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1. **58S scaffolds coated with Zein for bone regeneration (Research Paper)**

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Introduction: Bone defects are generated by fractures, trauma, congenital bone malformations, skeletal disorders, and tumor removal. Tissue engineering is an innovative method of producing tissue grafts. 58S is a bioactive glass made up of three components: 58% SiO2, 38% CaO, and 4% P2O5. Zein is FDA- approved polymer, it is natural, biodegradable, and biocompatible, and it has the ability to assist bone regeneration. In this study, we prepared a porous scaffold of 58S bioactive glass and coated with Zein and evaluated bioactivity, porosity, and cell adhesion.

Methods: Bioactive glass scaffolds were created using the replica plating method, subsequently, the manufactured scaffolds were coated with Zein (7%w/v) via immersion. Coated scaffolds were characterized with the scanning electron microscope, and morphology, cell adhesion, and bioactivity of them were evaluated. The porosity of coated scaffolds was estimated via the Archimedes procedure.

Results: The SEM results showed that cells adhered and proliferated on coated scaffolds. In addition, SEM images of bioactivity assessment revealed that the Hydroxycarbonate apatite crystals were deposited on prepared scaffolds. Moreover, the Porosimetry experiment presented that coated scaffold's Porosity was around 60 %.

Conclusion: the acquired results demonstrated that the manufactured scaffold is biocompatible, bioactive, and porous and could be a suitable candidate for bone regeneration

Keywords: bone tissue engineering, bioactive glass, Zein, scaffold

A look at proposed cancer care solutions based on personalized medicine (Review)

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Introduction: Cancer has long been considered a genetic disease characterized by a myriad of mutations that drive cancer progression. Recent accumulating evidence indicates that the dysregulated metabolism in cancer cells is more than a hallmark of cancer but may be the underlying cause of the tumor.In the clinical management of cancer with personalized medicine will be to integrate the comprehensive knowledge of tumor gene alterations, of tumor and microenvironment gene and protein expression profiling, of host immune competence,... This approach could result in the identification of individual prognostic and predictive parameters, which could help the clinician in choosing the most appropriate therapeutic program(s) throughout the entire disease. Therefore, the purpose of this study is to investigate new methods of cancer care based on personalized medicine.

Methods: In this article, a collection of articles dealing with the topic of the proposed cancer care based on personalized medicine from pubmed, google scholar, nature databases with the keywords Personalized medicine, Cancer management, Patient-derived organoids, Breast cancer, Cancer care , Ovarian cancer, Lung cancer,… were searched and finally 150 articles related to the subject were found and analyzed.

Results: The results of the studies showed: Three-dimensional (3D) modelling systems, from cell lines to organoid or tumoroid cultures, represent enhanced starting points from which improved translational outcomes for women with ovarian cancer will emerge. Consideration of molecular testing for a driver mutation is imperative for all providers caring for patients with a new suspected lung cancer diagnosis, as discovery of an actionable mutation will have dramatic implications in regards to patient survival and quality of life. Tumor genomic profiling is the standard of care for breast cancer that could contribute to taking steps to better management of malignancies. Circulating tumor DNA (ctDNA), accurately described by the term liquid profiling (LP), enables real-time assessment of the tumor mutational profile as a minimally invasive test and has therefore rapidly gained traction, particular for the management of cancer patients. Also Given the potential for cancer organoids to accurately recapitulate the intra- and intertumoral biological heterogeneity associated with patient-specific cancers, eliminating the undesirable technical variability accompanying cancer organoid culture is necessary to establish reproducible platforms that accelerate translatable insights into patient care. researchers are digging into personalized medicine for the management of

chemotolerance to increase cancer survivors with better quality of life. Recently, various genes/polymorphisms have been explored to be used as predictors of drug response and severity of cancer-linked symptoms.

Conclusion: According to the results of the studies and the impact of personalized medicine in the care of cancer patients according to the patient's family tree, Three-dimensional (3D) modeling systems, molecular testing, Tumor genomic profiling,... led us to identify the optimal dose of the Personalized drug and find relevant molecular targets that can help in disease management and introduction of effective treatments.

Keywords: Cancer care , Personalized medicine , Organoid , Tumor

A novel multi-epitope vaccine against SARS-CoV-2 variants of concern strains applying immunoinformatics approaches (Research Paper)

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Introduction: A newly emerged Coronavirus, SARS-CoV-2, which causes the Covid-19 disease, emerged in Wuhan in December 2019. Currently, Millions of deaths have been attributed to SARS-CoV-2, raising the call for efficient vaccines and treatments worldwide. Due to changes in the virus genome followed by mutations, variants with higher transmission ability and pathogenicity have emerged and raised excessive concerns about the efficiency of the developed vaccines. This study aimed to design a multi-epitope vaccine that targets the primary SARS-CoV-2 strain and its five variants of concern using immunoinformatics approaches.

Methods: B-cell, cytotoxic T lymphocytes, and helper T lymphocytes epitopes of the conserved and mutated positions of different SARS-CoV-2 surface glycoproteins were predicted and attached utilizing appropriate linkers. To provoke the immune response, the cholera toxin B subunit was also utilized as an adjuvant.

Results: This designed vaccine showed strong binding to the tool-like receptor in molecular docking analyzes (energy score of -1186.6). In silico cloning study also showed high and soluble expression of the final multi-epitope vaccine in the Escherichia coli (DH5) expression system. Further immunoinformatics analyses have shown the designed vaccine's high safety, stability, and efficacy, suggesting that our vaccine is a promising candidate against primary SARS-CoV-2 and its variants of concern strains.

Conclusion: In this study, the vaccine designed by immunoinformatics tools showed specific reactivity to Toll-like receptor. Given the validation of other epitope-based vaccines, our vaccine might be capable of providing strong immunity in a wide range of populations.

Keywords: Multi-Epitope vaccine, SARS-CoV-2, Variants of Concern (VOCs), COVID-19

A review of deep learning in healthcare, along with challenges and opportunities (Review)

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Introduction: The impact of deep learning in real-world clinical environments has become increasingly evident over the last few years. Deep learning algorithms can consistently provide high-quality results when used in clinical settings. Deep learning is preparing to change healthcare in more ways than just purely clinical applications. Deep learning is able to help detect genetic diseases like Turner's syndrome, hemophilia, and sickle cell anemia through the study of genes. This leads to finding future treatments and future medications. While deep learning has the potential to transform medical care, it still faces many obstacles, including inadequate data and interpretability issues. The article discusses how deep learning can be applied to precision medicine and next-generation health care, as well as some of the challenges, opportunities, and potential applications of this method.

Methods: Pubmed, Google Scholar, and Scopus databases were searched for related studies in the literature.

Results: In the last decade, deep learning (DL) has received unprecedented attention for its applications in the diagnosis and analysis of biomedical problems. There are several challenges that remain unsolved regarding deep learning's application in health care, despite the promising results obtained using deep architectures. This type of learning is difficult to interpret and requires a large amount of data. Aside from the quantitative performance of algorithms, understanding why algorithms work is also important in health care. Providing the medical professionals with an interpretable model is crucial to convincing them of the predictive system's recommendations for action. The goal of deep learning is to learn from data. It requires large amounts of data, however, for this learning to occur. Medical datasets, on the other hand, are generally biased and limited in nature.

Conclusion: In the future, advancements in IoT and edge computing will bring about a new model of DL that will support these technologies. Furthermore, a deep learning model must also be able to be interpreted since the more interpretable the model, the easier it will be to comprehend its predictions. In the field of interpretable deep learning, there are a number of new approaches and techniques available. Research in this field is still needed to find new and reasonable solutions to the key challenges, however.

Keywords: Healthcare; Deep Learning; interpretability

A review of effect of nutrition on prevention of cervical cancer (Review)

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Introduction: Cervical cancer is one of the most common malignancies in women. Every year, more than half a million women are diagnosed with cervical cancer and this disease leads to more deaths. From 300,000 people worldwide. High-risk subtypes of human papillomavirus (HPV) are the cause of this disease in most cases. prevention can be achieved by modifying the host immune system through a nutrient-mediated program. For optimal immune response function, several factors are needed, one of the most important of which is proper nutrition.

Methods: The present study is a review study that was conducted in 2021. Related articles gathered by searching keywords, Cervical Cancer, Prevention, Nutrition in Google Scholar, PubMed, Science Direct databases. After studying the found articles, a general conclusion was extracted from all the articles and finally, by merging the results of all the articles studied in this field, the present study was written.

Results: According to research, different categories of factors are effective in preventing cervical cancer, which are mentioned below: Nutrients Vitamin A Vitamin A deficiency causes oxidative stress that prevents cells from repairing. Adequate amounts of vitamin A in the diet may help prevent HPV infection. Taking too much vitamin A may increase the risk of HPV infection.Retinol for reproduction Base mucosal cells and the synthesis of protein blocks are required. Retinol deficiency may be associated with an increased risk of squamous cell metaplasia and HPV infection and may inhibit the early events of cervical cancer. There are more than 600 different types of carotenoids. They can be released into vitamin A in the body. Lutein, zeaxanthin and lycopene are the most common carotenoids. Vitamin D Vitamin D has roles such as modulating cell growth, neuromuscular function and immunity and reducing inflammation, and this vitamin can play an effective role in improving insulin resistance in HPV infection. Vitamin D deficiency can Causes persistent HPV infection, resulting in CIN, so high vitamin D intake may suppress persistent HPV infection and prevent CIN. Folate Folate (vitamin 9) plays an important role in red blood cells, DNA synthesis, repair and methylation, and cell proliferation. Higher folate levels are significantly inversely associated with a positive risk of HPV infection.In people with high folate levels, persistent HPV infection HPV secretion may decrease, and folate secretion may increase as a result of folate, which prevents HPV fusion, and inhibits varying degrees of CIN. Vitamin C Vitamin

C has several important functions that help protect and maintain healthy cells, skin, blood vessels, bones and cartilage, and also help heal wounds, so Vitamin C may reduce HPV infection. Data and prevent the development of CIN and cervical cancer. Vitamin E (tocopherol) Vitamin E protects cells against oxidative DNA damage and mutagenesis, thus preventing the development of certain tumors. Tocopherols have been suggested to protect against HPV persistence by enhancing immunological functions and modulating the inflammatory response to infection. Vitamin E may extensively inhibit HPV infection as well as the development of CIN and cervical cancer. Polyphenols Polyphenols are the most abundant antioxidants consumed by humans and their total consumption is up to 1 gram per day. Can be divided into two main groups: flavonoids and non-flavonoids. The most common natural polyphenols used to prevent and treat cervical cancer. Polyphenols by inducing apoptosis, growth retardation, inhibition of DNA synthesis and modulation of pathways Signal transmission inhibits HPV cell proliferation. Polyphenols can be used in combination therapy with chemotherapy or radiation therapy for cervical cancers. 3. Foods The vegetables Protective properties of vegetables and fruits are due to the presence of low molecular weight antioxidants that protect human cells and their structure against oxidative damage. Consumption of more vegetables reduces the risk of HPV persistence. Prevent cervical cancer by starting HPV infection. Fruits The effects of fruit consumption on the progression of cervical cancer are similar to vegetables. Moderate adherence to the Mediterranean diet reduces the risk of HR-HPV infection. In addition, low fruit consumption Relatively correlated with HPV persistence, repeated consumption of fruits may prevent the development of cervical cancer.

Conclusion: According to the above, health care workers should be trained to follow a diet rich in antioxidants, fruits and vegetables containing multivitamins and other micronutrients to prevent cervical cancer in women.

Keywords: Nutrition, Prevention, Cervical cancer

A review of Hemodialysis and pregnancy (Review)

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Introduction: Although pregnancy in women on hemodialysis is not common (incidence rate:1-7%), but in recent decades due to medical advances, the fertility rate of these people has increased. The most important fertility problems in women on dialysis are chronic anovulation, infertility, sexual dysfunction, abortion, and stillbirth. If the pregnancy continues, women on dialysis face serious problems. The present study was conducted with the aim of determining the effect of hemodialysis on pregnancy.

Methods: In this study, Persian and English articles published in SID, Google Scholar, Pubmed, Springer, Scopus and Science Direct databases using the keywords dialysis in pregnancy; end stage renal disease; hemodialysis; peritoneal dialysis; Intensive dialysis regimen was reviewed without restrictions on publication date and 20 articles were selected according to the inclusion criteria.

Results: Even if recently acquired knowledge has improved the outcomes of pregnancies with dialysis, these pregnancies are still a great challenge and require multidisciplinary collaboration. A woman may already be on dialysis, either in case of acute kidney injury that appears for the first time during pregnancy, or if existing renal pathology worsens during pregnancy and becomes necessary (often during the third trimester). Providing intensive hemodialysis is a common treatment approach when dialyzing pregnant women. Maternal and fetal outcomes can be improved. The objective is to maintain a satisfactory clinical status and maternal blood, urea, nitrogen (BUN) levels ≤80 mg / dl and creatinine 5-7 mg / dl for opportune fetal development and birth. Routine pharmacological treatment should continuously be individually adjusted as to the number of medications and dosage. The most important complications that may occur in such pregnancies include miscarriage, stillbirth, preterm labor, preeclampsia, hypertension, intrauterine growth restriction, low birth weight, and congenital anomalies.

Conclusion: Intensive hemodialysis might improve fertility along with maternal and fetal outcomes, but requires careful follow up and management from a multidisciplinary team that includes nephrology professionals working closely with professionals from obstetrics. The strategy choice must consider treatment availability, costs, and maternal/social aspects until future studies provide more reliable evidence.

Keywords: dialysis in pregnancy; end stage renal disease; hemodialysis; peritoneal dialysis

A review of hypotheses for the pathophysiology of vitiligo and comorbidities, as well as effective treatment techniques (Review)

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Introduction: Vitiligo is a complicated illness produced by hereditary components, metabolic variables associated with cellular oxidative stress, melanocyte adherence to the epithelium, and immunology (innate and adaptive) that results in melanocyte invasion. Although the condition does not cause immediate physical damage, it can have a significant impact on a patient's psychological well-being resulting in psychosocial distress and social stigmatization. Several theories have been proposed to explain the pathogenesis of this pigment. However, the exact pathogenesis is still unclear. The most widely accepted theory is that vitiligo is an autoimmune disorder that affects genetically predisposed individuals. Autoimmune disorders associated with vitiligo include hypothyroidism, thyroiditis, adrenal insufficiency, and pernicious anemia in 20-30% of patients with vitiligo. the average age of onset of vitiligo varies between genders and geographic regions. This disease usually starts at the peak age of 10 to 30 years. It affects around 0.5-2% of the global population, with up to 1.1-2% of Asians affected. It is well-established that vitiligo is not a pure melanocyte defect. This is due to the dynamic interplay between genetic and environmental factors that cause the autoimmune destruction of melanocytes. Melanocytes are localized not only in the epidermis and the region of the hair follicle protrusion, but also in the structures of the inner ear and eyeball, and therefore vitiligo may be accompanied by hearing and vision disorders. A better understanding of individual etiological factors in the Differentiating between vitiligo subtypes is critical for prognosis and deciding on appropriate treatment options. New and evolving treatment approaches Understanding the intracellular molecular and signaling mechanisms, as well as the cytokine profile, in the pathogenesis of vitiligo has paved the way for the development of various innovative vitiligo therapies.

Methods: Three databases were reviewed for relevant research up to 2022: Google Scholar, PubMed, and Medline. Keywords searched: "Associated disorders", "Kinds of vitiligo", "Treatment", "Oxidative stress", "Cell therapy", "Micropigmentation", "Vitamin D analogs ", " TWEAK" Papers on ideas and disorders associated with vitiligo were evaluated first, followed by articles on new research for the creation of effective therapies.

Results: There are no particular topical or systemic medications for vitiligo at the moment. Studies suggest that miRNAs may play a role in the etiology of vitiligo and may be used as biomarkers. It is important to learn more about miRNAs and their role in order to better understand the molecular process of vitiligo development. TWEAK is a multifunctional cytokine that belongs to the family of tumor necrosis factor receptor ligands. According to the current findings, TWEAK may play a role in the pathogenesis of vitiligo, differentiate between segmental and nonsegmental vitiligo, be a potential predictor of focal vitiligo fate, and be a promising therapeutic target in vitiligo. Vitiligo can be caused by the presence of a specific type of cell called TRM cells, which have been shown to play a key role in the development and flare-up of human vitiligo. This suggests targeting these cells might be an effective long-term therapy strategy for the condition. KRTAP10-11, IP6K2, and C9 were proposed as potential biomarkers for the pathogenesis and prognosis of vitiligo patients' responses to epidermal cell transplantation. According to existing studies, combining topical calcipotriol or tacalcitol with NB-UVB may improve the therapeutic effects of vitiligo, with tacalcitol having a greater benefit than calcipotriol. Micropigmentation may be a final resort for vitiligo patients who have not responded to regular medical and surgical therapies.

Conclusion: Despite advancements, the cause of vitiligo remains unknown. The fundamental problem in developing pathophysiology models is integrating various notions, such as oxidative stress and autoimmune response patterns. We now understand that differentiating between types of vitiligo is crucial for evaluating prognosis and selecting viable treatment options. The coexistence of vitiligo with autoimmune diseases is significant and points to an autoimmune etiopathogenesis of the condition. Phototherapy and other non-surgical treatments, such as phototherapy and topical agents, as well as numerous surgical techniques, are available as treatment alternatives for the condition. There is currently no therapy for vitiligo. Several remedies, however, have been developed as a result of advances in understanding vitiligo, with over 80% of individuals having some degree of re-pigmentation.

Keywords: Vitiligo, TWEAK, Autoimmunity, Pathogenesis, Therapeutics

A review of inflammatory effects of sleep deprivation on cognitive processes in Alzheimer's disease (Review)

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Introduction: Sleep disturbances, one of the characteristic symptoms of Alzheimer's disease (AD), has been proven is related to the pathophysiology of AD and can influence the cognitive functions in patients with AD. Sleep deprivation has been reported to be associated with inflammation. Evidence links neuroinflammation to cognitive deficits in AD. In this paper, we aimed to discuss the role of inflammation as a consequence of sleep deprivation in Alzheimer's progression and declining cognitive functions.

Methods: A search was conducted on PubMed, Cochrane Library, and Web of Science databases from 2010 to 2022 using the terms "sleep deprivation", "Alzheimer's disease", "cognition" and "inflammation".

Results: AD, the most common type of dementia, is characterized by the progressive loss of neurons, which typically leads to severe impairments in cognitive functions including memory and learning. There is a great deal of evidence suggesting Neuroinflammation as main part of the pathological progression of AD, but the molecular mechanisms are still not clear. Sleep deprivation has been associated with a chronic inflammatory state leading to inflammatory pathologies, including neurodegenerative diseases. Findings from sleep deprivation studies indicate that sleep deprivation is associated with increases in cytokines such as IL-1, IL-6, IL-17, IL-1β and TNF and induces an activation of vascular endothelial markers (i.e. E-selectin, s-intercellular adhesion molecule, s-ICAM-1). Interestingly, among people with chronic sleep deprivation, it appears that vulnerability to inflammation is increased after an episode of sleep loss. Also, sleep loss induces a systemic inflammation characterized by the release of several molecules, such as cytokines, chemokines, and acute-phase proteins; all of them may lead to changes in cellular components of the blood-brain barrier and induces blood-brain barrier disruption. Raised serum pro-inflammatory cytokines have been associated with a cognitive decline in Alzheimer's disease.

Conclusion: Taken together, sleep deprivation has been shown to cause neurocognitive impairment such as impaired memory and learning. Inflammatory processes may be an important biological mechanism linking

deprivative sleep to cognitive impairment and should be considered as a risk factor for developing and progressing Alzheimer's disease. Hence, the correction of sleep deprivation could be a preventive agent of severe cognitive decline in patients with Alzheimer's disease.

Keywords: sleep deprivation, Alzheimer's disease , cognition , inflammation

A Review of Interventions affecting Domestic Violence during Pregnancy and lactation (Review)

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Introduction: Domestic violence means the violent and domineering behavior of a family member against another member or members of the same family. Nowadays, domestic violence against women has been widely recognized as an important public health problem. Violence in pregnancy can affect a woman's ability to breastfeed in addition to its many consequences for the pregnant woman. The aim of this study is to investigate the interventions performed in the field of domestic violence during pregnancy and lactation.

Methods: The present study is a domain review study. In this study, 477 articles were searched through E.search by entering the desired keywords in the Pubmed, Science Direct, Cochrane Library, SID, Magiran and Irandoc databases from the time period covered by these Banks were acquired until 2021. Finally, 10 intervention studies in the period from 2001 to 2021, which investigated the interventions carried out in the field of domestic violence on pregnant and lactating women, were investigated.

Results: Based on the total of 10 studies, 1 study on cognitive counseling, 1 study on educational-supportive intervention, 1 study on breastfeeding counseling, 1 study on solution-oriented counseling, 5 studies on supportive counseling and 1 study on routine domestic violence screening in The pregnancy had paid off. In one study, breastfeeding counseling for abused mothers was not associated with a reduction in the duration of exclusive breastfeeding. In 5 studies, after supportive counseling, improvement in quality of life, increase in the use of safety behaviors, improvement in family and social support, increase in access to community resources, increase in the use of referral services and reduction in maternal depression were reported.Also, in 1 study, after solution-oriented counseling, after counseling, physical, mental and sexual violence in the intervention group decreased significantly (P=0.001) and in addition, the quality of life scores effectively decreased in The intervention group improved considerably compared to the control group (P=0.001).

Conclusion: The results of this study showed that making this type of interventions in the care program of pregnant and lactating mothers under

domestic violence are recommended in order to increase the health of the mother and the baby and increase exclusive feeding with breast milk.

Keywords: domestic violence, partner violence, violence during pregnancy, breastfeeding

A review of national preparedness against monkeypox virus (Review)

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Introduction: Introduction and Objective: Monkeypox virus (mpxv) was first isolated and identified in 1958, when monkeys shipped from Singapore to a Danish research facility became ill, however, the first confirmed human case in It was in 1970 that the virus was isolated from a child in the Democratic Republic of Congo who was suspected of having smallpox. The purpose of this study is to examine the country's readiness against this epidemic as soon as possible and to reduce the social, economic and life effects of this virus.

Methods: Materials and methods: The present study is a systematic review that was searched using the keywords mpxv, smallpox, epidemic in PubMed, Google Scholar, Elsevier and the desired articles.

Results: Findings: In the last two decades, Central Africa has seen an increase in the frequency of cases. MPXV may have emerged to occupy the ecological and immunological space vacated by smallpox virus. Countries should establish surveillance systems to detect emerging infectious diseases globally

Conclusion: Results: Considering that the disease caused by mpxv has no known clinical treatment, it is necessary to prepare the country's researchers to find clinical treatments, to make people aware of the dangers of this disease, to ensure the country's treatment infrastructure. To deal with it, he considered quarantine places and used smallpox vaccine and studied about it.

Keywords: mpxv, smallpox, epidemic , monkey pox

A review of the computer-aided detection role in the diagnosis of lung cancer in CT and PET images (Review)

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Introduction: PET/CT is a powerful diagnostic tool for cancer, but it has a primary disadvantage: it generates about 1000 slice images per scan. Since most cancer screening cases are normal, radiologists must identify a small number of abnormal lesions from many images without any oversight. This can be cumbersome, along with concern regarding the deterioration of diagnostic accuracy or fluctuation of results. Here, Computer Aided Detection (CAD) provides a digital output as a “second opinion” to support a radiologist’s diagnosis and assist in evaluating many images to identify lesions and arrive at the diagnosis. In this study, we focused on the automated detection of lung tumors, such as nodules, using PET/CT images.

Methods: Different terms explored in PubMed and Google Scholar databases: lung cancer, Computer-aided detection, CT, and PET. The obtained results were selected for the title and abstracts. Finally, 16 relevant papers were selected and reviewed in full text.

Results: Many modern CAD systems for lung nodules have been evaluated using sensitivity with FPs/case of ~5.0. Similarly, the sensitivity for detecting nodules using only CT images was 67.0%, with FP/case = 5.0. By combining CT and PET detection, sensitivity increased to 83.0% with FP/case = 5.0. Therefore, the sensitive nature of our hybrid scheme was 16% greater than that of the independent detection systems using only CT images. When the nodule size increases, it will likely merge with blood vessels, lung wall, and mediastinum. These types of nodules are difficult to detect in CT images using the detection algorithm for solitary nodules. Furthermore, significant increases in uptake can be accurately detected by PET. Because the CAD system integrates the detection abilities of two different types of imaging modalities, the sensitivity of the hybrid scheme is higher than that of the independent detection systems using either CT or PET. Both CT and PET detected 27.4% of the nodules. In contrast, 40.0% and 15.8% of the nodules were detected by CT and PET alone, respectively. These results indicated that the combination of CT and PET yields equivalent results. All the nodules

in the evaluation dataset were classified into three categories based on their diameter: <10 mm, 10–30 mm, and > 30 mm. observed that most nodules with diameters <10 mm were detected using CT images. These were not detectable by PET since the small nodule SUV was decreased due to the partial volume effect. On the other hand, 91.3% of the nodules with a diameter of more than 30 mm were detected using PET images. CT detection performance decreased since large nodules do not have a massive structure by fusing the mediastinum and chest wall, while PET detection was enhanced because of significantly high uptake values.

Conclusion: CT images detect solitary nodules using CNEF that were developed previously. The PET images are binarized based on the standard uptake values (SUVs) and detection of high-uptake regions. Initial candidate nodules are identified by combining CT and PET results. FPs among the leading candidates are eliminated using a rule-based classifier and three support vector machines (SVMs) with characteristic values obtained from CT and PET images. Founded that the sensitivity of the integrated results was 83.0% with FPs/case = 5.0, which are much more desirable than those obtained via independent detection methods using CT or PET. In summary, the results indicate that this novel hybrid method may be helpful in the detection of lung cancers, perhaps, particularly in mass-screening settings.

Keywords: Lung cancer, Computer-aided detection, CT, PET.

A review of the effect of ascorbic acid (vitamin C) on cancer treatment (Review)

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1. kheradgarayan motahar
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Introduction: Today, cancer is one of the most important causes of death. This disease has various types and so far, several methods are known for its diagnosis and treatment.

Methods: The main known method for treating all types of cancer is chemotherapy and radiation therapy. In addition to these methods, doctors suggest drugs and special diet to deal with this disease. One of the compounds that has attracted the attention of doctors and researchers in recent years is ascorbic acid.

Results: Ascorbic acid, also known as vitamin C, is important for preventing and slowing the progression of many diseases, including sepsis, periodontal diseases, and cancer. This vitamin is a type of water-soluble vitamin, has an important function as an antioxidant, and was discovered as an anti-scurvy agent. Also, vitamin C is an important nutrient that has a reducing effect, destroys free radicals and acts as an enzyme cofactor in cells. This combination is widely used in food and cosmetics.

Conclusion: Therefore, in this article, the results of the antioxidant effects of ascorbic acid in the treatment of cancer have been investigated.

Keywords: Key words: vitamin C - intravenous injection - oral use - complementary therapy

A Review of the Mechanisms of Resistance to MAPK Signaling Pathway Inhibitor Drugs in Cancer Therapy (Review)

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Introduction: Mitogen-activated protein kinase (MAPK) pathways regulate all aspects of life and are frequently altered in disease. MAPK pathways are three-kinase cascades in which the most upstream kinase (MAPKKK) responds to extracellular and intracellular signals and directly phosphorylates the middle kinase (MAPKK). The MAPKK exclusively phosphorylates and activates a MAPK, which typically has a large number of substrates that carry out specific cell fate decisions appropriate to the input signal. Cancer and drugs targeting the RAS-RAF-MEK-ERK pathway have made the most progress. Extensive research has been conducted on drugs that target this pathway, as well as mechanisms of sensitivity and resistance.

Methods: To find relevant articles, a search was conducted using the Google Scholar web search engine and the PubMed database. The keywords "cancer", "drug resistance “and” MAPK pathway" were used, and several articles were chosen for further investigation.

Results: Resistance to MAPK pathway inhibitor drugs can develop in a variety of ways, depending on cell type and cancer type, according to research papers on the subject. The RAS-RAF-MEK-ERK pathway is altered in nearly 40% of human cancers, primarily due to mutations in BRAF and its upstream activator RAS. MEK inhibitor drugs were the first to be developed, but despite their high potency, when administered alone, they produced disappointing clinical results. This was caused by the pathway's negative feedback amplifier property, which works to stabilize the output by influencing RAF. As a result, the combination of RAF and MEK inhibitors has become common in the treatment of certain types of cancer. Resistance to RAF and MEK inhibitors, on the other hand, leads to the discovery of other escape mechanisms, namely the role of adaptive network responses such as the JNK and p38 pathways. JNK is a cell death modulator that shares several substrates with the ERK pathway. The CJUN transcription factor, one of these shared substrates, promotes cell survival in cells treated with the RAF inhibitor vemurafenib. Combining a JNK inhibitor with vemurafenib clearly induces apoptosis. JNK inhibition has been shown to be effective in treating

vemurafenib-resistant melanoma cases where JNK works to reactivate the ERK pathway via other pathways, such as PAK (a kinase). The phosphatase PP2AC appears to influence the balance of the p38 and ERK pathways. P38 inhibitors promote cell proliferation in low-proliferation cells. P38 inhibitors promote proliferation in cells with low PP2AC expression by inhibiting ERK, while inducing cell death in cells with high PP2AC expression. Fructose-1,6-bisphosphatase (FBP1), a key enzyme in gluconeogenesis, inhibits ERK1/2 activation by the scaffold protein IQ-domain GTPase-activating protein1 (IQGAP1) in pancreatic ductal adenocarcinoma (PDAC) cells. Furthermore, resistance to RAF inhibitors and high glycolytic activity were observed in BRAF V600E and NRAS Q61K mutant cells from melanoma patients. Adding dichloroacetate, a glycolytic suppressor, to vemurafenib broke the drug resistance in these mutant cells. A number of studies have also suggested that amino acid metabolism may play a role in drug resistance to BRAF inhibitors. Specifically, it was discovered that serine biosynthesis had an effect on vemurafenib resistance.

Conclusion: Although the MAPK signaling pathway is important in many types of cancers and malignancies, making it an appealing target for cancer therapy, resistance to these inhibitory drugs can be achieved through a variety of mechanisms, including the activation of other pathways and metabolic modulators. Understanding this complex, context-dependent network is required for the development of effective drugs. Using computational models may be the key to overcoming this barrier.

Keywords: MAPK Pathway, Cancer, Drug Resistance

A Review on Osteoarthritis and Stem Cell Therapy (Review)

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Introduction: Osteoarthritis (OA) is a leading cause of disability worldwide and disease of an entire synovial joint characterized by clinical symptoms and distortion of joint tissues including cartilage, muscles, bones, menisci, and ligaments. Articular cartilage exhibits little or no ability for self-repair, resulting in progressive tissue loss and dysfunction following isolated cartilage injuries. The lack of effective repair also contributes to the widespread degeneration of the joint associated with OA. There are both intrinsic joint and extrinsic environmental risk factors for OA. It is often linked to age, gender, menopause, genetics, nutrition, and bone density that increases one's susceptibility to OA. These systemic factors, in addition to mechanical factors such as weight/body mass index, injury, repeated stress on the joint, surgery, and bone deformation play a role in OA severity. There is currently no cure for OA and most treatments are essentially symptomatic therapies to manage pain, stiffness, and swelling that are largely unsatisfactory. Currently, based on OA stages, there are different approaches. Pharmacologic management includes acetaminophen, aspirin, oral non-steroidal anti-inflammatory drugs (NSAIDs) and intra-articular corticosteroid injections. Aside from patient education, strengthening exercises, and weight loss, these drugs are recommended in a secondary manner. It has also been shown that physical and occupational therapy can be beneficial. Despite their efficacy for early management, these conservative treatments have little impact on underlying structural abnormalities. In addition, total joint replacement as a treatment for patients with end-stage OA is so invasive. Stem cells have extraordinary potential to contribute to novel treatment strategies for OA in different stages.

Methods: In this study, the method of a library collection, search in various texts, and authoritative scientific articles have been used.

Results: There are two regenerative therapeutic strategies for cartilage defects and osteoarthritis. Exogenous cell-based therapy entails delivery of autologous or allogeneic cells such as chondrocytes or mesenchymal stromal/stem cells (MSCs), or extracellular vesicles (EVs), either in suspension or seeded in a biomaterial. Alternatively, endogenous chondro progenitors, which reside in synovium (S), bone marrow (BM) and cartilage itself, could be targeted with pharmaceutical drugs or bioactive scaffolds to

trigger or enhance intrinsic repair. Among these approches, MSCs have been successfully isolated from several adult tissues including the bone marrow, adipose tissue, synovium, and peripheral blood. The wide use of MSCs in clinical trials is largely attributed to their ex vivo expansion capacity, easy accessibility and isolation from several adult tissues. The MSCs mechanism in joints is not clear and there are some hypotheses. Despite disappearing quickly from the target tissue after administration, MSCs are still able to exert chondroprotective and immunomodulatory effects. Since their therapeutic efficacy seems to be independent of their engraftment, it is now considered to be mainly paracrine mediated. The increasingly accepted model is that MSCs are found dormant in vivo as pericytes. These participate in the development of tissues, including synovium, and are involved in tissue repair during adult life. Once activated in response to signals associated with the injured environment, such as pro-inflammatory cytokines, a phenomenon generally referred to as “licensing,” they secrete factors, including chemokines and cytokines, to establish a regenerative environment. Proposed mechanism of action for tissue repair by endogenous MSCs are anti-apoptotic, anti-catabolic, anti-fibrotic, pro-chondrogenic, pro-angiogenic and immune-modulatory. The development of stem cell-based therapies for osteoarthritis also faces a number of challenges, such as the effects of age or disease on stem cell properties, altered stem cell function due to an inflammatory joint environment, and phenotypic instability in vivo that should be considered.

Conclusion: The development of stem cell-based therapies for OA is at a critical juncture. As a result of the extensive literature on stem cells, chondrogenic differentiation, and scaffold design, researchers and clinicians have been able to consider stem cells as a possible tool for modifying osteoarthritis progression. By using tissue engineering, osteoarthritic joints can be resurfaced to prevent or delay joint replacement and reduce the need for total joint replacements. There are, however, critical challenges specific to OA that threaten to obstruct the successful implementation of stem cell therapies. Therefore, it is clear that further studies are needed.

Keywords: Osteoarthritis, Stem Cell Therapy, Mesenchymal Stem Cells (MSCs)

A review on polyphenols and cancer (Review)

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Introduction: cancer is a leading cause of death worldwide, and this problem is increasing sharply. Much of this increase is due to aging worldwide populations, smoking, obesity, diabetes, alcohol intake, and genetic factors. Although different treatments are applied for curing cancer such as surgery, targeted therapies, radiotherapy, immunotherapy, and chemotherapy, some types of cancer cells are resistant and in some cases, these methods lead to dangerous side effects. Therefore, scientists are looking to use natural substances that directly fight cancer cells. Polyphenols are a large group of herbal compounds that are known for their structural features consist of a three-membered flavan ring and multiple phenol units. These compounds are found in fruits, green tea, coffee, wine, and cocoa. These organic agents are classified into several subclasses including catechins, flavonoids, catechins, isoflavones, curcuminoids, chalcones, and phenolic acids.

Methods: some studies represented that what makes these agents greatly beneficial is that they attack cancer cells directly. Free radicals that exist in our cells are the causes of oxidative stress. Oxidative stress is involved in various pathological states including cancer. Polyphenols have antioxidant effects and they are a severe barrier against the generation of free radicals. This property stabilizes free radicals and prevents them from damaging the cellular components. Moreover, polyphenols are able to induce cell death by altering the expression of apoptosis-related genes. Some studies showed that curcumin diminishes phosphorylation activation of the mitogen-activated protein kinase (MAPK) signaling pathway and increases PI3K/Akt protein expression. In addition, EGCG significantly increases the activity of caspase-3 and -7 as well as apoptotic cells.

Results: By studying several different tests on the effects of polyphenols on the cancer process, we concluded that the repeated use of these compounds with a certain dose can reduce the growth and proliferation of cancer cells and also prevent metastasis, in cases where the drug is used simultaneously. Polyphenolic compounds were used in chemotherapy, and the negative side effects of these drugs were reduced

Conclusion: In light of this review, Although there is little information about the effects of natural compounds in vivo, the absence of systemic side effects developed by polyphenols, and their epigenetic involvement in cancer biology,

make them particularly interesting. Finally, the aim of this paper is a short review of the use of polyphenols to fight cancer cells from different pathways.

Keywords: polyphenols, cancer, metastasis

A Review on Proton Mini Beam Radiation Therapy Efficiency and Applications (Review)

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Introduction: Radiation-induced toxicity is a major concern in radiotherapy which is dependent on the dose, dose rate and spatial fractionation of the dose. This study aimed to review the proton mini beam radiation therapy (pMBRT) technique and applications as an innovative method based on dose spatial modulation to increase skin sparing and reduce radiation toxicity.

Methods: The database of PubMed and Google Scholar explored with different combinations of terms: proton mini beam radiation therapy, spatial modulation, dose distribution, treatment response, survival rate. Totally 114 articles were obtained. The obtained results screened for title and abstract. Finally, 31 more relevant papers were reviewed full text and included in the study.

Results: Unlike the conventional proton therapy, the irradiation is carried out with a very narrow beam (diameter ≤1 mm), separated by gaps of 2 to 4 mm in pMBRT. This method is promising in terms of reduced side effects and superior tumor control for patients with high-grade glioma compared to common radiotherapy techniques. Also, has been widely used for radioresistant tumors close to a sensitive structure or pediatric cancers, in which dose escalation in the target volume without increasing the dose to adjacent normal tissues is essential. The superior normal tissue sparing and potential advantages in tumor control using pMBRT allows temporal fractionation of dose, which makes it possible to deposit higher and potentially curative doses in clinical cases where tissue tolerances are a limit for conventional methods.

Conclusion: pMBRT allows escalation of tumor doses and greater sparing of normal tissues which potentially improves the probability of local control for tumor and survival rate as well as reducing toxicity and improving quality of life.

Keywords: Proton Mini Beam Radiation Therapy, spatial modulation, dose distribution.

A review on Stem cells and injectable hydrogels for heart disease (Review)

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Introduction: Myocardial infarction (MI) occurs after the source of oxygen and nutrients to the cardiac muscle become decreases due to blocked coronary arteries. Heart failure causes fibrotic tissue growth and proliferation in the affected area of cardiac muscle lead to a very limited chance for regeneration because of the inability of the myocardium to self-regenerate. Consequent stiffness of the cardiac muscle after myocardial infarction leads to decreased cardiac output, arrhythmia, and sudden cardiac death. Therefore, myocardial tissue engineering(MTE) approaches with a variety of stem cells, including mesenchymal stem cells, cardiac and cardiosphere derived cells, induced pluripotent stem cells, embryonic stem cells, umbilical cord stem cells, and adipose-derived stem cells, have attracted significant attention as a therapeutic treatment for heart failure.

Methods: In this study, the method of a library collection, search in various texts, and authoritative scientific articles have been used.

Results: Myocytes are surrounded by an extracellular matrix (ECM) network that is produced by cardiac fibroblasts. The major ECM proteins in the myocardial ECM are collagen type I (approximately 85%, depending on the species) and collagen type III (approximately 11%). Various amounts of simultaneous collagens are responsible for the anisotropic mechanical properties in different regions of the heart but after MI and expression of the Pw1 gene, scar tissue create. For preventing this issue several ways provided that they include a patch-based system with stem cells (SCs) that need a surgical operation and also it can distribute the integrity of the electrical or mechanical signal, another ways are the use of injection routes that including intravenous infusion, intracoronary delivery, and intramyocardial injection. Among these ways intravenous the use of hydrogel for intramyocardial injection is more effectible, because hydrogel protects the cells from host inflammation, and enable functional integration with the injured myocardium furthermore, it can contain Growth factors (GF) like bFGF and VEGF for enhancing angiogenesis, TGF-β for ECM remodeling, IGF-1 for reducing fibrosis and TNF-a for reducing local inflammation attenuation. It is noticeable that the use of each stem call has pros and cons. bone marrow cells are including bone marrow-derived mesenchymal stem cells (MSCs),

hematopoietic stem cells, and endothelial progenitor cells. a bone marrow-derived mesenchymal stem cell is multipotent ability to differentiate into multiple mature cardiac cell lineages such as cardiac myocytes, endothelial cells, smooth muscle cells, and cardiac fibroblasts also, MSCs from bone marrow can play a role as pacemaker cells by the expression of the hyperpolarization-activated cyclic nucleotide-gated 2 genes (HCN-2). hematopoietic stem cells can be isolated from blood, bone marrow, and umbilical cord blood and Some studies report the ability of these stem cells to transdifferentiate into cardiomyocytes, but this has not been reproduced by all investigators working in this field. endothelial progenitor cells are very similar to hematopoietic stem cells, they are distinguished by their ability to respond to endothelial cell stimuli such as (VEGF), differentiate to form mature endothelial cells. Other cells are cardiac stem cells that they presenting c-kit, nkx2-5, gata4, flk-1, isl-1 antigens. Cardiac stem cells have higher angiogenic, antiapoptotic activity than other stem cells, high regeneration ability, no immunogenicity, they are adapted to the cardiac microenvironment, can also electromechanically coupled with host cells to allow synchronous contraction between the grafted cells and the host tissue but signification limitation of them are low cells population. embronic stem cells are the cell line with the most effective myogenic capabilities, but teratoma formation and immunogenicity are the major concerns in ESC, ethical concerns, incontrollable differentiation, arrhythmias. another one is insuce stem cells that like ESCs, iPSCs are multipotent and clonogenic. adipose-derived stem cells and umbilical cord stem cells also use in some studies. also, the use of mixed stem cell therapies like cardiochimeras and cardioclusters has been studied. for example, the Cardio Clusters are a 3D mixture of mesenchymal stem cells, cardiac progenitor cells, endothelial progenitor cells, and fibroblasts.

Conclusion: One of the major problems in the treatment of cardiovascular diseases is the inability of the myocardium to self-regenerate. Current therapies are unable to restore the heart's function after myocardial infarction. injectable hydrogel combined with stem cells SCs is necessary for optimal and effective myocardial recovery.

Keywords: stem cell,hydrogel, regenerative medicine

A review on the potential of embryonic stem cells in differentiation to hepatocytes (Review)

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Introduction: Embryonic stem cells (ESCs) were first identified in the mouse system and can differentiate into different cell types in vitro. This feature of stem cells has made them a good candidate for novel therapeutics in regenerating damaged tissues and organs. As with other tissues, there is a scarcity of donor livers and hepatocytes, which is compounded by the low recovery and proliferative capacity of adult primary hepatocytes. Besides their potential use for the treatment of liver disease, human embryonic stem cells (HESCs)-derived hepatocytes could be used to study the developmental biology of hepatogenesis.

Methods: The current research is a review on the available literature about differentiation of ESCs in to hepatocytes.

Results: ESCs are derived from the inner cell mass of blastocysts and have the capability of self-renewal and multilineage differentiation. ESC will differentiate and form an EB after removing feeder cells and culturing in suspension culture medium without leukemia inhibitory factor (LIF) or FGF2; The EBs will spontaneously differentiate into different cell types of the three germ layers including liver cells in adherent culture conditions. In order to avoid spontaneous differentiation of ESC forming a mixture of many kinds of cells, researchers have successfully induced ESCs to differentiate into liver

cells through the reconstruction of an appropriate in vivo microenvironment. The usual methods utilized to direct differentiation into liver cells fall into three classes: (A) soluble factor-induced approaches, (B) induction via interaction with diverse types of cells, and (C) induction by chromatin modification. Through gene manipulation hepatic cells were labeled and for the first time, a homogenous population of differentiated cell types was demonstrated. In addition, the hepatic- like cells were suggested to develop in a niche next to cardiac mesodermal cells and that aFGF may play a role in this differentiation. The differentiation towards hepatic-like cells were also demonstrated by using other factors, added insulin and dexamethasone to EBs cultured on collagen type I and showed that the cells express various endodermal genes.

Conclusion: HESCs have the ability of differentiation into cells with many features of primary human hepatocytes. Hepatocyte-like cells can be enriched and recovered based on asialoglycoprotein-receptor expression and potentially could be applied in drug discovery research and developed as therapeutics.

Keywords: Stem Cells, Stromal cells, Differentiation, Hepatocytes, Embryonic stem cells

A review on the Using medicinal plants as an alternative to antibiotics (Review)

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Introduction: the use of antibiotics has reduced child mortality and is critical for invasive surgeries and treatments such as chemotherapy. However, the number of infections caused by multidrug-resistant bacteria is increasing worldwide. Antibiotic resistance has been introduced as one of the biggest threats to human health. The advent of antibiotics changed the treatment of infections, but the development of antibiotic resistance threatened this achievement. One of the reasons for the development of drug resistance is excessive use of antibiotics and their indiscriminate and inappropriate prescription. The use of medicinal plants in treatment has a long history. Human societies learned the properties of different plants through trial and error. Years of use and trial and error taught humans to find the medicinal properties in which part of the plant, such as the skin, seeds, flowers, etc. The use of medicinal plants in different forms is the oldest medicinal method. Centuries ago in Iran, China, Egypt and India, the use of herbal medicines in traditional medicine for treatment has been common. The first instructions for making herbal medicine are from 5000 years ago. This instruction was discovered on a Sumerian clay slab. Examining historical Iranian manuscripts provides a lot of information on the use of medicinal plants. The Egyptian Medical Papyrus of Iberus, written around 1550 BC, is about plants and mentions 700 species of plants for treatment. Traditional Indian medicine or Ayurveda is one of the oldest health care and treatment systems. Plants were always used for different purposes because of their aroma, taste, color and properties. The concern about the dangers of chemicals has made them look for natural alternatives to chemical additives or poisons. Medicinal plants, unlike synthetic chemical drugs, cause less side effects. Plant extracts have biologically active compounds. As a result, they can be used in the treatment of diseases. Due to the presence of numerous secondary compounds, plant extracts show many therapeutic properties such as antimicrobial, anti-biofilm and antioxidant properties. For example, phenolic compounds have multiple biological effects, among which antioxidant properties can be mentioned.

Methods: Preparation of plant samples, such as grinding and drying, as well as different extraction methods, affect the preservation of secondary and effective compounds in the final extracts. For extracting and preparing plant samples, plant organs such as leaves, bark, roots, fruits and flowers can be used. Maceration, percolation, Soxhlet, microwave, sonication extraction and other methods can be used to prepare plant extracts. Maceration is a technique that has been widely used in medicinal plant research. Maceration

involved soaking the plant material in a sealed container with a solvent and letting it rest at room temperature for at least 3 days. After soaking for at least 3 days, the solution is clarified by filtration. The choice of solvents determines the type of compound extracted from the samples. Brewing and boiling follow the same principle as soaking. Each is soaked in cold or boiling water. Maceration technique is the most practical and simple method. In this method, the solvents used in the soaking process play an important role. Also, different solvents such as water, ethanol, methanol, hexane can be used. Each of these solvents as well as different extraction methods can further extract certain secondary metabolites. Then the effects of plant extracts on different microbes are investigated. Antimicrobial property testing methods include disc diffusion , agar dilution, broth macrodilution, broth microdilution, and a concentration gradient test.

Results: Research has shown that some medicinal plants such as Adiantum capillus-veneris, Quercus infectoria and artemisia have antimicrobial properties.

Conclusion: Extracts are hydrophobic and volatile compounds, studying them in order to increase the stability and consequently the efficiency of the extract can be improved.

Keywords: medicinal plants, antibiotics, antibiotic resistance, Maceration

A survey of the behavioral and neurobiological effects of prenatal stress on the GABA and Glutamate system (Review)

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Introduction: Prenatal stress (PS) is defined as the stress experienced by a mother before giving birth. PS can cause early and long-lasting effects on neurobehavioral development in both human and animal offspring and results in dysregulation of the major inhibitory (GABAergic) and excitatory (glutamatergic) systems in the CNS. A correct balance of activity of the GABA and glutamate systems is essential for neurodevelopment and CNS function. Dysregulation of this balance has been implicated in several neurological and/or psychiatric disorders. This study aims to highlight the new findings on some of the underlying mechanisms of GABA and Glutamate system dysregulation by PS, and the behavioral consequences.

Methods: The available literature in “PubMed”, “Google Scholar” and “ScienceDirect” databases was analyzed using the keywords prenatal stress, Glutamate, neurobiology, behavior, and the results with scientific evidence for behavioral and neurobiological effects of prenatal stress on GABA and Glutamate system were summarized.

Results: Alterations of the GABAergic and/or glutamatergic signaling during fetal development lead to a severe excitatory/inhibitory imbalance, a condition that may account for PS-precipitated anxiety-like behaviors. The hippocampus, frontal cortex, and amygdala are PS’s most affected brain regions. The amygdala plays an important role in the regulation of emotions and is inhibited by GABAergic neurotransmission, which prevents improper emotional and behavioral responses. PS has been demonstrated to affect the amygdala’s GABAergic neurons. Exposure to PS for a long time leads to the hippocampus's long-lasting dysfunction, which may continue to adulthood. Maternally stressed rats had increased anxiety-like behavior in adulthood, associated with altered expression of the α1, α2, β1–3, and γ2 subunits of the GABA receptor. Thus, we can conclude that PS may increase anxiety-related behaviors. Hippocampus is one of the brain regions responsible for memory stabilization. PS impairs memory function by leading to dysfunction of GABA in the hippocampus, and has been demonstrated to be one of the reasons for the seizure; PS can release stress hormones by the mother’s endocrine system. These hormones cause a significant elevation in the density of NMDA receptors in different brain regions, including the hippocampus. GABA

receptors consist of three groups of receptors (A, B, and C); the GABAA receptor is mainly involved in the regulation of neural excitability, anxiety, learning, and memory. Genetic alterations in this receptor have a role in some psychiatric or/and neurological disorders like epilepsy, depression, autism, and schizophrenia. PS increases the α5 subunit of the GABAA receptor in infant rats' hippocampus. The expression of the GABAA receptor δ subunit increases in patients with epilepsy. This subunit's function is as same as the α5 subunit's function but in dentate gyrus granule cells. Therefore, the alterations in the GABAergic system in certain brain structures such as the hippocampus mediate some aspects of PS-induced potentiation in seizure. Recent studies indicate that an imbalance between GABA and glutamate neurotransmission can be a significant mechanism underlying schizophrenia pathophysiology. Adult offspring of prenatal restraint stressed (PRS) mice, exhibit a deficiency in cortical GABAergic innervation. This is expected to result in aberrant synchronization of the firing rate of pyramidal neurons, a putative electrophysiological substrate of cognitive dysfunction in psychotic disorders. They show molecular disruption in chromatin remodeling at genes expressed in glutamatergic neurons, such as mGlu2/3 receptors, and exhibit a schizophrenia-like behavioral phenotype as well. These molecular alternations in PRS mice are alike those observed in the brain of schizophrenia patients, indicating a powerful correlation between schizophrenia symptoms and the altered epigenetic GABAergic/glutamatergic mechanisms. PS is a remarkable risk factor for the development of schizophrenia in the adult offspring of humans.

Conclusion: Prenatal stress, altering the GABA and Glutamate system mechanisms, causes many diverse neurological/psychiatric disorders such as behavioral abnormalities, anxiety, decreased learning and memory ability, epilepsy, seizure, schizophrenia, and some other disorders like autism, ADHD, major depression, bipolar disorder, infantile spasms, and even development of addictive states, which are beyond the scope of this paper. Therefore, pharmacological and psychotherapeutic interventions with regulatory effects on the excitatory/inhibitory balance can be attributed to the novel therapeutic target for PS-precipitated disorders.

Keywords: prenatal stress, GABA, Glutamate, neurobiology, behavior

A Survey on Iranian midwives' knowledge toward COVID-19 during pregnancy, delivery, postpartum, and neonatal feeding (Research Paper)

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Introduction: The COVID-19 pandemic has impacted care that maternal and newborn health professionals, especially midwives, provide. If they know in how to care for COVID-19 patients during pregnancy, delivery, and postpartum, they can manage these cases better. The study aimed to measure the knowledge of Iranian midwives about COVID-19 during pregnancy, delivery, postpartum, and neonatal feeding.

Methods: This cross-sectional study was conducted on 438 Iranian midwives from March to April 2021. Demographic information and knowledge of them were gathered using an electronic web-based questionnaire. The statistical analysis was performed using the SPSS software version 18.

Results: The mean age of participants was 31.8 ± 2.3. The mean knowledge score of midwives was 11.2 ± 2.8, which was moderate. 91.55% of Midwives were more knowledgeable about COVID-19 infection symptoms in pregnant women. 34.93% and 31.05% of midwives had correct knowledge about vaccination against COVID-19 during pregnancy and breastfeeding, respectively. Results showed no statistically significant relationship between demographic characteristics and knowledge of them ($P > 0.05$).

Conclusion: Midwives' knowledge about COVID-19 during pregnancy, delivery, postpartum, and neonatal feeding was moderate. Therefore, to improve the level of knowledge, educational programs by the Ministry of Health and Medical Education are necessary to design and implement.

Keywords: COVID-19, Knowledge, Breastfeeding, Midwifery, Pregnancy

ABL-1 protein (Research Paper)

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Introduction: ABL-1 is a protein in humans that is encoded by the ABL1 gene, which is located on chromosome 9. The gene found in mammals is called "c-Abl" and the gene in viruses is named "v-Abl". This proto-oncogene encodes a nuclear and cytoplasmic protein that is involved in cell division, differentiation, and binding. Mutations in this gene are associated with the development of chronic bone marrow leukemia (CML). Imatinib C29H31N7O1, also known as Geevec. It is used to treat cancers such as leukemia (cmL), acute lymphoma leukemia. It acts through the skill of bcr-Abl kinase serosinase, which reduces cell growth or apoptosis in some types of cancer cells. It works by blocking the function of an abnormal protein that signals cancer cells to multiply; this helps stop the cancer cells from spreading. In this study, we investigated the effect of imatenib on HNF4α protein by molecular docking method.

Methods: In this descriptive-analytical project, we used Chimera ‹PyRx software in order to analyze protein structure. Protein chains were examined using Chimera software. The most suitable chain was c chain, which had more amino acids than other chains, and the largest protein chain was Abl-1 Through this software, water molecules and all we removed the solvents from this chain and hydrogen ions and charge bar were added to the chain and finally saved in pdb format In the next step, we downloaded the structure of imatinib from PubChem site in SDF format. To perform the docking process, PyRx software was used.

Results: After docking with Pyrex software, 10 models were suggested, the first three models being the best docking modes, the results of which were obtained in the table below: According to docking results, we observed that imatinib with appropriate negative binding energy could be a suitable drug for binding to Abl-1 protein (-9 Kcal/mol).

Conclusion: Based on the results obtained This imatinib drug is effective on the ABL1 gene

Keywords: Bioinformatics, molecular docking, ABL-1, Imatinib

Acinonyx jubatus venaticus (Review)

Nastaran Dehghan,[1,*]

1.

Introduction: Acinonyx jubatus venaticus It is an endangered subspecies of cheetah, and according to estimates in 2019, only 12 of its collars were identified and had birth certificates in Iran. Currently, this cheetah is a symbol in the uniform of Iran's national football team. The Asian cheetah protection project has been started since 2010.

Methods: This animal used to live in desert areas in the region and its generation has been under the threat of total destruction for years. The results of the research in 2019 show that there are between 10 and 20 cheetah collars in the peripheral areas of the central desert, including Turan, Naibandan, Dere Anjir and Miandasht. This estimate is the result of ground mapping by more than 12,000 night vision cameras deployed in various locations.

Results: The Asiatic cheetah was once spread over large areas of Asia from the Arabian Peninsula and the Near East to the Caspian region, the South Caucasus, the Ghazal Qom desert and India, but currently it is on the list of animals on the verge of extinction of the International Union for Conservation of Nature and is exclusive to remote areas. It has fallen in the central deserts of Iran. The last documented report of cheetah in India dates back to 1974. From then on, the cheetah quickly disappeared from its entire territory. Since the 1970s, Iran has been known as the only habitat of Asian leopards. The Asian cheetah separated from the cheetah population in Africa between 32,000 and 67,000 years ago. At the time of the British rule over India, it was called the hunting panther. This name was derived from the cheetahs that were kept in captivity by the Indian royal family in large numbers to use them to hunt wild antelopes.

Conclusion: Acinonyx jubatus venaticus) Animals are going extinct and we should not let them die and become extinct due to climate factors or nutrition and predators that cause their extinction.

Keywords: Cheetah is a Persian word that is called cheetah because of its similarity with leopard.

Addressing Problems in Gene Therapy by Using Microfluidic Device
(Research Paper)

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Introduction: The potential use of gene- modified cell therapy in hematologic malignancies is often limited by complications related to effectively engineering and manufacturing cells with conventional delivery systems and is challenge specifically for immune cells. In fact, this life-saving therapy requires use of inefficient reagents and specialized equipment that can drive up the price of the treatment. Herein, we compared two different approaches for gene transfer into target cells: Nucleofection (Electrochemical Technique) as a 2D gene delivery and microfluidic device as a 3D gene transfer technology. In fact, we developed and used serpentine microfluidic chip for cell membrane penetration that permits delivery of DNA into Multiple myeloma cells

Methods: Myeloma Cells were grown in RPMI 1640 medium supplemented with 10% FBS. Then, cells were transfected using the Amaxa nucleofector II device (Lonza). Device is Designed and Fabricated by PDMS polymer. Myeloma cells and plasmids were introduced into the microfluidic transfection device. The percentage of GFP positive cells is analyzed by BD FACS Calibur Flow Cytometer

Results: We achieved high transfection efficiency (55.7% GFP) in myeloma cells with high cell viability (by PI staining) 24-48 hours after microfluidic processing compared to nucleofection that is toxic and rate of dead cells is very high

Conclusion: The significant differences in outcomes from the two techniques underscores the importance of understanding the impact of intracellular delivery techniques on cell function for research and clinical applications. Altogether, these results highlight the use of microfluidic device as a rapid and gentle delivery method with promising potential to engineer primary human cells for research and clinical applications

Keywords: Microfluidics, Transfection, Multiple Myeloma

Advanced biosensors for detection of pathogens related to livestock and poultry (Review)

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Introduction: With the growth of the world population and the development of agriculture, the prevalence of infectious diseases among livestock has expanded, which has a negative impact on public health, economy and agriculture. Conventional methods for detecting pathogens in culture and isolation from culture are very time- consuming and costly. Molecular polymerase chain reaction (PCR) methods are more sensitive. Real Time PCR (RT-PCR) is more specific, but requires sophisticated equipment. Using ELISA tests to detect virus antigens is time-consuming. As a result, the development of a reliable, rapid, accurate and sensitive diagnostic method for the identification of pathogens is of great interest to researchers. According to the above, the aim of this study was to identify some advanced biosensors for the detection of pathogens related to livestock and poultry.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Advanced biosensors for detection of pathogens related to livestock and poultry. After reviewing the relevant findings and evaluating the data quality, a total of 19 articles were analyzed.

Results: A biosensor is an analytical system that has biological detection. Factors (hormones, nucleic acids, enzymes, and cells) are fixed on the surface of a sensor that attaches to a transmitter that transmits and interprets the signal. Biosensors are made up of two parts: an element or a bioreceptor that detects the analyte in question and a transducer that produces a digital electronic signal proportional to the concentration of a particular analyte. Using a biosensor, results are achieved in a very short time. Staphylococcus aureus is one of the deadliest bacteria. Cultivation methods are traditional and time-consuming and other nucleic acid-based methods require qualified individuals and are also expensive. Antibody-based biosensors are used for

detection. Avian Influenza Virus (AIV(: Traditional methods for virus detection Reverse transcriptase polymerase chain reaction (RT-PCR) and Enzyme-linked immunosorbent assay (ELISA) are expensive and time-consuming .New method with biosensor technology using a small gold electrode to detect H7N1 with electrochemical techniques such as impedance spectroscopy. Escherichia coli (E. Coli) is a Gram-negative rod-shaped. This bacterium is usually harmless, but malignant strains can cause disease. Common methods for diagnosing E. coli include fermentation, culture, PCR assay, and enzyme-related immunosorbents, which have disadvantages such as reagent, cost, and length of time. Biosensors for the detection of E. coli are biochemical detection solutions that include: surface plasmon resonance, chemical light, quartz crystal microbalance system and electrochemistry

Conclusion: In this study, some advanced biotechnological methods that detect livestock and poultry pathogens early were investigated. Pathogens weaken production systems and increase veterinary costs and economic threats. Conventional pathogen detection techniques are often time-consuming and require complex equipment. One of the key challenges in farms is the slow absorption of these technologies in commercial farms, Therefore, the economic and managerial benefits of these advanced systems must be shown to individuals. Challenges such as sample preparation, service life, and system integration that hinder the implementation of these technologies. Addressing these issues will make it possible to make greater use of these biological technologies.

Keywords: biosensors, pathogens, livestock

Advances in nanomedicine to treat cancer-induced starvation (Review)

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Introduction: Cancer cells are distinguished from normal cells by high consumption of food and intense metabolism. One of the important advances in the field of nanomedicine is the treatment of starvation caused by cancer, which prevents angiogenesis and blood supply or consumes the glucose present in the cancerous mass. However, the use of nanomedicine in the treatment of this hunger has disadvantages such as low effectiveness, off-target toxicity, drug resistance, increased risk of metastasis, etc. In this study, we examine the studies conducted in the field of combining cancer starvation and nanotechnology.

Methods: In this review article, we collected the required data using keywords and using databases such as Google Scholar, PubMed, Scopus and ProQuest. In this study, the statistical population includes all the studies whose articles have been published until 2022. After reviewing the findings and evaluating the quality of the obtained data, 13 articles were analyzed.

Results: The combination of different types of drug delivery systems based on nanomaterials such as micelles, liposomes and dendrimers, with glycolytic enzyme inhibitors and glucose transporter inhibitors, anti-angiogenic drugs, GOX and CAT can be a more effective treatment. Glucose oxidase (GOx) has attracted more attention as glucose biosensors, which can oxidize glucose to gluconic acid and H2O2. According to a previous report, H2O2 at endogenous concentrations can induce malignant transformation of normal cells, but in turn leads to the death of cancer cells at high concentrations. Therefore, the use of GOx in tumor therapy not only consumes intracellular glucose, but also leads to the interruption of energy supply, but also raises the level of endogenous H2O2, causing stronger intratumoral cytotoxicity. But the

problem with this approach is that glucose starvation strategies usually affect both cancer cells and normal cells at the same time, secondly, cancer cells can resist a metabolic pathway by expressing alternative isoforms of the causative drug, called metabolomics. Special resistance.

Conclusion: Studies show that the combination of nanotechnology and cancer starvation with accurate drug delivery to the target tissue is a promising method to overcome the mentioned problems. Therefore, combining common cancer methods such as immunotherapy chemotherapy with nanotechnology can increase the effectiveness of the mentioned methods. However, off-target toxicity, metabolic plasticity and potential toxicity with nanoparticles still exist and require further studies.

Keywords: nanomedicine, cancer starvation therapy, Combined Modality Therapy, nanomaterials

Advantages of whole Genome Sequencing in Metagenomics Processes and DNA Biosynthetic Approach in Cancer (Review)

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Introduction: Recent technological and innovative advances in integrated and continuous imaging, sequence-based measurements and computational analysis have transformed our view of genomes in terms of their structure and dynamics in space and time. These advances provide a deeper understanding of genome functions and mechanical insights into how the nucleus is organized and functions spatially. These factors provide us with a wide range of complementary data and the opportunity to produce measurable and integrated models of the nuclear organization. Next-generation sequencing (NGS) is widely used to diagnose rare genetic disorders. Large differences in the inclusion of cost and effectiveness parameters have been identified between studies. The validity and scale of the results can therefore be questioned, which has prevented valid comparisons and widespread generalizations. Comparable decisions are needed to implement new NGS-based diagnostic methods in pediatric genetics and beyond. The aim of this study was to determine the benefits of whole genome sequencing in metagenomic processes and DNA biosynthetic approach.

Methods: This study was a secondary study with a narrative approach approach that in 2022 by searching for keywords such as, sequencing, NGS, genome, metagenomics, heterolog and gene clusters in valid databases such as, Scopus , Sciences Direct, Web of Sciences and PubMed. All input and output criteria of the study were examined. In this study, 15 articles were selected, of which 10 articles were included in the study

Results: According to studies from various articles, reported diagnostic efficiencies ranging from 3 to 70%, with a higher range of efficiencies for neurological symptoms and acute illness from 22% to 68% and 37-70%, respectively. Became. Diagnoses cause a range of changes with a higher frequency for acute disease reported from 67 to 95%. The frequency of species of unknown importance varied from 5 to 85% between studies with the potential to decrease in frequency over time and the higher rates identified in patients with non-European ancestors. This study provides evidence for a higher range of the diagnostic efficiency of exome / genome sequencing compared to standard genetic testing, especially in neurological and acute

symptoms. However it is essential to improve diagnostic accuracy and efficiency and to be able to analyze trends over time inhibits all Ca2+-dependent pathways in their signaling domain. Switched-off effectors/pathways are represented by white ellipses/arrows.

Conclusion: According to Results, genome sequencing has the potential for improvement and the process of clinical progression for patients undergoing genetic testing. Evidence of clinical utility is limited to the pediatric population.

Keywords: sequencing, NGS, genome, metagenomics, heterolog and gene clusters

Aerobic Exercise-Assisted Cardiac Regeneration by Inhibiting Tryptase Release in Mast Cells after Myocardial Infarction (Research Paper)

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Introduction: Cardiovascular disease (CVD) contributes critically to the mortality, morbidity, and economic problem of illness globally. Exercise is a share of everyone's life. Some evidence-based studies have frequently shown a progressive correlation between physical activity and good health.The effects of daily exercise on cardiomyocyte size, collagen content (fibrosis), and releasing mast cells (MCs') tryptase of the model of myocardial infarction (MI) were assessed.

Methods: 40 rats were coincidentally spread into sham+inertia (control), sham+exercise, infarction+inertia, and infarction+exercise groups. An experimental model of acute MI was induced in infarction groups. One week after surgery, exercising groups were allowed to an aerobic exercise program for six weeks. At the endpoint of the study, all examinations were performed.

Results: We found lesser fibrosis in sham+exercise and infarction+exercise groups compared to sham+inertia and infarction+inertia groups, respectively ($p = 0.023$, $p = 0.001$). Also, infarction groups were significantly lower than sham groups ($p < 0.05$) and the infarction+exercise group was significantly lower than the infarction+inertia group ($p < 0.05$). The effect of exercise on MCs while increased MC density and degranulation occur at the site of fibrosis, we demonstrated that exercise decreases both total MC density and degranulation in both sham and infarction groups ($p < 0.05$). Immunohistochemistry examinations were significantly higher expression of MCs' tryptase in infarction groups than sham groups ($p < 0.05$, $p < 0.0001$).

Conclusion: Exercise improves fibrosis and cardiac function in both healthy and MI rats by inhibiting released MCs' tryptase.

Keywords: Echocardiography; Exercise Therapy; Fibrosis; physiopathology; Tryptases.

Affect of Aspergillosis on The Other Types of Acute Respiratory Infections; A Cellular Investigation (Review)

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Introduction: Aspergillosis is the most common fungal respiratory infection that originates from the Aspergillus fungus, which is an aerosol mold. The prevalence of this Acute Respiratory Infection (ARI) in hospital conditions is one of the main problems of treatment, especially if the patients have other ARI (e.g., bronchitis, pneumonia, tuberculosis, and covid19).

Methods: A systematic review was conducted with keywords applied in online databases, including PubMed, Web of Science, Scopus, Science Direct, and Google Scholar from September 1979 to July 2022. Most relevant papers were retrieved and screened in three phases against inclusion criteria, based on their title, abstract, and their full texts, and eligible records were included in the review.

Results: Aspergillus infection is extremely dangerous in patients with immunodeficiency. The immune deficiency in patients can be acquired and caused by the presence of other infections in the body, in which case Aspergillosis with co-infection with the primary infection causes severe infection. Aspergillus can coexist with other pathogenic microorganisms (e.g., bacteria, fungi, and viruses) in patients. This coexistence increases the risk of infection and increases the risk of death due to ARI. Investigations showed that co-infection occurs through different cellular and molecular mechanisms (e.g., biofilm formation, and Inhibition of cytokines) with other pathogens at the levels of the immune and respiratory systems.

Conclusion: Exposure to the fungus, the individual's immune status, and lung status determine the pattern of the disease. Studies and observations show that Aspergillus can coexist with other microorganisms during processes. This symbiosis can be in the form of infectious synergy or inhibition. The result of this symbiosis is effective in the rate and severity of the infection of

microorganisms and in the respiratory system of patients with respiratory infections, it leads to the emergence or exacerbation of signs and symptoms of the disease.

Keywords: Aspergillosis AND Aspergillus AND Coinfection AND Respiratory Tract Infections

Affinity Capture of Erythropoietin on Boronate Functionalized Hydrogel Microparticles: Role of Spacer Arms on Adsorption Efficiency (Research Paper)

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Introduction: With the expansion of industrial production of various recombinant pharmaceuticals, it is essential to improve the purification efficiencies. developing boronic acid substrates as affinity adsorbents with appropriate spacer arms is essential to improve adsorption capacity of glycoproteins such as recombinant human erythropoietin (rhEPO). Therefore, this study compares the use of two amine activating agents (ammonia and ethylene diamine) with different chemical structure lengths as the spacer arms for covalent binding with boronate (CPBA) ligand to study the effect of ligand length and presence of amine functional groups in the boronate structure on affinity adsorption of a model glycoprotein (i.e. rhEPO) on agarose microparticles.

Methods: Immobilization of spacer arms: Agarose microparticles were activated with highly reactive epoxid groups according to Porath et al [18]. Then, the activated microparticles were aminated following Matsumoto et al [19]. For this purpose, NH3 and EDA respectively as two proportionally short and long length spacer arms were employed. Functionalization of the substrate with boronate affinity ligands: In order to functionalize the bed with boronate affinity ligands, 1.25 mL of activated and dried microparticles was placed in the reaction buffer of phosphate-buffered saline (PBS) solution of 0.1 molar (pH 7.4), 0.15 molar NaCl, 100 mM carbodiimide (EDC), 100 mM N-hydroxysuccinimide (NHS), and 50 mM 3-carboxyphenylboronic acid (CPBA) as affinity ligand. The reaction was carried out at ambient temperature for 2 hours. On completion of the reaction, the functionalized microparticles were washed with 0.01 M sodium phosphate buffer. The microparticles were stored in 20% ethanol at 4℃. In brief, two types of agarose microparticles namely EDA-CPBA and NH3-CPBA were prepared. By comparing the adsorption performance of NH3-CPBA and EDA-CPBA resins, the role of the spacer arm length and structure on glycoprotein adsorption was compared . In order to confirm the formation of favorable chemical bonds on agarose microparticles, Fourier-transform infrared spectroscopy (FTIR) was performed using PerkinElmer Spectrum Gx, Perkin-Elmer. Finally, the immobilized CPBA density was measured by elemental analysis (Thermo Finnegan). Affinity

capture of glycoprotein: To evaluate the effect of ligand structure (spacer arms) affinity capturing of rhEPO by two boronate functionalized microparticleswas conducted. To compare the ligands' performance, affinity capture efficiencieswere calculatedas ratio of the amount of captured protein (Mcaptured) to the amount of protein loaded (Mloaded) in the feeding stage [20] according to equation (1) Affinity capture efficiency (%) = (Mcaptured/Mloaded) × 100 equation (1)

Results: The results show that the adsorbent aminated with type 2 amine had a better performance in protein adsorption than the adsorbent aminated with type 1 amine. This can be due to two reasons. One is that the presence of two amine groups behind the CPBA ligand can improve the tendency of the ligand to capture proteins due to more significant electron withdrawal. Second, the employed type 2 amine holds four atoms thus can reduce the steric hindrance by providing a longer amine spacer arm which makes the ligands more accessible for the protein molecules to bind to. In conclusion, desiging the structure of boronate affinity ligand and the vicinal functional groups based on target biomolecules enhances the capturing capacity of boronate functionalized materials for further applications in diagnosis, separation and sensing of glycoproteins.

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Keywords: Boronate affinity materials, Protein Purification, Glycoprotein, Recombinant human Erythropoietin

Age-related diseases and public health implications (Review)

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Introduction: The percentage of national populations over age 65 has been increasing in the last 10 years. Clinicians and the public health community need to develop a culture of sensitivity to the needs of elderly population and its subgroups. Sensory changes, cognitive changes, and weakness may be subtle or may be severe in the heterogeneous population of people over age 65. Falls, cardiovascular disease, and difficulty with activities of daily living are common but not universal. This paper reviews relevant changes of normal aging, diseases, and syndromes common in people over age 65, cognitive and psychological changes, social and environmental changes.

Methods: A comprehensive literature search was carried out to assess different age-related diseases and public health implications in elderly population. Google scholar data base and PubMed has been searched. Epidemiological studies, experimental studies, inquiries or editorials on the mentioned theme published from 2015 until 2022 were included. specific keywords including “Public health”, “age-related diseases” and “elderly population” have been used.

Results: The review highlighted that older adult faced a range of physical, social and psychological challenges due to living with chronic conditions and required care and support in three main areas: 1) social activities and relationships; 2) psychological health; and 3) activities related to mobility, self-care and domestic life. It has been reported that some hearing and vision loss are a part of normal aging as is decline in immune function. Cardiovascular disease includes chronic ischemic heart disease, congestive heart failure, and arrhythmia, and osteoporosis and dementia are common chronic conditions at age 65. A recent study published in USA showed that osteoarthritis is the second most common chronic condition among American older adults and a common cause of chronic pain and disability. Osteoarthritis, diabetes, and related mobility disability will increase in prevalence as the population ages and becomes more overweight.

Conclusion: These population changes have considerable public health importance. Caregiver support, services in the home, assistive technologies, and promotion of home exercise programs as well as consideration of transportation and housing policies are recommended by recent literatures. For clinicians, judicious prescribing and ordering of tests includes a

consideration of life expectancy, lag time to benefit, and patient goals. Furthermore, healthy behaviors starting in early childhood can optimize quality of life among the oldest-old.

Keywords: public Health, age-related disease, aging, elderly population.

Aichi virus as a gastrointestinal virus? (Review)

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Introduction: The Aichivirus is a type of virus that is found in Japan in 1989. Aichi virus (AiV) is a cytopathic positive sense and ssRNA virus that is small and spherical. The genetic investigation has defined it as belonging to the family Picornaviridae, genus Kobuvirus.

Methods: It was first found following a 1989 outbreak of acute gastroenteritis in the Aichi Prefecture, which was likely linked to the raw oyster. It's been found in studies of Finnish youngsters, Pakistani children, and Japanese travelers since then.

Results: Viruses are the most prevalent cause of acute gastroenteritis, which are among the most common causes. Aichi viruses, for example, have been reported as novel viruses that cause epidemics of severe gastroenteritis in recent years.

Conclusion: In addition, multiple investigations in Japan, Germany, France, Tunisia and Spain found a high prevalence of AiV antibodies in adults (between 80 and 99 percent), indicating a high level of virus exposure. Possibly transmitted by contaminated food or drink via fecal-oral pathways. Vaccines that prevent illness transmission are currently unavailable.

Keywords: Human Aichivirus, Gastroenterits, Molecular epidemiology

Air conditioning of the electrospinning machine chamber (Research Paper)

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Introduction: Electrospinning is one of the most common technique that used in the tissue engineering [1]. In the electrospinning method, membranes consisting of micro and nanofiber are produced by evaporating the solvent from polymer solutions [2]. Indeed, the most commonly used solvents in that technique are anesthetic (e.g. chloroform) and toxic (e.g. dimethylformamide) [3]. Although the electrospinning of harmful solvents is carried out in a chamber with closed doors, it may endanger the health of the operators. Therefore, it is necessary to continuously ventilate the air inside the chamber. Since the electrospun fibers are very thin and delicate, the air flow inside the chamber may damage the fibers or interfere with the fiber formation. In this work, several configurations of the chamber with a fan are designed, and evaluated by simulation the flow field of the air inside the chamber. The fan is installed on the top of the chamber to suck the air containing the evaporated solvent, and in the other wall of the chamber, a mesh plate is considered to allow fresh air to enter the chamber. The simulation is carried out to investigate the effect of the airflow on the air condition and fiber formation. Several fans with different suction power are studied for air conditioning in a commercial electrospun chamber.

Methods: A commercial electrospun chamber with a dimension of 100×80×60 cm3 is selected for the simulation. The geometry of the camber is designed by Gambit software, and is shown in Figure 1. As shown in Figure 1, a fan is embedded on the top of the chamber which is simulated by a circular surface in the computational domain with small and concentrated grids. A rectangular strip is considered as the air inlet on the lower surface of the chamber is demonstrated by the pink color. The airflow field inside the chamber is simulated using Fluent software. Fans with low power are chosen to avoid damage the fibers. Therefore, the airflow is laminar, and the governing equations of the airflow are as below: where is the velocity vector, P is the pressure, is density, is the kinematic viscosity and ∇ is the gradient operator. For boundary conditions, a no-slip condition is set on the walls of the chamber. Different flow rates of 500-1800 $m3/h$ (correspond to various commercial fans) are set on the fan location. Initial zero velocity is set on the inlet surface when the fan is off. The physical properties of the air are considered at room temperature.

Results: The simulation result of the air flow field inside the chamber is shown in Figure 2 for a flow rate of 1800 $m3/h$. Figure 2-A illustrates the velocity vectors of the flow colored by the velocity magnitude (m/s). The highest velocity occurs at the fan location, which is 2.64 m/s and is shown in red color. The direction of the velocity vector at the fan plane is upward that confirm air exhaust. The magnitude of the velocity inside the chamber is lower than 1 m/s. Experimental test shows that it is small enough to ensure fibers do not damage. Two different directions are examined for the air inlet surface which are demonstrated in Figures 2-B and 2-C. In both cases, the path lines of the air are smooth and follow the wall of the chamber. There is no flow disturbance in the middle and center of the chamber where the electrospinning set is located.

Conclusion: Simulating the air flow field caused by the fan inside the electrospinning chamber gives valuable data about the magnitude and path line distribution. The obtained data are examined in an actual chamber. When the fan is on, the smell of solvent is not detected. That proves that the fan is working well. Moreover, no disturbance in the electrospinning process is observed despite the designed fan attached to the chamber.

Keywords: Air conditioning, Electrospinning, Toxic solvent, Simulation

AKAP4: a potential early biomarker in the diagnosis of breast cancer and immunotherapy target (Review)

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Introduction: Breast cancer is one of the most common cancer, especially in women related to death and early diagnosis is significant to manage it better and prevent the major problem and improve overall survival in patients. Screen tests are so important to detect breast cancer as soon as possible to increase the success rate of treatment. A-kinase anchoring protein 4 (AKAP4) is a scaffolding protein and it's binding to the regulatory subunit of protein kinase A (PKA). AKAP4 is known as Cancer testis (CT) antigens: a group of antigens used as early biomarkers. It's participated in the intracellular signaling of protein kinase–A. AKAP4 high expression in germ cells and cancer than normal cells. The present study aims to investigate the AKAP4 as an early detection of breast cancer and immunotherapy target for treatment.

Methods: In this study, a review was conducted to obtain relevant studies from the online databases Pubmed, Web of Science, and Scopus with "Breast cancer" and "AKAP4" as keywords from 2013 to September 2022 and only English studies was included. We reviewed all studies that considered AKAP4 as an early biomarker or immunotherapy target.

Results: Totally 5 related articles were reviewed. The data revealed that AKAP4 was expressed in various histotypes of breast cancer and it was detected in most patients with breast cancer. AKAP4 was detectable in all 4 stages of breast cancer (I-IV) in both tumor and peripheral blood. However, the expression of AKAP4 was significantly higher in stage IV, nodal involvement, and distant metastasis in peripheral blood. The studies demonstrated that anti-AKAP4 antibodies are present in patients' sera too and it can provide a better method of diagnosis. Due to the minimally invasive association with this method AKAP4 can consider a primary screen test. According to the presence of AKAP4 in all these stages, we can predict that it may consider as a tumorigenic factor; so some studies showed that AKAP4 can consider as an immunotherapy target and showed that knockdown of AKAP4 inhibited proliferation of breast cancer cells in vivo and in vitro. However, studies showed different result and we need more study to confirm this hypothesis.

Conclusion: AKAP4 is exclusively found in testicular tissue and It's not found in any other normal tissue. When AKAP4 is detected in other tissue or serum it can be considered as an early biomarker for cancer and malignant cells. Evaluation of AKAP4 was recently recognized as an early biomarker in breast cancer and it can help to more successful treatment and it can consider as immunotherapy target. However, more studies are needed to clear gray areas of the Role of AKA4P for breast cancer early diagnosis and treatment.

Keywords: Keywords: Breast cancer, AKAP4, Biomarker, Immunotherapy target

Allograft mineralized bone block; A suitable substitute for bone regeneration (Research Paper)

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Introduction: According to the increasing worldwide statistics of bone defects which could have an undeniable effect on the patient's quality of life, several investigations have been attributed to fabricate an ideal bone regenerative scaffold. Among different types of bone grafting, the clinical application of allografting have been progressed due to providing osteoconductive substitutes with similar characteristics to the native tissue without any limitations in resources. Nevertheless, there is still the risk of infection transmission and immunogenicity in this regard.

Methods: Herein, for the aim of overcoming these challenges, an allograft mineralized bone block was processed through decellularizing and lyophilizing after approving the sterility evaluations of the selected donor. The bock was evaluated using scanning electron microscopy (SEM) and image-j software.

Results: Based on the results, the final product was an interconnected porous structure with pore size ranges between 100-900 µm.

Conclusion: Therefore, it could be concluded that the prepared structure is an appropriate candidate for bone tissue regeneration.

Keywords: Allograft, Mineralized Bone Block, Bone Tissue Engineering, Regenerative Medicine

Aloe Vera and Cancer (Review)

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Introduction: For many years, Aloe is known to have many therapeutic properties which include; anti-microbial, anti-viral, anti-cancer, anti-oxidant, anti-inflammatory, skin protection, wound healing, and regulation of blood glucose and cholesterol. Several studies have illustrated the role of Aloe in cancer prevention and treatment, around 75 active compounds could potentially be of therapeutic value in cancer treatment.

Methods: I systematically searched on PubMed database. The combination of key words was Aloe and cancers. I read Aloe and its Effects on Cancer: A Narrative Literature Review which had use many articles about Aloe Vera and its effects on cancer and I used some of those articles to make my poster. I made the poster by Photoshop app.

Results: In fact, a part from whole Aloe, different compounds of Aloe have been identified to have anticancer activities involving many pathways.

Conclusion: Whether the whole Aloe or its compounds are considered, I found through different articles that Aloe is a medicinal plant that has acted well against many types of cancer.

Keywords: Aloe Vera, Cancer

Alpha-pinene improves learning and memory deficits after ischemia/reperfusion by inhibition of necrotic cells death (Research Paper)

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Introduction: The brain, including the hippocampus, is the most vulnerable organ in the body to ischemic reperfusion injury. The brain, including the hippocampus, particularly those in the CA1 region, will easily die-termed delayed neuronal death-when they are deprived from the blood supply. which include memory deficits, since hippocampus is well-known to play a pivotal role in the spatial memory regulation. α-Pinene is an organic compound of many aromatic plants and is known as a potent agent to possess antimicrobial, antioxidant, and anti-inflammatory properties. The present investigation is about finding the neuroprotective effects of α-Pinene by which improves learning and memory deficits after brain ischemia injury.

Methods: Twenty-eight male Wistar rats were randomly selected and allocated in the form of four groups (sham, α-Pinene, ischemia, ischemia+ α-Pinene). Ischemia was created by obstruction couple common carotid arteries in 20-min period. Saline as a vehicle and α-Pinene (100 mg/kg, intraperitoneally) were injected at the time of reperfusion. Spatial memory performances were evaluated by the Morris water maze. Necrotic cell death was detected by Nissl staining.

Results: The results showed that necrotic cell death in the CA1 area of hippocampus that increased by cerebral ischemia, significantly reduced with treatment of α-Pinene

Conclusion: This study for the first time found that α-Pinene treatment improved spatial memory impairments that induced by brain ischemia through preventing neuronal cell death. α-Pinene has significant neuroprotective effects and can be introduced as a therapeutic agent against cerebral ischemia-induced injuries.

Keywords: Alpha-pinene, Ischemic Stroke, spatial memory, Necrotic cell death

Alpha-pinene Inhibits Apoptosis of Hippocampus CA3 Cells Following Focal Ischemia/Reperfusion in Rats (Research Paper)

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Introduction: Cerebral ischemia causes loss of hippocampus pyramidal cells. Pinene (C10H16) is a bicyclic, double bond, terpenoid hydrocarbon. alpha-pinene among the best-known representatives of a broad family of monoterpenes and has anti-apoptosis properties. In this study, we investigated the neuroprotective effects of alpha-pinene in rats after global cerebral ischemia.

Methods: Male Wistar rats underwent a MCAO surgery for 1 hour. Saline as a vehicle and alpha-pinene at doses of alpha-pinene (50, and 100 mg/kg) were intraperitoneally injected immediately after reperfusion. 24 h after focal brain ischemia DNA fragmentation, apoptosis, in hippocampus CA3 area were detected using TUNEL assay.

Results: The results showed that treatment with alpha-pinene significantly reduces apoptosis (P <.05) in hippocampal CA3 area, compared to the ischemia group.

Conclusion: In conclusion, alpha-pinene treatment, found for the first time in the present study, reduces hippocampus CA3 injuries after cerebral ischemia through preventing neuronal apoptosis.

Keywords: Alpha-pinene, Ischemic, Apoptosis, Hippocampus

Amazing Roles of The Mitochondrial DNA in Cancer Metastasis (Review)

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Introduction: Tumor metastasis is a series of invasive and metastatic cascades in which tumor cells detonate from the original tumor to reach surrounding or distal tissues to form new lesions. It is the result of the interaction between tumor cells and the tumor microenvironment. Metastasis is the main cause of death in tumor patients, with most patients dying from the spread of the cancer rather than the primary tumor. Mitochondrial DNA, the genetic material in mitochondria, encodes essential oxidative phosphorylation proteins and plays an important role in mitochondrial respiration and energy transfer. This genetic material has a circular structure and 37 genes. Maternally inherited mitochondrial DNA (mtDNA) is thought to contribute to cancer development and prognosis. mtDNA is an important factor in tumor initiation and progression. As more in-depth studies of mitochondrial-encoded factors emerge, this may lead to exciting advances in targeting mtDNA to inhibit tumor metastasis. This review summarizes the structure and function of the mitochondrial genome and the relationship between mtDNA and tumor metastasis. Our goal is to establish a framework in related fields and address the role of the mitochondrial genome in tumor metastasis.

Methods: The researchers used a new mouse model, a model of mitochondrial nuclear exchange called MNX, to investigate whether the mitochondrial genome influences tumor incubation and metastasis efficiency. In another study, Using cytoplasmic hybrid (cybrid) technology, Ishikawa et al. replaced the endogenous mtDNA of a poorly metastatic mouse tumor cell line with mtDNA of a highly metastatic mouse tumor cell line, and found that the recipient tumor cells acquired the metastatic potential of the transferred mtDNA.

Results: Studies have supposed that replacing mtDNA from poorly metastatic tumor cells with mtDNA from highly metastatic tumor cells in mice via cytoplasmic hybrid (cybrid) technology could result in better metastatic capacity. Thus, mtDNA alterations have an important role in enhancing a tumor's metastatic capacity. mtDNA mutations (m.13997G>A, p.P25L and 13885insC in the ND6) can enhance the metastatic potential of tumor cells by inducing complex I defects resulting in increased ROS production. These results indicate that mtDNA mutations can contribute to tumor progression by enhancing the metastatic potential of tumor cells. mtDNA mutations can also

enhance cancer metastasis by promoting apoptotic resistance in cancer cells via activating the PI3K/Akt signaling pathway.

Conclusion: If we can summarize the characteristics of mtDNA mutation between tumorigenesis and metastasis, this may provide a great direction for the early diagnosis of cancer and the prediction of tumor aggressiveness. To date, there is no clear evidence of a definitive relationship between mtDNA and tumor metastasis, but some non-random changes in the mitochondrial genome associated with tumor progression have been reported in many tumor types.

Keywords: Metastasis, Mitochondrial DNA, cancer, mtDNA, tumor

An attitude on apoptosis resistance as the most important causes of cancer cell growth (Review)

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Introduction: Morphological hallmarks of apoptosis in the nucleus are chromatin condensation and nuclear fragmentation, which are accompanied by rounding up of the cell, reduction in cellular volume (pyknosis), and retraction of pseudopods. Chromatin condensation starts at the periphery of the nuclear membrane, forming a crescent or ring-like structure. The chromatin further condenses until it breaks up inside a cell with an intact membrane, a feature described as karyorrhexis. The plasma membrane is intact throughout the total process. At the later stage of apoptosis, some of the morphological features include membrane blebbing, ultrastructural modification of cytoplasmic organelles, and a loss of membrane integrity. The aim of this study was an attitude toward apoptosis resistance as the most important cause of cancer cell growth.

Methods: This study was investigating an attitude toward apoptosis resistance as the most important cause of cancer cell growth from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed

Results: Apoptosis mechanisms must be understood in order to comprehend the etiology of diseases brought on by disrupted apoptosis. This could thus aid in the creation of medications that specifically target particular apoptotic genes or pathways. Due to their dual roles as initiators and executors of apoptosis, caspases play a crucial role in the process. Three different mechanisms can activate caspases. The intrinsic (or mitochondrial) and extrinsic (or death receptor) routes of apoptosis are the two often discussed starting processes. Both routes ultimately lead to the execution stage of apoptosis, which is a shared pathway. The intrinsic endoplasmic reticulum pathway is a third, less well-known starting pathway. Cancer can be considered as the outcome of a series of genetic alterations in which a normal cell undergoes a malignant transformation. One of the crucial alterations in a cell that results in this malignant transformation is the evasion of cell death. Apoptosis was associated with the removal of possibly cancerous cells, hyperplasia, and tumor development as early as the 1970s, according to Kerr et al. Therefore, decreased apoptosis or its resistance is key to the development of cancer. A malignant cell can develop a decrease in apoptosis or apoptosis resistance in a variety of ways. 1) disrupted the balance of pro-apoptotic and anti-apoptotic proteins, 2) reduced caspase function and 3) impaired death receptor signaling summaries the mechanisms that contribute

to evasion of apoptosis and carcinogenesis. A set of physically and functionally related proteins known as the inhibitor of apoptosis proteins control signal transduction, cytokinesis, and apoptosis. They are distinguished by the presence of the protein domain known as the baculovirus IAP repeat (BIR). There are currently eight known IAPs: Livin/ML-IAP (BIRC7), NAIP (BIRC1), c-IAP1 (BIRC2), c-IAP2 (BIRC3), X-linked IAP (XIAP, BIRC4), Survivin (BIRC5), Apollon (BRUCE, BIRC6), and IAP-like protein 2 (BIRC1) (BIRC8). IAPs are naturally occurring caspase inhibitors that work by attaching their conserved BIR domains to the active sites of caspases, increasing the destruction of active caspases, or preventing caspases from interacting with their substrates. the importance of abnormalities in apoptotic pathways in the development of carcinogenesis, as well as the viability and potential of numerous new apoptosis-targeting therapeutic approaches. Some perplexing and unsettling questions, however, such as whether these therapeutic approaches lead to tumor resistance and whether they may result in the mass death of normal cells, remain unaddressed. If there are any lessons to be learned from the conventional anticancer medications, which kill both normal and tumor cells, have severe side effects, and increase tumor resistance, then this is a real issue. On the other hand, if these compounds that target apoptosis are selectively working on a single pathway or protein, that would be advantageous clinically. Although many inhibitors of the Bcl family of proteins and some pan-IAP inhibitors are among the molecules that enter clinical trials, the majority of them act on multiple targets. Therefore, ongoing research should concentrate on methods that can specifically trigger apoptosis in cancer cells while sparing healthy cells.

Conclusion: The importance of abnormalities in apoptotic pathways in the development of carcinogenesis, as well as the viability and potential of numerous new apoptosis-targeting therapeutic approaches. Some perplexing and unsettling questions, however, such as whether these therapeutic approaches lead to tumor resistance and whether they may result in the mass death of normal cells, remain unaddressed. If there are any lessons to be learned from the conventional anticancer medications, which kill both normal and tumor cells, have severe side effects, and increase tumor resistance, then this is a real issue. On the other hand, if these compounds that target apoptosis are selectively working on a single pathway or protein, that would be advantageous clinically. Although many inhibitors of the Bcl family of proteins and some pan-IAP inhibitors are among the molecules that enter clinical trials, the majority of them act on multiple targets. Therefore, ongoing research should concentrate on methods that can specifically trigger apoptosis in cancer cells while sparing healthy cells.

Keywords: apoptosis, resistance, cancer, cell growth

An overview of breast cancer diagnosis and treatment based on new techniques (Research Paper)

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Introduction: Breast cancer is one of the most common cancers among women and is the first cause of cancer-related deaths in women. Breast cancer is a type of malignant tumor that arises from the cells of this organ. In breast cancer, the disease usually starts in the lobules or ducts of the breast, and then it can penetrate through the ducts and walls of the glands and attack the surrounding fat tissues or even other parts of the person's body. In order to reduce mortality from breast cancer, early detection is necessary for its treatment.

Methods: Diagnostic methods include local thresholding methods, random methods, Gaussing filters, along with morphological filters, wavelet methods, and fuzzy logic methods.) to reduce false positives, artificial intelligence methods and recently fuzzy logic works along with artificial intelligence are used.

Results: The treatments that are used for breast cancer today include radiation therapy, chemotherapy, surgery, and the use of radiopharmaceuticals.

Conclusion: Early detection of breast cancer with effective and efficient diagnostic and screening methods, currently mammography plays a more effective role than other methods in detecting breast cancer, plays an important role in reducing the incidence and mortality rate of breast cancer.

Keywords: breast cancer, diagnosis, treatment, new techniques

An overview of medical treatment of dermatophytes (Review)

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Introduction: Dermatophytes are the most common cause of fungal infections worldwide, affecting millions of people annually. Dermatophytes are filamentous fungi with the ability to invade keratinised tissue, such as skin, hair, and nails. Classically, they are divided into three genera: Trichophyton, Epidermophyton, and Microsporum. However, this classification is based on the phenotype of the species and led to misclassification of morphological mutants. In 2017, de Hoog et al. constructed a phylogenetic tree using sequences of the nuclear ribosomal internal transcribed spacers (ITS rDNA) and divided the dermatophytes into seven clades: Trichophyton, Epidermophyton, Nannizzia, Paraphyton, Lophophyton, Microsporum, and Arthroderma. Ringworm or tinea is one of the most frequent clinical aspect of dermatophytosis. Among the tinea infections, tinea corporis, tinea cruris, tinea pedis, and onychomycosis are the most predominant types. The dermatophytes T. rubrum, T. interdigitale and T. mentagrophytes, are the main aetiological agents of dermatophytosis of skin and nails in humans.

Methods: Medical treatment of dermatophytosis consists of topical and/or oral antifungal agents. There are many topical agents for treating several less severe forms of tinea. The azole derivatives, such as clotrimazole, miconazole, econazole, and oxiconazole, are the generally used. Agents from the allylamine family, such as terbinafine and naftifine, are also used. Other topical agents, such as ciclopirox or amorolfine, can be effective in the less severe cases of onychomycosis. In the more severe forms of dermatophyte infections, oral treatment is generally employed. Topical (amorolfine, ciclopirox, efinaconazole, tavaborole, and luliconazole) and oral antifungals (terbinafine and itraconazole) are currently used for onychomycosis treatment. Azole antifungals (triazole class: efinaconazole and itraconazole; imidazole class: luliconazole), terbinafine, and amorolfine inhibit lanosterol 14α-demethylase, squalene epoxidase, and Δ14 reductase/Δ7-8 isomerase, respectively. These antifungals consequentially block ergosterol biosynthesis in fungal cells. Ciclopirox chelates polyvalent cations, such as Fe3+ and Al3+, resulting in the inhibition of metal-dependent enzymes responsible for degrading peroxides inside fungal cells. Tavaborole inhibits leucyl-tRNA synthetase and consequentially blocks protein synthesis in fungal cells.

Results: Terbinafine therapy of dermatophytosis is usually effective, yet increasing numbers of non-responding cases have been documented. Treatment failures and recurrences can be due to host factors such as poor

compliance, drug interactions and in cases of onychomycosis local nail factors. Terbinafine resistance in dermatophytes is typically rare, but reports have been increasing since 2017. It is associated with various point mutations in the squalene epoxidase target gene of T. rubrum and T. interdigitale. However, cases of terbinafine-resistant Trichophyton infections are also seen in other Asian and Middle Eastern countries such as Japan and Iran.

Conclusion: However, clinical resistance does not always correspond to the in vitro resistance and vice versa. This is because several factors influence outcome of an infection including the severity of infection, the host immunity, the timing and dosing of the therapy, compliance and the susceptibility of the infecting organism. Overall, clinical data would suggest that an antifungal combination regimen might be useful against an infection due to dermatophytes. It is interesting to note that even combining drugs acting against a common fungal target (i.e., ergosterol—azoles, allylamines, and morpholine drugs such as amorolfine), a positive interaction in terms of reduction of the MIC of both drugs is often observed. Also they indicate that an association of antifungal agents (systemic plus topic) is effective, and it might be useful in speeding up the clinical and microbiological healing of a superficial infection.

Keywords: Dermatophytes, antifungal agents, Topical, Oral

An overview of stem cells (Review)

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Introduction: In recent years , remarkable progress has been achieved in connection with stem cells , which promises new treatment solutions in difficult - to - treat diseases . These cells , which are present in all multicellular organisms , have the ability to divide and transform into very specific cells and are also able to replace lost and damaged cells . The self - renewal and differentiation ability of these cells promises a bright future in the field of regenerative medicine , cell therapy and pharmaceutical research . New technologies not only provide an unlimited source of autologous stem cells , but also enable the use of non - autologous cells . Of course , the therapeutic use of stem cells is associated with many limitations and obstacles , and therefore more research is necessary to understand their biology . In this article , the basic concepts , applications and limitations of use , and the perspective of the use of stem cells in the future have been reviewed .

Methods: 1. Gulotta LV , Chaudhury S , Wiznia D. Stem cells for augmenting tendon repair . Stem cells international . 2012 ; 291-431 . 2. Améen C , Strehl R , Björquist P , Lindahl A , Hyllner J , Sartipy P. Human embryonic stem cells : Current technologies and emerging industrial applications . Critical Reviews in Oncology / Hematology . 2008 ; 65 (1) : 54-80 . 3. Baraniak PR , McDevitt TC . Stem cell paracrine actions and tissue regeneration . Regenerative medicine . 2010 Jan ; 5 (1) : 121-43 . 4. Buecker C , Geijsen N. Different flavors of pluripotency , molecular mechanisms , and practical implications . Cell Stem Cell . 2010 Nov 5 ; 7 (5) : 559-64 . 5. Van der Jeught M , Taelman J , Duggal G , Ghimire S. Lierman S , Chuva de Sousa Lopes SM , et al . Application Of Small Molecules Favoring Naive Pluripotency during Human Embryonic Stem Cell Derivation . Reprogram . 2015 Jun ; 17 (3) : 170-80 . Cell 6. Guilak F , Cohen DM , Estes BT , Gimble JM , Liedtke W Chen CS . Control of Stem Cell Fate by Physical Interactions with the Extracellular Matrix . Cell Stem Cell 2009 ; 5 (1) : 17-26

Results: Stem cells exist as normal cells in embryonic and adult tissues . Recent studies in the direction The proof of the strong and powerful role stem cells in the field of treatment has begun . Stem cells with self - renewal potential and differentiate into special types of somatic cells . Their ability to produce new cells in medicine , drug discovery , Cell therapy and research are very important . In the past decades , many efforts have been made to find safe methods The cost and progress of stem cell cultivation has been done . The purpose of this review article : 1 (Explanation of the use of stem cells In medicine , drug discovery is sampling of diseases and toxicology

studies . 2 (Preparation of a summary of recent developments Stem cell technology , advantages and disadvantages of common cultivation methods .

Conclusion: The result of this discussion shows that the use of new cultivation methods can be used for the optimal use of stem cells be effective . Next , topics such as : types of stem cells , use of stem cells in drug discovery : 1) targeted recognition , 2) large - scale screening , 3) sampling of diseases , 4) drugs that stimulate proliferation and growth / poison studies We are dealing with science / automatic cultivation systems / combinatorial microarray and microfluidic cultivation systems .

Keywords: stem cell technology , medicine , drug discovery

An overview of the treatment of chronic myeloid leukemia based on its genetic profile (Review)

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Introduction: The Philadelphia chromosome, which contains the BCR-ABL oncogene, is a unique genetic defect that has been linked to the first human cancer, chronic myeloid leukemia (CML). In the field of hematologic neoplasia, it has since evolved into a paradigm for the identification of molecular mechanisms and focused therapeutic strategies. Other significant motifs in the Abl portion include the protein-interaction SH2 and the C-terminal nuclear localization signal (NLS), DNA- and actin-binding domains. This study's objective was to look at potential treatments for chronic myeloid leukemia based on gene profiles.

Methods: This study on the cellular and molecular basis of cancer and chronic myeloid leukemia based on gene profiles used scientific databases including Science Direct, Springer, Google Scholar, and PubMed.

Results: Results showed A hematological condition known as chronic myeloid leukemia (CML) is characterized by the malignant proliferation of bone marrow stem cells. A reciprocal t(9;22)(q34;q11) chromosomal translocation that results in the Philadelphia (Ph) chromosome, a derived 9q+ and a minor 22q-, is its cytogenetic distinguishing feature. The expression of the latter has been demonstrated to be both required and sufficient for the altered phenotype of CML cells. It contains the BCR-ABL fusion gene, which encodes a chimeric Bcr-Abl protein with an unregulated tyrosine kinase activity. Among human malignancies, CML is unique in that just one oncogene product has been found to play a significant role in its pathophysiology. The molecular and cell biology of CML has been extensively studied over the past 20 years thanks to the contributions of many researchers, providing the crucial foundation for the development of targeted therapy. It quickly became apparent that the Bcr-Abl oncoprotein is the best molecular target offered by CML cells because normal cells do not express it. In addition, the analysis of the signal transduction pathways impacted by Bcr-aberrant Abl's kinase activity revealed additional or alternative signaling stages that could be blocked to reverse the oncogenic effects of Bcr-Abl. Recently, immunological methods of identifying and eliminating leukemic clone have also received attention. These methods appear promising, especially in the context of eradicating residual disease following various forms of "debulking" therapy. Although early 1990s studies were focused on attempting to block BCR-ABL gene function via its RNA message, this

approach was never successfully converted into effective CML treatments. The exploration of small compounds that could interact with and inhibit this oncoprotein was thus moved to when the structure and mechanisms of action of the Bcr-Abl protein, the end result of the chromosomal translocation, were clarified. In CML, one of the two BCR-ABL junctions, called e13a2 (formerly b2a2) and e14a2 (previously b3a2), is typically present in the mRNA molecules that are transcribed from the hybrid gene. An oncoprotein with a molecular weight of 210 kDa is produced from both mRNAs. The tyrosine kinase activity of the usually controlled Abl protein is constitutively triggered by the pairing of "alien" Bcr sequences, which gives the p210Bcr-Abl its leukemogenic potential. Bcr acts by promoting dimerization of the oncoprotein such that the 2 adjacent Bcr-Abl molecules phosphorylate their respective partners on tyrosine residues in their kinase activation loops. By interacting with several effector proteins, the unchecked kinase activity of Bcr-Abl then usurps the physiological functions of the regular Abl enzyme, leading to uncontrolled cellular proliferation, decreased adherence of leukemia cells to the bone marrow stroma, and decreased apoptotic response to mutagenic stimuli. It is currently unclear how much each of these factors contributes to the phenotype of chronic phase CML.

Conclusion: The SH1 domain of Bcr-Abl is an obvious molecular target since it is crucial to the leukemogenicity of the oncoprotein. An isoflavonoid called genistein and an antibiotic called herbimycin-A were found to be possible candidates in early tests of natural products for substances capable of inhibiting this catalytic activity. Adenosine triphosphate (ATP) or a substrate can compete with synthetic molecules with competitive chemical structures for occupancy of the binding site in the kinase domain. This has been the subject of subsequent research.

Keywords: chronic myeloid leukemia, genetic profile, Philadelphia chromosome

Analysis of solvent effects on collagen nanofibers (Review)

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Introduction: introduction: Tissue repair refers to the replacement of damaged parts by living cells including mimicking the extracellular environment as the natural niche of the cell for tissue regeneration, which increases adhesion and cell growth. Collagen is a key component of the extracellular matrix. Its characteristics include its nature in reconstruction and restoration and the dimensions of the resulting fibers, and the degree of porosity and high bonding strength. In addition to the molecular weight of the polymer, which affects its viscosity, the type of solvent should also be considered.

Methods: In this research, articles between 2012 and 2022 were selected from Science Direct and Scopus, which were screened after identifying the articles.

Results: In the conducted research, there is a direct relationship between the type of solvent and the diameter of the fibers. In research that used acetic acid and DMSO. It was from nanofibers with a diameter of 200to 639 nm. In another study, hexafluoropropylene HFP trifluoroacetic acid TFA was used and the fiber diameter was reported between 220 and 415. In a similar study, the weight percentage of polyvinyl alcohol was used along with collagen, which according to the feeding rate Between 0.02 and 0.1 and 0.3, the diameter of the formed fibers was 90 to 240 nm

Conclusion: The modeling and arrangement of nanofibers, it has a lot to do with the type of solvent. Among these, properties such as dielectric constant, surface tension, and even output flow rate are also important. And due to the fact that some solvents are toxic, they can cause a change in the structure of nanofibers and the nature of the fibers. Therefore, it seems that the choice of solvent and mixing material is very important. Probable strategies can be based on error testing, but according to numerical calculations and in order to reduce the number of tests, computational analysis can be used.

Keywords: collagen-Nanofibers-Solvent -extracellular matrix

Analysis of the expression of selected miRNAs (miR-17-5p and miR-20-5p) and LncRNAs (LINC01605 and FAS-AS1) involved in the apoptosis signaling and their target gene, Caspase 3 in glioblastoma multiform (Research Paper)

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Introduction: Glioblastoma multiform (GBM) is an invasive cancer, that causes high mortality in patients. Disruption of the apoptosis process is one of the main pathogenesis of the disease. Recently, LncRNAs and miRNAs have been shown to play an important role in the process of apoptosis. In this study, we examined the expression changes of miRNAs (miR-17-5p and miR-20-5p) and LncRNAs (LINC01605 and FAS-AS1), as well as Caspase 3 in GBM patients.

Methods: In this study, 100 patients participated in two groups of 50 individuals, including 50 GBM patients as the case group, and 50 healthy individuals as the control group. Using RT-PCR, the expression changes of miRNAs (miR-17-5p and miR-20-5p), LncRNAs (LINC01605 and FAS-AS1) and Caspase 3 were examined in both groups.

Results: Expression of LINC01605, miR-20-5p and miR-17-5p increased in patients, while expression of Caspase 3 and FAS-AS1 decreased; the difference was statistically significant between the two groups. In addition, it was found that these factors have the appropriate sensitivity and specificity as diagnostic markers. In order to evaluate the diagnostic value of CASP3, LncRNAs (LINC01605 and FAS-AS1) and miRNAs (miR-17-5p and miR-20-5p), the receiver operating characteristic (ROC) curves were performed. Analysis showed, that there was an indirect relationship between the expression of miR-20-5p and miR-17-5p with patients' sex, however, no significant relationship was observed between them. An indirect relationship was also found between patients' gender. However, there was a direct relationship between FAS-AS1 and patients gender, but no significant relationship was observed between them (P > 0.05). Then the Area Under the Curve (AUC) values were analyzed. ROC curve analysis of genes showed the following information (Sensitivity: 92% and specificity: 64% for Caspase 3, Sensitivity: 40% and specificity: 84% for LINC01605, Sensitivity: 60% and specificity: 88% for FAS-AS1, Sensitivity: 94% and specificity: 60% for miR-17-5p, and Sensitivity: 88% and specificity: 74% for miR-20-5p). These genes

can be used as diagnostic biomarkers to discriminate GBM patients from control subjects.

Conclusion: Finally, LINC01605, FAS-AS1, miR-20-5p, miR-17-5p and Caspase 3 can be used as apoptosis predictors in the GM patients.

Keywords: miR-17-5p, miR-20-5p, Apoptosis, Glioblastoma Multiform, Caspase 3

Anatomy of the Uterus from the Point of View of Iranian Medicine and Its Comparative Analysis with Modern Medicine (Review)

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Introduction: Introduction: Knowledge of the anatomy and physiology helps a lot in the diagnosis and treatment of diseases. Investigation the ancient medical texts shows that the physician had an accurate and sharp view of the different body systems, and this increases the need to use traditional medicine texts. Therefore, the aim of this research was to investigate the anatomical issues of the uterus from the ancient traditional medicine and compare it with the findings of modern medical anatomy.

Methods: Method: This is a descriptive review study that investigated reference texts such as Ibn Sina's Canon, Tashrih-e-mansoori, Khawarizm shahi's collection and Abdolvahab Tafreshi's book. Then a comparison of the contents with the book of anatomy was made and the similarity and differences of the contents were examined.

Results: Results: The results of this research showed that the physician of ancient Iranian medicine were familiar with the various parts of the internal reproductive system, including the uterus (Zehdan), fallopian tubes (Oieh e Rahemi), cervix (Fam e Rahem), isthmus (Tangeh Kipo), and vagina (Onog e Rahem). The descriptions of the anatomy of the female internal reproductive system include the appearance, structure, anatomical adjacencies and uterine ligaments that appear in the form of pictures and drawings in books. The blue-red uterus is represented as an inverted male penis. Three layers of the uterus, serous, muscular and lining, have been introduced. Adjacents of the uterus, bladder, rectum and intestine are mentioned. Spindle-shaped neck introduced with a circular collar in the middle of the uterus. Cylindrical and 3-layered vagina that protrudes forward and is covered by hymen in girls. Main ligaments of the uterus are broad peritoneal ligament, round ligament and cardinal ligament.

Conclusion: Conclusion: The descriptions mentioned about the uterus and the internal reproductive parts of the female sex are very consistent with the modern facts of anatomy and are explained in detail with pictures in the ancient medical books.

Keywords: Anatomy, traditional medicine, uterus, modern medicine

Anthrax (Review)

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Introduction: Anthrax is globally a zoonotic and fatal disease that can infect mostly herbivores and also humans. The causative agent of anthrax is Bacillus anthracis, which is Gram positive, capsulated, non-motile and aerobic or facultatively anaerobic, belonging to the family Bacillacae. It produces spores that can persists for decades in the soil despite extreme temperatures, chemicals and even ultra-violet radiation, which can cause an outbreak after a climate shift. The severity of the disease is due to production of endotoxin. The endotoxin has three components (which are proteins): Edema factor(EF), protective antigen (PA)and lethal factor(LF). Individually these proteins are non-toxic, but they can become lethal if allowed to combine and interact within the cells of the exposed human or animal.

Methods: Two plasmids, pXO1 and pXO2, play the key role in the pathogenicity of Bacillus anthracis. They are responsible for the production of anthrax toxins and the formation of a poly-γ-d-glutamic acid (PGA) capsule that this capsule protects the bacilli from phagocytosis. Anthrax infection in humans has been categorized into two; Agricultural and Industrial. Agricultural cases occur when people come in contact with tissues from infected or death animals these include veterinarians, butchers, slaughterhouse workers, Industrial cases are those that occur during cleaning and processing of infected animal products.

Results: There are 4 types of anthrax: a) Cutaneous anthrax (skin anthrax): it happens by skin penetration or touching any infected products. It mostly effects arm, hands, face, neck and foot. This form is about 95% in society and is a very less dangerous form. Its symptoms for 1 to 7 days. It looks like an insect bite with a black centered painless sore on the skin and it can easily treated with antibiotics. b) Gastrointestinal anthrax: it happens by eating uncooked foods which the spore enters to the body. c) Inhalation anthrax: this happens by breathing in places where anthrax spores are found. It is the most dangerous form and can become chronic. symptoms are fever, shortness of breath, coughing, headache, and fatigue. d) Injection anthrax: it has been seen in people dealing with the Heroin injections. This form shows the redness along the site of injection, swelling. As the disease stay long will cause the failure of the organs, shock and also causes the meningitis.

Conclusion: This disease is common in developing countries like the Sahara Desert in Africa, central and southwestern Asia (Turkey, Labnan, Syria, Iran, Egypt), and the Caribbean. Several periodic outbreaks of anthrax were reported. Also In Kenya, anthrax outbreaks occur continuously from different parts of the country. anthracis in spleen tissue by realtime PCR should be considered as the method of choice for rapid confirmation of anthrax. In comparison to conventional PCR, real-time PCR is more sensitive For necropsy findings we have incomplete or absent rigor mortis with dark tarry blood oozing from the mouth, nostrils, anus, and if the carcass is opened, several necropsies observed include blood being dark thickened and failing to clot, hemorrhages on the serosal surface of the abdomen, thorax, epicardium, endocardium, and gastrointestinal tract mucosa and enlarged, dark red, or black, soft, semifluid spleen. Also in the skull meningitis might be seen.

Keywords: anthrax , disease , animals , bacillus anthracis

Anti leishmania effect of pistacia Atlantica subspecies Kurdica on leishmania major (Research Paper)

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Introduction: Leishmaniases are a group of diseases caused by several species of flagellated protozoan parasite, Leishmania, being primarily transmitted through the bite of female phlebotomine sand flies. Approximately 350 million individuals inhabiting in 88 countries in the tropics and subtropics are affected by leishmaniases.(7) A number of risk factors may be involved in the increase of exposure to the sand flies and subsequent Leishmania-associated morbidity, including expansion of urban areas along with forest destruction and migration of people to the endemic regions. Based on the involved sites of the body, clinical disease manifests as cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis (MCL) and visceral leishmaniasis (VL). Based on the published literature, CL is the most common form, with the annual incidence rate of 0.7 – 1.2 million cases. Most of the CL cases have been reported in six countries, comprising Brazil, Columbia, Algeria, Afghanistan, Iran and Syria.(6) In Iran, CL is a seemingly prevalent parasitic infection, with almost 20,000 new cases annually, that are being sorted into two major forms: i) anthroponotic cutaneous leishmaniasis (ACL) due to Leishmania tropica (L. tropica), transmitted by Phlebotomus sergenti (Ph. sergenti) and resulting in dry sores, ii) zoonotic cutaneous leishmaniasis (ZCL) caused by L. major, transmitted by Ph. papatasi and yielding secretory, wet sores. Altogether, successful treatment of CL requires long-lasting administration of obsolete, toxic drugs, i.e., pentavalent antimonials such as sodium stibogluconate and meglumine antimoniate, which may be associated with the emergence of drug-resistance isolates. Other new and efficacious therapeutic options such as amphotericin B are expensive and/or demonstrate lower efficacy.(7,1) Such concerns have directed researchers towards research and development (R&D) on the much cheaper and more efficient compounds. Medicinal plants represent a huge repertoire of therapeutic compounds for healing purposes of different types of wounds, including those related to CL. About 250,000 medicinal plant species have been documented around the world, while only 6% have been characterized biologically and functionally. Herbal medicine is much better accepted globally than synthetic medications; thus the discovery of a plant-based therapy for CL lesions is of utmost importance.(6,14) According to the recent findings, the anti-leishmanial activity of quinoline, flavonoids, saponins, terpens, tetralenes and alkaloids derived from medicinal plants have been shown on some

Leishmania species. (15,14,10) The present study was done to evaluate the anti-leishmanial efficacy of the extract of a pistachio tree, called Pistacia atlantica, subspecies Kurdica on L. major lesions in mice, in comparison with the standard glucantime treatment.

Methods: 2.1. Parasite culture and maintenance Standard L. major strain (MRHO/IR/5/ER) was retrieved from the Parasitology Department of Tarbiat Modares University, Tehran, and cultured in the Roswell Park Memorial Institute (RPMI-1640) medium supplemented with 10% fetal bovine serum (FBS), 100 IU/ml penicillin and 100µg/ml streptomycin. Culture flasks were incubated at 24±1 oC and checked using an invert microscope on a routine basis. 2.2. Induction of Leishmania lesions Upon reaching the stationary phase, the Leishmania promastigotes were enumerated and a 0.2 ml volume of the parasites (containing 106 promastigotes) was prepared and injected into the base of the tail of BALB/c mice. About 25 days later, lesion was formed at the injection site(FIGURE1) . In order to confirm the presence of Leishmania within lesions, direct sampling was done on glass slides, fixed with methanol, air-dried and stained using Giemsa solution and subsequently examined using light microscopy (100× magnification). 2.3. Treatment groups For this aim, 30 BALB/c mice were sorted into the following groups: 5% plant-based ointment (5 mice), 25% plant-based ointment (5 mice), 50% plant-based ointment (5 mice), glucantime therapy (5 mice), negative control (5 mice) and eucerin (5 mice). A control group was considered for the evaluation of lesion progression, length, recovery, animal mortality and the presence of parasites. All mice in experimental groups were checked regarding disease progress or recovery, length and duration of lesions, presence of the parasites as well as mortality. The diameter of each lesion (millimeter) was measured at first and in the end of the experiment using a caliper. The parasite burden in the lesions was determined during 6 weeks using a grading system for Leishmania lesions, initially (before treatment) and at the end of the experiment (before killing mice). For this purpose, the lesions were sanitized using 70% ethanol and samples were prepared from the exudates using a lancet. The preparations were air-dried, fixed with methanol, stained using Giemsa solution and then assessed regarding the parasite burden, as follows: no parasite per 10 cultures (negative), one parasite per 10 cultures (1+), 1-10 parasites per 10 cultures (2+), 10-100 parasites per 10 cultures (3+), 100-1000 parasites per 10 cultures (4+), and over 1000 parasites per 10 cultures (5+ and more). 2.4. Statistical analysis The significance level of the obtained results among experimental groups was evaluated using One-way ANOVA test and SPSS v21.0 software (SPSS Inc., Chicago, IL, USA). The difference between experimental and control group was assessed using T-test. Of note, a P<0.05 was considered as statistically significant. (3)

Results: 3. Results This experiment was conducted during 6 weeks and the mean ± standard deviation (SD) of lesion measurement at the end of each

week is provided in Table 1. Based on one-way ANOVA statistics, it could be inferred that there was a significant difference regarding time and treatment in the wound diameter. With respect to the calculated P-value for time variable (P < 0.05), there was statistically remarkable difference among different time periods, so that the mean of the measured lesion was different regarding 6 weeks of experiment, and there observed a statistically significant difference in terms of the time of lesion measurement. Based on Figure 2, there was a statistically significant difference in the diameter of the CL lesions during 6 experimental weeks, while in eucerin-treated group the diameter of lesions even increased during this period. It was deduced that in all treatment groups there was a statistically significant difference between sampling time and the parasite load in lesions. In all groups except of eucerin the parasite load was the highest in the first week and the least in the sixth week. The results corroborated that the parasite load differed in the treatment groups based on sampling time in each week. It was, also, noteworthy that the highest and lowest parasite load belonged to eucerin and 50% Pistacia atlantica extract ointment groups, respectively.

Conclusion: The results of the present study along with previous findings shows that Pistacia atlantica plant extract possesses potent leishmanicidal activities in vitro and in vivo. Also, it is recommended to determine the efficacy of different concentrations of Pistacia atlantica extract along with various routes of administration in the human CL cases.(3) Additionally, the prediction, isolation, purification and application of the effective compounds found in the Pistacia atlantica extract is highly suggested for future studies.

Keywords: Leishmania major Promastigotes Pistacia atlantica

Anti-inflammatory Effects of Mesenchymal Stem Cells-derived Exosomes on Endometriosis (Research Paper)

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Introduction: Among the most prevalent disorders affecting women globally is endometriosis. Endometriosis has become more common recently as a result of a number of genetic and environmental causes. Inflammation is one of the key pathogenic processes associated with endometriosis. We used exosomes formed from menstrual blood-derived stem cells (MenSCs) to treat endometriotic stem cells since the therapeutic effects of mesenchymal stem cells are delivered through paracrine functions and generation of extracellular vesicles and exosomes containing various growth factors and cytokines.

Methods: Menstrual blood samples (2-3 ml) from healthy and endometriosis women were collected. MenSCs were isolated by the Ficoll density-gradient centrifugation and characterized by flow cytometry. Secreted exosomes were isolated from healthy MenSCs (NE-MenSCs) based on the protocol of the Exocib kit (Cib Biotech Co) and used to treat endometriotic cells (E-MenSCs). various genes related inflammation, were analyzed using Real-Time PCR, from which some were evaluated in protein level as well.

Results: We evaluated several key inflammatory genes that are expressed at high or moderate levels in MenSCs. Compared with NE-MenSCs, E-MenSCs showed higher expression of IL-1β, IL-6 and IL-8. NF-kB, and COX-2, while similar expression of HIF and TNF-α genes was observed in both healthy and endometriosis cell lines. MSC-Exo surprisingly suppressed all inflammatory genes studied in the endometriosis cell line compared to untreated E-MenSCs. two main inflammatory markers IL-6 and IL-8 were analyzed using ELISA method. IL-6 and IL-8 were expressed at a lower level in E-MenSCs treated with MSC-Exo than in untreated E-MenSCs. ER expression may serve as a prognostic biomarker of aggressive endometriosis. ER-α gene had

remarkably higher expression in E-MenSCs rather than NE-MenSCs. It was observed that MSC-Exo did not change ER-a gene expression levels in the E-MenSCs group as compared to NE-MenSCs. ELISA was performed to quantify the ER-a concentration. ER-α expression showed no significant change after exosome-treated E-MenSCs.

Conclusion: MenSCs-derived exosomes can be used as a better therapeutic option for the improvement of endometriosis compared to conventional treatments. The present study shows that exosomes isolated from menstrual blood stem cells reduce the abnormal secretion of inflammatory factors as well as cell proliferation in endometriosis cells.

Keywords: Endometriosis, Exosomes, Menstrual blood, Mesenchymal Stem Cells

Antibacterial Activities of Medicinal Plants (marshmallow) (Review)

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Introduction: Today, the use of herbal medicine is expanding, and plant therapy has moved up the scientific study agenda in the majority of nations. Higher plants' potential as a source of novel pharmaceuticals is yet mostly untapped. Only a small portion of the estimated 250 000– 500,000 plant species have undergone phytochemical investigation, and even fewer have been subjected to biological or pharmacological screening. Antimicrobial agents are abundant in medicinal plants. Different nations employ plants as medicines, and they are the source of potential and potent pharmaceuticals. This study's goal was to look into the antimicrobial properties of medicinal plants.

Methods: The following subjects were covered in the articles we selected: research that looked at elements that affect the antibacterial mechanisms of medicinal plants (marshmallow), papers exploring the advantages and uses of medicinal plants in the fight against bacteria, and articles looking at the antibacterial mechanisms of medicinal plants on bacteria. For research on the antibacterial properties of medicinal plants, we consulted the databases PubMed, Scopus, Science Direct, and Google Scholar.

Results: Marshmallow (Althaea officinalis) is a medicinal plant, and many nations throughout the world employ its roots, leaves, and flowers in traditional medicine. Peptins, starch, mono- and disaccharides, mucilage, flavonoids, antioxidants, coumarins, scopoletin, tannin, asparagines, and several amino acids are all present in this herb. In addition to having antibacterial (both Gram-positive and Gram-negative bacteria), antifungal, anti-inflammatory, anti-mycobacterial, and anti-cough properties, the extracts made from marshmallow's roots and flowers also have antiviral, anti-yeast, anti-complement, and free radical scavenging activities. Without having any negative effects on the users, the aqueous extract of marshmallow is also useful in reducing hyperlipidemia, inflammation, and gastrointestinal ulcers as well as in preventing platelet adhesion.Through the inhibition of cytokinin, interleukin-6, and tumor necrosis factor synthesis and release, this plant can also reduce inflammation. The main immunomodulatory effects of the marshmallow root extract are the increases in phagocytic and macrophage activities16 and the number of T lymphocytes. Because of this, using

marshmallow instead of other remedies for bacterial, viral, and fungal infections would be a smart idea.

Conclusion: Plants have always been a great source of novel medicinal molecules throughout history. Motaharinia and colleagues demonstrated in a study from 1390 that marshmallow extract has more antifungal properties than marshmallow root. Additionally, they claimed that among these extracts, ketoconazole had the strongest antifungal activity on Malassezia furfur. Previous research indicated that marshmallow extract had antibacterial effects on a variety of microorganisms, including fungus. Some plants' antibacterial abilities are still unknown. As a result, learning more about the antimicrobial qualities of endemic plants, in particular, can help us understand how these plants affect the development of significant bacterial diseases. The health of living things is currently seriously threatened by antibiotic resistance. It is essential to look for affordable anti-microbial materials that are also effective. As a result, medicinal plants can serve as an effective alternative to chemicals.

Keywords: bacterial resistance, Antibiotic, Medicinal Plants, marshmallow

Antibacterial effect of alcoholic and aqueous extract of Propolis on Staphylococcus aureus and Pseudomonas aeruginosa (Research Paper)

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Introduction: Pseudomonas aeruginosa and Staphylococcus aureus can usually cause disease in humans. Propolis extract is known as an antimicrobial compound that affects bacteria. This research aims to determine the antimicrobial activity of propolis extract on bacteria strains in vitro and the pattern of antibiotic resistance.

Methods: In this research, the antibacterial effects of propolis alcoholic extract on Pseudomonas aeruginosa and Staphylococcus aureus bacteria (Kirby-Bauer method) and dilution in the tube, determining the Minimum Inhibitory Concentration (MIC) and the Minimum Bacteria Concentration (MBC) was evaluated. SPSS was used for statistical analysis.

Results: Based on the results, antimicrobial activity, non-growth halo diameter of Pseudomonas aeruginosa and Staphylococcus microorganisms were determined, and Staphylococcus aureus showed the highest sensitivity and Pseudomonas aeruginosa showed the highest resistance to propolis alcoholic extract.

Conclusion: The results of the antibiotic resistance pattern showed that Pseudomonas aeruginosa is only sensitive to gentamicin, while Staphylococcus aureus is resistant to most antibiotics. Conclusion: The alcoholic extract of propolis hadn't only an inhibitory effect but also antibacterial properties on Pseudomonas aeruginosa and Staphylococcus aureus bacteria.

Keywords: Propolis, Antibiotic Resistance Pattern, Staphylococcus aureus, Pseudomonas aeruginosa.

Antibacterial Effects of Peganum harmala Seed Extracts on Drug-resistant Clinical Isolates of Acinetobacter baumannii in North of Iran (Research Paper)

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Introduction: Background: Acinetobacter baumannii is one of the most common and important causes of hospital-acquired infections. Due to its intrinsic resistance to antibiotics, A. baumannii can survive in the hospital environment for a long time and target hospitalized patients. Therefore, treatment and prevention of hospital-acquired infection with these bacteria require identification of new an tibacterial agents with no or fewer side effects and toxicit

Methods: Antimicrobial susceptibility of the isolates was determined using the Kirby-Bauer method according to the Clinical and Laboratory Standards Institute document M100-S25 (2015). Antimicrobial activity of the ethanolic and aqueous extracts of P. harmala against drug-resistant A. baumannii isolates was determined by the agar well diffusion method. In addition, broth microdilution susceptibility testing was carried out to determine the minimum inhibitory concentrations (MICs) of the extracts. Finally, active compounds with antimicrobial activity were identified by gas chromatography-mass spectrometry

Results: The frequencies of the multidrug-resistant, extensively drug-resistant and pandrug-resistant A. baumannii isolates were 37.2%, 58.2% and 61%, respectively. The MIC90 of the aqueous extract of P. harmala was 1024µg/mL, which was four times less than that of its ethanolic extract (4096 µg/mL). Similarly, the MIC50 of the aqueous extract of P. harmala was significantly smaller than that of the ethanolic extract ($P < 0.05$). According to the results, vasicine/peganine and 8-hydroxy deoxy peganine were the most abundant (39.94%) bioactive compounds in the aqueous extract of P. harmala.

Conclusion: The aqueous extract of P. harmala had excellent antimicrobial effects on the resistant A. baumannii isolates.

Keywords: Acinetobacter baumannii, Drug Resistance, Peganum harmala, Nosocomial Infection

Antifungal effect of Artemisia austriaca extract on common Candida species(albicans, glabrata, parapsilosis, krusei) in Iran (Research Paper)

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Introduction: Candida species are one of the most common fungal diseases. Today, drug resistance is observed in fungi, especially in candida species, so researchers are looking for suitable alternatives; one of these choices is plant extracts because Plants have different metabolites with strong antimicrobial effects. In this study, we used Artemisia austriaca extract against a group of pathogenic fungi.

Methods: Plant extraction was performed using the Soxhlet apparatus. Candida samples were randomly chosen. The resistance and sensitivity of the candida species to plant extracts were investigated by the disk diffusion method. MIC was done by microdilution method; finally, MBC was also measured.

Results: According to the results obtained, among the studied species, the best antifungal effect was observed on Candida albicans. The growth inhibition zone of this fungus was 21±0.5mm. The MIC of the plant in Candida albicans was 31.25mg/ml, and MBC was 62.5mg/ml.

Conclusion: The results show that artemisia extract has a significant antifungal effect. Artemisia extract has the ability to have a more substantial antifungal effect against common Candida species. The present study indicates that Artemisia extract can be used in control and prevention models.

Keywords: Artemisia austriaca ,Candida albicans, Candida glabrata, Candida krusei

Antifungal Effect of Copper Oxide Nanoparticles on Candida Species
(Research Paper)

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Introduction: Candida species are one of the opportunistic associates of the common flora of skin, mouth and vagina that is known to initiate severe fungal infections. Between the new agents utilized as antimicrobials, nanoparticles are under especial consideration. Copper oxide nanoparticles (CuO NPs) are broadly used for their high biocompatibility, nontoxicity and simple organization. These NPs have exclusive features such as high surface to volume ratio that initiate them as relevant antimicrobial agents. The aim of this study was to evaluate the antifungal effects of CuO NPs against Candida species.

Methods: Copper Oxide Nanoparticles were synthesized. These nanoparticles are approved by transmission electron microscope, and nanocomposite structure was also confirmed by scanning electron microscope. Then, the minimum inhibitory concentrations (MICs) of CuO NPs for twelve Candida albicans strains were determined in microdilution broth technique according to CLSI M27-A3/S4.

Results: The results of this study indicate that the effects of CuO NPs are comparable to amphotericin B as standard antifungal. The MIC50 value of CuO NPs was determined at the range of 2-32µg/ml for Candida albicans strains. Higher concentrations of CuO NPs (32 µg/ml) were effective on the Candida cell growth, resulting in 100% reduction in the optical density in sabouraud dextrose broth medium.

Conclusion: Our findings indicated an excessive antimicrobial effect of CuO NPs against pathogenic Candida species and could reduce the growth of all established Candida sp. Thus, CuO nanoparticles can be consumed in treatment of infections initiated by this fungus.

Keywords: Copper oxide nanoparticles; Antifungal; Candida Species.

Antifungal Effect of Nano-Zno against Aspergillus species (Research Paper)

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Introduction: Zinc is a barely active element and a strong reducing agent; due to reduction, it can oxidize to form zinc oxide, which is very beneficial to prepare zinc oxide nanoparticles.(ZnO) ZnO is the most commonly used Zn nanoparticle, because of its low price and high productiveness. Many findings revealed that ZnO could be used as an antifungal agent. In this study, antifungal effects of Nano-ZnO were studied against Aspergillus species.

Methods: Eight clinical strains of Aspergillus niger and one standard strain (Asp. niger; PTCC 5154) were cultured on potato dextrose agar slants for 10 days at 25 °C. Then spores were harvested with Tween 80 (0.1%). The final spore concentration of suspension was reached 106 spore/ml. Serial dilutions of nano-ZnO were prepared and inoculated with strains and incubated at 37°C for 24 and 48 hours. Their antifungal effect was evaluated by the minimal inhibitory concentration (MIC) according to CLSI-M38-A3.

Results: The results showed antifungal activity against Asp. niger at the range of 1-8µg/ml. Higher concentrations of nano-ZnO (8µg/ml) were effective on the Aspergillus growth, resulting in 90% reduction in the optical density in SDB medium.

Conclusion: According to our results, nano-ZnO has a significant antifungal effect against Asp.niger. this study was focused on just one species of Aspergillus. Thus, more critical evaluations have to be done on various species in different dilutions of nano-ZnO.

Keywords: Aspergillus niger, Nano-Zno, Antifungal Effect

Antimullerian hormone and polycystic ovaries: A systematic review study (Review)

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Introduction: Polycystic ovary syndrome (PCOS) is a complex endocrine disorder with reproductive, psychological, and metabolic health consequences. Its prevalence has been reported up to 5-10%. Since various studies have suggested the relationship between the Antimullerian hormone and polycystic ovarian, this hormone can be highly beneficial in diagnosing this disease.

Methods: To get relevant studies from the English and Persian databases such as PubMed, Scopus, Web of Science, Iran Medex, SID, and Magiran, the English and Persian keywords (Polycystic ovaries and Antimullerian hormone with all possible search combinations) have been searched.

Results: Out of 1680 articles, 7 studies (1 cross-sectional 3 cohorts 3 case-control) were eligible according to the study criteria. All studies were evaluated based on the STROBE index. Our analysis revealed that higher levels of Antimullerian hormone could play a vital role in increasing the risk of polycystic ovaries. There was one study that suggested there is no relationship between AMH and PCOs.

Conclusion: The results of most studies showed a significant association between higher levels of Antimullerian hormone and polycystic ovaries. While a study has reported conflicting results. Therefore, it is highly recommended that further studies should be conducted in this area.

Keywords: Antimullerian hormone, polycystic ovaries, polycystic ovary syndrome

Antioxidant and anti-inflammatory properties of natural compounds (Review)

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Introduction: Oxidation protection is thought to prevent some chronic diseases. Inflammation occurs in bacterial, viral, fungal or parasitic diseases, and millions of people around the world suffer from inflammatory problems caused by such diseases. According to the treatment of inflammation based on chemical drugs, including non-steroidal anti-inflammatory drugs and glucocorticoids, which have various side effects such as heart toxicity, hepatotoxicity and immunodeficiency, natural anti-inflammatory products have been considered by many researchers as an alternative to conventional therapies for inflammatory disorders due to their relative safety, efficacy, and availability. These products contain compounds such as sugars, pantothenic acid, phenolics, flavonoids, fatty acids, vitamins, minerals.

Methods: Many studies have reported that there is a relation between the antioxidant and anti-inflammatory properties of natural compounds. In this review, first, oxidation and inflammatory process and the bioactive compounds especially phenolic compounds in natural products will be examined in general. Then, based on the results of various studies, mode of action of phenolic compounds as antioxidant and anti-inflammatory agents, antioxidant tests, expression of inflammatory factors such as interleukins and immune modulators, will be evaluated at in-vitro and in-vivo levels. The mechanisms of these effects will also be investigated as much as possible.

Results: Natural compounds are a wide group, ubiquitous in plant-based foods, and possess a remarkable anti-inflammatory capacity due to their multiple inhibitory activities of proinflammatory mediators. Form various studied and researches, it will be concluded, natural products have significant antioxidant and anti-inflammatory effects that exert anti-inflammatory effects by acting on various drug targets and cellular messaging pathways. The mechanism of action may be by preventing the formation of free radicals in inflamed tissues.

Conclusion: Researchers propose dietary natural compounds especially phenolics as a potential natural alternative for the treatment of inflammation and related diseases, with minimal or null adverse side effects.

Keywords: Inflammation, Antioxidant properties, Anti-inflammatory properties, Phenolic compounds, Natural comp

Antioxidant Treatment in Polycystic Ovary Syndrome (Review)

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Introduction: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among reproductive-aged women with various prevalence from 5-21%. This syndrome is associated with wide spectrum complications in different aspects of health, including reproductive (hyperandrogenism, hirsutism, anovulation, infertility, and menstrual disturbance), metabolic (obesity and diabetes mellitus as well as cardiovascular risk), and psychological features (mood disorders and decreased quality of life). Some characteristics of PCOS such as obesity and abdominal adiposity, androgen excess, and insulin resistance can develop oxidative stress in these patients. Nowadays, the use of antioxidants in management of women with PCOS has attracted lots of interests. Indeed, PCOS is a condition with significant decrease in serum antioxidant and vitamins levels and these women are in an increased risk of oxidative status (OS). OS occurs from the imbalance between reactive oxygen spices production and antioxidant defenses. The present study was conducted to review the extent of antioxidant treatment and PCOS.

Methods: A comprehensive literature search was carried out to assess if antioxidant Google scholar data base. Epidemiological studies, experimental studies, inquiries or editorials on the mentioned theme published from 2015 until 2022 were included. specific keywords including “Polycystic ovary syndrome”, “PCOS”, “antioxidant” and “antioxidant treatment” have been used.

Results: Studies reported significantly increased concentrations of oxidative stress biomarkers including plasma thiobarbituric acid reactive substances (TBARS) and malondialdehyde (MDA) and significantly lowered levels of superoxide dismutase (SOD), catalase (CAT), vitamin C and vitamin E in PCOS patients. Antioxidant supplementation has been shown to improve insulin sensitivity and other health threating conditions in women with PCOS. One study revealed that calcium and vitamin D supplementation had a significant effect on follicle growth and response to main PCOS treatment. NAC (N-acetyl-cysteine) is an antioxidant that derivative from the amino acid L-cysteine. NAC can have effects on insulin receptor activity as well as insulin secretion and subsequently increase glucose utility. Previous studies showed NAC can have effect on levels of circulated insulin and insulin sensitivity in PCOS women with hyperinsulinemia. Although some studies didn’t find any significant differences between women with and without PCOS regarding to

serum Zn levels, a research team believes zinc supplementation for PCOS women has some beneficial effects on cardio metabolic risk factors.

Conclusion: Despite the important role of alternative medicine especially antioxidants in management of PCOS women, there are not many well-designed papers or detailed literature reviews report in this field, especially in Iran. In the other hand, the available studies addressing antioxidant use in PCOS women yielded controversial results. For overcoming these limitations, updating our knowledge on this field and a critical appraisal of all available studies might be helpful to guide clinical practice. Collectively the results of all reviewed studies in this paper showed that antioxidants and vitamins have positive effects in management of PCOS and its' complications, although it seems more studies is necessary in this field because evidence are not enough to identify an optimum antioxidant management in women with PCOS.

Keywords: Reactive oxygen species, antioxidant defences, Oxidative stress, Polycystic ovary syndrome

APPLICATION OF ARTIFICIAL INTELLIGENCE IN EMBRYO SELECTION (Review)

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Introduction: As fertility rates have declined in recent years, assisted reproduction techniques (ART) have been more widely used. In vitro fertilization (IVF) results are influenced by many variables and their interwoven relationships. Embryo quality is unquestionably a crucial determinant of a successful IVF outcome. Artificial intelligence (AI) has been widely employed to enhance and automate embryo selection in recent years. We discuss the latest studies on AI in embryo selection in this review.

Methods: The current study employed a review method that searched for studies published in PubMed, Web of Science, and Google Scholar up to April 2022. Without consideration for language, databases were searched for relevant keywords. All relevant studies are included in this study.

Results: Several models have been developed, and while some of them have shown potential, there are still numerous obstacles to overcome. Some models provide a single still image of the embryo, while others have a time-lapse video of the embryo's development. Female age, number of previous treatments, stimulation procedure, clinic-specific parameters, and manual annotations of morphological and kinetic data could all be included in other samples. Including such entries can dramatically improve performance metrics. The majority of studies used convolutional neural network (CNN) to develop their models. There were considerable differences in model optimization between the studies. Because of the wide range of input, embryo population, and outcome, it's difficult, if not impossible, to compare AI performance outcomes across studies.

Conclusion: According to the findings of our study, AI has a lot of potential for the future of embryo selection; nevertheless, they still have a long way to go before they can claim to be as good as clinical embryologists in predicting outcomes.

Keywords: Artificial intelligence, embryo selection, In vitro fertilization

Application of BAM15 as a fat-burning molecule in the treatment of obesity and related disorders (Review)

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Introduction: Obesity is the source of various diseases in the world. More than 650 million people worldwide are obese. Many genetic and environmental factors, including: basal metabolism rate, satiety, hormonal function, movement activities and nutrition, provide the basis for obesity. There are currently only a few treatments for obesity, and people who take these drugs are usually able to lose weight over a long period. Treatment of obesity requires new and standard drugs. This new research is a very effective step in the drug discovery process. Recently, a molecule called BAM15 has been discovered that reduces weight by increasing body metabolism without affecting the amount of food eaten, muscle mass, increased body temperature, or toxic biochemical and hematological markers. BAM 15 as an uncoupler reduce the production of ROS, and as a result, by reducing inflammation and oxidative stress, they can treat disorders related to mitochondrial oxidative stress, including ischemic damage, Parkinson's disease, Alzheimer's, insulin resistance, aging, heart failure, sepsis, Non-alcoholic fatty liver disease, cancer, and have a favorable effect on disorders such as obesity that benefit from increased energy consumption.

Methods: In vitro studies, using different concentrations of Bam-15, the effect of this molecule on factors such as glucose absorption, fatty acid uptake, and the expression of genes involved in metabolic pathways were investigated. Body temperature, body weight, and daily food intake were also measured in Bam 15-treated mice.

Results: Bam 15 stimulates insulin signaling and glucose and fatty acid uptake in an AMPK-dependent manner. It also limited the expansion of fat in the liver and kidney in C57BL/6J mice, thereby preventing diet-induced obesity while improving glycemic control.

Conclusion: Collectively, the studies show that pharmacological mitochondrial isolation with BAM15 has powerful anti-obesity and related disease effects.

Keywords: BAM15, Mitochondrial uncoupler, Obesity

Application of biosensors in maintaining food safety (Review)

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Introduction: With the expansion of modern agriculture and the development of food industry, the quality and quantity of food increased significantly. Food safety is of great importance as it affects the awareness of consumers socially and economically and can endanger their lives. Factors that threaten this immunity include: heavy metals, pathogenic agents, used poisons, pesticides and veterinary drug residues. In recent years, various measurement and evaluation methods have been developed by researchers. Among these techniques, electrochemical biosensors/food toxin converters are among the most powerful tools used in this field. These tools increase the speed of food contamination screening and foodborne illness management by using corrective actions. This technique has many advantages, including high sensitivity, cheapness, suitable size and high analysis power. Also, nanomaterials used in the food industry, having food additives, antioxidant and antimicrobial properties, increase the shelf life and quality of food products. Combining nanomaterials with biosensors and creating nanobiosensors has improved sensing capabilities for environmental applications. Therefore, the expansion and development of nanobiosensors using the properties of nanomaterials in relation to specific biological materials is a more suitable alternative for easy and timely diagnosis of plant diseases. Therefore, it is necessary to have a rapid detection technology that can adapt to the diversity and complexity of food safety.

Methods: In the forthcoming systematic review, the required data were collected using keywords and citing valid databases such as Scopus, PubMed, Google Scholar and ProQuest. The statistical population includes all studies conducted until 2022 in the field of Application of biosensors in maintaining food safety. After reviewing the relevant findings and evaluating the quality of the data, 18 articles were analyzed.

Results: Today, the application of nanobiosensors in the agricultural and food industries is expanding to increase the productivity of natural resources, which contributes to the sustainability and efficiency of the agricultural and food sector. Nanobiosensors can be applied through agriculture, soil and moisture assessment, natural resources, soil pH assessment, disease management, detection of pathogenic organisms and chemicals, and detection of adulterated substances unsafe for humans, up to the commercialization stage. A limited number of industries such as Roche, Nippon and IBM etc. are associated with the manufacture of nanobiosensors due to their wide range of applications. Commercialization of nanobiosensors in agriculture and food industries is very little reported. Although there are reports of commercial nanobiosensors in diagnostics and medical applications. The versatility of nanobiosensors is another aspect that needs more attention. The development of a part of nanomaterials based on biosensing can increase the commercialization of nanobiosensors with portable sizes. In the coming years, nanobiosensor devices can be connected with GPS system to help precision and smart agriculture. As a result, farmers can make better decisions on irrigation, fertilization, pest control and proper harvesting of natural resources. Based on the above discussion, it can be concluded that electrochemical sensors based on 2DM have many advantages such as high speed, easy operation, low cost and time, maintaining food safety, environmental monitoring and material detection in various fields. This review mainly introduces the preparation methods, structures and properties of 2DMs and their applications in various electrochemical detection. Through the design of functional nanomaterials and the fabrication of sensor electrodes, the performance of electrochemical sensors is increased.

Conclusion: Finally, implantable biosensors and surface scanning biosensors offer innovative tools for future research. By improving the connection between nanomaterials and modified electrodes, it is possible to increase the bond strength of nanomaterials on the surface of the electrode so that it is easy to separate the changes of nanomaterials on the electrode and thus improve the stability of electrochemical detection. The high cost of fabrication, automation tests, results validation and validation of field trials that miniaturize industrial prototypes for production is still a major challenge. In addition, there is no market to compensate and bear all these costs. This may be the reason why there are fewer commercial nanobiosensors. However, extracting new nanomaterials from waste biomass can be a cost-effective alternative. New programs and methods based on CRISPR-Cas12a promote the development of numerous diagnostic solutions and have great potential in medical diagnosis, environmental monitoring, and especially food diagnosis.

Keywords: Biosensor, Food Safety, Biosensing Techniques

Application of Chitosan bio materials in dentistry (Review)

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Introduction: Chitosan is a kind of polymer that is basically found in the exoskeleton of crustaceans and some fungi. This polymer is biocompatible, biodegradable and non-toxic. Moreover, chitosan can induce the induction and integration of bones. These properties made the application of these materials important in medicine and dentistry. Therefore, this study is aimed to review the application of chitosan biomaterials in dentistry.

Methods: in this review article , the required data were collected from citing and keywords database like pubmed, science direct and Google scholar, the reviewed studies are about until 2021 in the field of application of chitosan in the dentistry and its effection on health and human life. After study and evulating the datas, 18 articles are chosed and analysed

Results: Many studies have been performed on different applications of chitosan biomaterials in dentistry. It has been reported that chitosan can reduce the bacterial adhesion. it is a solution to left a small proportion of the adhering bacteria alive. so, it shows a good application for oral health. Moreover, the application of nanoparticles with a copper-chitosan hybrid structure in dentistry has been reported. Chitosan improves adhesion and copper not only strengthens the tooth surface but also has antibacterial properties, prevents bacteria growth, and disrupts and destroys the caries-causing compound. Therefore, this combination showed a good effect on tooth enamel surfaces and can be an effective treatment for dental plaques. Nano chitosan along with nano calcium with anti-demineralization property can be used to increase the hardness of enamel through preventing demineralization process producing by acetic. In an experiment in which the participants used a mouthwash containing 5% phosphorylated chitosan in a period of fourteen days to remove the plaques on the teeth, two types of plates were reported. One plate was thin and the other plate was thick, that the thick and accumulated plate was the old plate. In general, this experiment showed that the phosphorylated chitosan destroys plaques and prevents

gingivitis and tooth decay. Chitosan-fluoride microparticles can be used as a controlled release of fluoride. These particles provide a means to increase fluoride absorption, and are used in dental care products that prevent tooth decay. Chitosan is an inhibitor of platelet aggregation on tooth enamel.

Conclusion: According to the results of research studies on chitosan, chitosan reduces bacterial adhesion and increases tooth enamel hardness in tooth problems. It is hard due to its structural complexity and synthetic limitations. All of these properties suggest that this biomaterial can be a promising biomaterial for dental applications. However, its production cost is high and we hope it will be solved by conducting further research and chitosan will be used in other parts of medicine.

Keywords: chitosan

Application of in silico simulations to genetic studies (Review)

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Introduction: About 13% of all deaths worldwide are due to cancer. Oncology is fundamentally based on prognostic aspects. These days, biomedical science relies heavily on computer support to analyze extensive data, quantify dynamic and multiscale events, or similarly simulate complex models. Computational models have been used for intracellular and intercellular aspects, tissue and organ-specific. In this regard, we focus on assessing and predicting tumor growth. The mathematical basis of tumor growth was explained in the middle of the last century. We take in silico modeling of tumor growth as an initial tool and further develop it into a new web-based simulation that is uniformly accessible to biomedical scientists and clinicians. Focusing on visualizing features is key to learning and understanding ding. Therefore, features are essential for knowledge discovery. The possibilities and accessibility of our simulation and visualization approach may ultimately encourage researchers and clinicians to advance the tumor research field toward personalized medicine. Future integrations will include biomolecular networks such as drug-protein interactions or patterns of genetic variation.

Methods: We studied and reviewed related articles by searching for keywords such as nanotechnology and in silico methods on reliable scientific sites such as PubMed and Science Direct and by entering the time filter from 2019 to 2022. We succeeded in presenting this review article.

Results: Our goal is to provide a comprehensive and extensible simulation tool to visualize tumor growth. According to tumor growth activity, computational models for different types of tumors, from animal and human models, that deal with individual stages of tumor development. Understanding tumor heterogeneity concerning personalized cancer therapy represents the ultimate goal of computational tumor growth modeling. Using tumor growth data and related gene data and providing an open source database for tumor growth data are significant steps forward to support scientific collaborations and clinical programs and ultimately help fight cancer.

Conclusion: We believe our approach provides an impetus to advance in silico modeling towards 3R and a better understanding of tumor dynamics. We emphasize the computational modeling approach of biological systems and the development of computational modeling tools for simulation and reproducibility experiments in biological research. In silico methods overcome the lack of wet testing facilities and succeed as dry methods in terms of reduction, modification and replacement. Animal testing is also known as the 3R principles. Our visualization approach to simulation allows for more flexible use and accessible extension to facilitate understanding and gain new insights. In silico modeling and other computational techniques help answer critical questions in cancer research.

Keywords: Nano technology,In silico metod,cancer

Application of magnetic bacteria in cancer treatment (Research Paper)

HOSSEIN AMERI SHAHRABI,[1] HOSSEIN SAYAF,[2,*]

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Introduction: In recent years, the use of natural compounds to fight cancer has received attention due to the few side effects and promising effects. Recently, many natural treatment methods against cancer have proven that magnetic bacteria can be successful in magnetosome-based methods. The treatment of cancerous tumors is very difficult because the metabolism and oxygen levels of the cells in the outer and inner parts of the tumor are completely different, and this makes the treatment difficult. Researchers at McGill University and Polytechnic University in Canada used magnetic bacteria to solve this problem. These bacteria are easily guided by a weakened magnetic field and reach the tumor site and deliver medicine. Another advantage of these bacteria is that they tend to migrate to places without oxygen, and the core of the tumor is exactly where the concentration of oxygen is low. Also, the magnetic field required for the movement of bacterial nano-robots is very weak and does not harm the body. Researchers at McGill University and Polytechnic University in Canada used magnetic bacteria to solve this problem. These bacteria are easily guided by a weakened magnetic field and reach the tumor site and deliver medicine. Another advantage of these bacteria is that they tend to migrate to places without oxygen, and the core of the tumor is exactly where the concentration of oxygen is low. Also, the magnetic field required for the movement of bacterial nano-robots is very weak and does not harm the body.

Methods: The standard strain of Magnetospirillium Griffis Waldens type MSR-1 with special code (DSM6361) was purchased from Detschesammlung von microorganismen und zellkulturen, Germany. This strain was grown in the special culture medium of DSMZ, Germany. To prepare the material culture medium, according to the standard method, DSMZ Medium 380 (Germany) of Magnetospirillum bacteria was used. A solution of mineral elements and a solution of vitamins in a volume of one liter and a solution of ferric quinate in a volume of 100 milliliters were prepared. For each liter of mother solution, 10 milliliters of vitamin solution, 5 millimolar solution of mineral elements, 2 millimolar solution of ferric quinate, 0.68 grams of KH2PO4, 0.37 grams of succinic acid, L(+)-Tartaric Na-thioglycolate, 0.05 gram Na, 0.37 gram acid Resazurin gram and 0.12 NaNO3 acetate, 0.05 gram 0.5 mg was used. Before mixing these compounds, the pH of the solution containing mineral elements was raised to 6.5 by adding KOH or potassium hydroxide and deoxygenated with the help of N2 gas. Ferric quinate solution and mineral elements were autoclaved for 15 minutes with a pressure of 15 pas at a

temperature of 121 degrees Celsius. After autoclaving, when the temperature of the solution reached 45 degrees Celsius, the filtered vitamin solution was added to it. The vitamin solution contains Pyridoxine-Thiamine-, Riboflavin, Nicotinic acid, HClHCl·2H2O, Folic acid. Other materials were obtained from Merck, Germany. With a sterile needle, some of the MSR-1 bacteria inside the medium was removed and injected into the bacterial culture medium, and then placed in an anaerobic jar and connected to the anoxomat device for charging, and for 1 week to 10 days for the growth of the bacteria in the incubator. After 1 week to 01 days when the bacteria grew on the liquid medium, it was removed from the liquid medium and cultured on DSMZ solid culture medium in a linear culture and in an anaerobic and aerobic jar at 82 Celsius degree was kept for 1 week to 01 days. In order to identify the bacteria from the warm staining and evaluate the movement of the bacteria under the microscope, it was done using a magnetic magnet. For this purpose, some of the grown bacteria was removed with a syringe and placed on a glass slide, and distilled water was poured on it, and the movement of the bacteria was observed and recorded under a light microscope by placing a magnet from the north and south poles. In order to closely examine the bacteria and observe the iron nanoparticles inside, photography was done with a Zeiss EM900 electron microscope. To observe the sample using an electron microscope, a few drops of the thickened culture medium containing bacteria were removed and poured onto the grid (copper grid). After drying, the WFI (injection water) was placed in a special chamber and was observed and photographed by an electron microscope (Ziemens 300kv) in the laboratory of Khaja Nasir Tusi Air and Space College (41). To separate and The purification of magnetosomes was done using a physical method, where the bacterial wall was broken using a French press (Thermo company, Germany) and the cell extract was obtained. This device causes cell lysis by direct pressure. The way it works is that by centrifuging the culture medium at 7000 revolutions per minute, it separates the bacteria from the medium. At the end, the sediment obtained is removed from the outlet of the device. About 100 grams (based on bacterial OD calculations) of Magnetospirillium griffis waldens cells extracted in 50 ml of 50 mM HEPES and 4 mM EDTA by passing three times through the French press (2000IB/IN2) to break the bacterial cell wall. Kurd (all the mentioned buffers that were used for magnetosome extraction contain phenylmethylsulfonyl fluoride as a protein inhibitor). Healthy cells and cell debris were separated by a centrifuge at 10,000 rpm. The supernatant liquid was passed through the magnetic separation column (the column was placed between two magnets, which produces a strong magnetic field and is a magnetic iron absorber). First, the magnetic particles were extracted with 50 ml of 10 mM HEPES and 200 mM NaCl. (pH=4.7) then it was washed with 100 ml of 10 mM HEPES. Then the column was cleaned of magnetic particles and the magnetic particles were removed from the column with 10 mM HEPES buffer by flushing or by pressure and kept in the refrigerator. For molecular identification, DNA

extraction was performed using a kit (Azma-Iran) according to the instructions of the kit. For more precise identification and for amplification, specific primers MT12166 of magnetospirillium griffis were used. Polymerase chain reaction was performed using a thermocycler (Bio Rad-USA). All reaction components were purchased from Yekta Azam Equipment Company. The reaction mixture includes: 52 microliters of Master Mix (includes PCR buffer with a concentration of 100 times, magnesium chloride, dNTP, Taq DNA polymerase enzyme), 3 microliters of DNA, 2 microliters of primers (5)

Results: After preparing the BM-PEI-siRNA nanocomposites and determining the amount of light scattering and measuring the potential, which were respectively +96.1, 3.77-49.5, they were selected to enter the cell. Laser scanning microscope observations showed that these composites become a quenching effect in the vicinity of the nucleus and this composite prevents the growth of Helia cells, which depends on the dose and amount of the composites. Using orange-ethidium bromide staining, it was shown that these nanocomposites cause cell wall apoptosis. According to a research conducted in 2018 by Fatemeh Hashminejad et al. on the cytocidal effect of the magnetosome of the bacterium Magneto-Spirillium Griffith-Waldnerber on the breast cancer cell line: It has been shown that magnetic nanoparticles synthesized by magnetic bacteria can be more effective in treating cancer by hyperthermia method than chemically synthesized nanoparticles. Chemically synthesized nanoparticles are very small and less than 20 nanometers in size.

Conclusion: After preparing the BM-PEI-siRNA nanocomposites and determining the amount of light scattering and measuring the potential, which were respectively +96.1, 3.77-49.5, they were selected to enter the cell. Laser scanning microscope observations showed that these composites become a quenching effect in the vicinity of the nucleus and this composite prevents the growth of Helia cells, which depends on the dose and amount of the composites. Using orange-ethidium bromide staining, it was shown that these nanocomposites cause cell wall apoptosis. According to a research conducted in 2018 by Fatemeh Hashminejad et al. on the cytocidal effect of the magnetosome of the bacterium Magneto-Spirillium Griffith-Waldnerber on the breast cancer cell line: It has been shown that magnetic nanoparticles synthesized by magnetic bacteria can be more effective in treating cancer by hyperthermia method than chemically synthesized nanoparticles. Chemically synthesized nanoparticles are very small and less than 20 nanometers in size. According to the above report, it can be said that the size of the structure of magnetic nanoparticles has a great effect on their effectiveness in dealing with cancer. The results of various researches show that magnetic nanoparticles enhance the performance of anticancer drugs such as doxorubicin and cisplatin in killing cancer cells through enhancing the production of reactive oxygen species or other unknown mechanisms. In other

words, magnetic nanoparticles increase the cytotoxicity of anticancer drugs and play an important role in drug delivery to tumor cells.

Keywords: Magnetic bacteria - treatment of cancer-cancer

Application of mesenchymal stromal cells in osteoarthritis (Review)

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Introduction: In today's modern and machine world, humans are exposed to various disorders and bone tissue injuries. A high percentage of elderly people suffer from osteoarthritis (OA), a common chronic disease affecting the joints with erosion of articular cartilage, inflammation of the synovium, and resorption of the underlying subchondral bone that resulting persistent pain and disability and high costs to society. Current treatments for OA are largely limited to analgesics and anti-inflammatory drugs that only provide symptom relief. Orthopaedics tissues, such as bone, cartilage, and tendon, involve cells that are difficult to culture and grow in vitro for reconstruction of damaged tissues. Recently, developments in stem cell research has have to exciting attempts to use stem cells for orthopaedics tissue regeneration owning to their potential to regenerate tissues without producing scar tissue that is generally associated with healing processes.

Methods: In the current review study, PubMed, Google Scholar, and Scopus databases were searched to find relevant articles. The search was conducted in English and the words searched included bone, bone regeneration, joint diseases, osteoarthritis, mesenchymal stromal cells, orthopaedics and stem cell.

Results: Pre-clinical experiments and clinical trials have demonstrated that mesenchymal stromal cells (MSC) related therapy is a promising option for

the treatment of cartilage lesions and OA owning to their potential to differentiate to both bone and cartilage. In this regard, pre-clinical studies have demonstrated that the cartilage of the joint can be protected from degeneration, and the development of OA can be delayed through intra-articular injection of MSCs isolated either from adipose tissue or from bone marrow and some clinical trials have shown decreases in inflammation and pain. In general, MSC related therapies for cartilage lesions and OA include tissue engineering of MSC transplantation, scaffold-free injection of stem cells and cell-free injection of exosomes into the injured joints. MSCs act through multiple pathways: (1) as “trophic” cells, secreting various factors that are immunomodulatory, anti-inflammatory, anti-apoptotic, proangiogenic, proliferative, and chemo attractive; (2) in conjunction with cells native to the tissue they reside in to enhance differentiation of surrounding cells to facilitate tissue regrowth. Moreover, exosomes are a kind of soluble biological mediator isolated from MSCs culture media in vitro. MSC-derived exosomes could protect cartilage and bone from degradation in OA. Furthermore, it has been exhibited that MSC-derived exosomes could attenuate OA by stimulation of chondrocyte migration and proliferation.

Conclusion: The stem cell-based strategies as a promising therapy will ultimately lead to the repair of injured or damaged joints. Among different types of therapies, MSC therapy for OA could be a safer, cheaper and a more efficient therapy modality that provide exciting and promising strategies for repairing bone, curtilage, tendon and other tissues.

Keywords: Stromal stem cells, Osteoarthritis, Orthopaedic diseases, Bone, Regeneration

Application of Nano-Drug Delivery System based on nanoparticles in enhancing cancer treatment: A review (Review)

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Introduction: Cancer has now become one of the most important causes of death in the world. In the last two decades, more attention has been paid to the replacement of more effective and specific treatments with low side effects and more anticancer activity. One of these purification methods is the use of nanoparticles. Nano-drug delivery systems (NDDS) are drug-loaded functional nano-carriers with a diameter of 10 x 1000 nm and composed of various natural or synthetic materials that are used for targeted delivery and controlled release of therapeutic agents. In this abstract, we provide an overview of the recent application of nano delivery systems in the treatment of cancer.

Methods: In this review, 10 articles were selected using keyword search (Nano-Drug, Cancer, Tumor, Therapeutic Agents, Delivery System, and Chemotherapy) in databases such as Scopus, PubMed, and Google Scholar after reviewing relevant findings and evaluating data quality. All studies were conducted from 2016 until 2022 in the field of nano delivery systems and cancer.

Results: The focus of this review is on providing chemotherapy drugs with higher therapeutic efficiency. One of the most promising methods to develop a type of NDDS for cancer therapy is layer-by-layer assembly of a multilayer film on nanoparticles followed by optional pattern removal. Adverse events were promising for BIND_014, and the selection of patients with PSMA-positive CTCs before treatment is a promising strategy for targeted therapy of PSMA, which could have a therapeutic and toxic advantage over docetaxel-based chemotherapy.

Conclusion: Based on the research, LbL assembly technology can not only achieve the formation of homogeneous nanoparticles but also produce other heterogeneous NDDS with different components and complex structures such as multilayers. In addition, the thickness, the surface charge, and the morphology of the multilayers can be well controlled by adjusting the assembly conditions. Since the use of nanoparticles in strengthening immunotherapy, radiation therapy, and chemotherapy has resulted in more anti-cancer effects and common side effects, and the possibility of multimodal treatment has been provided, research on this subject is progressing rapidly. It can be hoped that with future research and developments, this method will be used in medical centers and a big step will be taken to improve patients' health.

Keywords: Nano Delivery System, Cancer therapy, Chemotherapy, Nanoparticles

Application of stem cells in cardiovascular disorders (Review)

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Introduction: Introduction: One-third of all daily deaths are caused by cardiovascular disorders, making them one of the leading causes of death worldwide. One of the most recent and secure approaches to treating patients suffering from cardiovascular disorders such as ischemic heart and peripheral blood vessel disease is the use of stem cells.

Methods: Method: The current study is a descriptive-review analysis on the usefulness of stem cells derived from diverse sources in healing cardiovascular disorders. The selected papers have been published and are indexed in scientific databases such as PubMed, ISI, and Scopus. In this studied tried to properly explain the ability and mechanism of stem cells to increase or improve the healing process in cardiovascular disorders such as ischiatic condition.

Results: Result and discussions: Multipotent stem cells as well as precursors isolated from several tissues, including bone marrow, have been demonstrated to be able to restore the physiological activity of ischemic organs by enhancing their angiogenic potential. It has been demonstrated that stem cells can increase the blood flow to the ischemic area of the heart and speed up the repair process of the damaged areas through secretory (paracrine) mechanisms and differentiation into the endothelial cell line.

Additionally, mesenchymal stem cells (MSCs) have been successfully used to treat patients who have had heart attacks and strokes. Recently, it has been reported that the injection of MSCs can restore heart function by secreting paracrine substances, despite the fact that they are essentially distinct from cardiac cells like cardiac muscle cells. Additionally, it has been discovered that MSCs release all paracrine substances in membrane vesicles known as exosomes, which exist in blood, urine, saliva, semen, serum, etc. They are also involved in various pathological processes such as cardiovascular, etc.

Conclusion: Conclusion: Stem cells induce proliferation in the surviving heart tissue and result in rebuilding and improving the damaged heart's tissue. Therefore, this novel treatment approaches can be recommended as an alternative of invasive surgical procedure for patients suffering from cardiovascular and heart failure.

Keywords: Keywords: Stem Cells, Cardiovascular, Heart Failure, Cardiac, Mesenchymal Stem Cells

Application of stem cells in the treatment of nervous system diseases (Review)

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Introduction: Introduction: Stem cells are a population of undifferentiated cells that have the ability of proliferation, self-renewal and differentiation into specialized cell types. There are many reports about the potential of these cells in treating nervous system disorders.

Methods: Methods: The current study, which was carried out by exploring reputable medical databases, is a descriptive review of the potential benefits of stem cells in the treatment of nervous system illnesses.

Results: Results: Parkinson's, MS, Alzheimer's, stroke, brain and spinal cord injuries, amyotrophic lateral sclerosis, SMA, and cerebral palsy are a few of the neurological conditions that have been treated by cell therapy. For instance, stem cell transplantation may result in the production of chemicals that promote the survival or recovery of damaged nerve cells and lower inflammation in MS disease. Mesenchymal cells can be injected intravenously to travel within brain lesions and increase the survival rate of brain cells. Additionally, the injection of mesenchymal cells lessens the disease's severity and enhances the quality of life for MS patients. The researchers discovered that adult adipose tissue stem cells are among the best cells for treating MS because they improve sexual dysfunction and social interactions. Recent studies have shown that hematopoietic stem cell transplantation can stop the

progression of MS disease in 70% to 80% of individuals for 4 to 5 years. Dopaminergic progenitor cells, which are produced from fetal cells and can serve as a renewable resource with high capacity, are also found in Parkinson's disease. And this approach is being studied. In the past 20 years, there has also been a surge in interest in using cell replacement therapy to treat neurodegenerative illnesses like Huntington's. The idea of treating spinal cord injuries with stem cells produced from human umbilical tissue and cells derived from bone marrow has been supported by a number of peer-reviewed articles and case reports. The potential for combined allogeneic stem cell therapy for spinal cord injury: By giving spinal cord injury patients treated at our centers stem cells Mesenchymal generated from umbilical cord tissue, we have witnessed benefits. Stem cells can help with all of these issues in cases of really complicated spinal injury. They are able to regenerate an environment, repair dead tissue, and produce new nerve cells.

Conclusion: Conclusion: Neurological problems can be treated with cell therapy, which is an intriguing and successful technique. Up till now, mesenchymal stem cells, neural stem cells, embryonic stem cells, and other cells have all been utilized to treat neurological diseases under in vitro condition and may soon represent a novel therapeutic approach for the management of neurological disorders.

Keywords: Keywords: Stem Cell, Nervous system disorders, Parkinson, Alzheimer

Aptamer-based Diagnostics for Cardiac Troponin (Review)

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Introduction: One of the leading causes of mortality worldwide is myocardial infarction (MI) which occurs due to a decrease in the blood supply to the heart, causing the expiration of myocardial tissue. The diagnosis of MI relies on the detecting of some cardiac protein biomarkers. A possible biomarker for the early detection of acute myocardial infarction (AMI) is cardiac troponin I (cTnI). Aptamers are well-known receptors that contain specific nucleotide sequences and have a high affinity for binding to a particular cell of interest. The employment of aptamers as a means for detecting cardiac markers, such as troponin, can be considered as an alternative to conventional techniques like liquid chromatography, chemiluminescence, and enzyme-linked immunosorbent assay (ELISA). This brief review aims to look at aptamer-based cardiac troponin assays.

Methods: In the present review, we collected and analyzed articles found on the PubMed and Google Scholar databases using the Aptamer, Cardiac Troponin I, Myocardial Infarction, and Bioreceptors keywords.

Results: The results from various studies revealed that aptamer-based approaches to detecting cTnI are aptamer-based surface-enhanced resonance Raman spectroscopy (SERRS) and electrochemical aptamer-based biosensors. Aptasensor could be proper alternatives to conventional methods, though it was only recently that they were able to attract the attention of medical and diagnostic researchers. Furthermore, recent efforts in the field of aptamers have led to the development and expansion of aptamer-based diagnostic methods for cardiac biomarkers.

Conclusion: A critical challenge in controlling the high rates of MIs on a global scale is to find a quick way to predict the risk of heart attacks. Furthermore, conventional methods are extremely costly and do not exhibit a high detection speed and are extremely costly. On the other hand, aptamer-

based methods are suitable alternatives due to their low cost, rapid detection, and high specificity in cTnI diagnosis. According to the results of this review, it seems that aptamers will likely to replace antibodies in the point-of-care system shortly.

Keywords: Aptamer, Bioreceptors, Cardiac Troponin I, Myocardial Infarction.

Aptamer-based Lateral Flow Assays (Review)

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Introduction: The use of point-of-care devices has been extensively promoted in the past few decades. One of its common types is lateral flow assays (LFA), a portable, simple, and low-cost method that can be an appropriate candidate for diagnostic testing. This method is generally employed in food, agriculture, and biomedicine. Furthermore, numerous studies have been done on aptamers and their applications. Aptamers are short single-stranded oligonucleotide sequences with a 3D conformational structure to bind to the designated targets, and due to their low production cost and acceptable stability, they could be a proper alternative to antibodies. Therefore, combining the potential of aptamer and LFA can create a suitable platform for developing point-of-care devices. Compared with antibodies, aptamer-based LFAs have been less frequently used in a commercial setting. This review discusses aptamer-based LFA, its applications, advantages and, drawbacks.

Methods: According to the results of the search in the PubMed and Google Scholar databases, aptamer-based LFA, and more specifically, its advantages, disadvantages, and the necessary steps for its commercialization, have been discussed in some papers.

Results: Aptamers can be a suitable alternative to antibodies due to their low production cost and high stability. This method is used to rapidly detect antibodies, β-conglutin, hormones such as salivary cortisol, etc. However, one of the disadvantages of utilizing aptamers is that their affinity can be reduced by changing environmental variables such as pH.

Conclusion: The combination of aptamer potential with point-of-care approaches such as LFA has significantly contributed to advancements in

diagnostic procedures. The presence of different targets, ease of application, and quick response have drawn attention to the use of this method. Numerous improvements have been made in aptamer-based LFAs during the past few years, but unfortunately, none have made this method commercially applicable. One possible way to commercialize this technique is to use it in line with the diagnostic tests of Covid-19. It can be expected that aptamers in LFA will increase compared with antibodies.

Keywords: Aptamer, Aptamer-based LFA, Antibody, Lateral flow assays, Point-of-care.

Aptamer-based Technologies for Biomarker Discovery (Review)

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Introduction: Exploration and determination of human disease biomarkers lead to early detection, accurate therapy, prognosis, and response to treatment.

Methods: Efficient and sensitive methods revealing clinical biomarkers are limited due to various technical problems facing the current technologies.

Results: Aptamers are single-stranded oligonucleotides that can selectively and specifically bind to a wide range of targets with high affinity. Besides, compared to their counterparts, aptamers have advantages, including ease of synthesis, flexible chemical modification, stability in various conditions, and low immunogenicity. Recently, aptamer-based strategies, such as Cell-SELEX and SOMAScan technology, have revolutionized biomarker discovery. Through Cell-SELEX, scientists can use various nucleic acid aptamers to identify cell surface biomarkers of multiple cells. With SOMAScan technology, thousands of proteins of diverse biological specimens can be analyzed to become a multiplexed proteomics platform for biomarker discovery.

Conclusion: A brief review will be presented to introduce technologies based on aptamers in the field of biomarker discovery.

Keywords: Nucleic acid Aptamer, SAMAScan, Cell-SELEX, Biomarker, Cancer, Diagnosis

Aptamers: potential future targets to control drug-resistant bacteria (Review)

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Introduction: Antibiotics have been very effective in controlling pathogens, and resistance mechanisms developed in bacteria, but due to the increasing gap between the therapeutic effects of antibiotics and drug resistance, finding new antimicrobial agents are needed, which can be overcome by aptamer-based antimicrobials. Aptamers can interfere with the pathogen's biochemical pathways and interfere with the pathogen's conjugation process to prevent infection and reduce the pathogenicity of bacteria. In order for aptamers to interfere with the biochemical processes of a pathogen, they must be selected as receptor protein antagonists, as they must inhibit the pathogen's ability to infect.

Methods: Articles from 2005-2022 were reviewed in Google Scholar, PubMed, and Scopus databases with the keywords aptamer, aptasensor, and microbial drug resistance. And extracting information from basic studies.

Results: A study was conducted to inhibit PPK2 based on aptamer. Inorganic polyphosphate (polyP) is responsible for roles in bacterial virulence and stress resistance and is regulated by PPK protein families. PPK2 was characterized and used to develop DNA-based aptamers that inhibit the enzyme's catalytic activity. The selected aptamer showed strong selectivity for binding with PPK2 and inhibited it after binding. In another study, an RNA aptamer was chosen to bind to bacterial type IVB pili. This aptamer binding was able to inhibit the entry of pili-containing strains of pathogenic bacteria into human monocytic leukemia cells. Several DNA aptamers were developed to target and control infections caused by E. coli via lipopolysaccharide (LPS) or whole-cell O157:H7 as targets. who developed an aptamer-based colorimetric detection method for O157:H7 using truncated DNA aptamers against LPS, with a detection limit of 10,000 CFU/mL. Furthermore, in a similar study, DNA aptamer on a hydrothermally grown ZnO nanowire array was used to construct a high-performance photoelectrochemical aptasensor for the

detection of O157:H7, with a detection limit of 1.125 CFU/mL. A DNA aptamer targeting the outer membrane proteins of S. enterica serotype Typhimurium was selected and an aptamer-based trapping PCR detection method with a detection limit of 1 CFU/mL was developed using it. This aptamer was widely used in various detection methods based on different aptasensor technologies, with detection limits ranging from 1 to 1000 CFU/mL.

Conclusion: This review states that aptamers can be generated against whole pathogens, pathogen components, pathogen or disease markers, microbial toxins, or pathogen-infected host cells for pathogen detection or disease diagnosis. These aptamers can then be combined with different platforms to optimize detection speed, convenience, cost-effectiveness, and simplicity. For therapeutic purposes, aptamers can be directed against (1) surface components of pathogens or host cell receptors to prevent host cell entry or drug delivery, (2) essential proteins and enzymes to prevent pathogen propagation, and (3) chose microbial toxins to relieve the symptoms.

Keywords: Aptamer, Aptsensor, Microbial drug resistance

Aquaporin-8 lowexpressed as a strong possible contributer to development of Colon adenocarcinoma (Research Paper)

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Introduction: Colon adenocarcinoma (COAD) is a type of common malignant tumor originating in the digestive tract. This research aimed to find a significant expressed gene Aquaporin-8 in the COAD patients compared to control samples. AQP8 transport water into and out of cells according to the osmotic gradient across the membrane.

Methods: At the outset gene Expression data analysis of GSE100179 achived from the NCBI Gene Expression Omnibus(GEO) () then to find validation of expression analyses and reinforce the percent of survival between the cancer patients and control samples performed by GEPIA2() database. Single nucleotide polymorphism (SNPs) of AQP8 extracted from dbSNP software () and for finding deleterious SNPs used SIFT Database(),UniProt () and MIRNASNP(). For perceiving of Biophysical variation of deleterious SNPs used HOPE data base (). Through ENRICHR, KEGG, REACTOM gene ontology information, Molecular function involvement and located of Biological pathway were figured out. In addition miRWalk and String databases were used to detecting significant Protein and miRNA interactions with AQP8 in 3'UTR position. Then the chosen miRNA was investigated in LncRRIsearch and LncBase to find significant and strong interactions with LncRNAs and construct a predictive ceRNA network.

Results: based on microarrey analysis,AQP8 have a significant up_regulation compared to control groups in the COAD samples((|logFC| =-5.07744 , adj. P value = 2.96E-10). Result of miRNAWALK displayed possible miRNA-mRNA interactions (hsa-miR-330-5p) as a significant interactor to AQP8 mRNA . Sellected miRNA was searched in LNCRRIsearch and LncBase v-2 () and LINC00940 ,RMDN2-AS1 had the strongest interactions.

Conclusion: Based on the above analysis of several databases, we identify AQP8 is lowexpressed in COAD and make a possible ceRNA network among hsa-miR-330-5p, LINC00940 ,RMDN2-AS1.

Keywords: Colon adenocarcinoma , Aquaporin-8 ,Cancer ,Database , cRNA

Arrayed Hollow Channels for Enhanced Oxygen Transport in Three Dimensional-porous Silk Scaffolds Stimulate Osteogenic Activity of Pre-osteoblasts for Bone Tissue Engineering (Research Paper)

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Introduction: Cell-seeded scaffolds play a key role in bone tissue formation during bone regeneration. Silk fibroin is a promising natural biopolymer to promote effective bone regeneration, because of its versatile processability, controlled degradability, biocompatibility, hydrophilicity, and compression resistance, as well as its ability to stimulate cell adhesion, proliferation, and differentiation. A major obstacle for clinical application of 3D-porous silk fibroin scaffolds for bone regeneration is a high death rate of cells throughout the scaffold under low oxygen condition. Cell growth and distribution can be accelerated inside a 3D-prous silk fibroin scaffold by using hollow channels, since these channels promote oxygen and nutrient delivery to the central zone of the scaffold. More detailed knowledge of oxygen diffusion, as well as cell proliferation and distribution inside channeled 3D-porous scaffolds is still needed to further promote bone cell behavior inside 3D-porous scaffolds. Therefore, in this study we aimed to investigate whether arrayed hollow channels would further improve oxygen diffusion and enhance cell behavior, i.e. pre-osteoblast viability, proliferation, penetration depth, differentiation, and mineralization inside 3D-porous silk fibroin scaffolds by using finite element (FE) modeling and experiments.

Methods: Scaffold fabrication: 3D-porous silk fibroin scaffolds without and with channels of 0.5 or 1 mm diameter were fabricated (scaffold diameter: 2

cm; scaffold height: 1 cm; channel number: 12; channel diameter: 0.5, and 1 mm). Scaffold characterization: Physicomechanical properties of 3D-porous silk fibroin scaffolds, i.e. pore structure (scanning electron microscopy (SEM)), pore size distribution (image J software), and water uptake, as well as mechanical properties, i.e. compression modulus, and ultimate compression strength (universal compression testing machine) were determined. Finite element (FE) modeling: FE modeling was used to quantify the oxygen and cell density distribution inside 3D-porous silk fibroin scaffolds without or with channels of 0.5 and 1 mm diameter during 14 days. Cell culture and scaffold bioactivity: MC3T3-E1 pre-osteoblasts were seeded at 5x105 cells/cm3 on 3D-porous silk fibroin scaffolds, and cultured up to 21 days. Oxygen distribution (Oxygen Sensor Microx TX3 PreScens), as well as pre-osteoblast spreading (SEM), proliferation (AlamarBlue® fluorescent assay), and expression of proliferation and osteogenic genes (RT-PCR) were determined. Statistical analysis: Data are mean±SD from at least 3 independent, separate experiments. Differences were tested with two-way ANOVA combined with Tukey's multiple comparison test using GraphPad Prism® 8.0, and considered significant if p<0.05.

Results: FE modeling: FE modeling revealed a significantly more uniform and homogeneous oxygen concentration, as well as higher cell proliferation inside 1 mm channeled 3D-porous scaffolds than inside non-channeled and 0.5 mm channeled scaffolds. Physicomechanical properties: Experimental results indicated that the scaffold contained a network of interconnected pores with a diameter ranging from 50 to 200 µm, with an average pore diameter of 66.6 ± 24.9 µm (mean ± SD). Normalized water uptake during 2 h was higher inside 1 mm channeled scaffold than in non-channeled and 0.5 mm channeled scaffolds. Compressive modulus was not significantly different between the non-channeled, 0.5 and 1 mm channeled scaffolds. Oxygen transport: the oxygen concentration significantly increased inside 0.5 mm and 1 mm channeled scaffolds (2.3-2.4-fold) compared to non-channeled scaffolds at day 9. Cell proliferation: the cell number was higher inside 0.5 mm and 1 mm channeled scaffolds (1.1-1.3-fold) compared to non-channeled scaffolds at day 14. Gene expression: Expression levels of proliferation marker gene Ki67, and osteogenesis-related genes Runx2, Ocn, Fgf2, Dmp1, and Mepe were assessed after 4, 7, 14, and 21 days. Fgf2 expression was significantly enhanced inside 0.5 mm and 1 mmm channeled scaffolds after 4 days, while decreased after 21 days. Ki67 and Runx2 expression was significantly enhanced inside 0.5 mm channeled scaffolds after 7 days. Moreover, Ocn expression was significantly enhanced inside 0.5 mm channeled scaffolds after 21 days. In addition, Mepe expression was significantly decreased inside 0.5 mm and 1 mm channeled scaffolds after 14 days.

Conclusion: In conclusion, arrayed hollow channels inside 3D-silk fibroin scaffolds successfully improved oxygen transport, cell viability, spreading, and

proliferation, as well as osteogenic activity of the scaffolds. The mechanical properties of the channeled scaffolds were not significantly different from non-channeled scaffolds. These results are promising to further develop innovative 3D scaffolds containing arrayed hollow channels for bone tissue engineering.

Keywords: Bone tissue engineering Channeled 3D-silk scaffold FE modeling Oxygen delivery Pre-osteoblast

Assay the expression of recombinant human PD-1 mRNA in transfected cancer cells (Research Paper)

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Introduction: Programmed cell death protein-1 (PD-1)/PD-L1 pathway is one of the immune checkpoint pathways involved in the regulation of the immune responses and the suppression of anti-tumor defense. Soluble PD-1 improves immune responses and increase mortality of tumor cells as well; the aim of this study was to produce the soluble recombinant human PD-1 construct and also assess the expression of recombinant PD-1 mRNA in the transfected cells.

Methods: We designed and produced soluble recombinant human PD-1-GFP-pcDNA3.1/hygro construct. This construct could be expressed in the hypoxia condition due to its VEGFa promoter. We transfected this construct into the MDA-MB-231 cells. After that, we lysed the transfected cells and extracted shPD-1 mRNA. cDNA was synthesized by use of Oligo dt and random hexamers primers. Quantitative real time PCR was performed for determination of the amount of recombinant human PD-1 by the fallowing primers; 5'AGCCACAACGTCTATATCATG3' as the forward primer and 5'AGGTAGTGGTTGTCGGGC3' as the revers primer.

Results: Real time PCR results showed the lower CT value for transfected cells, which indicate the high expression of recombinant human PD-1 mRNA in the transfected cells and no in the non-transfected cells.

Conclusion: shPD-1 gene expression in mRNA showed the susceptibility of PD-1-GFP-pcDNA3.1/hygro construct for expression in cancer cell lines. Therefore, this construct might be used for cancer research (such as some colorectal cancers) with high expression of PD-1-PDL1/2.

Keywords: Recombinant, PD-1, mRNA, Transfected, Cancer cell

ASSESSING THE EFFECT OF POLYURETHANE/MULTIWALL CARBON NANOTUBES SCAFFOLD ON HUMAN ENDOMETRIAL STEM CELLS ATTACHMENT AND VIABILITY (Research Paper)

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Introduction: Nanofibrous scaffolds have lately been employed as three-dimensional (3D) scaffolds for neural tissue engineering (NTE). Because of the electrical conductivity and physical similarity to the extracellular matrix, electrospun nanofibers incorporated with carbon nanotubes (CNTs) offer enormous potential for use in neural tissue regeneration. Our goal is to create 3D scaffolds employing conductive electrospun microfibrous substrates to provide an optimal microenvironment for improving cell viability and supporting cell engraftment in neural tissues.

Methods: Multiwall CNTs (MWCNTs) were incorporated into polyurethane, and electrospun fibers were produced. Approximately 5x104 human endometrial stem cells (hEnSCs) were cultivated on the scaffolds. Scanning electron microscope (SEM) was used to examine cell attachment, the diameter and microstructure of the nanofibers. DAPI labeling was also utilized to assess cell attachment and viability by staining the nuclei of hEnSCs.

Results: The SEM analysis results revealed that produced fibers were continuous, had no beads, and had a surface that was uniformly smooth. The average diameter of nanofibers was about 200nm. The mats had a porous and homogeneous fibrous architecture. Based on SEM and DAPI findings, it is possible to see the attachment and distribution of cultured cells on the scaffolds as well as the interactions between the cells and the scaffolds.

Conclusion: We produced and characterized polyurethane-MWCNTs scaffolds for NTE applications. Our results demonstrated that the created 3D nanofibrous scaffolds provide an adequate microenvironment for promoting cell adhesion and viability. The findings provided evidence of the potential for these types of scaffolds to be used in NTE.

Keywords: Polyurethane, Multiwall carbon nanotubes, Electrospinning, Nanofibrous scaffolds, Stem cells

Assessment of Staphylococcus epidermis antibiotics resistance (Review)

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Introduction: Staphylococcus epidermidis is the most important member of the group of coagulase-negative Staphylococci and the cause of 75% of infections in this group. This microorganism is part of the natural microflora of the skin and mucous membranes of the human body. One of the important factors in causing hospital infections in babies and people with fixed medical prostheses. The treatment of infections caused by this bacterium has become a challenge for the health system due to the increase in antibiotic resistance.

Methods: Some articles that investigated the antibiotic resistance of S.epidermidis were studied and this article was written.

Results: According to these articles, biofilm is the most important factor in bacterial pathogenicity. Most of the time, S.epidermidis shows resistance to many antibiotics such as penicillin, amoxicillin, methicillin, rifamycin, fluoroquinolones, gentamicin, tetracycline, clindamycin, and sulfonamides. Resistant organisms are commonly found in the gut.

Conclusion: It is concluded that the antibiogram method alone isn't suitable for the infection treatment caused by this microorganism, then choosing the best treatment method is very important.

Keywords: Infection, Staphylococcus epidermis, Antibiotic Resistance

Assessment of the relationship between CD34 and CD133 serum levels and nephropathy in patients with type 2 diabetes (Research Paper)

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Introduction: Diabetic nephropathy is one of the most common microvascular complications of diabetes mellitus. Diabetic nephropathy is a metabolic disorder caused by chronic hyperglycemia, which causes a wide range of dysfunction in kidney cells and ultimately leads to the complete loss of kidney function Purpose: The aim of this study was to investigate the relationship between serum levels of CD34 and CD133 as markers of endothelial cells and progenitors with the severity of nephropathy in type 2 diabetic patients.

Methods: This cross-sectional analytical study was performed on 37 patients with type 2 diabetes with nephropathy (DPN) and 30 patients with diabetes without nephropathy referred to Mashhad hospitals in 2020. Lipid profile, Creatinine, Uric acid, Insulin, Insulin resistance, Blood pressure registered and serum levels of CD34 and CD133 were assessed by ELISA method in all patients. Insulin resistance was measured using the HOMA-IR formula. The Cockcroft-Gault formula used to estimate Glomerular filtration rate (eGFR). The software used in this study is SPSS v.24, and the significance level of the tests is considered less than 5%.

Results: Thirty seven diabetic patients with nephropathy (Case group) with a mean age of 58/76 ± 11/72 years including 54/1% of women, and thirty patients with diabetes without nephropathy (Control group) with a mean age of 53/90 ± 10/38 years including 53/3% of women were studied. BMI, diastolic blood pressure, fasting blood sugar, HbA1C, LDL, creatinine, uric acid, insulin, eGFR, CD34 and CD133 in DPN patients were significantly different from the control group (P<0.05); While age, sex, systolic pressure, cholesterol, HDL, and triglyceride were not significantly different between the two groups (P>0.05). In the DPN group, CD34 has a significant direct relationship with CD133 (P<0.05). The severity of nephropathy was significantly associated with decreased levels of CD34 and CD133.

Conclusion: The results of this study show that DPN can directly reduce the CD34 and CD133 markers in the body and increase the rate of secondary complications in these patients, so these two markers can be used to control or even therapeutic purposes in DPN patients.

Keywords: Type 2 diabetes, diabetic nephropathy, CD34, CD133

Association between 15 insertion/deletion genetic polymorphisms and risk of schizophrenia using pooled samples (Research Paper)

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Introduction: Schizophrenia is a psychiatric syndrome that affects approximately 1% of the world population and is among the top 10 reasons for disability. Genome-wide association studies showed that multiple common variants, each with small effect, are associated with schizophrenia. More than 100 loci are significantly associated with schizophrenia. In this case-control study, we investigated the association between 15 insertion/deletion (Indel) polymorphisms in APOB, ADRA2B, PDCD6IP, LRPAP1, TLR2, DHFR, VEGF, HLA-G, TPA, DBH, UCP2, FADS2, MDM2, TP53, SLC6A4 genes and schizophrenia risk using pooled samples. DNA pooling is a well-established method for reducing the cost and effort of large-scale association studies. DNA pooling combines DNA from numerous persons into a single sample which can be genotyped just once, instead of genotyping every individual.

Methods: In the present case-control study, 361 individuals with schizophrenia and 360 healthy individuals were included in the study. Genomic DNA was extracted from blood samples by boiling method. Two pooled samples (healthy control and schizophrenia groups) were prepared by mixing of equal amounts of extracted genomic DNA. PCR was used to determine the allele frequency of each polymorphism. The band intensity, which has been measured with ImageJ software, has high level of accuracy as an indicator for determining the relative amounts of DNA.

Results: The results showed that the Del alleles of HLA-G 14bp Indel (OR=1.23, 95% CI=1.01-1.52, p=0.045) and the TPA 300bp Indel (OR=0.67, 95% CI=0.54-0.82, p<0.001) had a significant association with the risk of schizophrenia. However, significant differences were not observed in the other insertion/deletion polymorphisms studied in this research.

Conclusion: There is no study on TPA 300bp Indel polymorphism and risk of schizophrenia, but previous studies showed that abnormal function of TPA is related to the pathogenesis of schizophrenia and tPA actively participates in the mechanisms of neurogenesis and angiogenesis, which might justify not only the impaired neurogenesis but also the low prevalence of neoplastic diseases among schizophrenics. The present study shows that the insertion allele is associated with an increased risk of schizophrenia. HLA-G 14bp Indel is associated with HLA-G expression and function. This genetic variant also

influences brain morphometric measures and HLA-G could be an important biomarker for schizophrenia. Further, low levels of sHLA-G were shown to have a significant impact on Clinical Global Impression (CGI) severity in people with schizophrenia. Our study demonstrates that the deletion allele is associated with an increased risk of schizophrenia. Future case-control genetic association studies are needed to conclude that these polymorphisms are risk factors for schizophrenia.

Keywords: Insertion/deletion polymorphisms, Schizophrenia, Pooled samples, personalized medicine

Association between Mir32 rs7041716 Polymorphism and Breast Cancer in Iranian Women (Research Paper)

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Introduction: About 5–10% of breast cancers (BC) are considered hereditary, from which the known BC genes account for 3–4%. Since mutations that are known to increase breast cancer risk within families are quite rare, identification of polymorphisms related to the disease is very important. Among the different biomarkers, polymorphism in Mir genes has attracted a lot of attention. In present study, association between Mir32 rs7041716 polymorphism and BC was examined in Iranian women population.

Methods: At first, sampling was done from 100 women with BC and 105 normal women. Then DNA was isolated from the samples. The quality and quantity of extracted DNA was determined using electrophoresis on agarose gel and nanodrop device. Finally, by using specific primers and tetra-primer ARMS PCR method, the rs7041716 (A > C) was investigated.

Results: The results of electrophoresis on agarose gel and nanodrop device showed that the isolated DNA has good quality and quantity. Statistical analysis revealed that the frequency of C allele and CC genotype in women with BC is higher than normal women. In addition, odd ratio analysis revealed that the C allele in the heterozygote genotype may increase the risk of BC as 2.9-fold.

Conclusion: According to the obtained results, the Mir32 Rs7041716 polymorphism can be used as a genetic marker in the diagnosis of BC.

Keywords: Breast cancer, MIR32, Tetra-arms PCR, rs7041716.

Association Between Periodontitis and Risk of Alzheimer's Disease: A Systematic Review of Current Evidence (Review)

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Introduction: Alzheimer's disease (AD) is the most frequent cause of dementia in older adults and a major global health issue for geriatric patients, leading to progressive cognitive impairment and behavioral problems. Periodontitis is a common oral infection considered a “low-grade systemic disease” causing the secretion of proinflammatory cytokines and elevation of C-reactive protein (CRP). The aim of the current review is to investigate the pathophysiology and possible association between periodontitis and AD according to released evidence.

Methods: The data were collected using literature retrieved using relevant keywords and MeSH terms in MEDLINE, PMC, Scopus, Google Scholar, and ProQuest. After full-text screening and quality assessment, a total of 17 articles were included in the final report.

Results: Alzheimer's disease is a complex neurodegenerative disorder associated with aging with several etiologies for its onset and progression. The development of extracellular amyloid plaques and intraneuronal neurofibrillary tangles is this disorder's most notable identifying feature (NFTs). Tau, a protein connected to microtubules, is found in hyperphosphorylated forms in NFTs. Reactive astrocytes and activated microglial cells are closely related to A-P plaques. The formation of A-P in the cerebral microvasculature is a result of inflammation. Pro-inflammatory cytokines, reactive oxygen and nitrogen species, and nitrogen may all contribute to neuroinflammation. These elements play a crucial role in the activation of microglia and the promotion of NFT formation. Spirochete plaques or masses resemble senile AD plaques in the brain. The tissue-invasive periodontal pathogens that cause periodontitis include Aa, Pg, Pi, Tf, and Fn. Spirochetes were found in 93.7 percent of AD cases and 33.3 percent of controls.

Conclusion: AD and periodontitis exhibit the same chronicity-related characteristics, with inflammation as their common denominator. Periodontitis has risk factors in common with disorders linked to cognitive impairment. The methodical management of geriatric patients requires constant coordination between the dentist and the neurosurgeon

Keywords: Alzheimer's Disease; Periodontitis; Oral health; Systemic Disease; Systematic Review

Association between polymorphism and ceRNA network of differential expressed gene in resistance and sensitive non-small-cell lung cancer to radiotherapy (Research Paper)

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Introduction: Lung cancer has been counted as one of the most malignant tumors which people in both poor and well-developed countries may face it. Nowadays, radiotherapy is one of the main arms of oncology in the post-surgical process of lung cancer patients. Radioresistancy, an important limiting factor, decreases the efficacy of radiotherapy for lung cancer patients. References determine the microRNAs (miRNAs) as important regulatory agents which can participate in radiation responses such as radioresistance or radiosensitization. On the other hand, studies have shown that resistance or sensitivity of the patients to the treatment can be related to single nucleotide polymorphisms (SNPs). Thus, the aim of this study is to investigate the effect of the two regulatory factors, miRNA and SNP, in the CPS1, which, based on our bioinformatic approaches, plays a role in the radioresistance in lung cancer.

Methods: Gene expression data of lung cancer cell lines were obtained from the National Center for Biotechnology Information (NCBI), Gene Expression Omnibus (GEO), and then analyzed by GEO2R to find differentially expressed genes (DEGs). Furthermore, miRWalk was utilized to find significant miRNA-mRNA interactions in the coding sequence (CDS) region. Additionally, the selected miRNA was searched in LncBase v.3 to find strong interaction with lncRNAs and construct a predictive competing endogenous RNA (ceRNA) network. The Pathway enrichment analysis was carried out using the hub for long non-coding RNAs (lncHUB) and Kyoto Encyclopedia of Genes and Genomes (Kegg) online databases. SNPs of carbamoyl-phosphate synthase 1 (CPS1) were extracted from the Database of Single Nucleotide Polymorphisms (dbSNP), and identification of deleterious SNPs brought out from the Sorting Intolerant From Tolerant (SIFT) database. Biophysical validation of deleterious SNPs was realized from HOPE software. CrisPam was used to identify the suitable clustered regularly interspaced short palindromic repeats (CRISPR) system to target the SNP.

Results: Based on microarray analysis, CPS1 has a significant down-regulation in the radioresistance of non-small-cell lung cancer (NSCLC) cell

lines samples compared to radiosensitive NSCLC samples (log fold change; logFC: -7.65, adjp-value < 1.54E-15). Analysis of possible miRNA-mRNA interactions revealed hsa-miR-27b-5p as a significant interactor to CPS1 mRNA. This miRNA was then searched in LncBase v.3 (marrow), showing that CPS1 Intronic Transcript 1 (CPS1-IT1) had the strongest interactions. Kegg reveals that CPS1 has an effect on nitrogen metabolism, arginine biosynthesis, alanine, aspartate, and glutamate metabolism; by using LncHUB, we found that CPS1 and CPS1-IT1 affect arginine biosynthesis. From all of the extracted SNPs on the coding region, SIFT online software revealed that rs28940283 is the most significant deleterious SNP in the protein-coding region CPS1. Based on the biophysical validation of HOPE, the mutated residue is located in a domain crucial for the protein's functionality and in contact with another domain that is also essential for the activity. The mutation can disturb the interaction of these domains, which might affect the protein's function. CrisPam suggests xCas9 and Streptococcus pyogenes Cas9 (SpCas9)-NG to target the SNP rs28940283.

Conclusion: In conclusion, we noticed that radioresistancy in NSCLC is associated with regulatory agents such as miRNA and SNP. rs28940283 can promote resistance in lung cancer cells by changing the correct folding and protein interactions of CPS1 and the misregulation of glutamine amidotransferase type-1 activity which can cause a reduction in the CSP1's function. Moreover, an interaction with hsa-miR-27b-5p forms a possible ceRNA network that can lead to the downregulation of the CPS1.

Keywords: Cancer; SNP; ceRNA; Radiotherapy.

Association of maternal vitamin D deficiency and increased autism risk: a review of literature (Review)

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Introduction: Autism is a complex neurobehavioral condition that affects communication through social interactions impairments. Vitamin D deficiency is a worldwide problem and Low vitamin D has been hypothesized as an environmental risk factor for Autism. According to high incidence of vitamin D deficiency and inadequacy during pregnancy that even reached up to 96 to 99.4 percent, and also the role of maternal vitamin D in brain development, cognitive function, and psychological function and its association with improved mental and psychomotor development, our study is to clarify if there is a relationship between maternal vitamin D deficiency and increased autism risk.

Methods: A literature search was conducted in electronic databases and we queried PubMed, Google Scholar, and Science Direct databases. The search strategy used the terms: autism, autism spectrum disorder, maternal, gestational, prenatal vitamin D deficiency, vitamin D adequacy during pregnancy. No restrictions were considered.8 studies were included in this review.

Results: studies showed that Mothers in autistic group had significantly lower maternal serum levels of the vitamin D, so there is an association between increased offspring risk of autism and low vitamin D serum levels, even a study shows more than the twofold increased risk compared with the sufficient group.

Conclusion: vitamin D substitution during pregnancy with safe, cheap and accessible supplementation may present an opportunity for prenatal intervention to prevent and reduce the risk of autism.

Keywords: Autism spectrum disorder, Autism, Vitamin D, pregnancy

Association of the SOD2 rs2758339 (A/C substitution) Polymorphism with the risk of breast cancer in Iranian women (Research Paper)

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Introduction: Breast cancer is the most common cancer among women affecting up to one third of them during their lifespans. Genetic polymorphisms can change the risk of breast cancer due to changes in gene expression or protein structure. It has been suggested that oxidative stress plays an important role in breast cancer carcinogenesis. Manganese superoxide dismutase (MnSOD/SOD2) is one of the major antioxidant enzymes that is responsible for the detoxification of reactive oxygen species in the mitochondria and plays a key role in maintaining the balance of free radicals in the human body. Several single nucleotide polymorphisms have been well defined in the gene encoding SOD2, including the potentially functional polymorphism of rs2758339. The aim of the present study is to investigate the association between rs2758339 (A/C substitution) polymorphism and the risk of breast cancer among Iranian women.

Methods: This study included 100 breast cancer patients and 100 healthy individuals as a control group. Genotyping of rs2758339 was done by polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) methods. Values are presented as mean ± SD for age, weight, height and BMI, and as % for other variables. P values (P < 0.05) were calculated using t-test for continuous variables and Chi-square test for categorical variables.

Results: Breast cancer patients and the control group were compared for the C allele (OR 1.130, 95% CI 0.760 - 1.681; P=0.543) of the rs2758339. Statistical analysis showed that there was no significant association between rs2842980 (A/C substitution) polymorphism and the risk of breast cancer.

Conclusion: The present data revealed that the rs2758339 polymorphism of SOD2 is not risk factor for breast cancer.

Keywords: breast cancer, SOD2, rs2758339, PCR-RFLP

Association of the SOD2 rs5746136 (T/C substitution) Polymorphism with the risk of breast cancer in Iranian women (Research Paper)

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Introduction: Breast cancer is the most common cancer among women affecting up to one third of them during their lifespans. Genetic polymorphisms can change the risk of breast cancer due to changes in gene expression or protein structure. It has been suggested that oxidative stress plays an important role in breast cancer carcinogenesis. Manganese superoxide dismutase (MnSOD/SOD2) is one of the major antioxidant enzymes that is responsible for the detoxification of reactive oxygen species in the mitochondria and plays a key role in maintaining the balance of free radicals in the human body. Several single nucleotide polymorphisms have been well defined in the gene encoding SOD2, including the potentially functional polymorphism of rs5746136. The aim of the present study is to investigate the association between rs5746136 (T/C substitution) polymorphism and the risk of breast cancer among Iranian women.

Methods: This study included 100 breast cancer patients and 100 healthy individuals as a control group. Genotyping of rs5746136 was done by polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) methods. Values are presented as mean ± SD for age, weight, height and BMI, and as % for other variables. P values (P < 0.05) were calculated using t-test for continuous variables and Chi-square test for categorical variables.

Results: Breast cancer patients and the control group were compared for the T allele (OR 1.956, 95% CI 1.312 - 2.916; P=0.0009) of the rs5746136. The CT (OR 0.218, 95% CI 0.099 - 0.478; P=0.0001) and TT (OR 0.158, 95% CI 0.055 - 0.451; P=0.0003) genotypes of the rs5746136 showed significant differences between breast cancer patients and controls compared to CC genotype.

Conclusion: It is indicated based on our data that the risk of breast cancer decreased with “CT” and “TT” genotypes of the rs5746136 variant compared with the controls in Iranian women.

Keywords: breast cancer, SOD2, rs5746136, PCR-RFLP

Associations between air pollution exposure and pregnancy outcomes following In Vitro Fertilization: a review of literature (Review)

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Introduction: Nowadays air pollution is a global health concern. According to World Health Organization (WHO), almost 99 percent of the global population breathes air that contains a high level of pollutants. Among its multiple adverse impacts reported on human health, we can mention adverse effects on reproductive health and fertility. fifteen percent of reproductive-aged couples are affected by infertility. increasing the number of families with fertility problems, results in more requests for the use of assisted reproduction techniques (ARTs). In vitro fertilization (IVF) is a common form of ART involving the manipulation of oocytes outside the body. In this procedure, the egg is removed from the ovaries and fertilized with sperm in a laboratory, and then returned to the woman's uterine to develop as the embryo. Considering IVF and embryo transfer (ET) have risks and side effects, the success rate, and the pregnancy outcomes are important. Associations between air pollution with various pollutants and adverse pregnancy outcomes have been described by several authors. To summarize the evidence, we will review the association between exposure to air pollutants and pregnancy outcomes following IVF in this article.

Methods: A literature search was conducted in electronic databases, and we queried PubMed, Google Scholar, and Science Direct database to identify all relevant studies published before August 2022. Combinations of terms and descriptors related to air pollution, fertility, and In Vitro Fertilization (IVF) technique and MESH search terms were used: air quality, air pollution, air pollutants, in vitro fertilization, fresh embryo transfer and frozen-thawed embryo transfer, pregnancy outcomes, pregnancy rate, live birth. No time or language restrictions were adopted, and queries were limited to human studies. 27 cohort studies were included in this review.

Results: pollutants included in these studies were: particulate matter (PM), nitrogen dioxide (NO2), carbon monoxide (CO), sulfur dioxide (SO2), and ozone (O3). pollutant exposures were studied in different periods of IVF including before oocyte retrieval, the time between oocyte retrieval and embryo transfer, and after embryo transfer. The results showed that air pollutants can significantly affect the IVF pregnancy outcome. For all exposure periods, O3 was positively associated with implantation and live birth. Exposure to PM2.5 and PM10 before oocyte retrieval has an adverse effect on IVF outcomes and showed positive associations with biochemical

pregnancy loss. IVF success rates were highest when PM concentrations were lowest and PM10 and CO levels were also inversely associated with intrauterine pregnancy. Likewise, Increased NO2 and SO2 were associated with a lower pregnancy rate and decreased probability of intrauterine pregnancy, however, there was a controversy about whether NO2 significantly modifies reproductive success.

Conclusion: metabolites and biologic pathways involved in inflammation and oxidative stress, associated with high exposure to air pollutants, may mediate the lower probability of live birth and increase adverse pregnancy outcomes following ART. Thus, to improve IVF successful outcomes, exposure to air pollutants should be limited, and prospective cohort studies are warranted to investigate the underlying mechanisms accounting for this association.

Keywords: air pollution, air pollutants, in vitro fertilization, IVF, pregnancy outcomes

AtefeYadollahy khales (Review)

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Introduction: The Newborn Metabolic Screen is a special test used to test baby for certain serious medical conditions. The goal of the screen is to identify babies who have these disorders before they ever get sick, and to help them get treatment as soon as possible. Liquid chromatography-tandem mass spectrometry (LC–MS/MS) has greatly increased the screening possibilities by monitoring levels of amino acids and acylcarnitines. Measuring different amino acids and acylcarnitines can be used to detect up to 45 different inherited disorders depending on how diseases are counted

Methods: The Newborn Metabolic Screen is performed by pricking your baby's heel and putting a few drops of blood onto special filter paper. The filter paper is allowed to dry and is then sent to the State Health Department. The blood is analyzed by the lab to identify babies who are at higher risk to have a medical condition. If the screen indicates the baby might have a medical problem, a member of the newborn screening follow-up unit will call baby's doctor with the results. If we cannot identify the baby's doctor, we may call parents directly to get this information

Results: Newborn screening with LC–MS/MS , now allows physicians to diagnose a disease even before a single clinical symptom is noted, allowing for better treatment planning and better outcomes.

Conclusion: Newborn screening has been considerably changed and expanded by the availability of LC–MS/MS technology. As new methods have been developed new challenges have been revealed, regarding which diseases to screen for, how to confirm diagnoses quickly and accurately and how to follow up on patients identified through the program.

Keywords: Newborn screening, screening, Metabolic, Liquid chromatography

Bacteria and Cancer (Review)

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Introduction: Genetic, environmental and dietary factors have often been studied to induce cancer, and the effect of bacteria on cancer has been less studied. In the past, bacteria were not thought to cause cancer. William Russell first reported the effect of bacterial infection on carcinogenesis in 1890. In 1926, Thomas Glover was able to isolate bacteria from pleomorphic organism and help treat cancer patients with antibacterial serum. Other scientists, such as William Coley, Gunther Enderlein, Josef Issels, Royal Rife, Florence and Seibert continued their research. Bacteria cause cancer by two mechanisms, including chronic inflammation and the production of carcinogenic bacterial metabolites. Helicobacter pylori causes gastrointestinal cancer by causing chronic inflammation in the stomach. Inflammation caused by H. pylori induces cell proliferation and also produces mutant free radicals that cause cancer. H. pylori has been identified as the first cancer bacteria by the International Agency for Research on Cancer. H. pylori, Salmonella typhi, Streptococcus bovis and Chlamydia pneumoniae cause gastric, gallbladder, colorectal and lung cancers by different mechanisms. Salmonella typhi causes gallbladder cancer by producing typhoid toxin and damage to DNA and changes in the cell cycle. Porphyromonas gingivalis, Fusobacterium nucleatum, Treponema denticola and Streptococcus anginosus cause oral cancer by causing chronic inflammation, increased cell proliferation, suppression of the immune system and production of carcinogens. Bacteria can also be used to treat cancer. Live, attenuated or genetically modified bacteria or anaerobic bacteria such as Clostridium and Bifidobacterium can be selectively colonized in tumors and fight cancer cells.

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Results: Pathogens cause cancer by producing carcinogens and inducing the immune system. Bacteria such as Fusobacterium spp, Borrelia burgdorferi, Escherichia coli, Mycoplasma spp, and Salmonella enterica can cause cancer. Bioengineering bacteria can also fight cancer by targeting cancer cells.

Conclusion: The hypothesis that the bacterial genome enters the human genome and causes cancer has not yet been confirmed and further studies are needed. Treatment of cancer with bacteria has disadvantages such as pathogenicity, negative interaction with chemical drugs and genetic changes of microbes.

Keywords: Bacterial Infections, cancer, Helicobacter pylori, oncogenic bacteria, carcinogenesis.

Bacteria, the cause or cure of colorectal cancer (Review)

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Introduction: Colon cancer is one of the most commonly diagnosed malignancies with an upward trend of morbidity. The incidence and mortality of colorectal cancer (CRC) have been increasing over the last 25 years. Some factors can increase the risk of CRC, for example, obesity, sedentary lifestyle, smoking, alcohol intake, diet, and diabetes. It has recently been recognized that the gut microbiome has a key role in colorectal carcinoma development. The human gastrointestinal tract contains more than 100 trillion bacteria, fungi, and viruses. Gut microbiota is involved in the transformation of food components into oncometabolite.

Methods: several studies have demonstrated an association between changes in microbiota composition and an increased risk of CRC. various bacterial strains are associated with CRC, such as Fusobacterium nucleatum, and Escherichia coli. Some studies showed that Fusobacterium nucleatum expression increased in tumor tissue, and this bacteria was also more abundant in feces from CRC patients. E. coli has the potential to cause intestinal inflammation via toxins such as colibactin, which has also oncogenic potential. In addition to bacterial virulence factors, some microbial metabolites affect the development of CRC, like glucuronic acid.

Results: Pathogenic bacteria may participate in the pathogenesis of CRC when the gut microbial homeostasis is disturbed. In contrast, some other types of bacteria such as Lactic acid bacteria as probiotics can reduce inflammation. Probiotics make a variety of biological benefits, containing the anti-activity of pathogenic bacteria, regulating the immune system, and preventing CRC. Increasing studies in this field shows that gut microbiota plays a vital role in the development of CRC. Despite this, some other bacteria such as lactic acid bacteria with probiotic properties will probably be a powerful tool for combating CRC.

Conclusion: The goal of this review is to show the relationship between gut microbiota and the development of CRC as well as the potential mechanisms of microbiota involved in the treatment of CRC.

Keywords: colorectal cancer, microbiome, probiotics, gastrointestinal tract, bacteria

Bacterial Resistance to Antimicrobial Biocides: an insight into molecular mechanisms (Review)

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Introduction: Antimicrobial Biocides are extensively employed as preservatives, disinfectants, and sterilizers in hospitals, industry, and the household. Antimicrobial Biocides are commonly used to eliminate bacteria from the surfaces of objects, transmission media, and surfaces. Iodophors, quaternary ammonium compounds, peroxides, phenols, chlorides, and glutaraldehyde are the six primary groups of Antimicrobial Biocides utilized in hospitals worldwide. In clinical settings, the most prevalent antiseptic and disinfectant biocides are chlorhexidine digluconate (a biguanide that disrupts the cell membrane), benzalkonium chloride (a quaternary ammonium compound that disrupts the cell membrane), triclosan (a bisphenol that blocks lipid biosynthesis), and formaldehyde (an aldehyde, alkylating agent). Reduced susceptibility of bacteria to antimicrobial biocides results from the selection pressure resulting from the bacteria's continuous use and recurrent exposure to substances employed to increase their productivity. Due to the diminished efficiency of antimicrobial biocides, antimicrobial biocides resistance has become a serious threat to life and health and the logical use of resources. This factor restricts their usage as antimicrobials. Several outbreaks of nosocomial infections have been attributed to tainted biocide solutions. A second problem is the paucity of data linking biocide tolerance and resistance to certain medically necessary antibiotics. Multiple investigations have demonstrated bacterial resistance to various biocides due to the presence of resistance genes. Resistance to Antimicrobial Biocides is caused either by the acquisition of foreign mobile genetic elements or by an innate genetic adaptation process. This article examined the resistance mechanisms of Antimicrobial Biocides-resistant bacteria on biofilms, cell membrane permeability, efflux pumps, degradable enzymes, and disinfectant targets. Efflux might be the quickest and most efficient stress resistance mechanism for bacteria. The Qac genes, which are situated on some plasmids that might transmit resistance by conjugative transfer, are the most often reported Antimicrobial Biocides resistance genes. Uncertainty remains

about whether the Qac genes can be transmitted via transformation or transduction. Studying the variables influencing bacterial resistance to antimicrobial biocides can lead to the discovery of innovative solutions to the problem of decreasing antimicrobial biocide efficacy. It has been established that the interaction between probiotics and bacteria, as well as the addition of 4-oxazolidinone, can suppress the production of biofilms.

Methods: Different databases such as Google Scholar, PubMed, Scopus and Web of Science were searched.

Results: Studies have shown that there is a significant relationship between molecular mechanisms and antimicrobial biocides resistance.

Conclusion: By decreasing the expression of efflux pumps, chemicals such as eugenol and indole derivatives might enhance bacterial sensitivity. The significance of these discoveries in anti-Biocide resistance has been established.

Keywords: Bacterial Resistance ; Antimicrobial Biocides; molecular mechanisms

Bacterial Vaccine against bacterial infections and cancer (Review)

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Introduction: Today, we need bacterial vaccines due to the increase in antibiotic resistance genes and bacterial infections. There are several types of bacterial vaccines, such as toxoids, subunit vaccines, killed whole-cell vaccines, OMV, and live attenuated vaccines. The dry form of live or attenuated bacteria can be used to produce live and attenuated bacterial vaccines, which increases the thermal stability of the bacterial vaccines. Bacteria such as Clostridium and Bifidobacterium that are severely anaerobic can be used as vaccines to treat solid tumors, some bacteria attack and destroy tumors through the mechanisms of chemotaxis and hypoxia, and immune processes. Some bacteria, such as E. coli, Helicobacter pylori, Pseudomonas aeruginosa, Borrelia burgdorferi, Shigella, Salmonella typhi, Neisseria meningitis, and Acinetobacter baumannii can produce outer membrane vesicles (OMV). The outer membrane of germ-negative bacteria is enclosed and is often associated with cellular components such as toxins, DNA, outer membrane components, etc. That produces OMV and acts as the bacterial vaccine. glycoconjugate vaccine is a vaccine that contains a bacterial O-antigen. To produce the glycoconjugate vaccine, the bacterial lipopolysaccharide (LPS) must be isolated and purified, then remove the toxic lipid A and pure O-antigen are produced. The O-antigen was bound to the carrier proteins by chemical or recombinant methods. To produce a bacterial vector vaccine, the antigen gene is inserted into the bacterial plasmid and chromosome, then the bacteria express the antigen. To produce a vector viral vaccine, the Mycobacterium tuberculosis antigen gene (for example Rv034133-4) was inserted into the HAdV-35 and HAdV-5 virus genome, and a viral vaccine was produced. This antigen is expressed on the surface of the virus and as a vaccine stimulates the immune system. The recombinant bacterial antigen is produced and conjugated to an antibody. Antibody against the receptor of dendritic cells (CLR), thus vaccine is better presented to the immune system. Omics science (such as genomics, proteomics, metabolomics, metagenomics, and transcriptomics) can also speed up and improve vaccine design.

Methods: Kunda NK, Wafula D, Tram M, Wu TH, Muttil P. A stable live bacterial vaccine. European journal of pharmaceutics and biopharmaceutics.

2016 Jun 1;103:109-17./Mayer RL, Impens F. Immunopeptidomics for next-generation bacterial vaccine development. Trends in Microbiology. 2021 Nov 1;29(11):1034-45. Shrestha A, Sadeyen JR, Iqbal M. Enhancing protective efficacy of poultry vaccines through targeted delivery of antigens to antigen-presenting cells. Vaccines. 2018 Dec;6(4):75. Lin IY, Van TT, Smooker PM. Live-attenuated bacterial vectors: tools for vaccine and therapeutic agent delivery. Vaccines. 2015 Dec;3(4):940-72. Draper, S., Heeney, J. Viruses as vaccine vectors for infectious diseases and cancer. Nat Rev Microbiol 8, 62–73 (2010). https://doi.org/10.1038/nrmicro2240 Serruto D, Rappuoli R. Post-genomic vaccine development. FEBS letters. 2006 May 22;580(12):2985-92. Siles ML, Lugo AC, McConnell MJ. Vaccines for multidrug resistant Gram negative bacteria: lessons from the past for guiding future success. FEMS Microbiology Reviews. 2020 Dec 8. Bekeredjian-Ding I. Challenges for clinical development of vaccines for prevention of hospital-acquired bacterial infections. Frontiers in immunology. 2020 Aug 5;11:1755. Shkair L, Garanina EE, Stott RJ, Foster TL, Rizvanov AA, Khaiboullina SF. Membrane microvesicles as potential vaccine candidates. International Journal of Molecular Sciences. 2021 Jan;22(3):1142./Kay E, Cuccui J, Wren BW. Recent advances in the production of recombinant glycoconjugate vaccines. npj Vaccines. 2019 May 1;4(1):1-8. Ihssen J, Kowarik M, Dilettoso S, Tanner C,/Wacker M, Thöny-Meyer L. Production of glycoprotein vaccines in Escherichia coli. Microbial cell factories. 2010 Dec;9(1):1-3. Lu G, Shan S, Zainab B, Ayaz Z, He J, Xie Z, Rashid U, Zhang D, Mehmood Abbasi A. Novel vaccine design based on genomics data analysis: A review. ScandInavian Journal of Immunology. 2021 Mar;93(3):e12986. Nooraei, S., Bahrulolum, H., Hoseini, Z.S. et al. Virus-like particles: preparation, immunogenicity and their roles as nanovaccines and drug nanocarriers. J Nanobiotechnol 19, 59 (2021). https://doi.org/10.1186/s12951-021-00806-7 Draper, S., Heeney, J. Viruses as vaccine vectors for infectious diseases and cancer. Nat Rev Microbiol 8, 62–73 (2010). https://doi.org/10.1038/nrmicro2240 Jan AT. Outer Membrane Vesicles (OMVs) of Gram-negative Bacteria: A Perspective Update. Front Microbiol. 2017 Jun 9;8:1053. doi: 10.3389/fmicb.2017.01053. PMID: 28649237; PMCID: PMC5465292. Henriques-Normark B, Normark S. Bacterial vaccines and antibiotic resistance. Upsala journal of medical sciences. 2014 May 1;119(2):205-8.

Results: The rise of antibiotic-resistant genes has threatened public health, and it has become one of the most important health problems for communities. Bacterial vaccines can prevent infectious diseases and reduce antibiotic-resistant infections. Types of bacterial vaccines include: toxoid, subunit vaccines/polysaccharide vaccines, conjugate vaccines, inactive vaccines, live attenuated vaccine, and recombinant vaccines. Omics science can also improve the design and production of bacterial vaccines.

Conclusion: Due to the increasing diversity of antibiotic resistance genes, some bacterial vaccines can't prevent resistance genes. It is difficult to design and produce bacterial vaccines that can stimulate the immune system. Increasing the data of genomics, proteomics, transcriptomics, glycomics and lipidomics in bioinformatics databases can help to better design the vaccine.

Keywords: Bacterial Vaccines, live or attenuated bacteria, Outer Membrane Vesicles (OMVs), glycoconjugate vacc

based on gene expression profiling and systems miR-28-5p regulates the expression level of GLUD1 gene in multiple sclerosis patients: a study biology analyses (Review)

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Introduction: Introduction: MS is a disease related to the nervous system that can affect the brain and spinal cord. This condition causes a wide range of potential symptoms, including vision problems, problems with hand or foot movement, and emotional problems. In this disease, the body's immune system mistakenly It attacks its natural tissues.

Methods: Methods: expression (GEO) and then analyzed by GEO2R to find differentially expressed genes by the target gse21924. The gene was selected from the David site in the kegg-pathway section. In the next step, we use the mir-walk site of the desired gene and select Mir. On the DIANA Tool site, we select the miRNA-lncRNA section and execute the search for the desired miR.The next step is to examin the relationship between the lnc genes, use the lncRRISEARCH site. Finally, from the kegg site, we find the signaling pathway in which the desired gene is involved, and from the string site, it enters the desired gene that we have chosen, and then gives us the proteins that are related to it

Results: Results: The GLUD1 (logFC: 1.988, adj.P.Val: 0.005387) could regulate the multiple sclerosis progression as a high expressed mRNA in the patients. MiR-28a-5p (score: 1, energy: 0.95, 3utr) and lncRNA A1BG-AS1 (interaction energy: -12.06 kcal/mol) regulates the expression level ofGLUD1 in the regulation of Nitrogen metabolism signaling pathways. Based on the protein-protein interaction analysis, GPT2 and GLS2 proteins have significant interaction with GLUD1 Mentioned proteins could regulate the MS status by modulating the Nitrogen metabolism signaling pathway.

Conclusion: Conclusion: miR-28-5p and lncRNA A1BG-AS1 regulate the expression level GLUD1 in regulating the Nitrogen metabolism signaling pathways in Multiple Sclerosis patients. High expression of GLUD1 protein increases Multiple Sclerosis development risk, and miR-28-5p and lncRNA A1BG-AS1can control this dysregulation.

Keywords: Key words: lncRNA,GEO,microRNAr. Multiple Sclerosis

Bioinformatic analysis of new synthesized benzylidene and indandione derivatives binding to β-amyloid fibrils (Research Paper)

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Introduction: Neurodegenerative diseases are some protein structure related diseases. While no applicable treatment is available, scientists have been worked on preventive treatments which acquire early diagnosis. ThT is a probe which has been widely used for diagnosing amyloid structures. While exposing to native protein, ThT shows no significant fluorescence intensity, but when it is placed inside amyloid structure, its fluorescence intensity increases and can be used as a sign of amyloid presence. Considering that positively charged ThT is unable to cross blood brain barrier and its fluorescence intensity will decrease in high concentration of beta amyloids, developing new lack of charge diagnosing agents with higher binding affinity to amyloids has become an issue of interest.

Methods: In this study we have employed some bioinformatic server and software for analyzing binding site and affinity of our compounds to amyloid structures. Compounds' 2D and 3D structures have been drawed using Chem Draw from Chem Office package. For getting amyloid beta structure we have used (2beg) pdb file from RCSB server. 3D structures have been energy minimized using gromacs software (gromos54a7 forcefield). These optimized forms have been used for docking process in auto dock 4.2 software and final complexes have been made using Lamarckian genetic algorithm.

Results: Our analysis has revealed that synthesized structures have shared same binding site with ThT and shown better binding affinity to beta amyloid structure.

Conclusion: These compounds are suggesting to be novel probes for early diagnosing of neurodegenerative diseases. Further studies including in vivo studies are needed.

Keywords: Beta amyloid, Neurodegenerative diseases, Amyloid structure diagnosis, Thioflavin T

Bioinformatic study on the role of PI3K/AKT pathway and LncRNAs in Prostate Cancer (Research Paper)

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Introduction: Prostate cancer is the most frequent cancer in men. Aging process, ethnicity, and genetic factors are three recognized risk factors for PCa. The state of tumor differentiation is highly correlated with a group of genes that have been discovered. The phosphatidylinositol 3-kinase (PI3K)/AKT pathway plays an important role in PCa carcinogenesis, according to a huge amount of evidence.

Methods: To achieve this goal, GEO data base and KEGG pathways were used to gain information about PI3K/AKT pathway and LncRNADisease data base was studied to choose lncRNAs associated with prostate cancer. The result showed that SCHLAP1 with Score: 0.9989 is linked to PCa.

Results: PI3K/AKT pathway result in apoptosis and proliferation of PCa cells and tumor metastasis and invasion by regulating several pathways. PI3K/AKT pathway is stimulated by The CCR9-CCL25 axis and IL-6, giving rise to PCa cell apoptosis resistance. IGF-I/PI3K/Akt signaling can lead to activating androgen receptor (AR), resulting in cell proliferation. Inactivation of PTEN can negatively activate AKT and mTOR. The aim of this study is to find the rule of PI3K/AKT pathway in the process of prostate cancer. We identified high SChLAP1 expression as significantly prognostic for metastatic disease progression of prostate cancer.

Conclusion: Based on the studies, it is concluded that PI3K/AKT signaling plays a significant role in PCa tumorigenesis. The mechanisms of PI3K/AKT in PCa tumorigenesis are multiple; inflammation, cell cycling, and angiogenesis are involved in this signaling. In additional we characterize a lncRNA termed SChLAP1overexpressed in a subset of prostate cancers.

Keywords: Prostate Cancer, SChLAP1, PI3K/AKT pathway, LncRNA

Bioinformatics analysis of hsa-miR-3615 and hsa-miR-302c-3p as novel candidates for the regulation of SSBP1 overexpression in Glioblastoma (Research Paper)

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Introduction: Brain cancer is almost a rare disease, but Glioblastoma(GBM) is the most common type of brain cancer, accounting for about 15% of primary brain tumors, which is considered one of the most hazardous cancers in the world. [1]in this analysis, we examined disease-related genes with over-expressed in GBM cancer to discover miRNAs that provide possible biomarkers and methods to improve the treatment and control of this disease. Therefore, we have targeted the bioinformatics analysis of the pathways of these genes and the influencing factors on their expression control.

Methods: we acquired the gene expression data with the comparison of 34 GBM tumors and 13 control samples (GSE50161) from the NCBI Gene Expression Omnibus(GEO) (http://www.ncbi.nlm.nih.gov/geo/). In this analysis, all genes that were over-expressed in GBM have been checked with the criteria of a threshold value of |logFC| >1 and an adj.P-value< 0.05. The pathways of genes were checked by the Kegg section in the enrichr database. [2][3] In addition, by using the miRWalk database, we noticed the interactions of our target genes with the related microRNAs, which determined the position and role of our found data (Score: 1.00)[4].

Results: Single Stranded DNA Binding Protein 1 gene selected in GEO2R analysis with adj.P.Val= 6.05e-11 and a threshold value of |logFC|=1.57. In continuance of the process, using UniProt[5], geneCard[6], and EnrichR[7], we understood that SSBP1 plays a very important role in the positive regulation of DNA-dependent DNA replication (GO:2000105) and DNA unwinding involved in DNA replication (GO:0006268). By analysis of possible miRNA-mRNA interactions discovered hsa-miR-3615, hsa-miR-302c-3p as significant targets for SSBP1 with negative free energy and worthy align score were found. [8] As well as our further analyzes by LncBase v.3[9] in relative to the role of lncRNAs with our target microRNAs, we discovered the role of SNHG1, HOTAIR, H19 to express several lncRNAs to interact with our target miRNAs.[10]

Conclusion: Brain cells become carcinomatous and escape from apoptosis by overexpressing SSBP1. Our predicted ceRNA network including the

mentioned LncRNA and miRNA can regulate the development and metastasis of GBM by affecting the expression level of SSBP1 by regulating the cell cycle.

Keywords: Glioblastoma cancer, miRNA, LncRNA, ceRNA

Bioinformatics and systems biology analysis of the gene expression and RNA interaction profiling in the Esophageal cancer-related signaling pathway (Research Paper)

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Introduction: Esophageal cancer (EC) is the eleventh most common cause of cancer worldwide and the sixth most common cause of cancer-related mortality [1]. The purpose of this study is to find a novel differentially expressed genes (DEGS) in the EC patients compared to control samples and signaling pathway.

Methods: gene expression data of EC patients (GSE161533) was obtained from the NCBI Gene Expression Omnibus (GEO) and then analyzed by GEO2R to find differentially expressed genes (DEGs) and validation of expression analyses performed by GEPIA2 [2] and ENCORI [3] database. Through GeneCards [4] and Enrichr [5], gene ontology information and biological pathway involvement were understood. Furthermore, miRWalk [6] was utilized to find significant miRNA-mRNA interactions. And the selected miRNA was searched in LncBase V.3 [7] to find strong interactions with LncRNAs and construct a predictive ceRNA network.

Results: Based on microarray analysis, MMP1 have a significant up-regulation in the EC samples, compared to control (|logFC| =6.779 , adj. P value =3.67e-23). This gene encodes a member of the peptidase M10 family of matrix metalloproteinases (MMPs). Proteins in this family are involved in the breakdown of extracellular matrix in normal physiological processes, such as embryonic development, reproduction, and tissue remodeling, as well as in disease processes, such as arthritis and metastasis. And the product of this gene is involved in the PPAR signaling pathway. hsa-miR-324-5 (score=1 , energy=-29.2) is a novel suppressor for MMP1. hsa-miR-324-5p have a RNA interactions with SLFNL1-AS1 and LINC00863 LncRNAs.

Conclusion: MMP1 is overexpressed in EC and forms a possible ceRNA network among hsa-miR-324-5p , SLFNL1-AS1 and LINC00863. So we assume that this network can participate in PPAR signaling pathway.

Keywords: Esophageal cancer; microarray analysis; signaling pathway; ceRNA network.

Bioinformatics data analysis and signaling pathways related to gene expression profile in clear cell renal cell carcinoma (Research Paper)

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Introduction: Clear cell renal cell carcinoma (ccRCC) is the most common solid lesion within kidney, and its prognostic is influenced by the progression covering a complex network of gene interaction [1]. in the last ten years ,research has been moving from being experimented in a real life lab to a virtual lab environment where analysis of data are done[2].

Methods: First , the gene expression data of ccRCC disease (GSE168845) received from Gene Expression Omnibus (GEO) database and then used GEO2R to find the expressed genes and analysis . then, for check potential correlation between the found gene and clear cell renal cell carcinoma disease used to ENCORI[3] and GEPIA2[4] databases . next to found worthy pathways signaling and ontologies used Enrichr [5] and for finding interactions between protein-protein used from String[6] . also for checking the interactions of mRNA-miRNA in 3`UTR , LncRNA-mRNA , LncRNA-miRNA and used miRWalk [7] , LncRRIsearch[8] and Lncbase.v3[9] data bases in order.

Results: The gene that called PTGER3 was found by analyzing data of GEO data base and found out that the expression was significantly reduced in ccRCC. (Log FC = -9.78 and adj.p.val = 1.43E-08). The prostaglandin EP3 receptor, also known as ep3, is a prostaglandin receptor for prostaglandin E2 (PGE2) that encoded by the human gene PTGER3 . this receptor may have many functions which involve digestion , nervous system and kidney reabsorption activities .[10] . The EP3 receptor is expressed in vessels as well as in the thick ascending limb and collecting duct, where it antagonizes vasopressin-stimulated salt and water transport. There for, PTGER3 involved in prostaglandin E receptor activity and also the regulation of lipolysis in adipocytes and negative regulation of secretion that related to renal cancer. The analysis of potential miRNA-mRNA interaction indicated hsa-miR-6837-5p as possibility significant factor for intended gene mRNA. In LncRRIsearch resulted good interaction between KCNQ1QT1 , LINC01239 and TSIX LncRNAs and mRNA. At last , searched hsa-miR-6794-5p miRNA in LncBase.v3 and found a potential intraction for AL160006.1 LncRNA .

Conclusion: There for, PTGER3 is low expression gene in ccRCC cancer and had strong interaction between KCNQ1QT1 , LINC01239 and TSIX and has-miR-6837-5p and possibility interaction between has-miR-6794-5p and AL160006.1.

Keywords: Clear cell renal cell carcinoma , Cancer , PTGER3 , Micro array

Bioinformatics study of the role of miR-21 in colorectal cancer tumorigenesis (Research Paper)

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Introduction: Colorectal cancer (CRC) is the growth of cancer cells in the colon or rectum (part of the large intestine). The disease is caused by abnormal growth of cells that can invade or multiply in other tissues in the body. 1.5 million new cases of this disease are reported annually in the world and it is one of the most common cancers after skin, breast and stomach cancers. MicroRNAs (microRNAs) are short single-stranded sequences about 18 to 25 nucleotides in size and are responsible for regulating the expression of genes called epigenetic alterations. MicroRNAs can be tumor inhibitors or oncogenes, miR-21, depending on the type of mRNA they inhibit. It stimulates, proliferates and invades cells and inhibits apoptosis. Therefore, in the present study, we evaluate the bioinformatics role of miR-21-3p and miR-21-5p in the tumorigenic pathway of colorectal cancer.

Methods: In this study, target miRNAs are extracted from Target scan, Vir-Mir, Miranda and miRNA path bioinformatics databases and the sequence and properties of miRNAs are investigated. The RNA22 bioinformatics database is then used to predict the target miRNA and used to confirm the predictions made. Thus, by inserting the miRNA sequence obtained from the miRBase site and the desired gene sequence obtained from the NCBI site, in the FASTA format, the complementary relationship between the miRNA and the target gene is determined based on the P value. The P-value indicates the possibility of accidentally binding to the target miRNA; The lower the value of p-p, the more significant it is and indicates that miRNA has a better chance of binding to the target gene. Finally, data analysis will be performed using SPSS software and a significant P value of less than 0.05 will be defined.

Results: The bioinformatic evaluation performed in this study showed that 21-miR is an increased oncogene in colorectal cancer, which can play a role in metastasis and disease invasion by affecting some molecular targets involved in signaling pathways.

Conclusion: high levels of 21-miR are associated with poor prognosis and lower survival of patients with the disease. Therefore, 21-miR can be used as a suitable and effective biomarker in determining prognosis as well as

treatment response; Because this microRNA plays a role in the clinical sensitivity and specificity in the diagnosis of colorectal cancer.

Keywords: Rectal Cancer - Biomarker - Algorithm

Biological behavior study of SH-SY5Y neuroblastoma cells on PCL/Gelatin nanofiberous scaffold containing Mg/Al-Layered double hydroxide (Research Paper)

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2.

Introduction: Nerve tissue engineering (NTE) is an effective approach for repairing damaged nerve tissue. In this regard, nanoparticle-incorporated electrospun scaffolds have aroused a great deal of interest in NTE applications

Methods: In this study, layered double hydroxide (LDH)-incorporated polycaprolactone (PCL)/gelatin (Gel) nanofibrous scaffolds were fabricated by electrospinning technique. The biological properties of scaffolds were examined by MTT assay, SEM analysis and. qRT-PCR.

Results: The results revealed that the inclusion of LDH nanoparticles into the PCL/Gel scaffold has improved biocompatibility in comparison with the pure PCL/Gel mat. The LDH-enriched electrospun PCL/Gel scaffolds exhibited a considerable impact on cell attachment and proliferation. The gene expression results showed that the neuron-specific (γγ) enolase (NSE) gene expression was significantly decreased in the scaffolds containing 1 and 10 wt% LDH compared to the scaffold without LDH, whereas in the scaffold with 0.1wt% LDH, a slight increase in expression was observed.

Conclusion: It can be deduced that electrospun PCL/Gel scaffolds containing LDH with optimum concentration can be a promising candidate for nerve tissue engineering applications.

Keywords: Layered double hydroxide, electrospun,SH-SY5Y neuroblastoma cells, scaffold, differentiation

Biological stability of therapeutic proteins (Review)

Afsaneh Farjami,[1,*]

1.

Introduction: The physicochemical and biological stability of therapeutic proteins is influenced by several environmental stress factors and agents. Therapeutic proteins should be evaluated using the appropriate techniques to establish their biological stability, which refers to their resistance to changes in biological activity, potency, toxicity, and immunogenicity in response to diverse environmental conditions. The biological activity of therapeutic proteins necessitates physicochemical stabilities that cannot ensure their efficacy and safety. There have only been a few experiments on both physicochemical and biological stability. Therefore, therapeutic proteins usually lack well-documented stability studies. This article aims to offer an overview of the effects of different environmental conditions on the bioactivity of therapeutic proteins.

Methods: A literature search was conducted on Scopus, PubMed, and Web of Science up to August 2022 for this purpose. We performed a title/abstract/keywords search for "Therapeutic proteins," "stability," "therapeutic proteins," and "stress parameters."

Results: The findings showed that several stress characteristics, including elevated temperature, pH, freeze-thaw, oxidative agents, light, mechanical stress, metal ions, and oxygen, have a detrimental influence on the stability of therapeutic proteins and result in unique degradation processes. Bioassays play an essential role in the stability studies of therapeutic proteins and may detect any change in their structure and bioactivity that standard physicochemical approaches cannot discern. Although physicochemical techniques are useful for identifying a product's purity, identity, and integrity, they are incapable of assessing the higher-order structure of therapeutic proteins; hence, the findings cannot be attributed to bioactivity. Therefore, bioassays based on the MoA are commonly necessary to investigate the bioactivity of therapeutic proteins. At least one functional bioassay is needed to assess bioactivity, however, more bioassays may be required if the product's mechanism of action is not entirely understood. Cell-based potency test, which employs a live cell-based system to generate a physiological response from interaction with therapeutic proteins, is the most widely used method for evaluating bioactivity. Activation of the receptor, cell signaling, receptor binding, and internalization of product molecules often occur due to the interaction between living cells and therapeutic protein products. Using living cells, tissues, or creatures makes bioassays more variable, less exact, and more robust than physicochemical methods.

Conclusion: Even while physicochemical stability alone cannot ensure the safety and effectiveness of biologic products, it is essential for the bioactivity of therapeutic proteins. To evaluate therapeutic protein stability comprehensively, it is required to examine both biological and physicochemical stability using the proper analytical methods.

Keywords: Therapeutic proteins, Stability, Bioassay, Bioactivity

Biomedical applications of silica-based aerogels: A review (Review)

Samin Hamidi,[1,*]

1.

Introduction: Silica-based aerogels are the applicable and well-known porous materials that has become the interest of the biomedical community. Silica aerogels are prepared from silica gels where the liquid is drawn out of the network structure so that its three-dimensional structure is not disturbed. Looking at from a nanotechnologists perspective, silica aerogels will have a special place in nanotechnology due to their porous structure, low weight, pore size regulation, and expanded surface. Aerogels have great potential for a variety of biomedical applications. These unique properties of aerogels have led to their use in biomedical fields such as drug delivery, antibacterial, and regenerative medicine. Engaging with materials whose characteristics can be customized is very important in the medical field. This review summarizes biomedical applications of number of aerogels and discusses the potential toxicity induced by silica aerogels.

Methods: PubMed, Scopus, Google Scholar, Embase, and Web-of-Science databases were searched using several combinations of keywords, including ‘Antimicrobial feature’, ‘Tissue regeneration’, ‘Drug delivery’, and ‘Drug delivery’.

Results: The application of silica-based aerogels in biomedicine is highly appreciated owing to their customized structure and their surprising parameters that could provide applied methods and solutions in different areas. Applications such as drug delivery, tissue engineering, and antibacterial is receiving scientist's consideration, making silica aerogels more and more interesting as a multi-application biomaterial to benefit healthy life. Silica aerogels are superior over the other nanomaterials because of their high porosity, low density, and tailorable structure, which turns them being as delivery platform for drug and bioactive materials and a platform for implants and antibacterial agents. It is assumed that drugs' stability, pharmakokinetic and dissolution rate could be affected through adsorption onto aerogels. It is undoubtedly an advantage since developing a new drug requires much time and, more importantly, financial expenditures. Therefore, it is necessary to continue research in this direction.

Conclusion: While tremendous advances in silica aerogels have been made, more investigations are needed to handle the difficulties associated with these materials' commercialization and medical applications. However, to accept silica aerogels in the market, the preclinical and clinical stages must be fully

tested. Furthermore, affordable product cost and improved biological characteristics of silica aerogels will also determine the speed of commercialization in this journey. Thus, silica aerogels with in vivo and in vitro studies provide alternative platforms for new therapeutic applications.

Keywords: Antimicrobial feature, Tissue regeneration, Drug delivery, Toxicology

Biomolecules-based gold nanomaterials as theranostic agents in diagnosis and treatment (Review)

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Introduction: Nanotheranostic is a great approach based on the combination of therapy and diagnosis in improving personalized treatment. Gold nanomaterials(GNMs) due to their unique features such as non-toxicity, and optical properties such as localized surface plasmonic resonance (LSPR) are appropriate for theranostic applications. LSPR depends on GNMs, in such wise that LSPR changes with different bio-functionalization. The interaction of biomolecules (DNA, amino acids, and peptides) with GNMs could generate various gold nanostructures with tunable LSPR features with different theranostic applications. This review has examined biomolecule-based GNMs as theranostic agents in the diagnosis and treatment of disease.

Methods: Keywords of gold, nanostructures, theranostics nanomedicine, and surface plasmon resonance are searched in ScienceDirect, PubMed, and Scopus databases. The papers of the years 2012-2022 were examined for information extraction.

Results: Plasma proteins- templated gold nanoclusters (Au NCs) exhibit a highly effective ROS generation under visible irradiation. Human plasma proteins- stabilized Au NCs show spectroscopic and photodynamic therapy features that possess both cancer diagnostic and treatment. Gold nanodumbbells conjugation with nucleolin-targeted DNA aptamer AS1411 as a targeted gold nano theranostics have revealed high efficacy in near-infrared II photoacoustic imaging-guided photothermal therapy for subcutaneous 4T1 tumors. Site-specific conjugation of a thermally sensitive elastin-like polypeptide to gold nanoparticles exhibited simultaneous photothermal /photoacoustic /X-ray computed tomographic imaging and PTT of melanoma.

Conclusion: According to studies, biomolecule-based GNMs could perform as theranostic nanoplatforms with tunable features such as tunable LSPR features. Therefore biomolecules-based GNMs possess wider therapeutic and diagnosis applications which should be explored in the future.

Keywords: Gold, nanostructures, theranostics nanomedicine, surface plasmon resonance

Biosensors And Diagnosis Technologies for Urinary Tract Infections (Review)

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Introduction: Urinary tract infections are the most common bacterial infections in infants, children, and adults. Complicated factors such as obstruction of urinary stones, indwelling catheters, and urinary tract surgery increase the risk of urosepsis, which has a mortality rate of up to 20%. Early identification of these microorganisms leads to faster recovery and fewer complications. However, these traditional methods of urine culture and urinalysis or microscopy are the standards of the bacteriology laboratory, which can be complex and time-consuming. To solve these problems, biosensors are recognized as an efficient and emerging technology that provides a powerful diagnostic platform for Infectious diseases have become. Biosensors can be used in understanding the mechanism of some diseases and disorders, in diagnosing and treating diseases and their complications, and in identifying their causes, as well as in other related sciences such as pharmacy, advanced drug delivery systems, and identifying new drugs and evaluating their biological activity.

Methods: This study is a systematic review with the keywords: Urinary Tract Infection (UTI), Biosensors, Patient, Bacterial, Diagnostic reliable scientific databases, and sites, including PubMed, Google Scholar, Scopus, Science Direct, Sid was conducted between 2012 and (August) 2022 and 40 articles were found in the initial search, after removing duplicates and evaluating the title and abstract, 19 articles related to the research selected, and the Total conclusions were made based on the information available in various selected articles.

Results: Sensor technology has developed greatly over the past decades and has become interdisciplinary research and industrial field. Sensors consist of three main parts: 1- Detecting part: This part must be able to selectively identify a specific material or a specific type of material. This part is where the interaction between the detector and the target analyte takes place. 2-Transducer: This part converts the interaction between the detector part and the target analyte into a visible signal. There are different types of converters. 3- The third part interprets the signals generated in the transducer into usable information. Biosensors are used in both research and diagnostics. The most important biosensors used in the field of UTI diagnosis include Dual signal amplification via enzyme-based target recycling, Magnetoelastic sensor-based technology, electrochemical endotoxin sensors based on TLR-4/MD-2 complexes, Aptamer based biosensors, Microcantilever array biosensors, Limulus amoebocyte lysate. It is an assay. It is also expected that biosensors can be used in the identification, quantification, and monitoring of more specific bacterial species. Biosensors may have a wider application in diagnostic approaches.

Conclusion: Generally, Biosensors provide an early and accurate determination of urinary pathogens, which is key to the management of UTIs. The ability to initiate evidence-based therapy guided by rapid profiling of bacterial pathogens and antimicrobial susceptibility can improve patient care and help prevent the emergence of multidrug-resistant pathogens. The successful development and implementation of these technologies have the potential to usher in the era of precision medicine to improve patient care and public health, but more studies are needed in this field.

Keywords: Urinary Tract Infection (UTI), Biosensors, Patient, Bacterial, Diagnostic

Biosensors for Environmental Monitoring: A review (Review)

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Introduction: In recent decades, environmental pollution caused by human and industrial activities has been the source of climate change, and on the other hand, it has a negative impact on human health and quality of life. This has led to increasing concerns about this, and countries are looking for innovative tools and early warning systems to monitor the quality of air, water, and soil, as well as the exact time and place of pollution. In this context, biosensors are of interest due to their cost-effectiveness, speed of operation, and in-situ and real-time evaluation. Biosensors can convert a biochemical reaction into a measurable signal by combining a biological diagnostic agent with a transducer. Despite the advances in the field of environmental monitoring, there are shortcomings of expensive equipment and time-consuming traditional analytical methods (chromatographic technique). Also, the increasing number of polluting sources is associated with the increasing need for warning and control systems in the place of pollutants.

Methods: In this review, statistics and required data have been collected using keywords such as Biosensors, and Environmental Pollution, citing reliable databases such as PubMed, Google Scholar, and Scopus. Data quality was evaluated and the most relevant articles from 2017 until 2022 were reviewed.

Results: Nowadays, biosensors such as immunosensors, aptasensors, genosensors, enzymatic biosensors, and nanophotonic transducers are used to detect and monitor various environmental pollutants. The detection elements in these biosensors are antibodies, aptamers, nucleic acids, enzymes, and photons respectively. Biosensors are fast, specific, sensitive, reusable, maintenance-free, and also provide early warning systems and portable diagnostic tools. Examples of biosensors and diagnostic systems are reviewed in this study. - Biosensors as simple, sensitive, and miniaturized

methods for detection and monitoring of pesticides such as organophosphorus insecticides - aptasensors for detection of acetamiprid from wastewater samples; In these biosensors, silver nanoparticles are doped on graphene oxide nanocomposite and these nanocomposites are excellent support for aptamer stabilization. Recently, the distinction of targets with different functional groups and rehybridization has increased. The reason for this is the development of aptasensors for ease of modification, thermal stability, laboratory synthesis, and the possibility of designing their structure. - Optical transducers: These types of biosensors have significant advantages, including being cheaper, faster, and using fewer reagents, high sensitivity, and not requiring labels and complex labeling methods. nanophotonic transducers for label-free environmental monitoring have offered other advantages such as immunity to electromagnetic interference, high sensitivity, wide bandwidth, and more importantly, miniaturization capacity and portability due to the scalable technologies used to manufacture them. The most common nanophotonic biosensor is the surface plasmon resonance (SPR) sensor. The function of this biosensor is based on the change of reflectance on a metal layer in close contact with a biological environment. The SPR sensor has been widely developed and commercialized. There are difficulties in miniaturizing this technique and turning it into a portable instrument, and it has a limited number of channels to perform simultaneous measurements. In recent years, many advances have been made in the field of optical biosensors with higher energy.

Conclusion: Despite the promising features of biosensor devices as ideal environmental monitoring tools, these devices were not possible to use in the field due to their miniaturization level and their full functionality outside the laboratory. Nanophotonic biosensors based on evanescent sensing have advantages such as sensitivity, rapidity, selectivity, multiplexing, cheapness, multiplexing, label-free detection, and lab-on-a-chip integration, and are considered a suitable choice for portable point-of-care detection. And they have also passed the stages of laboratory proof in terms of multiplexing and miniaturization in compact platforms. This new technology will soon pass through the experimental stages and enter the marketing and market phase. The value of these nanophotonic biosensors in 2013 was estimated at 39.11 billion, and predictions have given a double value for this technology in the future.

Keywords: Biosensor, Environmental Monitoring, Nanophotonic biosensors

Biosensors to detect graphene-based cholesterol (Review)

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Introduction: Graphene-based nanomaterials with unique morphological properties are very useful for sensing applications. Highly sensitive electrochemical and biosensors are of great importance not only for biomedical applications and clinical diagnostics, but also for environmental protection. Therefore, this study aimed to determine the effect of a graphene-based biosensor on the detection of cholesterol.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of biosensors to detect graphene-based cholesterol, a total of 16 articles were analyzed.

Results: After searching, 28 articles were found, and finally 12 articles were included in the study. Based on the results, biosensors can be classified according to the conversion mechanism: Biosensors, optical detection, thermal detection, ion sensitivity, electrochemical, and Malhotra sensors. Graphene-based sensors have shown good sensitivity and selectivity for the detection of glucose, cholesterol, hemoglobin, H2O2, small biomolecules, DNA, heavy metal ions, and toxic gaseous molecules. The use of graphene can avoid problems associated with NP and CNT metal alloys.

Conclusion: The unique properties of graphene-based materials (fast electron transfer, high thermal conductivity, excellent mechanical flexibility, good biocompatibility, high electrochemical activity, and easy surface functionalization) make them applicable for electrochemical analyte identification and biosensors with excellent results. Cholesterol biosensors are

considered an important tool for the clinical analysis of numerous diseases such as cardiovascular diseases. Therefore, there is a need to develop the most effective and accurate device for effective cholesterol monitoring.

Keywords: Biosensing Techniques, Graphite, Cholesterol

Biosynthesis of magnetic iron nanoparticles by Lactobacillus casei and investigation of antibacterial potential of them (Research Paper)

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Introduction: Magnetic iron nanoparticles were used as drug carriers in the drug delivery system, and due to increased drug absorption and controllable and targeted drug release, they have been widely used in MRI imaging techniques, and the manufacture of anti-cancer and anti-tumor drugs have been used. Due to the wide applications of magnetic iron nanoparticles, several solutions have been presented for their synthesis, the most important of which are chemical methods. Still, in recent years, researchers have invented a new technique in which living organisms such as plants, bacteria, fungi, and algae are used as a bioreactor for the synthesis of nanoparticles, called biosynthesis or green synthesis. This research used the green synthesis method to produce magnetic nanoparticles, and the ability of Lactobacillus casei in The green synthesis of iron magnetite nanoparticles has been investigated.

Methods: prepared 1mM of Fe2so4 solution, and the supernatant of each of the Lactobacillus casei was added. The biosynthesis of MINPs was proved by UV-vis, XRD, FTIR, and TEM. The antimicrobial effect of MINPs was performed by disk diffusion method and MIC and MBC on Bacillus cereus, Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa.

Results: change of the indicates the biosynthesis of MINPs. Peaks in 441-450nm were observed in the UV-vis spectrophotometer. XRD and FTIR results also confirmed the biosynthesis of MINPs. The size of MINPs was between 20-30nm, and the shape was spherical. The results of the antimicrobial effect of MINPs by disk diffusion and MIC methods were Bacillus cereus 26± 0.5 and 30± 1.2, Staphylococcus aureus 21± 1 and 40± 0.8, Escherichia coli18 ± 0.5 and 65± 1, and Pseudomonas aeruginosa 14 ± 2 and 80 ±0.0

Conclusion: The results showed that all three species of Lactobacillus could biosynthesize MINPs, which has a suitable antimicrobial effect against gram-positive and gram-negative bacteria .

Keywords: Biosynthesis, Magnetic Iron Nanoparticles, Lactobacillus casei

Breast Cancer and the Effect of Environmental Factors Involved (Review)

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Introduction: There are many genes as well as environmental factors involved in the risk of breast cancer. This study aimed to determine the effect of different environmental factors in the incidence of breast cancer in patients admitted in Imam Khomeini Hospital, Tehran. Estrogen hormone, age, weight, Dietary habits, vitamins, cigarette smoking and family history were concerned as risk factors.

Methods: The data were analyzed using the computer software SPSS for windows (version 11). The case-control study was conducted in 100 breast cancer patients and 100 healthy people as control.

Results: An increased association was found with patients becoming pregnant in high age, being pregnant for more twice in life period and who have had abortion. Using anti Pregnancy pills also is an important factor in the risk of breast cancer as a huge number of patients were using these kinds of tablets. Being over-weight also is a risk factor for breast cancer. Very few patients were using vitamins as it is an agent to reduce the risk of cancer. Positive association was also found among people using red meat and the number of using in the weak. No association was observed with age and risk of breast cancer. Factors like tea consumption and using fast food also resulted in positive association with breast cancer. We found no statistically significant association between positive family history and breast cancer risk.

Conclusion: This study shows that some of the environmental factors are important in increasing the risk of breast cancer.

Keywords: Breast Cancer, Environmental Factors.

BREAST CANCER TREATMENT AND INFERTILITY (Review)

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Introduction: Breast cancer is the most common malignancy in women with a significant increasing incidence during the reproductive life. Effect of the treatment leads to a premature depletion of the ovarian follicle reserve occurs in more than one-third of patients resulting in permanent infertility. The aim of this study is reviewing breast cancer treatment and infertility.

Methods: This review has been conducted based on analysis of available literature indexed in PubMed database between 2015 and 2022. Specific keywords including “breast cancer” and “infertility” have been used. Experimental and review articles on the mentioned theme were included.

Results: The chemotherapeutic, total dose given, the patient's age at treatment, the drug combination and finally whether targeted therapy is used or not, have been shown to modify the impacts of treatment on fertility rate of the patients. Alkylating agents are the most toxic ones. In young breast cancer patients, there is a trend to modify regimens to achieve less gonadotoxicity. Evidence regarding tamoxifen, the main used endocrine drug, is scarce and controversial on its direct effect on ovarian reserve. There are not enough studies on the impact of aromatase inhibitors on fertility. Also, HER2-directed agents have not yet demonstrated significant ovarian toxicity and there are scarce data on their effect on fertility.

Conclusion: Fertility impairment induced by adjuvant treatments and potential risk associated with pregnancy are not well studied and no standard strategy to preserve fertility in breast cancer patients is available so far. More studies are required.

Keywords: Breast cancer treatment; Fertility; Infertility

Breast Cancer; Investigation of common environmental factors (Review)

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Introduction:
Breast cancer is a disease in which malignant cells originate from the breast tissue and multiply irregularly and increasingly. This cancer is considered one of the most common and deadly cancers among women. Its prevalence is increasing in all countries, especially western countries. One of the most important worrying factors for women's health is the aim of this study is to determine the impact of environmental factors on breast cancer.
Various factors play a role in the occurrence of breast cancer in women, which are divided into three general categories: unchangeable, changeable and other factors. The unchangeable factors include age, family history, late menopause, early menstruation and genetic predisposition. The effect of these factors is as follows. is that the prevalence of breast cancer increases in women after the age of 35, as well as
women who have late menopause or the onset of menstruation before the age of 12, and those who have a family history of this cancer or similar cancers such as ovarian, colon, etc. The risk of breast cancer are variable factors including obesity, exercise, contraceptives
, and hormone use, which have a dramatic effect on the risk of breast cancer, women who are overweight and
obese after menopause, or not having enough physical activity, as well as frequent use of pills Hormonal contraception&nbs

p;increases the risk of this cancer in women.

Methods:
he current study is a systematic review that was conducted by searching Google Scholar and sid, elmnet, elseveir, and jove search engines using the keywords cancer, breast cancer, women and their English equivalents in the time range of 2012 to 2021. And 100 articles with the desired topic were found, based on free access to the full text of the article and suitability to the desired topic,
8 articles were selected and used.

Results:
According to the findings, environmental changeable factors have a significant impact on breast cancer because they can be changed and modified, they can be very helpful in preventing breast cancer, and it is suggested that after the age of 35, women should have sufficient physical activity, fitness, and regular checkups for prevention. have this disease

Conclusion:
Therefore, it is possible to reduce the risk of breast cancer in women by encouraging and guiding women to regular checkups and a healthy diet and exercise.

Keywords:
Cancer, breast cancer, women, neoplasm

Building a blockchain system to create a secure authentication environment for medical information management (Review)

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Introduction: The use of advanced health care programs "remote information system" and "telematics" requires an integrated approach to apply the social, financial, cultural and political effects and remove the barriers of information technology and communication technology. Security and privacy are two important and critical features used to build a high security authentication protocol. Blockchain is a technology that has good features such as decentralization, independence, integrity, immutability, verification, error tolerance, anonymity, auditability, and transparency, which ensures high security for people. Putting blockchain into healthcare is proposed to eliminate the barriers and problems of data exchange inherent in electronic health record (EHR) systems that are disparate. Damage to privacy in medicine and health care causes a lot of economic and credit losses to hospitals and other health institutions, and may also cause various damages to patients and endanger their lives. Therefore, privacy is very important in medicine. The purpose of this review is to Design of Secure Authentication Protocol for Telecare Medical Information System Using Blockchain.

Methods: In the following article, we collected the required data by using key words using reliable databases such as Google Scholar, ProQuest, Scopus and PubMed. Our statistical population consists of all the studies that have been conducted until 2022. After reviewing the findings, we reviewed 14 articles.

Results: 1. In Telecare Medicine Information System (TMIS), the anonymity of patient is very critical and the violation of patients privacy can cause serious security issues 2. According to the results, electronic files and private

health records are the most useful in using blockchain technology. Access control, interoperability, provenance and data integrity are all issues that are meant to be improved by blockchain technology in this field. 3.Providing secure authentication of people, the existence of a two-way, distributable and scalable process without a failure point, is possible by using the combination of public key construction and blockchain, which creates a secure environment for the electronic health network.

Conclusion: Thus, various cryptographic techniques based on distinct factors helped to protect the privacy of data and anonymity of patient .This system can improve the protection and privacy of patient records and prevent tampering . Blockchain is a potent and viable technology for patient access and exchange of health information. However, this technology remains at the prototype level and has limited functionality. Also, low throughput and high latency along with lack of technical stability of blockchain is one of the disadvantages of this technology. Blockchain is an ideal choice for improving existing computing systems in various ways. As one of the network-enabled technologies, cloud computing has been broadly adopted in the industry through numerous cloud service models. Fusing blockchain technology with existing cloud systems has a great potential in both functionality/performance enhancement and security/privacy improvement.

Keywords: privacy, Blockchain, Electronic Health Record

Can Engrafted Neural Stem Cells Amend Behavioral Deficits in Alzheimer's Disease? (Review)

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Introduction: Alzheimer's disease (AD) is a form of progressive and irreversible dementia that results from the accumulation of amyloid-beta plaques (Aβ) in the neuronal environment. In recent years, stem cell therapy (SCT) to the degenerative neurological disorders have provided the basic for the development of new therapeutic strategies but there are still many significant hindrances toward progressing to effective methods for SCT. In this article we will review whether and how engrafted neural stem cell (NSCs) can improve cognition in AD.

Methods: This review article has been extracted from 7 article that has indexed in PubMed and Google Scholar and published from year 2016 to 2022. The search terms include "Neural Stem Cell", "Alzheimer's Disease" and "Transplantation".

Results: NSC engraftment to the brain of transgenic AD mice reduced Aβ42 peptide levels and plaque formation as well as the levels of proinflammatory cytokines interleukin (IL)-1B and IL-6 that can improve cerebrovascular function. While NSC therapy improved performance on the Morris water maze test which is necessary for spatial learning and memory function in young mice. Notably, the levels of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and vessel density in the cortex and nerve fiber density in the hippocampus of NSC-injected mice were significantly enhanced.

Conclusion: NSC transplantation may influence spatial memory and behavioral deficits in AD by reducing Aβ plaques and proinflammatory cytokine levels and improving the level of neurotrophic factors and nerve fiber density in the cortex and hippocampus. However, further studies are required to confirm the positive impact of NSC transplantation on AD.

Keywords: Neural Stem Cell, Alzheimer's Disease, Transplantation

Causes of brain tumors (Review)

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Introduction: A brain tumor is an intracranial neoplasm within the brain or in the central spinal canal. Primary malignant brain tumors affect about 200,000 people worldwide every year. Brain cells have special characters. Due to the specific properties of brain tumors, including epidemiology, growth, and division, investigation of brain tumors and the interpretation of results is not simple. Research to identify the genetic alterations of human tumors improves our knowledge of tumor biology, genetic interactions, progression, and preclinical therapeutic assessment. Obtaining data for prevention, diagnosis, and therapy requires sufficient samples, and brain tumors have a wide range. As a result, establishing the bank of brain tumors is very important and essential.

Methods: The cause of most brain tumours is unknown, but there are several risk factors that may increase your chances of developing a brain tumour. age – the risk of getting a brain tumour increases with age (most brain tumours happen in older adults aged 85 to 89), although some types of brain tumour are more common in children. radiation – exposure to radiation accounts for a very small number of brain tumours; some types of brain tumours are more common in people who have had radiotherapy, CT scans or X-rays of the head. family history and genetic conditions – some genetic conditions are known to increase the risk of getting a brain tumour, including tuberous sclerosis, neurofibromatosis type 1, neurofibromatosis type 2 and Turner syndrome.

Results: Researchers know brain tumors develop when certain genes on the chromosomes of a cell are damaged and no longer function properly, but they aren’t sure why this happens. Your DNA in your chromosomes tells cells throughout your body what to do — it tells them when to grow, when to divide or multiply and/or when to die. When brain cell DNA changes, it gives your brain cells new instructions. Your body develops abnormal brain cells that grow and multiply faster than normal and sometimes live longer than normal. When that happens, the ever-growing crowd of abnormal cells takes over space in your brain. In some cases, a person may be born with changes in one or more of these genes. Environmental factors, such as exposure to large amounts of radiation from X-rays or previous cancer treatment, may then lead to further damage. In other cases, the environmental injury to the genes may be the only cause. Only about 5% to 10% of people with brain tumors have a family history of a brain tumor.

Conclusion: Unfortunately, brain tumors cannot be prevented. But you can reduce the risk of brain tumor by avoiding environmental risks such as smoking and exposure to excessive radiation. If a first-degree biological relative (sibling or parent) has been diagnosed with a brain tumor, it is important to tell their health care provider. Because whether or not the tumor is hereditary must be checked

Keywords: Brain Tumor, DNA, radiation, genetic, age

CCL21 and HSPA1A differentially expressed in ischemic heart disease (Research Paper)

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Introduction: Myocardial ischemia occurs when blood flow to the myocardium obstructed by a partial or complete blockage of a coronary artery by atherosclerosis. Rupture of plaques lead to myocardial infarction. The aim of this study is to identify important differentially expressed genes and their regulatory miRNAs in ischemic heart disease.

Methods: The expression profiling array of adipose tissue of 5 patients and 5 Control samples were obtained from the GEO database (GEO accession: GSE 152326), and the samples were analyzed. Genes with differential expression patterns were isolated with the GEO2R by P.value < 0.05 and logfoldchange (LogFC) # 1 investigation. In addition, miRNAs targeted 3´-UTR of selected genes were examined through miRcode database.

Results: The results showed that 3744 genes had differential expression among the samples in which C-C motif chemokine ligand 21 (CCL21) gene was the highest downregulated gene with logFC = -4.607 and p.value= 0.00001978. Heat shock protein family A (Hsp70) member 1A (HSPA1A) gene was the highest upregulated gene with logFC = 2.369 and p.value= 0.00078007. Further, miR-138 with two and miR-146 with one target sites might have regulate the expression of CCL21 and HSPA1A, respectively.

Conclusion: Our analysis showed that analysis of differentially expressed genes and 3´-UTR target sites related microRNAs in adipose tissue of ischemia could help to find accurate biomarker.

Keywords: ischemic heart disease, adipose tissue, differentially expressed genes

Cell surface vimentin detection in cancer cells by peptide-based monoclonal antibody (Research Paper)

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Introduction: Vimentin is a prominent intermediate filaments (IFs) protein expressed in different mesenchymal origin cell types. Besides a wide range of cellular function roles associated with vimentin expression, its dysregulation and cell surface expression in the induction of malignancy properties have been reported extensively, making it a promising cancer-specific target. Therefore, this study aimed to generate and characterize anti-vimentin monoclonal antibodies.

Methods: A 14-mer synthetic peptide from the N-terminal region of vimentin was conjugated to keyhole limpet hemocyanin (KLH) and used for immunization of Blab/C mice and monoclonal production by conventional hybridoma technology. The monoclonal antibody was purified using affinity chromatography of supernatants from the selected hybridoma cells. ELISA, Immunoprecipitation-western blotting (IP-WB), Immunocytochemistry (ICC), and flow cytometry were employed to characterize the produced monoclonal antibody in terms of interaction with vimentin immunizing peptide as well as vimentin protein.

Results: Amid the several obtained producing anti-vimentin antibody hybridoma, 7C11-D9 clone (IgG1 isotype with kappa light chain) showed higher reactivity with the immunizing peptide, led to its selection for purification and characterization. The purified antibody could detect vimentin protein in IP-WB, ICC and flow cytometry of the normal and cancerous cells with different origin.

Conclusion: Taken together, 7C11-D9 anti-vimentin monoclonal antibody might be used as immune diagnostic or immune therapeutic tools where detection or targeting of vimentin in a wide range of organisms is required.

Keywords: Antibody, Cancer, Peptide, Vimentin, Targeted therapy

cell therapy; a way curing for Parkinson diseases (Review)

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Introduction: One of the most common neurodegenerative diseases is Parkinson's disease (PD). The second most common after Alzheimer's disease. because of a loss of nerve cells in the substantia nigra (SN), which is part of the basal ganglia in the brain. SN plays an important role in control motor-like movements and how it influences your brain's chemistry.Loss of nerve cells in SN causes no release of dopamine or very little release, which leads to a disorder. Thus A way to increase dopamine to renewance of dopaminergic cells. The method that makes this possible is cell replacement strategy.Stem cells can divide and differentiate into different cells with unique specializations. stem cells have two main sources:adult body tissues and embryos.

Methods: There are four sources of stem cells for DA production: embryonic stem cells from fertilized eggs, neural stem cells from the embryonic or adult brain, or stem cells in other tissues. There are two methods for transplanting stem cells in PD patients: In the first method, stem cells are differentiated into dopamine-producing nerve cells in laboratory conditions. As a result, we will have an unlimited number of dochumenseric cells. In the second method, substitute stem cells or progenitor cells are introduced into the body and differentiation takes place there, which, after implantation in, striatum or substantia nigra nigra differentiates into a dopamenseric cell. In relation to the movement of stem cells through the blood-brain barrier, the cells are mainly administered intravenously, which can cross the blood-brain barrier. Although Mesenchymal stem cells can cross the blood-brain barrier when they are administered through an administered IV. However, the treatment of neurological diseases is difficult due to the presence of the brain barrier.

Results: Today, there is no useful cell therapy for the treatment of PD, but the most important scientific result of clinical trials with human fetal mesenchymal tissue transplantation is that cell therapy can be helpful and effective in the treatment of PD. Low availability and occurrence of dyskinesia. Also, during the last two decades, rapid and significant progress has been made in this direction. when the first human embryonic mesencephalic tissue was transplanted to the striatum in these patients, it was possible to detect the absence of transplanted neurons and increase the ability to survive. They have the ability to work in the brain of a fifty-sixty year old person who is affected by a chronic disease. The treatment of this disorder has been obtained through clinical trials that have been carried out since then, and evidence has been obtained that shows that these transplanted dopamine

have the ability to innervate the striatum and release dopamine. The effects of transplantation can last for at least ten years. which provides the possibility to quit the drug, however, the degeneration of dopamine neurons of the patient continues.No data have shown that the disease process compromises graft survival.

Conclusion: All existing treatment methods related to tuberculosis therapy are still in the developmental stage from a clinical point of view and should only be performed in small groups of patients. Stem cell transplant methods that have been performed so far have not provided any clinical benefit to patient groups that cannot be achieved with other Parkinson's treatments. However, cell therapy has a potential advantage, and that is, to replace certain neurons that have died or been damaged, so that the release of dopamine restores functional synapses at denervated sites in the striatum, which in the best case is the nigrostriatal system. To rebuild That we can achieve the science of how to produce the number of dopamine neurons in a large number of stem cells and how to implant them and also direct their growth, which causes the restoration of the dopamine system. There is hope that In the future, we will be able to provide patients with effective cell-based treatments that will restore the brain's function in Parkinson's patients.

Keywords: Parkinson's diseases, cell therapy, neurodegenerative disease, neuron stem cell

Cellular senescence pathway associated to pulmonary arterial hypertension (Research Paper)

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Introduction: Pulmonary arterial hypertension (PAH) is a frequent complication of congenital heart disease (CHD) and relates to type of the underlying cardiac defects and repair history. Some common underlying causes of pulmonary hypertension include high blood pressure in the lungs' arteries due to some types of congenital heart disease, connective tissue disease, coronary artery disease, high blood pressure, liver disease. The aim of this study was to evaluate the important signaling pathways in PAH.

Methods: The expression profiling array of patients with PAH and Control samples were obtained from the GEO database (GEO accession: GSE131793), and the samples were analyzed. Genes with differential expression patterns were isolated with the GEO2R by P.value < 0.05 investigation. Signaling pathways analysis was performed using Enrichr database.

Results: The results showed that 3363 genes had differential expression among the samples. In addition, pathway analysis demonstrated that cellular senescence with p= 0.00009805 is the main important signaling pathways in PAH patients and RB1, CDKN1A, ITPR3, PIK3R1, ETS1, MUC, ATM, MYBL2, MAP2K3 were important genes among differential expressed mRNAs in this pathway.

Conclusion: All in all, our analysis in line with previous reported showed that analysis the expression of cellular senescence genes might help to find novel diagnostic biomarker for PAH.

Keywords: Pulmonary arterial hypertension, marker, cellular senescence

Cerebral Glioblastoma: A Review on Genetic Alterations, Signaling Pathways, and Clinical Managements (Review)

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Introduction: Gliomas are the most common type of primary brain tumors, accounting for about 30-80 percent of all brain tumors and malignant tumors, respectively. World Health Organization (WHO) has classified tumors into four grades, based on malignancy, with grade I tumors having the least malignant behavior and grade IV tumors the most. Glioblastoma, previously known as glioblastoma multiform (GBM), belongs to grade four, which is the most malignant form. It can also be the most feared type of primary brain tumor not only for its aggressiveness and high levels of proliferation but also for its effects on the quality of life. This tumor, on average, usually develops at the age of 64 with a 14.8 percent of survival rate at 2 years. Therefore, among common gliomas, glioblastoma has the least survival rate. There is also a molecular classification for glioblastoma that comprises of four subtypes, based on different gene alterations. These subtypes include classic, mesenchymal, proneural, and neural glioblastomas. Despite different methods available for diagnosis, treatment, and management of patients with glioblastoma, prognostic factors such as age, gender, the extent of tumor resection, and neurological status play an important role in the overall outcome of a patient. While various factors can be used to classify glioblastoma, generally, it is characterized into primary and secondary glioblastomas, which was first presented by Hans Joachim Scherer (1906 - 1945), the German neuropathologist.

Methods: This review concentrates on cellular and genetic drawbacks that can lead to the appearance of glioblastoma. National Center for Biotechnology Information (NCBI) was the main source used for writing this review article, followed by Google scholar.

Results: Several genetic alterations and cellular pathways are involved in the appearance and progression of glioblastoma, including loss of heterozygosity (LoH), TP53 mutation, isocitrate dehydrogenase 1 (IDH1) mutation, P16INK4/RB1 pathway, and EGFR/PTEN/Akt/mTOR pathway. The majority (70%) of primary glioblastomas are caused by LoH, and it mostly occurs in older people. Secondary glioblastoma is mainly manifested by TP53 mutation and usually affects younger people. Understanding the alterations and cellular mechanisms involved in glioblastoma is important in developing new therapeutic regimes. Surgery, radiation therapy, temozolomide, and TTFields are the four most important therapeutic options available for treating patients.

Conclusion: Glioblastoma is a malignant and hardly-survived tumor that uses different cellular pathways and manifests various genetic alterations for its development. LOH10q and TP53 mutation were the most frequent gene alterations recognized in primary and secondary glioblastoma, respectively. Due to recent advances in understanding the cellular and molecular complexity of this tumor, several promising medical approaches have been included in treatment strategies, including the usage of nutlins, TMZ, and TTFields. Although this tumor is the toughest among gliomas, there is hope for new and better therapeutic options, which may ease the diagnosis and treatment process of this invasive tumor.

Keywords: Glioblastoma, EGFR, LOH, P53, TMZ

Cesarean section and preterm birth: A systematic review study (Review)

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Introduction: Premature birth is the common cause of neonatal mortality and childhood disability. Preventing preterm birth is a priority worldwide, albeit the exact cause is poorly understood. A large number of studies have suggested that there may be an association between cesarean delivery and subsequent preterm birth as a result of poor outcomes of cesarean sections.

Methods: This review was conducted to obtain relevant studies from the English databases Pubmed, Scopus, Web of Science, and Persian databases Iran Medex, SID, and Magiran with the English and Persian keywords cesarean section and preterm birth with all possible search combinations.

Results: Out of 2641 articles, 10 cohort studies were included based on the study criteria. 10 studies were of high quality and 4 studies were of medium quality according to the STROBE index. In general, The sample size of studies which were carried out from 2000 to 2020 ranged from about 30000 to 8000000. Our analysis showed that, cesarean section can increase the rate of preterm birth in following pregnancies.

Conclusion: A history of a previous cesarean section can lead to an increasing preterm birth rate in the subsequent pregnancy.

Keywords: Cesarean section, preterm birth, premature, cesarean delivery

Challenges and opportunities of use social media in medical education: A narrative review (Review)

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Introduction: Social media is a place where people can share, exchange, and communicate their ideas and knowledge. As a result, social media has become the new trend in communication and learning and its use in the field of medical education is increasing dramatically. Despite the increasing presence of social media in medical education, few studies have been conducted to determine their advantages and disadvantages. This review aimed to synthesize evidence regarding the use of social media in medical education, to identify features associated with positive and negative outcomes.

Methods: This is a narrative review study conducted in September 2022 using the keywords related to “social media”, “medical education” and “medical students” that searched in scientific databases including PubMed, Web of Science, Scopus, and Google Scholar search engine. After the initial search, screening was done by two authors in two stages: primary screening (inclusion criteria such as studies published between 2012 and 2022, English-language studies, original, intervention, and observation articles) then secondary screening (the title and abstract were for relevant to applying social media in educational interventions at each level of physician education included, and irrelevant articles such as patient training were removed). Finally, we independently extracted 1001 articles initially and combined data from articles that met the inclusion criteria (7 articles).

Results: The results of this study showed that the benefits of social media in medical education include: sharing educational materials (6 studies), the role of facilitating professors (4 studies), simplifying immediate group interaction,

networking and learning from others (4 studies), Saving time and ease of access (3 studies), instant feedback and quick response (3 studies), strengthening the student-teacher relationship and promoting educational interaction (3 studies), geographically free and distance learning (2 studies) , communication of people with different interests (2 studies), informal supplement for medical education (2 studies), access, student participation, flexibility and dynamics of these groups (1 study), replacement of expensive forms and surveys (1 study), peer education and increasing the vertical transfer of knowledge (1 study), faster identification of weak students (1 study), cost-effective (1 study), suitable for clinical communication (1 study), suitable bed for facilitating, speeding up and creativity in The educational process (1 study), is free (1 study) and saves time and money (1 study). Also, the disadvantages mentioned for social networks in medical education include privacy and respect for patient rights when transferring patient information (3 studies), distraction in studying (3 studies), lack of organization and quality assessment of posts, and failure to transfer all content (3 studies), dependency (3 studies), time lost from the students (2 studies), bad behavior of others (2 studies), the anonymity of people (2 studies) and peer pressure (1 study). Also, some have expressed the use of these tools with a sense of freedom and comfort, and some have considered participating in groups under the supervision of universities with a sense of lack of freedom in expressing their opinions. It was stated that marketing topics should not be discussed in educational groups.

Conclusion: This study stated the educational challenges and opportunities of social networks in medical education. Today, the use of social networks among students in medical education is common and affects the learning process, health, and personal life of learners. The benefits of using social networks in education have been shown, although disadvantages have also been mentioned for it, such as dependence and excessive use, lack of privacy, etc. In this study, solutions such as determining specific policies in the organization, designing an app are recommended by the university organization with high security, the presence of professors as supervisors and facilitators, and parents being informed about the student's program. Also, based on the reviewed studies, it is suggested that medical institutions guide students on how to get the most out of social networks, policies, and how to avoid its disadvantages. Also, he has created authentic pages in the social network so that authentic materials are available to students.

Keywords: social media, messaging, medical education, medical student, medical training

Changing oxidative stress parameters in the testis of depressed rats under hesperidin treatment (Research Paper)

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Introduction: Depression is a current and disabling disease. The prolonged psychological stress is a causative factor for depression, which leads to increase in MDA levels, oxidative stress, and depressive symptoms. Depression causes hormonal imbalance which can affect the testicles. Extra ROS production and exhaustion of anti-oxidative defenses trigger pro-inflammatory. The levels of different oxidative stress markers (MDA, SOD) are found to be altered in depressive disorders MDA status is used as a biomarker for oxidative stress. The study aims to investigate the effects of hesperidin on MDA and SOD factors of oxidative stress in the testis tissue of depressed rats.

Methods: In this experimental study, we used 24 adult male rats. The animals were divided into four groups. The control groups that received saline for 14 days, the depressed group that received reserpine (0.5mg/kg) for 14 days, the hesperidin group that received hesperidin (20mg/kg) for 14 days, and the depressed group was treated with hesperidin, they first received reserpine for 14 days for induction of depression and then received the hesperidin (20mg/kg) for 14 days. In this study, a forced swimming behavior test was performed to confirm the induction of depression. 24 hours after the last injection, animals were sacrificed and the level of MDA and SOD were measured in the testis. The basis of the tissue MDA measurement method is based on reaction with thiobarbituric acid (TBA), and extraction with butanol. Data were analyzed by using One-Way ANOVA.

Results: The results showed that in the forced swimming test, as an index of depression induction, the mobility time increased significantly between the depressed group and the hesperidin treatment group (p<0.05). The level of MDA has changed significantly between groups treated with hesperidin and the control group The result shows the level of SOD between groups was not changed significantly.

Conclusion: It seems that hesperidin as an antioxidant can improve the MDA factor in oxidative stress in depressive rats.

Keywords: Depression, Hesperidin, Oxidative stress, MDA, SOD

Characterization of nano lipid system containing curcumin extract in order to prevent tooth decay by Mozafari method (Research Paper)

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Introduction: The aim of this research was optimization curcumin characteristics for oral hygiene application. Curcumin-loaded starch nano-particles were developed for enhancing adhesion property with enamel surface and best anti-bacterial effect against Streptococcus mutans.

Methods: The study was the experimental one. The nanoparticles synthesize was based on precipitation and ionic gelation method. Nanoparticles characterization was done by scanning electron microscopy, dynamic light scattering and determination of zeta potential. In addition, minimum inhibitory concentration (MIC) was assessed to evaluate the antibacterial properties of nanoparticles against Streptococcus mutans. The binding amount of nanoparticles to hydroxyapatite was evaluated and finally, the curcumin release from the nanoparticles was also assayed.

Results: The average size of optimized starch nanoparticles were about 58 nm. Also, zeta potential was -15, mV. Loading contents of nanoparticles were 89% measured by optical density from standard calibration curve of curcumin. In addition, minimum inhibitory concentration (MIC) of nanoparticles against Streptococcus mutans, was 0.204 and 0.438 mg/mL for starch nanoparticles and pure curcumin, respectively. It was also found that starch nanoparticles had inhibitory effect on bacterial biofilm.

Conclusion: Curcumin-loaded starch nano-particles improve adhesion properties and interactions with enamel and prevent dental caries of Streptococcus mutans.

Keywords: Streptococcus mutans, Curcumin, Dental caries.

Characterization of Quinolone Resistance in Klebsiella pneumoniae Isolates from Municipal sewage in Ardabil province, Iran (Research Paper)

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Introduction: Antibiotic-resistant genes and bacteria enter the environment in several ways. One of the main points of entry for bacteria that are resistant to antibiotics into the environment is municipal sewage. Public health is in danger when released into the environment because treating bacterial infections is adversely affected by the prevalence of antibiotic-resistant microorganisms in the human population. There are now fewer alternatives for treating infections brought on by Klebsiella pneumoniae (K.pneumoniae) due to the recent emergence of resistant forms of this bacterium, particularly those resistant to fluoroquinolone medications. This bacterium can cause pneumonia, septicemia, meningitis, diarrhea, and bacteremia in infants. In this regard, the primary resistance mechanisms to fluoroquinolone antibiotics in gram-negative bacteria include mutations in DNA gyrase and topoisomerase IV and plasmid-mediated antibiotic resistance genes. In this work, K. pneumoniae isolates from municipal sewage in Ardabil province, Iran, were examined for genetic alterations in the gyrA and parC genes and the frequency of plasmid-mediated quinolone resistance (PMQR) genes.

Methods: From municipal sewage, 250 K.pneumoniae isolates were obtained. The isolates were initially detected using standard biochemical testing. Then, using PCR and the proper temperature settings, molecular identification of the 16S ribosomal RNA gene was carried out to confirm K.pneumoniae species. Additionally, agar dilution and the disk diffusion method were used to test antibiotic sensitivity. Additionally, DNA sequencing was carried out to look at mutations linked to quinolone resistance as well as PCR was used to determine the presence of the PMQR, gyrA, and parC genes.

Results: In the current investigation, 210 (85%) of the isolates of K.pneumoniae lacked ciprofloxacin resistance. 133 isolates of K.pneumoniae

with ciprofloxacin resistance and 17 isolates with Asp87Asn mutation in the GyrA gene. 166 isolates were found to have the S80I mutation in the ParC gene. Furthermore, 156 K.pneumoniae isolates carried the qnrS gene, and 143 isolates had the qnrB gene, according to PCR screening for PMQR determinants. Additionally, 182 K.pneumoniae isolates were found to contain the aac(6')-Ib-cr gene. However, none of the isolates had any of the qnrA, qnrC, qnrD, or qepA genes.

Conclusion: Our study's findings demonstrated that the FQ resistance rate was high. Concerning findings included the incidence of PMQR genes in K.pneumoniae isolates as well as alterations in DNA gyrase and topoisomerase IV. Additionally, the interaction of these resistance mechanisms is crucial in establishing high-level FQ resistance. Municipal sewage, therefore, has a significant potential for bacterial and gene resistance to spreading to natural ecosystems and can be hazardous to human health.

Keywords: Municipal sewage; Quinolone Resistance; Klebsiella pneumoniae

Characterization of recombinant alpha-toxin AnCra1 from Iranian scorpion Androctonus crassicauda venom and its effects on mammalian sodium channels function (Research Paper)

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Introduction: Alpha-scorpion toxins with long-chain peptide and four disulfide bonds represent diverse pharmacological profiles for various subtypes of voltage-gated sodium channels. Obtaining the natural toxins are difficult and time-consuming process, which represents the major difficulty to interpreting analysis of their structural and functional properties. This study describes the toxin peptide and plasmid construct containing the gene coding for mammalian toxin AnCra1 from the Iranian scorpion Androctonus crassicauda venom.

Methods: We have established genetic construction of fusion protein in pET32a + vector containing thioredoxin (Trx-tag), enterokinase cleavage site and 6xhistidine-tag for efficient expression in Escherichia coli strain RG2 (DE3). The soluble expressed peptide, then purified by Ni–NTA resin affinity chromatography and its purity was confirmed by reverse-phase HPLC and mass spectrometry. Toxicity of recombinant AnCra1 in comparison with native toxin was assayed in NIH mice. The electrophysiological assays of rAnCra1 was examined on hNav1.5 and hNav1.7 channels expressed on HEK293 cell line.

Results: The expression of the TrxA 6 × His -AnCra1 fusion protein was successfully done in RG2 (DE3) and the molecular weight of purified rAnCra1, was determined 7433.54 Da. Recombinant AnCra1 exhibits approximately high toxicity, as reflected by their lethal doses that it was certainly 3.34 ± 0.04 µg per mice. The electrophysiological data showed that rAnCra1 selectively inhibits the fast inactivation of hNav1.7 channel (EC50 = 136.7 ± 6.6 nM)

Conclusion: Our findings demonstrate that the rAnCra1 is structurally and functionally analogous to alpha excitatory toxins; furthermore, expression and purification of bioactive scorpion toxins in bacterial cells can be a practicable and efficient way to obtain a novel source of toxin peptides as tools to study the function and physiological responses of ion channels.

Keywords: AnCra1 · Alpha-scorpion toxin · Recombinant expression · Voltage-gated sodium channel

Checking the ways for Prevention of tuberculosis in HIV patients (Review)

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Introduction: These days, Many people in The World are living With HIV. Given that they have Immunodefiency, and also there are some limitations about B.C.G vaccine injection for HIV patients, They are in danger of catch the tuberculosis more than others. also, HIV helps to faster progression of tuberculosis. therefore, scientists are trying to find ways to prevention of Tuberculosis in HIV patients and save their life.

Methods: At this article, other projects had been analyzed and with finding the connection between them some ways to prevention tuberculosis are written. We used articles with DOIs like "10.1080/17476348.2019.1569518" and "10.1038/nrmicro.2017.128" with the titles "Advances in the diagnosis, treatment, and prevention of tuberculosis in children" and "Pathogenesis of HIV-1 and Mycobacterium tuberculosis co-infection"

Results: 3. Results 3_1. Prevention of tuberculosis As we know, the tuberculosis(TB) and HIV pathogenesis are similar in some ways. Generally, some of the ways to prevention of tuberculosis are not eating junk and unhealthy food, diagnosis, check-up and not smoking. 3_2. HIV and tuberculosis As it was said, one of the most famous factors for tuberculosis is HIV; having HIV and its pathogenesis inside the blood help TB. There are some factors that can effect on body. If HIV infect someone, the possibility of getting tuberculosis will increase. 3_3. precis At least, prevention of HIV and cure will help the person to not get tuberculosis. There are too many measures to prevention these two illnesses; for example eating healthy, exercising, doing some check-ups.

Conclusion: contracting tuberculosis is more dangerous for HIV patients Than normal people. creating healthy lifestyle for HIV patients and also diagnosis and cure HIV are effective in prevention of TB. in the future, we can research about this topic's details. for example about more effective exercises. At least, we can say that the actions that are done because of HIV, can effect on TB, too. So it's important that what is the person, who has tuberculosis, eating and doing.

Keywords: tuberculosis; HIV; prevention; B.C.G vaccine;

Chemical composition and biological properties of Iranian propolis (Review)

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Introduction: Propolis is a natural product that is produced by honeybees from parts of plants, buds, and exudates. It has pharmacological and biology properties, which are related to its chemical composition. The general composition of this substance varies in different geographical locations and climates. The biological characteristics of propolis are attributed to its chemical composition especially polyphenols and flavonoids.

Methods: Having regarded the importance of acquiring drugs from natural sources, the purpose of the literature review was to summarize recent studies (PubMed, Scopus) on progress in active ingredients, pharmacological effects and extraction methods.

Results: Flavonoids, phenols, terpenes, and aromatic acid compounds are the main chemicals that characterize the different extracts of Iranian propolis. The diversity of flavonoid compounds in Iranian propolis showed the typical pattern of “poplar” propolis. Flavanone was the most dominant compound of flavonoids that were important for antioxidant activity. The extracts of most types of Iranian propolis and its flavonoids showed greater antibacterial activity against Gram-positive bacteria. Cytotoxic effect of extracts on cancer cell lines showed that ethanolic extracts had more inhibitory effects on cell lines than the other extracts. The obtained results of Iranian propolis supported anti-inflammatory effects on cancer cells.

Conclusion: The mechanism of action of propolis is still unclear, due to the synergistic interaction of the ingredients of propolis, and this natural substance has multi-target activity in the cell and it may play a promising role in the complementary medicine. The broad-spectrum biological potentials of Iranian propolis present it as an ideal candidate for the development of new, potent, and cost-effective herapeutic product.

Keywords: Biological, Chemical composition, Flavonoids, Propolis

Chimeric Antigen Receptor(CAR) T-Cell Therapy in Malignant Solid Tumors (Review)

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Introduction: Chimeric antigen receptor (or CAR) T-cell therapy, is a brand new shape of immunotherapy that makes use of specially altered T cells to extra especially target cancer cells, they may become a useful and effective therapy in the treatment of any kind of malignant solid tumors, for example, brain tumors (like Glioblastoma), breast cancer, Pancreatic cancer, and other cancerous tumors. The immune system is the body's protection against infection and cancer. it is made of unique cells and organs that defend the body from infection and most cancers. Immune cells or antibodies can be produced inside the laboratory beneath tightly controlled situations after which are given to patients to treat most Cancers and Solid Tumors. This personalized "Living Drug" can be effective in opposition to some human diseases.

Methods: A search became carried out in PubMed with the keywords "Chimeric Antigen Receptor" and "CART cell". The documents of interest were selected, and an essential review of the facts became completed. Chimeric Antigen Receptor (CAR) T-cell therapy entails genetic amendment of a patient's autologous T-cells to express a CAR specifically for a tumor antigen, observed through ex vivo cell enlargement and re-infusion returned to the patient. CARs are fusion proteins of a particular single-chain fragment variable from a particular monoclonal antibody and one or extra T-cell receptor intracellular signaling domains. This T-cell genetic change might also occur through viral-based gene transfer techniques or nonviral strategies. which includes CRISPR/Cas9(a simple two-component system used for effective targeted gene editing), DNA transposons ("jumping genes", that can move and integrate to different locations within the genome), or direct transfer of in vitro transcribed-mRNA by electroporation (a powerful tool for transient genetic modification of cells).

Results: Chimeric antigen receptor T (CAR-T) cell therapy has appeared as an efficient solution for relapsed or refractory "liquid tumors" Leukemia and Lymphoma. The medical achievement of CAR T-cell therapy in blood cancers has generated enthusiasm for checking out the technic in solid tumors. but, the biology of solid tumors is more complicated than that of hematological malignancies. This type of immunotherapy has revolutionized the treatment of oncological diseases, and the potential uses in sarcoma and carcinoma have lately been defined.

Conclusion: In this review, the principle design of CARs, the main genetic modification techniques, the potential uses in the treatment of Solid Tumors, Limitations of cancerous solid tumor treatment, are described. Chimeric Antigen Receptor T-cell clinical trials have generated incredible consequences inside the early results of CAR T-cell therapy for sufferers of blood cancers. They may become a useful and effective therapy in the treatment of malignant solid tumors in sarcoma and carcinoma.

Keywords: Chimeric Antigen Receptor CAR T-cell therapy Solid Tumor carcinoma sarcoma

Circuitry and regulatory mechanisms Of Mitochondria (Review)

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Introduction: Mitochondria are the major source of energy for the cellular activity, by ATP generation via oxidative phosphorylation. Emerging evidence of the last decade indicates that mitochondria form a highly dynamic intracellular network that executes the “quality control” of the organelle's population in a process that implies their fusion, fission and autophagic degradation (known as ‘mitophagy’). Mitochondria regulate the operation of intracellular signalling cascades, generate reactive oxygen species (ROS), execute fatty acids β-oxidation, participate in aminoacid metabolism, pyridine synthesis, phospholipid modifications, calcium regulation and cells survival, senescence and death. The homeostasis of any healthy cell implies also a controlled regulation of mitochondrial mass and function, as an adaptive response to safeguard the mitochondrial (mt) DNA and to meet the energy demands vital for cellular function.

Methods: The present study was conducted by systematic review. To access the Circuitry and regulatory mechanisms of Mitochondrial genomic and energy transduction machinery, articles indexed in databases Science Direct, PubMed, Scopus, Google scholar, web of science, Embase and Medline were used over 2018 to 2021. According to the defined criteria, finally 17 Full text articles were reviewed in this study.

Results: Transcriptional networks Transcription of the mitochondrial genome occurs bidirectionally from the L-strand promoter and H-strand promoter located on opposing mtDNA strands at OH and produces a polycistronic transcript spanning nearly the entire length of the mitochondrial genome A widely accepted model for the assembly of the mitochondrial transcription initiation complex maintains that mitochondrial transcription factor A (TFAM) interacts via its C terminus with mitochondrial transcription factor B2 (TFB2M) and subsequently recruits mitochondrial RNA polymerase (POLMRT) to the promoter region. MITOCHONDRIAL BIOGENESIS MACHINERY Mitochondrial biogenesis is a complex process. Indeed, mitochondria are organelles that harbor their own genome (mtDNA). In mammalian cells, mtDNA is a circular molecule, which encodes for 13 mRNAs, 22 tRNAs, and 2 rRNAs. All 13 mRNAs of mtDNA encode 11 subunits of the ETC complexes I, III and IV, and 2 subunits of ATP synthase (complex V). Mitochondrial biogenesis is regulated at the transcriptional level, by nuclear proteins. The main actor of this process is a transcription complex composed of four

proteins that belong to the same family: heme activator proteins (Hap) 2, 3, 4, and 5 Hap2p, Hap3p, and Hap5p form a complex that is bound to nuclear DNA, and Hap4p is the co-activator of this complex, a functional homolog of peroxisome proliferator-activated receptor γ (PPARγ) coactivator-1 (PGC-1α, see below). Hence, activity of the overall complex is mostly dependent on Hap4p. The HAP complex regulates the expression of genes encoding several proteins such as proteins of the Krebs cycle or proteins of the OXPHOS system. Mitochondrial genes expression depends on the RNA polymerase Rpo41 and its accessory transcription factor Mtf1 The process of mitochondrial biogenesis takes place mainly in healthy cells. Interesting, in cancerous cells enhanced oxidative phosphorylation and mitochondrial biogenesis were correlated with invasion and metastasis

Conclusion: Mitochondria are not static organelles but are mobile and dynamic. Recent findings provide evidence of direct connections and communication between mitochondria as well

Keywords: Mitochondrial genomic, energy transduction, MITOCHONDRIAL BIOGENESIS, Transcriptional networks

Circular RNA: biogenesis, function and roll in disease (Review)

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Introduction: circular RNAs are a category of preserved single-strand RNA molecules driven from deoxyribonucleic acidic or coding (DNA) exon and intron sequences by precursor RNA back–splice. circRNAs type covalently closed, continuous stable loops while not a five finish cap and a three finish poly(A) tail. circRNAs are attributed to their attainable contributions to sequence regulation through a spread of actions, together with sponging microRNAs, interacting with RNA-binding proteins, regulation transcription and splice, and macromolecule translation. In recent years, it's been disclosed that circular RNA will play a crucial and potential role in the progression and development of diseases notably cancer and DM. A growing studies of analysis is shown that the expression patterns and characteristics of circRNAs may partially make a case for the flexibility of circRNAs as potential biomarkers or therapeutic targets. within the gift review, the researchers gift this understanding of cricRNAs biogenesis, restrictive mechanisms, and a review of recent findings and circRNA as potential biomarkers and their role within the development and progression of diseases

Methods: For this article, we searched for keywords such as cancer, circRNA, genetic, diabetes, stomach cancer, lung cancer, breast cancer, disease, etc., and searched for topics such as circRNA in cancer, the function of circRNA, Biogenesis of We used circRNA, circRNA, and disease and... to search in different databases. For this article, we used to review and research articles with different IF.

Results: Aberrant expression of circRNA, alongside the dysregulation of mRNAs, miRNAs, and incRNAs, is concerned with the pathologic process of medicine malignancies. Some circRNAs have currently been shown to possess prognostic worth alone or together with illustrious cancer markers. circRNAs have the potential to be used as therapeutic targets in cancer The junction sequence allows reverse junction for a selected circRNA while not poignant the parental mRNA. Mammalian cells will acknowledge peripheral circRNAs from foreign varieties. Not all circRNAs are non-coding. circRNAs with different and distinct expression in tissues as well as suppressing and inhibiting and affecting the expression of other mRNA, incRNA and miRNAs

can be associated with various cancers such as lung cancer, stomach cancer, intestinal-gastric cancer, esophageal cancer, pancreatic cancer, cancer Liver and breast cancer. Many circRNAs have associated degrees of abnormal expression in growth tissue/blood/exosomes of growth patients.

Conclusion: The study of circRNAs could be a novel analysis field that has emerged with the fast development of technology. various vital roles of circRNA are highlighted, especially their operation in diseases starting from cancerous to noncancerous pathologies and their growth and progression, which remains less understood.CircRNA is currently renowned for interacting with polymer binding proteins, dominant conjunction, translations, etc. Increasing proof indicates that circRNAs play polar roles in physiological and pathological processes, expressing different sorts of circRNA square measure overexpressed in numerous cancer and diabetic cell lines and, if guided, will regulate the expansion and proliferation of those morbid cells. more studies on this ancient polymer can give a big perspective on cancer and polygenic disorder analysis. Furthermore, additional controlled and large-scale clinical studies square measure needed before cancer-specific circRNAs may be suggested for designation and treatment notably in cancer CircRNA's most significant functions square measure that they act as a possible biomarker in cancer and polygenic disorder because of their stability and tissue-specific, creating them associate degree acceptable candidate for biomarker studies. The discovery of circRNAs has beyond question enriched the content of polymer restrictive networks and has offered new approaches for the event of clinically translatable diagnostic prognostic biomarkers and therapeutic targets for cancer.

Keywords: CircRNA, Cancer, genetics, disease

Circulating Tumor DNA (ctDNA) in Hematological Malignancy (Review)

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Introduction: Tissue and bone marrow biopsies and other invasive and unpleasant procedures remain the gold standard for cancer diagnosis and surveillance. These procedures involve physical risks, and a single biopsy cannot account for the spatial heterogeneity of tumors. This review discusses the current knowledge and landscape of liquid biopsy ctDNA in hematological malignancies.

Methods: This study performed by using collected article in English were available on details of the main topic since 2000 to 2022 in Scopus, PubMed, Web of Science with keyword ctDNA, liquid biopsy, hematological malignancy, cancer. Articles were selected on the basis of the exclusion criteria and after reviewing were included in the study.

Results: With breakthroughs in noninvasive cancer detection and monitoring, doctors, especially hematologists, have become increasingly acquainted with the term "liquid biopsy." the concentration of cfDNA in cancer patients is often greater than in healthy individuals, indicating that the amount of cfDNA could be utilized for cancer screening. Circular tumor DNA (ctDNA) analysis has advanced fast for cancer detection, characterization, and monitoring. Increasing clinical evidence demonstrates this technology's capabilities as a diagnostic test. The full potential of ctDNA liquid biopsy in the diagnosis, characterization, and management of solid and hematological malignancies will be found through clinical trials that test its effectiveness in the real world

Conclusion: Much research has shown that ctDNA could be used as a noninvasive biomarker for disease monitoring in the past few years. However, few published research supports the use of ctDNA in hematological malignancy. In conclusion, ctDNA surveillance may help detect hematologic cancer patients at risk of recurrence before established clinical criteria.

Keywords: ctDNA, liquid biopsy, hematological malignancy, cancer

Clinical and Histological Types of Breast Cancer : an Overview (Review)

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Introduction: Breast cancer is the most frequently diagnosed life-threatening cancer in women and the leading cause of cancer death among women. In the last two decades, research related to breast cancer has led to extraordinary progress in our understanding of the disease. Moreover, breast cancer occurs when cells in breast grow and divide in an uncontrolled way while creating a mass of tissue called a tumor. Symptoms of breast cancer can include feeling a lump in breast, experiencing a change in the size of breast and seeing changes to the skin on breast. Furthermore, there is numerous types of breast cancer which I elaborate them in the following sentences.

Methods: To begin, non-Invasive Breast Cancer cells that are confined to the ducts and do not invade surrounding fatty and connective tissues of the breast. Ductal carcinoma in situ (DCIS) is the most common form of non-invasive breast cancer. Lobular carcinoma in situ (LCIS) is less common and considered a marker for increased breast cancer risk. Also, Invasive Breast Cancer cells that break through the duct and lobular wall and invade the surrounding fatty and connective tissues of the breast.

Results: Oancer can be invasive without being metastatic, spreading, to the lymph nodes or other organs. Either, Lobular carcinoma in situ (LCIS, lobular neoplasia), the term "in situ," refers to cancer that has not spread past the area where it initially developed. Further, LCIS is a sharp increase in the number of cells within the milk glands (lobules) of the breast. Ductal carcinoma in situ (DCIS), the most common type of non-invasive breast cancer, is confined to the ducts of the breast. For example, ductal comedocarcinoma.

Conclusion: Additionally, infiltrating lobular carcinoma (ILC), ILC is also known as invasive lobular carcinoma. ILC begins in the milk glands (lobules) of the breast, but often spreads (metastatizes) to other regions of the body. More, infiltrating ductal carcinoma (IDC), IDC is also known as invasive ductal carcinoma. IDC begins in the milk ducts of the breast and penetrates the wall of the duct, invading the fatty tissue of the breast and possibly other regions of the body. in addition, there are types that are less, for example, Medullary

carcinoma is an invasive breast cancer that forms a distinct boundary between tumor tissue and normal tissue or mutinous carcinoma which is also a rare breast cancer formed by mucus-producing cancer cells. There are others, such as tubular carcinoma, inflammatory breast cancer and Phylloides tumor.

Keywords: Breast Cancer

Clinical applications of nanotechnology in dentistry (Review)

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Introduction: Nanotechnology is science, engineering and technology that is performed at the nano-scale, which is about 1 to 100 nanometers. Nanotechnology is one of the important topics in dentistry. Nano hydroxyapatite, nano composite, nano filler, nano zirconia are some types of nano materials, which are widely used in medical sciences. There are promising results for the various applications of these materials in dentistry and according to the extensive research that is being done in around the world; we will probably face the discovery and increase of new nanomaterials. The purpose of this review is to investigate the application of nanotechnology in dentistry.

Methods: In this review study, after searching keywords (Nanotechnology, Dentistry and Clinical Applications) in databases such as Scopus, PubMed and Google Scholar, finally 17 articles were examined. All studies conducted until 2022 were in the field of nanotechnology in dentistry.

Results: The use of silver nanoparticles in tooth filling increases the beauty and mechanical quality of composites and prevents secondary tooth decay by minimizing the growth of biofilm and lactic acid. The addition of nano ZrO2 is suitable for increasing the mechanical properties of teeth. Fluoride toothpaste is suitable for early caries lesions; studies show that nano hydroxyapatite and fluoride have a synergistic effect. The use of organic-free implant paste consisting of two-dimensional magnesium phosphate nano-crystals, which have an incomparable ability and unique healing around the implant, has been proven. Adding silica nanoparticles to Fuji stones and inside the teeth makes it softer. A new orthodontic cement made using nCaF2 with small particle size and high surface area has antibacterial and demineralization properties, which for the first time has increased the potential to inhibit WSL by significantly increasing enamel hardness.

Conclusion: Despite the wide applications of nanomaterials in dentistry, there are also concerns in this field, for example, the discoloration of dental materials and dental plaque after integration with silver nanoparticles in some studies shows that more research is needed in this field.

Keywords: Nanotechnology, Dentistry, Clinical Applications

Clinical Decision Support Systems and internet of things for Personalized Healthcare System : A Review (Review)

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Introduction: Recent years have seen a phenomenal change in healthcare paradigms and IOT enables a common platform for seamless exchange between healthcare devices and stakeholders followed by an advanced analysis of the shared pool of data due to the rapid proliferation of wearable devices and smartphones, the Internet of Things enabled technology and with help of e-health, such as electronic record systems, telemedicine systems, personalized devices for diagnosis, etc is evolving healthcare from conventional hub based system to more personalized healthcare system (PHS). Also, it marks the foundation of Clinical Decision Support Systems which act as an assistive tool for medical personnel and count significantly toward decision support systems thanks to its efficient data analytics, enabling to have a holistic visualization of the healthcare scenario.

Methods: We searched English original articles in PubMed/Medline database using the MeSH, keywords including "internet of things" and " Clinical Decision Support System" from 2012 to 2022. It then excluded the articles about heart failure to do a focused review on Clinical Decision Support systems and internet of things.

Results: thanks to IoT, decision support systems can do more, by spanning their knowledge to the health records of the patients as well as deeper insights into the data. This work discusses an anIoT-based model that serves as the one-stop platform for all the inter and intra-entity communications in healthcare, as well as the assistive tool for the patients as well as medical personnel. Thereby, the decision support system is illustrated using k-means clustering and considering several physiological parameters impactful for cardiovascular diseases. It illustrates the foundation of decision support system in this scenario, for in-system prediction of the risk of a person for cardiovascular diseases.in other research CDSS, automated prediction and diagnosis PredictAD (Predict Alzheimer's Disease) is a project for developing a standardized and objective solution that would enable an earlier diagnosis of Alzheimer’s disease, improved monitoring of treatment efficacy, and enhanced cost-effectiveness of diagnostic protocols.

Conclusion: The Internet of Things paradigm represents the vision of the next wave of the ICT revolution. IoT-enabled technology in PHS will enable

faster and safer preventive care, lower overall cost, improved patient-centered practice, and enhanced sustainability. But, we are aware that the goals set up for IoT in healthcare are not easily reachable, and there are still many challenges to be faced, consequently, this research field is getting more and more impetus. Researchers with different backgrounds are enhancing the current state of the art of IoT in healthcare by addressing fundamental problems related to human factors, intelligence design and implementation, and security, social, and ethical issues. Future IoT-enabled PHS will be realized by providing highly customized access to rich medical information and efficient clinical decision-making to each individual with unobtrusive and successive sensing and monitoring.

Keywords: Internet of things, Clinical Decision Support System, IOT, CDSS

Cloning and expression of human interferon gamma in Escherichia coli
(Research Paper)

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Introduction: Human interferon gamma (hIFN-γ) is a glycoprotein that is produced by normal T and killer cells. hIFN-γ is often used in research due to its many roles in the immune system, such as antiviral activity, antitumor activity, and control of cellular apoptosis. The production of hIFN-γ in bacterial cells is associated with the formation of insoluble inclusion bodies. To overcome this problem, a protein fusion method was used.

Methods: In this study, based on the SUMO fusion system, the hIFN-γ along with the sumo tag was successfully cloned in the pET21b vector and expressed in Escherichia coli. The expression of hIFN-γ was induced by adding IPTG to a final concentration of 0.5 mM. at 24°C. Finally, the hIFN-γ was purified with a nickel column and treated with SUMO protease enzyme, in order to separate the SUMO part from the hIFN-γ protein.

Results: SDS-PAGE showed a protein band of about 35 kDa including sumo protein and hIFN-γ. Subsequently, the hybrid protein was treated with SUMO enzyme and hIFN-γ with a molecular weight of about 17 kDa purified.

Conclusion: SUMO fusion enhances protein expression, solubility, and purification of protein in E. coli. Also, SUMO fusion enhances the level of protein production. We by using this method produce the soluble hIFN-γ in E. coli.

Keywords: human interferon gamma, SUMO tag, solubility, Escherichia coli, purification

Co- localization of Flt1 and tryptase of mast cells in skin wound of rats with type I diabetes: Initial studies (Research Paper)

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Introduction: Random skin flap (RSF) is commonly used in plastic and reconstructive surgery, but its distal part often occurs ischemia. Type 1 Diabetes mellitus (T1DM), may be detrimental for flap survival by provide sever ischemia. We sought to determine the influence of DM on the relation between mast cells and angiogenesis by examining tryptase and Fms-like tyrosine kinase 1 (Flt-1), a well-known vascular endothelial growth factor receptor (VEGFR-1), in the surviving areas of RSF in healthy and diabetic rats.

Methods: 16 male rats divided into healthy and diabetic groups. T1DM was created in the diabetic rats, followed by generation of a RSF in both the control and diabetic rat. On day 7, the surviving areas of each RSF were recorded. Then animals were euthanized, and numbers of vessels, mast cells and co-localization of mast cell tryptase and Flt-1 were analyzed.

Results: T1DM decreased survival areas in the RSF compared to the healthy rats, with higher percentage of intact and degranulated mast cells. T1DM elevated the expression percentage of tryptase and VEGFR-1in the proximal and middle areas of the survival parts of the RSF in most diabetic rats.

Conclusion: Generally, our results showed that mast cell degranulation might have a positive correlation with VEGFR-1 and in this current model of ischemic tissue in diabetic rats, this finding could lead to poor angiogenesis and weakened blood vessel function, which might result in decreased RSF survival. Additional molecular mechanisms that pertain to the effects of DM on ischemic tissues healing such as this RSF model should be determined by further investigations.

Keywords: Angiogenesis; Flap; Ischemia; Vessel.

Co-treatment of Alpha-Lipoic Acid and Injectable platelet rich fibrin (i-PRF) bioscaffold can reduction of oxidative stress in mouse ovarian tissue following autotransplantation (Research Paper)

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Introduction: However, Ovarian tissue transplantation is best option for cancerous young woman. But, ischemia-reperfusion (I/R) injury remains the most important limitation of this method and Occurrence of oxidative stress then reduces the survival of autografted tissue. . Injectable platelet rich fibrin (i-PRF) is a liquid formulation of platelet rich fibrin (PRF) without the use of anti-coagulants. It contains a fibrin matrix resulted from fibrinogen molecules activation in plasma, leukocytes, circulating stem cells, platelets and growth factors. On the other hand Alpha-lipoic acid (ALA) is a powerful antioxidant that can inhibit oxidative stress and cell damage. In this study, we investigated the effect of co-treatment i-PRF bioscaffold and ALA on the Serum concentrations of malondialdehyde (MDA) and total antioxidant capacity (TAC) after mouse ovarian tissue transplantation.

Methods: Experimental samples consisted of three groups (n=6): control, autograft + saline (whole ovarian tissue transplanted in the gluteus superficialis muscle, saline directly injected into it), autograft + i-PRF+ ALA (first, the mice received 100 mg/kg" intraperitoneal injections of ALA, 30 minutes before transplantation than whole ovarian tissue transplanted in the gluteus superficialis muscle, i-PRF was directly injected into it). 7 days after ovary transplantation, the serum level of MDA and TAC were assayed. We Data analyzed dy one-way ANOVA and Tuckey's test and the means were considered significantly different at p-value < 0.05.

Results: In the the control group, the serum level of MDA significantly decreased in compare to other groups, while it showed a significant increase in the autograft group compared to the autograft + i-PRF+ ALA group ($p < 0.05$). Moreover, Serum concentrations of TAC decreased significantly in the autograft group compared to the control counterpart, whereas it increased significantly in the autograft + i-PRF+ ALA group compared to the autograft group ($p < 0.05$).

Conclusion: This results for the first time showed that concomitant use i-PRF bioscaffold and ALA can prevent IR damages in mice transplanted ovaries through reduction oxidative stress and improves thier function.

Keywords: Ovarian tissue transplantation, α-lipoic acid (ALA), Injectable platelet rich fibrin (i-PRF), Ischem

Collagen fibers extracted from the surface of the soft coral polyp Sarcophyton sp.: nature-inspired structure for the fabrication of tissue engineering scaffolds (Review)

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Introduction: Collagen is the main component of the extracellular matrix and the most abundant protein in the human body, which is widely used in the fabrication of tissue engineering scaffolds. Collagen solution is prepared during chemical processes, which destroy the native fibrillar structure of collagen, and its mechanical properties are reduced compared to native collagen. As a result, collagen-based scaffolds do not preserve the structure and mechanical properties of native collagen. To solve this challenge, we can take inspiration from nature. Over 3.8 billion years, nature has evolved objects highly efficiently using common materials. Understanding these processes and then being able to use and modify their mechanisms for the benefit of society leads to the improvement of many challenges.

Methods: Collagen fibers with a length of more than ten centimeters and a diameter of 5 to 10 micrometers were manually pulled out from the surface of the soft coral polyp Sarcophyton sp. and placed on the hydrogel with orientations desired to create a stable composite. This hydrogel can be made flat or tubular with a small diameter and used in various tissue engineering. This hydrogel was evaluated in terms of similarity to native collagen, mechanical properties, and biocompatibility.

Results: The amino acid content of these fibers was very similar to mammalian type I and II collagens, and the natural helical structure of collagen fibers was preserved in these extracted fibers. The mechanical properties of collagen fiber showed a superelastic behavior, and the elastic modulus increased with stress. The cell viability results showed that the coral collagen fibers were non-cytotoxic, and more than 80% of the cells survived.

Conclusion: This study showed that composites reinforced with collagen fibers extracted from soft coral exhibit superelastic behavior and biocompatible compositions similar to native tissues. This composite can be a

promising candidate for various tissue engineering such as blood vessels, skin, nerves, etc.

Keywords: Inspiration – Coral – Collagen fiber – Tissue engineering

Colon cancer diagnosis (Research Paper)

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1.
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Introduction: Cancer begins and spreads with the uncontrolled growth of body cells. The simple definition of cancer disease is as follows: the uncontrolled growth of body cells begins with disregarding the normal rules of cell division in the body. Normal cells of the body are constantly producing signals that indicate whether this cell should divide or differentiate into another cell or the life of this cell has ended. But cancer cells do not pay attention to these signals or they themselves produce these signals and are self-sufficient, which causes the uncontrolled growth of those cells and causes cancer [2]. Diagnosis and prevention of cancer is usually diagnosed with genetic tests, and patients are tested and examined based on clinical indicators, pathology or family history that can be verified. Genetic testing can be used as a prediction guide. Early detection of cervical, colon and lung cancer and timely intervention for treatment can improve a significant number of them and reduce the number of deaths [3]. Colon cancer is the third most common cancer worldwide and the fourth leading cause of cancer-related death, and with nearly 1.4 million new cases and 700,000 deaths, the prevalence of colon cancer is projected to increase worldwide. It is an increase that is predicted to reach 2.4 million people by 2035. In terms of geographical distribution, it compares the Human Development Index (HDI) between developed and developing countries. In countries with moderate to high HDI, prevalence and mortality are increasing (Eastern Europe, Asia and South America). Stabilizing or reducing the death rate is only in very advanced countries (United States of America, Australia, New Zealand, etc.). In the National Cancer Institute, colon cancer is defined as this, cancer is a disease in which the cells of the body divide abnormally without control and can attack the surrounding tissues. These cells can also spread to the affected parts of the body with the help of the blood and lymphatic systems. Colon cancer forms in the tissues of the colon. Rectal cancer and colon cancer are generally grouped together because they have many characteristics in common. There are many types of colon cancer, but about 96% of colon cancer is adenocarcinoma. Some other less common types of colon cancer include: Carcinoid Tumors that start in hormone-producing cells in the intestine. Gastrointestinal stromal tumors that develop in the interstitial cells of Cajal, in addition, sarcomas, which are very rare, can develop in blood vessels, muscles or connective tissues in the walls of the large intestine. Since most cancers are colorectal adenocarcinoma, we classify them into different groups. Adenocarcinoma begins in the epithelial tissues of the colon and intestine. Polyps are the most common precursor lesion of this type of cancer.

Mucus around the intestine can act as precursor lesions of colon cancer. Countries that have diets high in fat, red meat, and refined grains, and the amount of fiber and fruit consumption in them is low, the probability of colon cancer is higher in that society, and in addition to the diet, their living environment also has a great impact on the amount of colon cancer. He has colon cancer. Even with the progress of colon cancer science, the rate of survival and recovery is slow. Colorectal cancer prevention is a main goal for public health in different societies. The effects of diet on the occurrence of colon cancer are related to the fact that the diet is such that it prevents intestinal inflammation and reduces the risk of colon cancer. Foods that increase inflammation are high-fat foods and red meat. Vegetables have been studied a lot because of their protective effects against colon cancer, and some of their mechanisms include: epigenetic and xenobiotic regulation of metabolism, inhibition of cell proliferation and tumorigenesis, and their antioxidant activity. A high-fat diet (60% fat) is the background of colon cancer [4].

Methods: Required equipments are pH meter, balance, ultrasonic bath, fluorescence microscope. We use double distilled water to prepare solutions and dilute them. In order to remove the metal impurities in the carbon nanotubes and make them hydrophilic, we have to place them in a 0.2 M nitric acid solution for 15 hours until the surface of the carbon nanotubes oxidizes. Graphene oxide (GO) is obtained from graphite powder according to Hammer's method. For the synthesis of graphene nanocomposite and gold nanoparticles (rGO-AuNP), the method provided by Wang et al. was used. To measure the M2PK protein in feces, a number of stools from sick people should be collected and tested at different concentrations. Aptamer synthesis is the first step towards the production of our biosensor. First, we need to determine the sequence of our aptamer. Our aptamer structure..Aptamer sequence. It is used to detect colon cancer cells. We have to add parts to the beginning and end of the aptam, at the end of three primes we add amino-C6 and at the end of five primes we add fluorescein isothiocyanate (FITC). FITC is used to detect the connection between cells and aptamer using flow cytometer and fluorescence microscope. Aptamers are used for detection by chemically binding to our target cell or tissue. Four steps are used to create a link: 1) Creation of thiol group with 11-MUA coating on the electrode. 2) Activation of the COOH group in 11-MUA with ethyl (dimethylaminopropyl) carbodiamide (EDC) / N-hydroxysuccinimide (NHS). 3) binding with NH2 at the apex end of the aptamer. 4) coating with bovine serum albumin (BSA) to prevent non-specific binding. Before starting the diagnosis, we clean the electrode through the following four steps. 1) In order to bind thiol groups on the surface of the electrode, we place the electrode in ethanol/H2O solution at a ratio of 1/3 (V/V) for 18 hours. After 18 hours, we dry the solution with nitrogen gas. 2) N-hydroxysuccinimide (NHS) and N-ethyl-N-(3-diethylaminopropyl) carbodiimide (EDC) are used. EDC is used as a cross-

linker to form the amide bond, and NHS is used to activate the carboxyl group attached to EDC. We immerse the gold electrode in phosphate buffer containing salt (PBS) for 1 hour. This buffer, adjusted to pH 4.7, contains 2 mM EDC and 5 mM NHS. 3) After that, we immerse the electrode in Tris-HCl buffer for 2 hours. This buffer is adjusted to pH 7.6 and the ionic strength I is set to 0.14 and contains 0.4 µM of aptamer. 4) To prevent non-specific binding, we immerse the electrodes in distilled water containing 1% BSA for half an hour. We also put it in Tris-HCl buffer for 10 minutes to remove unlimited BSA. We use several different cells to verify the performance of the apta sensor to find out the level of aptamer working properly. Flow cytometry and fluorescence microscopy are used to evaluate the binding between aptamer and cells. For this purpose, we use FITC as a functional fluorescein molecule with an isothiocyanate reactive group (N = C = S), with the peak wavelength of the excitation and emission spectrum from 495 to 519 nm. After determining the desired range of detectable current, we determine the positive and negative control of these tests All electrochemical measurements are performed at 25 °C in PBS containing K3 [Fe(CN)6] at a concentration of 1 mM]. PBS adjusted to pH 4.7 was used as electrolyte. In this measurement method, cyclic voltammetry (CV) is used as an electrochemical method. The connection of colon cancer cells to aptamer using fluorescence microscope and using microscopic images has already been diagnosed. Flow cytometry is the best method to confirm binding between target cells and aptamer. Using negative and positive control cells, we distinguish. By comparing the control chart, we distinguish between positive and negative. We examine different concentrations of 12, 25, 50, 100, 1000, 17000 cells per milliliter to find the best concentration for cancer detection [1].

Results: According to the research done by different people and scientists, different methods have been identified to diagnose colon cancer. Each of these methods has its own characteristics. But some methods cause late diagnosis and other treatment methods are not working and the cancer has progressed a lot. But this method of tests done by different people has shown that it has the ability to identify in the first stages, which helps both the treatment of the person and the doctors to choose the right treatment and to treat the person in a shorter time. advance

Conclusion: According to the studies, this method has the ability to identify a person's disease in the first stages, which helps both the treatment of the person and the doctors to choose the right treatment and to advance the treatment of the person in a shorter time. Due to its accurate sensors and specific identifiers, this method can correctly diagnose the disease and reduce the additional costs of the person and make it a much better result of the treatment. Of course, this method required more and more detailed laboratory research.

Keywords: Cancer - large intestine - nanoparticles - colon cancer

colorectal cancer and CDH3 Gene (Research Paper)

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Introduction: Colon adenocarcinoma (COAD) is one of the most common types of gastrointestinal malignancies, and studying molecular mechanisms can be an important step in the prevention process. cadherin3(CDH3), a gene encoding P-cadherin, which is one of the main components of adherens junctions and is closely related to the development and development of various types of tumors(1).One of the non-specific clinical symptoms of this cancer is very fast progression and metachronous metastasis, which is the cause of death with colon adenocarcinoma (COAD)(2).

Methods: First, gene expression data of COAD patients (GSE50114) were obtained from NCBI gene. And then of (GEO) expressed genes were analyzed by GEO2R And using the Encori database, DIY expression, survival, and co-expression charts were checked, the Enrichr database was used to analyze the signaling pathway. And the signaling pathway was checked in KEGG and Reactome database.Then, from the String data, we were able to check the interaction between genes, and with Mirwalk, miR was selected and the relationship between miR expression in COAD disease was checked in Encori LncBase, lncRResearch obtained the list of lncRna and its accuracy was checked in the gene card website. And in lnc base, lnc related to miRna was investigated And finally ceRNA was predicted.

Results: CDH3 was found to be a significantly up-regulated gene in COAD tissue compared to normal human tissues. In addition, COAD patients with higher levels of CDH3 in their tumor tissues survive longer compared to patients with moderate to low levels (3). CDH3 gene regulates tight junction & estrogen signaling pathways & adherens junction ⁄It is associated between miR-1250-5p and LAMP-a51 And because this lcnc gene It regulates the CDH3 gene and regulates the signaling pathway on COAD disease, and expression disorder causes COAD disease. and LAMP-a51 expression disorder causes COAD dieses disorder .

Conclusion: miR-1250-5p LAMP-AA1 and LAMP-a51 regulate the dieses state by regulating CDH3 expression.

Keywords: Colorectal cancer;Data analysis:CDH3 Gene

Combination treatment with antibody-drug conjugates targeting Ror1 and Sortilin induces tumor regression in a mouse model of breast cancer (Research Paper)

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Introduction: Triple negative breast cancer (TNBC) is highly invasive, metastatic and recurrent. Antibody drug conjugate (ADC) has received widespread attention in novel breast cancer therapy approaches. Among the tumor related antigens, Ror1 and Sortilin are among the most promising targets. The aim of this study is to produce immunoconjugates against these two molecules and measure their efficacy in vitro and in vivo separately and in combination with each other to overcome the stated limitations associated with cancer cells.

Methods: In this study, expression of Ror1 and Sortilin antigens in breast cancer cell lines, MDA-MB231 and 4T1 were evaluated using flow cytometry and immunocytochemistry. Monoclonal antibodies were conjugated to DM1 by Sulfo-SMCC linker and anti-tumor activity of anti-Ror1 and anti-Sortilin antibodies and their respective ADCs were assessed in vitro and in vivo.

Results: Flow cytometry revealed an increased expression level of Ror1 at 54.84 ± 2.63 (P <0.001) and 40.7 ± 2.54 (P <0.001) of MDA-MB231 and 4T1 cells, respectively. Immunocytochemical analysis confirms these findings. There is a substantial difference in the level of apoptosis caused by the Ror1-ADC compared to intact antibody. The highest rate of apoptosis was seen in the MDA-MB231 cells with a rate of nearly 50% for Ror1-ADC. Sortilin-ADC could induce 45.2% of apoptosis in 4T1 cells. Examination of in vivo activity revealed better tumor growth impediment in the two recipient groups, Ror1-ADC and Sortilin-ADC compared with BALB/c mice receiving the same amount of Ror1 and Sortilin antibodies (P <0.05). while antibody treatment showed no apparent effect on breast tumor growth, the mice survival rate increased compared to irrelevant-mAb group. In the case of the ADC

combination treatment group, the results are remarkably indicative of success with a high percentage of tumor growth control.

Conclusion: Our study reveals the important role of Ror1 and Sortilin in the survival of breast cancer cells. Our findings also suggest that mAb-DM1 compounds have strong and selective antitumor activity in vitro and in vivo that augment their possible use as a Therapeutic agent in targeted cancer therapies, especially TNBC cancers with high heterogeneity that makes treatment choices more challenging.

Keywords: Triple negative breast cancer; Antibody-drug conjugates; Sortilin; Ror1

Comparative study of carboplatin and cyclophosphamide effects on p53 protein using molecular docking method (Research Paper)

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Introduction: Tumor protein P53, also known as p53, cellular tumor antigen p53, is any isoform of a protein encoded by homologous genes in various organisms, such as TP53 (humans) and Trp53 (mice). This homolog (originally thought to be, and often spoken of as, a single protein) is crucial in vertebrates, where it prevents cancer formation. As such, p53 has been described as "the guardian of the genome" because of its role in conserving stability by preventing genome mutation. Carboplatin, sold under the trade name Paraplatin among others, is a chemotherapy medication used to treat a number of forms of cancer. This includes ovarian cancer, lung cancer, head and neck cancer, brain cancer, and neuroblastoma. It is used by injection into a vein. Cyclophosphamide, also known as cytophosphane among other names, is a medication used as chemotherapy and to suppress the immune system. As chemotherapy it is used to treat lymphoma, multiple myeloma, leukemia, ovarian cancer, breast cancer, small cell lung cancer, neuroblastoma, and sarcoma. It is taken by mouth or injection into a vein. In this descriptive-analytical study, we investigate carboplatin and cyclophosphamide effects on P53 protein using molecular docking method.

Methods: In this study, we used pubchem.ncbi.nlm.nih.gov, www.drugbank.com,and www.uniprot.org to examine carboplatin and cyclophosphamide. Also software ViewerLite, AutoDockTools-1.5.6, Chimera 1.15 and PyRx were used.

Results: After performing molecular docking separately for carboplatin and cyclophosphamide, we found that conformation1 of carboplatin with negative binding affinity and RMSD had a better effect on P53 protein.

Conclusion: According to docking studies, we found that carboplatin had a better effect on P53 protein to induce apoptosis and prevent cancer cell growth.

Keywords: Molecular docking, P53 protein, Carboplatin, Cyclophosphamide

Comparative study of fluorouracil and fludarabine effects on p53 protein using molecular docking method (Research Paper)

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Introduction: Fluorouracil (5-FU) is a pyrimidine analogue used as an antineoplastic agent to treat multiple solid tumors including colon, rectal, breast, gastric, pancreatic, ovarian, bladder and liver cancer Fludarabine is a purine analogue and antineoplastic agent used in the therapy of chronic lymphocytic leukemia (CLL) and in immunosuppressive regimens in preparation of hematopoietic cell transplantation (HCT) TP53 is found in increased amounts in a wide variety of transformed cells. TP53 is frequently mutated or inactivated in about 60% of cancers. TP53 defects are found in Barrett metaplasia a condition in which the normally stratified squamous epithelium of the lower esophagus is replaced by a metaplastic columnar epithelium. The condition develops as a complication in approximately 10% of patients with chronic gastroesophageal reflux disease and predisposes to the development of esophageal adenocarcinoma In this descriptive-analytical study, we investigate fluorouracil and fludarabine effect on p-53 protein using molecular docking method.

Methods: In this study, we used the Pub Chim site at pubchem.ncbi.nlm.nih.gov, Dragbank www.drugbank.com, and www.uniprot.org to examine Fluorouracil and Fludarabine derivatives. Also from the software ViewerLite, AutoDockTools-1.5.6, Chimera 1.15 and PyRx were also used. In this article, we first saved fluorouracil and fludarabine from a pub site as a pdb file.

Results: According to Docking studies, we found that conformation of fluorouracil 1 with negative binding affinity and RMSD had a better effect on P53 protein to induce apoptosis and prevent cancer cell growth.

Conclusion: better effect on P53 protein to induce apoptosis and prevent cancer cell growth.

Keywords: p53 fluorouracil and fludarabine molecular docking method

Comparative study of the effect of the Favipiravir drug on NEF protein (TNIP1_Human) using molecular docking method (Research Paper)

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Introduction: Introduction: Favipiravir, sold under the brand name Avigan among others, is an antiviral medication used to treat influenza in Japan. It is also being studied to treat a number of other viral infections, including SARS-CoV2. Drug pyrazine carboxamide derivative.[1] NEF is one of many pathogen-expressed protein, known as virulence factors, which manipulate the host's cellular machinery and thus allow infection, survival, or replication of the pathogen. TNIP1_Human (UniProt name).[2] In this descriptive-analytical study, we investigate the Favipiravir drug on TNIP1_Human (NEF) protein and its effect on using the molecular docking method

Methods: PubChem.NCBI.nlm.NIH.gov, Dragbank website, and uniprot website. From software, Chimera1.15 and PyRx were also used.This article first saved the Favipiravir drug from the site as a pdf file.We edited the target protein using Chimera1.15 software. NEF protein had three chains and, in this study, we only used the chain for another adaptation, and the rest were removed. Also, this software removed water molecules from the protein, and hydrogen molecules were removed. Then using PyRx software, we started the molecular docking in which the appropriate grid box was selected

Results: Result: After performing molecular docking for the Favipiravir drug, the results are shown in the table below Binding affinity (kcal/mol) :-4.3 Favipiravir Binding affinity (kcal/mol) RMSD upper bound:0 RMSD lower bound:0.0

Conclusion: According to Docking studies, we found that conformation of Favipiravir drug with negative binding affinity and RMSD had not to effect on NEF protein.

Keywords: NEF , docking , Favipiravir , pubchem , uniprot.

Comparative study of the findings of the first complete blood cell count in determining the outcome of patients diagnosed with covid-19; A cross-sectional study (Research Paper)

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Introduction: Background: Coronavirus 19 has become a global health threat that has affected high-density areas, such as military barracks. There is an urgent need for an accurate and robust risk assessment tool to assess the prognosis of the disease, which is also easy and cost-effective to implement. Aims: The aim of this study was to compare the findings of the first complete blood count in discharged patients with Coronavirus disease with the death.

Methods: Methods: This retrospective cross-sectional study was performed on 213 patients with a definitive diagnosis of Coronavirus disease. The findings of the first Complete blood count (CBC) were compared to estimate the survival of discharged and deceased patients. Data were analyzed by using Medcalc.20.013 software.

Results: Results: The frequency of death was 35.2%. The increase in white blood cell had a poor predictor of death (ROC = 0.66). The decrease in hemoglobin in predicting death lacked Diagnostic Estimates (ROC = 0.58). Platelet augmentation was not effective. Mean corpuscular volume increase had poor detection Estimates (ROC = 0.60). Increase in red blood cell distribution width had poor detection Estimates (ROC = 0.66). The increase in neutrophils was good in predicting death (ROC = 0.70). The decrease in lymphocytes was good in predicting death (ROC = 0.70). The increase in Neutrophil to Lymphocyte Ratio was good in predicting death (ROC = 0.70). The increase in Platelet to Lymphocyte Ratio was poor Diagnostic Estimates in predicting death (ROC = 0.67). The increase in Systemic Immunity Inflammation index in predicting death had poor diagnostic Estimates (ROC = 0.68).

Conclusion: Conclusion: The results of the present study showed that demographic factors have no effect on survival prediction. Based on the first findings of CBC test, three factors predicting death risk prediction (Neutrophil increase, Lymphocyte decrease and Neutrophil-Lymphocyte Ratio increase) with good diagnostic Estimates. This indicates that this diagnostic test is

accurate and inexpensive in predicting the deterioration and survival of Coronavirus disease patients.

Keywords: Keywords: Coronavirus disease, Survival, Complete Blood Count, Prediction rate

Comparing the effect of Galantamine and Rivastigmine on beta-amyloid protein using docking method (Research Paper)

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Introduction: Galantamine and Rivastigmine are cholinesterase inhibitors and are used to treat mild to moderate Alzheimer's disease. The main role of these drugs is to reduce the progression of clinical symptoms of Alzheimer's disease. In Alzheimer's disease, the central cholinergic neurons are disturbed due to the reduction of choline synthesis and its consumption. Cholinesterase inhibitors that reduce the breakdown of acetylcholine in the brain can be considered as a suitable drug. One of the events of Alzheimer's disease is the deposition of different proteins in the brain of Alzheimer's patients. These proteins accumulate in the extracellular spaces in the form of amyloid deposits, one of these proteins is amyloid-beta. The reasons for the accumulation of amyloid-beta protein are the excessive production of this protein and the inability to remove amyloid-beta from the brain, which can be involved in the development of Alzheimer's disease. In this investigation, a comparative study of the effect Galantamine and Rivastigmine, on beta-amyloid protein, which is involved in the formation and progression of Alzheimer's disease, has been done using the molecular docking method.

Methods: In this study, the website www.uniprot.org was used to investigate amyloid-beta protein. Also, used the pubchem.ncbi.nlm.nih.gov site to check the information of the drugs considered in this article. Chimera 1.15 and PyRx software were used for docking. At first saved amyloid-beta structure from a Uniprot site as a pdb file. Then the 3D structures of Galantamine and Rivastigmine drugs were saved in sdf format. Specifications of Galantamine: MF: C17H21NO3. Galantamine is a tertiary alkaloid and a competitive inhibitor of acetylcholinesterase enzyme, which is considered as a therapeutic target for Alzheimer's disease. Galantamine was extracted from botanical sources, such as Galanthus nivalis. As an inhibitor of acetylcholine, Galantamine prevents its breakdown in the synaptic space and increases its neurotransmission. This drug was approved by the FDA in 2001 for the treatment of mild to moderate Alzheimer's. Specifications of Rivastigmine: MF: C14H22N2O2. It is a reversible cholinesterase inhibitor. Rivastigmine is a carbamate ester and a tertiary amino compound. Rivastigmine is a parasympathomimetic or cholinergic agent for the treatment of mild to moderate dementia of the Alzheimer's type. Editing of the target protein was done by Chimera 1.15 software. Amyloid-beta protein has 4 chains, in this study only chain A was examined and the rest of the chains were removed. Using this software, water molecules were removed from the structure and

hydrogen molecules were added. After optimizing the structure, we used PyRx software to perform molecular docking and the gridbox was as follows: scores centers X= 0.992678 [95.41000366210938, 103.9000015258789, 208.07000732421875] Y= 0.963918 [109.41000366210938, 107.9000015258789, 214.07000732421875] Z= 0.71395 [91.41000366210938, 109.9000015258789, 174.07000732421875]

Results: After performing molecular docking for two drugs Galantamine and Rivastigmine, the results were obtained according to the following table: RMSD upper bound RMSD lower bound Binding Affinity(kcal/mol) Galantamine 0.0 0.0 -6.0 Conformation 1 9.708 7.537 -5.8 Conformation 2 4.709 2.596 -5.8 Conformation 3 8.68 6.569 -5.8 Conformation 4 8.553 7.325 -5.7 Conformation 5 4.379 1.799 -5.7 Conformation 6 28.189 25.699 -5.6 Conformation 7 8.848 6.653 -5.6 Conformation 8 15.953 14.135 -5.6 Conformation 9 The result of Galantamine docking RMSD upper bound RMSD lower bound Binding Affinity(kcal/mol) Rivastigmine 0.0 0.0 -5.0 Conformation 1 12.301 10.829 -4.7 Conformation 2 13.18 10.539 -4.7 Conformation 3 12.766 10.493 -4.5 Conformation 4 13.1 10.917 -4.5 Conformation 5 11.692 10.705 -4.5 Conformation 6 5.708 2.704 -4.4 Conformation 7 11.517 10.224 -4.4 Conformation 8 7.942 5.168 -4.4 Conformation 9 The result of Rivastigmine docking

Conclusion: According to the investigations, Conformation1 of Galantamine with negative binding affinity -6.0 and RMSD 0.0 has a better effect on amyloid-beta protein and preventing the progression of Alzheimer's disease.

Keywords: Alzheimer's disease, Galantamine , Rivastigmine , beta-amyloid protein , docking method.

Comparing the effect of Tetrabenazine, Deutetrabenazine and haloperidol drugs on huntingtin protein (Research Paper)

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Introduction: Huntington's is a hereditary disease that is often inherited and is caused by the huntingtin protein. Huntington's is a brain disease that progresses over time. Although there is no definitive treatment for this disease today, doctors prescribe three drugs Tetrabenazine, Deutetrabenazine and Haloperidol to control the disease and reduce its complications. In this research article, we used the molecular docking method to investigate the interaction between these drugs and huntingtin protein.

Methods: in this research paper, we used molecular docking methods. for this purpose, we downloaded the structures of drugs and protein from uniport and pubchem website after this, we prepared the protein by making some changes in the chimera program. at the end, we used the pyrx program to dock and analyse the results.

Results: all three drugs have a suitable binding affinity (more negative than 5) and also in at least one of the conformations, they have RMSD lower band and RMSD upper band equal (0.0)

Conclusion: According to docking studies, we found that all three drugs tetrabenazine, deutetrabenazine and haloperidol have a good interaction with huntingtin protein. Although, according to the numbers, Haloperidol drug has obtained a better result of docking with huntingtin protein compared to the other two drugs due to its very suitable binding affinity in conformation 1 .

Keywords: Huntingtin protein - Molecular docking - Tetrabenazine - Deutetrabenazine - Haloperidol

Comparison Achillea millefolium extract antimicrobial action and antibiotic resistance isolates Staphylococcus aureus and Enterococcus feacalis from clinical and standard samples in Isfahan Hospital

(Research Paper)

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Introduction: S.aureus and E.fecalis are important factors that cause disease in people, while antibiotic resistance increase rapidly in the world in recent years. Then researchers trend toward herbal cures. The aim of this study, check the antimicrobial activity of A.millefolium extract and antibiotic resistance for S.aureus and E.fecalis.

Methods: Achillea millefolium was provided and dried. Then extract methanol, ethanol, and Easton extract from the plant. Standard samples included extract S.aureus and E.feacalis collected from IROST. A total of 6 clinical specimens (3 S.aureus and 3 E.feacalis) were taken from Isfahan hospital and identified all isolates. Antibiotic resistance was assessed using disk diffusion method for Vancomycin, Cefazolin, Gentamicin, Tetracyclin, Ciprofloxacin, Oxacillin, and Trimethoprim-Sulfametaxole. Kirby-Bauer antibiogram conventional method was performed for the determination of antibiotic resistance bacteria. Antibacterial activity of extracts was evaluated by disk diffusion method, Concentration of herbals that inject was 0/5, 0/250, 0/125,0/0625 mg/ml.

Results: Most S.aureus are resistant to Cephazolin, Tetracycline, Oxacillin, and Vancomycin, and E.fecalis show resistance to Cephazolin and Vancomycin. Herbal extracts affect bacteria but not as much as antibiotics.

Conclusion: In this study, samples showed vancomycin and cefazolin resistance, which was an alarm of the most important reason for antibiotic resistance used a lot of them by people, especially B-Lactam antibiotics cause resistance to several drugs. To prevent and decrease antibiotic resistance must use antibiotics under supervision with suitable doses. Various concentrations of methanol, ethanol and acetone extracts have antibacterial resistance but it was so little. The results showed that A.millefolium hadn’t

enough effect on gram-positive bacteria, maybe it affects gram-negative bacteria. Suggested examination extract of A.millefolium on gram-negative bacteria.

Keywords: Achillea millefolium, Staphylococcus aureus, Enterococcus feacalis, antibacterial resistance.

Comparison check The effect of drugs novantrone(Mitoxantrone) & prozak (Fluoxetine) on protein MBP by molecular docking method (Research Paper)

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Introduction: Protein information:Myelin basic protein (MBP) is a protein believed to be important in the process of myelination of nerves in the nervous system. MBP maintains the correct structure of myelin, interacting with the lipids in the myelin membrane. MBP was initially sequenced in 1971 after isolation from bovine myelin membranes. Drug information :novantrone(Mitoxantrone): Mitoxantrone for the treatment of leukemia and other cancers It is also used to treat multiple sclerosis (MS). This drug is known as a group of drugs that They are known as anthracandiones and they slow down or stop the growth of certain cells (including cancer cells and cells that affect the body's natural defenses). prozak (Fluoxetine): Fluoxetine is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class . It is used for the treatment of major depressive disorder, obsessive–compulsive disorder (OCD), bulimia nervosa, panic disorder, and premenstrual dysphoric disorder. The scope of this work is much more than the mentioned materials.The purpose of this project is to compare the effects of novantrone(mitoxantrone) and prozak(fluoxetine)on mbp protein.

Methods: Doking articles are done in a descriptive_analytical way. Pyrx and chimera's applications are used in this article .First , we searched for the desired protein through the uniport site , then we choosed its human sample and searched for its molecular form it gave us a variety of protein samples , we choosed a sample that has fewer chain and it has more initial and terminal nucleotides then we saved the protein file in pdb format . We searched for the drug we want (novantrone /prozak) through the pubchem site then saved its three-dimensional structure in sdf format. To do the docking process with the chimera program we removed the extra chains , water molecules and ions and we added hydrogen . finally , we performed the process on chain (a) . we saved the final file in pdb format.

Results: According to the docking results of the drug effect preozak(Fluoxetine) on protein MBP Compared to drugs novantrone(Mitoxantrone) It is better.

Conclusion: According to the docking results of the drug effect preozak(Fluoxetine) on protein MBP Compared to drugs novantrone(Mitoxantrone) It is better.

Keywords: MBP protein, novantrone(Mitoxantrone), prozak (Fluoxetine), MS disease, Molecular docking

Comparison of nucleotide alignment and protein feature of OPA gene in Neisseria meningitides and Neisseria gonorrhoeae (Review)

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Introduction: The genus Neisseria is the type of the family Neisseria cease. Members of the genus Neisseria are gram-negative mammals and reptiles, although some species are primarily human pathogens. The species can largely be defined as either pathogenic or commensal, with Neisseria gonorrhea and Neisseria meningitides being recognized as important human pathogens. The commensal Neisseria are largely confined to the upper respiratory treat of human. N. gonnorrhoeae subspecies Kochi was isolated from conjunctival cultures from patients in rural Egypt and was first distinguished in 1897. N. meningitides were isolated in 1887 by Weichselbaum from the cerebrospinal fluid of patients with acute meningitis . The genomes of N. meningitis strain MC58 (group B) and 22491 (group A) and the genome of the gonococcal strain FA1090 (unpublished) have been completely sequenced . The repertoire of genes encoded by N. gonorrhea and N. meningitides is highly homologous; identically expressing more than 90 percent of their genes . It is estimated that about 1607 potential proteins are expressed by N. meningitides. Genome analysis of the N. meningitides strain 22491 indicates that this organism encodes a complete set of enzymes for glycolysis (apart from fruk and PFA), gluconeogenesis, the pentose-phosphate, and Ed path-way, the pyruvate dehydrogenase complex and the TCA cycle. N. meningitides appears to be capable of de novo synthesize most of the amino acids (with the exception of asparagine and methionine), purine and pyrimidine nucleotides.

Methods: The protein and nucleotide sequence of the OPA Neisseria meningitides species was extracted from the NCBI site. BLAST, the complementary, reciprocal and online bioinformatics software, was the reference nucleotide sequence employed

Results: The result for 2-rune bacterial membranes as Neisseria meningitides and Neisseria gonorrhea were concluded. This includes a phylogenetic tree for sequence similarity survey, consensus sequences, percent of nucleotide between sequences, amino acids forming protein sequences, the forecast of epitopes, and the protein structure. The opacity proteins mediate a variety of

interactions between the bacterium Neisseria meningitides and its human host. OPA proteins cause the gonococcus to stick together in colonies and also binds the bacteria to cells containing carcinogenicity antigens.

Conclusion: The results showed compelling similarity between sequences, the percentage of proteins in reference sequences and amounts of elements in reference sequences. They have alternatively encountered diversity between sequences, forecasted the protein's location in the membrane and distinguished the structure of the proteins and epitopes.

Keywords: Neisseria gonorrhoeae, Neisseria meningitides, Nucleotide, OPA gene, Protein, BLAST

Comparison of the effect of liposomes of Peppermint extract and Cinnamon essential oil against Staphylococcus aureus with beta-lactamase gene isolated from packaged minced meat in Yazd (Research Paper)

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Introduction: Staphylococcus aureus is one of the most important pathogenic microorganisms in meat products, especially those that come into contact with the hand during repeated production. Beta-lactamase drugs, especially the new generation of Cephalosporins, is used to treat most infections caused by Staphylococcus aureus, but the production of beta-lactamase by some strains has failed to treat infections associated with the organism. The aim of this study was to evaluate the degree of contamination and compare the antimicrobial effect of liposomes Peppermint extract and Cinnamon essential oil on Staphylococcus aureus with beta-lactamase gene isolated from minced meat in Yazd.

Methods: For this purpose, sampling of 45 packaged meat distribution and supply centers in Yazd city was performed under hygienic conditions and all samples were tested for the presence of Staphylococcus aureus with beta-lactamase gene tested by biochemical methods and molecular confirmation with PCR test. Were placed. The antibacterial effect of the liposomes of red pepper extracts and red onion on the mentioned isolates was evaluated with the tests of minimum inhibitory effect (MIC), minimum lethal effect (MBC), well release and bacterial growth curve.

Results: The results showed that 17% of the samples were infected with Staphylococcus aureus bacteria with the beta-lactamase gene. The liposomes of Peppermint extract and Cinnamon essential oil showed a good antibacterial effect against these isolates, and in all tests, the liposomes of Cinnamon essential oil was more effective than Peppermint extract

Conclusion: By proving the stronger antimicrobial effect of Cinnamon essential oil liposomes, it is recommended that in dishes such as grilled types of meat prepared from minced meat, be sure to use the liposomes Cinnamon essential oil.

Keywords: Staphylococcus aureus, beta-lactamase, Peppermint extract, Cinnamon essential oil, minced meat.

Comparison of the effect of Salvia Rosmarinus and Lavandula essential oil liposomes on enterococcus isolated from packaged minced meat (Research Paper)

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Introduction: Enterococcus is one of the most important pathogenic microorganisms in meat products, especially those that come into contact with the hand during repeated production. The aim of this study was to evaluate the degree of contamination and compare the antimicrobial effect of liposomes Peppermint extract and Cinnamon essential oil on enterococcus isolated from minced meat.

Methods: For this purpose, sampling of 40 packaged meat distribution and was performed under hygienic conditions and all samples were tested for the presence of enterococcus tested by biochemical methods and molecular confirmation with PCR test. Were placed. The antibacterial effect of the liposomes of Rosmarinus essential oil and Lavandula essential oil on the mentioned isolates was evaluated with the tests of minimum inhibitory effect (MIC), minimum lethal effect (MBC), well release and bacterial growth curve.

Results: The results showed that 21% of the samples were infected with enterococcus. The liposomes of Rosmarinus essential oil and Lavandula essential oil showed a good antibacterial effect against these isolates, and in all tests, the liposomes of Rosmarinus essential oil was more effective than Lavandula essential oil.

Conclusion: By proving the stronger antimicrobial effect of Rosmarinus essential oil liposomes, it is recommended that in dishes such as grilled types of meat prepared from minced meat, be sure to use the liposomes Rosmarinus essential oil.

Keywords: Enterococcus, extract, Rosmarinus, Lavandula, minced meat

Comparison of the effects of ondansetron and metoclopramide during and after surgery (Review)

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Introduction: Nausea and vomiting is one of the most common problems during (in spinal and sedation patients) and after surgery in most patients. To prevent and control this problem, ondansetron and metoclopramide are commonly prescribed. Comparing the effectiveness, the appropriate time of use, benefits and side effects of these drugs can help us make the right choice in order to prevent and treat this problem.

Methods: This study is a review that was performed during the period (2016-2022), by searching in valid foreign databases like Scopus, google scholar, Pubmed with the English keywords "Ondansetron", "Metoclopramide", "Nausea", "Vomit", "Treatment of vomit and nausea", and performed in valid domestic databases with Persian keywords "متوکلوپرامید", "اندانسترون", " حالت تهوع" and "درمان حالت تهوع و استفراغ". In the first step, a total of 35 articles were found, and finally 15 articles (10 foreign articles and 5 internal articles) that were more in line with the subject and the purpose of the research were selected and studied and organized.

Results: In one of the studied articles, it is recommended to use metoclopramide to prevent nausea and vomiting during surgery in patients who have undergone spinal surgery for cesarean section. In other articles that studied nausea and vomiting after various operations such as middle ear surgery, laparoscopic cholecystectomy and appendectomy, the choice of ondansetron as the superior drug was significant. Some of these articles mentioned that ondansetron is effective in controlling nausea and vomiting up to 6 hours after the operation and another article mentioned even up to 24 hours of effectivity after the operation. In other postoperative hours, all studies agreed that there was no significant difference between ondansetron and metoclopramide.

Conclusion: Metoclopramide is better used to prevent nausea and vomiting during cesarean surgery. Ondansetron is more effective than metoclopramide for preventing and controlling postoperative nausea and vomiting for up to 24 hours. After 24 hours of surgery, no significant difference was observed between ondansetron and metoclopramide for the prevention and control of nausea and vomiting.

Keywords: ondansetron, metoclopramide, nausea, vomit, Treatment of vomit and nausea

Complications of Pregnancy in Women with Congenital Heart Diseases: A review study (Review)

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Introduction: The number of women with congenital heart disease (CHD) at risk of pregnancy is growing because over 90% of them are grown-up into adulthood due to progress in cardiologic and surgical interventions. Pregnant women with congenital heart disease are at increased risk for cardiac and neonatal complications. Various studies have mentioned the complications of pregnancy and childbirth in women with congenital heart disease. Therefore, the present study was conducted with the aim of reviewing the outcomes of pregnancy in women with congenital heart diseases.

Methods: In this study, Persian and English scientific articles published in Google Scholar, MEDLINE, Science Direct, PubMed and SID, using keywords Pregnancy, Delivery and Congenital heart disease were examined without time limit and finally according to the inclusion and exclusion criteria, 14 articles were selected and reviewed.

Results: The results of various studies showed that most frequent maternal complications during pregnancy and delivery are heart failure, arrhythmias, bleeding or thrombosis, and rarely maternal death. Complications of fetus are prematurity, low birth weight, abortion, and stillbirth. Risk stratification of pregnancy and delivery relates to functional status of the patient and is lesion specific. Medication during pregnancy and post-delivery (breast feeding) is a big concern. Especially prescribing medication with teratogenicity should be avoided. Adequate care during pregnancy, delivery, and the postpartum period requires a multidisciplinary team approach with cardiologists, obstetricians, anesthesiologists, neonatologists, nurses and other related disciplines. Caring for a baby is an important issue due to temporarily pregnancy-induced cardiac dysfunction, and therefore family support is mandatory especially during peripartum and after delivery.

Conclusion: Timely pre-pregnancy counseling should be offered to all women with CHD to prevent avoidable pregnancy-related risks. Successful pregnancy is feasible for most women with CHD at relatively low risk when

appropriate counseling and optimal care are provided. Maternal cardiac and neonatal complication rates are considerable in pregnant women with congenital heart disease. Patients with impaired sub pulmonary ventricular systolic function and/or severe pulmonary regurgitation are at increased risk for adverse cardiac outcomes.

Keywords: Pregnancy, Delivery, Congenital heart disease, Complication

Computational and research strategies in Covid-19 (Review)

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Introduction: SARS-CoV-2 was the first severe epidemic of the digital age. Computational approaches have been widely used in the effort to deal promptly and effectively with the resulting global health crisis. Bioinformatics and computational biology are important in understanding and analyzing protein dynamics, primarily in relation to sequence, structure, and evolution-based analysis (which tracks changes in protein composition over time). We need to constantly learn more about viruses and their variants. Therefore, the need for rapid and effective computational analysis of the disease and its mutations is essential to reduce its potentially harmful effects.

Methods: The present study is a review study that has been compiled using electronic resources in reputable databases such as PubMed, Scopus, Google Scholar, ISI, Science Direct related from 2019 to 2022.

Results: A variety of computational approaches have been explored and are underway in the hope of better understanding how Covid-19 works to develop effective diagnosis and treatment. Investigate the importance of active signaling pathways, for example, using a set of randomly generated signaling pathways to identify the most important signaling pathways for drug prediction and drug composition. A fast and cost-effective computational method has been developed for the initial prediction of the impact of emerging viral species at the molecular level. With this early prediction, there will be a great opportunity for the scientific community to do more research. On the other hand, we know that one of the best diagnostic strategies for Covid-19 disease is lung imaging. To reduce the burden on radiologists of interpreting these images, "artificial intelligence diagnosis" can be very effective and useful. These images can be easily entered into the artificial intelligence system and receive diagnostic results in a few seconds.

Conclusion: The field of bioinformatics and computational biology is wide in terms of coverage. It can be limited to protein at the molecular scale to analyze specific protein interactions or extended to study the global progression of the disease. The significant assistance provided by computing programs during the epidemic is believed to motivate redoubled efforts to

further develop and adopt them, with the aim of increasing preparedness and critical response to current and future emergencies.

Keywords: Coronavirus 2019 (Covid-19), Bioinformatics, Computational tools, Public health.

Computational approaches on the Conjugation of a biogenic polyamine with a model enzyme (Proteinase K) (Research Paper)

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Introduction: In order to understand the influence of polyamines on proteins, we used bioinformatics simulation methods including molecular dynamic simulation and ducking methods on the interaction of proteinase K (PK) as a model enzyme combined with spermine (as a polyamine).

Methods: Molecular docking is one of the best theoretical methods to investigate the correct binding site of small ligands (such as polyamines) on enzyme or protein. Molecular dynamic (MD) simulation is a powerful tool to investigate the protein alterations in the presence of ligand over a define time scale

Results: The molecular simulation results demonstrated that spermine could spontaneously bind and alter the structure of PK. Overall; the results showed that spermine could bind to PK and improve its stability and activity, thereby promising various biotechnological and industrial applications. Molecular dynamic studies showed that spermine acted as a stabilizer. The molecular docking results showed that the combination process is spontaneous (negative value of ΔG°).

Conclusion: These results are is in agreement with experimental results, and also revealed that spermine was especially on the surface of the enzyme with different hydrogen and hydrophobic interactions and stable PK as model enzyme

Keywords: Bioinformatics insights, Proteinase K (PK), polyamine, Molecular dynamic and ducking simulations

Correlation between Janus kinase 2 (V617F) gene polymorphism and the Risk of thrombophilia in the Iranian population (Research Paper)

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Introduction: Thrombophilia is a defect in blood coagulation that raises the risk of myeloproliferation and thrombosis. Thrombophilia can be arises from hereditary and acquired defects in the coagulation system. Acquired disorders include heparin-induced thrombocytopenia, antiphospholipid antibody syndrome, neoplasia, use of oral contraceptives (OCP), pregnancy and childbirth, old age, hyperlipidemia, congestive heart failure. Hereditary causes of thrombophilia is mutations in the genes that control blood coagulation. One of the most important mutations is V617F in Janus kinase 2 gene. The purpose of this study was to determine the mutation V617F in the Janus kinase 2 (Jak2) gene using molecular methods in the field of thrombophilia diagnosis.

Methods: Blood sample were collected from 148 people suspected of thrombophilia who referred to medical centers in different cities of Iran. DNA was extracted from the blood samples using DNA extraction kit. The quality and quantity of extracted DNA was determined using electrophoresis on agarose gel and nanodrop device. Finally, by using specific primers and with the help of Allele-specific PCR method, the desired mutation was investigated.

Results: The results of electrophoresis on agarose gel and nanodrop device showed that the extracted DNA has good quality and quantity. In terms of JAK2 V617F polymorphism, 14 people were JAK2 V617F mutation (9.5%) and 134 people were wild-type.

Conclusion: According to the obtained results, the JAK2 V617F polymorphism can be used as a genetic marker in the diagnosis of thrombophilia.

Keywords: Janus kinase 2, Thrombophilia, Allele-specific PCR, V617F

Correlation between Plasminogen activator inhibitor-1 (4G/5G) gene polymorphism and the Risk of thrombophilia in the Iranian population (Research Paper)

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Introduction: Thrombophilia is a type of coagulation disorder that increases the risk of thrombosis. Thrombosis in the placenta's capillaries, which can obstruct the flow of nutrients between the mother and the fetus, may lead to abortion. The 4G/5G polymorphism in the plasminogen activator inhibitor type 1 (PAI-1) gene promoter is one of the key determinants in the onset of thrombophilia in women who experience recurrent miscarriages. The purpose of this study was to determine the mutation 4G/5G in the PAI-1 gene using molecular methods in the field of thrombophilia diagnosis.

Methods: Blood sample were collected from 148 people suspected of thrombophilia who referred to medical centers in different cities of Iran. DNA was extracted from the blood samples using DNA extraction kit. The quality and quantity of extracted DNA was determined using electrophoresis on agarose gel and nanodrop device. Finally, by using specific primers and with the help of Allele-specific PCR method, the desired mutation was investigated.

Results: The results of electrophoresis on agarose gel and nanodrop device showed that the extracted DNA has good quality and quantity. In terms of PAI-1 (4G/5G) polymorphism, 102 people (69%) were homozygous wild (AA), 36 people (24%) were heterozygous (AC) and 10 people (7%) were homozygous mutant (CC).

Conclusion: According to the obtained results, the PAI-1 4G/5G polymorphism can be used as a genetic marker in the diagnosis of thrombophilia.

Keywords: Plasminogen activator inhibitor-1, Thrombophilia, Allele-specific PCR, 4G/5G

Correlation of adiponectin/leptin ratio with infertility and abortion in Iranian women with polycystic ovary syndrome (Research Paper)

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Introduction: Adiponectin and leptin are two adipocyte-derived hormones that modulate the hypothalamic–pituitary–ovarian axis functions. Considering the opposite effects of leptin and adiponectin on different biological processes, the adiponectin/leptin ratio has been introduced as an emerging biomarker, and recent studies highlight its correlation with BMI, obesity, metabolic syndrome, insulin resistance, insulin levels, coronary artery disease, and stroke in different populations in Europe and Asia. This study aimed to assess the correlation of adiponectin/leptin ratio with infertility and abortion in Iranian women with PCOS.

Methods: A data set of 127 women with PCOS (including 57 infertile patients and 70 patients with a history of recurrent abortion) and 37 healthy control was enrolled in this study. Leptin and adiponectin were measured by ELISA kits.

Results: Our results showed that with every 0.01 unit increase in adiponectin/leptin ratio, the chance of infertility decreases by 18%. Also, each 0.001 unit increase in adiponectin/leptin ratio could decrease the chance of abortion by 18% in PCOS women.

Conclusion: The results of this study showed that the adiponectin/leptin ratio is correlated with a decreased risk of infertility and abortion in PCOS patients.

Keywords: PCOS; Infertility; Adiponectin/leptin ratio; Abortion

Correlation of HOMA-IR/Adiponectin ratio with infertility and abortion in Iranian women with polycystic ovary syndrome (Research Paper)

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Introduction: PCOS is a common endocrine-metabolic disorder in women of reproductive age. The association of abnormal adiponectin levels and insulin resistance with PCOS was observed in several investigations. Recently, some studies introduced the HOMA-IR/Adiponectin ratio as a biomarker of metabolic syndrome. The aim of this study was to assess the correlation of the HOMA-IR/Adiponectin ratio with infertility and abortion in Iranian women with PCOS.

Methods: A data set of 144 women with PCOS (including 57 infertile patients and 70 patients with a history of recurrent abortion) and 50 healthy control was enrolled in this study. Adiponectin levels were measured by ELISA kits. Homeostasis model assessment of adiponectin (HOMA-Adiponectin) was calculated using the following formula: fasting insulin (μU/L) × fasting glucose (mmol/l)/22.5.

Results: Our results showed that with every 0.01 unit increase in HOMA-IR/Adiponectin ratio, the chance of infertility increases by 7%. Also, each 0.001 unit increase in adiponectin/leptin ratio could increase the chance of abortion by 6% in PCOS women.

Conclusion: The results of this study showed that the HOMA-IR/Adiponectin ratio is correlated with an increased risk of infertility and abortion in PCOS patients.

Keywords: PCOS; Infertility HOMA-IR/Adiponectin ratio; Abortion

COVID-19 infection diagnosis (Research Paper)

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Introduction: The worldwide affected covid-19 disease has caused deaths and irreparable economic problems. The best way to deal with such a horrible disease is to use correct and fast diagnostic methods to prevent transmission and spread of the disease. One of the methods used currently for the detection of infected patients is the LAMP method, which is an isothermal nucleic acid amplification method. The high sensitivity and specificity of this method, speed, and simplicity of analyzing the results have led to an increase in interest in it.

Methods: In the present study, 34 Oro-nasopharyngeal swab samples were first analyzed using the gold standard qRT-PCR method, and then the colorimetric RT-LAMP method was used to evaluate the possibility of SARS-COV-2 virus detection using the LAMP technique. In this study, 3 pairs of primers specific to the orf8 gene were used for the LAMP reaction and the results were evaluated according to the color change of the reaction mixture. Also, in this study, a lateral flow assay combined with the RT-LAMP method (RT-LAMP-LFA) was designed to detect the SARS-COV-2 virus. In this test, first, the virus genome was amplified using the RT-LAMP method and with the help of the LF primer labeled with digoxigenin and the LB primer labeled with biotin, and then the amplified products were evaluated on a lateral flow strip using the anti-digoxigenin antibody conjugated with gold nanoparticles on the conjugation pad, Goat Anti-Mouse IgG on the control line and streptavidin on the test line. In the RT-LAMP-LFA method, the heated samples were used instead of the extracted RNA.

Results: The results of the RT-LAMP method showed a sensitivity of 93.33% (77.93-99.18% CI:95%) and a specificity of 75% (19.41-99.37% CI: 95%) compared to the qRT-PCR technique. Also, the sensitivity and specificity of the RT-LAMP-LFA method for the detection of SARS-COV-2 virus for 44 positive samples and 22 negative samples were evaluated 100% and 77.27% respectively.

Conclusion: The results of this study showed that the RT-LAMP-LFA method can provide a quick and simple test for the detection of SARS-COV-2 virus by eliminating the time-consuming step of RNA extraction.

Keywords: COVID-19; SARS-COV-2; diagnosis; qRT-PCR; RT-LAM

COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses (Review)

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Introduction: Coronaviruses belong to the Coronaviridae family in the Nidovi-rales order. Corona represents crown-like spikes on the outer sur-face of the virus; thus, it was named as a coronavirus

Methods: All coronaviruses contain specific genes in ORF1 downstream regions that encode proteins for viral replication, nucleocapsid and spikes formation [25]. The glycoprotein spikes on the outer surface of coronaviruses are responsible for the attachment and entry of the virus to host cells (Fig. 1). The receptor-binding domain (RBD) is loosely attached among virus, therefore, the virus may infect multiple hosts [26,27]. Other coronaviruses mostly rec-ognize aminopeptidases or carbohydrates as a key receptor for entry to human cells while SARS-CoV and MERS-CoV recognize exopeptidases [2]. The entry mechanism of a coronavirus depends upon cellular proteases which include, human airway trypsin-like protease (HAT), cathepsins and transmembrane protease serine 2 (TMPRSS2) that split the spike protein and establish further pene-tration changes [28,29]. MERS-coronavirus employs dipeptidyl peptidase 4 (DPP4), while HCoV-NL63 and SARS-coronavirus require angiotensin-converting enzyme 2 (ACE2) as a key receptor

Results: Most importantly, human coronaviruses targeting vaccines and antiviral drugs should be designed that could be used against the current as well as future epidemics. There are many companies working for the development of effective SARS-CoV-2 vaccines, such as Moderna Therapeutics, Inovio Pharmaceuticals, Novavax, Vir Biotechnology, Stermirna Therapeutics, Johnson & Johnson, VIDO-InterVac, GeoVax-BravoVax, Clover Biopharmaceuticals, Cur-eVac, and Codagenix. But there is a need for rapid human and animal-based trails as these vaccines still require 3–10 months for commercialization. There must be a complete ban on utilizing wild animals and birds as a source of food. Beside the development of most efficient drug, a strategy to rapidly diagnose SARS-CoV-2 in suspected patient is also required. The signs and symptoms of SARS-CoV-2 induced COVID-19 are a bit similar to influenza and seasonal allergies (pollen allergies). Person suffering from influ-enza or seasonal allergy may also exhibit temprature which can be detected by thermo-scanners, hence the person will become suspected. Therefore, an accurate and rapid diagnostic kit or meter for detection of SARS-CoV-2 in suspected patients is required, as the PCR based testing is expensive and time consuming. Different teams of

Chinese doctors should immediately sent to Eurpean and other countries, especially spain and Italy to control the over spread of COVID-19, because Chinese doctors have efficiently con-trolled the outbreak in china and limited the mortality rate to less than 3% only. The therapeutic strategies used by Chinese, should also be followed by other countries.

Conclusion: The novel coronavirus originated from the Hunan seafood market at Wuhan, China where bats, snakes, raccoon dogs, palm civets, and other animals are sold, and rapidly spread up to 109 countries. The zoonotic source of SARS-CoV-2 is not confirmed, however, sequence-based analysis suggested bats as the key reservoir. DNA recombination was found to be involved at spike glycoprotein which assorted SARS-CoV (CoVZXC21 or CoVZC45) with the RBD of another Beta CoV, thus could be the reason for cross-species transmission and rapid infection. According to phylogenetic trees, SARS-CoV is closer to SARS-like bat CoVs. Until now, no promising clinical treatments or prevention strategies have been developed against human coronaviruses. However, the researchers are work-ing to develop efficient therapeutic strategies to cope with the novel coronaviruses. Various broad-spectrum antivirals previously used against influenza, SARS and MERS coronaviruses have been evaluated either alone or in combinations to treat COVID-19 patients, mice models, and clinical isolates. Remdesivir, Lopinavir, Ritonavir, and Oseltamivir significantly blocked the COVID-19 infection in infected patients. It can be cocluded that the homolo-gus recombination event at the S protein of RBD region enhanced the transmission ability of the virus. While the decision of bring back the nationals from infected area by various countries and poor screening of passengers, become the leading cause of spread-ing virus in others countries.

Keywords: Coronaviruses-COVID-19-Origin-Outbreak-Spread

CRISPR/Cas9 Tool for MicroRNAs Editing in Cardiac Development, Function, and Disease (Review)

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Introduction: There is emerging scientific proof that the CRISPR/Cas9 system can target small noncoding RNAs, like miRNAs. CRISPR/Cas9 technology provides a unique gene-editing approach with stability. MiRNA dysregulation can result in numerous diseases, such as a number of pathological processes associated with heart disease. Many miRNA molecules have been discovered as being involved in the modulation of fibrosis and cardiac hypertrophy, as well as the regulation of cardiomyocytes.

Methods: Pubmed, google sccholar

Results: The results demonstrate the high efficiency of the CRISPR/Cas9 method for studying the result of the deletion of miRNAs in cell physiology. Studies display that miRNAs strongly affect organ evolution and concentration of miRNAs can involve in the differentiation, development, and function of organs so that at low concentrations miRNAs may target one or a small group of mRNAs and at high concentrations, it may affect different groups of mRNAs. CRISPR/Cas9 tools can be used to eliminate small areas of DNA and determine miRNA in cases where similar groups of miRNAs are in the same strand, also CRISPR/Cas9 genome-editing method is more strong system in stopping miRNAs than previous methods such as antisense inhibitors.

Conclusion: we critically examine the current status and recent progress of miRNA-targeted therapeutics through the CRISPR/Cas9 system, besides another emerging strategies to specifically combine different delivery platforms and cell-fate engineering for the clarification of miRNA function and miRNA-based therapeutic intervention.

Keywords: CRISPR/Cas9, MicroRNAs, Cardiac Development and Disease

Critical Thinking for Undergraduate Medical Students: benefits and barriers (Review)

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Introduction: Critical thinking is one of the major principles in the universities of the third millennium which is expressed as one of the aspects of thinking that has been accepted as a way to overcome difficulties and facilitate access to information in life. This kind of thinking helps individuals to differentiate correct information from incorrect information and make an accurate assessment and decision on events. As medical staff and medical students are a group of people who majorly interact with difficult situations that refer to human life, the most valuable property of an individual, they need some skills to make rapid and accurate decisions; therefore, it seems that critical thinking could help them in this term. The present study is designed to review the last knowledge about the roles, benefits, and barriers of critical thinking for undergraduate medical students; whether it is necessary to improve this skill during the learning in medical faculties, or not.

Methods: To determine the aims of the present study, a comprehensive systematic search was conducted through electronic databases including PubMed, Scopus, Embase, and Web of Science with the keywords “Critical Thinking”, “Medical Education”, “Medical Students”, and other related MeSH terms up to August 2022. Original studies, review studies, and references of the review studies were included. Finally, the associated studies which investigated the roles, benefits, barriers, limitations, and features of critical thinking in undergraduate medical students were reviewed.

Results: According to the reviewed studies, eight chrematistics were identified for critical thinking which are defining a problem, asking questions, examining evidence, avoiding emotional reasoning, analyzing assumptions and biases, avoiding oversimplification, tolerating ambiguity, and considering other interpretations. These features finally help an individual, e.g medical student, to avoid medical/clinical errors, increase productivity, better clinical decision making, bring in innovation through creativity, develop confidence, climb the leadership ladder, get higher grades, succeed in a career, and learn throughout life. Overall, reviewed studies were unanimous that low self-

esteem, lack of risk-taking, and lack of motivation to risk are the primary barriers to critical thinking in undergraduate medical students.

Conclusion: In conclusion, it can be stated despite thinking critically can improve the performance of the medical staff and medical students, it seems necessary to investigate its barriers and limitation in more detail which can help us to find better solutions for teaching and learning critical thinking.

Keywords: Critical Thinking, Medical Education, Medical Student

Current insights into nanodelivery of natural coumarins for anticancer approaches (Review)

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Introduction: Cancer is among the most leading causes of death worldwide. The number of new cancer cases per year is expected to rise to 23.6 million by 2030. Among clinical approaches that have been employed for cancer treatment, use of chemical drugs, alone or in combination with surgery and radiotherapy, is a routine modality. However, severe side effects and rapid emergence of drug resistance in cancer cells are major problems in chemotherapy that need to be overcome. In recent years, nano-pharmaceutics has been emerged as an attractive field to develop and improve efficacy of anti-cancer drugs. On the other hand, increasing interest in the use of natural products for cancer chemotherapy has been observed. In this regard, recent studies have reported that the encapsulation of natural products into different delivery systems enhances their efficacy by increasing bioavailability, reducing side effects and improving target-specific activity.

Methods: Published articles including key words cancer therapy, natural coumarins, sustained drug delivery and nanoparticle were extracted in databases PubMed, Web of Science and Scopus.

Results: Coumarins are a large class of phenolic substances found in plants with a wide range of pharmacological properties. Auraptene (AUR) is the most abundant geranyloxy coumarin found in nature with great anti-cancer effects. However, poor solubility of AUR is the main reason for its low bio-distribution and delivery to targeted sites. To overcome this limitation, AUR has been nano-encapsulated with biodegradable and biocompatible copolymers, consist of polycaprolactone (PCL), polyethylene glycol (PEG) and poly-D, L-lactide (PLA), which improved therapeutic indexes of AUR. Galbanic acid (GBA) is an active sesquiterpene coumarin that its anti-cancer activities are also limited due to low solubility. Recently, it has been reported that nanodelivery of GBA with PLA-PEG and solid lipid nanoparticles (SLNs) have increased its hydrophilic property. Curcumin is another valuable natural coumarin with poor solubility and bioavailability that both compromise its clinical application to a great extent. Hence, different types of bio-nanocarriers have been used for effective delivery of this agent to different target sites, such as protein-based nanopolymers (including as albumin, zein and silk),

polysaccharide nanoparticles (including chilosan, alginate and cellulose) and copolymers including PCL and PEG.

Conclusion: As proved by recent reports, use of nanocarriers has greatly improved biocompatibility, biodegradation and delivery of natural coumarins. Nevertheless, further in vivo and clinical studies are required to facilitate safe administration of nanocarriers in cancer patients.

Keywords: Nanodelivery, Anticancer effects, Natural coumarins

Current Prevention and Treatment Strategies to Control Monkeypox (Review)

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Introduction: Monkeypox infection is an ongoing global outbreak caused by the Monkeypox virus (MPXV), an enveloped double-stranded DNA virus with manifestations similar to smallpox. MPXV is primarily spread by close, sustained physical contact (skin-to-skin, sexual, or respiratory droplets) or fomites. Currently, no specific approved treatments and preventive approaches have been developed for MPXV infection, however, some strategies have been suggested to be effective. The present study aimed to reflect the current opinion on the potential application of pharmacological and preventive strategies such as antivirals, as prophylaxis against monkeypox infection

Methods: This study was a narrative review performed in 2022. We searched four keywords "Monkeypox virus", " Monkeypox", "Treatment", " and "Prevention" in six databases including PubMed, Scopus, Science Direct, Web of Science UpToDate, and Google scholar to determine the related documents on the main objective of the study.

Results: A review of current studies revealed that several medical countermeasures are available for orthopoxviruses such as monkeypox. According to CDC monkeypox treatment guidelines, most people with monkeypox recover fully within 2 to 4 weeks without the need for medical treatment. According to the US Strategic National Stockpile (SNS), there are three smallpox vaccines such as ACAM2000® (live, replication competent vaccinia virus), Aventis Pasteur Smallpox Vaccine (APSV) (an investigational replication-competent vaccinia), and JYNNEOSTM (live, replication incompetent vaccinia virus) (also known as IMVAMUNE, IMVANEX, MVA-BN). The Advisory Committee on Immunization Practices provides recommendations for the use of pre-exposure prophylaxis (PrEP) for individuals with job-related exposure to orthopoxviruses and high-risk exposure groups such as gay, bisexual, and other men who have sex with men (MXM) in the current outbreak. They are required to be vaccinated with either ACAM2000® or JYNNEOSTM as pre-exposure prophylaxis (PrEP). Also, vaccination as post-exposure prophylaxis (PEP) is recommended for healthcare workers and people with high-risk exposure to case patients in the infectious period.

Conclusion: The necessary therapeutic option for monkeypox virus infection is supportive care. Moreover, respiratory and hemodynamic support and skin lesion treatment are recommended. Currently, there are no specific treatments approved for monkeypox virus infections, however, there are several options, including antiviral agents (e.g., brincidofovir, cidofovir and tecovirimat) and immune therapies (e.g., vaccinia immune globulin intravenous (VIGIV)) for patients with moderate to severe symptoms or who are at high risk of severe disease. Future studies on monkeypox virus infection treatment are required to find novel strategies on prevention and treatment of monkeypox virus outbreak.

Keywords: Monkeypox virus, Prevention, Vaccine interventions, Antivirals

Cutaneous adverse reactions after COVID-19 vaccine: A Systematic Review (Review)

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Introduction: vaccine aversion, even to minor side effects (SEs), might raise vaccine hesitation at a time when mass vaccination is most needed. Mistrust in safety data provided by pharmaceutical corporations, according to the WHO's Strategic Advisory Group of Experts on Immunization (SAGE), may play a crucial role in diminishing vaccination acceptance levels. As a result, independent research on vaccine safety and SEs is a valuable asset in increasing public trust in COVID-19 vaccines and their efficacy. As a result, the goal of this systematic review was to collect cases of cutaneous SEs to COVID-19 vaccines in order to describe the timing and morphology of cutaneous SEs to COVID-19 vaccines and to understand differences in cutaneous SEs between the two vaccine doses in order to direct vaccine counselling.

Methods: The present study was conducted by systematic review. To access the Cutaneous adverse reactions after COVID-19 vaccine, articles indexed in databases Science Direct, PubMed, Scopus, Google scholar, web of science, Embase and Medline were used. Keywords including COVID-19; SARS-CoV-2; adverse event; vaccines; delayed inflammatory reaction; vaccine reaction; COVID-19 vaccine; cutaneous adverse reaction; COVID-19 skin; COVID-19 vaccination reaction; COVID-19 vaccine rash; coronavirus vaccine; vaccine allergy were searched over 2018 to 2021. According to the defined criteria, finally 66 Full text articles were reviewed in this study.

Results: The results of the present study showed that Pain, Tenderness Warmth, Itch, Redness, Swelling, rash and Herpes zoster are the most common. Additional less common reactions included Fatigue, headache, feverishness, and myalgia, Chills, Fever (¬38°C), Joint pain, Malaise, Muscle ache, Nausea, anaphylaxis, tachycardia, tachypnea and notable tongue swelling Lymphadenopathy (axillary or regional) and Arthritis. Reactions were more common after the first dose. Symptoms were more common near the injection site but were also seen in the neck, chest, lower back and face. Cutaneous adverse may occur immediately or even after 30 days.

Conclusion: cutaneous reactions to COVID-19 vaccination are typically minor and self-limited, and should not discourage vaccination. Allergic-type cutaneous symptoms, as well as effflorescence and angioedema, are transient and infrequently associated with anaphylaxis. However, more research into the side effect profile of COVID19 vaccines is required.

Keywords: COVID-19 vaccine, SARS-CoV-2, minor side effects, cutaneous adverse reactions, cutaneous reactions

Cytochrome P450 isoenzymes induce ROS during detoxification of chemical carcinogens that Besides causing DNA damage can lead to interference in multiple intracellular signaling pathways, notably MAPK/P13K-AKT/NF-KB/HIF-1 (Research Paper)

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Introduction: It is estimated that liver cancer is the fifth most frequently diagnosed cancer and the second most common cause of cancer-related deaths among men and that it is the seventh most frequently diagnosed cancer and the sixth leading cause of cancer-related deaths among women worldwide[1][2]. In contrast to men, women experience relatively low incidences and mortality rates from Hepatocellular carcinoma (HCC) [1]. CYP1A2 and CYP2C19 encode members of the cytochrome P450 superfamily of enzymes. The cytochrome P450 proteins are monooxygenases that catalyze many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids[3][4]. CYP1A2 and CYP2C19 may be associated with the occurrence of HCC. Cytochrome P2C (CYP2C) subfamily members (CYP2C19) are known to participate in clinical drug metabolism and are known to metabolize many xenobiotics, including the anticonvulsive drug mephenytoin, omeprazole, diazepam and some barbiturates that cause chemical carcinogenesis[5].

Methods: GSE112790 dataset Affymetrix was chosen and Microarray analysis was based on the bioinformatics tools (R programming language and online databases). to find differentially expressed genes (DEGs) in HCC samples compared to (Fifteen adjacent liver tissues obtained from patients with metastasis of colorectal cancer who had not received chemotherapy were used as control.) [6]. The GEO online database was used to find this dataset. In this study 54,676 genes were analyzed. The limma was used to conduct the DEG analysis on expression data, 144 low-expression genes and 172 high-expression genes were identified, which were selected for subsequent experimental research. The genes with logFC > 2 & logFC < -2 are considered as the differentially expressed genes (DEGs) in this dataset. The adjusted p-value (adj. P. Value) < 0.001 is considered the statistical significance level. Interaction between microRNA and LNCRNA using LNCRresearch was investigated. The Pathway enrichment analysis was carried out using KEGG and Reactome's online databases. All miRNAs were regained from DIANA-Tar Base v.8 and miRNA-mRNA interactions were investigated. The expression of lncRNAs in different tissues has been examined by the lnCAR databases. The expression of genes in HCC was

compared by Gepia2 databases. The protein-protein interaction analysis has made by STRING online software.

Results: we found that the expression of mRNAs CYP1A2 and CYP2C19 in tumor tissue from HCC patients compared to the control group has decreased (adj. P. Value < 0.001). Interaction analysis of CYP1A2 and CYP2C19 mRNAs with MALAT1and NEAT1 lncRNAs illustrated that these RNAs have a single local base-pairing interaction (Energy = -21.76 kcal/mol) and (Energy = -12.48 kcal/mol). miRNA interaction analysis revealed that hsa-miR-27a-3p could regulate the expression of CYP1A2, CYP2C19 mRNAs and MALAT1, NEAT1 lncRNAs in cell line HUH7.5 from liver tissue in an interaction axis. CYP1A2 and CYP2C19 have a significant interaction that Played an important role in linoleic acid metabolism. CYP1A2 and CYP2C19 could regulate the following signaling pathways: Chemical carcinogenesis-reactive oxygen species, Drug metabolism-cytochrome p450, Chemical carcinogenesis-DNA adducts and Chemical carcinogenesis-receptor activation. CYP1A2 plays a role in the Chemical carcinogenesis-reactive oxygen species (ROS), one example of which is the induction of oxidative stress. ROS are also generated due to induction the of the various cytochrome P450 isoenzymes during detoxification of chemical carcinogens. Increased ROS generation often has been linked to DNA damage that can lead to damage to bio-macromolecules, gene mutations, altered gene expression and activation of oncogenic pathways. Besides causing DNA damage, ROS further induces multiple intracellular signaling pathways, notably MAPK/P13K-AKT/NF-KB/HIF-1. These signaling routes can lead to cancer proliferation, angiogenesis and metastasis to exposed cells. Furthermore, this study showed that CYP2C subfamily members can interact with CYP1A2. Besides, metabolizing IQ and MeIQx, CYP1A2 can also form DNA adducts (dG-C8-MeIQx, dG-N-MeIQx). A variety of cancers, such as liver, lung, colon, and breast, can be affected by DNA adducts.

Conclusion: CYP1A2 and CYP2C19 mRNAs could be two prognostic biomarkers. MALAT1 and NEAT1 lncRNAs expression levels have a significant positive correlation with the expression of CYP1A2 and CYP2C19 mRNAs in HCC. Hsa-miR-27a-3p could form a complex network with CYP1A2, CYP2C19 mRNAs and MALAT1, NEAT1 lncRNAs in cell line HUH7.5 from liver tissue. CYP1A2 induces oxidative stress. Increased ROS generation besides DNA damage can lead to damage to bio-macromolecules, gene mutations, altered gene expression and activation of oncogenic pathways. ROS also further interferes in multiple intracellular signaling pathways, notably MAPK/P13K-AKT/NF-KB/HIF-1.

Keywords: HCC, MAPK/P13K-AKT/NF-KB/HIF-1 signaling pathways, ROS, complex network, MALAT1, NEAT1

Delivery of CRISPR/Cas9 for Genome Editing: Review Abstract Articles (Review)

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Introduction: In recent years, genome engineering technologies based on the CRISPR-associated RNA-guided endonuclease Cas9 has provided the ability to rapidly and economically introduce sequence-specific modifications depends on the generation of double-strand break (DSB) and DNA repair process into the genomes of cell and organisms. CRISPR/Cas system is the most flexible and user-friendly platform for genome editing. Gene modification can be introduced into the animal genome through homologous recombination and embryonic stem cell technology. Genetically modified animals, especially gene knockout editing is one of great interest in the prevention and treatment of human diseases. Safe and efficient delivery of CRISPR/Cas9 systems is still a challenge. In this review, we discuss CRISPR/Cas9 delivery methods for Genome Editing.

Methods: CRISPR/Cas system is the most flexible and user-friendly platform for genome editing. Safe and efficient delivery of CRISPR/Cas9 systems is still a challenge. Non-viral vectors, viral vectors, and physical delivery are the most widely used method for delivery of CRISPR/Cas9 for genome editing.

Results: Viral vectors are efficient in gene delivery, but they have some contraindication due to many drawbacks such as off-target effect, immunogenic and inflammatory responses, limited packaging capacity, and high cost in production. Non-viral vectors, including Nano carriers and nanoparticles such as Nano polymeric- and lipid-based structures, rigid nanoparticles, nanoparticles coupled to specific ligand systems including arginine–glycine–aspartate (RGD) peptide, porous silicon, mesoporous silica, metal–organic, cell-penetrating peptides. The physical delivery, including microinjection, electroporation and hydrodynamic delivery show high efficiency for the application in vitro, but not satisfy for in vivo application.

Conclusion: CRISPR/Cas9 technology has been used to generate target genome modifications. Genetically modified animals, especially gene knockout editing is one of great interest in the prevention and treatment of human diseases. Non-viral vectors based on Nano carriers plays an important role for targeting delivery of CRISPR/Cas9 systems due to increase the circulation time, low toxicity, biocompatibility, and facilitating scaled up. Nano carrier-based delivery systems suggesting that they can be potential promising platform for Safe and efficient delivery of CRISPR/Cas9 systems.

Keywords: CRISPR/Cas9, Genome Editing tools, Nano carriers

Depression and serum levels of heavy metals in human studies: a systematic review (Review)

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Introduction: Environmental pollutants, including heavy metals, can affect neurobiological processes. Depression is one of the most common neurologic disorders and some evidence has emerged showing that heavy metal pollutants are associated with depressive symptoms and their severity. Therefore, the current review was aimed at providing evidence of the relationship between serum levels of heavy metals and depression.

Methods: A literature search on PubMed, MEDLINE, SCOPUS, Web of Science, and google scholar has been conducted, and 21 articles published on the association of serum levels of Lead (Pb), Cadmium (Cd), Mercury (Hg), Arsenic (As) and depression in humans have been included, cited, reviewed, and summarized. The review included all field and community trials and observational studies in all population groups. Searching electronic databases, study selection, and data extraction have been conducted by two researchers independently. Pb and Cd levels were determined by atomic absorption spectrometry. Total serum Hg levels were determined using a direct mercury analyzer. The outcome variable depression was defined based on a diagnosis through records of hospitalization, physician's diagnosis, the treatment for depression, or otherwise stated International Classification of Diseases (ICD- 10). A narrative synthesis was implemented to summarize findings if meta-analyses were not appropriate.

Results: Depression was found to be significantly higher in males with higher serum Pb levels. An increased serum Cd level was associated with an increase in depression; however, inconsistent results were found in associations between blood cadmium levels and depressive symptoms in the elderly population. Higher levels of Hg were negatively associated with depression and with increased fish consumption. Reviewed studies were mostly measuring As in urine instead of serum; therefore, not included. Most

of the studies especially in the last decade tested the association by adjusting socio-demographics, family histories, lifestyles, smoking, and food intake variables. It is revealed that the observed symptoms in most cases are linked to the alteration of the functionality within monoamines pathways. These pathways generate from the dorsal raphe nucleus (5-HT pathways) to the amygdala and from the median raphe nucleus (mainly dopamine pathways) to the hippocampus. The two systems regulate successively evoked depression.

Conclusion: The review did not confirm a relationship between the levels of selected heavy metals and depression except for Cd. Further studies are needed to reduce the risks posed by heavy metals and to more comprehensively determine the effects of various environmental pollutants and their interactions.

Keywords: Heavy metal, Depression, Lead (Pb), Cadmium (Cd), Mercury (Hg)

Design of biological inhibitors to inhibit S2 subunit of spike glycoprotein in SARS_COV_2 (Review)

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1.
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Introduction: The coronavirus is the cause of the infectious pneumonia disease COVID 19, which since 2019 the World Health Organization (WHO) has declared as a global pandemic, which is still spreading. Spike protein in SARS COV2 virus is an important factor in pathogenesis, which includes two regions S1 and S2. The S1 subunit has the role of binding to the host receptor and the S2 subunit has the role of membrane fusion between the host cell and the virus. The S2 region is a more protected region than S1, so the probability of mutation in it is reduced. A region in S2 called FP (Fusion Protein) plays a vital role in membrane fusion, which starts the process of membrane fusion by entering the lipid bilayer of the host and disrupting the membrane structure. In this research, with modern bioinformatics methods, inhibitor design for the FP region has been done in order to prevent the occurrence of membrane fusion and disrupt the entry and proliferation of this virus.

Methods: The region related to FP in PDB:6VXX was considered from amino acid 788 to 806. Then amino acids with high interaction were determined for this sequence with the assumption that they can be complementary sequences of the intended sequence. These sequences were modeled using RaptorX, Swissmodel, and Phyer2 servers, and the accuracy of the built models was evaluated using the Procheck server. The binding energy of the designed models was calculated via the molecular docking method using the Haddock.version 2.4 server.

Results: The region related to FP in PDB:6VXX was considered from amino acid 788 to 806. Then amino acids with high interaction were determined for this sequence with the assumption that they can be complementary sequences of the intended sequence. These sequences were modeled using RaptorX, Swissmodel, and Phyer2 servers, and the accuracy of the built models was evaluated using the Procheck server. The binding energy of the designed models was calculated via the molecular docking method using the Haddock.version 2.4 server.

Conclusion: The results obtained from molecular docking showed that the designed models have a high tendency to connect to the FP region and the binding energy values calculated for the top 5 models are -120, -96, -93, -90.6 and -90.5 kcal/mol, respectively. As a result, these models can be used to

inhibit the spike protein from the FP region and prevent the virus from entering and infecting the host cell. These types of inhibitors can be useful and effective in making vaccines or antiviral drugs.

Keywords: FP,COVID19,Corona_virus

Designing a disinfectant formula for eye drops, detergent, and herbal pain reliever using special theine extract (non-toxic) of black tea plant and black date kernel liquid extract (Research Paper)

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Introduction: Nowadays, due to the industrial growth of countries, especially Middle Eastern countries, air pollution and its negative effects have become one of the major concerns of society, and every day it causes more pathogenic effects on the sensory and respiratory organs of people. Doctors and pharmacists and researchers and Researchers are trying to find new and more effective methods and drugs and treatments for this, one of the negative effects that air pollution causes for humans are eye diseases and problems, including ‹Redness of the eyes‹Burning ‹Watery eyes ‹Eye cord secretions ‹ Itching‹Dryness and tingling sensation in the eyes ‹Blurred vision and vision problems, watering and itching The effective treatment of doctors is to use sterile drops and eye washes to treat and heal these cases, which are mostly chemical and may have side effects over time. The design of a herbal drop that, in addition to washing and sterilizing the eyes, has pain-relieving properties is a solution that has been achieved after long research.

Methods: In order to perform this operation, we need extensive research to identify the most suitable plant and the most effective plant for this, which is extracted from scientific and globally approved sources, in addition, we need the science of pharmacy and the science of medicinal plants, extract extraction and pharmacopeia. For this, after identifying the plant and extracting the desired extract with the desired structure and chemical formula, the combination obtained from tea plants and black date kernels along with dibasic sodium phosphate monobasic sodium phosphate sodium chloride sodium edetate benzalkonium chloride It is combined and finally, the output is a clear and colorless solution consisting of acidic alkaline basic structures suitable for eye pH and suitable saline phosphate, which is the result of using advanced extraction devices and laboratory testing. In the first stage, the database of artificial intelligence (AI)-based laboratories have been used to replace animal testing, which will reduce the harm caused by the dangers to animals and increase high-tech research services.

Results: According to the conducted research, the result of the experimental tests shows the 67% effectiveness of this drop to solve the mentioned problems, and also through the additional stages of the test and the final output, it can be concluded that it is possible to improve the effectiveness of the drug. This percentage can be close to 90% effective and also by examining other samples of herbal eye drops that are designed with other

plants such as chamomile, we come to the conclusion that the resulting solution and the laboratory sample have high efficiency results. and also during Experiments and research have shown the effectiveness of this drop for the primary treatment of eye diseases, including lacrimal gland diseases and eye thyroid disease.

Conclusion: The result shows that this drop prepared from tea theine extract and black date kernel extract along with sodium and phosphate compounds will reduce eye pain and increase the moisture of the eyes with little harm. In addition, this drop is for eye diseases including the problems caused by According to the ongoing research, it is effective for lacrimal glands and eye thyroid and produces a suitable response for the patient.

Keywords: Eye drop Herbal Extract Tea theine Date kernel

Designing Clinical Trial for Immunotherapy of Metastatic Colorectal Cancer Patients by Autologous Cancer Vaccine (Research Paper)

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Introduction: Colorectal Cancer (CRC) is the second leading cause of cancer-related mortality. This disease has an adverse effect on the quality of life. Surgery and chemotherapy are standard methods for improving quality of life, reducing the number of tumors, and reducing metastases. In recent years, immunotherapy with cancer vaccines has been used to induce appropriate immune responses against cancer cells or tumor antigens. One of the cancer vaccines and active specific immunotherapies for CRC patients is an autologous colon cancer vaccine which used after surgery. This vaccine contains the sterile non-tumorigenic autologous tumor cells and BCG (Calmette-Guerin bacillus) in 4 doses injection after chemotherapy. The aim of this study is a different design of clinical trial in Iran for immunotherapy of colorectal cancer patients by autologous cancer vaccine.

Methods: We designed the distinct clinical trials schedule for immunotherapy of colorectal cancer patients by autologous cancer vaccine. This cancer vaccine will be able to use for 1; metastatic colorectal cancer patients, 2; all patients with resectable or non-resectable tumors can use this vaccine. 3; this immunotherapy has two additional doses (6 doses instead of 4 doses of common vaccine) in two periods, 3 doses will be injected before the chemotherapy and also 3 doses will be injected after the chemotherapy.

Results: This new different designing of clinical trials schedule for immunotherapy of metastatic colorectal cancer patients by non-tumorigenic autologous tumor cells was approved in Isfahan University of medical sciences and also Iranian Registry of Clinical Trials.

Conclusion: It is the first time autologous tumor cells have been used in an Iranian clinical trial. As a result of this study, patients with metastatic CRC can receive active specific aimmunotherapies at lower costs in Iran.

Keywords: Autologous Cancer Vaccine, Colorectal Cancer, Metastasis, Immunotherapy, Clinical Trial

Designing the Indigenous Allogeneic Cancer Vaccine for Immunotherapy of Metastatic Colorectal Cancer Patients (Research Paper)

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Introduction: Colorectal Cancer (CRC) is the fourth most common cancer in Iran. In some patient's surgery and chemotherapy as the standard methods could not prevent cancer recurrence. Therefore, in recent years, cancer vaccines or cancer cell immunotherapy have been used to encourage suitable responses against tumor antigens. One of the cancer vaccines for prevention of colon cancer recurrence after surgery is an allogeneic colon cancer vaccine, which is contained allogeneic cancer cells and adjuvant BCG (Calmette-Guerin bacillus). Usage of this vaccine could increase survival of patients with metastatic colon cancer. The aim of this study is designing the different allogeneic cancer vaccine for metastatic colorectal cancer patients in Iran.

Methods: This study designed the indigenous allogeneic cancer vaccine, which is contained some metastatic and non-metastatic colon and rectal cell lines. These cells express mutation form of KRAS, BRA, PI3KA, and P53, and also express high levels of APC, CEA, CD133 and EP cam. Part of these cells have miss match instability. This cancer vaccine will be able to use for metastatic colorectal cancer patients with resectable or non-resectable tumors in two periods of times, 3 doses before the chemotherapy and also 3 doses after the chemotherapy.

Results: The new indigenous allogeneic cancer vaccine for immunotherapy of metastatic colorectal cancer patients by non-tumorigenic colorectal cell lines was approved in Isfahan University of medical sciences and also Iranian Registry of Clinical Trials.

Conclusion: Our study is the first immunotherapy by indigenous allogeneic colorectal cancer vaccine in Iran. This immunotherapy provides the active

specific immunotherapies for metastatic CRC patients with the lower cost in Iran.

Keywords: Allogeneic Cancer Vaccine, Immunotherapy, Metastasis, Colorectal Cancer

Detection of tetracycline using aptasensors (Review)

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Introduction: Tetracycline is a broad-spectrum antibiotic used in the therapy of human and animal. Residual tetracycline in food are often used as model compounds to develop aptasensors. Until now, more than 100 advanced aptasensors toward tetracycline have been developed. The purpose of this research is to investigate recent advances in aptasensors for detection of tetracycline

Methods: In the forthcoming systematic review, the required data were collected using keywords and citing valid databases such as Scopus, PubMed, Google Scholar and ProQuest. The statistical population includes all studies conducted until 2022 in the field of Detection of tetracycline using aptasensors. After reviewing the relevant findings and evaluating the quality of the data, 18 articles were analyzed.

Results: After the TET aptamer modified onto multi-walled carbon nanotubes (MWCNTs-CS)/ interdigital array microelectrode (IDAM), the EIS presents an apparent increase, which was due to the inhibition effect of the macromolecules for electron transfer. After incubated with TET, the aptasensor has a significant change in impedance, but the non-specific oligonucleotide modified sensor almost stayed unchanged. The main reason lay in that the oligonucleotide cannot be combined with TET and TET cannot be bound to the electrode to prevent electron transfer, leading to the invariability in the impedance value.

Conclusion: Antibiotics are widely used and cause the development of antibiotic-resistant bacteria, allergic reactions and various side effects on human health. Therefore, ultrasensitive assays for the detection of tetracycline are of great interest. Such advanced aptasensors promise to overcome many challenges as biosensors are highly sensitive, easy to operate, and portable.

Keywords: Tetracycline, Aptasensor, Biosensor

Detection of aminoglycoside resistance genes in Enterococcus faecalis strains isolated from a clinical sample in Shahrekord (Research Paper)

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Introduction: Background and Objectives: Today Enterococci resistance to some drugs has gained widespread that it would cause complications in the treatment of infections caused by these bacteria. The purpose of this study was the evaluation of resistance to aminoglycoside antibiotics in Enterococcus faecalis by multiplex PCR.

Methods: 130 suspects Enterococcus isolates were collected from laboratory Shahrekord. Bacteria were identified by routine microbiological tests. Susceptibility testing towards aminoglycosides antibiotic using disk diffusion method. Finally, Multiplex PCR assays were performed to identify aminoglycosides antibiotic resistance genes.

Results: Out of the 130 isolates, 75 isolates were Enterococcus faecalis. The highest resistance towards Tetracycline and Streptomycin and the highest sensitivity to Vancomycin. PCR results showed the prevalence of aac (6')-Ie-aph (2")-Ia,ant(4')-Ia and aph (3') – IIIa, genes to be in order of %60, %26/6, and %56 , respectively. Ten isolates possessed all three genes.

Conclusion: According to the results of high-level antibiotic resistance, periodic tracking of antibiotic resistance genes in clinical samples is recommended.

Keywords: Enterococcus faecalis, Aminoglycoside genes, Antibiotic Resistance

Detection of isoniazid resistance strains of Mycobacterium tuberculosis by multiplex allele-specific polymerase chain reaction (MAS-PCR) in Ardabil, Iran (Research Paper)

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Introduction: Mycobacterium tuberculosis (MTB) is the major causative agent of a highly contagious disease called tuberculosis (TB). Tuberculosis (TB) is one of the top 10 causes of death among poverty-related infectious diseases (IDoPs), a major public health problem worldwide and is one of the most common life-threatening infections, with high rates of multidrug-resistant tuberculosis (MDR-TB). Drug-resistant tuberculosis (DR-TB) occurs in many parts of the world. The global rise of drug-resistant MTB strain, especially the significant prevalence of isoniazid (INH)-resistance, constitutes a significant challenge to global health. Isoniazid is one of the first-line drugs for tuberculosis treatment, and there are increasing reports of the development of resistance to this drug in many parts of the world. In most cases, mutations in the KatG and inhA genes are the cause of isoniazid resistance. Efforts to control tuberculosis have encountered serious problems with the emergence of drug-resistant Mycobacterium tuberculosis (MT), and rapid diagnosis of resistance can play an essential role in controlling and preventing the disease. Therefore, this study was conducted to evaluate the prevalence of mutations in genes associated with isoniazid (INH)-resistant MTB in Ardabil, Iran.

Methods: In this cross-sectional study, 111 Sputum and bronchoalveolar lavage (BAL) samples which microscopically were positive for MTB, were collected from patients referred to Ardabil Province Health Center from July 2016 to June 2020. Clinical specimens were subjected to DNA extraction using a specific lysis buffer and boiling method. The multiplex allele-specific polymerase chain reaction (MAS- PCR) and specific primers were employed for identifying mutation in inhA and KatG genes.

Results: Overall, based on the MAS-PCR method, 23(20.71%) of infected samples were resistant to isoniazid. The frequency of mutations in KatG and InhA genes was 10.81% and 9.9%, respectively.

Conclusion: This study showed the high mutation rate in the KatG gene which would be valuable for providing appropriate treatment regimens and tuberculosis management. Detection of resistance alleles in the KatG and inhA genes for INH could serve as markers for MDR-TB strains. The MAS-PCR is a useful method to detect mutations in the KatG and inhA genes. this molecular method is not only simple and inexpensive but also provides accurate and reliable results in less time than other methods. In addition, rapid diagnosis of INH-resistant MTB would accelerate the modification of TB treatment regimens. Timely infection control measures could reduce the risk of the development and transmission of multidrug-resistant TB.

Keywords: Mycobacterium tuberculosis, Isoniazid (INH), Drug resistance , tuberculosis (TB)

Determination of frequency, risk factors and antibiotic resistance pattern of nosocomial infection caused by Gram-positive cocci in Shahid Mostafa Khomeini hospital during April 2014-March 2020 (Research Paper)

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Introduction: Introduction: Gram-positive bacteria, especially gram-positive cocci such as coagulase-negative staphylococci and Staphylococcus aureus, are very important pathogens in the hospital environment, including urban and field hospitals during wars and natural disasters. Gram-positive organisms have highly variable growth and resistance patterns. Misuse of broad-spectrum antibiotics increases nosocomial infections. This is not only a major health care problem, but also imposes great economic losses on society.

Methods: Materials and Methods: This retrospective cross-sectional study was performed on 263 patients with at least one gram-positive cocci culture. These patients were hospitalized in the adult ward of Shahid Mostafa Khomeini Hospital from April 2014 to March2020. Isolates were differentiating by laboratory tests and antibiotic sensitivity and resistance were evaluated by standard disk diffusion methods. Data were analyzed using Medcalc statistical software.

Results: Results: The results of this study showed that the Isolate of Staphylococcus coagulase negative was in the first place with 36% infection. The most common risk factor for this bacterium was vascular catheters. Staphylococcus aureus was in second place with 33% infection and the most common cause was endotracheal intubation. Enterococcus isolate was in the third place with 25% infection and the most common cause was urinary catheter. The best effective drugs on gram-positive cocci were vancomycin and ciprofloxacin and the highest resistance was observed in erythromycin, amikacin and clindamycin. Prolonged hospitalization and hospital ward were effective risk factors.

Conclusion: Conclusion: According to the results of the study, the use of effective antibiotics according to the patient's antibiogram can be useful in the better effectiveness of treatment.

Keywords: Keywords: Nosocomial infection, Antibiotic resistance, Gram-positive cocci, Risk factors

Determining the Functional Effect of COVID-19 on Adametase 13 Protease activity in Patients with TTP (Thrombotic Thrombocytopenic Purpura): A Systematic Review (Review)

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Introduction: Thrombocytopenic purpura (TTP) is a blood condition that affects 3 to 10 adults per million population in one year and is deficient in (<10%) ADAMTS13 (a di-integrin and metalloproteinase), a protein. The cut is defined for the phone. Thrombotic microangiopathies are a group of disorders that are mainly related to endothelial dysfunction. These endothelial disorders are caused by several imbalances between platelets, the endothelium, the immune system, and the production of cytokines. With the advent of Covid-19 vaccines, the severity of hospitalization of patients and the progression of Covid-19 disease in the acute condition is greatly reduced. Autoimmune hematologic complications such as vaccine-induced immune thrombocytopenia (VITT), immune thrombocytopenic purpura (ITP), and TTP have also been reported after COVID-19 vaccination. The pathophysiology of TTP de-Novo remains unclear after vaccination with two schools of thought. First, it expresses undetected latent TTP, which is shown by patients after a stimulus (vaccine) with the onset of symptoms within a few days of receiving the vaccine. Second, it increases the potential for the formation of autoantibodies against ADAMTS13, which it presents through molecular mimicry mechanisms. In addition, there is evidence that ADAMTS13 deficiency alone is not sufficient for acute relapse in patients with acquired or recurrent TTP. There is a need for a "second shock" in the form of infection or inflammation for acute TTP deposition, in which case the COVID-19 vaccine was considered. (Thrombotic Thrombocytopenic Purpura).

Methods: This is a secondary study (Systematic Review - 2022) looking for preferred case reports for systematic reviews and meta-analysis recommendations (PRISMA) that we searched in the PubMed, EMBASE, and EBSCO databases for published studies on TTP. There were no restrictions based on language, age, or country of origin. The first search was conducted on May 1, 2022, followed by an additional search on May 12, 2022. The two authors independently screened all search results from three databases at the title and abstract level, and if any, the discrepancies were resolved. By discussion or judgment by the third author. We retrieved all available

resources in the studies provided for additional resources. The following keywords were used to identify the reports: "COVID-19" [Mesh] AND "TTP [Mesh]" OR "Purpura" [Mesh] AND "ADAMTS13 Protein" [Mesh] AND "COVID-19 Vaccines"

Results: Normally in the body, proteases called Adams to break down 13 von Willebrand multimeters, and in its absence, these multimers remain, causing platelet binding and aggregation. This deficiency is inherited or more commonly acquired as a result of the production of antibodies against Adams 13 and if its activity level reaches less than 10%, thrombotic thrombocytopenic purpura disease develops and its five symptoms include fever, Thrombocytopenia is microangiopathic hemolytic anemia, renal failure, and neurological symptoms. In its peripheral blood smear, there are red blood cells in the form of schistocytes. The enzyme is lactate dehydrogenase and its diagnosis is based on clinical evaluation of thrombocytopenia and microangiopathic hemolytic anemia. Assay for the activity of Adams 13 is not widely available. Thrombotic thrombocytopenic mortality is relatively significant, reaching about 10% at 18 months after starting steroid treatment and plasma replacement.

Conclusion: Evaluation of thrombocytopenia after vaccination poses an important diagnostic dilemma, and physicians should consider the likelihood of TTP given the associated mortality and the need for appropriate treatment, as the risk of TTP mortality without early treatment is -80. 90% remains high.

Keywords: COVID-19, TTP, Purpura, ADAMTS13 Protein, COVID-19 Vaccines

Determining the relationship between HPV virus and the occurrence of malignant or premalignant colorectal lesions: a review study (Review)

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Introduction: Colorectal cancer is the third most common tumor and the fourth cause of mortality caused by cancers; the incidence rate of which in Iran is about 5000 new cases per year. On average, the 5-year survival rate for this malignancy is 64.4%. Human papilloma virus is a DNA virus that infects the cells of the epithelial basal layer and after the integration of the virus DNA into the cell genome, it leads to the over expression of E6 and E7 oncogenes. This ultimately leads to a decrease in the activity of the Rb and P53 genes; and in this way it is associated with mucoepithelial cancers. Considering the high prevalence of HPV infections and colorectal cancer in the country, the aim of this study is to investigate the possible role of HPV in the occurrence of malignant or pre-malignant lesions of the colorectal.

Methods: In this study, published articles on the possible role of HPV in colorectal cancer in Iran and the world were reviewed and the results and parameters involved in this topic were evaluated and compared. In this study, PubMed, Web of Science, EMBASE, Scopus ,and Google Scholar databases were searched.

Results: In order to determine the relationship between HPV and colorectal cancer, it is necessary to be able to detect the genome of the virus in cancerous or precancerous lesions, but not in healthy tissues. Some studies have shown that 14-84% of colorectal cancer cases were positive for HPV DNA, while others did not find a significant relationship between the two. In a study conducted in Turkey, 81.2% of cancer tissues contained HPV genome, however, in the studies conducted in Iran, despite the different findings regarding the presence or absence of HPV genome in biopsies obtained from patients with colorectal cancer, in most studies, there was no significant relationship between the presence or the role of HPV with the occurrence of colorectal cancerous or precancerous lesions .

Conclusion: Conclusion: In Iran, despite the different findings regarding the presence or absence of the virus genome in the samples taken from patients; No significant relationship has been found between the presence of HPV and the occurrence of colorectal cancer. It is felt that extensive studies with a sufficient sample size will clarify the dimensions of this issue

Keywords: colorectal cancer, HPV, oncogene

Determining the relationship between nsSNPs genome sequencing in human SLC2A2 gene and phylogenetic function of nucleotides (Review)

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Introduction: DNA sequencing (DNA) is a process in which the sequence of nucleotides in a DNA molecule is determined. The DNA of living organisms consists of a special sequence of nucleotides. DNA sequencing allows scientists to examine the relationships between organs and their phylogenetic relationships by comparing DNA between different organs. Glucose transfer through the eukaryotic cell membrane is carried out by members of the glucose transporter family (GLUT), which are mainly divided into three classes (I, II and III) based on phylogenetic relationship. In humans, a class I member called GLUT2 is encoded by the carrier family of salt 2, the facilitated glucose transporter 2 gene (SLC2A2) on the third chromosome. The requirement for DNA sequencing was first proposed by Francis Crick's theory. Protein-mediated movement of glucose in cell membranes is made possible by GLUT2, a transmembrane transporter protein. Regulates glucose uptake and insulin secretion into pancreatic cells. Modern DNA sequencing uses powerful methods that allow DNA sequences to be identified in a very short time. This technology has made it possible for many companies to offer their customers methods for home DNA testing. An example of DNA sequencing DNA sequencing In the past and in the early years of the invention of this technology, it took a long time and sometimes several years to achieve the result, but now with the development of technology, DNA sequencing can be done in a few In addition to DNA sequencing, services such as DNA sequencing also offer services such as single-nucleotide polymorphism tests to identify and study genetic changes and mutations in the human genome. Sequencing Target Areas although whole genome sequencing using NGS genome techniques is an optimal and community-based method, it is not available in many research and clinical laboratories. The aim of this study was to determine the relationship between genome sequencing and phylogenetic function of nucleotides

Methods: This study was a secondary study with a narrative approach approach that in 2022 by searching for keywords such as sequencing, NGS, genome, phylogenetics, nucleotides and mutations in valid databases such as Scopus, Sciences Direct, Web of Sciences and PubMed. All input and output criteria of the study were examined. In this study, 15 articles were selected, of which 10 articles were included in the study

Results: There are 13 extracellular domains, 12 interstitial domains and 5 cytoplasmic domains in human GLUT2. The risk of Fanconi-Bickel syndrome (FBS), diabetes, breast cancer (BC) and Alzheimer's disease (AD) is associated with poor GLUT2 function. The most common form of genetic mutation is single nucleotide polymorphism (SNPs). Non-synonymous SNPs (nsSNPs) can lead to amino acid changes and subsequent changes in phenotype. In this study, intra-silicon analysis was performed to find the phylogenetic relationship of human GLUT2 protein and the potential adverse effects of nsSNPs in its coding region. Identification of different variants using sequencing of the whole genome is of particular importance to the identification of genetic variants of a particular trait. Variants that make some people more susceptible to the disease A study of the entire genome through sequencing was initially performed on variants that are common in the community, but with NGS methods and sequencing of the entire genome, it is possible to study variants with abundance. Provided less.

Conclusion: Using this method, the binding site of some transcription factors and genes under its control can be identified. The Methyl-Seq technique is also used to map the genome methylation pattern and to identify regions that are differentially methylated.

Keywords: sequencing, NGS, genome, phylogenetics, nucleotides and mutations

Determining the role of induced mesenchymal and pluripotent stem cells in the treatment of liver cancer (Review)

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Introduction: Primary liver cancer is the seventh most common cancer and the second most common cause of cancer death in the world. Cirrhosis and liver failure are common clinical signs of liver disease. The liver is constantly exposed to harmful damage from external and endogenous toxins, so it needs a way to heal the damage. Globally, hepatocellular carcinoma (HCC) is the leading histological type of liver cancer, accounting for more than 75% of all liver cancers. Liver transplantation is known as the best and most effective treatment for the final stage of liver disease. But it was limited due to lack of organs and high costs. Today, stem cell therapy has received increasing attention due to its attractive effectiveness in the treatment of liver disease, especially cirrhosis, during clinical trials. In recent years, mesenchymal stem cells (MSCs) have been used as an alternative approach to the treatment of liver disease has been suggested. This study aimed to determine the role of mesenchymal stem cells and induced pluripotent stem cells in the treatment of liver cancer. Mesenchymal stem cells can be defined as pluripotent cells with self-renewal capacity that can create many distinct and unique types of mesenchymal cells. At present, the mesenchymal stem cells used in clinical therapy and basic experimental research are mainly derived from bone marrow, umbilical cord, adipose tissue, amniotic fluid, menstrual blood, and so on.

Methods: This study is an initial observational study of the analytical study with a group approach that in 2022 by searching for keywords such as Mesenchymal Stem Cells, Bone Marrow, Pluripotent Stem Cells, Liver Neoplasm in the MeSH database and reputable databases such as Science Direct, Pub Med and Web of Science were performed and 15 articles were extracted and 10 of them were reviewed and included in the study.

Results: Mesenchymal stem cells (MSCs) can be differentiated into hepatocytes, promote liver regeneration, inhibit liver fibrosis, and induce liver apoptosis, particularly through paracrine mechanisms. Studies have shown that liver regeneration after hepatectomy is characterized by specialized phenotypic examination, meaning that each cell is responsible for replicating

its cell type. Normal liver regeneration occurs primarily through the proliferation of mature hepatocytes and bile epithelial cells (BECs). Liver cancer stem cells (LCCs), which are identified by specific surface markers, are responsible for tumorigenesis, recurrence, metastasis, resistance to chemotherapy, and poor prognosis of HCC. That is, hepatocytes make other liver cells, and this is true of most other types of hepatocytes, including BECs and hepatocytes (HSCs). Stem cells are not usually associated with physiological proliferation of the liver, except for Kupffer cells and hepatic sinus endothelial cells (LSECs), both of which can be derived from bone marrow stem cells. Remarkably, in the case of impaired hepatocyte proliferation or BECs, the inactive cell type can become a damaged cell type and effectively act as an optional stem cell. A chemotactic protein from the family of CXC proteins produced by bone marrow stromal cells SDF-1a and its chemokine receptor CXC receptor 4 (CXCR4) in a variety of cells and tissues including immune cells, brain, heart, liver, kidney, lung, and spleen are expressed. SDF-1a promotes stem cell migration to damaged tissue by binding to CXCR4 on the stem cell membrane

Conclusion: Recently, extensive research has been devoted to examining the relationship between HCCs and MSCs. The function of mesenchymal stem cells in the development, development, and treatment of HCC is highly controversial. An increasing number of studies show that mesenchymal stem cells have dual properties of suppressing and promoting tumors through various molecular signaling mechanisms.

Keywords: Mesenchymal Stem Cells, Bone Marrow, Pluripotent Stem Cells, Liver Neoplasm

Development of a sensitive Sandwich ELISA method for detection of the SARS-CoV-2 (Research Paper)

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Introduction: Diagnosis of COVID-19 is based upon clinical and in vitro approaches. Sensitive diagnostics are of major importance for rapid and accurate detection of infectious agents including the SARS-CoV-2. In this regard, the current study was designed to develop a sensitive Sandwich ELISA (S-ELISA) kit for the detection of SARS-CoV-2 whole particles as a serious threat to human beings.

Methods: For the development of a sensitive S-ELISA platform, our recombinant scFv antibody (which is developed by in-depth bioinformatics studies) was used as a primary antibody for coating the microtiter ELISA plates. Thereafter, the washing step was performed and blocking was done with the tween 20 in PBS buffer. The whole viral particles were added to ELISA plates in 20µg/well concentration. Incubation was done and the secondary antibody (the positive serum samples from COVID-19 patients) was applied as a detection antibody to each well. After the addition of HRP-conjugated A+G antibody and three times washing with PBST, reactions were developed through the addition of TMB (3, 3', 5, 5'- tetramethyl benzidine).

Results: The gathered results showed the specific binding capacity and high affinity of the purified scFv for the detection of SARS-CoV-2.

Conclusion: In the current study, the potent in-vitro reaction of the introduced recombinant scFv turns it into a possible candidate for diagnostics and by further investigations, it may be utilized as potent therapeutics.

Keywords: SARS-CoV-2; Sandwich ELISA; recombinant scFv antibody; sensitive

Development of Diagnostic Biomarkers in the Inflammed and Non-Inflamed Intestinal Mucosa of Patients with Crohn's Disease Using Bioinformatics Analysis (Research Paper)

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Introduction: Despite having no known etiology, Crohn's disease (CD), an inflammatory bowel disorder, is frequently associated with genetic, immunological, and environmental variables. In the current work, the postulated molecular pathways in the inflamed and non-inflamed intestinal mucosa are subsequently explained using the transcriptional signatures we uncover in CD patients.

Methods: We have access to the GSE83448 gene expression profiles via the Omnibus gene expression database (GEO, https://www.ncbi.nlm.nih.gov/geo/). We conducted Gene Ontology (GO) keywords and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways searches using the web tool DAVID (https://david.ncifcrf.gov/) to enhance the identification of the biological activities of DEGs. Using the GEO2R instrument, DEGs were found in the inflamed and non-inflamed intestinal mucosa of CD patients as compared to the control group. Using the Cytoscape application, DEG protein-protein interaction (PPI) networks along with significant modules and hub genes were constructed.

Results: Patients' intestinal mucosa was divided into group's inflamed and non-inflamed intestinal mucosa using the biomarkers connective tissue growth factor (CTGF), matrix metallopeptidase 2 (MMP2), integrin alpha M (ITGAM), cadherin 1 (CDH1), JUN, collagen type I alpha 2 chain (COL1A2), collagen type III alpha 1 chain (COL3A1), C-X-C motif chemokine ligand 8 (CXCL8), serine protease inhibitor clade E member 1 (SERPINE1), and periostin (POSTN).

Conclusion: The development of new molecular targets and diagnostic biomarkers for both inflamed and non-inflamed intestinal mucosa in CD patients may be a result of these findings.

Keywords: Crohn's disease, Inflamed, Non-inflamed, Differentially expressed genes, Diagnostic Biomarkers

Development of novel human antibody against Naja oxiana snake venom (Research Paper)

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Introduction: Snakebite is one of the health concerns worldwide. Naja oxiana is one of the venomous snakes with a high mortality rate. Anti-serum therapy is the only treatment of the victims. However, in some cases, antiserum injection leads to some side effects in host like serum sickness and anaphylactic shock. It is crucial to develop a neutralizing agent with low side effects. The human antibody library (non-immunized library) was used to isolate specific antibodies against N.oxiana venom components.

Methods: Four rounds of biopanning were performed to enrich scFv-displaying phages against the venom of N. oxiana. Enrichment of scFv-displaying phages against N. oxiana venom was analyzed by polyclonal Enzyme-Linked Immunosorbent Assay (ELISA). Specific antibody fragments against N. oxiana venom were selected through monoclonal ELISA, and were expressed in E. coli bacterial cells. Purification of the selected clones was performed by using nickel affinity chromatography. Neutralization and protective capacity of specific antibody fragments were analyzed in C57BL/6 mice (i.v. injection).

Results: Results of biopanning and polyclonal ELISA demonstrate a successful enrichment process. Five specific antibody fragments with the highest signal in monoclonal ELISA were selected, expressed, and purified. The purity of expressed antibody fragments was monitored by SDS-PAGE and western blot. The selected antibody fragments were able to neutralize two LD50 of N. oxiana venom and protected all mice when injected 15 min post-envenomation.

Conclusion: The data indicate that such selected antibodies are promising tools for further studies and in the development of novel protective agents against N. oxiana venom.

Keywords: Naja oxiana, snake venom, human antibody, phage display.

Diagnosing laryngeal reflux with voice disorders using pharyngeal pH examination:A systematic review study (Review)

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Introduction: Laryngeal reflux (LPR) is an inflammatory disease of the upper gastrointestinal tract. It involves the retrograde movement of liquid and gas contents of the stomach through the esophagus to the pharynx and throat. Many laryngeal disorders have been attributed to LPR, including: reflux laryngitis, subglottic stenosis, contact ulcers and granulomas, and even laryngeal carcinoma. Analysis of the pH study characteristics of LPR patients may improve the understanding of the pathophysiological mechanisms of LPR. In clinical practice, objective diagnostic methods are also used, such as pH monitoring, pH-MII monitoring, oropharyngeal pH monitoring or pepsin detection test. Pharyngeal pH monitoring is a standard management of laryngeal reflux (LPR). Scores metrics including: number of reflux episodes, reflux time, and Ryan score. The present study was conducted with the aim of investigating patients with voice disorders caused by LPR by monitoring the pharynx.

Methods: Search method: In this article, we collected the required data by using keywords and also by searching in data bases such as Google Scholar, Scopus, ProQuest and PubMed. Our statistical population is all available articles published until 2022. After evaluating the findings as well as the quality of the data, we analyzed a total of 14 articles.

Results: The threshold for detecting acid reflux events was considered to be 5.5 and 5 for upright and lying positions, respectively. The results of oral and pharyngeal pH monitoring showed that out of 161 patients, 82 patients had non-acid reflux and 79 patients had acid reflux. Among patients who were diagnosed with acid reflux, 62% had acid reflux in the upright position, 25% had acid reflux in the supine position, and 13% had acid reflux in both the supine and upright positions. The number of patients with vertical LPR was significantly higher compared to supine LPR. In addition, comparing the vertical LPR group with the lying LPR group in terms of pH results, the number of LPR episodes and the total Ryan score in the standing group were significantly higher than the lying group. However, the percentage of time

below baseline pH and parameters of the longest reflux period were significantly higher in the supine group. Information on the prevalence of LPR in the population is scarce. A study from Greece estimated 18.8% based on RSI criteria, while a second Greek study reported an LPR prevalence of 8.5%. The efficiency of 24-hour two-probe pH monitoring (acid exposure in the proximal probe greater than 0.02%) for diagnosing LPR is low, and changes in diagnostic criteria should be considered. The frequency of LPR assessed by RSI and RFS in patients with voice disorders is approximately 47%. This suggests that causes other than gastroesophageal reflux, such as allergies, should be investigated in approximately 25% to 50% of patients with voice disorders. Approximately half of patients with voice disorders have LPR, and only a subset of these patients have evidence of GERD.

Conclusion: Fiber optic laryngoscopy (RFS) findings in addition to RSI seem to be important in diagnosing the possible cause of reflux in voice disorders and can be an indicator to start anti-reflux treatment. Acid exposure time as measured in the proximal probe of a dual 24-hour pH probe may need to be re-evaluated as one of the diagnostic criteria for LPR.

Keywords: larynx, reflux, voice disorders

Diagnosis and treatment of acute lymphoblastic leukemia in Iran (Review)

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Introduction: Acute lymphocytic leukemia (ALL) is a malignancy of B or T lymphoblasts characterized by uncontrolled proliferation of abnormal, immature lymphocytes and their progenitors which ultimately leads to the replacement of bone marrow elements and other lymphoid organs resulting in a characteristic disease pattern.Blood cancers represent the world's fifth most prevalent type of cancer, accounting for about 8% of all cancers. Leukemia is the fourth leading cause of death among Iranian children aged 5 to14 years. The most prevalent cancer of children in the world and in Iran is ALL. The peak incidence age of ALL is between 2–5 years, and it is more common in males. The high incidence and prevalence of leukemia are associated with significant mortality, incurring high diagnostic and therapeutic costs in Iran. This review is amid to discuss the status and challenges associated with ALL management in Iran

Methods: In this review, relevant studies were searched in scientific databases fusing Based on their title, and keywords associated with ALL and Acute lymphocytic leukemia from 2016 to march 2022. Out of 623 studies, 32 articles related to our aim according to the inclusion criteria of this review article, were studied.

Results: Information regarding ALL in Iran is scarce; however, many efforts have been made to overcome these barriers. Nevertheless, major obstacles to successful treatment in Iran and LMIC remain poor adherence, abandonment of treatment, and lack of supportive therapy and new therapeutic agents.

Conclusion: Further improvements in survival should be pursued by developing more Iran registries, forming cooperative groups, developing educational models to facilitate earlier diagnosis and prevention of complications, better support therapy and management of infections, and adapting treatment strategies.

Keywords: Acute lymphoblastic leukemia; Iran; Therapeutics

Diagnosis and treatment of cancer using microorganisms (Review)

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Introduction: cancer is a group of diseases that arise as a result of uncontrolled proliferation of transformed cells and is one of the most common causes of death, and it shows that we should look for a new way to treat it, which we are investigating bacterial therapy. . This method is non-invasive and it is possible to work on changing their ability in genetic engineering. Example: release of specific compounds and changes in metabolite pathways. Secretion of toxins and enzymes, including lipase and protease, and its effect on the hypoxic area of the tumor. A combination of bacteriotherapy and radiotherapy or immunotherapy can also be an effective method.

Methods: This is a research and review with PubMed and Google, the focus of which is the diagnosis and treatment of cancer using microorganisms.

Results: Probiotics are the most well-known microorganisms in the treatment of cancer and by, changing the intestinal flora, they reduce the absorption of carcinogenic and mutagenic substances, and Salmonella typhimurium has an anti-mutagenic effect, and in relation to the coagulation bacillus, with or without the presence of S9, between -40 50% and in relation to Lactobacillus acidophilus between 50-55% anticancer effect. Salmonella and Clostridium are effective in controlling tumor growth and increasing survival in animal models.

Conclusion: Bacteriotherapy method: A:Proliferation of tumor-specific bacteria which has the least negative effect on healthy cells B:Plasmid DNA transfer to mammalian cells by bacteria C:Use of tetanus, botulonium and diphtheria bacterial toxins in two bacterial methods and bacterial toxins that bind to tumor surface antigen The location of bacterial colony formation allows the detection of metastatic tumors by 4methods: bioluminescence, fluorescence, magnetic resonance and positron radiation. Transferring plant cytochrome P450 to E.coli bacteria can also turn it into an anti-cancer drug factory.

Keywords: cancer, Probiotics , Bacteriotherapy ,microorganisms

Diagnosis and treatment of type 1 diabetes at the dawn of the personalized medicine era (Review)

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Introduction: Type 1 Diabetes (T1D) is a likely life-threatening multifactorial autoimmune sickness characterized through manner of technique of T-cell-mediated destruction of pancreatic β cells, resulting in a deficiency of insulin synthesis and secretion. It requires cautious manage to avoid extreme long-time period complications, alongside coronary heart and kidney contamination, stroke, and absence of sight. Insulin replacement, stays the mainstay of treatment for the large majority of T1D patients today, but this technique fails to accumulate most dependable blood glucose manage in loads of individuals. With advances in our facts of early diploma diabetes development, diabetes stratification, and the characteristic of genetics, T1D is a promising candidate for a customized treatment technique, which desires to apply "the right treatment on the right time, to the right patient. Innovative techniques of accomplishing stepped earlier insulin mediated glycemic manage are becoming to be hard to patients, even as tissue transplants, genetic change and stem-cell therapies are showing promise in pre-medical models and human trials mainly subgroups of patients.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus, PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of diagnosis and treatment of type 1 diabetes at the dawn of the personalized medicine era. After reviewing the relevant findings and evaluating the data quality, a total of 29 articles were analyzed.

Results: By comparing healthy kidneys and kidneys with diabetic nephropathy (after death), gene expression patterns were identified. Preclinical trials of gene treatment were achieved with the aim of preventing or delaying the onset of type 1 diabetes, correcting insulin deficiency, promoting the feature and proliferation of pancreatic beta cells, modulating the

immune tool and inflammatory responses, or inducing insulin secretion via manner of technique of non-beta (which encompass intestinal K cells and hepatocytes, skeletal muscle). Through the over expression of wonderful genes, diabetes can also furthermore be handled or averted in extreme techniques. Klotho is an antiaging gene that is expressed in mouse and human pancreatic islets A mixture of gene treatment and immunomodulation can be helpful. The truth that some immunotherapies display their effectiveness first-class in a wonderful age organization is remarkable. (People of brilliant, sometime replies to brilliant treatments.) Several brilliant techniques to supply insulin-producing cells from embryonic stem cells were positioned so far. Removing the bone marrow and then transplanting autologous hematopoietic stem cells, which desires to preserve your autoimmune destruction of the pancreas and re-installation tolerance, is a few different ways to cope with T1D.

Conclusion: The appreciation of contamination and heterogeneity begs for the format of custom designed precision treatment centered on specific features, alongside age and specific immune phenotypes, that can distinguish corporations of patients on the concept of their contamination entity. Perhaps the most promising innovation in T1D treatment has been the exploration of the functionality of stem cells. Different treatment strategies ought to be available for brilliant patients, brought in an integrated, objective, quantitative and evidence-primarily.

Keywords: type 1 of diabetes ،personalized medicine ،Individualized Medicine ،Therapeutics type 1 of diabetes

Diagnosis of myocardial infarction by a new generation of biosensors (Review)

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Introduction: Myocardial infarction is a leading cause of death in developed and developing countries. Myocardial infarction occurs due to a lack of oxygen supply to the heart muscle. Since the necrosis and heart damage is irreversible in myocardial infarction and 85% of damage arises during the first two hours after the heart attack, the early diagnosis of this phenomenon is critical by safe, quick, and cost-efficient methods. Electrocardiogram studies as the main approach are not sufficient for early diagnosis of myocardial infarction, so detecting and monitoring relative biomarkers levels in plasma or saliva has attracted a huge of attention. Biosensors with electrochemical mechanisms and based on nanoparticles are very effective in monitoring the onset and progression of heart disease. These biomarkers include protein C, troponin I (cTnI) or T (cTnT), serum amyloid A, C-reactive protein, hearttype fatty acid-binding protein, myoglobin, and creatine kinase

Methods: The present study is a systematic review study that was conducted with strategy (or-and) in multiple databases (SID, ISC, PubMed, ISI), with a time limit (2016- 2021) and keywords such as biosensor, biomarker, heart disease, myocardial infarction, and heart attack. 39 studies were screened simultaneously by three researchers in 3 stages and finally, 20 studies related to the subject were obtained.

Results: Various biosensors have been developed to address the problems of traditional diagnostic and treatment methods, which have many advantages, such as low cost, mobility, reliability, repeatability, and require a small amount of solution to perform the test. Most studies emphasize the use of biosensors and provide practical and important details for the diagnosis of cardiovascular disease by biomarkers. Nano biosensors in combination with nanomaterials, provide powerful analytical substrates for the detection of cTnI

and cTnT. Some of the studies determined perspectives on the future of new methods and devices in this field.

Conclusion: Although biomarkers and sensors are approved by various researchers, the use of nanotechnology provides new methods to extend the accuracy of tests and accelerate the response to be considered.

Keywords: Myocardial infarction, Biosensors, Biomarkers, Nanotechnology

Diet and osteosarcopenic obesity: a potential for therapeutic application (Review)

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Introduction: Osteosarcopenic obesity (OSO) syndrome describes a decrease in skeletal muscle strength and bone mass and an increase in adipose tissue at the same time. So far, many preventive and therapeutic methods for OSO have been studied. The best of them in terms of having the least side effects and minimizing social and economic costs is to follow a proper diet and physical activity. Accordingly, in current study we aimed to examine the dietary factors associated with this syndrome.

Methods: The keywords including osteosarcopenia, nutrition, diet and osteosarcopenic adiposity were searched in PubMed, Scopus, and Google Scholar search engines until April 2022. After evaluating the quality of the data, 14 articles examining the relationship between dietary factors and OSO were entered the study and reviewed.

Results: Literature reviews showed, adequate dietary intakes of protein (1 gr/kg/day, high quality and branched-chain amino acids), low-fat dairy (especially fermented such as yogurt and cheese), fruits, vegetables, legumes, whole grains, nuts, seeds, berries and prunes are associated negatively with OSO. Moreover, the diets rich in micronutrients such as vitamin D, K, E, Calcium (from dairy or non-dairy), potassium, Magnesium and omega-3 fatty acids (from vegetable or animal sources) reverse the risk of OSO. On the other hand, excessive consumption of phosphorus, sodium, iron (mostly in processed foods and red meat), trans fatty acids, saturated fatty acids, omega-6 fatty acids, fructose (not in fruits) and refined grains increase the risk of OSO. Furthermore, preventing sudden weight loss, malnutrition, lack of energy, obesity and getting enough sleep (normal circadian rhythm) and exercise (yoga, pilates and tai chi) can be useful in managing and improving osteosarcopenia.

Conclusion: Diet can well changed the pathological aspects of osteoporosis, sarcopenia and obesity. This proves the need for more care and lifestyle modification during this period. Also, more comprehensive research is needed to better understand these relationships and to take appropriate interventions to remove barriers to rehabilitation.

Keywords: osteosarcopenia, nutrition, diet, osteosarcopenic adiposity

Differences and distinctions between covid 19 and monkey pox (Review)

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Introduction: In December 2019, Covid-19, a virus that causes acute respiratory disease, was identified in Wuhan, China. This new virus caused widespread and rapid infection. The World Health Organization declared the outbreak of the Covid-19 virus on January 31, 2020 as a public health emergency and international concern, and the treatment included general supportive care, respiratory support, symptomatic treatment, nutritional support, psychological interventions, etc., but the monkeypox virus was the first Once isolated and identified in 1958 when monkeys were sent from Singapore to a Danish research facility, monkeypox, a rare disease caused by infection with the monkeypox virus, was endemic in several countries in central and western Africa. Cases of infection in people outside of Africa are often associated with international travel or imported animals. However, the first confirmed human case was in 1970 when the virus was identified in a child in the Democratic Republic of the Congo who had suspected smallpox.

Methods: The current research is a systematic review that was studied using the keywords covid19, monkey pox, epidemic in PubMed, Google Scholar, Elsevier, and the desired articles.

Results: Case fatality rates of up to 11% have been reported, research has shown that vaccination with the traditional smallpox vaccine confers immunity against monkeypox, but since the eradication of smallpox in 1980, routine smallpox vaccination has been discontinued. Due to the limited knowledge of patients and health workers and the lack of diagnostic tools and treatment protocols, it is challenging for management in this field. This not only limits the level of care provided to those affected, but may also put other patients and health personnel at risk of infection.

Conclusion: Monkey pox is a viral disease like covid-19, but unlike it, it is not an emerging disease. The smallpox vaccine creates resistance to the monkeypox virus, unlike the covid-19 virus, human-to-human transmission is negligible and it can be transmitted through contact with large respiratory droplets and skin lesions. Contamination or the creation of a large epidemic like Covid-19 is less

Keywords: monkeypox, covid19, epidemic

Differential Effects of Graphene Materials on Human Skin Cell Metabolism and Function (Review)

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Introduction: In recent years, Graphene-based nanomaterials (GBNs) have attracted attention for their promising applications in biomedical. Adequate information is lacking despite rapid progress in the development of new applications about how GRMs (graphene-related materials) could affect human health, particularly regarding such highly exposed barriers as skin. In this review study we aimed to provide a general overview about Differential effects of graphene materials on the human skin cells.

Methods: In this systematic review, we collected the data we needed by using keywords and also by referring to reliable databases such as PubMed, Scopus, Google Scholar and ProQuest. The statistical populatio n of this study includes all studies conducted until 2022. After reviewing relevant findings and evaluating data quality, we analyzed 15 articles.

Results: Considering the potential cutaneous effect of carbon nanomaterials, researchers evaluated the in vitro effects of GBMs on human skin HaCaT keratinocytes, a spontaneously immortalized non-tumor cell line, which is used to evaluate the toxicity of several compounds at the skin level. Over the past decade, sublethal doses of GRM have been shown to induce neitherapoptosis or necrosis can have a deleterious effect on human cells by altering cellular metabolism and homeostasis. After dermal exposure, the toxic effects of GBMs remain unknown. Skin contact with carbon nanomaterials such as graphite is associated with more skin problems. Graphene oxide (GO) is more useful than other GRMs because it is soluble in water. Previous studies have explained how GO induces cytotoxicity through increased reactive oxygen species (ROS). This causes the intrinsic apoptosis pathway (mitochondria) to be activated and also causes necrosis. According to the evidence, FLG in high concentrations interacts with HaCaT

keratinocytes in causing significant damage to mitochondria as well as altering the plasma membrane. The different physicochemical properties of GBMs, like their composition used for their production could ultimately influence their interaction with cells and their cytotoxicity. Using the mitochondrial activity of HaCaT cells, the effect of GOs and FLG on cell survival after exposure (24 to 72 h) was evaluated. Considering that FLG is significantly less in reducing mitochondrial activity than GO3, it can be said that the oxidation state of the substance affects the cytotoxic potential. It seems that, contrary to the absence of anti-proliferative properties, the effect of GOs and FLG on HaCaT cells indicates a significant damage in the plasma membrane levels. Data report that long-term exposure to low GBMs concentration induces only slight cytotoxic effects. According to previous studies, different GRMs can stimulate cytotoxicity and cause necrosis, apoptosis and autophagy. All these processes are related to cellular stress.

Conclusion: In limited time, GO and FLG had different effects on cell death. Both compounds reduced cell motility to a similar extent in a dose-dependent manner. Since actin remodeling and cell migration are impaired by treatment with free GRMs, results suggest that processes like wound healing could be compromised. In new scaffolds, one of the promising candidates is graphene foam, which plays a role in skin tissue regeneration and, bioengineering and it is therefore essential to understand the mechanisms governing its toxic effects and to determine the exact toxicity range for each GRM to choose the best one for each specific need with the least damages, besides that we can create different low and high oxygen graphene for different uses.

Keywords: graphene, toxicity, skin

Differentiation of mesenchymal stem cells derived from adipose tissue into insulin- producing cells using flavonoid compounds of walnut green skin in diabetic model rats (Research Paper)

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Introduction: For many years, the use of stem cells to treat diabetes has become a global challenge in regenerative medicine; So that studies with a history of nearly 50 years have proven that stem cells can perform repeated divisions and remain undifferentiated, but if there is a specific stimulus in the environment, they are able to differentiate into different types of dedicated cells; Therefore, this research aimed at the differentiation of adipose-derived mesenchymal stem cells (AD-MSCs) into pancreatic beta cells using the flavonoid compounds of walnut green skin in order to produce or increase insulin hormone at the level of clinical study.

Methods: In this experimental study, the differentiation of AD-MSCs into insulin-producing cells was started under the flavonoid extract obtained from the green skin of walnut with doses of 50 and 100 mg/ml for three weeks. To make rats diabetic, streptozotocin with a dose of 60 mg/kg was injected intraperitoneally. In order to check the differentiation of cells, morphology test, Dithizone staining (DTZ) and insulin measurement were used by ELISA method. At the end, blood was taken from the animals and the levels of glucose, creatine, urea and uric acid and the expression level of specific genes of pancreatic cells namely PDX1 and NGN3 were evaluated by RT-PCR method.

Results: The results showed that under the influence of flavonoid compounds, the differentiated cells were transformed from spindle-shaped to round or clustered cells, and the DTZ-specific staining of the cells was positive and insulin secretion was also proved. The level of serum glucose, creatine, urea and uric acid decreased and the expression level of insulin-producing genes PDX1 and NGN3 showed a significant difference in the experimental groups ($P \geq 0.05$).

Conclusion: The findings of this study showed that in addition to the flavonoid compounds in walnut green skin, they can effectively differentiate AD-MSCs into insulin-producing cells. It has even been able to increase the amount of insulin hormone production through the differentiation or production of new pancreatic beta cells.

Keywords: Diabetes, Adipose Tissue-derived Mesenchymal Stem Cells, Flavonoid, Differentiation, Pancreatic beta

Disease pathogenesis, therapeutics and the outcomes of genetic and non-genetic elements in vitiligo: An Overview (Review)

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Introduction: Vitiligo is a long-standing progressive autoimmune disorder that's characterized by the absence of pigment within the skin and therefore the loss of melanocytes. Melanocytes are found within the basal layer of the epidermis in many tissues involves the skin, hair follicles, eyes, inner ear, bones, heart, and brain, and along with the keratinocytes form the epidermic unit, whose main perform is to provide and distribute melanin by a complex method known as melanogenesis. Melanogenesis is decided genetically however is influenced by many intrinsic and extrinsic factors. The intrinsic factors are free by close cells, as well as keratinocytes, fibroblasts, inflammatory, neural, and endocrine cells, and the extrinsic elements, encompass ultraviolet radiation and medicines. Nowadays there has been a rampant advance in determining the molecular and genetic factors influencing the disease process and the relationship between several cytokines and signaling pathways with the pathogenesis of the disease has been determined. An autoimmune hypothesis predominates and is supported by several factors: its association with other autoimmune diseases, high levels of antibodies against melanocytes found in 10% of patients with vitiligo, susceptibility loci associated with vitiligo in genome-wide association studies that encode immunomodulatory proteins, and lastly, an inflammatory infiltrate seen at the periphery of active lesions. In biochemical theory, damage to melanocytes is due to an imbalance in oxidative stress. Higher levels of hydrogen peroxide in vitiligo patients and increased superoxide dismutase activity support this theory. Another hypothesis is the melanocytorrhagy theory, which proposes that defective cell adhesion leads to detachment and transepidermal loss of melanocytes with exposure to autoantigens and activation of the immune system leading to melanocyte injury. Eventually, the convergence theory states that the presence of a combination of several pathways causes vitiligo, including genetic background, sensitivity to environmental changes, altered epidermal microenvironment, intrinsic melanocyte defect, and autoimmune response. Clinically, vitiligo appears as achromic patches that increase in number and area over time. Therapy strategies aim to halt the disease, achieve repigmentation, and prevent a recurrence.

Methods: A thorough search was done using the terms "vitiligo," "autoimmune"', "oxidative stress", "repigmentation," "JAK inhibitors," "TNF-α inhibitors," and "IL inhibitors" on databases including Google Scholar, Medline, and PubMed. The study was created after a thorough analysis of pertinent English-language papers and review articles. This article sought to provide a thorough analysis of all biological and more recent targeted treatments used to treat vitiligo, as well as their effectiveness and any potential side effects.

Results: Vitiligo is a multifactorial ailment with a tricky interaction among various factors regarding genetic and non-genetic elements along with non-immunological and immunological elements. The remedy modalities in vitiligo have frequently been nonspecific and generalized like topical immunosuppressive, phototherapy, surgical techniques with modest efficacy, and potential adverse effects. Owing to higher information on the pathophysiology, there's the viable emergence of more modern unique centered treatment options aimed toward proscribing ailment development and attaining repigmentation with a good safety profile.

Conclusion: Despite recent significant advancements in our understanding of vitiligo, its pathophysiology and causation are still unknown. There are still questions concerning what ultimately leads to the destruction of melanocytes, and further research is required to fully understand the etiology of vitiligo. A better knowledge of pathophysiology has led to the development of newer, more focused medicines with a high safety profile that attempts to slow the progression of the disease and achieve repigmentation. JAK inhibitors are the only class to date with outcomes that are both promising and well tolerated; but, like any immunosuppressant, they carry the danger of reawakening latent infections and a few systemic side effects. Comparing adjuvant phototherapy to monotherapy can result in a better response. Despite TNF-α inhibitors have been utilized in a few cases, it is most effective when vitiligo is present in conjunction with other chronic autoimmune disorders for which it is prescribed. Additionally, before beginning treatment, patients should be informed of the possibility of their condition getting worse or developing de novo vitiligo. Also, IL inhibitors have not been very good at achieving the desired response. Numerous new therapies are under development, and the majority of available information about them is provided by case studies or series. However, more randomized controlled trials are required to better evaluate their effectiveness.

Keywords: Vitiligo, Autoimmunity, TNF- α inhibitors, JAK inhibitors

Down syndrome (trisomy 21) (Review)

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Introduction: Down syndrome is known as trisomy 21, a condition in which people have 47 chromosomes per cell instead of 46 per cell. Trisomy 21 is caused by an error in cell division. This extra chromosome occurs randomly and is dependent on the mother's age. Basically, the older the mother is, the higher the chance of it occurring in the fetus. But the interesting thing here is that most of the affected children are born to mothers under 35 years old because the number of children born to these mothers is more than that of mothers over 35 years old in the society. The incidence of Down syndrome is estimated to be between 1 in 1,000 and 1 in 1,100 live births worldwide. Characteristics of children with Down syndrome: Distinctive features such as flat face, small ears, slanted eyes and small mouth, short hands and feet Loose joints. Below average intelligence Many children with Down syndrome are also born with heart, intestinal, ear or breathing problems. These health conditions often lead to other problems, such as respiratory tract infections or hearing loss. But most of these problems can be treated. Impulsive behaviors. Weak analysis power. Mental retardation. Low learning bias. Short attention span. Obsessive distraction Treatment: There is no definite treatment for it. But it must be acknowledged that early intervention, high quality health care, good educational opportunities, proper nutrition and many other interventions make a big difference in a person's life. According to research, if the mother's gestational age is older than 35 years, the probability of the baby's Down syndrome increases. Also, if they have previously given birth to a child with Down syndrome, the probability of having a new child increases. Sometimes it is seen that the parents' genes are equal, but one of those genes is not in the right place. The mother or father may not have this disease themselves, however, it is possible that their child will have one of the types of Down syndrome. Trisomy 21 This model is the most common type of Down syndrome in the fetus, in which each individual cell receives three copies of chromosome 21 instead of two. Translocation Down syndrome In the previous model, a separate copy was created from chromosome 21. But in this model, the extra chromosome sticks to the previous chromosome 21. As a result, the number of chromosomes remains the same as 46 Mosaic Down syndrome This type can be considered the rarest model of this disease in which only some cells have an extra chromosome. Therefore, the symptoms of Down syndrome are much less common in these people prevention: Sonography of N.T Between the 11th and 14th week, using ultrasound, they check the fold on the back of the fetus's neck. Triplicate experiments Between weeks 15 and 18, the mother's blood should be checked with some tests and the desired factors should be measured. Combination test This test combines the

screening results of the first 3 months of pregnancy, blood tests and NT ultrasound with the quadruple screening of the second 3 months. DNA testing This test is performed without cells and in which the genetic material and DNA present in the mother's blood are analyzed Genetic ultrasound Between 18 and 20 weeks of the fetus, the doctor must combine the results of the blood test with the result of a very accurate ultrasound and examine the details. Diagnostic tests: sampling of placental villi. amniocentesis Subcutaneous umbilical cord blood sampling Improving people's lives through: occupational therapy, speech therapy and physiotherapy. Enrollment in special schools. There is no conclusive scientific research that shows that Down syndrome is caused by environmental factors or parental activities before or during pregnancy All 3 types of Down syndrome are genetic disorders (related to genes). But only 1% of all cases of Down syndrome have a hereditary component, meaning they are passed from parent to child through genes.

Methods: by study and reviwe simmilar articles

Results: By performing screening tests and diagnostic tests, it is possible to prevent the birth of genetically defective babies.

Conclusion: It is a genetic disease that is caused by the presence of an extra copy of chromosome 21. It causes symptoms such as: small nose, upper eyelid slits, short stature, mental disability in them. Heart problems are seen in half of them. There is no treatment for the disease and it is before birth. The baby should undergo diagnostic tests for prevention.

Keywords: Trisomy 21. Down syndrome. Genetics. Chromosome. DNA

Down-regulation of HSD17B13 and the role of rs76926692 as potential factors in development of Liver Hepatocellular Carcinoma: Bioinformatic analysis of proteomics data (Research Paper)

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Introduction: Liver Hepatocellular Carcinoma (LIHC) is one of the most hazardous cancers. Although many significant breakthroughs have been made in medical treatments, LIHC is one of the most common causes of death universally.

Methods: Expression analysis of GSE136247 was obtained from GEO2R online software, and the GEPIA2 database confirmed expression analysis. After using the mirwalk database, a microRNA was picked up, and its correlation with HSD17B13 was studied. Single nucleotide polymorphism (SNPs) of HSD17B13 acquired from dbSNP and detection of deleterious SNPs from SIFT database. Then, structural modifications of these SNPs were checked in HOPE software in order to recognize the reasons for this harmful effect on the development of LIHC.

Results: According to the microarray analysis, HSD17B13 has a notable down-regulation in the LIHC samples compared to controls. Chose the best-interacted miRNA, which was hsa-miR-7974 with HSD17B13. Moreover, after performing a correlation analysis between these two applying Encori, the result obtained from 370 samples of LIHC supported the previous finding that hsa-miR-7974 down-regulates HSD17B13 in this disease due to the convincing R=-0.201 and p-value=9.86e-05. Based on the Reactome database, HSD17B13 plays a role in numerous signaling pathways associated with LIHC, such as MAPK family signaling cascades, Receptor Tyrosine Kinases, and Hedgehog. The down-regulation of HSD17B13, which has oxidoreductase activity, involves the progression of LIHC. Among plenty of deleterious SNPs in the coding region of HSD17B13, rs76926692 is one of the most significant deleterious ones. In this SNP, Proline residue mutates to Glutamine at position 260. This mutant residue is larger and can't fit the protein core, which may cause a problem in the binding process, and less hydrophobicity, which causes hydrophobic interactions deficiency which can cause a problem in folding correctly. Furthermore, since this mutation happened at the highly conserved residue, it is likely to have a devastating effect on the protein.

Conclusion: In conclusion, several pieces of evidence were in agreement with the down-regulation of HSD17B13 in LIHC, and rs76926692 can encourage the development of LIHC by modifying the folding and the interactions of this protein.

Keywords: Liver Hepatocellular Carcinoma, Single nucleotide variations, Microarray, Data analysis

Down-regulation of MBP in MAPK signaling pathway by miR-15a-3p might promote the multiple sclerosis status: high-throughput bioinformatics investigation (Research Paper)

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Introduction: Due to a better understanding of the mechanisms behind relapsing-remitting multiple sclerosis, various disease-modifying drugs have been produced during the past several decades through immune system control or suppression. However, the options for treating progressive multiple sclerosis are still largely unsatisfactory and challenging [1]. We used high-throughput data analysis in this research to identify new regulatory RNAs (both protein-coding and non-coding) in MS patients.

Methods: To identify novel potential dysregulated regulatory mRNAs in MS patients relative to controls, the GSE38010 [2] microarray dataset was downloaded and analyzed. Affy package [3] obtained the raw data from Bioconductor (http://bioconductor.org/). The limma software was used to normalize the raw data and analyze differential expression (DE) [4]. The Enrichr [5] online database (https://maayanlab.cloud/Enrichr/) was used for pathway enrichment and gene ontology (GO) analysis. To identify new regulatory miRNAs for possibly dysregulated mRNAs, an investigation of microRNA (miRNA)-mRNA interactions was carried out using the online tool miRWalk [6] (http://mirwalk.umm.uni-heidelberg.de/).

Results: Based on high-throughput microarray data analysis, the MBP gene has a significantly low expression in the MS samples (logFC: -6.465, adj. P. Val: 0.010899). miRNA-mRNA interaction by mirwalk revealed that hsa-miR-15a-3p regulates the expression of the MBP gene (score: 1, binding energy: -23, number of pairings: 18) by maintaining an RNA interaction by the seed region in the 3'UTR of MBP mRNA. Based on Enrichr, MBP regulates the Neural crest differentiation and MAPK signaling pathways. Positive regulation of metallopeptidase activity (GO:1905050) and positive regulation of chemokine (C-X-C motif) ligand two production (GO:2000343) are the two main biological processes regulated by MBP.

Conclusion: By suppressing the expression of MBP, miR-15a-3p regulates the Neural crest differentiation and MAPK signaling pathways by involving the positive regulation of metallopeptidase activity. MBP is a significant low-

expressed mRNA in MS patients. So, miR-15a-3p could promote MS by playing a role in the low-expression of MBP.

Keywords: Microarray analysis, Systems biology, Multiple Sclerosis, RNA interaction network

Drug resistance pattern of Escherichia coli isolates from typical lesions of poultry colibacillosis and detection of florfenicol and colistin resistance genes by PCR (Research Paper)

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Introduction: Escherichia coli is the causative agent of colibacillosis in poultry leading to heavy economic losses and increased antibacterial use in poultry flocks with a consequence of increased drug resistance. In order to reduce drug resistance, as a global problem, and to establish better health among humans, animals and environment, a periodical monitoring of drug resistance rate is required. The aims of this study were to investigate the resistance of Escherichia coli isolates to different antimicrobial agents and also to detect florfenicol (cfr, fexA, floR) and colistin (mcr-1) resistance genes among isolates.

Methods: One hundred Escherichia coli isolates originated from typical lesions of colibacillosis were collected from poultry referred to a private laboratory in Tehran and University bacterial collection and the drug resistance of isolates to 16 antimicrobial agents including ampicillin, neomycin, gentamicin, enrofloxacin, flumequine, difloxacin, chloramphenicol, florfenicol, Fosbac, erythromycin, colistin, tetracycline, oxytetracycline, trimethoprime+sulfa, linco-spectin and doxycycline was determined by using disk diffusion method. Then, the chromosomal and plasmid DNA were extracted and florfenicol (cfr, fexA, floR) and colistin (mcr-1) resistance genes were detected among all isolates by using polymerase chain reaction test (PCR).

Results: Based on antimicrobial susceptibility test, the highest resistance was observed to erythromycin, doxycycline and tetracycline and the lowest resistance rate was found to linco-spectin, gentamicin and Fosbac. All isolates

were resistant to at least one and 10% of isolates were resistant to at least 12 antimicrobial agents. The 16% of the isolates belonged to one identical pattern and 35% of isolates each belonged to a separate pattern. Among 85 tested isolates, 40 and 52.94% of the isolates showed floR gene on their plasmid and chromosomal locations, respectively. However, no isolate was positive for fexA, cfr and mcr-1 resistance genes.

Conclusion: The findings of this study demonstrated the high frequency of resistance to commonly used antimicrobial agents among E. coli isolated from colibacillosis. Detection of resistance genes increases the researchers' knowledge on the epidemiology of drug resistance. This information indicates the necessity for implementation of the right management programs for poultry farms and rational antimicrobial therapy besides periodic antimicrobial susceptibility monitoring.

Keywords: Colibacillosis, Colistin, Drug resistance, Escherichia coli, Florfenicol

Dysregulation of EZH2/CDKN2A/CDKN2B in a ceRNA network promote thyroid carcinoma (Research Paper)

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Introduction: Thyroid carcinoma (THCA) represents the most common endocrine malignancy, among all endocrine carcinomas.The genetic alterations identified in THCA fail to distinguish tumors with different clinical behaviors, such as extra-thyroidal extension and lymph node metastasis[1]. In recent decades, miRNAs and lncRNAs have been considered as potent biomarkers in cancer. Therefore, in this bioinformatics approach, the goal was to discover a biological network of genes, miRNAs and lncRNAs which have a remarkable impact on progression of THCA

Methods: Initially, (GSE104005) raw data was achieved from the NCBI Gene Expression Omnibus(GEO) and analyzed by GEO2R in order to find genes with significant increase in expression regulation. Further, validation of expression analysis performed by GEPIA2[2] and ENCORI[3] databases to select differentially expressed genes (DEGs). In this investigation DEGs with adjusted p-value<0.05 and |logFC| >1.2 were considered significant. EZH2, CDKN2A, and CDKN2B were selected. The pg. 2 possible correlation between the selected genes and thyroid carcinoma is reinforced by GEPIA2. Furthermore, biological pathway involvement are processed Through Reactome[4] and NRICHR[5] databases. Moreover, STRING[6] and Genecards[7] are utilized to find significant protein-protein interactions and the exact interaction among these genes .In addition, selected genes were searched in Mirwalk[8] to find significant miRNA-mRNA interactions and hsa-miR-4289 is identified a significant mutual miRNA among these three genes . In addition, with the purpose of finding lncRNAs related to this network, the miRNA was searched in LncBase V.3[9] and MALAT1 and XIST were selected as suitable lncRNAs that construct a predictive ceRNA network among them

Results: GEO data analysis by GEO2R indicated, that EZH2 , CDKN2A and CDKN2B as significantly up-regulated genes in the THCA samples, compared to control (DEGs with adjusted p-value < 0.05 and |logFC| >1.2 were considered significant).The product of EZH2 mRNA is Histone-lysine N-methyltransferase EZH2, the Catalytic subunit of the PRC2/EED-EZH2 complex (PRC2), which methylates 'Lys-9' (H3K9me) and 'Lys- 27' (H3K27me) of histone H3, leading to transcriptional repression of the affected target gene. The expression of PRC2 is positively regulated in growing cells

and also plays a crucial role in oxidative stress, caused by oncogenic signaling, through trimethylation of CDKN2A and CDKN2B loci. Analysis of possible miRNA-mRNA interactions indicated hsa-miR-4289 is a significant interactor to EZH2 mRNA and also CDKN2B and CDKN2A mRNAs.Co-expression analysis by ENCORI revealed a conciderable co expression among hsa-miR-4289 and all those selected mRNAs. This miRNA was then processed in LncBase v.3 as a result MALAT1 and XIST have strong interactions with this miRNA.

Conclusion: In conclusion, overexpression of EZH2 along with CDKN2A and CDKN2B in THCA forms a possible ceRNA network among hsa-miR-4289, MALAT1, and XIST.This investigation could be suggested novel CeRNA interactions among lncRNA, mRNA, and miRNA for the candidate diagnostic and prognostic biomarkers associated with THCA by microarray analysis.

Keywords: Thyroid carcinoma; EZH2; CDKN2A; CDKN2B; CeRNA

Dysregulation of VDR-associated lncRNAs in patients with multiple sclerosis (Research Paper)

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Introduction: Long non-coding RNAs (lncRNAs) have been shown to influence pathoetiology of multiple sclerosis (MS). We aimed at identification of expression levels of three vitamin D receptor-associated lncRNAs, namely SNHG6, SNHG16 and LINC00346 in the circulation of MS patients compared with healthy subjects. Expression of SNHG6 was significantly lower in MS patients compared with controls (expression ratio (ER) (95% CI)= 0.39 (0.22-0.69), adjusted P value=0.0015) and in female patients compared with female controls (ER (95% CI)= 0.28 (0.13-0.59), adjusted P value=0.0001). Expression of SNHG16 was also lower in total MS patients compared with total controls (ER (95% CI)= 0.24 (0.1-0.57), adjusted P value=0.0001). Expression of LINC00346 was lower in total patients compared with controls (ER (95% CI)= 0.03 (0.009-0.09), adjusted P value<0.0001).

Methods: Four mL of whole peripheral blood was acquired via venipuncture from MS patients and healthy subjects in EDTA tubes. Hybrid-RTM blood RNA extraction kit (GeneAll Biotechnology Co Ltd., South Koera) was used for extraction of total RNA. After verification of appropriate quality and concentration of RNA, cDNA was synthesized using High-Capacity cDNA Reverse Transcription kit (Applied Biosystems). Expression of SNHG6, SNHG16 and LINC00346 were quantified in the rotor gene 6000 Corbett Real-Time PCR System by using SYBR® Premix Ex TaqTM (TaKaRa, Japan). B2M gene was used as normalizer.The Statistical Package for the Social Sciences (SPSS) v.18.0 (SPSS Inc., Chicago, IL) was used for statistical assessments. GraphPad Prism version 9.0 for Windows (GraphPad Software, La Jolla California, USA) was used for depiction of graphs.

Results: There was no significant difference in expressions of SNHG6, SNHG16 and LINC00346 between male and female patients. There was no significant correlation between expressions of SNHG6, SNHG16 and LINC00346 lncRNAs and age, disease duration, age at onset or EDSS. LINC00346 had the AUC values of 0.84, 0.82 and 0.94 in differentiation of total MS patients from total controls, female patients from female controls and male patients from male controls, respectively. SNHG6 could separate female patients from female controls with AUC of 0.79. Finally, SNHG16 could separate male patients from male controls with AUC of 0.73.

Conclusion: these lncRNAs might be proposed as putative peripheral markers for MS and potential contributors in the pathogenesis of MS.

Keywords: Multiple sclerosis, lncRNA, SNHG6, SNHG16, LINC00346

Effect of evening primrose (Oenothera biennis) on vaginal bleeding in induction of missed abortion (Research Paper)

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Introduction: Hemorrhage is one of the three main causes of maternal mortality worldwide. Considering the observed beneficial effect of evening primrose in some gynecological and obstetric procedures, this study was conducted with the aim of the effect of evening primrose on vaginal bleeding in induction of missed abortion.

Methods: In this randomized clinical trial, 148 women referring to Niknafas Hospital in Rafsanajn with diagnosis of missed abortion were randomly allocated into two 74-subject groups. The intervention group used 2000 mg vaginal evening primrose capsules the night before the hospitalization, while the control group did not receive any medication. Both groups received an initial dose of 800 µg of vaginal misoprostol after admission and the next dose was given three hours later if necessary. The required information from the patients' files was recorded in the relevant checklist and analyzed with spss software and chi-square, t-test and Fisher's exact statistical tests.

Results: There was no statistically significant difference in the level of vaginal bleeding when referring for abortion induction in the intervention and control groups (p>0.05). There was a statistically significant difference between the level of vaginal bleeding during hospitalization and during the ejection of uterine contents in the two groups (P < 0.05), so that this bleeding was less in the intervention group than in the control group. In the intervention group, 90% of the cases were mild bleeding, 8.6% moderate, and 1.4% severe bleeding, and in the control group, 74.3% mild bleeding, 24.3% moderate, and 1.4% severe bleeding were recorded.

Conclusion: Administration of 2000 mg evening primrose vaginally at the night before induction of a missed abortion is effective in reducing bleeding in this process. More studies in this field are suggested.

Keywords: Missed abortion, misoprostol, evening primrose, bleeding.

Effect of Honey Addition on Total Phenol of Different Herbal Teas
(Research Paper)

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Introduction: Herbal teas contain phenolic compounds that also have antioxidant property in our daily diet. Honey is a natural sweetener that also contains antioxidant properties. In this work, the effect of honey addition on total phenol of some herbal teas were investigated

Methods: The honey samples were collected during spring and summer seasons (2020) and the honey was extracted by louveaux methodology. On the basis of our melissopalynological study, honey samples are classified as natural polyfloral honey obtained from two different honeys in the southern slopes of Central Alborz. 2 types of honey (with different doses of pollens in honey) were added into 5 different herbal teas (Malva Silvestre's (Malvaceae), Cmaellia scinencies (Theaceae), Origanum (Lmiaceae), Cydonia oblonga (Rosaceae), Stachys lavandulifolia (Lamiaceae)) at 3 different temperatures (40oC , 55 oC , 70 oC), and the changes of total phenolic content were determined

Results: The highest total phenolic content (574.5 mg/kg) was related to Malva Silvestre's that was mixed with natural polyfloral honey 1 at 70 oC. The lowest total phenolic content (171 mg/kg) was related to Cydonia oblonga that was mixed with natural polyfloral honey 2 at 70 oC.

Conclusion: The total phenolic content of the honey-added-tea samples were found to be increased.

Keywords: Honey,Total Phenol,Teas

Effect of metal nanoparticles in bone tissue repair (Review)

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Introduction: Since tissue develops different organs and serves as the primary scaffold for body shape, it is essential to the organization of multicellular organisms. In recent years, the research for efficient methods to promote tissue regeneration has been more intense

Methods: Nanoparticles are essential to the engineering of bone tissue healing. According to their composition, size, and form, nanoparticles often interact differently with bone cells and tissue. The use of metal nanoparticles is a prime illustration of this

Results: Metal nanoparticles have special physiochemical characteristics that indicate they can act to repair bone tissue, including antibacterial effects, the shape memory phenomenon, low cytotoxicity, stimulation of the proliferation process, good mechanical and tensile strength, acceptable biocompatibility, significant osteogenic potential, and the capacity to control cell growth pathways.

Conclusion: These particles' benefits and drawbacks are examined critically, and their significance for bone tissue engineering is emphasized.

Keywords: bone tissue, magnetic nanoparticles ,repair

Effect of nanomedicine mechanical properties on tumor targeting delivery (Review)

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Introduction: Conventional antitumor managements do not have precise results and are associated with serious risks. These cases cannot completely eliminate the tumor and in addition, they have severe side effects. But recent advances in nanotechnology have led to the rapid development of various nanoparticle (NP)-based drug delivery systems (including liposomes, polymeric carriers, metal nanoparticles, carbon nanostructures, etc.) to deliver therapeutic agents especially to solid tumors. Nanomedicines circulate in the body and are partially absorbed by macrophages of the reticuloendothelial system. Then, they continue to penetrate and release drugs into the tumor. Finally, they accumulate in the tumor and have therapeutic effects. Size of nanomaterials below 100 nm and poor clearance of nanomaterials at the tumor site. Both allow enhanced penetration and retention (EPR) of NPs in the tumor. Improved bioavailability of insoluble drugs, increased antitumor therapeutic effect, and increased patient compliance are just some of the advantages of NPs, but recent studies have raised questions about the true benefits of this technique. Nanoparticles must overcome several complex biological barriers, including high interstitial fluid pressure, dense tumor extracellular matrix, blood flow limitation, etc., to successfully eradicate the tumor. This is why only 0.7% of NPs reach the tumor site.

Methods: In this systematic review, the data required for this study were collected using keywords and based on reliable databases such as Google Scholar, PubMed, Scopus and ProQuest. In this study, our statistical population includes all articles registered until 2022. After reviewing the relevant findings and evaluating the quality of the obtained data, 17 articles were analyzed.

Results: Considering the obstacles mentioned for the penetration of nanoparticles into the tumor, various physicochemical parameters of nanoparticles have been studied to increase tumor penetration. NP size is

one of the determining factors, the optimal value of which is between 10 and 50 nm. Anti-angiogenic therapy that can normalize tumor vasculature has been proposed as a means to improve NP delivery to tumors. Blockade of vascular endothelial growth factor receptor 2 in mammary tumors greatly improves the delivery of small (12 nm) NPs. Another advanced combination technique is extracellular matrix (ECM)-degrading enzymes such as losartan, which reduces tumor collagen content and successfully enhances the delivery of NPs such as Doxil. Two other methods are: different expression of receptors (such as folic acid receptor, integrin, etc.) on the surface of normal and malignant cells and modifying the surface of nanoparticles with polyethylene glycol and covering them with cell membrane. Self-assembled peptide nanohydrogels (such as peptides with b-sheet structure, peptides with b-hairpin structure, etc.) are currently the most efficient nanocarriers for antitumor drug delivery. Peptide nanohydrogels have tumor inhibition properties and localization ability, and they have high injectability with intratumoral delivery.

Conclusion: The focus of cancer nanotherapies is expected to expand in the coming years due to the multifunctional design and functionality of nanomaterials. To achieve the most favorable pharmacokinetics, delivery to tumors with appropriate time resolution and taking into account the local microenvironmental conditions of tumors should be considered. The development of new nanomaterials will be an important driver for progress in this field. However, a better understanding of the fundamental processes involved is necessary to overcome major obstacles in cancer nanomedicine, and we can also consider various mutually limiting factors. However, there are still some important questions that need to be answered, such as what technology do we need to safely and precisely manipulate nanoparticles? And what are the retention effects caused by tumor lymphatic drainage? Etc.

Keywords: Drug Delivery Systems, Neoplasms, nanomedicine

Effect of vitamin E supplementation on cardiometabolic risk factors, inflammatory and oxidative markers and hormonal functions in PCOS (polycystic ovary syndrome): a systematic review and meta-analysis

(Research Paper)

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Introduction: Polycystic ovary syndrome (PCOS) is a common endocrinopathy among reproductive-age women. Various therapeutical approaches are currently used to manage or control symptoms associated with PCOS. This systematic review intended to assess the effects of Vit E supplementation on cardiometabolic risk factors, inflammatory and oxidative markers, and hormonal functions in PCOS women based on the clinical trial's results.

Methods: The databases including PubMed, Scopus, Cochrane, Web of Science, and Embase were used to find all relevant studies. The authors reviewed all relevant clinical trials via systematic evaluation of abstracts and titles. Searches were conducted on August 1, 2020. After the initial search and reading of the article's title and abstract, 353 articles were reviewed; finally, 12 articles met the inclusion criteria.

Results: We found that vitamin E can improve PCOS hormonal profile by decreasing testosterone and LH levels and by increasing progesterone and FSH levels. It can also reduce insulin resistance, cholesterol, LDL, and TG levels among these patients, it can also improve their cardio-metabolic profile. We also found that vitamin E supplementation can decrease oxidative stress in PCOS.

Conclusion: Vitamin E supplementation can positively affect the patients who are diagnosed with PCOS in regards to metabolic and hormonal parameters.

Keywords: Vitamin E, PCOS, cardiometabolic risk factors

Effects of folic acid-chitosan in targeted drug delivery nanosystem with antitumor application in breast cancer model in Balb/C mice (Research Paper)

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Introduction: Introduction: Breast cancer is the most common type of cancer among women with a death rate of almost 50% and its frequency has increased over the past years. Selenium (Se) nanoparticles have antioxidant and anti-pathogenic effects. The use of nanoparticles coated with folic acid-chitosan (FA-Cs) is one of the new targeted treatment methods. Chitosan increases the duration of drug release from designed nanoparticles. Folic acid molecules can also be used at the level of nanoparticles to increase the specificity of drug binding to cancer cells. Therefore, the aim of the study was to use folic acid-chitosan coating in the drug delivery system containing selenium nanoparticles with anti-tumor application in the breast cancer model in Balb/C mice.

Methods: Materials and methods: First, selenium nanoparticles were synthesized with compounds such as selenium oxide and ascorbic acid, and then were coated with folic acid-chitosan. The nanoparticles prepared in the study were injected intraperitoneally with 5-day intervals and Breast cancer induced in Balb/C mice. The studied groups include the control group, Curcumin group, SeCsFA group and SeCurCsFA group, with 8 mice in each group. The weight and the size of tumors were measured with scales and calipers. After 25 days, the mice were euthanized and the final tumor weight was checked in different groups.

Results: Results: The results of examining selenium nanoparticles using a scanning electron microscope showed that the shape of the particles was spherical and uniformly distributed, and their size was about 200 nm. In the control groups, Curcumin group, SeCsFA group and SeCurCsFA group, tumor size was 9.25, 3.82, 7.87 and 0.63, respectively, and tumor weight was 24.125, 25.87, 21.9 and 22.73.

Conclusion: Conclusion: According to the results of using selenium nanoparticles loaded with curcumin coated with folic acid-chitosan by

increasing the specificity of the drug connections and increasing the drug release time, it increases the antitumor activity in the breast cancer model in Balb/C mice.

Keywords: Keywords: breast cancer, folic acid-chitosan, drug delivery, selenium nanoparticles, Balb/C mice

Effects of Interval training on expression of G6Pase gene in hepatocyte of Streptozotocin-Nicotinamide induced Type-2 diabetic male rats (Review)

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Introduction: Insulin dysfunction or inadequate insulin secretion leads to type 2 diabetes (1). About 90% of these patients are type 2 diabetic ones (2, 3). According to the World Health Organization, there has been a global increase in the number of people with diabetes from 108 million to 442 million in the past decade (4). One way to maintain glucose homeostasis is to regulate hepatic gluconeogenesis. Suppression of gluconeogenesis by controlling the expression of genes affecting it is one of the methods to restore normal blood glucose levels for the treatment of type 2 diabetes (6). PGC-1α gene is downstream intracellular genes involved in gluconeogenesis that regulate the expression of enzymes such as G6Pase. Glucagon regulates the expression of PGC-1α (7), thereby controlling the transcription of gluconeogenic enzymes such as G6Pase. G6Pase is one of the key enzymes involved in gluconeogenesis that converts glucose 6 phosphate to glucose. The presence of this enzyme allows the tissue to release glucose into the blood (8). Insulin inhibits PGC-1α activity(7). Physical activity is an effective strategy in improving type 2 diabetes (9 However, further studies are needed to evaluate in detail the relative effect of exercise (10). G6Pase is an important insulin signaling gene in liver and involved in diabetes, studies have shown that the role of G6Pase is influenced by PGC-1α in regulating type 2 diabetes (14); thus better understanding the role of G6Pase may open a clear horizon for an effective therapeutic strategy. However, the pathways of hepatic gluconeogenesis signaling in diabetics in response to different types of exercise with varying intensity and duration are not completely clear, and studies at the level are not sufficient. Therefore, identifying the effect of exercise training on hepatic gluconeogenesis in diabetic patients and how to regulate the genes involved in it, is an undeniable necessity to find a milestone in helping to reduce diabetes complications. In the present study, the effect of 10 weeks of Interval training on the expression of G6Pase gene in the liver of streptozotocin-induced diabetic rats was investigated.

Methods: In This study was performed in an experimental design on 16 diabetic male Wistar rats (mean weight, 220±20 g). After type 2 diabetes induction (with nicotinamide-streptozotocin), the samples were divided into two groups of Interval and Controlled. The training program was 10 weeks

and five times a week, with a gradual increase in speed. 48 hours after the last training session, liver tissue samples were taken after an overnight fast. Fasting glucose, serum insulin, insulin resistance, G6Pase gene expression in hepatocyte were measured in both groups. The obtained data were compared using independent t-test. The significance level was considered to be p<0.05.

Results: Independent t-test showed that 10 week Interval training significantly decreased the fasting glucose (P-value< 0.001) and increased serum insulin (P-value< 0.001). But, the changes in insulin resistance (p=0.266), the expression of G6Pase (p=0.492) were not significant in the exercise group compared to the control group.

Conclusion: The results of the present study showed that 10 weeks of interval exercise can significantly decrease fasting glucose and increase blood insulin and this regulation and control of glycemia and improvement of blood glucose and insulin levels without affecting the expression of G6Pase gene have expressed. Therefore, further studies are needed to align different genes and their complex relationship to the pathway of hepatic gluconeogenesis under the influence of different types of exercise. According to the results of this study, which indicated a decrease in fasting glucose and an increase in serum insulin, it can be concluded that interval exercise may be used as a non-pharmacological treatment to improve type 2 diabetes. However, given the limited research on the cellular and molecular domain of diabetes and exercise training, and because of the limited scope of the present study, further laboratory and field studies are needed to elucidate other mechanisms that may be involved. Future research to understand the mechanisms involved in all types of exercise with a glycemic control approach may provide new avenues for regulating insulin sensitivity in people with type 2 diabetes.

Keywords: Interval exercise, G6Pase, Type 2 diabetic, Streptozotocin

Effects of malnutrition in infancy on DNA methylation in the prenatal period (Review)

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Introduction: Methylation is a complex molecular mechanism that regulates the course of numerous biochemical processes that are responsible for the correct reading of the genetic information stored in DNA, maintains the stability of the genome, and controls the process of gene transfer. Methylation is one of the epigenetic processes that is not related to changes in the nucleotide sequence of DNA. While epigenetic changes occur at any stage of life and can be inherited, they are influenced by external factors, such as: lifestyle (in particular, diet, weight disorders and physical activity), as well as drugs and substances. Toxic, they change. DNA methylation is an epigenetic mechanism to modulate gene expression, which is involved in cell differentiation and tissue organization, and can be used as a predictor of future disease risks.

Methods: In the upcoming systematic review, Scopus, PubMed, Google Scholar and ProQuest databases were used to cite and collect studies. These studies were collected and used using keywords during the years 2018-2022. A total of 19 articles were analyzed.

Results: The composition, structure, and function of the brain depend on the availability of appropriate nutrients, including lipids, amino acids, vitamins, and minerals. In addition, endogenous gut hormones, neuropeptides, neurotransmitters, and gut microbiota are directly influenced by dietary composition. Therefore, food quality is effective on brain function and as a result mental health, mood and cognitive function. For example, studies have implicated maternal dietary factors and the first days after birth in the risk of behavioral and emotional problems in children. Increased intake of unhealthy

foods and decreased intake of nutrient-dense foods in early childhood were independently associated with internalizing and externalizing behaviors in young children. These behaviors are early indicators of secondary mental health problems. Additionally, children whose mothers had consumed more unhealthy foods during pregnancy showed higher levels of externalizing behaviors. DNA methylation regulates the temporal and spatial patterns of transcription in response to internal and external signals and plays an important role in cell differentiation and tissue organization during general and neurodevelopment. Experiments showed that arsenic and cadmium interact with DNA methyltransferases. Also, exposure to environmental chemicals such as heavy metals and polychlorinated biphenyls causes developmental disorders in neurological functions.

Conclusion: In conclusion, early life nutritional exposure plays a role in modulating early vulnerability factors for mental health problems in children. Good dietary practices are important for mental health as well as physical health throughout life. Thus, it is likely that the combined effect of genome-wide DNA methylation changes, with a limited contribution from each specific locus, translates into an epigenetic risk architecture that can, in association with additional factors, affect subsequent long-term physical and mental health. In childhood malnutrition ideally, the focus should be on optimal energy status in relation to overall food intake, activity and body composition. However, if improving food intake and activity is impossible, as may be the case in older adults, the focus should be on key nutrients related to epigenomics and cognition, including those involved in DNA methylation, DNA repair, histone modifications, and ncRNA function are related. . However, more research is needed in this area.

Keywords: methylation, DNA, malnutrition

Effects of nano propolis on the proliferation and wound healing: in vitro study on A375 melanoma cancer cell line. (Research Paper)

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Introduction: Skin cancer is the most common type of cancer. It is a disease in which malignant (cancerous) cells are formed in melanocytes. Melanoma is the most aggressive skin tumor with malignancy, metastasis, and high mortality. Malignant melanoma comprises 2% of all cancers. The success rate of current chemotherapy is relatively low because of multidrug resistance and its side effects. Therefore, there is a need to discover new, safe, and effective compounds and low-cost against melanoma. Propolis, as an herbal compound (an emerging strategy for preventing or treating melanoma), can be used for cancer treatment due to flavonoids in the composition. Bees produce Propolis by mixing the enzymes in their saliva with different parts of the plant. Propolis has anti-bacterial, anti-fungal, anti-parasitic, antioxidant, anti-inflammatory, and antitumor properties, as well as a booster for the immune system. An essential issue for using Propolis is overcoming to limitations of bulk Propolis and protein structural changes. Hence, converting Propolis into nanoparticles could become more reactive following the reduction of their surface area to volume.

Methods: 1. propolis extraction: To extraction of Iranian Propolis (using 200gr Propolis with 1700ml ethanol 70%), the mixture was kept in the dark container for 14 days with moderate shaking. The resulting extract was filtered, and after rotary evaporating, it was freeze-dried. Propolis chemical contents were evaluated by X-ray crystallography (XRD). 2. nano propolis preparation:

Propolis dried (powder was dissolved in 80% alcohol) sonicated with Tween 80 and 20 and distilled water. Then characterization of nanoparticles was determined by DLS and Zeta potential. 3. Cell viability: first A375 cells (5*103) were seeded on a 96-well plate with high glucose DMEM containing 10% FBS (fetal bovine serum) and 1% Pen Strep for 24h. Then, the cells were treated with different concentrations of Propolis for 24 and 48h. Negative and positive control contained medium and 15% DMSO, respectively. MTT solution was added to each well and incubated for 24h. Next, DMSO was added to dissolve the blue formazan crystals. Absorbance was read at 570 and 630 nm by a microplate reader. 4. wound healing: After seeding the cells in the 12-well plate and receiving 80% confluency, the cells were treated with IC50 concentration and a control sample. Then, a scratch was created in each well using a blue tip, and the wells were imaged for 48h.

Results: 1.Nano propolis characterize: The DLS showed particle sizes from 1 to 40 nm, and the zeta potential determined the surface charge to be -110, which prevents aggregation. 2.MTT assay: Nanoparticle-propolis had different effects in two time periods of 24 and 48 hours with concentrations of 10, 20, 40, 50, 60, 70, 80, 90, and 100(µl/ml). The IC50 in these two times was shown as 86(µl/ml) and 60(µl/ml), respectively. Compared to the control group, cell viability decreased significantly in 48 hours. Therefore, the effective concentration and the optimal time to continue the study were 60(µ l/ml) and 48 h, respectively. 3.Wound healing: The wound width in the control group changed from 0.5 to 0.1(µm) from 0 to 48h compared with the IC50-treated group (with no changes). The correlation between time and wound healing was negative, with a coefficient of -0.84.

Conclusion: The study of nano propolis on the A375 cancer cell line showed that it could have cytotoxic effects in a dose-dependent manner, which was proven using the MTT test. in addition, the wound healing test also showed that nano propolis could prevent cell migration. As a result, nano propolis can be a suitable candidate as a therapeutic nutritional supplement along with chemotherapy drugs. Of course, extensive clinical studies are needed to confirm the positive effects of this natural product.

Keywords: Propolis, nano propolis, cancer, MTT assay, wound healing

Effects of stem cells on improving fertility and ovarian follicles (Review)

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Introduction: The major functions of the ovaries are to govern the health of the female by regulating endocrine status and the production of mature oocytes. Female sex hormone secretion and reproductive ability decrease with aging. One of the ovarian diseases is Primary Ovarian Insufficiency (POI) in which ovarian function is lost before 40 and causes infertility. The percentage of POI is increasing every year. Therefore, it is important to find a treatment for this disorder. In this regard, many studies have been recently conducted on the effectiveness of stem cells in the treatment of ovarian ageing. This research is amid to review these studies and discuss the stem cells properties, which are effective in improving ovarian function.

Methods: In this review study, after searching through databases of PubMed and goggle scholar, 9 articles were finally selected to study. the focus of these articles is on the effects of stem cells on fertility and Ovarian follicles.

Results: A recent study reported that MSCs repair injured cells via paracrine activity or direct cell-to-cell interaction. MSCs can stimulate tissue regeneration by promoting angiogenesis and cell viability via paracrine activity through cytokines and extracellular vesicles. Various studies suggested interesting interaction between the paracrine effect of MSCs and the cell surrounding. Various types of MSCs derived from different resources such as umbilical cord-derived MSCs, adipocyte-derived MSCs and bone marrow-derived MSCs have been applied in the treatment of a variety of women's infertility disorders, including premature ovarian failure. Human placental MSCs (hPMSCs) can inhibit oxidative stress and apoptosis, thereby improving ovarian function. Paracrine signaling is a key mechanism whereby Human placental MSCs (hPMSCs) promote endometrial repair via the release of key bioactive molecules but safety concerns in using allogenic MSC as a biological drug remain.

Conclusion: according to the existing studies, ovarian aging and the decline in fertility that occurs in women over 40 with age is an inevitable issue that led researchers to look for ways to postpone this issue. Various methods have been proposed, including the use of MSCs, and animal model studies have been carried out in this field, but more studies and clinical trials are needed to be sure of the lack of complications of the methods or the definite effect.

Keywords: Stem cells,paracrine, ovarian

Efficacy of Fish-Derived Bioactive Peptides on K562 cell line (Research Paper)

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Introduction: Bioactive peptides are generally inactive oligopeptides activated by metabolic processes, such as enzymatic hydrolysis, intestinal digestion, and fermentation. These peptides are low in molecular weight, easy to digest, and also are more function than native proteins. One of the great source of biological peptides is extracted from fish, and as researches showed fish-derived protein peptides have anti-cancer, anti-inflammatory, antioxidant, and cytoprotective functions.

Methods: K562 cells after culture in RPMI culture medium and HEK293 in DMEM culture medium and incubation at 37°C temperature with 95% humidity and 5% CO2, when they grew enough to perform MTT test in 96 plate culture house and then After treatment with extracted peptides and adding MTT dyes and DMSO in specific time intervals, the results were evaluated with ELISA reader. Hoechst's test was used to investigate the occurrence of apoptosis, and the cells were cultured in 24 house plates and treated with peptides, and the results were evaluated with a fluorescence microscope.

Results: After treatment of the cells with these extracted peptides and MTT assay evaluation, a decrease in cytotoxicity and an increase in antiproliferative effects were observed in K562 cell line, and there was no effect on HEK cell line. In addition Hoechst test and pictures taken form fluorescence microscopy showed the effect of induction of apoptosis on K562 cell line

Conclusion: Therefore, bioactive peptides with anti-cancer activity provide new opportunities in drug development for the treatment of cancer because they specifically target cancer cells and have little or no toxicity on healthy cells and tissues.

Keywords: CML cancer, bioactive peptids, K562 & HEK293 cell lines, apaptosis

Efficient electrochemical methods for the detection of dopamine in vivo (Review)

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Introduction: Neurotransmitters are chemical messengers that allow neurons to communicate with each other or stimulate glandular or muscle cell responses. One of the important members of this family is dopamine (3,4-dihydroxyphenethylamine). It plays several important roles in the central nervous system, cardiovascular, renal and hormonal systems. Neurological disorders such as schizophrenia, Alzheimer's and Parkinson's disease show abnormal levels of dopamine. Due to the wide range of physiological and pathophysiological effects of dopamine, accurate the measurement of dopamine and its metabolites in biological systems is of great clinical importance. Dopamine detection in blood or urine samples is usually done in specialized laboratories using methods such as ELISA (enzyme-linked immunosorbent assay) as well as other spectroscopic, fluorescence, colorimetric and electrochemical methods. Electrochemical methods have been proposed due to relatively high response speed, high sensitivity, specificity and the use of relatively simple and inexpensive equipment. Nanoparticles are usually used for electrochemical analysis. Nanoparticles have distinct physical and chemical properties that make them uniquely suitable for the development of advanced electrochemical sensors. In this context, the main goal of this work is the effective detection of dopamine based on electrochemical methods.

Methods: Search method: In this systematic review, we collected the data we needed by using keywords and also by referring to reliable databases such as PubMed, Scopus, Google Scholar and ProQuest. The statistical population of this study includes all studies conducted until 2022. After reviewing relevant findings and evaluating data quality, we analyzed 15 articles.

Results: A wide variety of electrode materials have been proposed to increase the selectivity of dopamine detection. More important recent examples include: the use of tyrosinase-based biosensors for the detection of

phenolic compounds, including dopamine, consisting of a carbon fiber microelectrode coated with a biocatalytic layer containing tyrosinase in a chitosan biopolymer matrix. - Carbon fiber microelectrodes in the presence and absence of metal oxide using a chitosan composite mixture shown as a stabilization matrix, electrochemical sensor based on ZnO that oxide nanoparticles on the glass surface of the carbon electrode taken in ambient conditions. Cyclic voltammograms responded to dopamine in the absence and presence of metal oxides. However, in the absence of metal oxides, a slight increase in dopamine depletion current, while the response of the implantable enzyme-based biosensor to induced dopamine production in the rat brain indicates that the sensor works effectively and that the materials used in The sensor fabrication and the enzyme/electrochemical coupling process of dopamine detection make this sensor a good candidate for use as an implantable sensor. However, higher amounts of enzyme do not improve the performance of the biosensor. Higher enzyme concentrations may have saturated the surface of the existing microelectrode and changed the diffusion and permeability characteristics of the layer, making less enzyme accessible to the substrate or carbon fiber to the reaction product.

Conclusion: The implantable enzyme-based biosensor using a natural chitosan biopolymer and a mixture of ceria/titania-based metal oxide nanoparticles has several unique features such as the recovery of the reaction product by an enzymatic/electrochemical method. The recycling process minimizes electrode deactivation. In addition, the electrode materials are biocompatible. While tyrosinase-based biosensors for dopamine described to date are characterized by detection limits in the micromolar range and relatively large electrode sizes. In addition, their use in vivo has not been demonstrated. It should be noted that this issue needs more studies.

Keywords: dopamine, Nanoparticles, Biosensors, Electrochemical detection

Electrochemical sensors for hepatitis C virus detection (Review)

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Introduction: Hepatitis C is the most common liver disease caused by hepatitis C virus (HCV) and can cause health problems such as cirrhosis and liver carcinoma. Today, the early stage of the disease is practically undiagnosed, so it is an important problem in modern public health. Access to cost-effective diagnostic methods that can be deployed in the field are the main obstacles in the way of controlling and eradicating a many endemic and emerging infectious diseases. The aim of this article is to investigate biosensors for the direct detection of HCV surface antigen.

Methods: In the forthcoming systematic review, the required data were collected using keywords and citing valid databases such as Scopus, PubMed, Google Scholar and ProQuest. The statistical population includes all studies conducted until 2022 in the field of Electrochemical sensors for hepatitis C virus detection. After reviewing the relevant findings and evaluating the quality of the data, 16 articles were analyzed.

Results: 1. The electrochemical signal of the oxidized product, 2,3-diaminobenazine, is used to determine HCV DNA. This strategy is capable of sensitive detection of HCV DNA in a wide linear range in the range of 0.5-10 nM and has a detection limit of pM405.0. 2. The recommended detection limit of electrochemical paper-based analytical devices (ePAD) was 18.2 pg mL-1 for hepatitis B surface antigen (HBsAg) and 1.19 pg mL-1 for hepatitis C surface antigen (HCVcAg). In addition, this proposed ePAD is also used in real clinical sera of patients to confirm its biological function. 3. Linear peptide was chosen as a cheaper and easier ligand for the preparation of HCV biosensor. The HCV biosensor obtained in the presence of interfering protein, channel albumin, showed selectivity towards E2. 4. Electrochemical detection of hepatitis C virus based on reduced magnetic nucleotides-assisted graphene oxide-copper nanocomposite, a DNA-assisted reduced magnetic copper oxide-graphene nanocomposite (mrGO-CuNCs), is proposed. 5. Bimetallic- Metal Organic Frameworks (MOF)- based HCV electrochemical biosensors have several advantages for use. Among these advantages are:

being cheap; high selectivity and sensitivity; Linear detection range from 1 fM to 100 nm and very low detection limit (0.64 fM). Consequently, this method opens the door to design more electrochemical biosensors related to the electrical and catalytic activity of bimetallic MOFs.

Conclusion: Developed gene sensors enable selective and specific detection of hepatitis C. Also, the ePAD sensor is very promising as a usable, portable and expandable sensor for other biological assays. Furthermore, the developed electrochemical HCV sensor is a simple, rapid and inexpensive alternative to existing methods for HCV detection and paves the way for hepatitis C care diagnosis.

Keywords: Electrochemical Techniques, Hepacivirus, hepatitis C virus

Endocrine complications in children with malignancy (Review)

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Introduction: Endocrine disorder is caused by dysfunction (increase or decrease) of any of the endocrine glands. These disorders can be primary or secondary in relation to other diseases. One of the secondary endocrine disorders is the development of malignancies. One of the most important advances in medical science in recent years is the treatment of childhood malignancies, and this increases the life expectancy of these patients to survive. The management of childhood cancer has improved significantly. In the past decade, we have seen great progress not only in conventional treatment but also in the development of targeted therapy with the emergence of new therapies such as immunotherapy and molecular therapies for pediatric cancer. As survival increases, the effects of late cancer treatment have become a major medical issue in childhood cancer survivors. Most of these survivors experience at least one non-endocrine or endocrine complication. In the meantime, endocrine disorders are the most common complications in childhood cancer survivors, including hematologic malignancies, brain tumors, and sarcomas, and more than 50% of cancer survivors experience at least one hormonal disorder during their lifetime.

Methods: This systematic study was mentioned using key words and referring to reliable scientific databases such as Scopus, PubMed, Google Scholar and ProQuest from the studies that were conducted until 2022 and a total of 16 articles were reviewed.

Results: Strong evidence shows that a large percentage of childhood cancer survivors have endocrine problems and other complications in the prevalence of vision, hearing, cognitive, cardiac, pulmonary, and digestive disorders. Tumors arising near the hypothalamic-pituitary (HP) region and those treated with surgery or radiotherapy involving this region are at risk for HP dysfunction. HP dysfunction means growth hormone deficiency, which leads to impaired linear growth and short stature in adults. Deficiency and disorder

of LH and FSH hormones leads to early central puberty or late puberty, ovarian damage which ultimately leads to a decrease in ovarian reserves, ovarian failure, primary and secondary amenorrhea and early menopause in women, also leads to a decrease in sexual desire and Erectile dysfunction. In males Patients with ACTH deficiency may present with symptoms of adrenal insufficiency, including fatigue, nausea, anorexia, hypoglycemia, poor weight gain, and vulnerability to medical stressors. Also, the results of studies have shown that thyroid gland abnormalities are one of the most common endocrine complications, which can be seen as hypothyroidism, hyperthyroidism, or toxic thyroid in childhood cancer survivors. Among other complications after recovery from cancer, we can mention a decrease in bone density and the risk of osteoporosis and fractures caused by it, central diabetes insipidus with symptoms of polydipsia, polyuria and nocturnal enuresis.

Conclusion: As a result, many studies have shown that complications and chronic infectious diseases are observed among cancer survivors, especially recovered children. Several factors, including the length of treatment, age at diagnosis, tumor type, and genetic polymorphisms affect the severity and extent of complications after recovery. In this review, we summarize the current knowledge about endocrine sequelae among CCS and outline facts about lifelong surveillance of these patients, encouraging oncologists and endocrinologists to develop new follow-up guidelines and early detection that Minimize the consequences among these patients.

Keywords: Endocrine complications, malignancy

Endothelial cell derived microparticles as prognostic biomarker in multiple sclerosis (Review)

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Introduction: Microparticles (MPs) are submicron cell membrane derived fragments that increased in many physiological conditions like apoptosis or pathological conditions such as multiple sclerosis (MS) and many other diseases. MPs play a significant role in physiological processes such as inflammation, coagulation, and vascular function.

Methods: A systematic search was performed to identify studies published in multiple databases (sciencedirect, PubMed, ProQuest, Cochrane and google Scholar) up to 2022, and recently published abstracts were also reviewed. Using the key words such as MS, microparticles and endothelial.

Results: Increased Endothelial cell derived MPs (EnMPs) counts have been reported in MS. of the cerebral endothelial cells. EnMPs express different markers at their level. Expression of markers such as CD62E shows activated endothelial cells. Overproduction of microparticles in cerebrospinal fluid (CSF) has been reported in many patients, and these particles might be one of the major factor in the development of MS. Drugs used to treat MS, such as interferons, reduce the release of a number of EnMPs. Therefore, it is likely that EnMPs can be used as a functional and sensitive biomarker for the diagnosis and prognosis of the MS.

Conclusion: Endothelial dysfunction is evident in the incidence and exacerbation of MS. Prompt diagnosis and timely treatment can be very helpful. It is hoped that this will be possible by further understanding the EnMPs and their function.

Keywords: Multiple sclerosis, Microparticles, Endothelial cell

Engraftment of Three Types of Stem Leyding Cells (CD51+, p75-positive and Nestin-positive): A Treatment Strategy for Testosterone Deficiency and Testicular Leyding Cell Dysfunction (Review)

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Introduction: Testosterone is produced by stem leyding cells (SLCs), which reside in the testis interstitium. Testosterone deficiency (TD) is a public health concern which is characterized by various symptoms such as sexual dysfunction and osteoporosis. Since SLC replacement therapy has provided a long-lasting system for testosterone delivery, in this article I will review the engraftment of what types of SLCs have effect on TD.

Methods: This review article has been extracted from 5 article that has indexed in PubMed and Google Scholar and published from year 2014 to 2022. The search terms include “Stem Leyding Cell”, “CD51”, “Nestin”, “p75-positive”, “Testosterone” and “Transplantation”.

Results: p75 neurotrophin receptor positive ($p75^+$) cells demonstrated clonogenic self-renewal capacity and had differentiation potential into testosterone producing Leyding cells (LCs) in vitro and in vivo. GFP driven by the Nestin (Nes) promoter which have been identified as Nes-GFP^+ had the ability to extensive proliferation in vitro and when these cells grafted onto testes of LC-disrupted rat models, the Nes-GFP^+ cells produced testosterone. And these results are similar to the transplantation of $CD51^+$ SLCs that were successful in differentiating into mature LCs, and secretion of testosterone.

Conclusion: Transplantation of three types of SLCs, which are $p75^+$, Nes-GFP^+ and $CD51^+$ may influence TD and testicular leyding cell dysfunction by improving serum testosterone levels, meiotic and post-meiotic germ cell recovery and spermatogenesis which all of these influences might be regulated by the hypothalamic-pituitary-gonadal (HPG) axis. However, further studies are required to confirm the positive impact of $p75^+$, Nes-GFP^+ and $CD51^+$ transplantation on TD.

Keywords: Stem Leyding Cell, CD51, Nestin, p75-positive, Testosterone

Environmental toxins and the impact of other endocrine disrupting chemicals in women's reproductive health (Review)

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Introduction: Human fertility is decreasing anywhere withinside the world, and one in every of the critical motives is the accumulation of environmental pollution with interior our bodies of men and women. Therefore, this systematic evaluation has grown to be done at the effects of environmental pollution and one of a type endocrine disrupting chemical substances on women's reproductive health.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Environmental toxins and the impact of other endocrine disrupting chemicals in women's reproductive health. After reviewing the relevant findings and evaluating the data quality, a total of 20 articles were analyzed.

Results: Various research have established that the principal corporations of chemical substances that cause toxicity with in the reproductive tool are: solvents, asbestos, silica, metals together with chromium, lead and mercury, hair dyes and beauty products, persistent natural pollution and insecticides, smoking, endocrine disruptors chemical substances such as, tetrabromobisphenol A, bisphenol A, bisphenols F and S and bisphenol B. The worst productiveness disrupters are organochlorine compounds (dioxins, polychlorinatedbiphenyls, and chlorinated insecticides), bisphenol A (BPA), herbicides and organophosphate insecticides. Human exposure to environmental chemical substances is related to lengthy time period outcomes and acute toxicity, together with, cognitive disabilities, cancer, continual diseases, start defects, death, and has the cap capacity to be transmitted to the following generation. In addition, disruption of women's reproductive characteristic through way of endocrine disrupting chemical substances might also additionally moreover furthermore result in lack of

ovulation, beside the issue of hormone production, menstrual cycle disorders, infertility, and untimely growing older of fertility. Experimental statistics show that publicity to insecticides has a terrible impact on the cap capacity of the ovary to provide intercourse hormones in animal fashions and women. By developing the amount of hexachlorocyclohexane, polychlorinated biphenyls and dichlorodiphenyltrichloroethane withinside the blood of women, their fertility decreases. Women with the very awesome stages of polychlorinated biphenyls have an extreme 50% reduce charge in their cap capacity to get pregnant. Several insecticides together with malathion chlorpyrifos, endosulfan, and permethrin cause ovarian abnormalities after start, lower withinside the big variety of follicles, and decorate follicular atresia. While the increase withinside the degree of chlorinated bisphenols have grown to be related to a Lesser in inconvenient situations and fertilization charge for oocyte increase. No vast correlation has grown to be decided among polychlorinated biphenyls interest and its cap capacity to sell fibroid development. Epidemiological research rarely has investigated the affiliation among heavy metallic publicity and reproductive effects. Some researchers noted an affiliation among blood lead degree and infertility.

Conclusion: Extensive publicity to quite a few of notable chemical substances has brought on several abnormalities withinside the girl's reproductive tool and numerous animal species. Reproductive effects might also additionally moreover furthermore be dose-based and associated with lengthy-time period publicity and the interest degree of the compound present. Most to be had statistics deliver a lift to the proof for women's reproductive health-associated sports activities, sports of endocrine disrupting chemical substances. However, the actual mechanisms that cause the physiological, molecular changes and cellular aren't clear. In the future, guidelines ought to be made to lower human publicity to endocrine disrupting chemical substances and defend reproductive health.

Keywords: Environmental toxins, Reproductive, Women's reproductive health, Endocrine disrupting chemicals

Epidemiological and clinical observations of COVID-19 (Review)

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Introduction: Coronavirus Disease 2019 (COVID-19) pandemic remains a major public health threat in most countries. This article examines epidemiological and clinical observations as well as the link between vitamin D deficiency and covid-19.

Methods: COVID-19 disease is associated with the increased generation of pro-inflammatory cytokines, Creactive protein (CRP), acute respiratory disease syndrome (ARDS), pneumonia, and heart failure. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects pulmonary epithelial cells using the angiotensin converting enzyme-2 (ACE-2) receptor. Besides pulmonary epithelial damage, SARS-CoV-2 also infects macrophages through ACE-2 receptors and activates them. Macrophages, neutrophils, and T cells get activated through sustained elevation of cytokines including interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)alpha, resulting in type 2 pneumocyte apoptosis, and in some patients a path that leads to acute respiratory distress syndrome (ARDS). The host responses are sometimes amplified by an overwhelming expression of pro-inflammatory cytokines. This ‘cytokine storm’ is responsible for some of the serious manifestations of COVID-19 such as ARDS. Hypoxemia and bilateral lung infiltration are features reminiscent of severe viral pneumonia that result from endothelial injury, excessive cytokines, and immune overkill. Low levels of vitamin D can increase the likelihood of developing multiple acute and chronic ailments including cardiovascular and autoimmune diseases, diabetes, cancer, infectious diseases, dental caries (DC). Many retrospective studies have found an association between vitamin D levels and COVID-19 severity and mortality. In clinical studies, low levels of serum vitamin D were associated with acute respiratory tract infections including epidemic influenza.

Results: Studies in the pediatric population demonstrated that patients with COVID-19 had significantly lower vitamin D levels compared with controls. In addition, fever was significantly higher in patients who had deficient vitamin D levels compared with patients who had sufficient levels. Additionally, older adults with vitamin D deficiency and COVID-19 had worse morbidity outcomes compared with those who were not vitamin D deficient. A prospective, interventional study found that a high dose of calcifediol reduced the need for intensive care stays in patients infected with COVID-19. A few studies have also reported on a significant association between sun exposure, vitamin D, and susceptibility to and recovery from COVID-19.

Conclusion: Perhaps the most important finding was that vitamin D deficiency increased the risk of developing COVID-19 by a factor of 5 after adjusting for age. Prospective interventional studies are required to validate the hypothesis that vitamin D supplementation can be helpful for the prevention and treatment of COVID-19.

Keywords: COVID-19; acute respiratory disease syndrome (ARDS); vitamin D

Epigenetic regulation in human cancer: the potential role of epi-drug in cancer therapy (Review)

zahra mollaei,[1,*]

1.

Introduction: Epigenetics is the study of heritable, dynamic changes to the genome that take place without regard to the DNA sequence. Cohesive interactions with different enzymes and other molecular elements are necessary. Abnormal epigenetic changes can trigger genetic expressions at the wrong time and encourage the development of tumors. The epigenetic modifiers are becoming interesting targets in numerous cancer therapies since they are reversible and vulnerable to external influences. Numerous epi-drugs have recently been created and linked to clinical usage. Epi-drug use has demonstrated compelling outcomes, including enhancement of anti-tumor effects, overcoming drug resistance, and activation of the host immune response, whether used alone or in combination with chemotherapy or immunotherapy. The goal of this review was Epigenetic regulation in human cancer: the potential role of epi-drug in cancer therapy.

Methods: This study has written about Epigenetic regulation in human cancer: the potential role of epi-drug in cancer therapy from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed

Results: Results indicated Epigenetic modification mechanisms Histone modifications, non-coding RNAs, and DNA and RNA methylations, which are thought to be the primary regulatory mechanisms throughout cancer, can be used to classify the epigenetic alterations into three major categories. Despite this, strong data suggests that using epi-drugs alone or in conjunction with other medications can enhance the anti-tumor efficacy. However, one should not undervalue the related issues. First off, there are still many epigenetic chemicals undergoing laboratory research. How to convert the efficacy in vitro at nanomolar-scale concentrations into well-tolerated and effective clinical use would be the main difficulty for those molecules. In various cancer cell lines, it has been discovered that MG98 effectively reactivates silenced TSGs via downregulating DNMT1 and exhibits an inhibitory effect on proliferation. However, in clinical trials, it did not provide a meaningful response.

Conclusion: As Summary, another difficulty with epi-drugs is their off-target effects. The mechanism underlying epigenetic regulation is unclear due to its complexity, dynamic nature, and interdependence. Currently, certain widely used epi-drugs, including VPA, have a history of producing unintended epigenetic alterations. To facilitate their use in clinical therapy, such epi-drugs

must have a well-established safety profile. In the meantime, the development of resistance to some of the epi-drugs is posing a challenge. The PRC2 reduction shown in the resistant AML cells suggests that the targeted c-Myc expression may be recovered. Additionally, contributing to BETI resistance in triple-negative breast cancer (TNBC) is the hyperphosphorylation of BRD4.

Keywords: Epigenetic, cancer, epi-drug, cancer therapy

Epigenetic Regulations of ACE2 and COVID-19 (Review)

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Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a member of the coronavirus family that causes an infectious disease called the Coronavirus disease 2019 (COVID-19). The angiotensin-converting enzyme 2 (ACE2) type I membrane receptor which acts as a passway for the entrance of the virus to the host cell is a member of the Renin-Angiotensin pathway. The expression level of ACE2 is high in the lung, and the spike protein on the SARS-CoV-2 can bind to this receptor. The regulation of expression levels of the ACE2 gene is dependent on key regulatory elements for chromatin modification and transcription factors. Epigenetics is the changes in gene expression that do not involve changes to the underlying DNA sequence, and it happens at the level of histone proteins, RNA and DNA. The epigenetic changes in DNA methylation of the ACE2 gene and histone proteins, located near the ACE2 promoter, affect SARS-CoV-2 infection outcomes in different ages and genders. Epigenetic compounds such as Valproic acid (VPA), which shows antiviral effects through Histone Deacetylase (HDAC) inhibition, represent promising candidates for use as COVID-19 treatments.

Methods: In a bioinformatic study, four available genome-wide DNA methylation human datasets were examined to recognize the relation between DNA methylation profiling related to ACE2 and susceptibility risk for COVID-19 related to age and gender. Another study using molecular docking and bioinformatics showed that VPA targets and inhibits the active sites of the HDACs from classes I and IIa specifically. In another study, for investigation of VPA effect on inhibition of SARS-CoV-2 infection through decreasing ACE2 expression, first VPA was used for Huh-7 and HK-2 cell lines treatment, and then the cells were infected with SARS-CoV-2 which had been obtained from a nasal swab. Then, the ACE2 expression level in these cells was measured by RT-PCR and western blot. To verify the hypothesis of downregulation of the ACE2 through HDAC inhibition with VPA, several HDAC inhibitors with the same and different functions rather than VPA were applied in HK-2 and Huh-7 cell lines. Then, the expression level of ACE2 was analyzed.

Results: Higher levels of ACE2 expression are correlated with greater susceptibility to SARS-CoV-2 infection and viral loads. Based on a comparative analysis of DNA methylation in various tissues, the cause of high expression of ACE2 in the lung is the hypomethylation of three CpG sites around the ACE2 promoter. Moreover, during aging DNA methylation level is

decreased and led to differential methylation patterns of several genes. Thus, the probability of contracting Covid-19 increases with aging. Also, analysis of DNA methylation at two CpG sites related to the ACE2 gene shows that females are significantly hypomethylated compared to males. Moreover, the ACE2 gene is located on the X chromosome that is under X-inactivation in females. However, this gene can escape from this inactivation. Therefore, it may explain the higher ACE2 expression observed in females and the higher rate of infection in females. In addition, histone modifier enzymes such as HDACs seem to be related to enhanced levels of ACE2 expression in COVID-19 patients. HDACs normally repress transcription by removing acetyl groups from histones and resulting in chromatin compression, so their inhibition is usually associated with increased gene expression. However, recent studies have reported that HDACs can cause transcription stimulation. In the case of COVID-19, free ACE2 on the surface of the cells is reduced due to binding to spike protein of the virus, and following Angiotensin (Ang) II accumulation, Angiotensin Receptor (ATR) 1 is activated and sends a signal into the nucleus to stimulate the HDACs. These enzymes, in turn, lead to ACE2 upregulation. Decreased expression of the ACE2 at mRNA and protein levels due to using HDAC inhibitors as same as VPA shows the fact that the ACE2 downregulation is caused by HDAC class I inhibition.

Conclusion: Epigenetic regulation of the ACE2 gene, including DNA methylation and histone modifications, has a significant impact on the outcome of SARS-CoV-2 infection. Gender and age-related differences in ACE2 DNA methylation observed in the respiratory system cause pathological differences in patients with COVID-19. Epigenetic medicines such as VPA, which affects ACE2 expression through HDAC inhibition, will play a promising role in COVID-19 therapy.

Keywords: Epigenetics, DNA Methylation, ACE2, COVID-19

Epigenetics advancing personalized nanomedicine in cancer therapy (Review)

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Introduction: Epigenetic changes are introduced as a shape of genetic extrude in chromatin and therefore genes, if it does now not have an effect on the totality of the gene, but impacts the way the gene is expressed. In the studies completed on a fertilized egg, they were able to use genetic and epigenetic codes, turn the egg into natural components, which incorporates tissues, organs with specific structures and functions. Since first-class 0. 1% of the human genome is specific, if it changes, we see plenty of range with interior the human population. According to WHO, maximum cancers is taken into consideration as a severe hazard to human fitness with inside the international and is known as the second one purpose of death. The prevalence of numerous life-threatening cancers is increasing, genuinely so with inside the USA in 2018, we placed 17 million human beings laid low with maximum cancers. Among maximum cancers treatments, that could purpose epigenetic changes in an individual. The survival price of maximum cancers patients has superior little with inside the past, and we need new thoughts and strategies for maximum cancers' treatment. One of the treatments for maximum cancers and special illnesses is the treatment based totally absolutely, absolutely on epigenetic changes the use of custom designed remedy and little studies It has been completed due to its importance. The essential emphasis of this article is to create a connection among custom designed and with medication with regard to epigenetic changes in maximum cancers' management.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Epigenetics advancing personalized Nano medicine in cancer therapy. After reviewing the relevant findings and evaluating the data quality, a total of 22 articles were analyzed.

Results: Cancer manifests itself with inside the shape of hypo methylation in DNA and CPG and histone changes. Chemotherapy and radiotherapy are a few of the strategies to cope with maximum cancers, which due to the effect on epigenetics, purpose changes in gene expression, genetic mutations and instability in chromosomes. Today, new fields for maximum cancers' treatment are being created, which want It has superior the lives of patients and is used no longer first-class for the treatment of cancers but moreover for the treatment of illnesses together with kind 2 diabetes. The answer is treatment in specific human beings and predicting difficulty effects of drugs through scientific trials and discovery of latest drugs.

Conclusion: The essential emphasis of this article is to create a connection Today, NATO medication and epigenetic-based totally absolutely genuinely treatments are particularly have become used that first-rate changes were made in maximum cancers patients, but the survival of maximum cancers patients has now not changed with the ones treatments, and consistent with this difficulty, specific treatments based totally mostly on the aggregate of custom designed treatment in NATO medication and epigenetics. Consistent with the evidence, shows successful customized remedy because it specializes with inside the specific dispositions of absolutely everyone and their genetics. The truth that a large thing of the scientific and natural dispositions associated with the affected individual is even though unknown can motive the perception that focused treatments have failed. Customized NATO medication based totally mostly on Epigenetics is a suitable opportunity for scientific programs on patients with numerous illnesses. We want to supply effective treatments to patients with the improvement of knowledge related to genetic changes and the development of custom designed NATO medication.

Keywords: biomimetic nanoparticles, personalized nanomedicine, Epigenetics, nanomedicine, cancer therapy

Estimation haplotype frequency of XV-2c, KM.19, T854T, and TUB18 markers at the CFTR gene in Khorasan Razavi province of Iran

(Research Paper)

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Introduction: Haplotype phasing is an approach for the carrier detection and prenatal diagnosis of genetic diseases like cystic fibrosis (CF), an autosomal recessive disorder, in a more convenient manner. The CFTR gene region contains several linked polymorphic markers to detect CF. Therefore, in this research, we investigated the efficiency of XV2c-KM19-T854T-TUB18 haplotype phasing in 14 nuclear families as CF cases and 75 unrelated healthy individuals as the controls referred to Mashhad University of Medical Sciences teaching hospitals in Northeastern IRAN.

Methods: We collected blood samples from 14 nuclear families as cases and 75 unrelated individuals as the controls. Then we extracted genomic DNA using the salting-out procedure. We genotyped four markers of XV-2c, KM19, T854T, and TUB18 by the PCR-RFLP method. We calculated haplotype frequency using FBAT and PHASE (Haplotype frequency estimation computer software).

Results: We designated the results of genotyping markers as follows: the digested and undigested alleles were termed number 1 and number 2, respectively. For each haplotype, each four-digit number represents the XV-2c, KM19, T854T, and TUB18 markers, respectively. Among the 15 estimated haplotypes identified for four biallelic markers in each case and control group, five haplotypes [2122, 1222, 2222, 2212, 1111] showed a frequency of more than 5% based on the FBAT program. Besides, nine haplotypes [2122, 1222, 2222, 2212, 1122, 1221, 1211, 1212, 2221] showed higher frequency (≥5%) based on PHASE program. Furthermore, except for the XV-2c marker, from all included polymorphisms of this study, only allele two was seen as a dominant allele in Khorasan Razavi population.

Conclusion: This case-control study showed that KM19 has the highest degrees of heterozygosity among cases; therefore, it may be more reliable when compared to other markers. We calculated its p-value as 0.03466125

based on the χ2 test for this marker which indicates a significant difference between cases and controls. Therefore in this study, we found KM19 a better indicator for genetic evaluations when compared to others. However, a combination of XV2c-KM19-T854T-TUB18 could be helpful. This investigation showed five informative haplotypes [2122,1222,2222,2212,1111], which could be valuable in performing carrier and prenatal diagnoses of the CFTR gene mutations in the Khorasan Razavi population. However, investigation for other potentially linked markers to the CFTR gene; is recommended to establish the best possible diagnostic approach.

Keywords: Cystic fibrosis (CF), Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), Linkage Analysis.

Evaluate the effect of co-treatment of Alpha-Lipoic Acid and Injectable platelet rich fibrin (i-PRF) bioscaffold on inflammation in mouse autotransplanted ovarian tissue (Research Paper)

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Introduction: Ovariaan tissue transplantation preserve fertility in patiant young woman and girls after chemotherapy and radiotherapy. nevertheless, ischemia-reperfusion (I/R) injury occurs during the early post-transplantation days leads to increased inflammation and eventually damage to autografted tissue. Injectable platelet rich fibrin (i-PRF) is a liquid formulation of platelet rich fibrin (PRF) without the use of anti-coagulants. i-PRF is bioscaffold and contains, leukocytes, circulating stem cells, platelets and growth factors. Alpha-lipoic acid (ALA) is also a strong free radical scavenger with anti-inflammatory properties. we aimed to research the effect of co-treatment i-PRF bioscaffold and ALA on the serum level of inflammatory factors such as interlukin 6, 10 (IL6,10) and Tumor necrosis factor-α (TNF-α) in the mouse ovarian tissue following transplantation.

Methods: Mice were divided into three groups: control, autograft + saline (whole ovarian tissue transplanted in the gluteus superficialis muscle, saline directly injected into it), autograft + i-PRF+ ALA (first, the mice received 100 mg/kg" intraperitoneal injections of ALA, 30 minutes before transplantation than whole ovarian tissue transplanted in the gluteus superficialis muscle, i-PRF was directly injected into it). Serum concentrations of IL-6, IL-10 and TNF-α were measured 7 days after ovary transplantation. Then the obtained data analyzed using one-way ANOVA and Tuckey's test and the means were considered significantly different at p-value < 0.05.

Results: The serum level of TNF-α and IL-6 in the autograft group increased significantly compared to the control group , while it showed a significant reduction in the autograft + i-PRF+ ALA group compared to the autograft group ($p < 0.05$). Moreover, Serum concentrations of IL-10 was significantly lower in the autograft group when compared to the control group, Whereas it showed a significant increase in the autograft + i-PRF+ ALA group compared to the autograft group ($p < 0.05$).

Conclusion: we results revealed that co-treatmentr i-PRF bioscaffold and ALA can Improve ischemic injuries in transplanted ovaries through decrease inflammatory factors.

Keywords: Ovarian tissue transplantation, α-lipoic acid (ALA). Injectable platelet rich fibrin (i-PRF). Ischem

Evaluating antilipemic effects of Silybum marianum versus Atorvastatin in atherosclerotic rabbits (Research Paper)

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Introduction: Atherosclerosis is a chronic inflammatory disease that remains the major cause of mortality, morbidity and disability in the developed world. The incidence of cardiovascular disease (CVD) varies from one region to another and it seems to be higher in Iran. Disorder of plasma lipoprotein and metabolism of lipids are the most recognized risk factors. Increased permeability to low-density lipoprotein (LDL) and its sequestration in the extracellular matrix plays role in the pathogenesis of atherosclerosis. In contrast to the LDL with atherogenic potential, HDL particles prevent atherosclerotic plaque formation. HDL transports cholesterol reversely from the peripheral tissues to the liver and acts as an anti-inflammatory and anti-oxidative agent. Recent studies have shown a correlation between CVD and triglyceride components, apolipoproteins, such as chylomicron, VLDL, LDL, and HDL. Several studies show that Milk thistle (Silybum marianum), a herbaceous plant, has potential anti-oxidative and immunomodulatory effects, reduces inflammation and inhibits oxidation of LDL. So, in this study, we aimed to evaluate the therapeutic effects of Silybum marianum seed extract.

Methods: Thirty-six male white New Zealand rabbits were divided into six groups as follows: control group; groups 2-6 were induced atherosclerosis by a high-fat diet, 2% cholesterol and 14% coconut oil, for eight weeks. Then: Group 2, was dissected; groups 3 to 6, animals were fed with the standard diet for the second eight weeks: Group 3, atherogenic control group (AC); group 4, Atorvastatin group (AV); group 5, Silymarin extract 1 (SM1), which were gavaged daily whit SMSE 100 mg/kg; group 6, Silymarin extract 2 (SM2), atherosclerotic rabbits were gavaged with SMSE high dose (200 mg/kg). After a therapeutic period with SMSE for two months, we evaluated serum concentrations of TG, TC, LDL, VLDL, and HDL were measured with biochemical kits from Pars Azmoon company- Iran.

Results: The serum levels of the lipid profile are shown in Table 1. There was a statistically (P< 0.05) increase in the mean concentration of TC, TG, HDL, LDL, VLDL in AC, AV and SM1 groups compared with the control group, while there were no significant differences between the control group and SM2 in the level of TC, TG and LDL. These results indicated that the high dose of SMSE was significantly more effective in lowering levels of TC, TG, LDL and VLDL than the low dose of SMSE and AV. Serum levels of the lipid profile of SM groups showed that they performed better than the values of the group treated with AV (VLDL in both doses, TG, TC and LDL in higher dose), indicating the effectiveness of the SMSE treatment. Table 1:The mean serum level of studied parameters in five groups Control Atherogenic Control Atorvastatin Silymarin (100mg/kg) Silymarin (200mg/kg) Triglycerides 71.50±7.2 162.16±11.2* 99.00±4.6*$ 102.83±5.9*$ 79.83±12.0$#@ Total cholesterol 29.50±4.0 220.00±18.3* 51.83±7.8*$ 55.16±7.2*$ 37.33±5.3$#@ HDL 17.16±2.8 53.66±7.5* 39.00±5.7*$ 36.33±2.2*$ 35.00±6.3*$ LDL 31.00±3.9 67.00±5.4* 44.16±4.9*$ 40.16±4.7*$ 33.66±3.9$#@ VLDL 8.50±1.9 25.50±1.9* 17.00±1.4*$ 19.16±1.7*$# 14.66±1.6*$#@ VLDL: Very-low-density lipoprotein; LDL: Low-density lipoprotein; HDL: High-density lipoprotein *P<0.05, level of significance compared with the control (c) group $ P<0.05, level of significance compared with the atherogenic control (AC) group # P<0.05, level of significance compared with the Atorvastatin (AV) group @ P<0.05, level of significance compared with the Silybum Marianum seed extract (SM1) group

Conclusion: Silymarin had affected lipid profile and 200 mg/kg SMSE was more effective than AV and even managed to control levels of TG, TC and LDL. Our results showed that rabbits treated with SMSE and AV experienced a significant increase in serum HDL and decrease in TC, TG, LDL and VLDL levels compared to atherosclerosis animals, meanwhile, the higher dose of SMSE was statistically more effective than the lower dose and AV. In accordance with results obtained by Radjabian (2010), SMSE can dose-dependently modify lipoprotein profiles. Other articles, demonstrated that Silymarin can affect the metabolism and the concentration of blood fats by inhibiting 3-hydroxy-3-methylglutheryl coenzyme A (HMG-CoA) reductase, a key enzyme in cholesterol synthesis, in the liver and also by lowering blood cholesterol by inhibiting its absorption in the gastrointestinal tract. In conclusion, this study indicates that SMSE, especially the high dose, may have good anti-atherosclerotic effects compared to Atorvastatin since it controls lipid profile.

Keywords: Atherosclerosis, Lipids, Silybum marianum, Rabbit

Evaluating of OCT-4 and NANOG was differentially regulated by a new derivative indole in leukemia cell line (Research Paper)

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Introduction: The potential exists to improve treatment through characterization of tumor stem cells and identification of therapeutic targets Using OCT-4 and NANOG genes. Here we have synthesized and investigated the potential of; New Indole-3-carbaldehyde derivative (NI-3-CD) in inhibiting the expression of self-renewal regulatory factors and cancer stem cell gene in a leukemia cell line NB4.

Methods: The NB4 cells were cultured in RPMI1640 medium contained NI-3-CD and I3F (15.12–1000 µg/ mL) for 24, 48 and 72 h. Inhibition of cell proliferation was assessed by trypan blue staining technique and MTT assay. The percentage of apoptotic cells was determined by flow cytometry analysis using Annexin V/PI apoptosis detection kit. The fold changes of NANOG/OCT4 expression against β-actin were determined by realtime-PCR technique. Western blotting analysis was also applied for evaluating the expression of NANOG/OCT4 at protein level. Data were analyzed by student t and repeated measure tests. Differences were considered significant if (P < 0.01).

Results: There was a significant difference in cell viability, when various concentrations of NI-3- were used for 24, 48 and 72 h in comparison to I3C regarding the cellular viability. Furthermore, the NI-3-CD, had markedly elevated anticancer activity than I3C (IC50 values for novel I3C in 24, 48 and 72 h were 225.77, 123.13 and 63.72 M respectively while for I3C were 728.05, 407.82 and 277.92 M respectively). Flow cytometry results exhibited an obviously significant augmentation in apoptotic NB4 cells. Real Time- PCR analysis indicated that the expression of NANOG/OCT4 was down regulated in compare to untreated control cells and I3C treated cells (P < 0.05). In concert with RT-PCR, western blot analysis showed that the OCT4

expression in NI-3-CD treated cells was also significantly decreased in compare to both untreated control cells and I3C treated cellular populations.

Conclusion: Our results imply that NI-3-CD treatment decreases the sphere-forming ability of NB4 cells. In summary, this study provides valuable information on the presence of stem-cell genes expression in NB4 cells.

Keywords: NANOG, OCT4, Antitumor, Indole-3-carbaldehyde, Treatment

Evaluation and comparison of the production of the quadrivalent HPV recombinant vaccine by VLP method in two models of enveloped and non-enveloped (Research Paper)

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Introduction: By 2022, about 220 human papillomavirus (HPV) genotypes have been identified. This large group of double-stranded DNA viruses is grouped into five genera (alpha, beta, gamma, mu and nu) based on the nucleotide sequence of the major structural protein L1, and can be classified into mucosal or cutaneous types based on their preferential infection site. Generally, HPV encodes at least six early genes (E1, E2, E4, E5, E6 and E7) and two late genes (structural L1 major and L2 minor capsid proteins). E1 and E2 are important for viral genome replication and its regulation, E4 promotes virion release from keratinocytes, while oncogenes E6 and E7 interfere with the host's cell cycle regulators to ensure viral genome replication.

Methods: To develop HPV-16 L1 / L2 chimeric protein VLPs, a neutralizing cross-epitope of the HPV-16 L2 gene was first inserted into the HPV-16 L1 gene. Chimeric L1 / L2 HPV-16 was then inserted into the pPICZA plasmid and expressed in Pichia pastoris (P. pastoris). Final purification of VLPs was performed using an ultra centrifuge (130,000 g) using a sucrose density gradient of 10-40% for 4 hours at 4 ° C. SDS-PAGE and Western blotting were performed separately for L1-HPV-16 and L2-HPV-16 proteins. 55 ng of purified VLPs for detection of L1 HPV-16 and L2-HPV-16 antibodies by ELISA test separately coated with ELISA wells using commercial L1-HPV-16 and L2-HPV-16 antibodies شد. Sera of 16 patients positive for HPV-16 and 85 serum negative for HPV infection were tested for HPV-16 antibody by ELISA and the results were compared with a commercial test kit.

Results: It can be stated with certainty that Licensed human papillomavirus (HPV) vaccines contain virus-like particles (VLPs) self-assembled from L1 major-capsid proteins that are remarkably effective prophylactic immunogens. However, the induced type-restricted immune response limits coverage to the included vaccine types, and expensive multiplex formulations, restrictive storage and distribution conditions drive the need for next generation HPV vaccines. Vaccine candidates based upon the minor structural protein L2 are

particularly promising because conserved N-terminal epitopes induce broadly cross-type neutralizing and protective antibodies.

Conclusion: In vivo, there are specific mechanisms that show how antibodies produced from L1 protein and L2 protein can neutralize HPV infection. Protein L1-raised antibody-mediated protection differs based upon antibody levels. High doses of protein L1 antibodies prevent viral BM binding leading to the Fc-mediated opsonization of antibody-bound viral particles by phagocytes, mainly neutrophils.

Keywords: human papillomavirus, HPV, VLP, protein L1

Evaluation of the effect of the methotrexate on expression changes of LncRNA HOXA-AS2 in acute lymphoblastic leukemia (Research Paper)

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Introduction: One of the characteristics of acute lymphoblastic leukemia (ALL), a blood cancer of the lymphoid line of blood cells, is the development of a sizable number of immature lymphocytes. Pale skin, fever, easy bruising or bleeding, swollen lymph nodes, and bone soreness may all be symptoms in addition to weariness. ALL develops quickly as acute leukemia and, if ignored, usually results in death within a few weeks or months. Only 10% of adult ALL patients and 30% of pediatric ALL patients survive, making ALL a disease with a terrible prognosis. In cancer tissues, HOXA-AS2 is elevated, which promotes this type of cancer cell migration and proliferation. the finding also suggested that HOXA-AS2 levels may be significantly up-regulated in the bone marrow tissues of leukemia patients compared with healthy subjects. Furthermore, results showed that HOXA-AS2 upregulated HOXA3, thereby activating EGFR/Ras/Raf/MEK/ERK signaling pathway in leukemia. Methotrexate is used to treat certain types of cancer (such as acute lymphoblastic leukemia, non-Hodgkin's lymphoma) and etc. Another folate-dependent mechanism that is impacted by methotrexate is the methylation of biomolecules. Furthermore, independently of the metabolism of folate, methotrexate has the ability to alter metabolic pathways and cellular functions. The aim of this work was to investigate the effects of methotrexate on the expression of the HOXA-AS2 gene in an acute lymphoblastic leukemia cell line.

Methods: Methotrexate was produced in two concentrations for the current study: 1µM and 10µM at 72 hours. A prepared dose of methotrexate was administered to the Jurkat E6.1 cell line, which was bought from the Pasteur Institute, 72 hours after cell passage. Following RNA extraction and cDNA synthesis, Real-Time PCR was used to examine the changes in the expression of HOXA-AS2 and GAPDH. Finally, Excel was used to create the diagrams, and Rest 2002 Software to analyze the data.

Results: Our research found that after 72 hours of methotrexate treatment at both concentrations, the expression of HOXA-AS2 reduced in contrast to the GAPDH housekeeping gene. According to the findings, changes in HOXA-AS2 gene expression reduces after 72 hours at a concentration of 1µM and 10µM decrease were statistically significant These changes included 1µM (0/998) and 10µM (0/851) at 72 hours, respectively. (P <0.001).

Conclusion: According to the present study results, alternation in HOXA-AS2 expression after treatment with Methotrexate, at two concentration were effective in the decrease of HOXA-AS2 expression. Evidence showed that Methotrexate has positive potential and efficacy because the drug was effective in decreasing gene expression in two concentrations in 72 hours.

Keywords: Methotrexate, LncRNA HOXA-AS2, GAPDH, Acute lymphoblastic leukemia

Evaluation of Antibacterial and Antiadenoviral Activity of Bacillus Clausii Supernatant and Its Effect on the Expression of Apoptotic Regulatory Genes Bax, Bcl-2 and MiR-145 in HeLa Cancer Cells

(Research Paper)

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Introduction: Bacillus clausii is being studied as a probiotic candidate. There is insufficient information on the antimicrobial and anticancer effects of B. clausii cell-free supernatant. The current study aimed to evaluate the antibacterial and antiadenoviral activity of B. clausii supernatant and its effect on the expression of apoptotic regulatory genes bax, Bcl-2 and miR-145 in HeLa cancer cells.

Methods: First, the cell-free supernatant (CFS) was prepared from a 24-hour bacterial culture, then its antibacterial effect on several gram-positive and gram-negative bacteria was evaluated using the microdilution method to calculate the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC). Adenovirus 5 (Ad5) espouse to the CFS under pre-treatment (incubation of cells with the CFS followed by Ad5 inoculation), pre-incubation (a mixture of co-incubated CSF/Ad5 added to cells), competition (adding Ad5 and CFS into cells at the same time) and post-treatment (cells inoculated with Ad5 and subsequently incubated with CFS) assays. Titer of virus and E1A level calculated by tissue culture infectious dose 50 (TCID50) and real-time polymerase chain reaction (real-time PCR) methods, respectively. After exposure to the CFS, expression levels of Bax, Bcl-2 and MiR-145 in HeLa cancer cells were evaluated using a real-time PCR method.

Results: B. clausii supernatant showed antibacterial activity against E. faecalis, S. aureus, MRSA, E. coli, P. aeruginosa, and A. baumannii. Ad5 titers in pre-treatment, pre-incubation, competition, and post-treatment assays with CFS (dilution:) decreased by about 4.61, 4, 3.9, and 3.1 Log10 TCID50/ml in comparison to control, respectively. Comparison of E1A expression levels between experimental assays and control showed similar findings of the viral titration. B. clausii supernatant during 48 h exposure to

HeLa cells increased the expression level of Bax, Bcl-2 and miR-145 genes to 9.1, 2.3 and 55-fold, respectively, in comparison to the untreated condition

Conclusion: The supernatant of B. clausii had an antibacterial effect against some gram-positive and gram-negative bacteria. It inhibits replication of Ad5 and increases the bax/Bcl-2 ratio in cervical cancer cell line. The bacterial supernatant upregulates the tumor suppressor miR-145. Therefore, B. clausii can be considered as a potent antimicrobial and anticancer agent. However, further studies are needed to determine its spectrum of antibacterial, antiviral, and anticancer effects.

Keywords: Antibacterial, Bacillus clausii, Bax, Bcl-2, miR-145

Evaluation of antioxidant and cytotoxic properties of Ephedra major extract and essential oil on A549 cell line of lung cancer and changes in expression of Bax and P53 genes (Research Paper)

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1.

Introduction: Introduction: Lung cancer is one of the most common types of cancer in the world and Iran. The antioxidant property of the variety plant sources is studied to obtain an efficacious drug against cancer. The objectives of the present study is to evaluate the antioxidant and anticancer effects of the essential oil and hydro alcohol extract of Ephedra's major plant against lung cancer A549 cell line.

Methods: Method: Ephedra plant extract and essential oil were extracted by soaking and Clevenger method respectively. The antioxidant activity of the extracts was measured using the DPPH test, and the phenolic content was measured by the Folin-Ciocalteu reagent. Also, the level of cytotoxicity, different concentrations of essential oil and extract of ephedra plant were evaluated on A549 cells at three times of 24, 48 and 72 hours using the MTT method. The expression changes of BAX and P53 genes was measured using Real time PCR method.

Results: Results: Our results showed that the concentration of phenolic content and antioxidant properties were higher in the ethanol extract than in the methanol extract. Cytotoxicity investigation indicated that IC50 of ephedra essential oil was 600 µl/ml and IC50 of ephedra plant extract was 750 µg/ml in 48 hours after treatment. Results of the study relevant that expression of BAX and p53 genes significantly increased under the influence of IC50 concentration of Ephedra essential oil and ethanol extract compared to the control group.

Conclusion: Conclusion: This investigation found that the extract and essential oil of ephedra major had cytotoxic properties on A549 lung cancer cells in higher concentrations and correlated by increasing the expression of BAX and P53 genes. So, these extracts can be used for the development of new drugs against lung cancer.

Keywords: Keyword: Ephedra major, lung cancer, Cytotoxic, antioxidant

Evaluation of bone-marrow micrometastasis effects on disease course in patients with esophageal cancer (Review)

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Introduction: Esophageal cancer is a type of invasive malignancy in which the risk of the involvement of blood vessels and lymph nodes at the time of diagnosis is high. The presence of metastasis in this malignancy can strongly affect the prognosis of the disease; however, some patients, despite not having detectable metastasis in the primary surgery, have shown recurrence due to the presence of micrometastasis. Bone marrow specimen immunohistochemistry (IHC) evaluation and anti-cytokeratin 18 antibody staining, which were obtained from the rib resection of patients with esophageal cancer, show that up to 90% of the cases have malignant cells. This study aimed to evaluate the association between bone marrow micrometastasis and histopathological and clinical behaviors of the tumor by comparing patients with or without bone marrow micrometastasis, followed by comparing neoadjuvant chemotherapy and surgery versus surgery alone in the prognosis of these patients.

Methods: This study reviewed the published literature on the association of bone marrow micrometastasis with the pathological behavior of the tumor and the application of neoadjuvant chemotherapy for the control of micrometastasis. The results and relevant parameters involved in this subject were evaluated. The published literature on PubMed, Scopus, Web of Science, EMBASE, and Google Scholar were used for the study.

Results: Approximately 53% of bone marrow micrometastasis cases do not have any significant differences in clinical signs in comparison to other patients. On the other hand, in some studies, there was a significant relationship between the presence of bone marrow micrometastatic cells with the tumor grade and stage N of the tumor. Nevertheless, there was no significant relationship between age, gender, and tumor length with micrometastasis. Additionally, the ten-year survival rate was 20% for those who only underwent surgery and 28% for those who underwent neoadjuvant chemotherapy followed by surgery, which was due to the micrometastasis reduction by neoadjuvant chemotherapy

Conclusion: Conclusion: Due to the critical role of bone marrow micrometastasis in determining the prognosis of this malignancy and its significant association with the tumor grade and stage N of the tumor, it is

required to carry out further studies with IHC or hematoxylin-eosin staining and neoadjuvant chemotherapy.

Keywords: Micrometastasis, Esophageal cancer, Neoadjuvant

Evaluation of coagulation parameters in COVID-19 patients with diabetes (Review)

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Introduction: Diabetes is the most common comorbid disease in patients with Covid-19 which leads to adverse clinical outcomes. On the other hand, coagulation disorders in Covid-19 patients are a major problem associated with high mortality. The aim of this study was to evaluate coagulation parameters in Covid-19 patients with diabetes.

Methods: A systematic search was performed using related keywords such as "COVID-19", "SARS-COV-2", "Diabetes", and "Coagulation parameters" in Pubmed, ScienceDirect, and Google Scholar databases from 2020 to 2022. In this study, 15 articles including original and observational articles were used.

Results: In diabetic patients with Covid-19, levels of D-Dimer, IL-6, C-reactive protein (CRP), and ferritin were significantly increased compared to non-diabetic patients with coronavirus. However, no significant differences were observed in platelet count, prothrombin time (PT), and relative thromboplastin time (PTT). In some studies, fibrinogen levels showed a significant increase, while in others, the increase was not significant.

Conclusion: In general, diabetic patients are at significant risk of coagulopathy and thromboembolism if they develop coronavirus disease, and even these risks can lead to mortality in these patients. Consequently, the evaluation of routine coagulation tests, especially D-Dimer, which is related to the prognosis of the disease, should be performed periodically and regularly in diabetic patients with Covid-19 and, if necessary, preventive measures should be taken.

Keywords: COVID-19, Diabetes, Coagulation, D-Dimer, CRP

Evaluation of developmental and efficacy of Pseudomonas exotoxin-based immunotoxins on brain tumors (Review)

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Introduction: Throughout history, cancer has attracted global health concern. This disease affects different target tissues, of which brain tumors are among the most dangerous. Microorganisms are one of the factors that transform normal cells into cancer cells. Due to the many side effects of traditional treatments, the world is looking for an alternative, more effective solution to treat this disease, the use of genetically modified microorganisms, which are hybrid molecules that are attached to bacterial or plant toxins to carriers of the genus Antibodies are formed that are linked by chemical bonding or genetic engineering to destroy pathological cells in various fields such as cancer, immune diseases or pain control. Penetration of protein drugs into the brain is very difficult due to the presence of protective barriers. The purpose of the current research is to investigate RIT derived from Pseudomonas Aeruginosa (PE), especially NBI-3001, which is an intravenous immunotoxin for the treatment of malignant glioma.

Methods: An online search of published medical articles through PubMed, Scopus, Web of Science, and Google Scholar using the terms "cancer," "brain tumor," "GBM," "Pseudomonas," "immunotoxin," "PE38," "NBI- 3001" were reviewed and screened and after evaluating the validity of the articles using SJR and MDPI databases, finally, more than 20 articles were carefully reviewed.

Results: Cancer is the cause of one of the six deaths in the world. But today, about 40% of cancers can be prevented, and with timely diagnosis, more than 80% of them can be treated with the help of new approaches. Many studies have been conducted on bacteria and their molecular mechanisms. The findings have shown that the cause of carcinogenesis is their continuous infection, and through this feature, they are used in cancer treatment. Brain tumors are one of the most dangerous diseases that can damage the brain and cause death. The cause of this type of cancer is a genetic mutation that leads to a change in tissue function. Glioblastoma in adults and medulloblastoma in children are the most common and aggressive malignant tumors. Patients with high-grade astrocytic tumors require new therapeutic approaches due to the highly heterogeneous and diffuse nature of astrocytic tumors. Advances in genomic and proteomic research have paved the way for personalized treatment based on the characteristics of the target tumor and its environment. Treatment with living bacteria that target the tumor is a unique

option because, in many treatment methods, the genetic structure of the tumor is effective in the treatment, but the effect of this method is on the depths of the tumor. It starts to multiply by selective colonization in the tumor, while in the rest of the body, it is cleared after a few days. The protective barriers of the brain make it difficult for the drug to penetrate. We discuss 2 new approaches to this problem: 1. blocking immune checkpoints 2. local treatment by new immunotoxins (RIT) and drug injection directly into the tumor. The high efficiency of RITs is due to factors such as very small molecular size, which makes it easier to penetrate solid tumors. Second, while retaining the specificity of Monoclonal antibodies, they have become more potent and have no known mechanism of drug resistance. Third, RITs can effectively kill quiescent, non-dividing cells, different from traditional chemotherapies. Finally, RITs have little cross-resistance with other agents and are also resistant to chemotherapy in cancer.

Conclusion: Due to their unique characteristics, recombinant immunotoxins are the best alternative or companion to traditional methods and a promising method for treating GBM. Since RIT-based treatment methods are considered a new platform in the treatment of brain tumors, cognition and understanding of this treatment method is It makes it possible for scientists to Development this method and discover its complementary steps and eliminate the complications caused by this treatment method. The current research examines therapeutic approaches based on RITs.

Keywords: tumor, Pseudomonas, immunotoxin, RIT, NBI-3001

Evaluation of Fetal Nuchal Translucency Threshold Alternatives for Down Syndrome Diagnosis (Research Paper)

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Introduction: One of the most common and well-known chromosomal disorders is Down syndrome (DS). DS is the most frequent genetic explanation of mild mental retardation. DS prenatal screening has been incorporated into Iran's prenatal care and consideration programs. The objective of the present study was to investigate the relationship between prenatal screening results (Trisomy 21 risk and nuchal translucency) and amniocentesis karyotype results to report the new nuchal translucency (NT) cut-point as a first trimester triage marker for pregnant women.

Methods: In this present prospective study, a total of 363 pregnant women were evaluated from March 2020 to March 2022 in Kerman, Iran. According to their prenatal screening test by determining the risk of trisomy 21 (combination of maternal serum levels of Alpha-fetoprotein, unconjugated estriol, and human chorionic gonadotropin multiples of the normal median (MoM) results with maternal age) and NT, the amniocentesis test had been done for each pregnant woman. Amniotic fluid cell culturing and karyotype analysis had been done. Moreover, the data were analyzed using descriptive and inferential statistical methods (SPSS Statistics software version 26).

Results: Positive combined prenatal screening for DS is when NT thickness overextended 4.0 mm. As pregnant women age, their gestational age changes this upper NT threshold value. In other words, the NT clinical test has a significant relationship with DS developing in fetuses (P-Value < 0.001). The best cut-point for NT clinical test was number 2.2050 and the sensitivity and specificity of this test were equal to 0.647 and 0.852, respectively. The laboratory test of DS had a significant correlation with Down syndrome risk (P-Value < 0.001). The best cut-point value for DS laboratory test (Trisomy 21 risk test) was 0.032 level, and the sensitivity and specificity of this test are 0.786 and 0.843, respectively. Also, one unit increase in Trisomy 21 (T21) Risk increased the possibility of developing DS by 18.11 times (P-Value = 0.013). The chance of developing DS in male fetuses was equal to in female fetuses (P-Value = 0.067).

Conclusion: The current study determined the association between prenatal screening results (risk of T21 and NT) and amniocentesis karyotype results and indicated possible alternatives for cut-points to DS and NT risks. Also, the two sexes were affected approximately equally. The present research provides insight into the most appropriate indications for NT value to apply in Iran's laboratories.

Keywords: Down Syndrome, Screening test, Nuchal translucency, Amniocentesis, Diagnosis.

Evaluation of frequency of cagA gene from Helicobacter pylori in patients with myocardial infarction (Research Paper)

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Introduction: Cardiovascular disease is one of the most important causes of death in industrial and developing countries, including Iran. Several studies have reported the association between chronic infections such as Helicobacter pylori and cardiovascular events. This research aimed to Evaluate the frequency of cagA gene from Helicobacter pylori in patients with myocardial infarction and its association with cardiovascular diseases as a risk factor. The result of this study can be significant in the timely diagnosis and treatment of cardiovascular diseases.

Methods: In this study, 194 patients with cardiovascular diseases were examined with intravenous blood, all obtained using standard techniques, and the rate of serum cholesterol, LDL, HDL, triglyceride, cardiac Enzyme, troponin, and IgG serum of each patient was measured by biochemistry Auto analyzer and ELISA system. Then DNA was extracted from samples, and the frequency of genes of the cagA, the gene was determined from H.Pylori in the patient via PCR, and then compared with Epiinfo software.

Results: Among 194 patients, cagA gene in 129 cases was positive (66/49%). Finally, comparing the biochemical parameters of the patients in both groups with positive cagA and negative cagA showed a significant difference in the rate of triglyceride, cholesterol, HDL-C, LDL-C, and AST between the two groups.

Conclusion: Additionally, the presence of cagA can increase the risk of affection for cardiovascular disease, especially in people under 50 years old.

Keywords: Cardiovascular disease, PCR, H.pylori.

Evaluation of gene expression of interleukin 25 (IL-25) in sputum of patients with persistent severe asthma (Research Paper)

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Introduction: Severe persistent asthma as defined by the European Respiratory Society is an asthma that has been in the stage of 4 or 5 of asthma as defined by Gina over the past year, which requires treatment with high dose inhaled glucorticoids and long-acting beta-agonist (LABA) with anti-leukotriene or theophylline. Interleukin-25 (IL-25) is a proinflammatory cytokine which is mainly produced by T lymphocytes or their precursors. Some lymphocyte subgroups produce interleukin-25, which activates neutrophils. The aim of this study, considering the role of interleukin 25 (IL-25) in inflammation and airway deformity, was to evaluate the level of this gene expression in patients with severe persistent asthma and to compare the level of this gene expression with clinical symptoms and pulmonary tests in this group of patients

Methods: In this semi-empirical study, patients with persistent severe asthma completed conscious satisfaction and then, sputum was sampled with a nebulizer by using hypertonic saline (an expectorant compound) to measure the interleukin-25 (IL-25) gene expression level in sputum and sample cytology. Sputum sampling was performed in two groups of 31 patients with asthma and 31 healthy individuals.

Results: The results of this study indicated that there is no significant difference between asthma stage and the interleukin-25 gene expression level, but in the correlation coefficient of graphs, there was a significant relationship between asthma stage and gene expression. The data showed that by increasing the interleukin-25 gene expression level in Patients which have severe persistent asthma with shortness of breath (Dyspnea), there is no significant difference in all individuals, but about shortness of breath (Dyspnea) with the IL-25 gene expression level, by increasing the level of this gene expression, There is a significant increase in the average of results in group 3 compared to group 2. In addition, there is a significant difference between gender and the interleukin-25 gene expression level in comparing women and men. As well as, it was observed that by increasing the interleukin-25 gene expression level, the rate of coughsin patients increases as well. Surveys show that there is a significant correlation between the interleukin-25 gene expression level and pre FEV1.

Conclusion: It is recommended that other inflammatory cytokines affecting persistent severe asthma which may make the disease more difficult to control, be investigated.

Keywords: severe Persistent asthma, Real Time, Interleukin-25 (IL-25), Sputum

Evaluation of gene expression of thymic stromal lymphopoietin (TSLP) in sputum of patients with persistent severe asthma (Research Paper)

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Introduction: Asthma, as a respiratory disease, is a chronic inflammatory complication of the all ways that causes narrowing of the airways and the development of sensitivity and resistance to air currents. This disease causes a lot of costs to the individual and the medical tem of the country every year. Also, because the population of asthmatics is increasing worldwide, thymic stromal lymphopoietin it is very important to study the factors that can aggravate the disease. The thymic stromal lymphopoietin gene is an important cytokine in the development of asthma and respiratory tract inflammation. This cytokine is expressed in various cells, including the airway epithelial cells. Many environmental factors such as allergens, germs, cigarette smoke, etc. can trigger the production of TSLP

Methods: In this study, TSLP gene expression in sputum of patients with stable severe asthma was investigated by RT-PCR. A total of 31 patients with asthma and 31 control samples were studied.

Results: The results showed that there was no significant difference between the control and asthma groups in terms of TSLP gene expression distribution. Also, a significant linear correlation was observed between TSLP gene expression and body mass index and asthma severity .the relationship between age, gender, cough and shortness of breath with gene expression intensity in people with severe asthma was not significant, but there was a significant difference between asthma severity and TSLP gene expression And as the severity of asthma increases, so does gene expression.

Conclusion: It seems that by suppressing the expression of TSLP or creating polymorphisms in this gene this disease can be reduced. It is recommended that other inflammatory cytokines affecting persistent severe asthma, which may make the disease more difficult to control, be investigated.

Keywords: severe Persistent asthma, Real Time, thymic stromal lymphopoietin (TSLP), Sputum

Evaluation of genes expression in Multiple sclerosis disease: In silico study (Research Paper)

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Introduction: Multiple sclerosis (MS) is a chronic inflammatory and demyelinating disease of autoimmune origin. Major contributors to the MS development include exogenous, environmental, and genetic factors. MS is characterized by multifocal and temporally scattered damage to the central nervous system (CNS) resulting in axonal damage. Current therapeutic options for progressive multiple sclerosis are comparatively disappointing and challenging. One possible explanation is the lack of understanding of the pathogenic mechanisms underlying progressive multiple sclerosis. In addition, imaging techniques and biomarkers are not yet well established. MS Genome-wide association studies have identified many genes involved in immune regulation, and the next step will be to elucidate how these genetic variations influence immune cell function to drive disease development and progression. However, much of the remaining genetic contribution to MS has not been elucidated. The main aim of this study is to investigation and prediction expression changes of some genes in MS disease.

Methods: First, the keywords MS or multiple sclerosis were searched in the GEO dataset, and the data of GSE146383 was selected for the study. In addition, in order to analyze these data, Transcriptome Analysis Console (TAC) program was used. Finally, the results of the study were also reviewed in the PubMed database.

Results: Considering the P-value < 0.05 and Log2FC > 5, Discoidin Domain Receptor tyrosine kinase1 (DDR1), Replication Factor C subunit2 (RFC2), and Heat Shock Protein (HSPA6) genes showed the most expression change in patients with MS disease compared to control samples.

Conclusion: The results of this study show increased expression of HSPA6, RFC2 and DDR1 genes. Therefore, these genes may play an effective role in the pathogenesis and treatment of MS. It is also suggested that the expression data of these genes can be used as a diagnostic biomarker in the diagnosis of this disease. Although the results of this study show new prognoses about MS disease, more studies are needed in this field.

Keywords: MS, Multiple sclerosis, DDR1, RFC2, HSPA6

Evaluation of genome extraction using magnetic nanoparticles (Review)

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Introduction: Genome isolation is a prerequisite for many molecular biology and genetic engineering techniques. Since the discovery of DNA and RNA, various methods have been developed and used to extract genomic content, and to date, efforts have been made to reduce contamination and optimize extraction time, quality and concentration.

Methods: In September 2022, our research was conducted on the ScienceDirect, PubMed, SID, and Scopus databases. Articles with irrelevant titles or abstracts were excluded. Finally, the most related articles were selected.

Results: Recent studies have shown the high efficiency of coated magnetic nanoparticles, especially silica-coated, compared to bare or uncoated nanoparticles.

Conclusion: Genome extraction using magnetic nanoparticles is an easy, fast, and efficient method that can provide a good quality nucleic acid product. In addition, the efficiency of magnetic nanoparticles can be greatly increased by improving the performance of magnetic separation, improving stability, and adding special functional groups.

Keywords: Magnetic nanoparticles, Genome extraction, Magnetic Separation, PCR, Fe3O4@SiO2

Evaluation of Health Anxiety in Nursing and Midwifery Students of Iran University of Medical Sciences During Covid-19 Crisis in 2021 (Research Paper)

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Introduction: With the spread of Covid-19 worldwide, young adults, often including students, are not only at risk for physical health but also mental health, stress and anxiety problems. Health anxiety is an obsessive and irrational worry about having a serious medical condition which most people experience, but the problem arises when the anxiety is excessive. The aim of this study was to investigate the level of health anxiety among nursing and midwifery students of Iran university of medical sciences.

Methods: The present descriptive study was performed on 191 nursing and midwifery students of Iran University of Medical Sciences after obtaining approval from the ethics committee. Data was collected by available sampling method, using demographic information checklist and 18-item health anxiety questionnaire, provided to students through the Porsline link and social networks in cyberspace. The collected data were analyzed by Spss-16 software and descriptive statistics were used to describe the data and chi-square inferential test to determine the relationship between demographic factors and health anxiety.

Results: 71.2% of the students participating in the study were women and the average age of students was 23.98 years. 65.44% of the participants studied at the undergraduate level. Also 177 of the participants (92.67%) did not have any underlying disease. The results showed that the mean health anxiety of the participants was 17.93. There was a significant relationship between health anxiety and having a history of underlying disease (P = 0.05).

Conclusion: The probability of health anxiety in medical students is higher than students in other fields, therefore it is suggested that special programs be considered to prevent the occurrence of health anxiety in this group.

Keywords: Health Anxiety, Covid-19, Students, Nursing, Midwifery

Evaluation of Patients with Tetralogy of Fallot by Cardiac MRI After Complete Surgical Repair in Rajaei Heart Center, Tehran, Iran (Research Paper)

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Introduction: Tetralogy of Fallot is the most common type of cyanotic congenital heart disease. The underlying mechanisms that contribute to heart dysfunction in patients with repaired tetralogy of Fallot are incompletely understood. In this study, we tried to evaluate the cardiac function indexes and residual complications after Fallot tetralogy complete surgical repair.

Methods: In this cross-sectional study, clinical data and information obtained from cardiac magnetic resonance (CMR) gathered from 150 consecutive patients with repaired tetralogy of Fallot. Cardiac function indexes and residual complications evaluated in the patients.

Results: Mean age of patients was 22.5±9.6 years. 60 patients (40%) were female and 90 patients (60%) were female. Mean of Left ventricular Ejection Fraction and mean of Right ventricular Ejection Fraction was 54.9±7.5 and 38.6±8.3 percent, respectively. Left ventricular Dilatation in 19 (12.7%) and Right ventricular Dilatation in 141 (94%) patients was observed. RVOT dilatation in 143 (95.3), residual pulmonary stenosis in 39 (26%), ASD (Atrial Septal Defect) in 1 (0.7%), VSD (Ventricular Septal Defect) in 40 (26.7%), PDA (Patent ductus arteriosus) in 11 (7.3%) and Delayed Enhancement of RVOT in 125 (83.3%) patients was positive.

Conclusion: Residual complications following repair of Tetralogy of Fallot, especially in the right ventricle, are common and CRM may be a diagnostic

instrument for follow-up in patients with congenital heart disease after repairing surgery.

Keywords: Tetralogy of Fallot, cardiac magnetic resonance, residual complications

Evaluation of rs10129954 polymorphism of DPF3 gene with non-obstructive azoospermia in Iranian men referring to Royan Institute (Research Paper)

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Introduction: Infertility is a major health problem worldwide and is estimated to affect 8–12% of couples in the reproductive age group. A large number of infertile men are suffering from idiopathic infertility. This infertility can be the result of mutations or other changes in the genes involved in spermatogenesis. Genetic factors account for at least 15% of male infertility. Men with azoospermia are at the highest risk of being carriers ofgenetic anomalies (25%). The most abundant source of genetic variation in the human genome is represented by single nucleotide polymorphisms. The polymorphism studied in this research is in the intronic region of the DPF3 gene (rs1012995). DPF3 is an important regulator of gene expression that acts through nucleosome repositioning. Double PHD fingers 3 (DPF3) is a human epigenetic factor found in the multi protein BRG1-associated factor (BAF) chromatin remodeling complex. Considering the important role of epigenetic factors in spermatogenesis, polymorphism in this gene can affect the function of this gene and these disorders may be associated with infertility in men. The aim of this study was to investigate the DPF3 gene polymorphism (rs10129954) in non-obstructive azoospermia patients in Iranian men referred to Royan Institute.

Methods: We studied this polymorphism in 96 infertile men with idiopathic azoospermia, and 100 fertile men with normozoospermia as a control group. DPF3 gene polymorphism (rs10129954) was analyzed using the ARMS PCR. to investigate the differences in genotypic and allelic frequency distribution between two groups Fisher's exact test and Chi-square test was used.

Results: Results showed that out of 96 infertile men, 19 (19.8%) had CC genotype, 33 (34.4%) had CT and 44 (45.8%) had TT genotype. Of the 100 fertile controls, 33 (33%) had CC genotype, 49 (49%) had CT genotype and 18 (18%) had TT genotype and P<0.001.

Conclusion: According to the obtained results, polymorphism (rs10129954) of DPF3 gene has a significant relationship with idiopathic infertility caused by non-obstructive azoospermia. In order to better understand the effective genetic factors, more research and larger populations are needed.

Keywords: DpF3 gene - Male infertility – Azoospermia - Polymorphism

Evaluation of Students Knowledge about Corona Virus and its Relationship with Stress during COVID-19 Epidemy in Shahrood (Research Paper)

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Introduction: Coronavirus disease 2019 is a serious respiratory syndrome that the whole world is facing since two years ago and it seems it has turned into a real dead end! Covid-19 is not a usual virus and impacts various aspects. Until now, we have been focused on the biological and clinical features of this illness but it's time to accept there are way too many things that need to be investigated. We conducted this study to target the psychological effects of the covid-19 outbreak and the correlation of individual's knowledge with their mental health. We mainly focused on university students to bring new insights on awareness and its correlation between stress level and protective manners during the covid-19 pandemic.

Methods: The online cross-sectional questionnaire was conducted from February 2020 to April 2020 of 300 students of Shahrood University of Medical Sciences and Technology (By random sampling) including background information and perceived stress questionnaire version 14 questions and awareness assessment questionnaire including virological information and clinical management, epidemics and ways to prevent. Parametric data were analyzed by two-way independent t-test and ANOVA, non-parametric data by Mann Withney, numerical variables by linear regression test, and nominal variables by Pearson chi-square.

Results: all 314 participants were divided into two groups based on their field of study: medical sciences (64%) and non-medical students (36%). results indicate that based on participant's score in the awareness assessment questionnaire There was a significant difference with a mean of 8.83 in non-

medical versus 10.24 mean in medical sciences in case of total awareness. notably, there was an inverse relationship between the level of awareness and stress and also the level of stress and preventive performance of individuals.

Conclusion: The Conclusion of these studies showed that increasing the level of awareness, can be effective in reducing stress levels and promoting mental health in students, and improving preventive behaviors to reduce the Covid 19 transmission chain. Therefore, one of the important tasks of the government and universities is to provide strategies to increase the level of awareness of students.

Keywords: COVID-19; distress; fear; knowledge; student

Evaluation of the antimicrobial and antifungal effect of nano-emulsions loaded by oil extract of Thymus kotschyanus (Research Paper)

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Introduction: The development of antibiotics has been a major breakthrough in medical world as a powerful means of curing diseases and preventing infections. However, in recent years, antimicrobial resistance has become one of the most significant medical concerns. Therefore, to tackle this issue alternative options such as implementing herbal oil extract as an antibacterial agent have to be taken into consideration. Nevertheless, the volatility, poor water solubility, as well as sensitivity to light and oxygen, are the main drawbacks of using essential oils. Therefore, nanoencapsulation of essential oil (EO) which was successfully used in our study appears to be a great way to enhance physiochemical attributes namely bioavailability, solubilization, and thermal stability.

Methods: In this study, the EO of Thymus kotschyanus which is a medicinal herb belonging to the Lamiaceae family was extracted by hydro-distillation method Clevenger type and the components of EO were analyzed by gas chromatography –mass spectrometry (GC-MS). Then, the EO was loaded into a nano-emulsion mainly made of Twin 80 and Span 60 as surfactants. It was synthesized by a high-pressure homogenizer and the thermal stability of particles was investigated at three (4, 25 and 40 C) temperatures for 84 days. Moreover, morphology of the nanoemulsions was evaluated by Transmission Electron Microscope (TEM) and Atomic Force Microscopy (AFM). The release of the EO from the nano-emulsion was investigated for 24 hours. Ultimately, the antimicrobial and antifungal impact of nano-emulsion was investigated by both micro-broth and macro-broth dilution tests against 6 species of gram-negative bacteria, 6 species of gram-positive bacteria, Aspergillus niger, and Candida albicans.

Results: Analysis of morphological characterization by AFM and TEM represented the spherical shape of nanoparticles. The outcome of measurements done by Nano Zetasizer reported an average size of 135 nanometers and revealed a regular distribution of nanoparticles. Furthermore, in the in-vitro drug release test, more than 55 percent of the loaded EO was released in the first 5 hours and the rest of the EO was secreted steadily until

the end of the assessment. The inhibitory effect of EO and Nano emulsion containing essential oil (NEO) is more than antibiotics on gram-negative bacteria such as Salmonella typhi (MBC and MIC of NEO = 1/56×10-2 / MBC of antibiotic = 6/25×10-2) and also their effect is remarkable on gram-positive bacteria like Bacillus subtilis (MBC and MIC of NEO = 4×10-4 / MBC of antibiotic = 7×10-4). However, no progress was seen in inhibiting the growth of Pseudomonas aeruginosa in various concentrations by neither the EO nor the NEO. In addition, both EO and NEO caused inhibition in the growth of Candida albicans and Aspergillus niger. Moreover, prior to all antibacterial tests the effect of the EO in inhibiting the growth of microorganisms was also assessed by measuring the diameter of inhibitory zone. Bacillus subtilis with inhibitory zone of 36 mm was the most susceptible bacteria.

Conclusion: According to the reports of current research, the nano-emulsion of Thymus kotschyanus has a noticeable antimicrobial and antifungal effect and can be a priceless source for curing diseases specially in case of multi drug antimicrobial resistance. Since in preparation of the nano-emulsion less oil extract is used, it can be assumed that the encapsulated EO represents higher efficacy in comparison with pure EO specifically in gram-negative bacteria. What is more, due to the accessibility of Thymus kotschyanus and feasible process of synthesizing the nano-emulsion, application of this nano herbal drug is highly recommended.

Keywords: Nano-emulsion, Thymus kotschyanus essential oil

Evaluation Of The Cost-Effectiveness Of Auditing-Feedback Intervention On Drug And Paraclinic Prescribing Indicators In The Social Security Organization Of Tehran between 2016 and 2018 (Research Paper)

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Introduction: One of the most important challenges in the field of pharmacotherapy is the inappropriate and irrational prescription of drugs, which itself causes unwanted consequences both from the perspective of society's health and from the perspective of cost in the health system. In order to prevent and reduce the amount of irrational drug prescription and consumption, various solutions have been proposed by the World Health Organization and implemented by many countries. One of the most effective solutions proposed in the field of management strategies is the implementation of an audit-feedback intervention on the performance of doctors' prescriptions. Therefore, in this study, the cost-effectiveness of auditing-feedback interventions on drug prescribing and paraclinical indicators in Tehran Social Security Organization with the aim of using the results of this study in planning, policy development and resource allocation management to develop strategies to promote rational drug prescribing was investigated.

Methods: First, in order to evaluate the level of effectiveness, intervention effectiveness indicators were determined and their values were extracted using TDMS software. Then, the calculation of changes in the indicators was examined, and at the end, the growth rate, the calculation of gross profit due to the implementation of the intervention and the calculation of net profit (savings) due to the implementation of the intervention were calculated by analytical methods.

Results: The changes in the average effectiveness indicators of the study showed that the average number of prescribed medicinal items and the amount of antibiotics prescribed in these 3 years have decreased. While the percentage of prescriptions containing serum, the average prescription of tests per prescription and the percentage of prescriptions containing tests to the total prescription have been increasing. The amount of prescription containing corticosteroid drugs and injectable drugs had a fluctuating trend. The important point is the calculation of the costs incurred for the

implementation of the intervention in relation to the changes in the effectiveness indicators, the results showed that the implementation of this intervention, in addition to controlling the amount of irrational prescription of this group of drugs, also saved drug costs from a financial point of view. So that the amount of savings based on the average reduction of medicinal items in this study was estimated as 29,561,193 dollars.

Conclusion: This study showed that the implementation of the audit-feedback intervention on the percentages of antibiotics and the average of pharmaceutical items written in physicians' prescriptions had made good progress. But in terms of the percentage of serum prescribed in the prescription, the percentage of tests and the average number of tests, as well as the percentage of injectable drugs and corticosteroids, it has not performed well. In order to improve it, education and culturalization to retrain some doctors to change their prescribing behavior, as well as pharmacists to advise patients and perform several interventions simultaneously, are needed.

Keywords: Rational drug prescription, Audit-Feedback intervention, Economic evaluation.

Evaluation of the effect of grape seed extract and punica granatum L on Aurora Kinase C protein by molecular docking method (Research Paper)

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Introduction: Grapes (Vitis vinifera) one of the world's agricultural and produced fruits, grape seed extract has Protects against toxic reproductive agents.(1) Grapes contain significant amounts of the carotenoid antioxidant lycopene. In men who are deficient in the carotenoid lycopene, this antioxidant can increase sperm motility and count. The carotenoid lycopene is important for healthy sperm, and men who are deficient in it usually suffer from fertility problems. Grapes contain significant amounts of the carotenoid antioxidant lycopene. In men who are deficient in the carotenoid lycopene, this antioxidant can increase sperm motility and count. The carotenoid lycopene is important for healthy sperm. punica granatum L (pomegranate) plant is a small shrub and is one of the oldest fruit plants. which can be used as a medicinal plant. It has been used for generations to treat ulcers, diarrhea and male infertility.(2) Serine/threonine-protein kinase component of the chromosomal passenger complex (CPC), a complex that acts as a key regulator of mitosis. The CPC complex has essential functions at the centromere in ensuring correct chromosome alignment and segregation and is required for chromatin-induced microtubule stabilization and spindle assembly. Also plays a role in meiosis and more particularly in spermatogenesis. Has redundant cellular functions with AURKB and can rescue an AURKB knockdown. Like AURKB, AURKC phosphorylates histone H3 at 'Ser-10' and 'Ser-28'. AURKC phosphorylates the CPC complex subunits BIRC5/survivin and INCENP leading to increased AURKC activity .(3) Herbal medicines, as a treatment method, have received a great deal of attention. In this study, we investigated the effect of grape seed extract and punica granatum L on Aurora Kinase C protein by molecular docking method.

Methods: In this descriptive-analytical project, we first downloaded the most suitable three-dimensional structure Of Aurora Kinase C protein in terms of resolution and number of suitable chains from the uniprot site in pdb format. We see some specifications of this protein below. Chain A was selected for the docking process because it is larger than the other chains and has the most amino acids. Released: 2019-05-15 Then, protein chains were examined using Chimera software. The most suitable chain in the protein was selected separately, which had more amino acids than other chains and the largest chain was the protein. Through this software, molecules were selected. We removed water and all solvents from these chains and hydrogen ions and charge bar were added to these chains and finally saved in pdb format. In the next step, we downloaded the structure of Aurora Kinase C drug

from Pubcheem site in SDF format. The information about grape seed extract drug was as follows: Exudate from seeds of the grape plant Vitis vinifera, composed of oils and secondary plant metabolites (BIOFLAVONOIDS and polyphenols) credited with important medicinal properties.(4) Molecular formula: C32H30O11 The information about punica granatum L drug was as follows: Ellagic acid is an organic heterotetracyclic compound resulting from the formal dimerisation of gallic acid by oxidative aromatic coupling with intramolecular lactonisation of both carboxylic acid groups of the resulting biaryl. It is found in many fruits and vegetables, including raspberries, strawberries, cranberries, and pomegranates. It has a role as an antioxidant, a food additive, a plant metabolite, an EC 5.99.1.2 (DNA topoisomerase) inhibitor, an EC 5.99.1.3 [DNA topoisomerase (ATP-hydrolysing)] inhibitor, an EC 1.14.18.1 (tyrosinase) inhibitor, an EC 2.3.1.5 (arylamine N-acetyltransferase) inhibitor, an EC 2.4.1.1 (glycogen phosphorylase) inhibitor, an EC 2.5.1.18 (glutathione transferase) inhibitor, an EC 2.7.1.127 (inositol-trisphosphate 3-kinase) inhibitor, an EC 2.7.1.151 (inositol-polyphosphate multikinase) inhibitor, an EC 2.7.4.6 (nucleoside-diphosphate kinase) inhibitor, a skin lightening agent, a fungal metabolite, an EC 2.7.7.7 (DNA-directed DNA polymerase) inhibitor and a geroprotector. It is an organic heterotetracyclic compound, a cyclic ketone, a lactone, a member of catechols and a polyphenol. It derives from a gallic acid.(5) Molecular formula: C14H6O8 To perform the docking process, pyrx software was used. In this software, after importing the protein as a receptor and the drug as a ligand, we obtained the binding site through the Deepsite site, the specifications of which were as follows: exhaustiveness = 8 center_x= 35.1554 center_y= 4.7732 center_z= 19.2287 size_x = 25.0 size_y = 25.0 size_z = 25.0

Results: After performing molecular docking separately for grape seed extract and punica granatum L, the results were as shown in the table below. The result of grape seed extract docking grape seed extract Binding Affinity(kcal/mol) RMSD lower bound RMSD upper bound Conformation 1 -6.9 0 0 Conformation2 -6.8 2.414 4.307 Conformation 3 -6.5 1.546 2.071 The result of punica granatum L docking punica granatum L Binding Affinity(kcal/mol) RMSD lower bound RMSD upper bound Conformation 1 -6.0 0 0 Conformation2 -6.0 0.105 6.183 Conformation 3 -5.9 2.519 5.889

Conclusion: According to Docking results, it can be concluded that grape seed extract can bind well with Aurora Kinase C protein with good negative binding energy. Proper orientation of drug within protein according to RMSD = 0 in pyrx method is another reason for this is

Keywords: grape seed extract , punica granatum L , Aurora Kinase C protein

Evaluation of the effect of Staphylococcus aureus cytoplasmic extract on U87 glioblastoma cell line and evaluation of the expression of apoptotic bax and bcl-2 genes (Research Paper)

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Introduction: Glioblastoma is one of the most common malignant diseases that develop in the spinal cord or brain, and its prevalence rate in Iran is faster than the global statistics of a decade and is one of the most serious causes of death in patients. So far, many treatment methods have been used for treatment, but these methods were transient, there was still a possibility of disease recurrence and they did not have a good effect on the patient's survival.In recent years, drugs such as bacterial toxins, different fractions, and cytoplasmic extracts have received attention in the treatment of various types of cancers. Therefore, the purpose of this study is to evaluate the effect of Staphylococcus aureus cytoplasmic extract and its function on U87 glioblastoma cell line and its effect on apoptosis induction.

Methods: U87 cell line cells were produced from Iran's teak reserves center and the cells were grown in suitable conditions. Staphylococcus aureus was also cultured in LB Broth at 37 degrees for 24 hours; Then, plant cytoplasmic extract was prepared by sonication and its contents were evaluated by SDS-PAGE. Lowry's method was used to determine and finally, the inhibitory effect of Staphylococcus aureus on cell proliferation and apoptosis was investigated through MTT test. The tumor cell was treated with an ideal dose of Staphylococcus aureus extract, and the expression rate of bcl-2 and bax genes was measured using Real-Time-PCR techniques.

Results: Cytoplasmic extract of bacteria prevented the continuation of the proliferation process in U87 cell line and induced apoptosis by increasing the expression of apoptotic gene bax and decreasing the expression of bcl-2 gene. In fact, based on the analysis performed between the case and control groups by means of a statistical test, it is observed that the expression of bcl-2 in the treatment cDNA cell based on the CT ranking is lower than the control group with a significant difference in variance, and also the expression of the bax gene in a sample of has been treated Attention to the CT rate is higher than the control group (P Value < 0.05).

Conclusion: These results proved that the cytoplasmic extract of Staphylococcus aureus has an inhibitory effect on proliferation in the U87 cell line, and by implementing more projects in the direction of identifying bacterial substances with anticancer properties, Staphylococcus aureus extract can be used. It has been named as a favorable candidate for inducing apoptosis in malignant tumors.

Keywords: Glioblastoma, Staphylococcus aureus, apoptosis, cell proliferation, U87 cell line

Evaluation of the Effect of the Cyclophosphamide on Expression Changes of LncRNA HOXA-AS2 in Acute lymphoblastic leukemia (Research Paper)

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Introduction: The most typical kind of teenager cancer is leukemia. Acute lymphocytic leukemia (ALL), which makes up around 78% of all teenager leukemia diagnoses in this demographic, is diagnosed about five times more commonly than acute myelogenous leukemia (AML). One of the most successful and often used antineoplastic medications is still cyclophosphamide. Additionally, it has strong immunosuppressive properties and is the most widely used medication in bone marrow transplants (BMT). It was initially synthesized to selectively target cancer cells, although the hypothesized mechanism of tumor specificity (activation by cancer cell phosphamidases) transpired to be irrelevant to its activity. Nevertheless, cyclophosphamide's unique metabolism and inactivation by aldehyde dehydrogenase is responsible for its distinct cytotoxic properties. Differential cellular expression of aldehyde dehydrogenase has an effect on the anticancer therapeutic index and immunosuppressive properties of cyclophosphamide. Long noncoding RNAs (lncRNAs) have important roles in diverse cellular processes and carcinogenesis. Homeobox (HOX)A cluster antisense RNA 2 (HOXA-AS2) is a 1048-bp lncRNA located between human HOXA3 and HOXA4 genes whose overactivation was previously found to promote the proliferation and invasion of solid tumors. However, its biological roles in leukemia remain unclear. The goal of this study was to see how Cyclophosphamide affected the expression of the HOXA-AS2 gene in a cell line that had been diagnosed with acute lymphoblastic leukemia.

Methods: Two Cyclophosphamide concentrations were created for the current study: 20 and 50 µM at 48 hours. After purchasing the Jurkat E6.1 cell line from the Pasteur Institute, it was given a prepared dose of cyclophosphamide 48 hours after cell passage. Following RNA extraction and cDNA synthesis, Real-Time PCR was used to examine the changes in the

expression of HOXA-AS2 and GAPDH. Finally, Excel was used to create the diagrams and Rest 2002 Software to analyze the data.

Results: The results of our findings showed that the expression of HOXA-AS2 in comparison with the GAPDH housekeeping gene decreased after 48hours of cyclophosphamide treatment at both of the concentration drug. According to the findings, changes in HOXA-AS2 gene expression decreased after 48 hours at a concentration of 1µM and 10µM decrease were statistically significant These changes included 20µM (0/958) and 50µM (0/923) at 48 hours, respectively. (P <0.001).

Conclusion: According to the present study results, alternation in HOXA-AS2 expression after treatment with cyclophosphamide, at two concentration were effective in decrease of HOXA-AS2 expression. Evidence showed that the cyclophosphamide has positive potential and efficacy because the drug was effective in decreasing gene expression in two concentrations in 48 hours. Therefore, cyclophosphamide can be a useful drug in controlling the expression of genes involved in acute lymphoblastic leukemia.

Keywords: LncRNA HOXA-AS2, GAPDH, Acute lymphoblastic leukemia, Cyclophosphamide.

Evaluation of the effects of Galega officinalis extract on spermatogenesis and testicular structure in diabetic rats (Research Paper)

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Introduction: The aim of this study was to assess the antioxidant potential of Galega officinalis extract on oxidative damage in testes and sperm parameters of diabetic rats.

Methods: In this investigation, 32 male Wistar rats were randomly divided into 4 groups: Control, Diabetic control, Diabetic treatment with G. officinalis extract, and the healthy group that received G. officinalis extract. An installation of distilled water was conducted in the control and diabetic groups. Also, treatment groups obtained Galega extract (50 mg/kg body weight) for 8 weeks. After the treatment period, all of the subjects were anesthetized, their blood samples were assumed, the insulin and glucose serum levels were measured, then the testes and epididymis were extracted and sperm parameters and oxidative stress markers were evaluated.

Results: In diabetic rats that received G. officinalis extract, Johnson's score and diameter of the seminiferous tubule remarkably increased as well as glucose plasma levels decreased and insulin levels increased. Also, during diabetes, an increase in the malondialdehyde (MDA) level and a decrease in the levels of superoxide dismutase (SOD) and catalase (CAT) enzyme activity were observed in the testes. The administration of G. officinalis extract (50 mg/kg BW) rectified these parameters. Moreover, the sperm parameters were reduced in the diabetic group, while the use of G. officinalis remarkably improved the noted disorders in the treatment groups.

Conclusion: The outcomes of this research prove the antioxidant role of hydroalcoholic extract of G. officinalis in the improvement of the testicular oxidative damage caused by diabetes.

Keywords: Diabetes, Oxidative Stress, Galega officinalis, Testis, Sperm parameters

Evaluation of the effects of high-intensity resistance training in patients with osteosarcopenia: as a way to prevent and improve complications (Review)

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Introduction: Osteosarcopenia is the simultaneous degeneration of skeletal muscle, decrease in muscle function, and loss of bone mass due to aging or low physical activity. The adverse consequences associated with it, including fractures, falls, increase in risk of insulin resistance and metabolic syndrome, depression, and loss of independence and even the risk of death, necessitate interventions against it. The purpose of this article is to evaluate resistance training as a strategy to stimulate the skeletal response and prevention the reduction of muscle mass in order to combat osteosarcopenia.

Methods: Information sources were searched in google scholar, PubMed and Scopus databases since 2017 using related keywords; Resistance training, Osteosarcopenia, HI-RT, high-intensity resistance training. Finally, the most relevant articles were examined.

Results: The results of this article are about the improve body composition such as significant optimize in MetS Z-score, Waist circumference and HDL-C and moderate arterial blood pressure; significant increase in maximum strength, maximum hip and leg extensor strength, Habitual gait velocity, LBM and SMI; and remarkable decrease in Total body fat mass, abdominal body fat percentage and Areal BMD at the total hip ROI. On the other hand, a slight improvement in osteoporosis markers and Handgrip strength maintained was also seen. They all leads improve a person's functional capacity.

Conclusion: The research works mainly focuses on reducing the social and economic costs of osteosarcopenia by improving the physical condition of the elderly. Although current drug therapies for osteoporosis have no effect on muscle mass, there is strong evidence that resistance exercise, along with a balanced diet, can have a dual effect on bone and muscle, all of which help improve function. Since there are many interactions between muscle and bone, additional research can be done to better understand these interactions, which will help facilitate the development of new therapeutic agents.

Keywords: Resistance training, Osteosarcopenia, HI-RT, high-intensity resistance training

Evaluation of the efficacy of using allogenic natural killer cells in the treatment of children with recurrent neuroblastoma after hematopoietic stem cell transplantation (Research Paper)

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Introduction: Neuroblastoma is the most common tumor seen in the first year of life, and is the most frequent extra cranial solid tumor of childhood. It is derived from neural crest cell, and may arise in the adrenal medulla or anywhere along the paraspinal sympathetic ganglia. Typically, neuroblastoma presents with bone pain, anemia, or in babies, hepatomegaly. It has a median age at diagnosis of 18 months. Nearly two thirds of patients present at diagnosis with evidence of metastatic disease and have poor long term survival due to residual disease, despite aggressive approaches, including high dose multi agent chemotherapy, surgery, radiation therapy and autologous stem cell transplantation.

Methods: The large retrospective study recently conducted by the center for international blood and marrow transplant research (BMTR) analyzed allogenic SCT from matched donors.

Results: The case of neuroblastoma is not well understood. The great majority of cases are sporadic and unfamiliar. Familial neuroblastoma in some cases is caused by rare germline mutation in the anaplastic lymphoma kinase (ALK) gene. Germline mutations in the PHOX2B or KIF1B gene have been implicated in familial neuroblastoma, as well. Neuroblastoma is also a feature of neurofibromatosis type 1 and the beck with Weidman syndrome. MYCN oncogene amplification within the tumor is a common finding in neuroblastoma. Neuroblastoma has been linked to copy-number variation within the NBPF10 gene, which results in the 1q21.1 deletion syndrome or 1q21.1 duplication syndrome. Tumor cells express surface molecules that either switch off or switch on NK cell mediated cytotoxicity. HLA class I molecules on tumors negatively regulate NK cell function by engaging immunoreceptor tyrosine based inhibition motifs (ITIM) bearing receptors. That include the inhibitory killer in kire receptors (KIRS, CD158), highly polymorphic clonally distributed receptors able to distinguish among different HLA-A, B and C allotypes, and CD94, NKG2A heterodimers, specific for non-classical HLA-E. KIR and CD94, NKG2A are differently expressed in CD56 bright CD16 and CD56 dull CD16+ NK cell subsets, which represent sequential stage of maturation. Tumor cells switch on NK cell function by expressing at the cell surface non-MHC class I, danger molecules that are

recognized by and array of activating NK receptors. In vitro treatment of NB cells with IFV-γ induced up regulation of HLA class I expression although decreasing their susceptibility to autologous NK cells, this up regulation of HLA class I molecules could enhance t cell mediated recognition. Patients were considered missing KIR ligand if the lacked one or more HLA class I ligand for their inhibitory KIRs. In contrast, patients with all ligands present possessed all HLA class I ligands for their inhibitory KIR. 152 patients were missing KIR ligand were compare with patient who received chemotherapy without ASCT and those who received ASCT. Twenty-one patients suffered from grade 3 or 4 gastrointestinal side effect: mucositis in 81% and nausea in 50%. Seven patients exhibited elevated liver enzyme (serum glutamate oxaloacetate transaminase and glutamate pyruvate transaminase) 3 times the upper limit of normal (ULN) and/ or elevated bilirubin.

Conclusion: High risk patients who currently have a dismal prognosis could benefit from multidisciplinary therapeutic protocol that include novel NK cell based immunotherapeutic strategic. The latter will take advantage of our knowledge about the presence or absence of NB associated interacting with activating, inhibitory receptors expressed by NK cell.

Keywords: neuroblastoma, brain cancer, stem cell transplantation, NK therapy, hematopoietic.

Evaluation of the frequency of oxa-23, oxa-58 and ndm genes in clinical samples of Acinetobacter baumannii by Multiplex-PCR method
(Research Paper)

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Introduction: Acinetobacter baumannii is the cause of a wide range of nosocomial infections. Antibiotic resistance of this organism is a major challenge worldwide. The aim of this study was to identify oxa and ndm genes by multiplex-PCR and to determine the pattern of antibiotic resistance.

Methods: This study was performed in a period of 8 months by collecting 25 bacterial plate isolates. Antibiotic susceptibility testing was performed on Müller Hinton agar medium by disk diffusion method. MPprimer software was used to design the primers. After data collection, the level of significance was assessed at $P<0.05$ using SPSS 22.

Results: Except for gentamicin, cefpime, ciprofloxacin and tobramycin, there is a significant relationship between resistance pattern and sensitivity. All Acinetobacter baumannii isolates were sensitive to ceftazidime. Also, 20% of the isolates were resistant to imipenem, which are considered carbapenem-resistant isolates of Acinetobacter baumannii. Of the 25 isolates studied, 5 isolates (20%) had oxa58 gene, 5 isolates (20%) had oxa23 gene and three isolates (12%) had ndm gene.

Conclusion: The results showed a high widespread of antibiotic resistance among Acinetobacter baumannii isolates, which emphasizes the need to develop programs in the control and treatment of this powerful pathogen. Also, the frequency of beta-lactamase-producing isolates in hospital isolates has been growing, which indicates the need for more attention of health centers in prescribing drugs.

Keywords: Acinetobacter baumannii, Antibiotic resistance, Multiplex-PCR, Nosocomial infection.

Evaluation of the rational use of meropenem: A retrospective study in southern Iran (Research Paper)

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Introduction: Inappropriate use of antibiotics results in the emergence of antimicrobial resistance. This study aimed to evaluate the appropriate use of meropenem in terms of initial indication and requiring renal dose adjustment in Shahid Beheshti Hospital, Shiraz, Iran.

Methods: This retrospective observational study was carried out in Shiraz from April 2018 to March 2019. A total of 159 patients of all age groups who received at least one dose of meropenem were included. Required data were obtained through paper-based and electronic medical records. The analysis was performed using descriptive-analytical methods.

Results: Based on the results, meropenem was mostly prescribed for the age range of 60-79 years (32.7%), followed by the age group of 80-99 years (31.4%). The initiation of meropenem therapy was inappropriate in 20.7% of patients. The most frequent indication for meropenem utilization was pneumonia (23.8%), followed by complicated skin and soft tissue infections, and sepsis. (16.3% and 15.0% respectively). Regarding hospital wards, the highest proportion of meropenem was prescribed in internal medicine wards. Most prescriptions (97.5%) were initiated empirically and only 2.5 % were based on culture results. Out of the 84 culture and sensitivity tests, only 12 (14.2%) results confirmed the susceptibility to meropenem. 36 of 84 (42.8%) specimens for microbiological testing were obtained prior to commencing any antimicrobial therapy. The most predominant isolated microorganism derived from cultures was Escherichia coli, followed by Staphylococcus aureus, and Acinetobacter baumannii. Dose adjustment due to renal function impairment was required for 54 patients. Despite that, only 20 (37.0%) of patients received adjusted doses.

Conclusion: The rate of inappropriateness in the study, especially regarding dose adjustment and the number of requests for culture and susceptibility tests, highlights the necessity of implementing new strategies to enhance the rational use of broad-spectrum antimicrobial agents.

Keywords: Inappropriate use, Meropenem, Indication, Carbapenem, antimicrobial resistance

Evaluation of the stability of the immune receptor FLAGELLIN SENSITIVE-2 (Research Paper)

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Introduction: In innate immunity, the immune receptor FLAGELLIN SENSITIVE-2 is regarded as the best model to study the functional properties of other receptors. FLS2 is involved in Mitogen-activated protein kinase signaling pathways which have a crucial role in innate immunity. FLS2 is essential in the perception of flagellin. Furthermore, FLS2 is directed for degradation by the bacterial ubiquitin ligase AvrPtoB. Considering the importance of the FLS2 receptor, it is needed to the stability of this protein.

Methods: The Isoelectric pH of FLS2 was measured to evaluate protein stability. In addition, aliphatic index and GC percentage were also measured. The calculated instability index for the studied proteins showed that the proteins whose instability index is less than 40 are stable, otherwise they will be unstable. Therefore the FLS2 protein is regarded as one of the stable proteins. Proteins with a very high aliphatic index (above 100) may be stable in a very high- temperature range. Average total hydropathy (GRAVY) indicates the protein hydrophobicity index. If the GRAVY calculated for a protein is negative, it means that the protein is non-polar, and if it is positive, it is considered polar. The solubility of polar proteins is higher than the solubility of non-polar proteins in solvents. Against the special solvents of each protein, non-polar proteins accumulate in the middle and polar proteins accumulate in the outer part. Non-polar proteins can be used as targets to transfer the drug to the desired point, by adding a specific signal to the protein to transfer to the desired part and placing the target substance (drug) in the protein, this design is done.

Results: Our results showed that the instability index for FLS2 protein is less than 33.53. Because the aliphatic index of the studied protein is high than 100 (106.31), this protein is very stable against heat and can maintain its tertiary structure at high temperatures. Moreover, the percentage of GC (percentage of guanine and cytosine in the study sequence) was 46.6%. GC content analysis showed that genes with high GC content were more resistant to heat than genes with lower GC content. GRAVY calculated for FLS2 protein is negative (-0.016) and indicates its non-polarity.

Conclusion: The results showed that FLS2 protein is almost one of the stable proteins and non-polar proteins. The results that are investigated in this study, help researchers to better understand the FLS2 receptor and other immune receptors in detail.

Keywords: protein stability, FLS2, receptor,, Isoelectric point, Aliphatic chains, Relative volume of protein

Evaluation the Effect of different concentrations at48hour Mercaptopurine (6-MP) on Expression Changes of CPEB2 in Jurkat E6.1 cell line (Research Paper)

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Introduction: In acute lymphoblastic leukemia (ALL), early lymphoid pioneer cells multiply and take the place of healthy hematopoietic cells in the bone marrow. A purine analog called mercaptopurine (6-MP) is used to treat autoimmune disorders and leukemia. It has both immunosuppressive and anticancer properties. The cytoplasmic polyadenylation element binding protein (CPEB), an mRNA-binding protein that controls cytoplasmic polyadenylation of mRNA as a trans factor in oogenesis and spermatogenesis, is very similar to the protein that this gene encodes. Studies on a related mouse gene suggested that this protein may have a role in transcriptionally inactive haploid spermatids. This investigation looked at how 6-mp altered the acute lymphoblastic leukemia Jurkat E6.1 cell line's expression of CPEB2.

Methods: 6-MP was prepared at dosages of 5 and 10 µM in this investigation. The Jurkat E6.1 (T-ALL) cell after cell passage was bought from the Pasteur Institute of Iran at the passage and treated by 6-MP for 48 hours at the indicated concentrations. The expression variations of CPEB2 and the housekeeping GAPDH gene were then assessed by Real-Time PCR, and the results of Real-Time PCR were analyzed by Rest 2002 Software. Next, RNA extraction and cDNA synthesis were carried out.

Results: According to our research, the expression of CPEB2 was significantly decreased after 48 hours of treatment with 6-mp at 5 µM compared to non-6-mp samples and GAPDH. According to the findings, a concentration of 5 M at 48 h was the best dose and time. At 48 hours, the expressions of CPEB2 at 5 and 10 µM dosages were 0.787 and 1.811, respectively (p-value < 0.001).

Conclusion: It may be inferred from the analysis of CPEB2 expression variations after treatment with 6-MP that a concentration of 5 µM was successful in suppressing CPEB2 expression. The findings revealed that the most potent concentration of the medication, 5µM 6-MP, caused a further drop in the expression of CPEB2. Over 48 hours, 6-mp had a good impact on the CPEB2 oncogene reduction process. At some of the concentrations examined, this reduction in expressions was statistically significant. Decreased gene expression at the concentration of 5µM demonstrated that the effect of the drug was dependent on concentration and with increasing dose of the drug; a decreasing gene expression was evident. The result suggests that 6-MP has a high potential for controlling and treating cancers.

Keywords: Acute Lymphoblastic Leukemia, CPEB2, GAPDH, Mercaptopurine 6-MP

Evaluation the Effect of Methotrexate on Expression Changes of LncRNA CPEB2 in Jurkat E6.1 cell line (Research Paper)

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Introduction: In acute lymphoblastic leukemia (ALL), early lymphoid pioneer cells multiply and take the place of healthy hematopoietic cells in the bone marrow. A purine analog called methotrexate is used to treat autoimmune disorders and leukemia. It has both immunosuppressive and anticancer properties. By boosting adenosine release, activating adenosine receptor A2a, and preventing the conversion of BH2 to BH4 in leukemia, methotrexate suppresses the activation of nuclear factor B (NF-B). This study set out to investigate the effects of methotrexate on the expression of the LncRNA CPEB2 in the acute lymphoblastic leukemia Jurkat E6.1 cell line.

Methods: In this study, methotrexate was prepared at 1and 10μM doses. After cell passage, the Jurkat E6.1 (T-ALL) was purchased from Pasteur Institute of Iran at the passage I was then treated with methotrexate at 48h with indicated concentrations. Then RNA extraction and cDNA synthesis were done and the expression changes of CPEB2 and the Housekeeping GAPDH gene were evaluated by Real-Time PCR. Finally, the results of Real- Time PCR were analyzed by Rest 2002 Software.

Results: our findings discovered that after 48 hours of treatment with methotrexate at 1μM, the expression of LncRNA CPEB2 was considerably lower than in non-methotrexate samples and compared with GAPDH. Conforming to the results, it has been found that a concentration of 1μM at 48h was the optimal dose and time. The expressions of LncRNA CPEB2 at the doses of 1 and 10μM at 48h were 0.721 and 1.521 respectively ($P<0.001$).

Conclusion: It may be inferred from the findings of the investigation into how the expression of CPEB2 changed while it was being treated with methotrexate that the concentration of 1μM was successful in suppressing CPEB2 expression. The findings revealed that methotrexate, at a

concentration of 1 μM, which is the drug's maximum potency, caused a further drop in CPEB2 expression. For 48 hours, methotrexate significantly slowed down the expression of the CPEB2 oncogene, and at some of the investigated concentrations, this effect was statistically significant. Decreased gene expression at the concentration of 1μM demonstrated that the effect of the drug was dependent on concentration and with increasing dose of the drug; a decreasing gene expression was evident. The result suggests that methotrexate has a high potential for controlling and treating cancers.

Keywords: Acute Lymphoblastic Leukemia, LncRNA CPEB2, GAPDH, methotrexate

Events life in parents children with ADHD (Review)

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Introduction: The purpose of this study was to established whether there was any relationship between diagnosis of ADHD and various problematic life events in parents of children monitored with a diagnosis of ADHA.

Methods: Two hundred forty nine parents of children followed up with a diagnosis of ADHA and one hundred forty six healthy controls with no diagnosis of ADHD in their children or themselves were included. DSM diagnostic criteria were used in diagnostic evaluation. Diagnostic criteria recommended for DSMV and ADHD symptom assessment scales Wender Utah rating scale.adult attention Deficit Hyperactivity disorder self-report scale were also used. Problematic life events were recorded on a data form prepared by the authors.

Results: Parents meeting a diagnosis of ADHD experienced nearly all problematic life events at a higher level compared to parents not meeting that diagnosis and to the healthy controls.

Conclusion: Parents of children diagnosis with ADHD are exposed to a high, lifelong level of ADHD associated life events. These parents should be evaluated in terms of diagnosis of ADHD.

Keywords: ADHD children parents

Evidence of an association between the embB gene and ethambutol resistance in Mycobacterium tuberculosis patients by multiplex allele-specific polymerase chain reaction (MAS-PCR) in Ardabil, Iran

(Research Paper)

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Introduction: Tuberculosis (TB) is an extremely infectious sickness due to Mycobacterium tuberculosis (M. tuberculosis) which is life-threatening. Recently, it was found that one of the most important factors for the rapid spread of TB is the development of resistance to valuable anti-TB drugs. Various drugs such as isoniazid (INH), rifampicin (RIF), streptomycin (SM), pyrazinamide (PZA), and ethambutol (EMB) are used to treat TB. improper use of these drugs leads to resistance. Ethambutol (EMB) is one of the first-line drug regimens for pulmonary tuberculosis therapy, and resistance to this drug is increasingly reported in many parts of the world. It should not be used alone but can be prescribed in combination with at least one other antituberculosis agent such as isoniazid. EMB is effective against strains of M. tuberculosis, but not so much against viruses, fungi, or other bacteria. Mutation in embB is the main mechanism of resistance. The purpose of this study is to investigate the relationship between the mutation in embB gene and ethambutol resistance in M. tuberculosis using the MAS-PCR method.

Methods: As part of a cross-sectional study, 63 infected sputum and bronchoalveolar lavage samples (BAL) were collected from patients referred to the Ardabil Provincial Health Center for TB between July 2016 and June 2020. The boiling method was used for whole DNA extraction from clinical samples as described previously. MAS-PCR method was employed for detection of mutations embB which confer resistance to ethambutol.

Results: In the present study, 34 out of 63 samples (53.96%.) harbored a mutation in embB gene which mediated resistance to ethambutol.

Conclusion: In this study, high mutation rates leading to resistance to EMB were observed. EMB-resistant MTB were common, especially those with an embB mutation. Tracking embB mutation among EMB-resistant isolates would be diagnostically and epidemiologically valuable. According to the results, "

MAS-PCR can not only be used as a simple and rapid method for detecting EMB resistance in M. tuberculosis strains but also provides accurate and reliable results in less time than other methods. Regular monitoring of drug resistance and expansion of drug resistance testing facilities is imperative to prevent the transmission of drug-resistant TB in the community and also, provide primarily valuable data in administrating suitable drugs for combating tuberculosis.

Keywords: Ethambutol (EMB), Mycobacterium tuberculosis, MAS-PCR, Drug resistance, Mutations

Examination of microRNAs related to oral cancer (Research Paper)

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Introduction: One of the top 10 most prevalent malignancies in the world is oral cancer which has a poor prognosis, a delayed clinical diagnosis, no known biomarkers for the illness, and expensive treatment options. Because each patient presents the treating doctors with a different set of issues, the care of oral cancer is a multidisciplinary endeavor that affects both survival and quality of life. This research aims to examine the potential impact of microRNA on gene expression.

Methods: The GEO2R software in the GEO dataset was used to analyze the study of the expression of genes related to all types of cancer on the dataset GSE31056. The DAVID database's most differentially expressed genes were examined to determine which gene was most responsible for the occurrence of oral cancer. Additionally, the miRWalk database was used to find the microRNAs linked to this gene. Identification of the microRNAs influencing oral cancer was made possible by the Human microRNA Disease Database (HMDD).

Results: The plasminogen activator, urokinase (PLAU) gene was shown to be the most beneficial gene in treating oral cancer, according to the findings. Regarding the miRWalk database's identification of hsa-let-7e-5p and hsa-let-7b-5p as PLAU-related microRNAs. Additionally, it was found by using the HMDD database that hsa-let-7b may be a microRNA involved in the development of oral cancer by miRNA-induced gene upregulation.

Conclusion: Understanding the mechanisms affecting the target gene's expression may allow us to alter the course of the disease, and identifying the implicated microRNAs as markers may assist in disease management. On the function of microRNAs related to the PLAU gene, more thorough research is required.

Keywords: oral, cancer, non-coding RNA, Bioinformatics, Database

Examining the advantages and disadvantages of using vaccines (Review)

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Introduction: This article examines the pros and cons of using vaccines and the side effects of using vaccines

Methods: The method of conducting this research is descriptive and analytical, and it is practical in terms of execution.

Results: A vaccine is a biological product that is specific against a microbial disease. Vaccines involve the killing or weakening of viruses or bacteria or the antigenic proteins derived from them. They are prescribed to prevent, cure or treat infectious diseases. The first time the vaccine was discovered by Edward Jenner, an English doctor, its real use is called immunology. Different vaccines have different methods of use, most are injectable, such as the Corona vaccine, and some are oral, such as the polio vaccine. Vaccines exist for diseases such as influenza, tetanus, chickenpox, shingles, HPV, measles, mumps, rubella and corona, but it has not yet been possible to produce vaccines for all diseases such as HIV. This article examines the effect of vaccines on different types of diseases, the advantages and disadvantages of using vaccines, and the side effects of using vaccines.

Conclusion: The use of vaccines can help in the treatment or prevention of disease, but it also has disadvantages. Vaccines can have side effects. Another disadvantage of vaccines is that each vaccine is produced specifically for a disease. In case of an outbreak of a disease, it must be Another vaccine should be produced and other vaccines will not be effective from the moment of implementation

Keywords: vaccine-Antigenetic-HIV-HPV

Examining the consequences of the corona virus disease on children aged 2 to 9 years (Review)

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Introduction: The corona virus was first introduced to the world at the end of 2019 in the city of Wuhan, China, as an agent that attacks the respiratory system was introduced. Since the outbreak of the pandemic that the World Health Organization announced in March 2020; Governments implemented policies to reduce the spread of the virus and protect citizens. In most countries, physical distancing measures and stay-at-home requirements created unprecedented restrictions on the activities of all people. Direct or indirect exposure to pandemic diseases and their consequences causes psychological and physical problems.

Methods: In this narrative review article, published articles from PubMed, science direct, SID, magiran, CINAHL and Iran medex, Scopus, ProQuest Elsevier indexes were searched from the beginning of the corona disease outbreak in 2019 to 2021. The search was done using the keywords child parents, mental, physical, activity and COVID-19 and all related articles were studied and reviewed.

Results: In this study, among the related articles, 50 articles that had common goals and also had a suitable sample size were reviewed and reported. The findings of a study showed that 10% of the patients who received clinical counseling and the patients who were hospitalized had high levels of stress, anxiety and depression. In other studies, the level of behavioral problems and hyperactivity (35.12%) of 2-3-year-old children has shown a higher increase than mental problems (14.11%). The findings of another study showed that at this age, having quality sleep, which is between 10 and 13 hours a day, is appropriate in the current situation, and they sleep later at night and wake up later in the morning; He has also reported a decrease in their half-day sleep. In terms of comparing the activities before and after the outbreak of Corona, no difference has been seen in the case of having houses with playground facilities (the presence of green spaces).

Conclusion: The results showed that children are at risk of the consequences of the quarantine resulting from the corona pandemic and there is a need for educational planners and community therapy to plan

programs, classes and online workshops to prevent the physical and psychological consequences of children.

Keywords: Corona virus, child, physical activity, mental health, parents

Examining the importance of the prevalence of HPV virus in the development of ovarian, uterine and cervical cancer (Review)

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Introduction: Cancers of the female genital tract are one of the most important causes of their death in the world. In this model of cancers, like other malignancies, prevention as well as timely treatment reduces mortality. However, the survival rate in people with severe metastasis is only 20%. Ovarian cancer (Oca) ranks first with 41.2%, and endometrial and cervical cancers rank second and third among gynecological cancers, respectively. The purpose of this review is the importance of the HPV virus on malignancies of the female reproductive system, especially in the areas of the cervix and ovaries. HPV is a small virus with double-stranded DNA and belongs to the Papillomaviridae family. Usually, infection with this virus does not lead to symptoms, but genital warts are observed in some types of it. If no action is taken to treat the human papilloma virus, the cells in the cervix grow abnormally and turn into cancer cells.

Methods: Cancers of the female genital tract are one of the most important causes of their death in the world. In this model of cancers, like other malignancies, prevention as well as timely treatment reduces mortality. However, the survival rate in people with severe metastasis is only 20%. Ovarian cancer (Oca) ranks first with 41.2%, and endometrial and cervical cancers rank second and third among gynecological cancers, respectively. The purpose of this review is the importance of the HPV virus on malignancies of the female reproductive system, especially in the areas of the cervix and ovaries. HPV is a small virus with double-stranded DNA and belongs to the Papillomaviridae family. Usually, infection with this virus does not lead to symptoms, but genital warts are observed in some types of it. If no action is taken to treat the human papilloma virus, the cells in the cervix grow abnormally and turn into cancer cells.

Results: In studies conducted on cancer tissue samples, it has been shown that almost 70% of these cancers are related to HPV infection. Evidence shows that the prevalence of HPV in people with genital cancer is increasing. More than 100 types of human papillomavirus (HPV) are known. According to studies conducted on cervical carcinoma tissue cases, it has been determined that HPV16 is more prominent than other HPV types with a prevalence of 63% in North America and 46% in Asia. In fact, persistent infection with high-risk HPV and integration of the virus genome with the host genome is the cause of malignancy. Also, the constant expression of viral oncoproteins E6 and E7 is necessary to maintain the growth of cells in this area. Genital tract

cancer is associated with HPV's affinity and affinity for certain squamous cells in the cervical epithelium or the vulnerability of cubical epithelial cells and potential embryonic stem cells, which are considered as target cells for HPV infection. The mechanisms by which HPV affects the upper genital tract are unclear. Anatomically, the fallopian tubes and endometrium are the continuation of the endocervical, and for this reason, infection may develop from this route. In addition, sperm cells may transmit HPV. Therefore, they act as a virus carrier during endocervical passage. Molecular methods such as PCR can be used for early and definitive diagnosis of HPV virus. First, DNA must be extracted from the paraffin blocks, then a PCR test is performed using MY09/MY11 primers, and the PCR product is placed in the electrophoresis machine, and finally the L1 gene belonging to the human papilloma virus (HPV) is determined. Compliance with personal and social health tips can have a significant impact on preventing HPV infection. Microbial infection, genetic predisposition and lifestyle may also play a role in the higher incidence of HPV in some areas. It should be noted that in addition to HPV, other microorganisms in the bacterial field such as Mycoplasma genitalium, Chlamydia trachomatis and Neisseria gonorrhea are also known worldwide as a risk factor for genital cancer.

Conclusion: To date, there have been achievements related to HPV infection and cancers of the female genital tract, which include anti-HPV vaccines and a variety of interferon drugs. But these methods have not been effective enough in the field of treatment and we still need prophylactic vaccines that can target more strains of this virus. Due to the widespread and threatening nature of this disease for women's health, the production of HPV vaccine is increasing in the world. It should be noted that scientists are trying to make vaccines with new formulations that can completely destroy this virus.

Keywords: Human papillomavirus, Ovarian and cervical cancer, female reproductive system

Examining the pattern of bacterial isolates obtained from urinary infection in Imam Khomeini Hospital in Shirvan city in 2021 (Research Paper)

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Introduction: Urinary tract infections are one of the major causes of complications and co-morbidities in patients with underlying diseases and constitute most of the reasons for going to the hospital worldwide. Sufficient knowledge of factors related to urinary tract infections can easily control the disease.Studies conducted in different communities show that gram-negative bacilli are the most common etiologic agents of urinary tract infections, and among them, Escherichia coli accounts for more than 80% of urinary tract infections. Considering the importance of urinary infections in this study, the prevalence rate and factors involved in causing urinary infections in Shirvan Imam Khomeini Hospital in 2021 were evaluated.

Methods: Urine samples were cultured in the laboratory of Imam Khomeini Hospital and the isolates isolated in positive cases were determined as uropathogens using microbiological and biochemical tests, including culture in blood agar media, mechanical and gram staining, test Citrate, urea test, bile squaline test, TSI environment, SIM test, 5.6% salt tolerance test, PYR test were performed.

Results: In 2021, a total of 5150 cases of urine culture were performed, of which 73 cases (4.7%) were positive. Among the positive cases, 65.7% were Escherichia coli, 20.55% Klebsiella species, 5.48% Pseudomonas aeruginosa, 2.73% Proteus mirabilis, 2.73% Streptococcus, 1.36% Staphylococcus saprophyticus and 1.36% Enterobacter.

Conclusion: According to the results, it is clear that the total number of positive cases of urine culture is reduced compared to previous studies, and among the positive cases, Escherichia coli is considered as the first cause of urinary infections by a large difference. The relatively low percentage of cases of Staphylococcus saprophyticus indicates a significant change in the causes of urinary infections from members of Gram-positive bacteria to Enterobacteriaceae.

Keywords: Urinary tract infection, enteric pathogens, prevalence rate

Examining The Receptors Involved In The Growth Of Cancer Cells And Their Effect On Cancer Treatment (Review)

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Introduction: The genetic and epigenetic changes that cause cancer enable cells to overproliferate and evade mechanisms that would otherwise regulate their survival and migration. Numerous of these alterations correspond to signaling pathways that regulate cell growth and division, cell death, cell fate, and cell motility. They can be understood in the context of wider signaling network distortions that fuel the progression of cancer, such as alterations in the tumor microenvironment, angiogenesis, and inflammation. Hyperactivation of these signaling pathways can result from mutations that turn cellular proto-oncogenes into oncogenes, whereas the inactivation of tumor suppressors eliminates important negative regulators of signaling. A closer look at the PI3K-Akt and Ras-ERK signaling pathways demonstrate how these changes dysregulate signaling in cancer and result in many of the defining traits of tumor cells. The aim of this study was to examine the receptors involved in the growth of cancer cells and their effect on cancer treatment.

Methods: The current study, which looked through academic databases like Google Scholar, Science Direct, Springer, and PubMed, Examines the receptors involved in the growth of cancer cells and their effect on cancer treatment.

Results: Results revealed that cancer cells exhibit a variety of distinctive traits. These are caused by cellular signal transduction dysregulation brought on by the genetic and epigenetic modifications that fuel cancer. This has an impact on not only the cancer cells themselves but also a larger signaling network that includes blood vessels, the immune system, the ECM, and other cells. In fact, systemic effects are ultimate what cause cancer patients to die because metastatic cancer is a disease that disrupts signaling throughout the affected person. Cancer therapies have been significantly impacted by pharmacological and antibody-based inhibitors that target signaling proteins downstream from these or proteins altered in malignancies. For instance, nonreceptor tyrosine kinase (NTK) Abl and receptor tyrosine kinase (RTK) ErbB2 inhibitors significantly lower patient mortality in chronic myelogenous leukemia and breast cancer, respectively. However, the incidence of recurrence is high due to the emergence of drug resistance. Other inhibitors, such as those that target B-Raf, EGFR, and the kinase ALK, generate substantial decreases in tumor volume and lengthen survival in patients with melanoma and non-small-cell lung carcinomas.

Conclusion: Due to the redundant pathways that regulate cell proliferation and survival, crosstalk between pathways, and feedback inhibitory mechanisms that result in pathway reactivation, the complexity of the cancer signaling network poses a significant obstacle to efforts to produce such anticancer treatments. There is the reason for optimism that methods based on targeting them will be effective because pathways like Ras-ERK and Akt-PI3K signaling regulate a wide range of characteristics of cancer cells, and because parts of these pathways, or upstream receptors, are frequently mutated in a number of cancers. However, there are a number of considerations that limit the effectiveness of medicines that target these pathways. For instance, adaptive responses to driver mutation inhibition involve rewiring of signaling pathways, and this is frequently the result of either the loss of feedback inhibition or the stimulation of stress pathways. Furthermore, despite the targeted pathways' blockage, elements from the tumor microenvironment may promote other pathways that keep cells viable. As an alternative, drug-resistant variants of the targeted protein or mutations in other pathways that get around the dependence on the targeted pathway may be selected for in some rare tumor cells, and epigenetic or stochastic changes in the state of tumor cells can also activate intrinsic resistance pathways.

Keywords: receptors, cancer cells, drug-resistant, epigenetic

Examining the receptors involved in the growth of cancer cells in cancer (Review)

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1. Msc of Molecular Genetic Department of Genetics, Zanjan Branch, Islamic Azad University, Zanjan, Iran.

Introduction: Many distinguishing traits are present in cancer cells. These are caused by cellular signal transduction dysregulation brought on by the genetic and epigenetic modifications that fuel cancer. This has an impact on not only the cancer cells themselves but also a larger signaling network that includes blood vessels, the immune system, the ECM, and other cells. In fact, systemic effects are ultimate what causes individuals to die from cancer, and metastatic cancer can be thought of as a systemic disease that affects signaling throughout the affected person. Examining the receptors involved in the development of cancer cells was the goal of this review study.

Methods: This review study has written about Examining the receptors involved in the growth of cancer cells in cancer from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: The study's findings were evident Cancer treatments have greatly benefited from pharmacological and antibody-based inhibitors that target signaling proteins downstream from these or proteins altered in malignancies. For instance, nonreceptor tyrosine kinase (NTK) Abl and receptor tyrosine kinase (RTK) ErbB2 inhibitors significantly lower patient mortality in chronic myelogenous leukemia and breast cancer, respectively. However, the incidence of recurrence is high due to the emergence of drug resistance. Other inhibitors, such as those that target B-Raf, EGFR, and the kinase ALK, generate substantial decreases in tumor volume and lengthen survival in patients with melanoma and nonsmall-cell lung carcinomas Due to the redundant pathways that regulate cell proliferation and survival, crosstalk between pathways, and feedback inhibitory mechanisms that result in pathway reactivation, the complexity of the cancer signaling network poses a significant obstacle for efforts to produce such anticancer treatments. There is the reason for optimism that methods based on targeting them will be effective because pathways like Ras-ERK and Akt-PI3K signaling regulate a wide range of characteristics of cancer cells, and because parts of these pathways, or upstream receptors, are frequently mutated in a number of cancers. However, there are a number of considerations that limit the effectiveness of medicines that target these pathways. Rewiring of signaling pathways, for instance, is connected to adaptive responses to driver mutation inhibition, and this is frequently caused by either a loss of feedback inhibition or an increase of stress pathways. In addition, elements from the tumor

microenvironment may promote other pathways that continue to support cell survival even when the targeted pathways are inhibited. Alternately, rare tumor cells may be selected if they have drug-resistant forms of the targeted protein or mutations in other pathways that avoid dependence on the targeted route. Additionally, epigenetic or stochastic changes in the state of tumor cells may trigger intrinsic resistance pathways.

Conclusion: The degree of intratumoral genetic variability makes things more difficult. This is much more prevalent than previously thought, according to recent findings derived from the sequencing of individual patient tumors' single cells and various tumor areas. Only 45% of mutations were discovered over the entire tumor in one study of kidney cancers. Single biopsies might not be enough to individually tailor a patient's treatment because of this heterogeneity, which also strongly influences intratumoral variance in susceptibility to medications that target signaling proteins altered in cancer.

Keywords: cancer cells, receptors, mutations, signaling pathway

Examining the relationship between health literacy and female students of Islamic Azad University, Bandar Abbas branch (Research Paper)

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Introduction: Health literacy is the level of a person's capacity to acquire, interpret, and understand basic information and health services that are necessary for making appropriate decisions. Also, nutritional behaviors are among health-related issues that are multi-causal and have an important impact on health. The present study was conducted with the aim of determining the relationship between health literacy and nutrition of female students of Islamic Azad University, Bandar Abbas branch.

Methods: The present research was descriptive and analytical and was conducted on 300 female students of Islamic Azad University, Bandar Abbas branch in 2019. Sampling was done by the available method and the study tool included a researcher-made, multifaceted questionnaire. Finally, after collecting the questionnaires using SPSS-23 software and with the help of descriptive and analytical tests and linear regression tests, the data were analyzed and reported.

Results: The mean and standard deviation of the health literacy score was (46.67±07.16). In this study, 16.7%, 8.27%, and 5.55% of people had inadequate health literacy, borderline health literacy, and adequate health literacy, respectively. Based on the results of one-way analysis of variance, there was a significant relationship between health literacy and education level. The results showed that there is a positive and significant relationship between health literacy and people's self-care behavior.

Conclusion: According to the findings of the study, increasing the level of health literacy can improve people's nutritional behaviors. Therefore, in educational activities, special attention should be paid to the level of health literacy of people.

Keywords: Health literacy, nutrition, female students

Examining the unit cost of inpatient which admitted with covid-19 in Tabriz (Research Paper)

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Introduction: covid-19 is a highly contagious viral disease caused by the acute respiratory syndrome of Corona 2 virus, which has had catastrophic effects on the world's demographics. This disease has placed a significant burden on the Iranian health care system.

Methods: This study is a descriptive study that was performed retrospectively and information was collected cross-sectional over a period of one year and examined the unit cost of patients with corona in two scenarios .Also, the costing approach of this study is a top-down method.

Results: The study showed that patients with covid-19 who were hospitalized in the internal wards of covid-19's daily hospitalization cost is 15,152,154 Rials and the average length of stay of each patient is 5 days and finally the unit cost of each patient is 75,760,770 Rials. Patients who are hospitalized in the intensive care unit are average and each day of hospitalization of these patients is 23,478,657 Rials and each patient is an average of 8 days of hospitalization, so the unit cost per patient was 187,829,254 Rials

Conclusion: The cost of treating patients with corona is a significant cost and has had a great economic burden on the Iranian health care system, so that appropriate policies are needed to reduce waste of resources.

Keywords: covid-19-inpatient -hospitalization-unit cost-cost analysis

Exosomes Derived from Bone Marrow Mesenchymal Stem Cells attenuate cytokine storm and ARDS in COVID-19 patients. (Review)

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Introduction: COVID19 pandemic is still one of the most important concerns of health care systems around the world due to the occurrence of life-threatening pneumonia. In severe cases, COVID-19 disease is associated with excessive immune response called cytokine storm. Cytokine storm is a potentially fatal condition associated with excessive activation of immune cells and production of inflammatory cytokines and chemical mediators. The cytokine storm induced by COVID-19 is associated with the severity of COVID-19 and progression to ARDS. ARDS is associated with acute and diffuse inflammatory damage of the alveolar-capillary barrier and increased vascular permeability and decreased lung compliance, leading to pulmonary fibrosis and hypoxemia. Inflammasomes are one of the most important components of innate immune response that strongly promote inflammation. Inflammasomes play a key role in the pathogenesis of many inflammatory diseases. inflammasome Activation is probably the cause of severe cytokine storm, leading to ARDS and multi organ failure. current treatments of ARDS including the use of an interleukin-6 antagonist drug called Toslizumab associates with side effects including sepsis, opportunistic infections such as mucormycosis, severe neutropenia, elevated liver enzymes, and coagulation disorders. Due to the limited effective treatment options and the significant side effects of current treatments for ARDS patients, more effective treatment strategies are needed to suppress the cytokine storm and restore fibrotic lung tissue. Bone marrow-derived mesenchymal stem cell exosomes (MSC-E) are a complex combination of signaling nano-vesicles exosomes and are novel, multi-targeted, next-generation biologic agents that contain chemokines, growth factors, mRNA, and microRNA with anti-inflammatory, regenerative, and immunomodulatory functions and could be the key to suppress the cytokine storm and improve antiviral defenses in COVID-19. In this study, we

aim to investigate the role of MSC-Es in suppressing cytokine storm and preventing the progression of ARDS in COVID-19 patients.

Methods: Our search was performed in PubMed, SCOPUS, Science direct, EBSCO, ProQuest for published literature until September, 2022 by keywords including COVID-19, exosome, cytokine release syndrome and acute respiratory distress syndrome. The extracted papers were studied and based on defined inclusion criteria, 12 articles from all obtained studies were selected in the current study.

Results: Several preclinical studies show favorable therapeutic effects of MSC-E administered intravenously in animal models of acute lung injury (ALI), ARDS, asthma, and other inflammatory diseases. The analysis of clinical findings indicates a decrease in alveolar inflammation, increase in lung edema clearance, repair of epithelial membranes, and decrease in other consequences of cytokine storm. Recently, several studies have focused on animal models of ARDS and ALI induced by LPS to understand the mechanism of action of MSC-derived exosomes in reversing fibrosis, ARDS, and acute lung injury. A study has shown that MSC-Es can reverse ALI through downregulation of nuclear erythroid factor 2 (NrF-2) and antioxidant response element (ARE), leading to ALI treatment. In another study, a positive association between the activation of the NF-κB pathway and the stimulation of the nuclear factor Kappa-B kinase subunit Beta (IKKβ) was reported. This study showed that MSC-E decreases IKKβ and its ubiquitination, thus inhibiting NF-κB and Hedgehog pathways, that both play a key role in epithelial-mesenchymal transition process and lung fibrosis. Also, treatment with MSC-E showed a significant decrease in IFNγ, TNFα, IL-6, and the oxygen saturation level improved significantly after 72 hours of treatment. few clinical studies have reported the safety and efficacy of exosomes derived from allogeneic bone marrow mesenchymal stem cells in the treatment of severe cases of COVID-19. Improvement of clinical status and the absolute number of neutrophils and lymphopenia with an increase in the mean number of CD3+, CD4+ and CD8+ lymphocytes were reported.

Conclusion: The results show that stem cell-derived exosomes are a promising therapeutic candidate for severe COVID-19 due to their immunogenicity, capacity to restore oxygen, reduce cytokine storm, restore immunity and repairing lung tissue in patients with lung fibrosis and are promising candidates for the treatment of severe cases of COVID-19.

Keywords: COVID-19, exosome, cytokine release syndrome, acute respiratory distress syndrome

Exploitation of two selected immunogenic proteins, OmpA and BauA, for protection against Acinetobacter baumannii infection (Research Paper)

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Introduction: Acinetobacter baumannii is a hospital opportunistic pathogen, which is a gram-negative and non-flagellated bacillus, which is considered as a common nosocomial infection with high mortality that mostly causes sepsis and meningitis. And infection of the urinary tract. Reproduction and persistence of A. baumannii in eukaryotes based on iron uptake functions including siderophore biosynthesis. Iron transfer into the cytosol is mediated by specific membrane receptors that detect iron-siderophore complexes. The expression of this Acinetobactin-mediated iron uptake system is critical for the intracellular growth of A. baumannii. OmpA is the most abundant membrane protein gram-negative bacteria and is also the major protein of bacterial pathogenesis. The production of new monoclonal antibodies against outer membrane protein A (OmpA) could be considered as a potential tool to improve the treatment of A. baumannii infections. A. baumannii is usually resistant to beta-lactams, aminoglycosides, rifampin, and fluoroquinolones. This bacterium has led to the use of new therapies such as vaccines. No vaccine is known for this bacterium, but it is still worth considering. In this study, we used two separately selected and recombinant proteins, OmpA and BauA, as vaccine candidates to evaluate immunogenicity against A. baumannii in a mouse model.

Methods: Based on a pre-designed primer from Shahed University Bank, BauA and OmpA gene fragments were extracted from the bacterial genome PCR and the clones simulated in pet28 were expressed in Escherichia coli BL21(DE3). The product was analyzed by SDS-PAGE method and purified by the Ni_NTA affinity chromatography method. These proteins were injected into BALB/c mice separately and in combination. The titer of IgG-specific antibody produced against each group was determined after experiment using the indirect ELISA method. Bacterial proteins were then identified by IgG immunoblotting.

Results: OmpA and BauA were already reported to raise antibodies against these proteins. The same results were obtained. The combination of the two antigens led to significant protection against A. baumannii in comparison to the single antigens.

Conclusion: Administration of the combined antigens triggers better protection than single antigens.

Keywords: Acinetobacter baumannii, Antigen, Antibody, Vaccine, OmpA, BauA

Exploring the HSA/DNA binding behavior of p-Synephrine, a naturally occurring phenyl ethanol amine with anti-adipogenic activity: multi spectroscopic and molecular dynamics approaches (Research Paper)

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Introduction: In traditional Chinese medicine, the Citrus aurantium plant is widely exerted for various problems such as indigestion, diarrhea, and respiratory problems. It contains multiple active ingredients such as p-Synephrine (SN), a phenyl-ethanolamine that is believed to exert lipolytic and thermogenic activity through the induction of beige adipocyte differentiation (1). SN has some structural similarities to ephedrine which was prohibited by the FDA in 2004 due to its association with cases of seizure and heart attack. However, according to many peer-reviewed studies, despite the similarities to ephedrine, SN consumption in typical doses results in no cardiovascular effects (2, 3). Nonetheless, this study aimed to provide a comprehensive and complete profile of the biomolecular interactions of SN to human serum albumin (HSA) and calf thymus DNA (ct-DNA) using a detail-oriented approach through a combination of different biophysical methods and molecular docking.

Methods: A wealth of information has been produced through a combination of the following protocols: fluorescence spectroscopy, Resonance Light Scattering (RLS), and viscometry measurements. The molecular docking method was employed to investigate the exact binding site of ligands in interaction with HSA and ctDNA.

Results: The emission spectra of HSA in the presence and absence of SN are demonstrated in Fig. 1. Obviously, in the presence of SN, the fluorescence intensity of HSA has been dramatically reduced and slightly blue-shifted towards lower wavelengths. Fig. 2 illustrates the RLS spectra of the HSA-SN complex. At first glance, it is observable that upon the addition of SN to the HSA solution, the RLS intensity increased. Meanwhile, the gradual addition of ct-DNA to SN solution induced an obvious quenching in the SN-DNA spectra. Moreover, the addition of various concentrations of SN to the ct-DNA solution resulted in a negligible change in the relative viscosity. Docking results indicate the positioning of SN in the Sudlow site I which is located in subdomain IIA of HSA. While the docking outcomes of the ct-DNA-SN complex show the propensity of SN towards the grooves of the ct-DNA.

Conclusion: The ability of SN to reversibly interact with HSA has been manifested through the occurrence of quenching in the emission spectra (Fig. 1). This interaction occurs spontaneously and consequently changes the conformation of the protein (4). In accordance with RLS data (Fig. 2), the interaction between SN and HSA has led to the formation of a new complex that is larger in size and shape. As confirmed by molecular docking, SN is able to attach to Arg 257, Arg 218, and His 242. This strong interaction with HSA is facilitated through hydrogen bonds and ionic interactions. As revealed by fluorescence data, SN is clearly amenable to forming a complex with ct-DNA and changing its conformation. The relative viscosity of ct-DNA remained almost unaffected as various concentrations of SN is added to the solution which further suggests the tendency of SN to interact with the grooves of ct-DNA (5). The docking results of the DNA-SN complex confirm the previous findings. This method has also revealed the ability of SN to bind to ct-DNA through hydrogen bonds and H-pi interaction.

Keywords: p-Synephrine, HSA, DNA, Fluorescence spectroscopy, molecular docking,

expression analysis of INHBA mRNA in colorectal cancer and Integrated analysis of ceRNA network (Research Paper)

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Introduction: Colorectal cancer (CRC) is one of the most common cancers in the world. Multiple factors and bio-processes are associated with tumorigenesis and metastasis of CRC [1]. Competitive endogenous RNAs (ceRNAs) theory has revealed a new mechanism of interaction between RNAs (mRNAs, miRNAs, and lncRNAs) that is used to find the involved genes. In this study, we used microarrays to detail gene expression and target novel biomarkers for diagnosis and curing CRC.

Methods: Our study aimed to define the potential biomarkers in CRC via the analysis of a competitive endogenous RNA (ceRNA) network. Therefore, bioinformatics analysis targets novel biomarkers for diagnosis and curing CRC. First, NCBI Gene Expression Omnibus (GEO) was selected to get the desired GSE (GSE 25071), and therefore the gene expression profile was analyzed by GEO2R to search out differentially expressed genes (DEGs) in CRC tissue compared to controls, so the gene was selected for further studies. The most significant gene (|logFC| > 3 and p value< 0.05) were selected and Then was taken to miRWalk 3.0 [2] to find miRNA. We searched for our target miRNA in LncBace v.3 [2], and CASC19 was selected as a suitable lncRNA. Ultimately, the pathways that the gene was involved in were analyzed and studied to find that role in Cancer.

Results: Based on the microarray analysis that was carried out, INHBA had selected as significantly up-regulated mRNA (|logFC|=5/07 and adj p-value = 3.33E-10), and based on miRWalk interaction analysis mir-21-3p had a significant strong interaction with mRNA (Score: 1, Energy: -24.1) and by using Kegg database pathways were examined individually [3]. INHBA is involved in Cytokine- cytokine receptor interaction and TGF-beta signaling pathways and signaling pathways regulating pluripotency of stem cells. In addition, mir-21-3p correlated with the most remarkable prognostic values of CRC patients [4], and this miRNA has RNA interaction with, CASC19 lncRNA.

Conclusion: Contemplating the above paragraphs, it is concluded that INHBA with mir-21-3p and its CeRNAs (competing endogenous RNAs) CASC19 act as a biological network with an important role in CRC. the mentioned lncRNA CASC19 expression is associated with tumor size, lymph

node metastasis, and distant metastasis, suggesting high CASC19 expression may promote CRC metastasis [5]. the participation of INHBA in a CeRNA network, as well as the signaling pathway, demonstrated the possibility of INHBA being a reliable biomarker for diagnostic and prognostic goals.

Keywords: colorectal cancer, mir-21-3p, INHBA, Biomarker

Expression of Bioinformatically Candidate miRNAs including, miR-205-5p, and target gene (HER3/SMAD4/PTEN), Targeting PI3K/AKT Pathway in Triple-Negative Breast Cancer (Research Paper)

Shadi Tanhadokht,[1,*]

1.

Introduction: Triple-negative breast cancer (TNBC) is an invasive and lethal form of breast cancer. PI3K pathway, which often activated in TNBC patients, can be a target of miRNAs. The purpose of this study was bioinformatic prediction of miRNAs targeting the key genes of this pathway and evaluation of the expression of them and their targets in TNBC.

Methods: We predicted miRNAs targeting PIK3CA and AKT1 genes using bioinformatics tools. Extraction of total RNA, synthesis of cDNA and quantitative real-time polymerase chain reaction were performed from 22 TNBC samples and normal adjacent tissues of breast

Results: Our results demonstrated that miR-205-5p were predicted to target HER3, SMAD4, PTEN and three of mRNAs in PI3K/AKT signaling pathway, respectively and were down-regulated while their target mRNAs were up regulated in clinical samples and cell lines. The analysis of the receiver operating characteristic curve was done for the evaluation of the diagnostic value of predicted miRNAs in TNBC patients

Conclusion: The findings of our studies showed that Mir-205-5p expression is associated with direct and indirect effects on its target genes (PTEN, SMAD4, HER3) in the tissue of breast cancer patients compared to controlling expression reduction or expression silencing , and leads to the activation of the signaling pathway towards cancer. It is likely that by modulating the HER3 gene, Mir 205 will also be regulated.

Keywords: Triple Negative Breast Cancer; MicroRNA; HER3; PTEN; SMAD4 ؛Bioinformatics

Expression of Epidermal Growth Factor Receptor by Odontogenic Cysts: A comparative Study of Dentigerous Cyst and Odontogenic Keratocyst (Research Paper)

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3.

Introduction: Compare with Dentigerous cyst, Odontogenic Keratocyst is one of exclusive developmental cyst with unique clinical and histopathologic features. Considering the determining role of epidermal growth factor receptor (EGFR) in cell proliferation and survival, and the controversial results of previous studies regarding the expression of this marker by the odontogenic cysts, this study aimed to compare the expression of EGFR marker by Dentigerous cyst (DC) and odontogenic Keratocyst (OKC) as two lesions with more common neoplastic transformation.

Methods: In this experimental study, 49 specimens (23 DCs and 26 OKCs) were evaluated. Immunohistochemical staining was performed using EGFR antibody. Evaluation of EGFR expression was made regarding to Tie-JUN Li et al. So, The location of EGFR expression in the epithelial cells (Basal layers, Suprabasal & basal , All layeres) were assessed through histopathologic sections.. Data were analyzed using the Mann-Whitney test, t-test and chi-square test.

Results: In The present Study, of 49 evaluated cases, the mean percentage of EGFR expression was 58.20±17.97% in the 23 DC and 78.05±19.27% in the 26 OKC specimens. The EGFR expression of OKC was significantly higher than DC (P=0.001). However, the Mann-Whitney test showed no significant difference regarding EGFR score (P=0.144). The chi-square test revealed no significant difference in expression of EGFR in the basal layer, basal and suprabasal layers and all layers (P=0.524).

Conclusion: The expression of EGFR marker in OKC was significantly higher than in DC, which may justify the progressive growth potential of OKC.

Keywords: Dentigerous cyst, Odontogenic Keratocyst, Odontogenic cyst

Expression of SARS-CoV-2 receptor binding domain (RBD) in prokaryotic system (Research Paper)

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Introduction: The receptor binding domain (RBD) is a part of the SARS-CoV-2 S protein, which binds to the host receptor and facilitates viral entry. RBD expressed in eukaryotic cells cannot meet the high expression yield and cost requirements for therapeutics and vaccines. There have been numerous studies suggesting that the RBD expressed by E. coli may induce protective immunity. Furthermore, RBD expressed in E. coli has been used for worldwide research purposes as a cost-effective antigen. In this study, we expressed RBD in the E. coli BL21 strain and evaluated the purified protein by SDS page and ELISA.

Methods: The plasmid and the sequence coding for RBD were treated with restriction enzymes. The RBD fragment was ligated into pET28a (+) using T4 DNA ligase. Then the expression construct was transformed into E. coli BL21, cultured in LB media, and induced with isopropyl b-D-1-thiogalactoside. A 15% SDS-PAGE was used to analyze the expression. For purification, the cells were lysed by sonication and recombinant RBD was purified by the NiNTA column. Finally, the recombinant RBD was refolded by the gradual elimination of urea by dialysis. The quality of purified RBD was assessed by SDS-PAGE analysis and ELISA.

Results: To produce a large amount of antigen for the biopanning process, the DNA sequence of the RBD protein of SARS-CoV-2 spike protein was synthesized and cloned into the PET-28a vector. Results of PCR analysis and DNA sequencing confirmed the recombinant PET-28a sequence at the appropriate size of ~ 4000 bp as shown in supplementary data 1. The recombinant protein was expressed in E. coli strain BL21, purified by NINTA column, and refolded by dialysis. The SDS-PAGE results showed 95% purification of the RBD protein. To ensure the accurate antigenicity and function of the RBD protein an ELISA test on pooled COVID-19 serum

samples was performed and the results revealed a high binding affinity of the serum antibodies to the RBD protein.

Conclusion: In conclusion, we expressed high yields of SARS-CoV-2 receptor binding domain protein in E. coli strain BL21. Our results indicate that expressed RBD is functional and can induce immune responses.

Keywords: Receptor binding domain (RBD), protein expression, E. coli BL21, COVID-19, SARS-CoV-2.

Eye redness, myalgia and diarrhea in elderly following COVID-19 infection (Research Paper)

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Introduction: In humans, viruses cause respiratory infections that are usually mild, including the common cold, or sometimes it can be fatal. The outbreak of coronavirus disease 2019 (COVID-19) occurred in Wuhan, China was more expansive than initially estimated, with cases now confirmed in several countries. Therefore, it is crucial to determine the clinical symptoms of COVID-19 in different age groups.

Methods: This study evaluated the presence of SARS-CoV-2 infection in 219 throat and nasal swab samples using Real-time PCR. All samples were collected from people with respiratory symptoms who went to the grand bazaar.

Results: Of 219 patients examined, 19 (8.6%) positive cases out of 219 for SARS-CoV-2 were found by using Real-time PCR. Among these 19 positive cases of SARS-CoV-2, 6 (2.7%) were under 5, 3 (1.3%) were between 5-18, 4 (1.8%) were between 18-50 and 6 (2.7%) were over 50 years old respectively. Most common symptoms in positive group was cough and despite other age groups, in patients over 50 years old, myalgia and diarrhea was common.

Conclusion: It seems that SARS-CoV-2 symptoms can vary in different age groups but unlike other age groups, in elderly, uncommon symptoms like eyes redness, myalgia and diarrhea seems is seen following COVID-19 infection.

Keywords: Respiratory Tract Infection, Diarrhea, Myalgia, COVID-19, Eye redness

Fabrication and evaluation of modified liposome with TPGS loaded with Doxorubicin and curcumin as an anticancer drug on MDA-MB231 cell line (Research Paper)

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Introduction: Vitamin E (tocopherol) is one of the fat-soluble vitamins and a strong antioxidant that increases the body's immunity level against various diseases such as Alzheimer's, diabetes, heart attacks, and all types of cancer. By being in the fat layer of the cell membrane and neutralizing free radicals, vitamin E prevents the destruction of the cell wall and plays a role as a pro-oxidant, a signal molecule, and regulator of gene expression, especially in the prevention of cancer and arteriosclerosis. Derivatization of vitamin E is very common to increase its stability in the water environment and increase its efficiency. D-α-tocopheryl polyethylene glycol 1000 succinate (TPGS) is one of the most common and widely used tocopherol derivatives, which, in addition to the properties of vitamin E, is widely used in the construction of drug delivery nanostructures. TPGS increases biocompatibility, drug solubility, and drug permeability in tissue and cell membrane. Also, TPGS can act as a powerful adjuvant to overcome multidrug resistance (MDR) in tumors, and for this reason, several nanomedicines based on TPGS have been developed. On the other hand, the use of natural compounds in improving the properties of chemotherapy drugs is of great interest. In the meantime, curcumin is a natural product that is of great interest due to its anti-cancer, anti-inflammatory, antioxidant, and antimicrobial properties. In this study, we used TPGS in the manufacture of liposomes and evaluated its effectiveness in increasing the effectiveness of curcumin and doxorubicin (DOX), which is a common chemotherapy drug, in inducing cell death in the MDA-MB-231 cell line in vitro.

Methods: In this study, DOX and curcumin will be loaded into the liposome made with TPGS and the efficiency of the resulting liposome in inducing cell death in the MDA-MB-231 cancer cell line compared to liposomes without TPGS will be evaluated in a case-control study in vitro.

Results: In the upcoming project, TPGS is loaded in liposomal structure and used for drug delivery against the MDA-MB-231 cancer cell line.

Conclusion: Our study successfully declares that TPGS loaded in Liposome nanocarrier with DOX and Curcomin coating had more anti-cancer effects than free TPGS. The present studies showed that Liposome nanosystems are suitable carriers for TPGS, compare to the free form.

Keywords: Cancer Therapy, Anticancer, Liposome

Factors related to the social health information needs of the families of students with cancer (Research Paper)

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Introduction: Continuous evaluation of parents' informational needs and related factors can increase the quality of child care. The purpose of this research was to determine the factors related to the information needs of families of children with cancer.

Methods: The current study was a descriptive-analytical cross-sectional study that was conducted on 300 families with children with cancer who referred to Peymaniye Hospital in Jahrom, who were included in the study as a purposeful and voluntary non-probability sampling. The information was collected by a researcher-made questionnaire with 48 items in 4 dimensions (access, presentation and exchange of relevant health information; provision of information about cancer by the treatment staff; health facilities and services and counseling; and social, economic and spiritual support) and collected and analyzed using SPSS software. The entry criteria included having at least one child with cancer in the family and the desire to participate in the research and the exit criteria, refusing to continue cooperation at any stage of the study.

Results: Parents' gender and child's age were related to the total score of the health information needs of the family of children with cancer and the second dimension of the four dimensions of these needs ($P<0.05$). Parents' gender, their level of education, the duration of the child's diagnosis, the type of cancer and the presence of a cancer patient in the second-degree family with the first dimension; Gender of parents and their level of education, place of residence, amount of income and age of the sick child are among the factors related to the third dimension; And the gender of the parents and their education, the amount of income and the age of the sick child had a significant relationship with the fourth dimension of the health information needs of the children's family ($P<0.05$).

Conclusion: Considering the relationship of some individual, background and socio-economic factors on the informational needs of the families of children with cancer, it is necessary for the health authorities to pay attention to these factors in order to provide and solve the aforementioned informational needs. Identifying the factors related to the health information needs of these families

can help the guardians of the health field to take measures to meet the health information needs of these patients and their families through face-to-face or non-face-to-face training, preparing pamphlets, brochures, Guide to do. Certainly, the optimal solution of such information needs will have a positive effect on the health of the sick child and the costs imposed on the family and the health system.

Keywords: social health, cancer

Familial vs. sporadic multiple sclerosis: VDR gene expression profile in an Iranian population (Research Paper)

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Introduction: Multiple sclerosis is an autoimmune inflammatory disease that affects the brain and spinal cord, causing the destruction of myelin and varying degrees of axonal degeneration. Many molecular mechanisms control the process of myelination in the nervous system. Alterations in each of these regulatory mechanisms lead to the impaired myelination. The Hippo signaling pathway is an important mediator of myelination in the nervous system and might contribute to the pathophysiology of MS.

Methods: This study examined via qPCR the RNA expression of YAP1, TAZ and CRB3 as the key effectors of the Hippo pathway and also, VDR in the peripheral blood of 72 MS patients including 35 sporadic and 37 familial MS patients; also, there were 74 healthy controls including 34 healthy first-degree relatives of the familial MS patients (HFR) and 40 healthy individuals without a family history of the disease (control).

Results: The results showed the increased expression of VDR in the sporadic group, as compared to other groups. There was also an increased expression of TAZ in the familial and HFR groups, as compared to the control group. The familial and sporadic patients displayed a significantly lower level of expression of YAP1 in comparison to the HFR group. The increased expression level in the sporadic patients and control group, as compared to the HFR group, was seen in CRB3, but there was no significant differential expression, as expected, in the familial group versus sporadic or HFR group. We also assessed different clinical parameters such as EDSS, onset age, family history of other autoimmune diseases and MRI characteristics of the patients. Our results showed a significant correlation between VDR

expression level and EDSS in the familial patients. Moreover, the effect of brain atrophy on the relative gene expressions was evaluated in the patient groups.

Conclusion: Overall, these findings suggest that Hippo pathway effectors and also, VDR gene, by controlling myelination, may play a potential role in the pathophysiology of the sporadic and familial forms of MS. Confirmation of different gene expression patterns in sporadic and familial MS groups in the future may have obvious implications for the personalization of therapies in the disease.

Keywords: Multiple Sclerosis; Family Research; Myelin; Real-Time PCR; Medical genetics

Fast-tracking of Staphylococcus epidermidis in the clinical sample in Isfahan city (Research Paper)

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Introduction: t is very important to use a fast and simple method in order to recognize Staphylococcus epidermidis isolates out of a broad range of bacteria. The appearance of resistance to beta-lactam antibiotics is one of the most usual resistance moods in Staphylococcus epidermidis.

Methods: In this study, 120 clinical samples were collected. The isolates were identified via common biochemical tests, and then the specific primers sesC were used to re-confirm Staphylococcus epidermidis isolates. After the identification of the genus and species of isolates, PCR and special primers were used to detect blaZ. The methicillin resistance was measured according to the agar screening procedure and then antibiotic susceptibility was measured by the disk diffusion method

Results: Out of 120 samples of nosocomial infections, 100 isolates of Staphylococcus epidermidis were identified by the phenotypic method. All of the isolates were confirmed by sesC PCR. from the 100 specimens, 80 (80%) samples in this study contained a blaZ gene. According to the agar screening method, 60% of isolates were resistant to methicillin. Staphylococcus epidermidis isolates were found to show the highest resistance to penicillin (93%), ceftriaxone (85%), amoxicillin (80%), cefocithin (65%), and the highest sensitivity to cephalexin (40%),cefazolin (39%).

Conclusion: The result of this study show increased resistance to beta-lactam antibiotics in Staphylococcus epidermidis isolates showing an earnest alarm to the healthcare system, thus it requires monitoring of antimicrobial pattern in Staphylococcus epidermidis to characterize a proper Staphylococcus epidermidis diet.

Keywords: Drug resistance-methicillin-resistant Staphylococcus epidermidis (MRSE)

Flaxseed biocoumpunds modified the TNF-α/IL6/SIRT1/NRF1/NPPA/FGF7 network in Myocardial infarction (Research Paper)

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Introduction: Cytokine storms and cytokine release syndrome (CRS) lead to cardiovascular disease. Phytochemicals and bioactive compounds of the herbals are vital sources of active agents and have potential approaches to preventing or therapy cardiovascular disease. Flaxseed contains phytochemicals, including secoisolariciresinol diglucoside, lignans, and linolenic acid (SAL), with anti-inflammatory and antioxidant activity.

Methods: Here, candidate hub genes, TNF-α, IL6, SIRT1, NRF1, NPPA, and FGF7, were selected based on in-silico analysis and artificial intelligence. Myocardial infarction (MI) was induced using H9c2 cardiac cells in hyperlipidemic and hyperglycemic conditions. RT-qPCR was conducted to evaluate the expression of genes.

Results: This study indicated that SAL compounds bound to the Il-6, SIRT1, and TNF-α as a druggable candidate protein based on the chemoinformatics analysis. This study indicated that the deregulation of TNF-α, IL6, SIRT1, NRF1, NPPA, and FGF7 networks in MI models and SAL compounds ameliorated the expression level of these genes. Furthermore, SAL compounds improved the function and myogenesis of H9c2 cardiac cells in hyperlipidemic and hyperglycemic conditions.

Conclusion: Moreover, our data indicated that phytochemicals obtained from flaxseed might have potential complementary treatment or preventive strategies for MI.

Keywords: cardiovascular diseases, Flaxseed, H9c2, chemoinformatic, hub genes

FMS-like receptor tyrosine kinase-3 Overexpression as a Potential Contributor to Development of Acute myeloid leukemia (Research Paper)

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Introduction: Acute myeloid leukemia (AML) is a cancer of the myeloid line of blood cells, characterized by the rapid growth of abnormal cells that build up in the bone marrow and blood and interfere with normal blood cell production. This study aimed to the analysis of relative expression of gene FMS-like receptor tyrosine kinase-3 (FLT3) in AML. FLT3 is a member of the class III RTK (receptor tyrosine kinase progenitor cells). Its expression in these cells means that FLT3 has an important role in the pathogenesis of AML. FLT3 mutations commonly co-occur with mutations such as cytogenetically normal AML and likely modulate prognostic impact. the prognostic impact of FLT3 mutation is still up for debate.

Methods: Gene expression data of AML patients (GSE114868) was obtained from the NCBI Gene Expression Omnibus (GEO) and a gene named FLT3 was selected for further study. Then FLT3 was analyzed by GEPIA2 to find differentially expressed genes. GEPIA2 database was used to support the possibility of a correlation between FLT3 and Acute myeloid leukemia, and it evaluated the correlation between the gene and patient survival. Through ENRICHR, KEGG, REACTOME databases, and Gene Cards, gene ontology information and biological pathway and Molecular function involvement were processed. miRNA SNP, dbSNP, SIFT, and UniProt were used to calculate the probability of each single nucleotide polymorphism (SNP) and Mutation based on the quality of the base assignments and the curves in the chromatogram files. Also, HOPE was used to analyze the impacts of point mutations on the structure and function carried out by a protein. STRING and miRWalk were utilized to find significant Protein and miRNA interactions with FLT3 mRNA in the 3'UTR region. Additionally, the selected miRNA was searched in LncRRIsearch and LncBase v.3 to find strong interactions with LncRNAs and construct a predictive ceRNA network.

Results: Based on analysis of the GEO dataset, The expression of FLT3 was shown increasingly (|logFC| = 6.71399118, adj. P value = 4.15E-40) in AML samples. Through ENRICHR, KEGG, and REACTOME pathways, FLT3 plays

a special role in Acute myeloid leukemia and it is a part of different molecular functions and biological processes such as lymphoid progenitor cell differentiation. Analysis of miRNA SNP, dbSNP, SIFT, and UniProt showed FLT3 mutations likely modulate prognostic impact. Based on String, the interaction of FLT3 has been shown with different proteins such as FLT3LG, GRB2, HSP90AA1, HRAS, NRAS, PTPN11, KRAS, PIK3R1, KITLG. Analysis of possible miRNA-mRNA interactions in miRNAWALK revealed hsa-miR-2115-5p (energy= -21.1) as a significant interactor to FLT3 mRNA. This miRNA was then searched in LncRRIsearch and LncBase v.3, and it had the strongest interactions with HELPAR (energy= -103.73), LINCO1215 (energy= -77.19), HCG18.

Conclusion: In conclusion, FMS-like receptor tyrosine kinase-3 (FLT3) is overexpressed in AML based on Analysis of different databases and forms a possible lncRNA and ceRNA network among hsa-miR-2115-5p, HELLPAR, LINCO1215, HCG18.

Keywords: Acute myeloid leukemia (AML), FMS-like receptor tyrosine kinase-3 (FLT3), Cancer, ceRNA

FoxP-dependent operant self-learning in Drosophila (Review)

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Introduction: The highly conserved FoxP family of transcription factors is involved in operant self-learning, a form of motor learning in different animals such as humans, zebra finches, and Drosophila. The FoxP genes mutant flies showed profound defects in operant self-learning, motor coordination, and performance of inborn behaviors.

Methods: The article is written based on recent results published on dFoxP.

Results: Palazzo and colleagues (2020) presented key data on the FoxP circuits associated with locomotion and object fixation in Drosophila using available lines and created lines by them. All three FoxP isoforms (FoxP-iA, FoxP-iB, and FoxP-iIR) are expressed in neurons, but not in glia and that not all neurons express all isoforms. These isoforms are expressed in, e.g., the protocerebral bridge, the fan shaped body, and in motorneurons, but not in the mushroom bodies. Furthermore, the expression of FoxP genes in the protocerebral bridge and motorneurons during development is required for the normal locomotion and landmark fixation in walking.

Conclusion: The results of flight simulator method demonstrated the significant impairment of dFoxP mutant flies in operant self-learning and habit formation. The alterations in brain structures as a result of mutation in dFoxP, can affect operant self-learning in Drosophila. Therefore, this conserved gene regulates operant self-learning and habit formation in flies.

Keywords: dFoxP, Drosophila, Habit, Operan self-learning

Frequency of bacteria isolated from blood cultures and compare antibiotic-probiotic resistance with silver nanoparticles (Research Paper)

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Introduction: Blood infections are very dangerous ones, especially if it is not treated properly, it can lead to high mortality. The purpose of this study is to investigate the frequency of separated bacteria from cultivated blood and to compare antibiotic-probiotic resistance pattern with silver nano-particles.

Methods: In this study, the bacteria in taken samples from patients are identified and The antimicrobial property of standandard Lactobacillus Acidophilus supernatant and silver nano-particles is investigated utilizing The Well Diffusion Agar method. The antibiogram test also is conducted for several antibiotics by applying the Disk Diffusion Agar method. In order to reduce the error, each test is repeated three times and diameter of non-growth zone and its antimicrobial ability is compared together.

Results: The results are analyzed by SPSS software, version 21 and P value <0.05 is considered meaningfully.From, the bacteria in taken samples from patients, four types of bacteria are identified; Staphylococcus aurous, Staphylococcus epidermidis, Klebsiella, Escherichia coli. Out of these bacteria, Escherichia coli get the maximum value of frequency and Staphylococcus epidermidis minimum. All of the identified bacteria have different reaction in relation to 10 types of antibiotics. Klebsiella shows the highest sensitivity toward novobiocin. The gram negative bacteria including Klebsiella and Escherichia resist to supernatant. Among the gram positive bacteria, Staphylococcus aurous shows the highest and Staphylococcus epidermidis the lowest diameter of non-growth zone to supernatant. For Staphylococcus aurous and Staphylococcus epidermidis, it shows MIC= 0.5 µl/ml , MIC=0.01 µl/ml to supernatant, respectively. Both bacteria do not have MBC. Klebsiella shows the maximum and Staphylococcus epidermidis the lowest sensitivity to silver nanoparciles. The value of MIC for Klebsiella, Escherichia coli, Staphylococcus aurous, Staphylococcus epidermidis are MIC= 0.12 µl/ml , MIC=0.6 µl/ml , MIC=0.6 µl/ml , MIC=0.12 µl/ml respectively and the amount of MBC for these bacteria are MBC= 0.25 µl/ml , MBC= 0.6 µl/ml , MBC=0.12 µl/ml , MBC=0.12 µl/ml respectively.

Conclusion: In this study Escherichia coli has the maximum frequency among the blood samples. This shows that these bacteria can be a common factor in blood infection. However, the most bacteria resist to antibiotics. So it needs to apply new methods to fight with infections. All gram positive bacteria in this study are sensitive to supernatant and the whole of bacteria are sensitive to silver nano-particles. These outcomes show the high anti-microbe potentiality in them.

Keywords: bacteremia, antibiotic resistance, probiotic, supernatant, Ag nanoparticle

Functional changes in miRNA due to Single Nucleotide Polymorphism in the rectal cancer (Review)

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Introduction: Rectal cancer is a disease in which malignant (cancer) cells form in the tissues of the rectum. Rectal cancer occurs when cells in the rectum mutate and grow out of control. The Rectum starts at the end of the final segment of your colon and ends when it reaches the short, narrow passage leading to the anus. In the current study, we have researched the reverse effect of a single nucleotide polymorphism (SPN: rs374284482) while converting C to T at the seed match of miR-1249-3p to 3'UTR sequence of ETHE1 gene. The ETHE1 gene is a member of the metallo-beta-lactamase family, which encodes iron-containing proteins. The ETHE1 gene located on chromosome 19.

Methods: For this purpose, GEO datasets showed the top 250 differentially expressed genes. The David database was used to cluster the gens and it revealed the involved genes in transcriptional misregulation pathway in cancer including ETHE1 gene. The miRNASNP-v3 database showed the relationship between studied miNA and SNP.

Results: The results showed that binding to the 3'UTR region of ETHE1, the miR-1249-3p blocks gene's expression, and acts as a tumour suppressor in rectal cancer. The occurrence of rs374284482 (C/T on chr22:45200977) in the seed match of miR-1249-3p (chr22:45200973-45200979) and ETHE1 (chr19:42506718-43506849), made the binding to be lost. It makes the gene not to be under the control of miRNA anymore and upregulation will occur.

Conclusion: Thus, our data suggest that rs374284482 is a disease-associated SNP since as a common polymorphism in miR-1249-3p affects the regulation of the ETHE1 gene and result in the genetic predisposition to rectal cancer. It is role in the tumorigenesis through somatic mutation Preliminary evidence suggests that these effects are mediated through target genes which expressions are affected by the SNP status.

Keywords: rectal cancer, ETHE1 gene, miR-1249-3p, rs374284482

Gene therapy for human colorectal CD44+ cancer stem cells(CSCs) using CRISPR/Cas9 system (Research Paper)

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Introduction: Colorectal CSCs have been therefore considered as a promising therapeutic target for colorectal cancer. The potential role of CRISPR/Cas9 in gene therapy has made it to become one of the hottest pots in cancer treatment. Different concepts of CRISPR/Cas9 mediated cancer therapy, including tumor related genes manipulating, tumor immunotherapy, tumor research modelling and anti-cancer drug resistance overcoming are established in various cancer types.

Methods: Geo dataset 100433 downloaded from Geo datasets. Genes are compared with logfc (fold change) for their expression in healthy and patients group and then sorted by their p-value. Also genes function and ontology are identified by DAVID database. Finally genes with most modification and related to critical pathway in immune system are selected and their best gRNAs(guide RNA) in CRISPR system are identified for editing by CHOPCHOP webtool.

Results: FOLR2 or folate receptor beta has hyperexpression among primary tumor patients. It plays an important roles in immune system and inflammatory response. The best gRNAs for this gene is identified through CHOPCHOP database.

Conclusion: Many experiences showed that immune genes play an important roles in cancer progression and metastasis, therefore they can be as a therapeutic target for CRISPR/Cas9 system and gene therapy.

Keywords: Colorectal cancer, CRISPR/Cas9, Gene therapy, gRNA

Generating 4T1 stable cell line that expresses EGFP and enhanced Firefly Luciferase for the cancer research study. (Research Paper)

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Introduction: most developments in cancer research have happened with the help of animal models. animal models give us hints that can reach us to a cure for cancer. despite all of those advantages animal models have limitations that can be misleading. First of all, the immune cells work differently in animal models such as mice than in the human so isolation and characteristic of immune cells that work against tumor is an important part. Secondly, a big problem in the use of animal models is how the tumor develops and spreads in the body. One solution to this challenge is Bioluminescence imaging which is high-throughput, cheap, and scalable. to answer those problems We have generated a 4T1 stable cell line that expresses enhanced firefly luciferase (fLuc+) and EGFP.

Methods: We have digested plex307-EGFP by BamHI that breaks upstream of the EGFP and then fLuc+-T2A has ligated into it. We have used plex307-fLuc+-T2A-EGFP, pspax, and pCAG-VSVG plasmids to produce lentiviruses that express EGFP and fLuc+. We transfected the 4T1 cell line with viruses and then do a selection by puromycine for two-week. finally, the single cell has been isolated from the pool by the limiting dilutions method.

Results: The fluc+ spectrum of the cell line confirms that the maximum emission of enhanced luciferase is 584nm. Also, EGPF expression has been confirmed by fluorescent microscopy.

Conclusion: The main purpose of present study is investigation of tumor developing in animal model

Keywords: 4t1, animal model, firefly luciferase, cancer, singel cell,

Generation of haploid spermatids on silk fibroin-Alg-laminin-based porous 3D scaffolds (Research Paper)

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Introduction: In vitro production of sperm is one of the most important options for fertility preservation in azoospermic men and prepubertal boys with cancer. Therefore, in this study, a biocompatible porous scaffold based on silk fibroin-Alg containing laminin was developed to differentiate mouse spermatogonia stem cells (SSCs).

Methods: After extraction and characterization of silk fibroin using SDS-PAGE analysis, stable porous 3D scaffolds were successfully prepared from combined solutions through a freeze-dried method. Then, structural and biological properties, biocompatibility, water absorption, degradability, and mechanical behavior of biomimetic scaffolds were characterized. Neonatal mice testicular cells were seeded on 3D scaffolds after confirmation of nature and their differentiation efficiency was evaluated using Real Time-PCR, flow cytometry, immunohistochemistry techniques, and H & E staining. The function of Leydig and Sertoli cells was also assessed using ELISA.

Results: Blend matrices showed uniform porous microstructure with interconnected network, which significantly maintained long-term weight and better mechanical properties than pure structures. The results of molecular analysis after 21 days of culture showed that the expression of differential markers (Acrosin, Scp3 and Prm1) in the 3D system containing laminin was significantly higher than other groups. The hormonal analysis confirmed the function of Leydig and Sertoli cells for the synthesis of testosterone and inhibin.

Conclusion: The usage of a 3D system containing laminin could lead to the differentiation of SSCs and the progression of meiosis to the stage of haploid spermatid that pave the way for new human infertility treatments in the future.

Keywords: Spermatogonia stem cells, Porous scaffold, Silk fibroin, Alg, Laminin

Genetic And Epigenetic Factors Associated with Varicocele (Review)

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Introduction: Varicocele is found in approximately 20% of adults and adolescents and in 19–41% of men seeking treatment for infertility. Most semen samples of patients with varicocele showed low sperm count, decreased motility, and morphological abnormalities. Infertility in patients with varicocele has a complex and multifactorial etiology, in which genetic alterations and environmental factors contributed to the disease progression, further reducing the spermatozoa quality and leading to infertility. The testicular damage has been attributed to increased scrotal temperatures and venous pressure, accumulation of toxic substances, hypoxia, hormonal dysfunction, autoimmunity, oxidative stress, and apoptosis. Here, I review the available literature regarding the genetic and epigenetic changes associated with varicocele.

Methods: A comprehensive literature search was carried out to assess genetic and epigenetic factors associated with varicocele. Google scholar data base and PubMed has been searched. Epidemiological studies, experimental studies, inquiries or editorials on the mentioned theme published from 2015 until 2022 were included. specific keywords including “varicocele”, “infertility” and “genetic and epigenetic” have been used.

Results: It has been suggested that patients with infertility and varicocele were observed to have significantly increased DNA-damaged sperm. Some studies in patients with varicoceles have reported an association between chromosomal abnormalities and microdeletions in the Y chromosome with the disease. The gametes of infertile men with altered sperm morphology and motility show high rates of chromosomal abnormalities, which originate mostly from meiotic errors. Abnormal meiotic segregation in spermatozoa of men with varicoceles has been reported. Mutations and gene polymorphisms are frequently observed in infertile men with varicocele. Several studies have demonstrated an association between varicocele and polymorphisms, including single-nucleotide polymorphisms (SNPs). Deletions in the mitochondrial DNA (mtDNA) of spermatozoa have been reported in men with varicocele. the expression of several miRNAs associated with oxidative stress in the spermatozoa of patients with varicocele has been evaluated in previous studies and reported reduced expression of miR-15a. miR-15a is also known to repress the expression of HSPA1B. The regulation of the HSPA1B by miR-15a may play an important protective role against cell stress throughout sperm maturation. Thus, these results help elucidate spermatic involvement in the pathology of varicocele.

Conclusion: Because of the multifactorial nature of varicocele, there are still no known biomarkers that could be identified in the early stages of the disease. Chromosomal disorders, mutations, polymorphisms, changes in gene expression, and epigenetic changes have all been reported to be associated with varicocele. Several studies are underway to unravel the genetic basis of this disease, as it is important to understand the origin and the aggravating factors to ensure appropriate guidance and intervention.

Keywords: Varicocele, Infertility, Epigenetic, Genetic.

Genetics and Molecular Mechanisms of Autism (alpha rhythm and power spectrum shape in children with ASD) (Review)

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Introduction: Early recognition of autism spectrum disorder (ASD) provides opportunities for early intervention and you can also achieve better development results. The use of infant electroencephalography (EEG) has shown promise in predicting the subsequent diagnosis of ASD and elucidating the neural mechanisms underlying the disorder. Given the high comorbidity of speech disorders, we and others hypothesized that language acquisition, including phonetic discrimination, is impaired in children subsequently diagnosed with ASD. Phonetic learning occurs rapidly in infancy, so the altered neural matrix in the first year of life may be a rapid and accurate indicator for the later diagnosis of autism. Autism spectrum disorder (ASD) is a severe neurodevelopmental disorder with core functions such as communication and social disturbance and stereotyped behavior (Chase et al., 2006). Currently, the incidence of ASD is increasing rapidly worldwide. Currently, the cause of ASD is unclear, and diagnosis is made primarily on the basis of subjective behavioral ratings and observational scales. Therefore, it is important to find objective indicators for a correct assessment.

Methods: As you have noticed just now, the junction action potentials recorded from the excitation electrode can be approximated very well by a Gaussian distribution. The standard interpretation of the Gaussian distribution is that it represents the result of a homogeneous process dependent on the parameters of the normal distribution. For example, the shape of the complex action potential of the sciatic nerve shows that very few neurons with high conduction velocities respond to the electrical activity represented by the first part of the complex action potential curve and neurons with very slow conduction velocities. . It is responsible for the electrical activity shown in the last part of the curve. The large-amplitude central portion of the complex action potential "peak" indicates that most neurons in the fixation nerve have conduction velocities between the two extremes, with most conduction velocities concentrated in the middle range, but fewer and more "extreme" ones. On the other hand, autism is associated with childhood seizures, but an association with TSC is not the only result. In 1981, Rijkkonen and Amnell studied 192 children with a diagnosis of (provoked) infantile seizures and found a prevalence of 12.5% according to established criteria. Using the same criteria, Hunt and Dennis (19) found that 58% of children with TSD and a history of childhood seizures had autism. Hunt and Shepherd suggested that the higher incidence of autism in TSC reflects a more fundamental relationship between the disorders. However, there appears to be a difference

in the autistic symptom profile of individuals with TSD compared to idiopathic autism.

Results: The identification of the TSC1 and TSC2 genes and the first characterization of protein products and their roles represents the significant advances in our understanding of TSC that have been achieved in the past decade. The different disease risks associated with TSC1 and TSC2 need to be clarified. Especially since prenatal diagnostic decisions can be based on them. The important functions of Hamatin and Tuberin seem to require the interaction of the two proteins, thus explaining the difference in TSC1 and TSC2 disease severity. Presumably, disease severity is actually determined by the rate of somatic mutations at the two loci. If this ratio is higher in his TSC2 site than his TSC1 site with TSC2, then he has a higher rate of second stroke and we predict he has more hamartomas and malformations with TSC2 than TSC1. These are all associated with Laplace's first and second error curves (based on Gaussian distribution)

Conclusion: These curves may have the same mean and the same variance. This is to be expected when they are all based on the same underlying process. The only difference is that the peak amplitude occurs when the same event is performed at three different "intensities". For example, for complex action potentials, alpha rhythm and power spectrum shape: different amplitudes may reflect more (or less) active neurons, better (or worse) recording technique, and so on.

Keywords: Gaussian distribution- autism- TSC- power spectrum shape- alpha rhythm

Genomic landscape of chronic lymphocytic leukemia (Review)

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Introduction: Chronic lymphocytic leukemia (CLL) is a B-cell neoplasm, defines as accumulation of apparently normal, mature CD5+, CD10 - , CD19+, CD20+, and CD23+ lymphocytes in the peripheral blood, bone marrow and lymphoid tissues. CLL accounts for 40% of adult leukemias, almost 70 years at diagnosis, and 1F:2M sex ratio. Family history is observed in 5–10% of CLL patients or other non-Hodgkin lymphoma which is the highest genetic susceptibility among hematologic neoplasms.

Methods: This study is a review of the genetic basis of Chronic lymphocytic leukemia, through assessing related articles using databases, ScienceDirect, PubMed and GoogleScholar.

Results: Cytogenetic: nearly 80% of patients have a recurrent chromosomal abnormality mainly, del (13q14.3), del (11q22.1)/ ATM, del (17p13.1)/ TP53), del (6q23.3)/ MYB, and +12. 50-60% of CLL patients have13q14 deletion that is the most common genetic defect. large deletions engage RB1gene with poor prognosis. Other recurrent copy number alternations also were reported: 1p, 1q23.2q23.3, 2p12p25.3, 3p21.31, 3q, 4p15.2p16.3, 6p25.3, 6p22.1, 6q, 7p, 7q, 8p21, 8q24.1, 9q13q21.11, 10q24, 11q22.3, 12, 14q24.1q32.3, 14q32 deletion, 15q15.1, 17q, 18p, and19. 14q24.1q32.33 deletion have been observer in 48% of patients. +2p is a recurrent abnormality in heterogeneous CLL populations. large scale studies identified chromothripsis in 4–5% of patients. Translocations, especially ones that not involve IGH, are rare in CLL. The t(14;19) (q32;q13) IGH/BCL3 is a recurrent translocation mostly found with trisomy 12. t(14;18)(q32;q21) results in IGH/BCL2 fusion . t(18;22)(q21;q11.2) BCL2/IGL and t(2;18)(p12;q21) IGK/BCL2 are observed as secondary aberrations in patients. Rarely MYC [t(8;14)(q24.1;q32) IGH/MYC t(2;8)(p12;q24.1) IGK/MYC and t(8;22)(q24.1;q11.2) MYC/IGL can be observed in CLL. translocations in 13q14 and 17p13 are unbalanced and deletions in the breakpoints were detected. Recently, a rare patient with trisomy 12 and t (14;18) was described. Considering the mutations of the IGHV gene (variable region of the immunoglobulin heavy chain) patients are classified in two molecular subtypes. mutated IGHV patients present an indolent CLL while, unmutated IGHV patients exhibit an aggressive form of CLL. Genome-wide association studies (GWAs) have recognized approximately 45 susceptibility loci for CLL mostly mapping to noncoding regions. Using next generation sequencing, 11 recurrent somatic copy number changes and 44 recurrent mutations in genes comprising, ATM,

SF3B1, NOTCH1, TP53, MYD88, DDX3X, CHD2, HIST1C1 (chromatin regulators), XPO1, RANBP2 (RNA export factors), RAS, MAP2K1, MAP2K3 (signal transducers), EGR2, IKZF3 (B-cell transcription factors), RPS15 (ribosomal proteins) and POT1 (telomere-associated proteins) were recognized. Down-regulation of PAX5 was shown via mutations of an enhancer found on 9p13. TP53, ATM, IGHV mutations and complex karyotype have an intensive poor prognosis. epigenetic profiling, exhibited differential DNA methylation between CLLs and controls. higher epigenetic heterogeneity observed in more aggressive CLL subgroups. Few epigenetic changes can be attributed as exactly CLL-specific alternations. Therefore, CLL patients classified in three epigenetic subgroups with a distinct clinical consequence: naive B-cell like, intermediate and memory B-cell like, With different IGHV mutational state. Non-coding RNAs 13q14 deletion includes LncRNA DLEU2, miR15-a/miR16-1 genes. These two microRNAs are essential in maintaining the balance of apoptosis of B lymphocytes. Besides, an alternative transcript in this locus raises cell cycle progression through cyclin D1 and angiotensin I converting enzyme 2. Other microRNAs involving in CLL encompass: miR-27b, miR-29a-c, miR-125b, miR-146a, miR-155, miR-202-3p, miR-150, miR-499, miR-574, miR-106a, and miR-9. As an example, miR-202-3p Promotes CLL progression and can be considered as a therapeutic target. High level of circRNA mc-COX2 is associated with CLL progression and prognosis. Various snoRNAs were recognized as potential biomarkers via assessment of the snoRNAs expression in CLL patients. SNORD116-23, SNORD116-29, SNORA36A SNORD94, SNORD116-1 were down-regulated in CLL. In patients, the SNORA31expression is associated with the expression of its host gene, (TPT1), which is a target of TP53.

Conclusion: CLL is heterogeneous clinically and genetically. Genetic analysis provides the basis of diagnosis, prognosis and treatment choices for the disease. Whole genome analysis revealed new CLL genomic drivers and molecular pathways that has encouraged scientists to fulfill new prognostic classifications and therapeutic targets. The major challenge in this area is how to apply our knowledge into clinical practice.

Keywords: Chronic lymphocytic leukemia, Cytogenetics, Next generation sequencing, Epigenetic, Non-coding RNAs

Genotypic comparison of Ornithobacterium rhinotracheale isolates from commercial chickens by using RAPD and MLST (Research Paper)

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Introduction: Ornithobacterium rhinotracheale (ORT) is a newly emerging respiratory bacterial pathogen that causes significant economic losses to the poultry industry. Previous studies in Iran showed high molecular and genetic similarity among ORT isolates by SDS-PAGE, ERIC-PCR and 16SrRNA gene sequencing during 1999-2009. The aim of this study was the genotyping of ORT isolates recovered from commercial chickens by using RAPD-PCR with OPG11 primer and multilocus sequence typing (MLST).

Methods: In total, 30 ORT isolates recovered from commercial chickens of Iran during 2000-2017 and confirmed by bacteriological, biochemical and PCR tests were used in this study. All 30 ORT isolates were subjected to RAPD-PCR with OPG11 primer. For MLST, 5 isolates were selected based on their RAPD patterns. Seven primer pairs were synthesized for amplification and sequenceing of seven housekeeping genes of adk, aroE, fumC, gdhA, mdh, pgi and pmi in MLST assay.

Results: In RAPD-PCR with OPG11 primer, 9 different genotypes were found. The DNA sequences of the distinct alleles of these seven loci of 5 ORT strains were compared with other alleles deposited in GenBank. Four out of 5 strains belonged to sequence type 9 (ST9) and one strain was found to be a new ST.

Conclusion: Based on the results of the present study, a new sequence type among ORT isolates of Iran was found that has not been previously reported

from elsewhere in the world. Further studies on more ORT isolates may help in identification of different sequence types and dominat ST in the country.

Keywords: Genotyping, MLST, Ornithobacterium rhinotracheale, Poultry, RAPD-PCR

Globozoospermia genetics and its association with egg fertilization (Review)

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Introduction: Today, fertility problems have become one of the major problems for young couples, so the study of genes involved in the emergence of abnormalities that lead to infertility in men and women is very important. globozoospermia is a severe sperm morphology abnormalities that lead to round head sperm. people with phenotype globozoospermia suffer from or completely lacking acrosome deficiency. due to the absence of acrosomic and round head sperm , the acrosomic reaction is impaired. to penetrate the sperm into the oocytes of the acrosomic enzymes, they begin to dissolve the plasma membrane, and the inner layer of the egg begins to liberate calcium granules and the The signaling cascade is launched. after the sperm penetrate the egg, the egg activation occurs.defects in each of these stages can lead to anomalies and infertility of the type of globozoospermia, and the article examines the genes involved in this process.

Methods: In this systematic review, the keywords of the globozoospermia, infertility, acrosome reaction, infertility treatment were found in Pubmed and Scholar Google and Scopus databases.

Results: Globozoospermia, including genes involved, can be mentioned Spata16, Pick1, GOPC, HRB, CSNK2A2 and DPY19L2. the mutation and removal in each of these genes can lead to globozoospermia. the expression of the Spaca1 gene is also reduced in globozoospermia. the expression level of the MRNA gene kifc1 was mainly observed in the testicles of patients with globozoospermia in the spermatide stage. the two SPATA16 and Pick1 genes play an important role in the Spermatogenesis process, as the Spata16 protein plays a role in organizing the Golgi and acrosomic granules organized in rounded and elongated spermatozoa. and Pick1 can adjust the transportation of the Golgi Network vesicles to the endoplasmic network. in

fact, Pick1 is involved in the transmission of vesicles from Golgi to the acrosome and collaborates with GOPC and CSNK2A2 in the construction of acrosome, although no globozoosperm man has been found to carry a mutation in the GOPC or CSNK2A2 gene, some of the cases of human globozoospermia are likely to be explained in these two genes. anyoploid levels, especially in chromosomes 1, 13, 15, 16, 21, XX and YY in sperm, are also significantly higher than a normal person.

Conclusion: Therefore, Spa16, Pick1, GOPC, HRB, CSNK2A2, KIFC1, Spaca1 and DPY19L2 genes are among the genes involved in the incidence of globozoospermia and aneuploid rate in chromosomes 1, 13, 15, 16, 21, XX and YY in sperm Patients with globozoospermia are also significantly higher than a normal person.

Keywords: Globozoospermia, Infertility, Acrosome Reaction

Graphene-based biosensor for specific detection of ovarian cancer cells (Review)

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Introduction: Ovarian cancer (OC) is nominated as one of the most aggressive gynecologic malignancies and is the main cause of gynecological malignancy-related mortality worldwide. So, developing an efficient early detection method for OC via a facile and low-cost approach is vital. Considering that graphene oxide has high biocompatibility, it is used as a promising new material at the forefront of material design for biomedical applications. Our goal in this study was to peruse the function of Graphene-based biosensors for specific detection of ovarian cancer cells.

Methods: For this research, existing articles in PubMed, Web of Science, Magiran, Sid, and Google Scholar databases that have been published till 2022 are systematically selected, and 16 articles are included in this study. This research is done in English considering the following keywords: Graphene-based biosensor, ovarian cancer, Cancer cells, and Graphene oxide.

Results: Due to the high water affinity and single-stranded DNA (ssDNA) sorption characteristics of GO, a GO-based qRT-PCR assay for the detection of miRNAs dependent on OC was designed and developed. In the GO-based qRT-PCR system, GO could significantly improve the sensitivity and specificity of the qRT-PCR assay by noncovalently interacting with primers and ssDNA and reducing the occurrence of non-specific amplification. Moreover, the detection of miRNAs associated with OC confirmed that GO-based qRT-PCR assay could differentiate benign ovarian tumors from OC.

Conclusion: Generally, findings provide robust evidence that surprisingly graphene-based flexible biosensors demonstrate highly sensitive and can be effectively used as a promising method for screening and improving the overall survival of patients with OC, but more studies are needed.

Keywords: biosensor, Ovarian Neoplasms, Neoplastic Stem Cells, Graphene oxide

Green synthesis of silver nanoparticles using aqueous extract of cassia fistula and evaluation of its healing potential in mice Model of Leishmaniasis (Research Paper)

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Introduction: Leishmaniasis is a serious problem that affects many people in the world. It causes significant morbidity and death in Asia, Africa, and the Americas, and there are serious side effects from the available therapies. Recent years have seen a rise in the use of biogenic silver nanoparticles and other nanoscale materials in medicine.

Methods: In this study, Cassia fistulaleaf extract was used to create silver nanoparticles (CF-AgNPs). Silver nanoparticles were synthesized after stirring for 24 hours in the dark. Fourier transform infrared spectroscopy, dynamic light scattering and zeta potential, UV-visible spectroscopy, and field emission scanning electron microscopy were used to examine the biosynthesized CF-AgNPs. In addition, the anti-leishmanial and antibacterial activities of biosynthesized CF-AgNPs alone and in combination with luteolin was tested. The L. major-infected BALB/c mice were treated with CF-AgNPs, luteolin (L), and CF-AgNPs/Lointments topically for 21 days in order to conduct the in vivo investigation.

Results: The color change of the reaction mixture to dark brown, absorption peak between 400-450 nm, and nano dimensions (70 nm) were the signs of the synthesis of CF-AgNPs. The results obtained from the toxicity test of nanoparticles on promastigotes of Leishmania major showed that nanoparticles were capable of killing the parasite at low concentrations. After 21 days of treatment of mice with ointments, histological evaluations were performed. In the negative control group, the number of inflammatory cells and amastigotes was much higher than in the group treated with CF-AgNPs/Lointment (p<0.05). On the other hand, the number of fibroblasts was significantly higher in the group treated with the CF-AgNPs/Lointment compared to other groups(p<0.05).The results showed that CF-

AgNPsointment alone had no significant difference in terms of the number of inflammatory cells, the number of amastigotes and fibroblasts compared to the negative control group(p>0.05).

Conclusion: Recent study has demonstrated that CF-AgNPs/L can act through multiple mechanisms against leishmania parasites and help wound healing process. Flavonoids are known to speed up epithelialization and enhance wound healing. On the basis of our results, CF-AgNPs/L can increase fibroblast function and reduce inflammatory cell infiltration and could be considered as therapeutic strategy for treatment of L. major.

Keywords: cassia fistula, Leishmaniasis, Silver nanoparticles, CF-AgNPs

Heat killed Saccharomyces boulardii improves the sperm viability of rats with cholestatic liver disease (Research Paper)

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Introduction: The nonpathogenic yeast Saccharomyces boulardii (S. boulardii) has beneficial effects on the human intestine, and thus has been prescribed as probiotics for the treatment of diarrhea. Several studies have demonstrated that this probiotic may interfere with cellular signaling pathways prevalent in a variety of inflammatory disorders, including liver fibrosis. Liver fibrosis is a chronic condition that is linked to a number of secondary conditions, including male reproductive failure. Due to safety concerns around the use of live probiotics, previous studies have demonstrated that alternatives to live probiotics, such as heat-killed bacteria or their fractions or purified components, have significant beneficial effects. The purpose of this study was to examine the protective effect of heat-killed S. boulardii against cholestasis-induced male reproductive failure.

Methods: Male Wistar rats were subjected to bile duct ligation to induce liver fibrosis. The study included 4 groups (n=8). The bile ducts of two groups were ligated while one group received heat-killed S. boulardii (BDL+ Heat killed S. boulardii) and the other received a vehicle (BDL). sham operated (Sham) and normal control (CN) either received vehicle. Using gastric gavage, heat-killed S. boulardii was administered one week prior to BDL and 3 weeks after BDL. At the end of the 28st day, blood samples were collected by heart puncture and sexual hormones including testosterone, LH, and FSH analyzed by ELISA method. In addition, the epididymis was isolated from the testis, and the concentration of sperm, as well as the percentage of live and abnormal sperm, were assessed. Furthermore, testicular tissue immediately frozen in RNA later and stored at -80 °C for assayed inflammatory genes expression such as TNF-α, IL-6, and IL-10.

Results: The level of sperm abnormality, LH and inflammatory genes such as TNF-α, IL-6 were significantly greater, while the level of sperm viability, sperm concentration and testosterone were significantly lower in the BDL group when compared to sham group ($p \leq 0.05$). In the BDL+ Heat killed S. boulardii the level of sperm viability was higher and IL-6 was lower than that in the BDL group ($p \leq 0.05$). Other sperm parameters, sexual hormones and TNF-α and IL-10 didn't significantly Changed Compared to BDL group ($P \geq 0.05$).

Conclusion: The results of this study showed that cholestasis has a negative effect on male factors that are linked to infertility. Exposure to chemicals at supraphysiologic concentrations results in cytotoxicity and testicular damage. Our findings suggest that heat-killed S. boulardii may be useful in the context of male infertility.

Keywords: Infertility; Saccharomyces boullardii; Liver fibrosis; Testis

Helicobacter pylori infection and multiple sclerosis: an updated meta-analysis (Review)

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Introduction: There is considerable controversy around the question as to whether Helicobacter pylori (H. pylori) infection has a protective or causative role in the development of multiple sclerosis (MS). This study evaluated published information to assess the association between H. pylori infection and MS.

Methods: We conducted a comprehensive systematic review of relevant observational studies in international databases. A random-effects model was used to calculate pooled odds ratio (OR) and 95% confidence interval (CI). I2 statistic was used to assess the between-study heterogeneity. Subgroup and meta-regression analyses were applied to identify the source of heterogeneity.

Results: In total, 22 studies (25 datasets) were eligible for the meta-analysis; 17 datasets had prevalence data and eight datasets had data on the mean titer of anti- H. pylori IgG. The pooled prevalence of H. pylori was 44.1% (908/2606) in the MS patients and 46.1% (1016/2200) in the controls, indicating a non-significant protective effect of H. pylori on MS (OR, 0.82; 95%CI, 0.58–1.17). In the subgroup analysis, studies that used ELISA yielded a significant protective association (OR, 0.59; 95%CI, 0.46–0.77), while a significant positive association (OR, 5.75; 95%CI, 2.40–13.76) was found in studies that used histological methods.

Conclusion: Our findings do not support the hypothesis that H. pylori infection represents a protective factor against the development of MS; however, the results varied depending on the diagnostic method(s). Further studies are needed utilizing accurate diagnostic methods to elucidate the association between active H. pylori infection and MS.

Keywords: Keywords: Multiple sclerosis, Helicobacter pylori, association, meta-analysis

Hemophagocytic Lymphohistiocytosis as the initial presentation of pediatric Acute Lymphoblastic Leukemia (Research Paper)

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Introduction: Hemophagocytic Lymphohistiocytosis (HLH) is a multisystem inflammatory syndrome that is rare and life-threatening. It causes immune dysregulation, prolonged hyper-inflammatory conditions, and cytokine storm. Acute lymphoblastic leukemia (ALL) is one of the malignancies which can have an initial presentation of HLH.

Methods: A case report study

Results: We presented a 7-year-old child who at first had manifestations of HLH based on pathology results and HLH-2004 criteria. She received chemotherapy treatment based on the HLH-2004 chemotherapy regime; after the chemotherapy treatment, she achieved complete remission and was successfully treated. About 48 weeks after starting chemotherapy, cervical lymphadenopathies and consistent fever were found. Based on the results of lymphadenopathy biopsy and bone marrow aspiration, the patient was diagnosed with precursor B-cell ALL.

Conclusion: We found that HLH could be the initial presentation of B-cell leukemia. It is essential to rule out B-cell leukemia in patients with secondary HLH.

Keywords: Hemophagocytic lymphohistiocytosis, Acute lymphoblastic leukemia, HLH, ALL

Hereditary anemia or thalassemia minor (Review)

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Introduction: Some people have a low level of hemoglobin in their blood, which is called anemia. There are various conditions, the most common of which occur when there is not enough hemoglobin because they do not get enough iron from food. Major is also a different type of deficiency. It is bloody. This is also due to not having enough hemoglobin, but it has nothing to do with iron intake from food. This is a hereditary blood disorder. Thalassemia is one of the types of blood disorders that occurs due to the decrease of a specific protein in the blood, namely hemoglobin. This protein helps to move oxygen in the body through its activity. If the amount of this important component in the blood reserve of our body decreases, the blood supply will be disturbed and as a result, symptoms such as lethargy, fatigue and paleness will appear. Its genes are always passed on from parents to children. But fortunately, most of the time this disorder is diagnosed during marriage and the birth of babies with this condition will be prevented. If a person is suffering from this disease, he will always have hemoglobins without one of the subunits, which is usually the beta subunit. As a result of this, the red blood cells will be smaller than normal and of course it should be said that this feature is recorded in the genetic code of the person. Therefore, if parents or one of them have this defective gene in their DNA, their child will suffer from anemia. It is only possible that there is a need to take folic acid supplements. But one important point is important in this disease and it will be related to the children of these people. These people should be careful not to marry someone who has this disorder like themselves. Because their child will suffer from the severe type of this anemia and will face dangerous complications and problems unlike the mild type. Of course, it should be said that in severe cases of minor anemia, symptoms such as facial bone deformity, reduced growth, abdominal swelling, depression and anxiety, and dark urine color were observed. Proper nutrition for people: First of all, we should know that a small amount of iron in food is always absorbed in the body of healthy people. But this is not the case in people with thalassemia! In fact, it should be said that the absorption of iron in the body of these patients is higher. Therefore, it is better to adjust the diet of these people in such a way that they get less iron from their diet. Calcium, vitamin D and folic acid prevent the absorption of iron in the body of these people. There are 2 types of iron in general, iron with iron and iron without iron. Non-dairy foods such as vegetables, yolks, eggs, beans, etc. are rich in iron, but some of this type of material is less. A person suffering from this type of anemia does not need to follow a basic and special diet unless prescribed by a doctor. Instead of vitamin C juices, use caffeinated substances due to less absorption of iron

and avoid vitamin A supplements and consume them after a meal rich in iron. Depending on the progress of the thalassemia disease, the type of treatment will also be different. For example, mild thalassemia, which is the most common type of thalassemia, will not need treatment. On the other hand, moderate thalassemia can be treated with blood transfusion But what requires a treatment process and couples are afraid of getting it is severe thalassemia. This type of thalassemia can be treated with the following treatments: Blood injection Iron chelate treatment bone marrow transplant surgery

Methods: by study and reviwe another articles

Results: It is a hereditary disease that often does not need treatment. In more severe cases, treatment is considered according to the doctor's order, and in rare cases, the symptoms show the need to have a diet.

Conclusion: Thalassemia is a Greek word derived from the two words thalasa meaning sea and blood meaning blood. It is not a single disease but includes a heterogeneous group of hereditary anemias. which is a disorder in the hemoglobin chain. It is manifested in two ways: minor and major, which are the most common genetic disorders and do not require special treatment, and are often shown as mild anemia in blood tests.

Keywords: anemia, genetic, hereditary, thalassemia, minor

high efficient green fluorescent protein (GFP) using novel molecular engineering approaches - beyond the biology (Review)

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Introduction: Green fluorescent proteins (GFPs) and GFP-like proteins from marine organisms, especially those from the jellyfish Aequorea victoria, called avGFP, have made significant contributions to cell biology. Because of their unique protein sequence, they have light-absorbing chromophores. avGFP attracted much attention after its cloning in 1992. Since then, many researchers have focused on identifying and improving fluorescent proteins with new qualities and enhanced properties for direct observation of dynamic processes in living cells and tissues. Molecular engineering of GFP as a powerful toolkit helps us to produce brighter fluorescent light at a specific wavelength or enhance photostability and photoactivation properties. Also, in some variants, chromophores form rapidly and Effectively. moreover, some engineered versions sense physiological signals within cells, like concentrations of free ions. actually, they act as biosensors.

Methods: In this review, we studied more than 40 articles from 1995 to 2022 from valid databases. clearly, we describe the structure and molecular characterization of GFP at first and then focus on the engineered versions, their novel properties, and developments.

Results: GFP as a popular protein molecule has been noticed in recent years and new desirable features have been added to it with various engineering methods. The evolution of cell biology was realized by using GFP as a reporter gene and monitoring the gene expression. In addition, other applications like using as intracellular markers, Subcellular localization, cell trafficking, biosensors, protein-protein interactions and photobleaching (to investigate protein dynamics in living cells) are remarkable. However, the wild type of GFP has limitations that must be overcome by protein engineering techniques or site-directed mutagenesis for optimal use.

Conclusion: In recent years GFPs and GFP-like proteins have been the subject of Many studies and so far many efforts have been made to overcome their structural and functional limitations. By using protein engineering techniques, limitations such as weak folding at 37°C, inappropriate absorption peaks, low photostability or low speed of chromophore formation have been

studied and solved to some extent. as a matter of fact, cell biology and molecular techniques are in progress, it is hoped that the limitations of GFPs and GFP-like proteins will be overcome completely and we will be able to design fluorescent variants with desired properties.

Keywords: green fluorescent protein, GFP, protein engineering, biosensors, cell visualization

High-throughput analysis of hub genes and key pathways in NASH using computational bioinformatics approach. (Research Paper)

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Introduction: Nonalcoholic steatohepatitis (NASH) explains the inflammatory form of NAFLD and is considered to be the hepatic manifestation of metabolic syndrome. Improvement of therapeutic outcomes of NASH may be best achieved by targeting significant pathologic pathways. However, the molecular mechanisms of NASH are still not well understood. The present study aimed to explore hub genes and key pathways in NASH using computational bioinformatics approach.

Methods: To identify the candidate genes, microarray dataset GSE164760 was downloaded from Gene Expression Omnibus (GEO) database, which including 74 NASH samples and 6 healthy samples. The differentially expressed genes (DEGs) were identified using R studio software. The protein-protein interaction network (PPI) was constructed using Search Tool for the Retrieval of Interacting Genes (STRING; http://string-db.org) online database. Degree and Betweenness centrality were determined using Gephi software. Pathway enrichment analysis was performed through Enrichr web server.

Results: A total of 5467 DEGs were identified (adjective p-Value<0.05). Eighty one downregulated genes(logFC<-1) and 466 upregulated genes(logFC>1) were analyzed. Four hub upregulated genes were with degree more than 20 and betweenness centrality>500. These include MDM2, KAT2B, RAB7A and HNRNPC. MDM2 was with the highest betweenness. KEGG pathway analysis revealed that upregulated key genes were mainly enriched in Ubiquitin mediated proteolysis(MDM2, Combined Score= 505.1), p53 signaling pathway(MDM2, Combined Score= 227.3), Endocytosis(RAB7A, Combined Score= 419.8), Autophagy(RAB7A, Combined Score= 298.5), Notch signaling pathway(KAT2B, Combined Score=134.7) and Spliceosome(HNRNPC, Combined Score= 171.4). Moreover, three hub downregulated genes were with degree more than 10. These included JUN, FOS and DUSP1. JUN was with the highest betweenness. KEGG pathway analysis revealed that downregulated key genes were mainly enriched in apoptosis(JUN, Combined Score= 1361.5) and MAPK signaling pathway(FOS and DUSP1, Combined Score= 599.3).

Conclusion: Hub genes and pathways identified in the present study help us understand the molecular mechanisms underlying NASH, and provide candidate targets for diagnosis and treatment of NASH.

Keywords: NASH, pathway analysis, hub genes, bioinformatics

Histopathological effects of Acesulfame Potassium on male rat gonads
(Research Paper)

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Introduction: Todays, there is an increasingly rapid rate of some diseases such as diabetes. Therefore, some Sugar substitute like Acesulfame Potassium is more popular than ever. This study investigated the effect of this Sugar substitute during pregnancy and life time on spermatogenesis.

Methods: In the present study, groups 1, 2, 3 and 4 were intraperitoneally injected with Acesulfame Potassium doses of 50, 100, 200, and 400 mg/kg bw/d during pregnancy, respectively. The control group received 0.5 ml of normal saline. After the lactation period, male newborn rats in each group were separated from their mothers and divided into two groups: (1) treated group and (2) untreated group. In the treated group, the rats were received intraperitoneal injections of ace K (50, 100, 200 and 400 mg / kg mg/kg bw/d) and the untreated group was kept without any injections until puberty period. The control group received 0.5 ml of normal saline. After anesthesia, the testis was removed and fixed in formalin, the hematoxylin and eosin (H&E) stained tissue sections were prepared and counted under a light microscope and the morphology of spermatogonium, spermatocytes and spermatids in 10 fields in slide was carefully examined. The offspring body weights in both groups were also examined.

Results: The number of spermatogonium, spermatocyte and spermatid showed no significant differences between the different groups and in comparison with the control group. Neonatal weight gain up to puberty was significantly higher in the "treated group" in the 50, 200mg doses.

Conclusion: This study showed there is no threat for spermatogenesis with consumption of Acesulfame-K during pregnancy and life time.

Keywords: Acesulfame Potassium; Spermatogenesis; Male rat gonads; spermatogonium,

HPV and cervical cancer (Review)

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Introduction: HPV is the most common sexually transmitted infection worldwide. The majority of sexually active people will contract HPV during their lifetime (approximately 75–80%). While most HPV infections (70–90%) are asymptomatic and will resolve on their own within 1–2 years, persistent infection (or multiple reinfections) can cause morbidity and mortality. There are around 200 different genotypes of HPV, of which more than 20 are known or probable carcinogens. Oncogenic strains of HPV (predominantly HPV 16/18, so-called “high-risk” strains) cause almost all cervical cancers.HPV also causes oropharyngeal (mouth, throat, tongue, and tonsils), vaginal,vulvar, penile, and anal cancers. Research suggests that HPV is also associated with sinonasal, conjunctiva, and lacrimal sac cancer. A rare but serious consequence of HPV infection is recurrent respiratory papillomatosis, whereby HPV infection can be transmitted by maternal HPV infection as well as individual sexual behaviours. HPV infection has also been associated with a higher risk of HIV acquisition. In addition, two strains of HPV (HPV 6/11, i.e., so-called “low risk” strains) are responsible for 96–100% of anogenital warts. While not deadly, anogenital warts can impact one’s quality of life and accrue substantial financial costs to health care systems.

Methods: HPV was the first virus that was recognized as the cause of cervical cancer and is widely distributed in mammals and about 40 of its genotypes can cause the infection of the mucous and skin epithelial cells of the anogenital area and other areas. In addition, endogenous hormonal factors have a relatively small effect on the growth of cervical and vaginal cancer and are one of the effective endogenous factors in the composition of vaginal microbiota. Because some of these microorganisms inhibit the growth of bacteria and viruses by producing bacteriocins and biosurfactants and regulate vaginal homeostasis. On the contrary, some of them produce substances that endanger the integrity of the vaginal epithelium and multiply pathogenic infections.

Results: Therefore, microbiota It is the first line of defense against infections. Also, according to scientific data, in female patients over 40 years of age, it is possible that persistent high-risk HPV infections play an important role in the risk of cervical cancer due to the reduction of estrogen and progesterone hormones.and an average adult has an 80% risk of contracting the HPV

infection by the age of fifty. Every year, 570,000 cases among females and 60,000 cases among males can be attributed to HPV infection among cancer cases. This uncoated virus is one of the DNA viruses whose genome contains double-stranded DNA. Another structure of this virus can be mentioned its specific proteins such as E1 and E2 proteins as factors identifying the origin of replication, E4 and E5,which play a role in the life cycle of the virus, and most importantly, oncogenic proteins E6 and E7, which target cell cycle regulators, including P53 and retinoblastoma proteins. Also, L1 proteins create species diversity.

Conclusion: High-risk HPV viruses can integrate inside infected cells and coordinate the expression program of a gene for the transcription of its oncogenic proteins (E6 and E7) and spread cancer. Persistent infection with high-risk human papillomavirus (HPV) is the cause of most cervical cancers . Over the past deca- des, there has been significant progress in primary and second- ary prevention of cervical cancer through HPV vaccination and screening.

Keywords: cancer; HPV; Uterus; Human papilloma virus

Human Papillomavirus and male fertility (Review)

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Introduction: Human Papillomavirus (HPV) is the most common global sexual transmitted disease among men and women. Most studies have been focused on HPV relationship with female fertility, however few of them studied about HPV relationship with male fertility. The aim of this review is to find out the possible effect of HPV on semen as well as male fertility.

Methods: A review literature search of eligible studies was conducted in the PubMed database from 2014 to 2022 for studies evaluating the association between HPV and male fertility using the following search strategy: ("Human Papillomavirus " OR "HPV") AND ("male fertility" or "male infertility") AND ("semen") AND ("sperm") as used keywords. 12 studies (systematic reviews and meta-analysis) were found and 10 studies were included in this review.

Results: All of the studies reported higher percentage of infection in infertile men. In the presence of HPV in semen compare to its absent: five studies reported decreasing sperm motility ,three studies showed increasing anti-sperm antibodies (ASAS), two studies reported decreasing in sperm concentration ,changing in sperm morphology was reported in three studies ,only one study found apoptosis in sperm cells ,one study reported decreasing in sperm count while another study did not find any difference and one study showed asthenozoospermia.

Conclusion: According to the higher prevalence of seminal HPV in infertile men compared to general population and also HPV's effect on some sperm parameters, it seems that seminal HPV infection might be a significant risk factor for men infertility however more research is needed to confirm HPV association with male infertility.

Keywords: Human Papillomavirus, HPV, male fertility, semen, sperm

Human papillomavirus vaccination in HIV and HPV -infected women (Review)

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Introduction: HPV contamination is the most, now not uncommon, place location of sexually transmitted contamination worldwide. High occurrence of present day and continual HPV Infections have been endorsed in immunocompromised individuals, which includes human immunodeficiency virus. Women inflamed with human immunodeficiency virus (HIV) are at substantially better chance than HIV uninfected ladies for continual human papillomavirus (HPV) contamination and development of cervical presences and invasive cervical most cancers; in addition, the prevalence of cervical most cancers will increase with extra extreme immunosuppression. There is growing proof that HPV-associated contamination and anal contamination keep to increase in HIV-inflamed populations. Compared to healthful humans, HPV has an unethical to persist longer amongst human immunodeficiency virus (HIV)-inflamed humans and strong organ transplant (SOT) recipients because of reduced CD4+ counts and immunosuppressive treatment, respectively. This very last outcomes in now not uncommon place genital warts and HPV-associated cancers. The extra, HPV vaccine (q HPV) is a prophylactic vaccine that is. regular and quite immunogenic in HIV-inflamed adults

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Human papillomavirus vaccination in HIV and HPV -infected women. After reviewing the relevant findings and evaluating the data quality, a total of 19 articles were analyzed.

Results: The top-notch weapon to control HPV contamination is primary prevention, which includes interventions associated with way of existence and sexual habits, and HPV vaccination. Current records advocate that prophylactic HPV vaccines are regular and immunogenic in top-notch HIV-incredible populations (children, woman adolescents, adults) and, through way of technique of extrapolation, in all possibility to lessen HPV associated most cancers' improvement amongst human beings with HIV contamination. In a pattern of HIV-inflamed ladies who have been HPV DNA and HPV seronegative, immune responses to HPV vaccination have been generally strong, and the vaccine changed into nicely tolerated. Both the quadrivalent and the bivalent HPV vaccine look like regular and genuinely immunogenic in extra younger HIV infected ladies. ART-treated, HIV-inflamed extra younger ladies and age-matched HIV-horrible ladies had comparable antibody responses to the quadrivalent HPV vaccine. In assessment, serology antibody responses to the bivalent HPV vaccine have been decrease in extra younger HIV-inflamed ladies in assessment with uninfected ladies. It is reliable to increase remarkable HPV-associated malignancies, specifically anal and oropharynxes most cancers

Conclusion: People inflamed with HIV are but at better chance of growing HPV-associated diseases .HPV vaccination is currently endorsed to be used in person ladies and men as lots as 26 years of age. The vaccines have been generally regular and nicely tolerated. Injection-net internet site online reaction changed into the most now not uncommon location horrible occasion of HPV vaccines endorsed. When the consequences of HPV vaccines have been in assessment to placebo in HIV-incredible humans, reconversion prices with withinside the vaccinated companies have been better than as in assessment to the placebo group. People with HIV have a better chance of growing HPV-associated tumors and quicker development of the contamination. Therefore, HPV prevention may be very crucial in HIV+ patients

Keywords: HIV-infection ‹HPV-positive females ‹Human papillomavirus vaccination

Human-Patient Simulators versus Case-Based Learning in Undergraduate Medical Students Training: A review of current evidence (Review)

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Introduction: Today, medical education is rapidly evolving; therefore, new educational methods and technologies are required to adapt to the changes and improve the quality of training. Over the past decades, the role of simulation in medical education is increasingly highlighted. Human-patient simulators are capable of both simulating real patient encounters and giving real-time, physio-logically accurate feedback; however, beyond their advantages, some medical education experts presented several disadvantages of the human-patient simulator training for undergraduate medical students. Therefore, the present study is designed to review the potential advantages and disadvantages of human-patient simulator training in comparison with case-based learning, as a standard method, in undergraduate medical students.

Methods: To determine the aims of the present study, a comprehensive systematic search was conducted through electronic databases including PubMed, Scopus, Embase, and Web of Science with the keywords “Human patient simulation”, “Case-based learning”, “Medical education”, and other related MeSH terms up to August 2022. Original studies, review studies, and references of the review studies were included. Finally, the related studies which comprised Human-based simulators versus case-based learning in undergraduate medical students' training were reviewed.

Results: According to the reviewed studies, advantages of the human-patient simulator training can be summarized as addressing gaps in clinical conditions or settings, structured feedback, ability to practice skills/build confidence, filling the need for faculty/clinical site resources, patient safety and quality, controlled environment, and faster time to competence. On the other hand, being unrealistic, focusing on specific competencies, requiring full participation/engagement of learners, faculty resources, financial resources, spatial resources, and questionable return on investment are known as its major disadvantages. Moreover, some trial studies have investigated the efficacy of human-patient simulators versus case-based learning for

undergraduate medical students. However, there were controversies in these studies. In detail, some studies have stated that the advantages of human-patient simulator learning were higher than superior to its disadvantages, while some others make the opposite statement. Furthermore, several studies did not find any significant different effects of human-patient simulator learning on undergraduate medical students' training. Based on what was stated in various studies, these different results could be due to the student topics, fields, quality of simulators, and attitude of the student to simulation-based learning.

Conclusion: Still, there are some gray areas about whether human-patient simulators are superior to case-based learning for undergraduate medical students, or not. It seems that further investigations are needed to resolve this ambiguity based on any faculty and its students' properties.

Keywords: Human Patient Simulation, Case-Based Learning, Medical Education

Identification of Candidate Genes in Recurrence and Non-Recurrence Endometrial Carcinoma Patients by an Integrative Analysis (Research Paper)

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Introduction: Endometrial carcinoma (EC) is one of the most prevalent tumors of the female reproductive system. Although numerous studies, including analysis of gene expression profile and cellular microenvironment have been reported in this field, pathogenesis of this disease remains unclear. The molecular profile of endometrial cancer has become an important tool in determining patient prognosis and their optimal adjuvant treatment. This study aimed to screen the candidate genes differentially expressed in recurrence and non-recurrence patients by bioinformatics analysis.

Methods: GEO database and GEO2R online tool were applied to screen the differentially expressed genes (DEGs) of EC from the microarray datasets. Protein-protein interaction (PPI) network for the DEGs was constructed to further explore the relationships among these genes and identify hub DEGs. Gene ontology and KEGG enrichment analyses were performed to investigate the biological role of DEGs. Besides, expression profile, and survival analysis of MFNG gene, as one of the top hub DEGs, were also investigated using Gene Expression Profiling Interactive Analysis2 (GEPIA2) to further explore the roles of these hub gene in the mechanism of EC tumorigenesis.

Results: A total of 551 DEGs were screened out as the DEGs with 369 upregulated and 182 downregulated in EC. The gene ontology analysis showed that these genes were significantly enriched in cell communication, biological regulation, and localization, etc. The KEGG pathway analysis showed that DEGs were enriched in T-cell activation, leukocyte cell-cell adhesion, and leukocyte activation, etc. More importantly, MFNG, ZAK, SOCS2, WNT4, SMO, SMAD9, USP39, PRKACG, SF3A3, TRAF7 were identified as the hub genes of EC. Expression validation by bioinformatics analysis also proved the expression of MFNG was differentially expressed in EC, but overall survival was not altered significantly.

Conclusion: MFNG involved in the pathogenesis of EC and might be a candidate biomarker for distinguishing recurrence and non-recurrence patients.

Keywords: Endometrial carcinoma, Bioinformatics analysis, Differentially expressed gene, Pathway, Biomarker

Identification of Colorectal Cancer Highly Associated CircRNAs Through Integrative Bioinformatics and ceRNA Networks (Research Paper)

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Introduction: Colorectal cancer (CRC) is the third most commonly diagnosed cancer worldwide and is the second leading cause of cancer-related mortality. Despite all advances, the overall survival and therapeutic efficiency of CRC is still poor, and there is a great need to identify key pathways involved in CRC pathogenesis, novel biomarkers and drug targets. Circular RNAs (circRNAs) are covalently closed RNAs that play critical roles in the cell, including regulating gene expression, which is mainly through sponging miRNAs. Numerous studies have shown that circRNAs are involved in tumorigenesis. Due to their high stability and specific cellular functions, they may be ideal biomarkers and drug targets for cancer. To identify dysregulated circRNAs in CRC with high statistical significance, a meta-analysis of microarray datasets was performed and the major circRNAs with regulatory effects on hub genes were investigated.

Methods: A total of 40 circRNA microarray samples from three GEO (www.ncbi.nlm.nih.gov/geo) datasets (GSE126094, GSE138589, GSE142837) were selected for this study. All datasets were from the same platform (GPL19978) and included cancer and paired normal tissues. First, quality control was performed. Samples of poor quality were removed. Log2 transformation and quantile normalization (using the Limma package in the R software) were performed when necessary. The batch effect was removed using the Combat function of the R package called "SVA". Meta-analysis of the three datasets was performed using two approaches: direct merging (DM) and random-effects model (REM). Differentially expressed circRNAs (DECs) were screened using the cutoff value of 0.05 Benjamini-Hochberg's adjusted P-value and |log2FC| > 1. CircRNAs identified by both the DM and REM methods were considered for further analysis. MiRNA targets of DECs were identified using the CircMine (www.biomedical-web.com/circmine) database. The most likely mRNA targets of the miRNAs were identified using the miRDB (score cut-off 90) web tool (http://mirdb.org/). The CircRNA-miRNA mRNA network, also known as ceRNA network, was constructed (Figure 1) using Cytoscape (v.3.8.9). CytoHubba, a Cytoscape plugin, was used to identify the top 10 hub genes of the ceRNA network. Then, the circRNAs interacting with these hub genes were analyzed as "crucial circRNAs." To identify the pathways involving crucial circRNAs, KEGG pathway enrichment analysis was performed.

Results: REM Meta-analysis of microarray datasets of circRNAs revealed 338 dysregulated circRNAs and DM revealed 125 dysregulated circRNAs. A total of 54 DECs, including 10 upregulated and 44 downregulated circRNAs, were identified by both the DM and REM meta-analysis approaches and used for further investigation. 193 miRNAs were identified as targets for DECs sponges and 567 genes were identified as targets for miRNAs. Based on the Maximal Clique Centrality (MCC) algorithm of CytoHubba, PTEN, AGO1, AGO3, AGO4, MAPK8, MECP2, NRAS, CCND2, ETS1, and ITGAV were identified as the major hub genes. Examination of the circRNA-miRNA hub gene network (Figure 2) revealed that seven circRNAs (hsa_circ_0000512, hsa_circ_0072387, hsa_circ_0001022, hsa_circ_0001525, hsa_circ_0041555, hsa_circ_0049356, hsa_circ_0061817) can potentially regulate the expression of key hub genes in CRC. The mTOR and FoxO signaling pathways, microRNAs in cancer, and EGFR tyrosine kinase inhibitor resistance were among the enriched KEGG pathways of the seven hub circRNAs.

Conclusion: In summary, the present study aimed to prioritize the most likely circRNA candidates that play a role in colorectal cancer and could be used as future biomarkers or drug targets. Two different approaches of the meta-analysis were performed to identify DECs with high statistical significance. In addition, seven circRNAs were identified as potential modulators of hub genes in CRC. Furthermore, this study provides a deeper understanding of circRNA-related competing endogenous RNA regulatory mechanisms in CRC pathogenesis and the major signaling pathways involved in CRC tumorigenesis.

Keywords: colorectal cancer, circRNA, biomarker, microarray, meta-analysis

Identification of DEGs in colon adenocarcinoma with peroxiredoxin2 enzyme siRNA transfected to HT29 and SW480 cells using RNA-Seq data (Research Paper)

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Introduction: Colorectal cancer (CRC) is a common malignant disease with high morbidity and mortality. Many researches have demonstrated that PRDX2 play an important part in various biological functions, such as the protection effects for intracellular lipids and proteins and the mediation role for cellular signaling pathways associated with cell proliferation, apoptosis and differentiation. In addition, overexpression of PRDX2 has been reported in various cancer tissues and cells, which is essential for tumor maintenance and survival by protecting cells against ROS injury and apoptosis. The aim of this study was to evaluate the expression of genes in the presence and absence of peroxiredoxin2 enzyme in HT29 and SW480 cells.

Methods: SRP075061 dataset was downloaded from NCBI>SRA, the sra file was converted to two fastq paired files with sratoolkit.2.11.3-ubuntu64 software under Linux. Quality control of fastq files was done with FASTQC software, and low quality reads were trimmed with Trimmomatic software and we mapped the trimmed file to hg38_genome using Hisat2 software and a sam file was obtained. In the next step, we converted the sam file to counts files using hg38.ncbi.refseq.gtf and finally, DEGs were identified using the DESeq2 package in R Studio software by threshold(FDR:0.05 and log2foldchange>1)

Results: Based on the results, in the HT29 cell line (control and siRNA transfected), upregulated genes include: ATL2, SNX2O, NSL1 and downregulated genes include: ND5, COX1, ATP6. In cell line SW480 (control and siRNA transfected) SLC9A3, SLC9A3-AS1, IL7R are upregulated genes and NECAP1, HMGCS1, KRT1 are downregulated genes.

Conclusion: Due to the important role of peroxiredoxin2 enzyme in cell proliferation, differentiation, apoptosis and signaling pathways, genes that up and down expression in the presence and absence of peroxiredoxin2 enzyme in cell, were used for prevention, diagnosis and treatment in patients with colorectal cancer.

Keywords: Colorectal cancer, peroxiredoxin2 enzyme, HT29, SW480

Identification of Dihydrodiol Dehydrogenase (DHDH) gene as a potential biomarker for Thyroid Carcinoma by bioinformatics analysis (Research Paper)

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Introduction: Thyroid carcinoma (THCA) is the most common endocrine malignancy, accounting for ~2.1% of all cancer diagnoses worldwide. It is mostly detected around the course of the thyroglossal duct or laterally in the neck, also in the subdiaphragmatic organs and distant places such as the mediastinum. Although most patients are asymptomatic, symptoms related to the size of the tumor and its relationship with surrounding tissues can also appear. It can occur at any age, as well as it is more common in young adults, the mortality rate is decreased due to early diagnosis, but it is different in racial groups. Dihydrodiol dehydrogenase (DHDH) encodes an enzyme that belongs to the family of dihydrodiol dehydrogenases, which exists in numerous forms in mammalian tissues and are involved in the metabolism of sugars and xenobiotics in the endocrine system. Given that the variability of incidence-based mortality in the different races has not been studied. The aim of this study is to investigate the DHDH gene in clinical parameters based on the Pathological stage in the four racial groups.

Methods: In this Descriptive-analytical study to identify genes involved in THCA development, we analyzed the Cancer Genome Atlas (TCGA) data. Besides, to facilitate our understanding of such genes that participated in tumor progression, we analyzed a database OncoDB to explore abnormal patterns in gene expression related to clinical data that were identified. Also, differentially expressed genes (DEGs) by the OncoDB online database were identified and then by the TMP method normalized. Finally, functional enrichment analysis was applied. Criteria for including patient data in the present study are demographic information such as race and pathological stage. The TCGA datasets related to THCA consisted of 50 normal, 505 Cancer samples, and 400 DEGs (|log FC| > 1; P < 0.05) in individuals with TCHA compared with the normal samples via using the available numerical mRNA expression values.

Results: The expression of the DHDH gene in TCHA increases about two times with LogFC =1, while it has a very low expression in normal tissue. The ONCODB data have been used to investigate the clinical effect of DHDH gene expression increase in the pathological stage. The expression profile of

DHDH was included: Cancer sample average3.7; Cancer sample median: 2.8; Normal sample average: 0.5 Normal sample median: 1; log2 fold change: 1.49. Also, the results of demographic information based on pathological stage chart analysis show that the expression in the late stage is higher compared to patients in the early stage. According to the average expression of the DHDH gene in 27 samples of African-American patients, 1 sample of AMERICAN Indians, 50 samples of Asians, and 324 samples of White patients are respectively 3.0, 4.5, 4.6, and 3.7. The higher average of expression of target gene compared to the median reported, which respectively as, 1.8, 4.5, 2.8, and 2.9and these values indicate increased expression in the samples. This gene was significantly related to demographic parameters such as race and pathological stage. Conforming to the analysis of gene expression with ANOVA-Pvalue=1.5e-09 in different stages of the disease, it can be concluded that with the increase in DHDH gene expression, the tumor size increases, and the disease progresses towards metastasis.

Conclusion: According to the larger number of samples and the lower average in whites, it is concluded that the increase in expression in Asian and African-American patients is more than in white patients and the distribution of data in these patients is more scattered. The results of this study collectively revealed that altered DHDH gene expression levels might be responsible for racial differences in the carcinogenesis of THCA and target gene expression promotes the progression of related pathological stages of THCA. Therefore, the DHDH gene is expected to become a molecular target for THCA treatment.

Keywords: DHDH gene, Thyroid carcinoma, Clinical Parameters, biomarker, TCGA

Identification of HLA-DQ2 & HLA-DQ8 Heterodimer Frequencies in People with Celiac Disease Or Suspected Symptoms (Research Paper)

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Introduction: Celiac disease is an Enteropathy, related to the immune system, which is defined as the permanent sensitivity to Gliadin, wheat or other Prolamins, available in barley, in people with genetic susceptibility. The main component of genetic predisposition lies in the HLA area on chromosome number Six. Celiac disease it has a considerable amount of companionship with HLA class II genes and particularly DQ2 and DQ8 heterodimers. In the present study, DQ2 and DQ8 heterodimers are examined in a small community of Iranian individuals with the celiac susceptibility symptoms.

Methods: DNA extracted from 50 peripheral blood samples were evaluated for HLA-DQ2 and HLA-DQ8 heterodimer frequencies using qualitative PCR and reverse dot-blot hybridization.

Results: The frequencies were 42% for HLA-DQ2, 6% for HLA-DQ2 and DR4, 18% for HLA-DQ8 and DR4, and finally, 4% for HLA-DQ2, DQ8 and DR4. Results showed generally, the frequency of DQ2 genotype (>50%) is higher than that of DQ8 genotype (20-30%). In this evaluation, no significant relationship was found between the age and gender parameters with celiac. The results of serology tests were in contrast with that of European countries. However, the outcomes achieved from the evaluation of relationship between symptoms and autoimmune diseases were similar to those from European countries.

Conclusion: The difference in DQ8 frequency, observed in Iranian population, with that of European countries could show an association between the genotype frequencies and races population. According to the obtained results, celiac has a significant spread in Iran. Therefore, its prevention and treatment require more attention and new health care policy making.

Keywords: Celiac, HLA-DQ2, HLA-DQ8, qualitative polymerase chain reaction, reverse dot-blot hybridization

Identification of LGALS3 /hsa-miR-1225-5p/XIST ceRNA network in HCV-associated hepatocellular carcinoma patients: Integrated high-throughput bioinformatics investigation (Research Paper)

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Introduction: Hepatocellular carcinoma (HCC) is a common cause of cancer-related death around the world [1]. Cirrhosis is the most important risk factor of HCC which can be developed by Hepatitis B and C. HCV is a potential risk factor for cirrhosis and liver cancer progress [1].

Methods: In the present study, we tried to identify a potential diagnostic mRNA, a novel miRNA and finally, a ceRNA network in hepatocellular carcinoma using bioinformatics analysis. At first, liver cancer Microarray dataset GSE14323 was obtained from a study at PubMed [2] and then, analyzed by GEO2R to find differentially expressed genes (DEGs). After selecting a significant gene from the data, it was analyzed by GEPIA2[3] and ENCORI[4] to confirm its expression rate in normal and tumor samples and investigate survival analysis to find a significant relationship between high-expressed and low-expressed groups in mortality. Through Enrichr [5] gene ontology information and biological pathway, involvement was understood. In addition, protein-protein interactions were analyzed by STRING [6] to identify probable pathways that selected mRNA can regulate indirectly. miRWALK database [7] was employed to find a novel mature miRNA which has significant interaction with the selected mRNA in the CDS region. Finally, the novel miRNA was searched in LncBase v.3 [8] to find strong interactions with lncRNAs and construct a predictive ceRNA network.

Results: by GEO2R analysis, LGALS3 was selected as an up-regulated gene (logFC=3.1, adj. P value=7.81e-22) in tumor samples. The significant high expression of this gene in liver cancer also was shown in GEPIA2 and ENCORI. Survival analysis showed that there is a significant positive relationship between the high expression of LGALS3 and increasing mortality (log-rank p=0.0037, HR (high) =1.7, p(HR) =0.0041). This gene encodes a protein named Galectin-3 which regulates apoptosis and innate immune system. It is also related to Ras family activation regulation pathway which has a crucial role in human cancer. MiRNA-mRNA interactions analysis showed that hsa-miR-1225-5p is a significant interactor to LGALS3 mRNA. And then, XIST was found as a LncRNA which had an interaction with hsa-miR-1225-5p according to LncBase v.3.

Conclusion: LGALS3 is an over-expressed gene in HCC patients and forms a predictive ceRNA network among hsa-miR-1225-5p and XIST.

Keywords: Hepatocellular carcinoma, LGALS3, ceRNA, integrated bioinformatics

Identification of potential biomarkers and molecular mechanisms involve in AML prognosis using Bioinformatics approaches (Research Paper)

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Introduction: Acute myeloid leukemia is a form of acute leukemia, which is characterized by an increase in the number of abnormal white blood cells [1]. The incidence rate of AML is 4.3 per 100,000 in the US (United States). The most common therapies for patients with AML are chemotherapy and allogeneic stem cell transplantation but most older patients show poor prognosis and survival [2]. Therefore it is expected that advancing therapeutic strategies, can affect patient outcomes, especially for elderly patients. After many years, the microarray is one of the recent advanced techniques which can analyze a large number of samples for cancer research and provides new insight to treat various diseases [4]. In this study, we try to identify potential biomarkers of AML, by comparing AML and normal samples using bioinformatics tools to enhance therapeutic strategies for patients with AML.

Methods: The microarray dataset was downloaded from the GEO database and differentially expressed genes were screened using R packages analysis. Additionally, functional enrichment analyses were performed based on David online tool, to gain the main molecular mechanisms associated with DEGs. Then for further analysis of DEGs, the protein-protein interaction (PPI) network was generated using the STRING database and Cytoscape software.

Results: A total of 459 DEGs including 125 up-regulated and 334 down-regulated DEGs were screened between AML/ normal samples. The result of the KEGG pathway analysis shows that DEGs were mainly associated with Hematopoietic cell linage and Transcriptional misregulation in cancer. The result of GO term analysis indicated that DEGs were significantly associated with B cell activation and immune effector process. Furthermore, ten hub genes were identified through PPI network analysis which among them TNF, FLT3, and CDC44 show the highest degree of connectivity.

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genes were identified through PPI network analysis which among them TNF, FLT3, and CDC44 show the highest degree of connectivity.

Keywords: AML, Leukemia, Bioinformatic, Microarray, Biomarker

Identification of two novel FUT1 mutations in people with Bombay phenotype from Iran (Research Paper)

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Introduction: Background and purpose: Bombay and Para-Bombay phenotypes are characterized by FUT1gene mutation and lack or little expression of H antigen expression on red blood cells. ABH antigens are not present in the body secretions Bombay individuals, while para-Bombay individuals can be secretors or nonsecretors. The aim of this study was to investigate the molecular basis of FUT1 and FUT2 genes in Iranians with the Bombay or Para-Bombay phenotype.

Methods: ABO phenotype analysis and routine serological tests were performed on 11 people with Bombay and Para-Bombay phenotypes. The coding regions of FUT1 and FUT2 genes were amplified by PCR followed by sequencing. The ABO genotypes were also determined by sequencing of exons 6 and 7 of the ABO gene.

Results: Serological investigations confirmed the Bombay phenotype in 8 samples and the Para-Bombay phenotype in 3 samples. Family members with the Bombay phenotype had the classic T725G mutation in the FUT1 gene, accompanied by deletion of the FUT2 gene. Other samples had A653G, C661T, C652G and A722C mutations in the FUT1 while FUT2 was silenced by G461A or C390T variants.

Conclusion: In this research, we identified two novel mutations in the FUT1 gene in individuals with the Bombay phenotype. This and previous works confirm the variety of FUT1 mutations. Bombay phenotype, Para-Bombay phenotype, H antigen, FUT1, FUT2

Keywords: Bombay phenotype, Para-Bombay phenotype, H antigen, FUT1, FUT2

Identifying the miRNA and mRNA-associated networks to reveal potential prognostic biomarkers for Breast cancer (Research Paper)

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Introduction: Despite significant breakthroughs in breast cancer diagnosis and therapy, the prognosis remains unfavorable. microRNAs (miRNAs) appear to play a key role in the genesis and progression of human malignancies, according to mounting data. However, most miRNAs' regulation mechanisms and clinical relevance in breast cancer are yet unknown.

Methods: The gene expression profiles for miRNA and mRNA were collected from the Gene Expression Omnibus (GEO), in this study we systematically analyzed the expression profiles of mRNA (GSE54002 dataset) and miRNA (GSE42525 dataset). Using Cytoscape, a miRNA-mRNA regulatory network was built and visualized. The STRING database was used to build the protein-protein interaction (PPI) network, and the cytoHubba plugin was used to extract hub genes. The functions and signaling pathways associated with these differentially expressed mRNAs were discovered using Gene Ontology and the Kyoto Encyclopedia of Gene and Genomes.

Results: We found 225 differentially expressed miRNAs (DEmiRNAs), and 665 DEmRNAs in total. The enrichment results from analyzing DEmRNAs was shown to be associated with Interactions between immune cells and microRNAs in tumor microenvironment, B Cell Receptor Signaling Pathway and Cancer immunotherapy by CTLA4 blockade. Also construction of PPI network fof the DEmRNAs showed 564 nodes and 3899 edges in total from which one most significant module was identified. We also selected the key deregulated miRNAs and mRNAs based on statistical significance.

Conclusion: Our results show the significant roles of miRNA-mRNA regulatory networks in breast cancer and identified a new prognosis predictor and some potential prognostic biomarkers as well as involved genes and miRNAs in patients with breast cancer.

Keywords: Breast cancer, GEO, DEmiRNAs, DEmRNAs, microRNA

Immune system functions and COVID-19 immunity (Review)

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Introduction: The immune system is the best natural defense against pathogens (such as viruses, bacteria, protozoa, fungi, and worms). This study aimed to review data related to natural immunity against coronation.

Methods: studies on natural immunity to the coronavirus were studied by searching scientific databases such as Google Scholar, Science Direct, and PubMed.

Results: The results of some of the studies have shown that the humoral response may be transient and incomplete, but in some people, strong immune responses and neutralizing antibodies have been seen after infection. temporary antibodies protection against coronavirus infection has been reported by General studies. The results showed that after the antibody level improved after 6 months, the infection significantly decreased. Studies of COVID-19 infection in China, in patients with and without symptoms, have shown that asymptomatic patients have an incomplete and transient immune response by decreasing IgG and neutralizing antibody levels. On the other hand, experiments showed reduced mortality related to plasma usage including high antibodies to hospitalized COVID-19 patients. The cellular immunity role in the defense against COVID-19 has been confirmed by some research. In patients with severe COVID-19 infections, lymphopenia occurs and also, and CD4 and CD8 T-cells decrease. Studies have confirmed that T CD8þ cell memory is approximately associated with the severity of different COVID-19. Le Bert and coworkers showed that COVID-19 results in long-term T-cell immunity to a structural protein of SARS-CoV-2. Grifoni et al studied the roles of viral proteins that successfully stimulate T cells. They then investigated the cells of some of the patients who had recovered from COVID-19 with viral protein components and showed that all patients had helper T cells sensitive to spike SARS-CoV-2 protein.

Conclusion: According to recent findings, antibodies against SARS-CoV-2 are developed in most of the recovered patients. Scientists are uncertain, however, if enough antibodies are produced to ensure future safety, what constitutes a good level of immunity, or how long protection lasts. Based on immune responses to closely related viruses such as those that cause SARS and the Middle East respiratory syndrome (MERS), current estimates suggest

that a high percentage of improved people may be protected against re-infection for one to two years due to humoral immunity and cellular immunity.

Keywords: Covid-19, infection, Immune system, cellular immunity

Immunity of Patients with Tuberculosis Combined with Diabetes (Review)

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Introduction: Tuberculosis (TB) is the most volatile infectious disease worldwide. Despite the availability of anti-tuberculosis tablets and the weakened BCG vaccine, no big cut-price with withinside the huge kind of TB times has been determined. Currently, one-1/three of the world's population is infected with latent Mycobacterium tuberculosis (M. Tb). At this stage, the person isn't infectious; however, TB can be reactivated due to granuloma liquefaction due to immunodeficiency or immune comp omission. The load of diabetes mellitus (DM) has multiplied dramatically in low- and middle-earnings countries (Mics). Tuberculosis is an essential risk for people with diabetes. Immunopathy due to diabetes or pre-diabetes is characterized in element via persistent inflammation driven via continual hyperglycemia and effects in several complications. Patients with diabetes are an awful lot more possibly to enlarge active tuberculosis (TB). Evidence suggests that people with TB and diabetes have a higher risk of adverse effects of TB treatment, which include not on time sputum conversions, TB treatment failure, relapse, and death. Considering the immoderate prevalence of diabetes worldwide, crucial steps have to be taken to understand, prevent and combat T2DM.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Immunity of Patients with Tuberculosis Combined with Diabetes. After reviewing the relevant findings and evaluating the data quality, a total of 21 articles were analyzed.

Results: The conclusion of the studies determined that progressed glucose control and near monitoring of patients with comorbidity of M. Tb and diabetes need to be finished to aid in effective treatment and recovery. In patients with T2DM, depletion of GSH may be very common, which also can moreover

furthermore motive greater pathogenesis. One of the cytokines that is crucial to limitation and contain M. TB infection is TNF-α. Two cytokines—IFN-γ and TNF-α—that may be crucial for manipulating and stopping M. TB from unfolding, respectively, are significantly compromised in people with T2DM. As GSH is depleted withinside the path of infection or T2DM, NF-κB may be activated and the production of IL-1, TNF-α, and IL-6—all inflammatory cytokines—may be up regulated. TNF-α is a genuinely crucial cytokine for granuloma formation in M. TB infection. TB infection first infects alveolar macrophages. M. TB uses its cell wall receptors to enter macrophages and pass their safety system. Different research has explored the immunological molecular mechanisms that specify the affiliation among TB and T2D. In diabetic patients, bacterial popularity via way of means of immune cells is altered, ensuing in better replication of M. tuberculosis.

Conclusion: In preceding studies, it is being verified that greater glucose withinside the systemic float can promote the development of ROS and the pro-inflammatory cytokines IL-1 and IL-6, which at immoderate concentrations can inhibit macrophage specificity. A balance of anti-inflammatory and proinflammatory cytokines plays a crucial role in retaining the granuloma form and M. TB infection containment. A cytokine cannot be labeled as “beneficial” or “detrimental”; rather, so you can produce supposed effect, it needed to be withinside the right net internet site online on the right time, but, as stated previously, overproduction can motive disarray, desensitization and malfunction. In this retrospective cohort evaluation of TB patients with type 2 diabetes in China, they determined that the usage of MET as a combination drug with contemporary recurring progressed sputum tradition conversion rate at the stop of 2nd month of TB treatment, in ordinary to a check from Korea, in addition, MET moreover multiplied the achievement rate of antiTB treatment as compared with one-of-a-kind ant hyperglycemic.

Keywords: Mycobacterium tuberculosis Infection ‹Tuberculosis ‹diabetes ‹ LipoatrophicDiabetes Mellitus

Immunogenicity and Reactogenicity in Q Fever Vaccine Development (Review)

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Introduction: Cornell Burnett, an obligate intracellular bacterium which, in humans, motives the contamination Q fever.it may purpose some of immoderate syndromes. Vaccination is as an alternative a fulfillment for prevention of numerous infectious diseases. This examines gives a pinnacle stage view of past and modern research on Q fever vaccine development, our statistics of immunogenicity and reactogenicity c. burnetii.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Immunogenicity and Reactogenicity in Q Fever Vaccine Development. After reviewing the relevant findings and evaluating the data quality, a total of 17 articles were analyzed.

Results: Elimination of this bacterium is as an alternative difficult, and vaccination is considered the extraordinary approach for prevention of infection in humans. Many vaccines in competition to C. burnetii were developed, but, best, a formalin-inactivated, whole mobileular vaccine derived from virulent. The best currently certified vaccine for use in humans is Q-VAX (Sequa's), an entire mobileular, formalin-inactivated vaccine. Although this vaccine gives an immoderate diploma of prolonged-term protection in competition to infection, immoderate network and systemic reactions are often reported, especially in people with preceding exposure to C. Burnetii and, Individuals receiving Q-VAX need to first undergo pre vaccination screening which encompass anti-C. Burnetii antibody titers and an intradermal pores and pores and pores and pores and skin test, a way which gives every fee and time to vaccination. As surrender to forestall end result of this barrier to vaccine availability, many research groups have investigated novel vaccines in competition to C. burnetii with diverse levels of fulfillment in equaling the defensive efficacy of Q-VAX on the identical time as reducing reactogenicity.

The future of Q fever vaccine development may additionally be described via manner of the favored features of a next-generation, superior vaccine. The use of Q-Vax and top-notch segment I WCVs as Theoretical stepping stones will likely allow for the rational popularity quo of those features. Phase I WCVs show many benefits which encompass outstanding immunogenicity, stimulation of prolonged lasting immunity, and a single-dose immunization regimen. The downsides of segment I WCVs encompass the capability for a PVH response and the accompanying bulky Pre-vaccination screening way at the issue of producing problems However, a growing wealth of facts of the defensive mechanisms of host immune responses to C. burnetii, investigations into the pathogenesis of reactogenicity to whole mobileular C. burnetii vaccines, and traits in novel vaccine generation can help facilitate development of greater strong vaccines in competition to this pathogen. Preventing their tremendous use. Antibody-mediated immunity on my own cannot manipulate infection.

Conclusion: Through those observations, it's far apparent That a complicated Q fever vaccine would possibly probably mitigate the capability for a post-vaccination Hypersensitivity response, set off protection at a comparable diploma to segment I WCVs, and Be administered via a single-dose regimen. The direction to a non-reactive Q fever vaccine that is trustworthy but require statistics of antigenic desires and immunologic responses that the C. burnetii location has now not but ascertained. As we preserve to remedy the mechanisms of C. burnetii–host interactions ‹we're capin a role to flow into closer to a next-generation Q fever vaccine so that you can benefit humans throughout the world.

Keywords: immunoinformatics ‹Coxiella burnetii Infection ‹Q Fever Vaccine ‹multi-epitope vaccine

Immunoinformatics design of a multi-epitope vaccine against tuberculosis (Research Paper)

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Introduction: Mycobacterium tuberculosis is a pathogen that has been known as a main cause of tuberculosis disease for many years. Although, global BCG vaccination has showed a high reduction in new cases, it has reported variable efficacy (0-80%) among different population. On the other hand, some limitations of live attenuated vaccines, have spurred researchers to develop alternative ones.

Methods: In this study using immunoinformatics tools, the sequences of five Rv0888, Rv2645, Rv3841, Rv3874 and, Rv3875 antigens, as well as Heparin-Binding Haemagglutinin (HBHA) as an adjuvant, were retrieved. Different epitopes were identified employing various databases, and the selected epitopes and adjuvant were linked together using appropriate linkers. Then, allergenicity, antigenicity, solubility and physicochemical parameters of the designed vaccine were analyzed. Moreover, homology modeling, refinement of the 3D model, and their validations were performed. In the next step, molecular docking studies of the designed vaccine with Toll-like receptor 4 (TLR4) proteins as a receptor was done.

Results: A vaccine with a length of 704 amino acids was designed by selecting the high ranked epitope sequences. Allergenicity, antigenicity, solubility and physicochemical parameters studies have shown that the protein is antigenic, non-allergenic, soluble and stable. Also, the comparison of the refined 3D and the original model indicated that the 3D structure was improved and the potential mistakes were minimized. Finally, the best-docked model of vaccine and TLR4 complex was selected. The results showed that vaccine can bind appropriately to TLR4.

Conclusion: The fundamental purpose of this study is to use bioinformatics tools to design an appropriate subunit vaccine. As a result, a subunit vaccine consisting of eight epitopes from five Mycobacterium tuberculosis antigens which was linked to HBHA adjuvant by GPGPG linker was designed. Various evaluations in this study as well as molecular docking between vaccine and TLR-4 showed that the designed vaccine can be a good candidate for

tuberculosis and it is hoped that satisfactory results will be achieved, in practice.

Keywords: Tuberculosis, Epitope, Vaccine, Mycobacterium tuberculosis, Bioinformatics

Immunotherapeutic Effects of Propolis in Cancer treatment (Review)

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Introduction: The increasing incidence of cancer has caused great concern around the world. Therefore, finding a safe and effective treatment has become one of the main goals of researchers. Immunotherapy is an effective method compared to common cancer treatments, in which the patient's immune system is activated to fight a certain group of diseases, including cancer, by targeting and destroying tumor cells specifically. Propolis is one of the most promising immune system modulating factors. Propolis, which is a bee product, has been used to treat diseases since ancient times with different biological activities such as antibacterial, antifungal, antiviral, antioxidant, anti-inflammatory, immunomodulatory, antitumor, and immunostimulatory effects. This natural healing agent contains about 300 bioactive compounds including chrysin, galangin, gallic acid, quercetin, cinnamic acid, apigenin, and caffeic acid. The purpose of this systematic review is to review the immunotherapeutic effect of Propolis on the immune system of cancer patients according to clinical and experimental studies.

Methods: A comprehensive systematic search of articles was conducted in PubMed, Scopus, scholar, and ProQuest with the entry terms “Propolis immunotherapeutic effect”, “Propolis and Cancer Immunotherapy, and “Cancer Immunotherapy” from 2000 to 2022. This search yielded 42 results, 8 of which were included in this systematic study.

Results: The researches have been conducted both in in vitro and in vivo studies. In the in vivo studies, mice have injected intraperitoneal with 50-100 mg/kg of propolis (water-soluble Propolis (WSP) or ethanolic extract of Propolis (for 7-21 days, and the results were compared with the control groups. It was found that Propolis induced antibody production, stimulated

and induced lymphocytes, induced some cytokines production (IL-1 and TNF), changed the macrophages tumoricidal activity, increased the production of lymphocyte-activating factors, neutrophils, raising the ratio of CD4/CD8 T cells, and total helper T-cells. It was also found that a combination of propolis with anticancer drugs (Cisplatin, Irinotecan) inhibited tumor growth, increased the antitumor activity of chemotherapy drugs, and reduced the toxic and genotoxic effect of cisplatin on normal cells without affecting its cytotoxicity on tumor cells.

Conclusion: Totally, the positive immunotherapeutic effects of Propolis in cancer confirmed without any major side effects at in vitro, in vivo and clinical studies which suggested its promising potential as an anti-cancer natural agent for the development of new drugs. Therefore, more clinical studies are needed on propolis indications and usage doses.

Keywords: Propolis, Immunotherapy, Cancer

Impacts of COVID-19: A research agenda to support people in their fight (Review)

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1. No, I have no affiliation

Introduction: The onset of COVID-19, hereinafter COVID, is an unprecedented time in history. It is not only a unique situation in our lifetime,. Indeed, there have been numerous terrible events that have taken place since the last pandemic but nothing that has had the global impact quite like COVID has. Little is known about when this will actually end and the uncertainty in various ways (e.g., economy, health) surrounding this pandemic is enormous—and much may hinge on how “lucky” we are with medical management and/or finding a vaccine. The World Health Organization, the Centers for Disease Control and Prevention, and numerous healthcare organizations around the world are working hard with the ultimate goal of managing the disease and its health impacts. But, until this pandemic can be in our rearview mirror, the impacts on health, healthcare, economy, labor market, supply chain, work and home life are manifold and potentially lasting for a long time. Some estimates suggest that about 50 % of the US workforce is now working from home [as of April 2020]. Even after the pandemic passes, there may be permanent changes to workplaces and jobs, with some organizations already planning for a future with significantly expanded [relative to pre-COVID] or even nearly perma-nent work-from-home for its employees (e.g., Byers, 2020; Conger, 2020; Khetarpal, 2020). I see no reason to belabor the extent of the short-, medium-, and long-term impacts of this pandemic, given how much has already been

Methods: Alvesson, M., & Kärreman, D. (2007). Constructing mystery: Empirical matters in theory development. Academy of Management Review, 32(4), 1265–1281. https://doi.org/10. 5465/amr.2007.26586822. Bala, H., & Venkatesh, V. (2013). Changes in employees’ job characteristics during an enterprise system implementation: A latent growth modeling perspective. MIS Quarterly, 37(4), 1113–1140. Retrieved from www.jstor.org/stable/43825784. Bariso, J. (2020). Google’s CEO just gave the entire company a day off. Here’s why. [Accessed 30 June 2020] https://www.inc.com/justin-bariso/googles-ceo-just-gave-entire-company-a-day-off-heres-why.html. Bettinger-Lopez, C. (2020). A double pandemic: Domestic violence in the age of COVID-19. [Accessed 30 June 2020] https://www.cfr.org/in-brief/double-pandemic-domestic-violence-age-covid-19. Byers, D. (2020). Twitter employees can work from home forever, CEO says. [Accessed 30 June 2020] https://www.nbcnews.com/tech/tech-news/twitter-employees-can-work-home-forever-ceo-says-n1205346. CDC (2020). Coronavirus disease 2019 (COVID-19): Racial & ethnic minority groups.

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Results: science, continues to provide a complement to the pursuit of discovery of medications and vaccines. I organized these into two sets of five each: focal groups that should be studied—i.e., underprivileged popu-lations, different countries and cultural contexts, women (vs. men), workers in healthcare (frontline workers), elderly and at-risk—and five general issues and special considerations—i.e., role of technology as the oxygen, pre- vs. mid- vs. post-COVID studies, constraints on data col-lection/research due to COVID, evolution of COVID, and focus on contextualization (generalizability is irrelevant).Together, these ideas present illustrations of projects that researchers can pursue to help us move toward better ways of living and coping with COVID.

Conclusion: The COVID pandemic has created unprecedented changes to all aspects of life but this has also presented unique research opportunities. In fact, they are not just opportunities but an imperative for science to get ahead of the pandemic and provide leadership in solving what is clearly the grandest of grand challenges the entire planet and its people have faced in a very long time. This article specifically presented op-portunities and focal issues for future research on five job-related is-sues—i.e., job loss, job changes, job outcomes, coping, and suppor-t—and five life/home-related issues—i.e., home life changes, children, life-related outcomes, social life, and support. In addition to this, I presented overarching possible research directions and considerations for researchers, editors, and reviewers, as science, especially social

Keywords: COVID-19 impacts Work life impacts Home life impacts Stress Satisfaction Work-family conflict

Implications and challenges related to adoption of Artificial Intelligence for the Healthcare Workforce (Review)

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Introduction: The rapid advancement of artificial intelligence (AI)-related technologies, especially in the healthcare sector, is evident to all. This review focus on how the health of human resource (HHR) is affected by AI. In the second part, HRH issues related to AI implementation are discussed.

Methods: To identify relevant literature, different keywords such as "artificial intelligence", "Healthcare Workforce", and "AI" were combined by Boolean operators in electronic databases like PubMed, Google Scholar, and Embase until August 2022. Journal articles written in English with available full text that examined the effect of AI on the Healthcare Workforce were included. Articles conducted in sectors other than healthcare were excluded.

Results: AI consists of a wide range of applications in healthcare such as decision support in clinical settings, automation of administrative tasks, automated imaging, drug design, and use of surgical robots. Thus, AI can affect HHR in different aspects. The results of applying AI can be categorized as follow: Performance, productivity, Workload, Workflow, satisfaction, and Physician-Patient Relationships. AI-based technologies can perform tasks that are labor and time-consuming, resulting in providing more free time for healthcare professionals to do more complicated tasks. AI can facilitate the workload of radiologists by faster scan time and reporting more accurate diagnoses. AI has leveraged three categories that can improve the workflow of healthcare providers. These consists of Clinical documentation, Quality-measurement reporting, and Point-of-care learning. By automation of these tasks, the workflow will change considerably so that physicians are free to do more complicated tasks that cannot be performed by machines. This ability will result in higher satisfaction for both providers and patients. As this patient tracking contributes to higher patient safety. However, AI brings advantages like increasing efficiency, quality, and return on investment, there are critical aspects that should be considered. AI-related issues are as follows: I) the regulatory and legal issues, II) ethical concerns about privacy and breach risks, III) infrastructure shortages, IV) the availability of data, and V) economic aspects.

Conclusion: It can be said that artificial intelligence has entered all aspects of daily life, and health care is not an exception. AI serves as an assistant in the

health sector with the potential to enhance efficiency and improve healthcare quality and the volume of care delivered to patients. It has to be noted that the replacement scenario is impossible, as the human workforce cannot be replaced by machines entirely. While considering the benefits of AI adoption in healthcare, different issues ranging from legal and ethical aspects to economic aspects should not be neglected.

Keywords: artificial intelligence, AI, healthcare, health workers, Healthcare Workforce

Importance of NF-κB signaling pathway in cancer (Review)

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Introduction: Introduction and aim: NF-B-mediated signaling pathways play a direct role in preserving cancer stem cell traits linked to tumor growth. An NF-B-dependent pathway may be responsible for the spread of cancer. Another significant characteristic of cancer cell is their lack of apoptosis and overexpression of ABC genes, which is associated with their resistance to cytostatic medications. Numerous signaling pathways, such as Notch, Sonic hedgehog (Shh), and wingless-type, are in theory linked to control of their self-replacement (Wnt). Investigating the role of the NF-κB signaling pathway in cancer was the goal of this study .

Methods: Search Method: This study was investigated the Importance of the NF-κB signaling pathway in cancer and based on reliable scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Results: The findings demonstrated that NF-B is widely expressed and mediates a variety of biological activities, including immunology, cell proliferation, inflammation, memory, and learning. The DNA-binding and dimerization functions of the NF-B family's members depend on a conserved n-terminal REL homology domain (RHD). These family members particularly include the five subunits of NF-κB, namely RELA (p65), RELB, c-REL, p50, and p52, and the NF-κB. The NF-κB subunits RELA, RELB, and c-REL additionally comprise a C-terminal transactivation domain (TAD). The IKK complex (IKK/IKK/IKK) is phosphorylated by the binding of ligands to their corresponding receptors (such as CD40) in a way that is dependent on C-IAP, TRAF2/3, and NIK (NF-B-inducing kinase). In turn, phosphorylated IKKs phosphorylate IB, which is then degraded by the proteasome and has its NLS unmasked within the p50/p65 NF-B dimer. The NF-B dimer is then translocated into the nucleus where it binds to specific target sites and triggers the production of the target gene. In contrast to this canonical NF-B signaling cascade, non-canonical NF-B signaling is mediated by the phosphorylation of IKKs via NIK, which in turn causes p100 to be phosphorylated before being processed by the proteasome to become p52. Binding to particular NF-B sites and the subsequent nuclear translocation of the p52/RELB NF-B dimer are followed by the activation of particular target genes. Due to its diverse physiological roles and target genes, the dysregulation of canonical and non-canonical NF-B signaling pathways is directly linked to a number of characteristics of cancerogenesis and cancer development. Specifically, epithelial-to-mesenchymal transition (EMT),

angiogenesis, invasiveness, and metastasis are all crucial tumor-promoting mechanisms that are mediated by canonical NF-B signaling. Cell proliferation is also stimulated, and apoptosis, the EMT, invasiveness, and metastasis are all prevented. In a wide variety of malignancies from different organs, NF-B was revealed to be constitutively active as a driver of such critical mechanisms initiating and propagating tumor growth. Additionally, numerous oncogenic mutations or a protracted, chronic inflammatory milieu might cause the NF-B subunits to become constitutively active. It has been demonstrated that persistent inflammation, which is brought on by elevated NF-B activity, promotes the development of a protumor genic microenvironment in colon cancer. However, NF-B has also been implicated in anti-inflammatory functions that have a direct impact on tumor development and treatment resistance. For instance, it has been observed that overexpression of the NF-B p50 homodimer in M1 macrophages associated with tumors inhibits inflammatory and antitumor responses in mouse fibrosarcoma. The NF-B p50 homodimer was also activated in human ovarian carcinomas with abnormal tumor-associated macrophage response to M1 activation signals, suggesting a context-dependent role for NF-B activity at least in malignancies linked to chronic inflammation.

Conclusion: Conclusion: In conclusion, there is strong proof that NF-B plays a crucial role in organ-specific malignancies. Despite the fact that cancer stem cells were discovered in 1994, the study of NF-function B's in tumor-initiating cancer stem cells is still in its infancy. Although surface markers are limited in their capacity to target cancer in terms of marker specificity, the NF-B family and the signaling pathways they mediate for both apoptosis and self-renewal may offer a viable target for therapeutic interventions.

Keywords: Keywords: NF-κB, signaling pathway, cancer, hedgehog

Importance study of Heat Stress Protein 70 (HSP70) in tardigrade (M. Tardigradum) (Review)

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Introduction: Extremophiles are organisms that have adapted or at least are tolerant to extremely harsh environments. Most extremophiles are single cellular organisms with simple structure, such as archaea and bacteria. Tardigrade were found in harsh environments such as Antarctica as well as in urban area, e.g., from activated sludge in a sewage treatment plant. All tardigrades require surrounding water to grow and reproduce, but some limno terrestrial species are able to tolerate almost complete dehydration. When the surrounding water evaporates, tolerant tardigrades lose almost all body water enter a metabolically inactive dehydrated stage called anhydrobiosis. The dehydrated tardigrades withstand various extreme conditions that normally disallow the survival of most other organisms: for example, low and high temperatures from (-273 °C to nearly 100 °C), high hydrostatic pressure (7.5 GPa), immersion in organic solvent and exposure to high dose of irradiation.

Methods: We reviewed about 22 articles were conducted from 2019 to 2022 in the world and Iran. We searched some key words such as astrobiology, extremophiles, tardigrade, HSP70, microbes in space in sciencedriect, Elsevier, PubMed and SID.

Results: Tardigrades, known colloquially as water bears or moss piglets, are a phylum of eight legged segmented micro animals. The 0.1 mm to 1.2 mm large animal, was firstly described by German zoologist Goeze in 1730. Tardigrade is Latin and means slow moving, because of their appearance and clumsy way of moving they are often referred to as water bears. Despite called HSP the induction is not only due to temperature effect but also to a whole other series of environmental stress factors. These proteins are highly conserved and ubiquitous in all organisms. They play a crucial role in folding newly synthesized proteins, intracellular protection against protein denaturing factors, folding, unfolding of damaged proteins, assembly of multi protein complexes, transport, sorting of proteins into correct subcellular compartments, cell cycle control and signaling and protection of cells against stress, apoptosis. HSPs are classified based on their molecular weight: HSP10, HSP40, HSP70, HSP90. Genes encode these proteins are conserved in all of the organisms they have been found, including tardigrades. Due to their function in the cell, HSPs are believed to enhance tolerance in cryptobiosis. We observed different levels of expression of HSP70 genes

across consecutive states of cryptobiosis in the tardigrade milnesium tardigradum and from the three recognized HSP70 isoforms, HSP70Π was the most relevant in recovering from anhydrobiosis (HSP70) induction in rehydrating tardigrade richtersius coronifer shows a similar gene expression pattern as observed in m. tardigradum. I expected to observe down regulation in HSP70 like 1 gene in the transitional state compared to other observed anhydrobiosis states active, preconditioned and dry. Previous studies with anhydrobiotic tardigrade m. tardigradum showed downregulation of HSP70 isoform 1 in the transitional state, suggesting the gene having no direct role in anhydrobiosis. In addition, HSP70 showed downregulation in the transitional stage in tardigrade R. coronifer.

Conclusion: we showed that in m. tardigradum three isoform of HSP70 are up regulated during a heat shock. However only isoform 2 was significantly induced in the transitional stage between the active and cryptobiotic stage and was found in the anhydrobiotic stage. Yeast studies showed that HSP70 does not protect the yeast from dehydration stress during desiccation. Thus, HSP70 is probably only translated after rehydration to fold newly synthesized protein and does not protect the cell during desiccation.

Keywords: astrobiology, extremophiles, tardigrade, HSP70, microbes in space

Improvement in curcumin application for preventing dental caries by embedding in nanoparticles (Research Paper)

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Introduction: The aim of this research was optimization curcumin characteristics for oral hygiene application. Curcumin-loaded starch nano-particles were developed for enhancing adhesion property with enamel surface and best anti-bacterial effect against Streptococcus mutans.

Methods: The study was the experimental one. The nanoparticles synthesize was based on precipitation and ionic gelation method. Nanoparticles characterization was done by scanning electron microscopy, dynamic light scattering and determination of zeta potential. In addition, minimum inhibitory concentration (MIC) was assessed to evaluate the antibacterial properties of nanoparticles against Streptococcus mutans. The binding amount of nanoparticles to hydroxyapatite was evaluated and finally, the curcumin release from the nanoparticles was also assayed.

Results: The average size of optimized starch nanoparticles were about 60 nm. Also, zeta potential was -15.4, mV. Loading contents of nanoparticles were 84% measured by optical density from standard calibration curve of curcumin. In addition, minimum inhibitory concentration (MIC) of nanoparticles against Streptococcus mutans, was 0.204 and 0.438 mg/mL for starch nanoparticles and pure curcumin, respectively. It was also found that starch nanoparticles had inhibitory effect on bacterial biofilm.

Conclusion: Curcumin-loaded starch nano-particles improve adhesion properties and interactions with enamel and prevent dental caries of Streptococcus mutans.

Keywords: Streptococcus mutans, Curcumin, Dental caries.

Improvement of mechanical properties of chitosan-based scaffolds using montmorillonite for tissue engineering applications (Research Paper)

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Introduction: A suitable scaffold for tissue engineering must have good mechanical properties. Materials such as ceramics and natural or synthetic polymers can be used to make scaffolds. Polymers alone have low mechanical properties, so using the composite mode, such as combining polymers with ceramics, became more popular. Composite materials are promising biomaterials used to produce 3D scaffolds. A combination of at least two properly selected phases collects the advantages of the components and minimizes the disadvantages of each component, thereby improving the overall properties compared to the characteristics of each component alone.

Methods: In this study, montmorillonite (MMT), an inorganic nanoparticle with a layered structure and a negative charge, was used to increase the mechanical properties of the chitosan (CS) scaffold. CS polymer with a positive charge can intercalate into layers of MMT. CS/MMT composite microfibers with different concentrations of MMT were prepared by microfluidic technique, and the characteristics of the microfibers were evaluated by a tensile test.

Results: The results showed that the MMT layers inside the CS matrix were well dispersed in microfibers with a low concentration of MMT. This exfoliation and uniform dispersion improved mechanical properties and significantly increased Young's modulus compared to CS microfibers. However, due to

non-uniform dispersion and aggregation of MMT nanoparticles at higher concentrations, Young's modulus started to decrease.

Conclusion: This study showed the effect of MMT inorganic nanoparticles in improving the mechanical properties, so we could significantly increase Young's modulus with its low concentration. Therefore, CS/MMT microfibers prepared by the microfluidic technique have the potential to be used in tissue engineering applications and can play a significant role in the regeneration of damaged tissues.

Keywords: Tissue engineering - Mechanical properties - Montmorillonite - Microfluidic technique - Chitosan.

Improving of transdifferentiation, function and survival rate in microencapsulated β-cell: in-vitro and in-vivo study (Research Paper)

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Introduction: The objective of the study is to efficiently transdifferentiate rat bone marrow-derived mesenchymal stem cells (BM-MSCs) into islet-like cells, and encapsulate and transplant them while maintaining vital properties like stability, cell proliferation, and metabolic activity for the treatment of T1DM.

Methods: Trans-differentiation of BM-MCs into islet-like cells induced by high glucose concentration combined with Nicotinamide, β-mercaptoethanol, β-cellulin, and IGF-1. Glucose challenge assays and gene expression profiles were used to determine functionality. Microencapsulation was performed using the vibrating nozzle encapsulator droplet method with a 1% alginate concentration. Encapsulated beta-cells that had been cultured in a fluidized-bed bioreactor to measure their metabolic activity and viability were then transplanted into the omentum of STZ-induced diabetic Wistar rats, and their blood sugar and weight were monitored for two months.

Results: Based on the induction protocol, PDX1, INS, GCG, NKx2.2, NKx6.1, and GLUT2 expression profiles revealed the specificity of generated pancreatic islet cells. Post-islet-like cell transplantation reduced the glucose levels of the streptozotocin (STZ)-induced rats significantly (P< 0.05). In contrast to treated, STZ-induced rats who did not receive encapsulated islets displayed a consistent decline in weight and died when loss reached >20 percent at day ~55.

Conclusion: Enhancing the conditions and means of differentiation and protection of encapsulated cells, particularly for pancreatic beta cells with a limited supply, may be a promising approach for safe cell therapy.

Keywords: transdifferentiation, microcapsules, endocrine beta-cells, mesenchymal stem cells, insulin secretion

In depth assessment of COVID-19 detection methods (Review)

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Introduction: The efficient methods for Corona Virus Disease 2019 (COVID-19) diagnosis can be considered a key tool to manage this disease. The gold standard in this area is real-time quantitative reverse transcription-polymerase chain reaction (qRT-PCR), a sensitive and specific method to detect SARS-CoV-2. Other methods for the diagnosis of this virus include other RNA-based techniques, CRISPR, serological testing of antibodies, ELISA, imaging technologies, and artificial intelligence. The main aim of this article is to review different diagnostic approaches and discuss their advantages and disadvantages.

Methods: Articles from the authenticated database such as Google scholar, PubMed, Science Direct, Scopus, and Web of Science were collected and refined according to the subject.

Results: Methods that are used for COVID-19 diagnosis can be divided into 4 distinct categories according to their detecting targets: The RNA-based methods: The technologies used for the detection of nucleic acid in COVID-19 include RNA sequencing (RNA-seq), real-time quantitative reverse transcription-polymerase chain reaction (qRT-PCR), droplet digital reverse transcription-polymerase chain reaction (ddRT-PCR), reverse transcription loop-mediated isothermal amplification (RT-LAMP), and clustered regularly interspaced short palindromic repeats (CRISPR). Their advantages include high sensitivity, specificity, and accuracy; their disadvantages are long testing times, and high equipment/personnel requirements. The immunologic-based methods: The immunologic methods for diagnosis of COVID-19 include the detection of antigens and antibodies and can detect recovered patients with COVID-19. Four kinds of methods including rapid antigen detection, antibody detection, nanoparticle-based lateral-flow assay, and enzyme-linked immunosorbent assay (ELISA) are widely used in the diagnosis of COVID-19. Their advantages include high sensitivity, specificity, and can detect recovered people; their disadvantages are slow detection speed, and cumbersome steps. The imaging methods: Different types of diagnosing COVID-19 imaging technologies include chest computed tomography (CT), chest radiography and lung ultrasound are utilized to different degrees.

Patients suffering from fever and cough, chest discomfort, and difficulty in breathing are usually diagnosed by imaging examinations. Their advantages include low risk of infection, and low equipment requirements; their disadvantages are the need for professional analysis, and difficulty to detect mild symptoms. The assistive technology methods: The primary purpose of assistive technology is to maintain or improve an individual's functioning and independence. Different types of diagnosing COVID-19 assistive technologies include blood testing, pooling test, artificial intelligence, and omics analysis. Their advantages include expense reduction, low equipment requirements, reduce the need for professionals, and can study disease mechanisms; their disadvantages are low sensitivity and specificity and need to be utilized in combination with other detection methods.

Conclusion: The gold standard for diagnosing COVID-19 is the real-time quantitative reverse transcription-polymerase chain reaction (qRT-PCR), which is a sensitive and specific method to detect SARS-CoV-2. Other methods for the diagnosis of this virus include other RNA-based methods, CRISPR, serological testing of antibodies, ELISA, imaging technologies, and artificial intelligence. Concerning the type of samples and stages of the disease, a combination of information on patient demographics and histories, clinical symptoms, outcomes of molecular and serological diagnostic tests, and imaging information is highly recommended to achieve an adequate diagnosis of patients with COVID-19.

Keywords: SARS-CoV-2; Diagnosis techniques

In silico analysis of the second and third structure of the immune receptor FLAGELLIN SENSITIVE-2 (Research Paper)

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Introduction: In innate immunity, the immune receptor FLAGELLIN SENSITIVE-2 is regarded as the best model to study the functional properties of other receptors. Flagellin, the main building block of the bacterial flagellum, acts as a pathogen-associated molecular pattern (PAMPs) triggering the innate immune response in animals and plants. In Arabidopsis thaliana, the Leucine-rich repeat transmembrane receptor kinase FLS2 is essential for flagellin perception. Demonstrate the specific interaction of the elicitor-active epitope flg22 with the ectodomain of the FLS2 receptor by chemical cross-linking and immunoprecipitation. FLS2 constitutes the pattern-recognition receptor that determines the high specificity of flagellin perception. Due to the important role of FLS2 in the defense system, it is important to investigate the secondary and tertiary structure of this receptor. Predicting of the secondary and tertiary structure of proteins is very important in subsequent protein studies and the study and identification of the function of unknown proteins. Predicting the tertiary structure of proteins can also be used in molecular docking.

Methods: In this study, the Phyre2 software was used to investigate the secondary structure of the FLS2 protein. Three-dimensional structure modeling was performed based on the selection of a pattern with a high resemblance to the target protein using the Swiss Model database.

Results: The results indicate that five similar structures were found in the protein database for FLS2, one of these structures, called the crystal structure of a c20f3A, had a similarity of 95%. The model chosen for modeling FLS2 protein in Protein BRASSINOSTEROID INSENSITIVE 1 (Plant steroid receptor ectodomain bound to brassinolide and SERK1 co-receptor ectodomain) (4lsx.1.A) contains 774 amino acids and discovered by X-RAY DIFFRACTION with a resolution of 3.30 angstroms The Identity of 4lsx.1.A pattern with target, protein is 30.78.

Conclusion: The results of this research can be used in future research and molecular docking and provide basic information to investigate other immune receptors.

Keywords: Receptor, FLS2, 3D structure, 2D structure, Swiss Model Phyre2, Docking

In Silico analysis on the identification of has-mir-4271 associated with IGFBP4 gene in gastric cancer (Research Paper)

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Introduction: Despite its high prevalence and mortality rate, gastric cancer (GC) can be prevented and detected globally, thanks to its genetic susceptibility. Helicobacter pylori infection, age, high salt intake, and low fruit and vegetable consumption are all factors contributing to the condition. In the present study, hub genes were identified and molecular mechanisms were revealed in GC.

Methods: Gene expression profiles were analyzed using GSE54129 from the GEO datasets. Gene Expression Analysis using GEO2R tool revealed the Differentially Expressed Genes (DEGs). Adj. p-value < 0.01 and log2FC (fold change) >3 were considered as the cut-off criteria. By using the DAVID database, enrichment analysis was conducted on the DEGs and their pathways with overlapping functions were identified in the KEGG database. The protein-protein interaction network graph (PPI) was obtained using the STRING database to analyze the interactions between DEGs. MicroRNASNP-v3 database revealed the miRNAs (miRs) associated with the Insulin Like Growth Factor Binding Protein 4 (IGFBP4) gene as well as the underlying signaling pathways that contribute to GC growth. The miRWalk database was used for detecting the interaction between IGFBP4 gene and associated miRs.

Results: Based on the current research, 24 DEGs were identified. The KEGG and DAVID databases showed that IGFBP4 gene is a member of the insulin-like growth factor binding protein (IGFBP) family, which controls the bioavailability, activity, and distribution of insulin-like growth factor (IGF)1 and -2 through high-affinity IGFBP/IGF complexesIn addition to being in the same family of proteins as insulin, IGF plays a role in the regulation of growth and development. Consequently, IGFBP4 can inhibit cancer cell growth by reducing IGF1 activity. Furthter results showed that By interfering with RNA-induced silencing complexes and interfering with the 3' untranslated regions of

target mRNAs, has-mir-4271 could exert a suppressive effect on the IGFBP4 gene's activity by acting as a regulator of gene expression.

Conclusion: These findings imply that IGFBP4 could be a potential target in gene therapy for gastric cancer. Blocking of IGFBP4 expression in GC cells represses the IGF1 activity and may provide a novel treatment approach.

Keywords: Bioinformatic analysis, biomarker, differentially expressed genes, KEGG pathway

In silico study of the interaction of insect, scorpion and frog venom peptides with the spike protein receptor binding domain of coronavirus: investigation of natural inhibitors of SARS-CoV-2 (Research Paper)

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Introduction: The spike protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) interacts with the angiotensin-converting enzyme 2 (ACE2) receptor in human cells and causes covid-19 infection. This protein is located on the virus membrane and is a triangular glycoprotein with two S1 and S2 domains, both of which are very important for SARS-CoV-2 infection. Interactions between S1 with the peptidase domain of ACE2 lead to the binding of the virus to the host, and then the S2 domain leads to membrane fusion and entry of the viral ribonucleoprotein complex and its entry into the host cell. RBD (receptor binding domain) of the S1 domain of spike protein represents a potential target for the development of anti-SARS-CoV-2 drugs which might have the potential to inhibit the entry of SARS-CoV-2 into the host cells. Then, we considered the interaction of the RBD domain with ACE2. Peptides are potential molecules to be tested against spike protein. Then some peptides targeting the spike protein to prevent infection by COVID-19 establishment were investigated. Considering the importance of spike protein interaction with ACE2 receptor, some antiviral peptides of the scorpion, insect, and frog venom were selected and their docking and molecular binding analysis with the RBD domain of coronavirus spike protein have been done.

Methods: In order to select a proper peptide for binding to SARS-CoV-2 spike protein of coronavirus, 22 small peptides from venom scorpion, frog and, insect were obtained via literature survey. Molecular modeling: There are various servers and software for modeling peptides. PEPfold3 server was used in this research because all peptides had less than 50 amino acids. Docking: In this research, the HADDOCK server was used for molecular docking for protein-protein interaction. The crystal structure of the RBD domain in complex with the ACE2 receptor is available in the PDB bank and was used in this study (PDB code: 6m17, chain E). Then, only the RBD domain of the spike protein was used. All 22 structures obtained from various antiviral toxins were considered for docking, and each peptide was individually docked to the RBD domain of spike protein through the HADDOCK server.

The binding residues that interact with ACE2 receptor were considered active residues in docking and included Lys 417, Tyr 453, Gln 474, Phe 486, Gln 498, Thr 500, and Asn 501. Also, all residues from peptides are considered active residues. The interaction between peptides and the RBD domain in each complex was obtained using Ligplot+ software and the prodigy server.

Results: All the 22 peptides that were modeled by the Pepfold3 server were analyzed in the Haddock server in terms of the degree of binding to the RBD domain. The results showed that 5 Venom antimicrobial peptides-9, Dermaseptin-s4, Magainins1, caerin1-9, and Magainins2 have a lower Haddock score than the control. Hence, they have a stronger binding affinity to the RBD of the domain. Two peptides Venom antimicrobial peptide-9 and Magainins1 with Haddock scores of -121.6 and -119.6 are the best in terms of binding score. Also, by comparing the hydrogen bonds between the receptor and the ligand in the control state and the two best states, it was shown that in the two top states, the interaction with active residues was more desirable. Therefore, these two peptides are better than the control, both in terms of the docking score and in terms of making hydrogen bonds with the desired points, and it is suggested that they can perform better in binding to the RBD of the domain with better quality than the binding of this domain to ACE2 and therefore, prevent the host cells from causing covid-19.

Conclusion: According to the obtained results, Venom Antimicrobial Peptide 9 (FFGHLFKLATKIIPSLFQ) and maginin (GIGKFLHSAGKFGKAFVGEIMKS) interacted better with the RBD domain of spike protein than other peptides. Among these two peptides, Venom Antimicrobial Peptide 9 with RBD domain interacts more effectively than Magainins. And it can inhibit the interaction of the spike protein with the ACE2 receptor, so the peptide "FFGHLFKLATKIIPSLFQ" can be considered as a potential drug for the disease of COVID-19.

Keywords: Venom peptides, Docking, spike protein, coronavirus, Angiotensin-converting enzyme 2

In vitro assessment of a rapid colorimetric method to detect ex-tracellular DNA in cerebrospinal fluid: a platform for rapid diagnosis of bacterial meningitis (Research Paper)

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Introduction: Rapid and organ-specific diagnosis of acute infections saves lives and resources. As part of the innate immune system, neutrophils trap and kill bacteria by way of neutrophil extracellular traps, which are composed of extracellular DNA released into bodily fluids during infection. A combination of sulfated glycan and aniline dye (test solution /strip test) was recently used to develop the rapid colorimetric extracellular DNA detector, which showed a positive result spe-cifically in the infected organ. In the present work we used stimulation of healthy neutrophils by bacteria and assessed experimentally the colorimetric reaction compared to CSF from patients

Methods: Fresh cerebrospinal fluid (CSF) samples were obtained from patients admitted to the neurosur-gical intensive care unit (n=55) and analyzed by rapid test. Neutrophils from healthy subjects (28 and 32 years of age, one female) were stimulated with bacteria and incubated in the test solution. The results were studied by spectrophotometer.

Results: A shift in absorption from the γ-peak (521 nm, pink, negative) to the α-peak (630 nm, blue, posi-tive), which was inhibited by pre-incubation with DNase I or antibiotics effective against the bacteria was observed through several controlled attempts on healthy neutrophils. Light mi-croscopy revealed that neutrophils in test-positive CSF samples (n=26) differed morphologically from test-negative samples (n=29), resembling the bacterial-stimulated healthy neutrophils. The absorption shift occurred in test-positive samples after addition of DNase.

Conclusion: A diagnostic method based on detection of extracellular DNA in CSF can be employed at point-of-care to distinguish meningitis at an early stage even in the damaged brain tissue.

Keywords: Antibiotic therapy; Neutrophils; Toluidine blue; Post neurosurgical infections; Rapid diagnostic

In vivo Cardiac Reprogramming as a Strategy for the Treatment of Heart Disease (Review)

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Introduction: Cardiovascular diseases (CVD), which account for approximately 33% of all deaths worldwide, are the leading cause of morbidity and mortality for people of most ethnicities. These conditions include heart disease, stroke, heart failure (HF), and myocardial infarction (MI). The adult human heart's inadequate potential for cardiac regeneration is the key factor that places CVD at the top of the mortality list. In place of other treatment modalities like heart transplantation, cardiac regenerative medicine can restore the structure and function of the heart.

Methods: One of the potential approaches in heart regenerative medicine is the use of de novo generated cardiomyocytes (CMs) in cardiac cell-based treatment. To do this, many types of multipotent and pluripotent stem cells (PSCs) have been investigated to create cardiac lineage cells, such as cardiac progenitor cells (CPCs) and CMs, which are needed in cardiac regenerative medicine. Direct reprogramming, also known as a direct conversion, is a recently developed technique that directly transforms somatic cells into cardiac cells in vitro and in vivo. Through the activation of cardiogenesis-related or pluripotency-inducing factors in non-cardiac cells, this cellular alchemy provides a quick and secure method for producing autologous cardiac cells. The definition of direct conversion is the creation of either a functional mature such as CM. That develops a second fully developed somatic cell without passing through pluripotency The ethical problems associated with ESCs are solved by this technique since the starting cells are patient-derived somatic cells (for example, skin-derived fibroblasts). This method has received attention for the past twelve years as a way to produce de novo cardiac lineage cells (CPCs/CMs). In general, there are two methods for direct cardiac conversion: short-term overexpression of pluripotency-inducing factors (such as Oct4, Sox2, Klf4, and C-myc [OSKM]) in somatic starting cells, which results in the formation of unstable intermediates that can be reprogrammed; and long-term overexpression of

cardiogenesis-specific factors such as transcription factors and miRNA in starting somatic cells may result in the formation of unstable intermediates that can be differentiated or regulated to have a cardiac destiny using signals that induce cardiogenesis.

Results: Importantly, direct cardiac conversion based on pluripotency factors, also known as partial reprogramming, is quicker and more effective in producing CM in vitro. Also using transgene-free, chemical-based methods, it is now possible to directly convert somatic mice and human cells into cardiac lineage cells.

Conclusion: Although it is difficult to convert cardiac fibroblasts into cardiac cells in vivo via heart-specific partial reprogramming. Furthermore, assuming the safety concerns are resolved, cardiac cells created utilizing a partial reprogramming approach might be a helpful platform for disease modeling, drug screening, and cardiac cell-based treatment. In this study, we have evaluated all the reports that have been worked on in vivo cardiac reprogramming.

Keywords: Cardiac reprogramming, partial reprogramming, pluripotency-inducing factors, cardiogenesis-specific.

In-Vitro Effects of Copper Nanoparticles on Common Bacterial Strains Implicated in Nosocomial Infections (Research Paper)

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Introduction: In recent years, the bacterial resistance to antibiotics has grown at a worrying speed. On the other hand, the rate of discovery of new antibiotics has failed to keep up with the emergence of resistance. Thus, there is a need for new approaches for fighting bacterial infections. We studied the antibacterial properties of copper nanoparticles (Cu Nps) on most culpable bacterial strains for nosocomial infections.

Methods: The effect of copper nanoparticles on in-vitro growth of standard and clinical strains of Escherichia coli, Methicillin-resistant Staphylococcus aureus (MRSA), Enterococcus feacalis, Klebsiella and Pseudomonas aeuroginosa was studied. Copper nanoparticles with average diameter of 23 nm were synthesized by electric arc evaporation technique. Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were determined and the antibacterial effects were compared to the common antibiotics used to treat these strains bymeans of disk diffusion method.

Results: The arc-fabricated copper nanoparticles were successfully synthesized. At 50 A, transmission electron microscopy (TEM), X-ray diffraction (XRD), and scanning electron microscope (SEM) analyses showed fabrication of relatively pure, dispersed and brown Cu Nps with average size of 23 nm. Escherichia coli and MRSA showed acceptable levels of susceptibility to Cu Nps; the effects of copper nanoparticles were greater than cephalexin in suppressing Escherichia coli colony formation while the Cu Nps were more effective than vancomycin in suppressing MRSA growth. Other strains showed resistance to Cu Nps.

Conclusion: Using copper nanoparticles may be a viable approach in treating or preventing infections caused by Escherichia coli or MRSA.

Keywords: Copper nanoparticles, Antibacterial, Bacterial resistance

Incomplete penetrance of ALDH1A3 gene associated with autosomal recessive anophthalmia in a large consanguineous family (Research Paper)

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Introduction: Anophthalmia and microphthalmia (A/M) are severe congenital defects of eye development. A variety of genetic and environmental factors contribute to A/M including mutations in the ALDH1A3 gene. These mutations cause autosomal recessive A/M mostly in consanguineous families of different ethnicities. Mutations in the genes have mainly shown full penetrance. Nevertheless, in this study, we present a case with homozygote mutation (c.709G>A) in the ALDH1A3 gene that was healthy without any eye abnormalities.

Methods: Before pregnancy, a 28-year-old woman without any clinical abnormality was referred to our center for genetic counseling since she had a 5-year-old boy suffering from non-syndromic bilateral anophthalmia. They were relative to a family in our previous study, where we detected a novel homozygous missense mutation (p. Gly237Arg) in exon 7 of the ALDH1A3 gene in the patients using whole exome sequencing. Accordingly, we checked the identified mutation in the case and her boy via Sanger sequencing. Next, we checked the mutation in her parents. Besides, we genotyped the cases bi-directionally in triplicate to verify the findings.

Results: The boy was homozygote for the mutation (c.709G>A) in the ALDH1A3 gene and showed bilateral anophthalmia. The mother was homozygote for the same mutation; however, she was healthy and did not show any eye abnormalities.

Conclusion: This case might present an incomplete-penetrance biallelic (c.709G>A) mutation in the ALDH1A3 gene.

Keywords: Anophthalmia; ALDH1A3; Incomplete penetrance

Increase in menopausal estrogen level with low L-arginine consumption in short period (Research Paper)

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Introduction: As defined during menopause, the production of estrogen hormone by the ovaries decreases. L-arginine is a semi-essential amino acid and precursor of nitric oxide (NO) and primary substrate of polyamines. Our aim was to show whether the timely use of this substance can increase the level of ovarian steroid hormone production in aged rats.

Methods: Female Wistar rats (36weeks, weighing 250 grams) were randomly divided into control and experimental groups after Pap smear test and confirmation of diestrous phase. L-Arginine (5-50 mg/kg), a NO precursor alone or in combination with L-NAME (5-25 mg/kg), a NO-producing enzyme inhibitor, during a period of (3 to 21 days once a day, intraperitoneally) was injected in rats. The control group received only saline 1 ml/kg. At the end, blood samples were prepared and steroid hormone levels were measured using an ELISA kit. Ovary and uterus samples were also collected and analyzed biometrically and histopathologically. Data were analyzed using ANOVA under $\alpha = 0.05$.

Results: Estrogen levels were higher in low doses and short periods of L-arginine (3 and 5 days) compared to the saline control group, and the ovaries showed a normal condition (without cysts). Also, using L-NAME alone or before L-arginine injection had no significant effect.

Conclusion: Consumption of low doses of L-arginine in short periods may resolve menopausal complications with metabolic changes.

Keywords: L-arginine, estrogen, menopause, rat

Increased transduction efficiency in microfluidic devices (Research Paper)

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Introduction: Gene therapy using lentivectors (LV) is a promising approach to treat many disorders such as multiple myeloma (MM). Multiple myeloma is a second most common malignancy that characterized by the accumulation of malignant plasma cells in the bone marrow. In this study, we targeted special antigen in MM, B- cell maturation antigen by using the droplet-based microfluidic device. There are limitations in manufacturing LV due to inefficient cell transduction. To overcome this problem, we designed a focused-flow droplet generator device to increase gene transfer efficiency.

Methods: Device designed by soft lithography technique. Human myeloma cells were transduced by LVV in our designed chip and plates as control. Transduction efficiency is assessed by determining GFP expression on FACS.

Results: Transduction efficiency was assessed at decreasing virus concentration (MOI) while keeping picodroplet size constant. Transduction efficiency in picodroplets was higher than controls in human myeloma cells at all MOI s tested.

Conclusion: transduction efficiencies in pico droplets are comparable to levels obtained with transduction in conventional methods, indicating efficient gene delivery to target cells. Overall, our study provides a novel approach to the field of gene transfer to cells, especially transfection -resistant cells.

Keywords: Lentivector, Transdduction,,Microfluidic

Inhibition of the miR-3928-5p/INHBA interaction by rs1479520687 (G/A) disturb the regular Activin signaling pathway by changing the expression level of INHBA protein as a potential biomarker of GC (Research Paper)

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Introduction: One of the most prevalent diseases and a leading cause of cancer-related death is gastric cancer[1].Additionally, due to the significant tumor heterogeneity, the therapeutic response and prognosis vary at different stages. Therefore, it is highly desired to investigate the molecular mechanisms behind cancer invasion, metastasis, incidence, and prognosis from a genomics viewpoint, since this could lead to highly sensitive therapeutic modalities[2]. The purpose of this study is to identify possible biomarkers, associated pathways, and proteins by identifying differentially expressed genes in GC using microarray analysis.[3]

Methods: For the gene expression analysis, GSE54129 microarray dataset was analyzed by GEO2R online software. GEPIA2 [4] and ENCORI [5] online databases were used to validate the differential expression analysis. Also, the survival and co-expression analyses were performed by GEPIA2 and ENCORI. STRING [6] online software was performed to demonstrate the protein-protein interaction analysis. Pathway enrichment and gene ontology (GO) analysis was performed by enrichr [7]. Finding the possible dangerous single nucleotide polymorphisms (SNPs) in the 3'UTR region of selected genes was performed by miRNASNP [8]. Analysis of the potential deleterious SNPs in the coding sequence (CDS) of selected genes was performed by SIFT database [9].

Results: Based on microarray data analysis, INHBA has a significant up-regulation in the gastric cancer samples, compared to control (logFC: 4.6813, adj. P. Val < 0.0001). GEPIA2 and ENCORI expression analysis validates the expression analysis results. Based on survival analysis, the high expression of INHBA has a significant positive correlation with the low survival rate of GC patients (HR: 0.029, logrank p: 0.028). Based on enrichr, INHBA regulates the activin signaling pathway. SNP analysis revealed that rs1479520687 (G/A) inhibiting the interaction of hsa-miR-3928-5p with INHBA mRNA (ΔG binding: -11.78 kCal/mol). Protein-protein interaction analysis

revealed that INHBA has significant protein interaction with ACVR2A, SMAD3, ACVRL1, and FST proteins.

Conclusion: Our findings revealed the overexpression of INHBA in GC; furthermore, this gene participates in some crucial cancer-related patways. Besides, this study suggests that it would probably play prognosis role in this cancer. Additional studies are required to validate our outcomes and enhance our insight about the function of INHBA in GC.

Keywords: bioinformatics, biomarker, systems biology, RNA interaction

Inhibitory Effect of Isoniazid on the Expression of Locomotor Tolerance Induced by Morphine in Male Mice (Research Paper)

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Introduction: Repeated administration of Morphine as an opioid may cause tolerance to its different actions, including locomotor stimulating effect. The purpose of the current study was to evaluate the effects of isoniazid, as a GABAergic drug, on tolerance to morphine locomotor stimulating effect in mice.

Methods: Fourteen groups of male mice (22-30 g) were used. Acute locomotor effects of morphine (0,1,5,10,20,and 30 mg/kg, s.c.) or isoniazid (0, 25, 50, and75 mg/kg, i.p.) was evaluated using an infrared activity meter for 20 minutes. Tolerance to the locomotor effect of morphine was induced by injection of morphine (30 mg/kg, s.c., twice a day for 3 days). On the test day (day 4), One h. before administration of morphine (30 mg/kg, s.c.), one group (as control) received saline and the other three groups received isoniazid (25, 50, and 75 mg/kg, i.p.).Then, the locomotor activity of the animals was evaluated for 20 minutes.

Results: Morphine showed biphasic effects on the locomotor activity of mice. While morphine decreased the locomotor activity in low dose (5 mg/kg), it increased the behavior in high dose (30 mg/kg). On the other hand, isoniazid showed no significant effect on locomotor activity. Moreover, chronic administration of a high dose of morphine could induce tolerance to its locomotor activating effects, Tolerance was shown in control animals that received a challenging dose of morphine (30 mg/kg) on the test day. The animals showed reduced locomotor activity even with the high dose of morphine (30 mg/kg). Administration of isoniazid before morphine inhibited the expression of locomotor tolerance induced by morphine. The animals that received isoniazid before morphine had higher locomotor activity compared with the saline-treated group.

Conclusion: Isoniazid may inhibit the expression of tolerance to the locomotor-enhancing effect of morphine.

Keywords: Isoniazid, Morphine, Tolerance, Expression, Locomotor Activity

Insight to approaches of gene therapy on cystic fibrosis Review article (Review)

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Introduction: Cystic fibrosis (CF) is caused by mutations in the gene encoding the cystic fibrosis transmembrane regulator(CFTR), a cyclic AMP-activated chloride channel. Mutations in CFTR lead to imbalanced water and ion movement across the airway epithelium, resulting in thichened mucus, chronic bacterial infection and inflammation, with progressive loss of pulmonary function. CFTR modulators offer therapeutic opportunities for a wide range of CFTR mutation, which should enable treatment for approximately 90% of CF patients. CF gene therapy clinical trials by delivery of CFTR performed with Adeno-associated virus (AAV) and adenovirus, as well as non-viral liposome formulations continue to offer promise but so far have not led to the hoped-for clinical breakthroughs that this upproach offers. Gene therapy is an attractive strategy for CF lung disease because it treats the underlying cause of the disease rather than its symptoms. While gene correction showed limited success in both cell and animal models, therapy for patients had proven to be more difficult. In-vitro studies have suggested that not all cells need to express normal CFTR to effect normal epithelial functions. In a mixing experiment where normal cells were mixed with CF mutant cells, only 6-10% of the epithelium needed to contain epithelia cells expressing normal CFTR to restore chloride transport similar to normal epithelia. Conversely, in a gene targeting study, up to 25% gene correction could restore mucus transport in homozygous F508del human airway epithelial cells. The number of cells harboring wide-type CFTR that is needed to translate into clinical benefit in patience remains unknown. However, theoretically correcting a stem cell population within the airways may provide a renewable and long-term source of endogenous cells capable of renewing the damaged epithelia with cells that express wild-type CFTR. There are no other clinical trials for CF gene therapy.

Methods: There are several gene delivery methods to introduce a therapeutic gene or gene targeting. Both non-viral and viral delivery vectors have been tested in CF gene therapy research. (i) Non-viral vectors: Non-viral vectors were developed as a strategy to deliver the CFTR gene. These non-integrating gene delivery methods do not disrupt the host genome and thus the risk of causing mutagenesis are low. Non-viral vectors are not restricted in the cargo load enabling larger donor DNA fragments to be used for gene

repair. However, the efficacy of gene delivery is comparatively lower than viral methods. To enhance gene transfer into the nucleus, a cationic lipid is used to formulate the plasmid DNA complexed with CFTR enhanced chloride transport by 20% in CF patients compared to non-CF levels. Using a nebulized cationic lipid pGM169/GL67A to deliver the donor DNA, up to 3.7% increase in CFTR function in the lungs of CF patients was observed.

Results: Gene therapy for cystic fibrosis will mean a completely different disease and life perspective for many patients. New approaches need to be pursued to propose a disease-modifying treatment for all patients. For those who bear rare mutations that might be responsive to current CFTR modulators, new ways of evaluating drugs in very scarce population are worked on.

Conclusion: an effective therapy to treat all CF remains a challenge. While the discoveries of new small molecule modulators have greatly advanced treatment for some CF, the Since the discovery of the CF gene over 30 years ago, it has become apparent that finding effectiveness of these lifesaving drugs have not been universally effective and rather limited to specific classes of mutations. Rare CFTR variants remain uncured. Now, with recent advances in new gene editing tools, and new animal models, new precise gene targeting methods to treat CF disease will emerge and lead to potential effective personalized therapies. With new advancements in gene editing technologies coupled with advanced cell models to test gene engineering approaches, this will lead to rapid developments of new therapies for all CF.

Keywords: Cystic fibrosis Disease Treatment Gene therapy Gene disease

insight to Cushing syndrome review article (Review)

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Introduction: Cushing's syndrome is a life-threatening disease. This disease can appear both exogenously and endogenously. Its exogenous disease is caused by a glucocorticoid or adrenocorticotropin hormone (ACTH). If it is endogenous, it is caused by a latent increase in cortisol or ACTH. CS can be ACTH dependent or not. research has shown that more than 20% of adults with CS are non-ACTH dependent. This is also the case for about 15% of children over the age of seven. Symptoms of CS include such as: cracked skin or striae(mostly seen on the sides, thighs and armpits), roundness of face and neck, visceral obesity, acne, bruising, swelling, short stature, hirsutism, hypercortisolism, hyperglycemia, increase LDL, decrease HDL, hypertension, hypercoagulability, osteoporosis, depression, fatigue, cognitive disorders, weight gain, proximal muscle weakness, adrenal and pituitary tumors, menstrual disorders, infection(skin infection, urogenital infection and etc), etc. the most common visual symptoms in CS are weight gain and BMI increase(BMI>30). which helps doctors in the initial diagnosis of the disease by observing these symptoms. this disease is followed by diseases such as diabetes, heart attack and stroke, thromboembolism. hypertension, thromboembolism and infection are the main causes of death in this disease.

Methods: Excessive increase in glucocorticoid plays significant role in this disease. glucocorticoid affects both inflammatory proteins and the immune system. Salivary cortisol is more common in patients with ACTH dependent. even a slight increase in cortisol can cause hypertension, and hypertension usually persists after treatment. Of course, this disease is less common in children and sometimes may be seen in infants, and also in patients with CS, the probability of pregnancy is very low. Pregnant women with CS have high cortisol, high blood pressure and skin cracks and are at high risk of death.in pregnant women with CS, there is a risk of miscarriage, premature birth, and intrauterine growth restriction. Due to physiological changes in pregnancy, the diagnosis of CS is difficult and complicated. Bone changes in this disease affect the physical and functional structure of the body.30% to 40% of patients suffer from bone fractures and 50% have osteoporosis. Their growth can fail. It leads to a decrease in bone mass and short stature in adulthood. the focus of osteoporosis is more on the spine. of course, it affects the ribs and long bones. hypertension is the most common symptom, affecting about 80% of people with CS. It increases cardiac output and increases peripheral vascular

resistance. Infection of viruses such as HPV, Herpes Zoster, COVID-19, etc. are more effective in this patients. Pituitary adenoma is a common intracranial symptom In CS that is a sign of benign. 25% to 35%pituitary adenoma is an invasive factor and has a profound effect on the secretion. the internal tumors of these patients are usually more than one centimeter long and the size of the tumors may not change annually.

Results: thrombosis is one of the most important symptoms, which is related to the age of individuals and occurs more in women than men. increases coagulation and fibrinolactic.so coagulation inhibitors are needed.

Conclusion: however, some factors cause an increase in false cortisol, such as mental and physical stress, chronic and acute obesity, pregnancy, chronic exercise, depression, alcohol, anxiety, drinking more than 5 liters of water a day, malnutrition, smoking and drug use.

Keywords: cortisol, viruses, pregnancy, hypertension, glucocorticoid

insight to teratogenc virus treatment review article (Review)

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Introduction: Teratogenic virus the causes of intrauterine infections in humans,which cause fetal death or congenital malformations in children. Teratogen is a substance, organism or process that can harm a fetus during pregnancy. Teratogens can be an infectious agent, medicines or drugs or types of environmental exposures . Teratogens may produce physical or functional defects in the human fetus after the pregnant woman is exposed to the substance.

Methods: Most of the teratogens act via an unknown mechanism on developing cells and tissues to start a cascade . Congenital anomalies can occur during the developmental stages of the embryo ,form abnormal genetics.they cause teratogenic agents there is a greater risk to the fetus,as these abnormalities may not be detected until birth. These are anomalies the origin of illness and disability after childbirth defects can also lead to death.

Results: In this article,the purpose of investigating rubella, Zika and covid-19 viruses. Rubella virus(RV) is one of the main causes of birth defects and fetal death as a function of infection in pregmant women. in 1941, an Australian ophthalmologist, Norman McAlister Gregg noticed, that infants born with congenital cataracts also had congenital heart disease.The birth defects seen in infants include blindness, deafness, congenital heart disease, mental retardation and neurological complications, all of them collectively referred to as congenital rubella syndrome (CRS). Zika virus infection in pregnancy,regardless of the trimester of pregnancy it have major or minor abnormalities . neurodevelopmental assessment shows that Zika can cause a developmental delay in infants with motor area. ZIKV infection can cause Zika disease, characterized by rash, pruritus, arthralgia, headache,myalgia, and fever, among others syndrome called Congenital Zika Syndrome (CZS). Some anomalies caused by intrauterine ZIKV infection can manifest postnatally, such as postnatal microcephaly and neurodevelopmental disorders, that could affect cognitive, motor, and social functions teratogens can be either different types of chemicals,drugs,physical radiationsor even infections. Congenital infections can be transmitted form mother to child through the placenta , childbirth ,or during childbirth . For the treatment of COVID-19 or its symptoms,many drugs are bening used ,with potential teratogenic risks,including combined therapy with hydroxychloroquine and

azithromycin .Both Zika and Covid-19 pose a threat to the health of pregnant women Although ZIKV disease and COVID-19 share many similarities, the vectors, transmission, and epidemiology are distinct . ZIKV is a single-stranded RNA virus from the flavivirus (or vector-borne pathogen) genus, primarily transmitted by the Aedes aegypti mosquito. In addition, the virus can be transmitted vertically from the pregnant person to fetus in all trimesters of pregnancy, through blood products, blood transfusion.

Conclusion: the measles virus is one of the most dangerous human teratogen viruses, and in general, teratogen viruses have severe risks for pregnant women and fetuses.

Keywords: Teratogenic.Virus .Rubella .Covid . Pregnancy

Insight to virus therapy review articles (Review)

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Introduction: This is how viruses are used as therapeutic agents to treat some diseases. This treatment falls into three categories: 1. Oncolytic virus therapy: A promising strategy against cancer. Oncolytic viruses (OV) can replicate in cancer cells but not in normal cells. Leads to dissolution of the tumor mass. Additionally, the main effect of OV is to stimulate the immune system. In fact, this is a particularly promising new treatment for metastatic cancer. 2. Viral gene therapy (gene transfer): In this method, non-replicating viruses are often used to deliver therapeutic elements to cells of inherited diseases. New genes are introduced into cancer cells or surrounding tissues, causing cell death or slowing the growth of the cancer. This therapy is very flexible, with a wide range of genes and vectors yielding successful results in clinical trials. It has been used, but can also be used alone or in combination with current therapies to make cancer a manageable disease. 3. Viral immunotherapy (immunotherapy): This method uses viruses to introduce specific antigens into the patient's immune system.

Methods: Unlike traditional vaccines, which use attenuated or killed viruses or bacteria to generate an immune response, viral immunotherapy uses genetically engineered viruses to deliver specific antigens. Recent clinical trials of 2nd and 3rd generation vaccines have shown promising results in a variety of cancers including lung, prostate, pancreatic and melanoma. New treatment options need to be developed to reduce or eliminate cancer mortality. For example, systemic toxicity of chemotherapy regimens, although less severe than in the past, often causes acute and delayed nausea, stomatitis, and mild cognitive impairment. Treatments for metastatic prostate cancer, while prolonging life, often cause hot flashes, sexual lethargy, incontinence, and the risk of fractures. We need new ways to reduce these symptoms and reduce death and cancer pain.

Results: Immunotherapy, or boosting the immune system to kill cancer cells, has been studied for more than 100 years. However, conventional immunotherapy has had limited success because cancer cells tend to develop mechanisms to evade immune detection. Various methods of gene therapy are used to overcome this limitation. Currently, gene therapy is used to produce recombinant anti-cancer vaccines. Unlike vaccines for infectious agents, these vaccines do not develop to prevent the disease, but treat or

prevent the immunos system from detecting cancer cells. First, sample of sick cancer cells They are well recognized by the immune system. These modified cells are cultivated and destroyed in the laboratory, and the contents of the cells are incorporated into the vaccine. Another new direction in this therapeutic approach is the use of oncolytic vectors to kill cancer. Oncolytic therapy vectors are usually viruses that have been genetically engineered to target and kill cancer cells. They are harmless to the rest of the body and aim only to infect cancer cells and induce cell death through viral replication, expression of cytotoxic proteins and cell lysis. Gene therapy can treat a wide range of inherited and acquired diseases, and viral vectors can become a better treatment method with therapeutic drugs. Currently available viral vectors for gene therapy are various viruses, including adenovirus (AVV) and retrovirus (retroviral vector). Also simplex virus type 1 (HSV-1 Vector), Reovirus and Newcastle disease virus are chosen in many cases because of their natural ability to target cancer as well as ease of genetic manipulation.

Conclusion: A wide range of diseases that can benefit from gene therapy, such as viral vectors with special needs (tissue-specific delivery and gene expression) Therefore, it is unlikely that a single vector system will be sufficient for all purposes of gene therapy. It is clear that the future of virus-based vectors is bright, and the potential to fight many human genetic diseases is within reach. But unfortunately, modern medicines are still associated with complications, and for many diseases we have a long way to go before finding the right treatment. However, gene therapy approaches promise an impact on human health in the future.

Keywords: AVV- gen therapy- virus therapy- immunothrapy Vector-vaccines

Integrated system biology investigation (in-silico) of Co-expression of the lncRNAs and mRNAs associated and multiple intracellular signaling Pathways, with the Cervical carcinoma (Research Paper)

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Introduction: Cervical carcinoma is the second, most common cause of death and the most malignant reproductive disease seen among females worldwide[1][2][3]. Dysregulated genes identified in cervical cancer clinical samples may help develop prognostic markers and therapeutic targets[3]. The expression mRNAs microarray from Gene expression profiling in cervical cancer tissue was analyzed. A single local base-pairing interaction occurs between mRNAs, miRNA interaction analysis reveals that miRNAs regulate the expression of mRNA and lncRNA in an interaction axis, and we also demonstrate strong interactions between miRNAs and lncRNAs. CDKN2A is known to be an important tumor suppressor gene[4]. CDKN2A, FOS and CCNA2 may be related to the occurrence of cervical squamous cell carcinoma[1][2][5][6][7]. The FOS proteins have been implicated as cell proliferation, differentiation, and transformation regulators. In some cases, expression of the FOS gene has also been associated with apoptotic cell death[4]. The protein encoded by the CCNA2 function as a regulator of the cell cycle[4].

Methods: Gene expression profiling in cervical cancer tissue GEO2R and DAVID database with GSE127265 was examined. The genes with logFC > 3 & logFC < -3 are considered as the differentially expressed genes (DEGs) in this dataset. The adjusted p-value (adj. P. Value) < 0.05 is considered the statistical significance level. miRNAs were regained from DIANA tools Tar Base v.8 databases, followed by Interaction lncRNAs and mRNAs by lncRRisearch databases and lncHUB databases. The DIANA tools TarBase v.3 were used to analyze miRNA–mRNA interactions. The Pathway enrichment analysis was carried out using the online databases KEGG and Reactome. The expression of lncRNAs in different tissues has been examined by the lnCAR databases. comparing the expression of genes in different tissue by Gepia2 databases and the protein-protein interaction analysis by STRING online software.

Results: We found that CDKN2A, FOS and CCNA2 mRNAs had the highest expression changes (adj. P. Val<0.05) in cervical cancer. miRNA interaction analysis revealed that hsa-let-7b-5p could regulate the expression of CDKN2A, FOS and CCNA2 and Linc01566 lncRNA in cell line HELA from Cervix tissue in an interaction axis which indicates the existence of a complex

network. Interaction analysis of CDKN2A, FOS and Linc01566 lncRNA illustrated have a single local base-pairing interaction (Energy = -22.25 kcal/mol) and (Energy = -12.34 kcal/mol). Besides, there are common pathways between CDKN2A, FOS and CCNA2 including Pathway in cancer, Human Tcell Leukemia Virus 1 Infection and Cell Cycle. Additionally, FOS is involved in the MAPK signaling pathway and CDKN2A plays an important role in the P53 signaling pathway that the MAPK and p53 signaling pathways lead to Apoptosis.

Conclusion: We identified the hub lncRNA-mRNA network involved in regulating various biological processes in cell line HELA from Cervix tissue. CDKN2A, FOS and CCNA2 mRNAs and also, Co-Expression Linc01566 lncRNA and hsa-let-7b-5p miRNA could be prognostic biomarkers in cervical cancer. Moreover, CDKN2A by using The Cell cycle and P53 signaling pathway, FOS with such an effect on MAPK signaling pathway/ Estrogen signaling pathway and CCNA2 Through a block of differentiation would be able to regulate the CELL proliferation in Pathway Cancer.

Keywords: cervical cancer, P53 signaling pathway, Apoptosis, CELL proliferation, complex network

Integrated systems biology and bioinformatics analyses of gene expression profile in pancreatic adenocarcinoma-related signaling pathways (Research Paper)

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Introduction: Pancreatic adenocarcinoma (PAAD) which is often associated with a poor prognosis is one of the most lethal diseases[1]. Over the last decade, The massive amounts of data and technology generated by Biological scientists and their analysis and interpretation cause Steadily, traditional approaches to laboratory work are changing towards the age of bioinformatics. [2]

Methods: At first, gene expression data of PAAD patients (GSE130221) were collected from NCBI Gene Expression Omnibus(GEO) database and analyzed by the GEO2R database to find differentially expressed genes (DEGs). Then GEPIA2[3] and ENCORI [4] databases were used to check and strengthen the possibility of a correlation between the found gene and pancreatic adenocarcinoma. Next, from Enrich[5] and Reactome[6] databases to check pathways and ontologies, and from string[7] – miRWalk[8] - lncRRisearch[9] - lncbase .v3[10] databases to find significant interactions between protein-protein, mRNA-miRNA in the 3'UTR region, LncRNA- mRNA, lncRNA-miRNA, and ceRNA were used.

Results: By analyzing the GEO database data, a gene called FAM83A was found whose expression was significantly increased and upregulated in the PAAD sample. (Log FC = 7.21 , adj.P.Val = 7.64E-4) . The product of this gene is a protein of 434 amino acids with the same name, which functions in the epidermal growth factor receptor(EGFR)signaling pathway. Activates both RAS/MAPK and PI3K/AKT/TOR signaling cascades downstream of EGFR. Required for the RAS/MAPK signaling cascade activation upon EGFR stimulation, it also activates both signaling cascades independently of EGFR activation In this way, it can lead to the induction of cancer in the pancreas(unirpot database) [11]. Analysis of possible miRNA-mRNA interactions revealed hsa-miR-939-5p as a significant factor for fam83a gene mRNA. Then this miRNA was searched in the LncBase v.3 databases and finally lncRNAs AATBC, DBET, LINC02554, H19 had the most and best interactions.

Conclusion: In conclusion, FAM83A is overexpressed in PAAD and forms a possible ceRNA network among hsa-miR-939-5p, AATBC, DBET, LINC02554, AND H19.

Keywords: Pancreatic adenocarcinoma, FAM83A , Cancer , CeRNA , Bioinformatics

Integrating multi-omics datasets and multimodal imaging features toward correct diagnosis and treatment of neurocognitive disorders (Review)

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Introduction: Neurocognitive disorders (NCDs) are heterogeneous group of diseases accompanied by cognitive decline. With the prevalence of nearly 50 million patients worldwide, NCDs rises exponentially with the increasing ageing population. Hence, early diagnosis which provides care at the earliest possible stage will improve the diseases outcome. Due to exploring the interactions across multiple types of biological features, multi-omics studies have the ability to provide a holistic view of causal and functional mechanisms associated with complex diseases. Moreover, utilizing multimodal imaging modalities in clinical and preclinical settings yields the complementary and complete visualization of diseases and their stages. Here, we present a viewpoint on how the diagnosis and treatment of neurocognitive disorders could be improved by multi-omics and multi-modal imaging data integration.

Methods: We searched relevant studies through PubMed/Medline and Google Scholar.

Results: The use of multi-omics and multimodal imaging modalities might have the potential to be the gold standard approach in the modern clinical practice to a correct disease diagnosis.

Conclusion: Novel data analysis methods are required to integrate multimodal molecular-omics and neuroimaging data acquired from multiple experiments in different conditions and to determine the relevance of the results to human disease.

Keywords: Neurocognitive disorders, multi-omics, multimodal imaging, data integration

Integrative analysis to prospect potential biomarkers related to colorectal cancer diagnosis via Artificial Intelligence (Research Paper)

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Introduction: Introduction: Even though colorectal cancer is one of the most prevalent digestive tract cancers, the exact rationales of the pathophysiological mechanism and related genes are still a puzzle. Therefore, gaining comprehensive insight into the pathomechanism and identifying hub genes associated with colorectal cancer susceptibility can shed light on current diagnostic and treatment methods. Text mining and artificial intelligence surveys have revealed a complex cross-talk between genomics, transcriptomics, epigenomics, methylomics, family history, and environmental terms like gut microbiota alteration, diet pattern, infection, metabolic disorders, mental conditions, and inflammation may all play a role in causing gastrointestinal damage.

Methods: Methods: In this comprehensive analysis, genome-sequencing and high-throughput data have been used to pinpoint the genes that make constitute the intracellular signaling networks that govern biological processes. On the other hand, data analysis of non-coding RNAs indicated the significant effects of epigenetics, microRNAs, and lncRNAs practice critical roles in the susceptibility, risk, development, and progression of tumors from normal to end-stage colorectal tumors.

Results: Results: Based on artificial intelligence surveys, protein-protein interactions network analysis, and enrichment of molecular signaling pathways related to colorectal pathogenesis and progression rate, we provided a list of significant differential expressions of genes, lncRNAs, and microRNAs that might present prospective molecular genetics markers. Hence we suggested that significant differential expressions of genetic markers with high connectivity and positive feedback loops, known as hub nodes, tend to become master switches in the development and progress of tumoral cells.

Conclusion: Conclusion: Here, we achieved comprehensive biomarkers for monitoring and follow-up of the colorectal state that could be practically significant efforts on prognosis and diagnosis approach.

Keywords: Keywords: Colorectal Cancer, Artificial Intelligence, Biomarkers

Interaction between mitochondrial related anti-oxidant genes, and cancer cells apoptosis induction by ELF-EMFs (Review)

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Introduction: Extremely Low-Frequency Electromagnetic Fields (ELF-EMFs) with frequencies from 0 Hz to 300 Hz which are classified as the non-ionizing radiation of the electromagnetic spectrum are not too strong to damage DNA or to induce thermal effects on tissue. On the other hand, ELF-EMFs can specifically inhibit cancer cell proliferation in vitro and in vivo; this may depict a bright promising future as a cancer treatment candidate. In this regard, different underlying mechanisms of action have been proposed for this anti-cancer effect. Recently, it has been stated that ELF-EMFs affect apoptosis-related molecular pathways through increasing reactive oxygen species (ROS) levels and changing the balance between ROS and the antioxidant system (oxidative stress) which modulate cell fate and orchestrate apoptosis. However, the exact source of ROS elevation induced by ELF-EMFs in cancer cells is not transparent. In this area, mitochondria, one of the major resources of ROS production, can be considered as the main mechanism in increasing ROS levels by ELF-EMFs and consequently apoptosis induction. Hence, the aim of this study is to review the impact of ELF-EMFs on the mitochondria and affected underlying pathways in different types of cancer cells.

Methods: Related articles were selected from databases like PubMed, Scopus, ScienceDirect, and Google Scholar with the following keywords: ELF-EMF, mitochondria, anticancer, ROS, apoptosis, and proliferation.

Results: Exposure to ELF-EMFs could up-regulate the MAPK signaling pathway which promotes the expression level of peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PPARGC1A, also known as PGC-1α). PGC-1α plays a key role in oxidative metabolism which can enhance mitochondrial biogenesis and mitochondrial respiratory chain activity. Also, PGC-1α activates a transcription factor called nuclear factor E2-related factor 2 (Nrf2). Increased ROS level by mitochondrial respiratory chain and imbalance between ROS and ROS scavengers, antioxidant enzymes, leads to

activation of Nrf2 which binds to the antioxidant response elements and promotes expression level of antioxidant enzymes such as catalases, superoxide dismutases (SODs), and glutathione peroxidases to balance redox status. On the other hand, ELF-EMFs exposure could induce sirtuin-3 (SIRT-3) expression level, the regulator of antioxidant machinery and mitochondrial oxidative responses. Overexpression of SIRT-3 increases the expression level of mitochondrial SOD (SOD2) and catalase in favor of maintaining redox balance. In addition, SIRT-3 reduces ROS levels by deacetylating forkhead box O 3a (FoxO3a), a transcription factor that increases the level of SOD2 and catalase.

Conclusion: As mentioned above, the accumulation of intracellular ROS levels and cellular oxidative stress can promote the expression level of PGC-1α to maintain redox balance by increasing the level of ROS scavengers. Hence, during oxidative stress in cancer cells, PGC-1α has an important role in cellular adaptation and reprogramming which leads to cancer cell proliferation and survival. Also, the promoted expression level of PGC-1α is related to metastasis and poor prognosis in patients with cancer. In this case, PGC-1α silencing leads to mitochondrial dysfunction which can reduce the viability and invasion of tumor cells and can induce apoptosis through mitochondrial apoptotic pathways. In addition, SIRT-3 can either affects the quality of function or the quantity of mitochondria. Knockdown of this mitochondrial deacetylase brings out mitochondrial dysfunction and reduces cancer cell viability. Thus, PGC-1α and SIRT-3 genes silencing become one of the therapeutic targets in cancer treatment programs. Also, reactive oxygen species molecules take part in various intracellular signaling pathways and it is demonstrated that ELF-EMFs influence multiple signaling cascades in exposed cells by means of ROS perturbation in favor of apoptosis activation processes. So, using these fields in association with PGC-1α and SIRT-3 silencing could be effective in cancer treatment.

Keywords: ELF-EMF, mitochondrial ROS, anti-cancer, PGC-1α, SIRT-3

Interaction Up regulated VCAN gene and mi RNA in pancreatic cancer (Research Paper)

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3.

Introduction: Pancreatic cancer (PAAD) is malignancies which is predominantly seen in men and at advanced age (40-85) and has an aggressive course. It accounts for2% of all cancers and 5% of cancer-related deaths .the disease is very difficult to detect as it has no early signs and spreads rapidly to surrounding organs is one of most deadly types of cancer.(1)

Methods: This investigation aimed to study expressed gene(VCAN)in data of pancreatic ductal adenocarcinoma and normal tissue . Expression analysis of GSE132956 achieved from GEO2R online software and validation of expression analysis performed by GEPIA2 and ENCORI database.(2)Single nucleotide polymorphisms (SNPs) of VCAN extracted from d b SNP and identification of deleterious SNPs Brought out from SIFT database (3)Based on microarray analysis ,VCAN have significant up-regulation in the PAAD samples,(fold change,.27_p.value0.013).(4)database was then used to reinforce the possibility of correlation between the VCAN gene and PPAD cancer. furthermore , mi R Walk were utilized to find significant mi RNA-mRNA interaction in the 3UTR region .(5)

Results: Analysis of possible mi RNA –mRNA interaction revealed has-miR-6895-3p as a significant connection to VCAN mRNA .This mi RNA was a novel mi RNA in the Pub med database .(6)The VCAN gene have 8number Ln c RNA in the Ln c R research data base and were RNA gene and significant Ln c RNA in the gene card data base .(7)The mi RNA have expression and survival significant by PAAD samples in the data base ENCORY .

Conclusion: In conclusion ,VCAN gene is a high expressed in PPAD patient and have assoieate significant by miRNA (has –miR -6895-3P)and ENST00000627551 and 7 number Lnc RNA another that to create a network ce RNA,

Keywords: Key word :PAAD _ pancreatic cancer

Interleukin-6 gene polymorphisms and gastric cancer: A Systematic Review and Meta-Analysis (Review)

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Introduction: Gastric cancer is the fifth leading cancer which common both in men and women in developing countries. Less than 5% of stomach cancers occur in people under 40 years of age, with 81.1% of that 5% in the age-group of 30 to 39 and 18.9% in the age-group of 20 to 29. Cancer is a multi-factorial progressive illness which advanced under the impact of genes. Interleukin-6 (IL-6) is a pleiotropic, pro-inflammatory cytokine involved in many biological processes, including cancer and autoimmune diseases. Different types of cancers were influenced by the three SNPs (rs1800795, rs1800796 and rs1800797) of the IL-6 gene. This study aimed to investigating Interleukin-6 gene polymorphisms and risk of gastric cancer as a Systematic Review and Meta-Analysis.

Methods: This study was performed based on the PRISMA guideline. Documents gathered by searching through the Web of Sciences, Scopus, PubMed/Medline, OVID, and COCHRANE databases which published before 0101/2022 that related to interleukin-6 gene polymorphisms and risk of gastric cancer. Articles were searched using standard keywords as well as Mesh and Mesh Entry and all probabilistic combinations of words using Boolean operators. Data searching, extracting and quality appraising were done by two researchers, independently. At last, Random-effects size based on Cochrane test and I2 were used. Data analysis was performed using the Comprehensive Meta-Analysis Ver.2, and the significance level of the test was considered less than 0.05.

Results: Based on the meta-analysis conducted in 14 included studies, the total sample size of patients with 7788. The IL-6 -572G/C polymorphism had significant relationship with the increasing risk of stomach cancer under four genetic models [C vs. G: OR = 1.16, [95%CI: 1.03–1.30], p-value = 0.0069; CC vs. GG: OR = 1.41, [95%CI: 1.10–1.81], p-value = 0.0076; CC vs. CG + GG: OR = 1.29, [95%CI: 1.07–1.55], p-value = 0.0080; CC + CG vs. GG: OR = 1.41, [95%CI: 1.09–0.81], p-value = 0.0088]. The IL-6 -596G/A polymorphism had no relationship with the increasing risk of stomach cancer under four genetic models [AA vs. GG: OR = 1.71, [95%CI: 0.54-5.34], p-value = 0.3551; AA vs. AG+GG: OR = 1.83, [95%CI: 0.6-5.37], p-value =

0.2846; AA+AG vs. GG: OR = 0.98, [95%CI: 0.54-1.76], p-value = 0.9657; AG vs. AA=GG: OR = 1.21, [95%CI: 0.67–2.2], p-value = 0.530]. As the same, the IL-6 -174G/C polymorphism had no significant relationship with the increasing risk of stomach cancer under four genetic models [C vs. G: OR = 1.12, [95%CI: 0.85-1.5], p-value = 0.4087; CC vs. GG+GG: OR = 1.07, [95%CI: 0.81-1.40], p-value = 0.6450; CC+CG vs. GG: OR = 1.08, [95%CI: 0.92-1.22], p-value = 0.4317; CG vs. CC+GG: OR = 1.041, [95%CI: 0.9–1.19], p-value = 0.6024].

Conclusion: Results from this study, more confidently showed that the IL-6 gene SNPs (rs1800795, rs1800796 and rs1800797) in humans are related with increased cancer risks. Therefore, these three polymorphisms of the IL-6 gene have the potential to be evaluated as a population based rapid, low-cost PCR prognostic biomarkers for different types of cancers diagnosis and research.

Keywords: Interleukin-6; Gene polymorphisms; Gastric Cancer

Investigating antimicrobial effect of the concentrated extract powder of Scrophularia striata plant on Streptococcus mutans and Streptococcus sobrinus strains (Research Paper)

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Introduction: acteria in the oral cavity, including Streptococcus species, can be an important cause of tooth decay and plaque in the presence of predisposing factors. This problem causes most people in the society to spend a lot of money on dentistry every year. Therefore, in order to prevent and treat properly, using a low-cost and safe method based on medicinal plants can increase the general health of the mouth and teeth. On the other hand, the consumption of natural compounds is also very important in preventing the emergence of antibiotic resistance of microorganisms that cause oral and dental infections. Therefore, the purpose of this study is to investigate the antibacterial effect of this valuable plant and to find a mouthwash formula based on medicinal plants and traditional medicine for oral and dental health.

Methods: In this research, first, extracting from the plant (S. striata) was done by maceration. Then, by using rotary devices and spray dryers, the aqueous extract was concentrated and powdered, and serial concentrations were also prepared from the concentrated extract powder. Finally, the minimum inhibitory and lethal concentration (MIC and MBC) concentrations of 20, 30, 40, 50, 60, 70, 80 mg/100 ml prepared from the mentioned plant, on the standard strains of Streptococcus mutans ATCC 35668 and Streptococcus subrinus ATCC 27607 was investigated.

Results: After exposing the bacteria to different concentrations of the extract, the results of their culture on tryptose soy agar medium show that the minimum inhibitory concentration for Streptococcus mutans is 40 mg and the minimum lethal concentration is 60 grams, and for Streptococcus subrinus The minimum inhibitory concentration was reported to be 30 gr/ml and the minimum lethal concentration was 50 mg/ml for this strain.

Conclusion: According to the results obtained in this research, the extract of Scrophularia striata plant can be used to make mouthwashes and effective drugs in controlling oral infections and tooth decay.

Keywords: Infection and tooth decay, Scrophularia striata, Streptococcus mutans, Streptococcus subrinus

Investigating ARRB1 gene expression under tumor microenvironment mimetic conditions in MDA-MB-231 cells (Research Paper)

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Introduction: Cancer is a complex disease that can be defined as a human disease with genetic heterogeneity. Because it is determined by a few special adaptations, such as pH dysregulation is a major symptom in solid tumors. Compared to normal tissue, solid tumors are characterized by extracellular acidification and intracellular alkalinization. Therefore, the study focuses on the different concentrations of glucose and hypoxia on the expression of the ARRB1 gene in the MDA-MB-231 breast cancer cell line.

Methods: The MDA-MB-231 cells were culture in RPMI culture medium with 5.5, 11, and 25 mM glucose and oxygen of %1 and %21. In the next step, the RNA was extracted and cDNA was synthesized. Finally, the expression of ARRB1 mRNA is checked by real-time PCR.

Results: MDA-MB-231 cells in hypoxia conditions and over time compared to other different treatments have adapted morphological. RAAB1 gene expression showed a significant increase ($P \leq 0.01$) in 24 hours. While this increase in 48 hours only in normal conditions of normoxia and 25 mM glucose at the level of $P \leq 0.001$ and in 72 hours of expression at the level of $P \leq 0.001$ showed a decrease in expression.

Conclusion: Increasing or decreasing the concentration of glucose and hypoxia changes the expression profile of cancer cells and can affect the condition type and step.

Keywords: pH dysregulation, hypoxia, solid tumors, ARRB1

Investigating changes in the expression of ATP4B and ATP4A genes as potential factors in gastric cancer: a study based on gene expression omnibus (GEO) and bioinformatics analysis. (Research Paper)

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Introduction: Gastric cancer (GC) is the fifth most common cancer and the third leading cause of cancer death in the world. Stomach cancer, also called gastric cancer, begins when the healthy cells of the stomach change and become abnormal and grow out of control, and the result of these excessive divisions is the formation of a tumor. This type of cancer is caused by glandular cells in the innermost lining of the stomach (mucosa). Risk factors for this disease include: include Helicobacter pylori infection, age, high salt intake, and diets low in fruit and vegetables. This study aims to discover a new mechanism that has shown the interaction between RNAs (mRNAs, lncRNAs, miRNAs). In cancer cells, these interactions (expression levels) change compared to normal conditions and provide useful information about the disease

Methods: The significance of gene expression in gastric cancer was analyzed by analyzing raw data (GSE29272) from the Gene Expression Omnibus (GEO) database and then by GEO2R to find differentially expressed genes (DEGs) and also from the databases miRWalk, KEGG PATHWAY, lncBase v.3, STRING, GeneCards were used.

Results: ATP4B gene with logFC=6.054, which has the highest expression change among the genes related to this disease, together with ATP4A gene with logFC=5.213 can be effective in gastric cancer and regulate the progress of this disease. Using the KEGG PATHWAY database, it was found that Metabolic pathways(Glucose metabolism in gastric cancer cells differs from that of normal epithelial cells) and Gastric acid secretion signaling pathways for these two genes can be effective in this disease by influencing these signaling pathways. Then miRWALK was used to find miRNAs for ATP4B gene mRNA in the 3UTR region of this mRNA and hsa-miR-518a-3p and hsa-miR-27a-5p miRNAs were selected. hsa-miR-518a-3p miRNA was used to find lncRNAs in lncbase v.3 database and LINC00987 and SCARNA9

lncRNAs were found to have strong interactions. ENCORI was also used to validate the selected lncRNAs. STRING was used to find the interaction between the protein of this gene and other proteins, and this protein is related to ATP7B and ATP12A proteins.

Conclusion: According to these findings, it can be concluded that the higher expression of ATP4B and ATP4A genes and the effect on the signaling pathway of gastric acid secretion and metabolic pathways, as well as the creation of a possible ceRNA regulatory network between hsa-miR-518a-3p and LINC00987, SCARNA9 and their regulatory effect on the mRNA of this gene, can cause stomach cancer.According to these findings, it can be concluded that the higher expression of ATP4B and ATP4A genes and the effect on the signaling pathway of gastric acid secretion and metabolic pathways, as well as the creation of a possible ceRNA regulatory network between hsa-miR-518a-3p and LINC00987, SCARNA9 and their regulatory effect on the mRNA of this gene, can cause Gastric cancer.

Keywords: Gastric Cancer , GSE29272 , ATP4B ,ATP4A , miRNA

Investigating genetic and non-genetic risk factors and breast cancer detection methods in the population of South Fars women (Research Paper)

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Introduction: Carcinogenesis is a multifactorial process that is stimulated by two factors: genetic and environmental causes. Breast cancer is the most common cancer diagnosed in women worldwide, with more than 2 million new cases in 2020 but comparing the national estimates of the incidence of cancer in Iran (152.7 per 100,000) with other countries in the world, can be considered a medium risk area for cancer. The number of breast cancer risk factors includes modifiable and non-modifiable factors. Biomarkers such as steroid receptors and HER2 play a key role in evaluating the clinical course, prognosis, and determining the type of breast cancer treatment. In the present study, the relationship between these biomarkers ER, PR, HERB2, and malignancy tumor (clinical histology), detection, stage, tumor size, and nongenetic risk factors are analyzed. Breast cancer has a high chance of cure if diagnosed early and treated appropriately

Methods: This study is based on the data collected from the samples of 109 patients with breast cancer who visited Gerash University of Medical Sciences between 1397 and 1399, and at that time, using the immunohistochemical method on paraffin block. It was done to evaluate the level of estrogen, progesterone, and HERB2 receptors, and other information was collected through a questionnaire and laboratory test. Data were entered into SPSS 26 software and analysis was performed using the Chi-square method (P less than 0.05 was considered significant).

Results: In the current study, the highest age of disease in women was in the range of 35-44 years (35.5%) and the lowest rate of disease in women was 25-34 years (10.3%). Of course, increasing age in the study group increases the probability The average age of the patients was 41.2. The results showed that there is a significant difference between the average body mass index

and breast cancer stages. As the stage of breast cancer increases in patients, the amount of body mass index increases. Entering the advanced stages of breast cancer increases the body mass index. Age has no effect on increasing or decreasing body mass index. People whose body mass index is above 30 are diagnosed with stage 3 and 4 breast cancer (P≤0.05). In terms of the cancer tumor detection method, in 56.1% of the cases, Tru cat biopsy was the most used method and Fine needle aspiration Biopsy (Fna) with a fine needle was the least used method in 7.5% of the cases. Regarding the types of breast cancer (based on the site of involvement) in the patients who used the Tru cat biopsy method, the highest rate of breast cancer is related to invasive ductal carcinoma. Statistically, this type of cancer constitutes 90.9% of cancer cases. to give In the current study, estrogen receptor ER is positive in 71.7% of patients, estrogen receptor PR is positive in 61.6% of patients, and Herb2 is 3+ in 32.3% of cases. A direct relationship between the absence of the receptor and metastasis was seen in these patients. ≤0.05) Regarding the tumor size, the largest tumor size was between 2 and 5 mm at the rate of 56.7%. The size below 2 mm was 26.5% and the size above 5 mm was 10.0% and 2.2% were multiple tumors. It was proved in this study that tumor size is related to the tumor stage. In the examination of the side involved in breast cancer, which is divided into 4 parts, right, left, and bilateral, in the present study, 52%, 44.9%, and 3.1% were recorded, respectively. In terms of the location of cancer in the breast, the most part of the breast that has the possibility of cancer is the outer upper quadrant of the breast. Examining the study of gland metastasis to other parts of the body (distant metastasis), the most metastasis was to bone, liver, and lung with an equal amount of 4.7%, and in the next stage, the brain with an amount of 1.9%.

Conclusion: In a study in the south of the country, the relationship between the absence of genetic markers with a bad prognosis (tumor metastasis), the low average age of patients compared to abroad is about 9 years, and the relationship of the disease with a high body mass index, the relationship of tumor size and Tumor stage, and high probability of tumor location were proved in this research, but cancer genetic markers and genes were not related to the age of the patients. Examining reports on the status and comparison of breast cancer risk factors in access to breast cancer prevention methods in different regions of Iran is very useful.

Keywords: risk factors, breast cancer , detection, steroid receptors, clinical histology

Investigating possible mental injuries and brain injuries of COVID-19 (Review)

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Introduction: With the spread of the covid-19 pandemic, scientists started researching this issue to clarify the different angles of the infection of this unknown and new virus. In addition to clarifying the occurrence of lung infection, signs of some psychological and physiological damage were proven. Our study presents the results of reports and articles from around the world about the possibility of psychological and physiological damage of covid-19 on the nervous system. In this study, 125 related articles until June 2021 from databases such as Scopus, Pubmed, Web of Science, Google Scholar, and Google, and using keywords covid-19 brain damage, covid-19 infection, disease imaging findings covid-19, mental health, and covid-19 were extracted. Articles that were not the purpose of this study were excluded from the research process and finally, 43 articles were used. Due to the possibility of the SARS-COV virus not passing through the blood-brain barrier, a specific cause for neuropathological injuries and brain encephalopathies has not yet been introduced, and this mechanism is still unknown. An increase in the volume of the gray matter of the brain in the hippocampus and the olfactory bulb and an increase in anisotropy in the white matter fraction of the brain were reported in people who were suffering from the acute form of this disease compared to people who were not suffering from the corona. And psychologically, the occurrence of some styles of Symptoms such as rumination and anhedonia were confirmed in this disease and in affected people.

Methods: In this study, 125 related articles until June 2021 were found from Persian and English databases such as Scopus, Pubmed, Web of Science, Google Scholar, Google, and using the keywords covid-19 brain injury, covid-19 infection. Imaging data of covid-19 disease, mental health and covid-19 were extracted. The articles that were not the purpose of this study were excluded from the research process and finally, 43 articles were used in our research.

Results: The SARS-COV2 virus is a beta corona virus with a similar structure to its predecessor, SARS-COV, which has a genetic similarity of 70% with SARS-COV and more than 50% with the Middle East Respiratory Syndrome virus (MARS) (14). By binding to angiotensin (ACE 2) receptors on the surface of lung epithelial cells, the virus implants in this tissue and causes

symptoms of viral infections such as viral pneumonia and symptoms similar to MARS and SARS-COV. (15).

Conclusion: Considering the physiological and immunological changes in patients with the new coronavirus and the emergence of mental disorders, as well as the proof of the presence of this virus in CNS fluids, it is possible to recommend In people who have acute symptoms, MRI imaging must be used after recovery to check the possibility of brain damage in these patients, and also in hospitalized patients with acute symptoms, this imaging must be used for CNS in case of any changes .in the brain. The central nervous system can quickly control or treat these symptoms before certain events occur. Also, the importance of health and mental health of people who visit high-risk places such as hospitals and public places, such as medical staff and people who visit the market, doubles. It is hoped that the results of this study will be used by all people, especially the treatment staff so that post-corona mental injuries can be prevented.

Keywords: psychological, brain injuries, COVID-19

Investigating the antimicrobial effect of Fusarium metabolite isolated from Zea mays on Escherichia coli (Research Paper)

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Introduction: Fungi, as one of the most important plant pathogenic agents, are the main source of bioactive secondary metabolites, and they are of significant importance in environmental interactions, among which metabolites can be antibiotics, toxins, and enzymes.

Methods: In this research, the antimicrobial properties of the secondary metabolite isolated from Fusarium were investigated against the Gram-negative Escherichia coli bacteria.

Results: The results of the microbial tests showed that the metabolites extracted from the Fusarium fungus had an antibacterial effect on Escherichia coli bacteria with a concentration equivalent to 31.25 microliters. per milliliter. Regarding the minimum lethal concentration of bacteria by fungal metabolites, it was found that the metabolites extracted from Fusarium mushroom had a concentration equivalent to 62.5 microliters/ml. In the test to determine the antibacterial property using the disk method, it was found that the concentration of 15.6, 31.25 and 62.5 microliters/ml of the Fusarium mushroom metabolite could create a non-growth halo with a diameter of 6, 13.91 and 17.13 microliters/ml.

Conclusion: According to the obtained results, it can be claimed that the use of fungal metabolites to control the growth or even the death of bacteria can be useful as an alternative to antimicrobial chemical compounds.

Keywords: fungus, secondary metabolite, Escherichia coli

Investigating the association between MiR_199a-5p, miR-3120d and renal cancer in PI3K pathways (Research Paper)

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Introduction: Renal cell carcinoma (RCC) is the most common type (>80%) of kidney cancer. Claiming more than 100,000 lives per year worldwide, RCC accounts for about 3% of all adult cancers and its incidence is rising. With newer therapies, the median survival period of patients with advanced RCC is about 26 months. MicroRNAs (miRNA), are small noncoding RNAs that are emerging as important modulators in cellular pathways and appear to play a role in tumorigenesis, cell cycle, proliferation and apoptosis. So we purpose to evaluate the role of Ras, IKK, NFkB1, PI3K by mir-3120d, 199a-5p in renal cancer.

Methods: The feature of microRNA was archived by using mirbase. Target genes and predict one were identified by mirtarbase and mirwalk 2.0. Gene expression in normal and tumor tissue was obtained from NCBI. Finally, the pathway enrichment analysis was performed by the KEGG and David. GENEMANIA used to find gene network.

Results: The result dedicated that mir-199a-5p and 3120d by inhibiting Ras which actives Raf1, MEK, ERK through phosphorylation prevent proliferation of cancer cell and angiogenesis. IKK, NFkB were inhibited by blocking PI3K, which actives Ras. So MYC, BCL through inhibition cell survival, suppress cancer. Mir-199a 5p, and 3120d by inhibiting Ras, PI3K, IKK, NFkB through preventing cell cycle, prevent cancer development. Mentioned microRNAs, block NFkB by inhibiting PI3K which actives Act. So NFkB by inhibiting VEGF, suppresses cancer through inhibition angiogenesis.

Conclusion: Mir-199a-5p, 3120d by effecting on Ras, IKK, NFkB1, PI3K, in PI3K-Act, RAS, TNF and renal pathway effect on proliferation, angiogenesis and cell survival. Mentioned microRNAs by acting as tumor suppressor prevent cancer development and tumor spread by inhibiting proliferation of cancer cell, angiogenesis and sell survival.

Keywords: MicroRNA, Renal cancer, Signaling pathways, Expression gene

Investigating the challenging effect of complete genome sequencing on accurate sequencing of complex human genomic regions (Review)

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Introduction: The role of genome organization in regulating gene activity during development has been the subject of considerable debate. Scientists publish the first complete, non-chat sequence of the human genome. Two decades ago, the Human Genome Project produced the first draft of the human genome sequence, but sequencing remained at 8% of the genome. , The University of California, Santa Cruz, and the University of Washington. NHGRI was the main supplier of this study. The consortium used the complete genome sequence as a reference to discover more than 2 million other species in the human genome. Next-generation sequencing (NGS) can identify mutations in the human genome that cause disease and has been widely used in clinical diagnosis. However, the human genome contains many polymorphic, low-complexity, and repetitive regions that are difficult to sequence and analyze. Despite their complexity, these regions contain many clinically important sequences that can provide treatment for human disease and improve NGS diagnostic function.

Methods: This is a narrative review study in 2022 by searching for keywords such as generation sequencing, genomes, chromosomes, genomic variants, microsatellites in MESH and reputable databases such as Science Direct, Web of Science, and PubMed were searched and 15 articles were found, of which 10 articles were included in the study

Results: Complete genome sequencing analysis significantly adds to our knowledge of chromosomes. Including more detailed maps for the five arms of the chromosome open up new avenues for research. These results help us answer basic biological questions about how chromosomes are properly separated and divided. These studies provide more detailed information on genomic variants in 622 medically related genes. To evaluate the accuracy of NGS analysis of these difficult regions, we constructed a deceptive silicon chromosome, along with corresponding synthetic DNA reference controls, encoding difficult and clinically important human genome regions, including repeats, microsatellites, and HLA genes, and immunity. The receivers of these controls provide a well-known ground truth reference based on which

the performance of various sequencing technologies, reagents, and bioinformatics tools can be measured. Using this approach, we provide a comprehensive assessment of short and long-sequence reading tools, library preparation methods, and software tools, and identify systematic errors and biases that distort our clarity in these difficult remaining areas.

Conclusion: Once a person has sequenced their genome, we will be able to identify all the variants in their DNA and use that information to better guide their medical care.

Keywords: generation sequencing, genomes, chromosomes, genomic variants, microsatellites

Investigating the chronic effects of curcumin and niosome curcumin on Alzheimer's rats by marble burying and object recognition tests (Review)

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Introduction: Introduction: Alzheimer's disease (AD) is one of the most common neurodegenerative diseases for which there are currently no effective drugs to prevent and treat. Exposure to aluminum chloride increases neurotoxicity and oxidative stress in the brain and causes memory disorders, and antioxidants counteract these effects. The curcumin antioxidant(CUR), which is a natural polyphenol, has anti-inflammatory properties and improves memory and learning by crossing the blood-brain barrier, and therefore can be used to treat neurological diseases associated with oxidative stress, inflammation, and apoptosis.In this study, we investigated the long-term effect of curcumin antioxidant and niosome curcumin on memory and learning and stress and anxiety levels of Alzheimer's rats by object recognition and marble burying tests.

Methods: Materials and methods: In this study, 56 male rats were randomly divided into 3 groups (n=8): 1)control (28 days of saline), 2)sham (14 days of ethanol), 3)aluminum chloride (Alzheimer's)(28 days), 4)aluminum chloride + curcumin, 5)curcumin (14 days), 6) niosome curcumin (7 days), 7) aluminum chloride + niosome curcumin. (Injection of drugs is intraperitoneal). Memory and learning were evaluated by the object recognition test on the 14th day, and stress and anxiety were evaluated by the marble burying test on the last day of injection.

Results: Results: The data analysis showed that the curcumin and Noisome Curcumin groups buried more marbles compared to the Alzheimer's group (p<0.001) and the sham group had a significant increase compared to the control group (p<0.001). The Alzheimer's group was not significant in comparison with the control group (p>0.05) and also the noisome curcumin and curcumin group had a significant increase compared to the control group (p<0.001). In the object recognition test, the preference index (d3) in the Alzheimer's groups Noisome Curcumin and curcumin recipients had a significant decrease compared to the control and Alzheimer's groups (p<0.001), and Alzheimer's and control groups and Curcumin noisome had a significant increase compared to the sham group (p<0.001).

Conclusion: Discussion and suggestions: The analysis of the behavioral data obtained from the marble burying test and the object recognition test showed that Alzheimer's disease causes memory and learning disorders and causes stress and anxiety in male rats, and curcumin and noisome curcumin improve these disorders.

Keywords: Alzhiemer, Marble Burying Test, Object Recognition Test, antioxidant, niosome

Investigating the Co-culture of different types of PC12 cell lines on myogenic development of rat adipocyte-derived stem cells (Research Paper)

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Introduction: Researchers are looking for a way to better the myogenic differentiation of stem cells. It has been found that various factors and conditions may increase the progenitor activity of adipose-derived stem cells (ADSC). In the current study, we tested whether PC12 cell lines could improve the ability of ADSCs to support the myogenesis.

Methods: Rat ADSCs were isolated, cultured in vitro, and identified using flow cytometry. Following that, purified ADSCs were co-cultured with three PC12 cell lines. MyoD mRNA expression was detected using real-time reverse-transcriptase polymerase chain reactions (Real-time RT-PCR) And the length of neurites of the PC12 cell lines was checked using ImageJ software.

Results: Our results reveal a significant difference in the mRNA expression of the MyoD gene between ADSCs and ADSCs and PC12 cell lines co-culture groups in myogenic differentiation culture medium (P<0.001) and PC12 cell lines effect improved expression of this gene. Current data revealed that the co-culture of ADSCs and PC12 cell lines could develop Long neurites formation in the co-culture group.

Conclusion: It was concluded that ADSCs/PC12 cell lines co-culture can lead to the formation of differentiated myoblasts in proximity to long neurites formations. These in vitro cell models can be used as basic research in Nero-muscle tissue engineering implanted into organ defects where muscle tissue and Neurological regeneration were required.

Keywords: adipocyte-derived stem cells (ADSCs), PC12 cell line, myogenesis, Skeletal muscle

Investigating the educational and consulting needs of operating room technologists working in selected hospitals: A multicenter cross-sectional study (Research Paper)

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Introduction: Introduction: Since each person has unique characteristics, his / her skills learning and learning needs are different, so the first and fundamentally step in education is, studing the educational needs. Determining the educational and consulting needs of operating room technologists in selected hospitals in Isfahan was the aim of this study.

Methods: Methods: It was a cross-sectional analytical study to determine the need for operating room technologists to improve their knowledge in the fields of general and specialized knowledge and management of the surgery field and improve their job motivation and holding comprehensive specialized training courses. Data collection tool was a researcher-made questionnaire that consisted of 48 items (46 items with three-point Likert (1-low 2- medium 3- high) and a description section for each item and 2 reresponse items) which after obtaining consent Validity and reliability (CVR> 0/62 and CVI> 0/79) (Cronbach's alpha coefficient = 0/904) were determined by 50 operating room technologists of selected hospitals in Isfahan by convenience sampling method with inclusion criteria.

Results: Results: 40 people completed the questionnaire. Most participants were female (32 and 80%). The average age of the participants was 31/40± 1/31 years. 18 staff (45%) had work experience in the range of 1-5 years. Kashani and Shahid Chamran hospitals had the highest (16 persons 40%) and the lowest (6 persons and 15%) orthopedic fields (8 persons and 20%) and ocular, pediatric and vascular (1 person and 2.5%), respectively and had

the most and fewest participants. The average scores of needs assessment in the fields of general and specialized knowledge, surgical management and the need and interest to improve the level of knowledge as well as the need of holding comprehensive specialized training and counseling courses for operating room technologists are 44/37± 1/06, respectively (average need Upwards), 28/50 ± 1/06 (average need) and 9/72± 0/30 (medium upward need) and the average scores of job motivation was 17/60± 0.40 (average upward motivation)) Was.

Conclusion: Conclusion: Inspite of holding continuous training courses and special services for hospital staff and the existence of training systems and sites, there is still a need for training in operating room technologists and it is suggested that using the results of this study, the useful course and appropriate training programs in accordance with the operating room profession, to be planned and implemented in the first place to promote general and specialized knowledge.

Keywords: needs assessment, operating room technologist, training, counseling, job motivation

Investigating the effect of alcoholic extract of Ansal onion (Urginea maritime) on reducing muscle and joint pain (Review)

hamidreza shojaei,[1,*]

1. im student

Introduction: Ansal onion (Urginea maritime) from the Lily family (Liliaceae) is a medicine that is used from the heart to local pain relief and cloves (Syzygium aromaticum) is used for hair loss, nose and throat pain, gastritis and side and stomach pain, aloe vera Aloe vera) is used to repair wounds and cracks in hands and feet, etc. Products that each have separate properties and the combination of these also adds new properties to the products, and now in this article the combination of the above products is examined and We explain how to make the spray.

Methods: 1 Norn S, Kruse PR. Cardiac glycosides: From ancient history through Withering's 2. J Stannard. SquillIn Ancientand MedievalMateriamedica, With Special Referencetoits EmploymentforDropsy. Bull N Y ACAD MED. 1974 Jun; 50(6): 684–713. 3. Stoll A. Sur les substances cardiotoniques de la scille maritime (Scilla maritima L). Experientia 1954; 10:282-297. 4. Aliotta G, De Santo NG,PollioA,Sepe J, Touwaide A. The diuretic use of Scilla from Dioscorides to the end of the 18th century. J Nephrol 2004;17(2): 342-347 -

Results: First, we prepare four samples of different products. Ansal cloves and onions and aloe vera, Ansal cloves and onions, Ansal onions and aloe vera, Ansal onion water and alcohol mixture, first we grind the cloves to the amount of 30 grams, then mix with 100 cc of 96% alcohol and 50 cc of water. and then we heat it for 1 hour and then we get the clove extract with a strainer and then we cut the onion into small pieces and pound it in a mortar and mix 150 cc of alcohol and 75 cc of water and We heat it and get the extract using a strainer and do the same for aloe vera and then store the combined extracts in the refrigerator for a while. After storing in the refrigerator, we mix the obtained solutions with hexane in such a way that we mix 20 ml of the obtained extract with 100 ml of hexane and then spray it on the desired area and with four indicators of response time and shelf life. We compare its side effects and patient satisfaction.

Conclusion: The combination of onion, clove and aloe vera performed better than other combinations in the tests, and the patient's satisfaction with this solution was more than other solutions, and its shelf life was also longer than other solutions. It had more side effects and a short shelf life, and due to the equal patient satisfaction with the two solutions of hexane and Ansan and the

solution of cloves and Aloe Vera and Ansan, considering the many side effects and the short response time of the solution of hexane and Ansan, our desired solution in the spray, It was a solution of aloe vera, cloves and ansal, so it was used as a solution in our spray

Keywords: Urginea maritime

Investigating the effect of amiodarone drug on IRBIT protein by molecular docking method (Research Paper)

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Introduction: Introduction: Amiodarone, a potent antiarrhythmic drug useful for both atrial and ventricular arrhythmias, has a combination of β-blocking, calcium channel blocking, and class III antiarrhythmic effects. In patients with acute onset of AF and also with left ventricular dysfunction, amiodarone or digoxin is recommended due to minimal negative inotropic effect. Amiodarone has serious systemic side effects. In addition, amiodarone is associated with a high mortality rate in patients with acute or chronic heart failure.(1) IRBIT (Inositol 1,4,5-trisphosphate-released IP3R binding protein) was identified as a molecule that regulates Ca2+ concentration by competing with IP3 for the IP3 1,2 receptor. Given that the activities of various ion transporters are regulated by IRBIT in a phosphorylation-dependent manner, IRBIT can act as both a sensor and an integrative modulator of the intracellular ionic environment.(2) The purpose of this study is to investigate the bioinformatics effect of amiodarone on IRBIT protein. Material and method: This research was carried out using a descriptive analytical method. In this study , To check the chemical structure of the protein, visit www. uniprot. org we use. And to check the structure of amiodarone from pubchem. ncbi. nlm. nih. gov we used. Also from the software chimera1.10 and PyRx were also used.

Methods: Material and method: This research was carried out using a descriptive analytical method. In this study , To check the chemical structure of the protein, visit www. uniprot. org we use. And to check the structure of amiodarone from pubchem. ncbi. nlm. nih. gov we used. Also from the software chimera1.10 and PyRx were also used.

Results: Result:In this study, In this study, we come to the conclusione that because amiodarone binding energy level is -6.0 . AND ALSO had 9 results and RMSD was zero ,which shows that drug amiodarone has a btter effect on the IRBIT protein

Conclusion: conclusion: In this study, we came to the conclusion that amiodarone drug has the best effect on IRBIT protein

Keywords: DOcking , Amiodarone , IRBIT Protein, Bioanformatics,

Investigating the effect of Ativan (lorazepam) on BCL-2 protein using molecular docking method (Research Paper)

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Introduction: apoptosis is programmed cell death that occurs in multicellular.BCL-2 protein as a proteo-oncogene in germ cells is involved in the regulation of cell apoptosis.This protein generally plays a role in inhibiting cell apoptosis.Ativan (Lorazepam) ischemically a short-acting anti-anxiety drug that belongs to a group of drugs called benzodiazepines.The purpose of thisresearch is to investigate the effect of Ativan (lorazepam) on BCL-2 protein.

Methods: This research was carried out by descriptive-analytical method. Chimera 1.10.2 and PyRx programs were used in this research, as well as Uniprot,Pubchem,PDB,Pubmed,drugs and Deepsite site.

Results: We started the analysis and the following results were obtained. Binding affinity 1: _7.5 Binding affinity 2: _7.1 Binding affinity 3: _7.0 Binding affinity 4: _7.0 Binding affinity 5: _6.9 Binding affinity 6: _6.8 Binding affinity 7: _6.8 Binding affinity 8: _6.7 Binding affinity 9: _6.6

Conclusion: The obtained results indicate that Ativan drug has a good effect on BCL-2 protein and in the near future this drug can be used to regulate BCL-2 protein and control it.

Keywords: Apoptosis , BCL_2 protein , Ativa, Lorazepam

Investigating the effect of azithromycin on intestinal microbiome and memory in male Wistar rats (Research Paper)

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Introduction: The covid-19 pandemic caused by the acute respiratory syndrome coronavirus (SARS-CoV-2) has affected millions of people around the world.Respiratory viral infections make patients susceptible to other infections and lead to increased mortality.The meta-analysis showed that the antibiotic azithromycin was prescribed the most to prevent and deal with secondary infections in patients with Covid-19.Despite the beneficial effects of antibiotics in preventing the growth of pathogenic bacteria and causing disease, these compounds can have adverse effects on the intestinal microbiome and change the intestinal bacterial population.New research suggests that there is a complex two-way relationship between the gut microbiome and the host that plays a role in human health as well as in disease pathogenesis. Changes in the composition and function of gut microbiota can affect gut permeability, digestion, metabolism, immune responses, and memory and learning. Based on this, in the present study, the effect of the antibiotic azithromycin on the gut microbiome and memory recall was investigated.

Methods: In this experimental study, adult male Wistar rats weighing 220-250 grams were divided into control and antibiotic groups.In the control group, normal saline (0.6 ml) and in the antibiotic treatment group, azithromycin (15 mg/rat with a volume of 0.6 ml) was gavage daily for 7 days.In order to investigate the effect of azithromycin on the intestinal microbiome, in both groups of the PCR test (to identify and investigate three bacterial species:Enterococcus faecalis and Lactobacillus acidophilus and E.coli) And stool culture was used before and after treatment.At the end of the treatment, the memory was evaluated with the help of the passive avoidance test and the new object recognition test and motor activity was checked by the locomotion device.

Results: In the passive avoidance test, azithromycin gavage significantly reduced memory recall compared to the control group (P<0.001).In the new object recognition test, a significant difference was seen in the memory evaluation between the control group and the experimental group (P<0.05). Examining motor activity did not show any significant difference between the control and azithromycin groups (P>0.05). Stool culture and comparing the number of bacterial colonies before treatment in both groups showed a

significant difference. It did not show any difference between the control group and the azithromycin group (P>0.05), but stool culture and counting of bacterial colonies after treatment showed a significant decrease in the number of bacterial colonies in the group receiving azithromycin compared to the control group. (P<0.05).Also, by conducting PCR test, it was found that the antibiotic azithromycin caused the destruction of two species (Enterococcus faecalis and Lactobacillus acidophilus) out of the three bacterial species studied in the test.

Conclusion: The results of this research show that the use of the antibiotic azithromycin with its effect on the gut microbiome leads to the destruction of beneficial bacterial species and probably in this way it can have a destructive effect on memory and learning.

Keywords: Azithromycin antibiotic, Covid-19, memory, gut microbiome, rat

Investigating the effect of date consumption during pregnancy, labor, childbirth and postpartum periods, a review article (Review)

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Introduction: Recent research has shown that the consumption of various substances during pregnancy has effects on the outcome of pregnancy. Dates, with the scientific name Phoenix dactylifera, are tropical fruits, and are one of the substances that have various effects when consumed in late pregnancy. The present study was conducted with the aim of investigating the properties of date consumption during pregnancy, labor, delivery and after delivery.

Methods: In this study, the articles published between the years 2010-2019 with the restriction of Farsi and English from the databases GoogleScholar, PubMed, SID, Civilica with the keywords Date Fruit, Pregnancy, Child birth, Pain, Labor and the Persian equivalents of these words are reviewed.

Results: Among the articles, finally 15 related articles were reviewed. Results include increased Bishop Score, dilatation, effusion, spontaneous labor. Reducing the duration of labor (first and second phases of labor), the need for induction and augmentation, the use of oxytocin after delivery, bleeding after delivery, on the other hand, it also affects the fetus, causing an increase in Apgar and heart rate, and Apgar minutes of 5 In the baby of people who use dates, it is more than the control group. Consuming dates also improves the blood indicators of mothers, including: increasing Hb, Hct, RBC, Platelet. After childbirth, it also reduces bleeding, strengthens the muscles of the uterus, and with the increase of estrogen, the mental state of the person improves.

Conclusion: Recommending the consumption of dates for an easier delivery without the need for induction and without side effects, to pregnant women in the last months before delivery.

Keywords: date consumption , pregnancy, labor, childbirth, postpartum periods

Investigating the effect of dinitrosoamine in stomach cancer (Review)

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Introduction: Globally, there has been a slight drop in both the incidence and mortality rate of stomach cancer in recent decades. It was the third most common cause of cancer-related fatalities globally in 2012, with an estimated 700,000 deaths and over one million new cases of stomach cancer. In Eastern Asia, particularly China, new cases made for about half of the global total. Geographical variations in the prevalence of stomach cancer were noted, suggesting that some modifiable factors may have a significant impact on the etiology of this malignancy. Of the various classes of chemical carcinogens, nitrosamines have probably contributed to a greater extent than most to the understanding of the process of initiation of carcinogenicity. These carcinogens belong to the chemical class of N-nitroso compounds, comprising the N-nitrosamines and the N-nitrosamides. A major difference between the two groups is that the nitrosamides are unstable at physiological pH and decompose nonenzymatically to reactive intermediates; whereas the nitrosamines (eg, dimethylnitrosamine, DMN) are chemically stable under physiological conditions, and their adverse biological effect is mediated through the formation of reactive metabolites after enzymatic conversion, mainly by microsomal mixed-function oxidases. In numerous animal species, the N-nitroso compounds have been proven to be poisonous, teratogenic, mutagenic, and carcinogenic. Additionally, a significant amount of species, tissue, and cell specificity may be shown in the carcinogenic action of these substances, and many of them are carcinogenic. Investigating the role of dinitrosoamine in stomach cancer was the goal of this investigation.

Methods: This study was investigating of Investigating the effect of dinitrosoamine on stomach cancer from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Therefore, it is an urgent demand to identify risk factors that can have a marked impact on this disease. The typical diet in most countries contains nitrates, nitrites, and nitrosamines. Nitrates and nitrites occur naturally in fruit and vegetables, which are regarded as an important part of a healthy diet due to the powerful evidence of beneficial health effects against cancer. In the same time, nitrates and nitrites are often used as food additives in processed meats such as ham, bacon, sausages, A high consumption of processed meats is linked to an increased gastric cancer risk, and many people consider nitrates/nitrites as the main reason for that. Nitrosamines are produced by chemical reactions of nitrates, nitrites and other proteins. N-

nitrosodimethylamine (NDMA) is one of the most frequently occurring nitrosamines in our dietary foods. NDMA is a potent carcinogen, capable of inducing malignant tumors in various animal species in a variety of tissues, including liver, lung, and stomach. A peculiarity of nitrosamines is the high degree of cell and organ specificity in inducing tumors. There is substantial evidence that the initiation of the carcinogenesis process by carcinogens of this group is linked to the metabolic competence of the target tissue or cell to convert these carcinogens into mutagenic metabolites and to the binding of those metabolites to cellular DNA. Alkylation occurs in the DNA at the N-1, N-3, and N-7 positions of adenine; the N-3, N-7, and O6 of guanine; the N-3, and O2 of cytosine; and the N-3, O4, and O2 of thymine; and the phosphate groups. The initial proportion of each DNA adduct depends upon the alkylating agent used.

Conclusion: N-nitroso compounds have been found to be carcinogenic in animal studies.49 Two nitrosamines (N-nitrosodiethylamine and N-nitrosodimethylamine) are classified as probably carcinogenic to humans by the IARC. Epidemiologic studies suggest a positive association between nitrosamines and gastric cancer risk, but the data are still inconclusive. Most epidemiologic investigations on nitrosamine and related food intake and gastric cancer risk have been case-control investigations, which support a positive association of nitrite, nitrosamine, processed meat and fish, preserved vegetables, and smoked food intake with risk for gastric cancer.

Keywords: N-nitrosodiethylamine, stomach cancer, carcinogenic

Investigating the effect of herbal medicines in the treatment of vaginitis: a review study (Review)

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Introduction: Vaginitis is characterized by abnormal discharge and discomfort in the vulva, vagina or both. Vaginitis is the most common reason for visiting gynecologists's clinics, which accounts for about ten million visits to the doctor every year. Vaginitis has well known treatments in conventional medicine, however, a group of patients have treatment resistant or recurrent vaginitis and are not satisfied with the adequacy of conventional treatments. Therefore, nowadays, researchers have turned to herbal medicines, which not only have beneficial effects, but also have not side effects caused by the use of chemical drugs. Therefore, the present study was conducted with the aim of determining the effect of herbal medicines in the treatment of vaginitis.

Methods: studies related to vaginal infections from reliable common medical sources including reference books of gynecologists and Google Scholar, Iran Doc, SID, Scopus and Science direct databases with key words leukorrhea, traditional vaginitis and vaginal discharge, plant, herbal medicine, complementary Chinese medicine and medicine were searched. All journal articles that were indexed in reliable databases including ISI, Pubmed, ISC, and Scopus or had scientific research points, including human, animal, and In Vitro studies, regardless of the time period of publication, were selected. Finally, according to the inclusion and exclusion criteria, 28 articles were reviewed.

Results: The results of the studies showed that in the treatment of bacterial vaginosis, Hypericum perforatum vaginal gel, Ginger vaginal cream, Zataria multiflora vaginal cream, Garlic vaginal cream and Propolis Vaginal Cream, extracts of St. John's wort, chamomile, calendula, yarrow, shepherd's purse and tea tree oil have been effective. For the treatment of vulvovaginal candidiasis, vaginal cream with garlic and thyme extract, Shirazi thyme vaginal cream, Shirazi chamomile and bee propolis vaginal cream, licorice vaginal gel, yogurt and honey vaginal cream, honey and cinnamon vaginal cream, honey vaginal cream, vaginal douche with baking soda, vaginal suppository with Nigella Sativa, consumption of unpasteurized yogurt, frankincense vaginal cream, lavender, Artemisa persica, Onosma

Chlorotricum, mountain savory, myrtle plant, white alum, fennel, parsley, cumin and black cumin vaginal cream and coconut oil are recommended. Trichomonas vaginitis can be treated with vaginal douching with tea tree essential oil, Allium hirtifulium and propolis vaginal cream.

Conclusion: The results of various studies showed that due to the positive effects of herbal treatments, they can be used as complementary or even alternative treatments to chemical treatments.

Keywords: leukorrhea, vaginitis, vaginal discharge, plant, herbal medicine

Investigating the Effect of Insufficient Sleep on the Immune Systems (Review)

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Introduction: Sufficient sleep is important for our health. Sleep and the circadian system exert a strong regulatory influence on immune functions. Both brain functions act synergistically and share neuroendocrine effector mechanisms to convey control over immune functions. In modern society, insufficient sleep has become an issue for many groups of people. Social networks, movies, long working hours, hard exams in schools and universities, etc. are responsible for this problem. In this article, we want to examine if insufficient sleep influences physical health.

Methods: This study was conducted in 2022 by searching for keywords such as Insufficient Sleep, Physical Health, Interleukin and Immune Systems invalid databases such as pub med and Google Scholar

Results: Circulating naive T-cells and production of pro-inflammatory cytokines, like interleukin-12 (IL-12), peak during nighttime, whereas cytotoxic effector leukocytes and production of the anti-inflammatory cytokine IL-10 peak during daytime. Sympathetic tone and cortisol levels show a circadian nadir during nighttime and are further suppressed by sleep, whereas growth hormone and prolactin show a circadian peak during nighttime and are further enhanced by sleep .increased concentrations of prolactin and GH as well as a decrease in cortisol hormonal changes characterizing early nocturnal sleep, could be responsible for a shift towards T helper 1 (Th1) cytokines during this time according to studies, during sleep, IL1 and IL6 increase so sleep deprivation decreases nocturnal IL1 and IL6. Both of these interleukins have important roles in the immune system. Differentiated immune cells with immediate effector functions, like cytotoxic NK cells and terminally differentiated CTL

Conclusion: According to the findings, it is better to set up a program to pay more attention to our sleep. We shouldn’t be careless about our sleep

because of work, study, movies, and social spaces. If we don't, we will lower our immune system.

Keywords: Insufficient Sleep, Physical Health, interleukin, Immune Systems

Investigating the Effect of Ketogenic Diets on Quality of Life in Women with Breast Cancer (Review)

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Introduction: Ketogenic Diets (KDs) are low-carb, high-fat diets that offer many health benefits such as weight loss and benefits against diabetes and epilepsy and cancer. On the other hand, breast cancer, the most common cancer diagnosed in women, is proven to be related to obesity. The purpose of this study is to investigate the effect of KDs on quality of life (QoL) in women with breast cancer.

Methods: Google scholar, Scopus and Pubmed databases were searched using related MeSH terms and keywords and Relevant articles were used in this review.

Results: The evidence reviewed in this paper shows that using a KD, as a complementary treatment for breast cancer, may improve patients' QoL by shifting brain's preference to use ketones as its primary fuel instead of carbohydrates. In addition, This diet also helps patients by reducing Reactive Oxygen Species (ROS) and maintaining homeostasis. Patients receiving KD showed improvements in Physical Functioning, Cognitive Functioning, Fatigue and Insomnia compared to whom received a Standard Diet (SD). It should be considered that KDs are not palatable for everyone and they might cause some side effects such as micronutrient insufficiency, nausea/vomiting and muscle loss therefore, patients should be screened for unwanted side effects.

Conclusion: This study indicated that consuming a KD compared to SD has the potential to improve some aspects of QoL in breast cancer patients. However, further studies conducted in this subject would be necessary to draw conclusions about more possible effects of KDs in QoL of Breast Cancer sufferers.

Keywords: Diet, Ketogenic; Breast Cancer; Quality of Life; Breast Neoplasms

Investigating the Effect of Mercaptopurine on Expression Changes of TUG1 in Acute Lymphoblastic Leukemia (Research Paper)

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Introduction: Most commonly affecting children, ALL is a kind of cancer that can also affect adults. Due to unchecked cell proliferation, obstructed differentiation, and obstruction of apoptosis, abnormally cloned leukemia cells accumulate in the bone marrow and other non-hematopoietic tissues, impairing normal hematopoiesis and immune function. Leukemia is a malignant clonal disease of hematopoietic stem and progenitor cells. The discovery of dysregulated molecules linked to leukemia thanks to rapid advancements in cell and molecular biology raises the possibility that the disease is influenced by the heterogeneity of cellular and molecular genetics. LncRNAs have a wide range of biological roles and intricate regulatory mechanisms, are typically found in the cytoplasm or nucleus, and demonstrate great functional variability. By boosting EZH2 recruitment and H3K27me3 levels at the miR-34a promoter in leukemia cells, the TUG1 gene epigenetically inhibits miR-34a expression. 6-mercaptopurine is a key component of the pharmacological therapy used to treat pediatric acute lymphoblastic leukemia (ALL) (6-MP). The therapeutic response to this prodrug is significantly influenced by its intracellular metabolism. The disposal of 6-MP involves a large number of metabolizing enzymes, and active 6-MP metabolites include 6-thioguanine nucleotides (6-TGN) and methylated metabolites, which are mostly methylation by the thiopurine S-methyltransferase enzyme (TPMT). The aim of this study was to investigate the Effect of mercaptopurine on Expression Changes of LncRNA TUG1 in Acute Lymphoblastic Leukemia, the Jurkat E6.1 cell line.

Methods: In this research, suitable doses of mercaptopurine were prepared according to the IC50 of the drug which consists of 5 and 10µM. The Jurkat E6.1 cell line was treated with mercaptopurine at 72h after cell passage. The expression changes of LncRNA TUG1 and GAPDH as the housekeeping gene were investigated using Real-Time PCR after RNA extraction and cDNA

synthesis. Finally, Rest 2002 Software was used to analyze the data, and Excel was used to create diagrams.

Results: The Results of the research showed that after 72h of treatment with mercaptopurine at 5 and 10µM, the expression of TUG1inecreased significantly as compared to the control group. according to the result, doses of 5 and 10µM of mercaptopurine over 72h were the optimal concentrations and time for this drug's effect. The expressions of LncRNA TUG1 were 2.38 and 1.899 at the specified concentrations and times.

Conclusion: basis of the results expression changes in TUG1 as a Tumor suppressor gene after treatment with mercaptopurine, both concentrations of the drug successfully increased TUG1 expression. generally, mercaptopurine had a positive effect on the LncRNA TUG1 increased mechanism over 72hour, and this increase in expressions was statistically significant (p-value 0.001). According to evidence, mercaptopurine has a high anticancer potential and affirmative treatment of that. Therefore, the mercaptopurine drug has been effective in the tested concentrations in the Jurkat E6.1 cell line. And it has proven its therapeutic efficiency, although more extensive studies are needed for more definitive results.

Keywords: GAPDH, LncRNA TUG1, Jurkat E6.1 cell line, Acute Lymphoblastic Leukemia

Investigating the Effect of Ni-Thiosemicarbazones complexes on Expression Changes of LncRNA TUG1 in Acute Lymphoblastic Leukemia (Research Paper)

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Introduction: leukemia that affects lymphoid progenitor cells in the bone marrow, blood, and extramedullary regions is known as acute lymphoblastic leukemia (ALL). Relapse has a significant impact on survival in ALL. The prognosis has improved and there has been a substantial advancement in ALL treatment over the past couple of decades. In a study of children's ALL outcomes, the Children's Oncology Group found that, between 1990 and 2000, 5-year survival rates rose from 83% to more than 90%. All child age groups have shown this to be true, with the exception of newborns under a year old. Even with these improvements, 20% or so of children with ALL still experience relapses. The term "long non-coding RNAs" (lncRNAs) refers to RNAs that are longer than 200 nucleotides. The importance of lncRNAs in a variety of cellular processes, including proliferation, differentiation, apoptosis, invasion, and chromatin modification, has been demonstrated in an increasing number of studies. In this regard, it has been shown that lncRNAs are dysregulated in human malignancies. TUG1 is a recently discovered oncogenic lncRNA that has been found to exhibit aberrant upregulation in a variety of cancers, including leukemia, hepatocellular carcinoma, bladder cancer, B-cell malignancies, and oesophageal squamous cell carcinoma. TUG1 knockdown has been found to inhibit colony formation, cell invasion, and/or cell proliferation in various malignancies. TUG1 has an interesting downregulated expression pattern in non-small cell lung cancer, indicating a tissue-specific role in carcinogenesis. TUG1 could be used in clinical settings as a prognostic biomarker for malignancies. Leukemia, pancreatic cancer, breast cancer, non-small cell lung cancer, cervical cancer, prostate cancer, and bladder cancer are only a few of the malignancies that thiosemicarbazones are effective against. The goal of this study was to investigate of Ni-thiosemicarbazones complexes affected the expression of LncRNA TUG1 in the Jurkat E6.1 cell line.

Methods: In this research, appropriate doses of the thiosemicarbazones complexes Ni were prepared according to the IC50 of the drug which consists of 46 and 48µM. The Jurkat E6.1 cell line was treated by Ni 72 hours after cell passage. The expression changes of LncRNA TUG1 and GAPDH as the housekeeping gene were investigated using Real-Time PCR after RNA extraction and cDNA synthesis. Finally, Rest 2002 Software was used to analyze the data, and Excel was used to create diagrams.

Results: The Results of the research showed that after 72 hours of treatment with thiosemicarbazones complexes Ni at 46 and 48µM concentrations, the expression of LncRNA TUG1decreased significantly as compared to the control group. According to the findings, doses of 46 and 48µM of Ni over 72 hours were the optimal concentrations and time for this drug's effect. The expressions of LncRNA TUG1 were 1.968 and 2.369 at the specified concentrations and times.

Conclusion: According to the findings of the study of expression changes in LncRNA TUG1 as a Tumor suppressor gene after treatment with thiosemicarbazones complexes Ni, both concentrations of the drug successfully increased LncRNA TUG1 expression. Overall, thiosemicarbazones complexes Ni had a positive effect on the LncRNA TUG1 increased mechanism over 72hour, and this increase in expressions was statistically significant (p-value 0.001). According to evidence, Ni -thiosemicarbazone complexes have a high anticancer potential and affirmative treatment of that.

Keywords: Ni -Thiosemicarbazones complexes, cDNA, LncRNA TUG1

Investigating the effect of nutrition on benign prostatic hyperplasia (Review)

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Introduction: The prostate gland is the largest appendage in mammals and plays a key role in reproduction. Its secretions make up 30 to 50% of semen and play an important role in sperm fertility. Benign Prostatic Hyperplasia Histopathology of BPH typically includes double epithelial and stromal hyperplasia of the transitional zone of the prostate. Several biological factors, including oxidative stress, inflammation, androgens, and increased expression of several growth factors, are associated with benign and malignant prostate disorders. Benign prostatic hyperplasia is the most common hyperplastic disorder in men and the most influential cause of lower urinary tract symptoms. Pathogenesis nutrition appears to correct benign prostatic symptoms in men suffering from lower urinary tract symptoms. Although there are several medications and treatments for this condition, nutrition may improve outcomes as a primary approach or in conjunction with BPH medications or procedures. The purpose of this review is to highlight the benefits of nutrition and dietary supplements in men with BPH and LUTS.

Methods: In the following article, we collected the required data by using key words using reliable databases such as Google Scholar, ProQuest, Scopus and PubMed. Our statistical population consists of all the studies that have been conducted until 2022. After reviewing the findings, we reviewed 14 articles.

Results: The researchers found a significantly lower risk of BPH among men who consumed at least four servings of vegetables per day compared to those who consumed less than one serving per day. In a randomized, double-blind, placebo-controlled trial, it was found that lycopene, a component found

in tomatoes, may inhibit the progression of BPH and may improve symptoms in patients given a dose of 15 mg/day for 6 months. Forgive A meta-analysis of 19 published studies found an up to 35% reduced risk of BPH among men who drank alcohol daily, but an increased risk of LUTS. A case-control study on 1369 patients with BPH and 1451 controls showed a direct relationship between starch consumption and BPH. Saw palmetto, native to Florida, has been shown in many older clinical studies to significantly improve the signs and symptoms of BPH. A review of 21 randomized controlled trials involving a total of 3139 men (including 18 double-blind trials) found that men treated with saw palmetto had reduced urinary tract symptom scores, less nocturnal enuresis, better urinary tract symptom self-report scores. A review analyzed the specific effects of sernilton and suggested that it improved subjective symptoms including enuresis, but compared with placebo, no significant improvement in urodynamic measures was observed. A review of beta-sitosterol studies included four double-blind trials in 519 men that lasted between 4 and 26 weeks. According to research, prostate health and vitamin B6 are directly related, and 3 mg of pyridoxine daily is recommended for young men aged 19-50.

Conclusion: Based on the collected results, nutritional modifications such as consuming less meat, simple starch, and more vegetables and fruits significantly help in the management of BPH and LUTS. These dietary patterns may modulate metabolic pathways that lead to obesity and diabetes; Two diseases that contribute to the development of BPH and LUTS.Dietary supplements should be used with caution. Saw palmetto as an agent may not help, while beta-sitosterol and rye pollen extract may. Such lifestyle changes may help with weight loss and stabilize insulin levels, which moderate the effects of BPH and LUTS and, as a side benefit, have a positive effect on cardiovascular health. Much of the available data on nutrition in relation to BPH is observational and should serve primarily as a guide to inform patients about healthy lifestyle interventions. Therefore, newer clinical trials with a larger study population are needed to confirm the effectiveness of these herbal products.

Keywords: Prostatic Hyperplasia, Lower Urinary Tract Symptoms, Nutrition

Investigating the effect of silver nanoparticles and graphene oxide in pcl scaffold on the viability of human fibroblast cells (Review)

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Introduction: The human body is made up of different tissues and these tissues are vulnerable. Today, we use tissue transplantation to treat some of these injuries. For tissue transplantation, we need cells that are strong on the scaffolds. We have used PCL scaffolding in this project. PCL scaffold is a type of polymer that consists of repeating units of hexanovate. PCL scaffold is inherently biodegradable and is widely used in drug delivery networks today. Graphene oxide is a carbon allotrope that is hydrophilic and has high solubility and is used in drug delivery and anticancer drugs. Also, silver nanoparticles have antibacterial properties and are used in wound dressings.

Methods: To carry out this research, first, graphene oxide was synthesized and silver nanoparticles were prepared and electrospun in PCL scaffold. Structure of nanofibers in The electron microscope was examined and then fibroblast cell culture was performed on the nanofiber scaffold. At the end of the life test Compatibility of MTT and DAPI staining was performed and examined with a fluorescent microscope.

Results: The results showed that the supramolecular PCL nanofibers coated with a mixture of graphene oxide and silver with a higher density were more similar to the natural ECM of the body and has shown a better ability to support cell growth and proliferation

Conclusion: The results showed that the supramolecular PCL nanofibers coated with a mixture of graphene oxide and silver with a higher density were more similar to the natural ECM of the body and has shown a better ability to support cell growth and proliferation

Keywords: silver nanoparticles, graphene oxide, pcl scaffold, microelectrocopy, Mtt

Investigating the effectiveness of gold nanoparticles against bacterial resistance (Review)

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Introduction: Antibiotics frequently lose their potency over time as a result of the formation and spread of drug resistance in bacterial infections. Up to billions of dollars, more in medical expenses are incurred each year as a result of the so-called "antibiotic resistance crisis" and iatrogenic diseases brought on by bacteria that are resistant to antibiotics. It is critically important to find novel antibacterial agents and therapeutic approaches in light of this dire situation. Based on their own distinctive physical and chemical properties, nanoparticles offer a universal platform for therapeutic applications and treat drug-resistant microorganisms. Antibacterial agents are projected to be replaced by the antibacterial activity displayed by nanomaterials such as silver, gold, copper, titanium, zinc oxide, and magnesium oxide. Investigating the efficiency of gold nanoparticles against bacterial resistance was the goal of this investigation.

Methods: This study was conducted on the subject of Investigating the effectiveness of gold nanoparticles against bacterial resistance, by collecting content from Science Direct, Springer, Google Scholar, and PubMed sites

Results: According to the findings of numerous research, gold nanoparticles are particularly desirable in a variety of medical disciplines because of their adaptable size, shape, surface properties, optical properties, biocompatibility, low cytotoxicity, high stability, and potential for multiple uses. Some researchers have already used gold nanoparticles (GNP) in tests on gum disease, dental caries, tissue engineering, dental implantology, and cancer diagnostics due to their nanostructure, high surface volume properties, and biocompatibility. Since GNP contains antifungal and antibacterial action, it can be added to some biological materials to give them antibacterial qualities, enhancing their suitability for various applications. Using gold nanoparticles as carriers for antibacterial medications, antibacterial drugs can connect to nanoparticles via noncovalent or covalent bonding, enhancing the antibacterial effects of the pharmaceuticals by improving their ability to reach the site of action. Under continuous laser irradiation, the photothermal effects of gold nanoparticles can serve as sterilizing agents. Gold is thought to be a benign nanomaterial, but the chemicals used to prepare and modify it might be poisonous. When gold nanoparticle concentrations are high, this toxicity may become apparent, although gold nanoparticles have an antimicrobial impact. They did not have harmful effects on healthy cells in certain

quantities. Modified gold nanoparticles not only demonstrate good antibacterial activity against standard strains but also have unique antibacterial activity against multidrug-resistant bacteria. After multiple generations of cultivation, it is not easy to induce bacteria that are resistant to gold nanoparticles.

Conclusion: Nowadays, with the quick advancement of nanoscience and nanotechnology, it has been suggested alternatives to conventional approaches for individuals to identify, fend against, and defeat a variety of ailments. Currently, silver and gold nanoparticles (AgNPs and AuNPs, respectively) have been developed as metal nanoparticles, which have many uses in the medical and pharmaceutical industries, including antibacterial and antibiofilm properties, drug delivery systems, diagnostic tools, and personal care and cosmetic products.

Keywords: gold, nanoparticles, bacterial resistance, antibiofilm

Investigating the effects of paliperidone, olanzapine, and eripiprazole on fmrp protein using molecular docking (Research Paper)

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Introduction: Fmr1 protein is involved in the regulation of protein synthesis and the development of neuronal synapses, communication spaces between neurons. Almost all cases of fragile X syndrome are caused by mutations in DNA fragments, the GCC triplet repeats, found in the FMR1 gene. Naturally, these repetitive sequences are repeated from 5 to 40 times, which also shows the symptoms of autism. Normally, these repetitive sequences are repeated from 5 to 40 times. In people with Fragile X syndrome, these sequences are repeated more than 200 times, and this high number of repetitions leads to the inactivation of the FMR1 gene and the absence of the fmrp protein code, disruption of the nervous system and the occurrence of symptoms related to Fragile X syndrome and the occurrence of autism symptoms. becomes The purpose of this study is to investigate three drugs, olanzapine, eripirazole and palperidone, and compare their effects on Fmr1 protein by molecular docking method.

Methods: Using molecular docking, which is an in silico method, we perform the desired experiments in a computer environment, and this is a descriptive-analytical study. We first extract the desired protein information on the pdb site and download it in pdb format. Then we extract the 3D structure of Elanzapine, Aripirazole and Palperidone drugs from the PubChem website and save them in sdf format. In the next step, we modify the Fmrp protein using the Chimera software, removing water molecules and charge flow in this software. And in the last step, through the Pyrex software, by specifying the coordinates of the drug placement through the deepsite site of the process. We start docking. The coordinates of the placement of the drug through the site's depp were as follows: Center x = 25 Center y = 25 Center z = 25

Results: After docking with Pyrex software, the results were according to the table below. Docking results of palperidone drug with fmrp protein Binding affinity(kcak/mol) RMSD -7.4 0.0 -7.2 3.114 -7.1 7.696 Docking results of Eripirazole drug with fmrp protein Binding affinity(kcak/mol) RMSD -6.6 0.0 -6.6 3.676 -6.5 1.205 Docking results of elanzapine drug with fmrp protein Binding affinity(kcak/mol) RMSD -6.0 0.0 -5.8 11.139 -5.3 12.064

Conclusion: According to docking results, palperidone drug with more negative binding energy and more suitable orientation is more effective on fmrp protein.

Keywords: palpizole elanzapine molecular docking fmrp autism

Investigating the efficacy of vemurafenib, regorafenib, gefitinib and erlotinib on serine/threonine specific protein kinase by molecular docking method (Research Paper)

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1.

Introduction: Serine/threonine-specific protein kinase or BRAF is a protein playing a role in regulating cell growth, signaling, cell movement, and apoptosis, and in case of mutation in the BRAF gene, there is a possibility of normal cells would turn cancerous. Mutant B-Raf proteins are involved in tumorigenesis and most are of high kinase activity known as gain of function mutations . Vemurafenib drug belongs to the category of enzyme inhibitors (kinase inhibitors) and is among the targeted cancer drugs blocking the growth of cancer by stopping a protein called BRAF. Regorafenib is a cancer drug containing the active ingredient regorafenib. It has tyrosine kinase inhibitory activity and prevents tumor growth. It is used for patients who used other cancer treatment drugs but did not recover. Gefitinib drug belongs to the group of anti-cancer drugs and by interfering with the growth of cancer cells, it slows down or stops their growth. It has an effect on a specific enzyme protein called tyrosine kinase and inhibits it. Erlotinib is one of the cancer drugs and tyrosine kinase inhibitors, interfering with the growth of cancer cells and preventing them from spreading in the body. The aim of this research is to investigate the bioinformatics inhibition of BRAF mutated proteins by a number of anti-cancer drugs and to study the effect of each of them in inhibiting BRAF protein.

Methods: This research has been done by descriptive-analytical method. In this study, to determine the effectiveness of the drug and the best mode of binding and energy of the drug to the, computer methods such as docking were used and the results were analyzed. The 3D structure of BRAF protein was selected from the Uniport website and downloaded in PDB format in order to perform the docking. This protein has a resolution of 6.8 Å. The three-dimensional structure of the desired drugs was selected from the PubChem website and downloaded in SDF format. Then, the 3D structure of the target protein was entered into chimera version 1.15 to prepare the protein. The desired protein has four chains, One chain was selected and the other unnecessary ones were removed from the structure, then water molecules were removed from the desired chain and hydrogen atoms and charges were added and saved in PDB format. Molecular docking was used in order to investigate the binding and interaction of the studied compounds. PyRx software was used for docking.

Results: According to the docking studies, we found that the vemurafenib compound has the most negative binding energy level among all the studied compounds.

Conclusion: vemurafenib has better affinity and RMSD effect on BRAF protein to inhibit it and prevent cancer growth.

Keywords: Bioinformatics, docking, vemurafenib, gefitinib, regorafenib, erlotinib, serine/threonine specific

Investigating the expression levels of microRNAs promoting angiogenesis (miR-296)in colon cancer samples and their pathological importance in diagnosis (Research Paper)

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Introduction: Colon cancer is the third most common cancer and the second leading cause of cancer death. Early diagnosis of colon adenocarcinoma is one of the most important challenges in cancer management. Due to the importance of identifying non-coding RNAs and their stability, this study aimed to investigate the expression levels of miR-296 of serum extracellular microvesicles in patients with colon adenocarcinoma and controls. This study is likely to lead to the identification of a non-invasive diagnostic biomarker for colon adenocarcinoma.

Methods: In this study, 40 patients with colorectal adenocarcinoma and 40 healthy cases were selected for blood sampling. Then exosomal vesicles isolated from serum based on differential centrifuge protocol. The size and morphology of the exosomal Nanovesicles were assessed by SEM electron microscopy. After RNA extraction from the exosomes was performed using trisol, polyadenylation and cDNA synthesis. The expression level of miR-296 was compared with the expression of U6snRNA gene as a reference gene for normalization of data in the patient's exosome with a healthy sample by real-time PCR.

Results: The findings of this study showed that the isolated exosomes have a spherical appearance with a size range of 30 to 150 nm. After real-time PCR, in Roc curve analysis, Area under curve (AUC) was calculated to be 0.76 for miR-296. Also, the ΔCt parameter showed a significant difference in serum exosomes of patients compared to healthy exosomal samples, miR-296 expression level was significantly higher in serum exosomes of colon adenocarcinoma than in normal serum exosomes. (P <0. 01). The expression level of miR-296 in Stage 3 shows a higher expression than Stages 1 and 2 (P <0.05). Also, the expression level of miR-296 in patients with lymph node metastasis showed higher expression than patients with no lymph node involvement (P <0.01).

Conclusion: The results showed that increased expression of miR-296 and miR-93 in the serum exosomes of patients compared to healthy samples could be a criterion for the diagnosis of colorectal cancer. In addition, the expression of these two miRNAs with the clinical pathological features of the disease can confirm their biomarker potential.

Keywords: Colon adenocarcinoma, Exosome, MicroRNA, Biomarker,miR-296

Investigating the expression levels of microRNAs promoting angiogenesis (miR-93) in colon cancer samples and their pathological importance in diagnosis (Research Paper)

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Introduction: Colon cancer is the third most common cancer and the second leading cause of cancer death. Early diagnosis of colon adenocarcinoma is one of the most important challenges in cancer management. Due to the importance of identifying non-coding RNAs and their stability, this study aimed to investigate the expression levels of miR-93 of serum extracellular microvesicles in patients with colon adenocarcinoma and controls. This study is likely to lead to the identification of a non-invasive diagnostic biomarker for colon adenocarcinoma.

Methods: In this study, 40 patients with colorectal adenocarcinoma and 40 healthy cases were selected for blood sampling. Then exosomal vesicles isolated from serum based on differential centrifuge protocol. The size and morphology of the exosomal Nanovesicles were assessed by SEM electron microscopy. After RNA extraction from the exosomes was performed using trisol, polyadenylation and cDNA synthesis. The expression level of miR-93 was compared with the expression of U6snRNA gene as a reference gene for normalization of data in the patient's exosome with a healthy sample by real-time PCR.

Results: The findings of this study showed that the isolated exosomes have a spherical appearance with a size range of 30 to 150 nm. After real-time PCR, in the Roc curve analysis, the area under the curve (Area under curve, AUC) for miR-93 was calculated to be 0.74. Examination by ΔCt parameter also showed a significant difference in the serum exosome of patients compared to healthy exosomal samples. This ratio of miR-93 expression in the serum exosome of colon adenocarcinoma was significantly higher than normal serum exosome (P <0.01). The expression level of miR-93 in Stage 3 showed higher expression than Stages 1 and 2 (P <0.05). The expression level of miR-93 in patients with lymph node metastasis was higher than in patients without lymph node involvement (P <0.01).

Conclusion: The results showed that increased expression of and miR-93 in the serum exosomes of patients compared to healthy samples could be a criterion for the diagnosis of colorectal cancer. In addition, the expression of these two miRNAs with the clinical pathological features of the disease can confirm their biomarker potential.

Keywords: Colon adenocarcinoma, Exosome, MicroRNA, Biomarker,miR-93

Investigating The Function Of Circular RNA In Diagnosis And Treatment Of Colorectal Cancer (Review)

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Introduction: Colorectal cancer (CRC) is one of the most common malignant tumors of the digestive tract,is a serious disease characterized as uncontrolled division or abnormal growth of colon or rectum cells. (CRC) is the second most common adult cancer in women and the third most common in men, and it is the fourth leading cause of cancer death.The risk of developing CRC is affected by genetic, epigenetic and environmental factors. Circular RNAs (CircRNAs) is a class of endogenous noncoding RNAs, and are generated from back-splicing events and defined by covalently closed circular configuration without 5' end caps and 3' polyadenylated tails. Compared with linear RNAs, CircRNAs are much more stable than linear RNAs (with a half-life beyond 48 h) which have a high degree of stability and potential effect on gene regulation. Among the lncRNAs, circular (circ)RNAs are a group of naturally occurring endogenous ncRNAs having transcript lengths of hundreds to thousands of nucleotides. circRNAs have been investigated as specific targets for diagnostic and prognostic detection of CRC. These non-coding RNAs are also linked to metastasis, proliferation, differentiation, migration, angiogenesis, apoptosis, and drug resistance, illustrating the importance of understanding their involvement in the molecular mechanisms of development and progression of CRC. circRNAs have unique associations with tumour size, staging and overall survival in CRC that lend circRNAs the potential to serve as diagnostic and prognostic biomarkers. We aim to provide insight in the development of therapy and clinical decision-making.

Methods: circRNAs as biomarkers for colorectal cancer ; Several circRNAs have been proposed as useful therapeutic targets for CRC. For instance, hsa_circ_022382 which is derived from the human FADS2 gene is overexpressed in 200 CRC tissues, where CircFADS2 overexpression was positively associated with clinicopathological features. In another study, hsa_circ_0026344 was shown to be significantly downregulated in 32 CRC patients compared to paired adjacent non-tumorous tissues. circRNAs in predicting response to chemoradiotherapy; hsa_circRNA_0001313 is one of the upregulated circRNAs in radio-resistant CRC tissues. Inhibition of hsa_circRNA_0001313 induces radio-sensitivity, reduced cell viability, and

increases caspase-3 activity and colony formation by negatively modifying miR-338-3p in CRC cells. Another recent study reported that CircDDX17 was down-regulated in CRC, and its overexpression induced inhibition of 5-Fu resistance, blocked tumor growth, and CRC progression via sponging miR-31-5p . Interestingly, Circ-32883 was upregulated in CRC tissues and its overexpression was positively associated with chemoresistance through its potential action as a sponge for miR-501-5p. This miRNA binds to EML5 mRNA, inhibiting its expression. Thus, promoting resistance to FOLFOX therapy.

Results: CircFADS2 expression may therefore be a promising biomarker for prognostic investigation in CRC patients . The expression of hsa_circ_0026344 was correlated with tumor size and lymph metastasis. Functionally, circRNA-0026344 overexpression significantly suppressed CRC cell proliferation and colony formation as well as promoted apoptosis by regulating miR-21 and miR-31 levels . Targeted therapy, chemotherapy, and multiagent regimens, for example, FOLFIRI (5-FU and irinotecan) and FOLFOX (5-FU oxaliplatin) can be applied as the standard treatment of CRC. Recent studies have shown that different ncRNAs such as circRNAs, may play important roles in the regulation of chemoresistance and affect the sensitivity of tumors to chemotherapy and radiotherapy through modification of various signaling pathways, including cell cycle, proliferation, apoptosis, and DNA damage repair .

Conclusion: circRNAs are an ideal biomarker in cancer, and are stably expressed in exosomes, blood, and saliva, where specific circRNAs have been indicated as promising prognostic or diagnostic biomarkers already. Abnormal expression of circRNAs has been observed in a wide range of human malignancies and their dysregulation can alter gene expression networks, leading to dramatic changes in cell fates, including cancer initiation and progression. circRNAs can be both oncogenicand anti-oncogenic, so could potentially be utilized in the treatment and prognosis of colorectal cancer. Although recent advances on circRNAs have highlighted some interesting insights, much work remains to be done to translate circRNAs into clinical application for clinical patient benefit.circRNAs have significant potential for the treatment and diagnosis of CRC.

Keywords: circRNAs ,Colorectal cancer , biomarkers , oncogenic

Investigating the Impact of Social Media on the Health of the Elderly: A Systematic Review (Review)

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Introduction: The aging population and social media are currently the two main social phenomena. Social media greatly increases public access to health information, and as a result attracts older people who care more about their health. Under the influence of social media, the real life experiences of the elderly become more and more connected to the online world, and the impact of the Internet on healthy aging can not be ignored. Therefore, the purpose of this study is to investigate the impact of social media on the health status of the elderly in a systematic review.

Methods: To achieve this goal, the researcher conducts a systematic review of studies without time constraints by searching for the keywords Elderly, Social Media, Health in the authoritative scientific databases Scopus, PubMed, Web of Sciences and Google Scholar on June 15, 2022. Explore the contract. Inclusion criteria include studies in English, the presence of keywords in the title and abstract of articles, studies including the participation of the elderly and studies focusing on the impact of social media on the health of the elderly, and exclusion criteria include the absence of one of the keywords in the title and abstract Articles and abstracts without full text. The quality of the studies was also assessed based on the JBI checklist.

Results: A total of 753 articles were obtained and evaluated, and finally, out of 753 evaluated articles, 13 articles were carefully reviewed and included in the study. In general, the results of a series of studies showed that there is a positive and significant relationship between the use of social media and the health of the elderly. Social media has increased the levels of health management for the elderly. The positive effects of social media on the health of older people include: meeting emotional needs, communicating face to face with family and friends, expanding social relationships with people with common interests, increasing mental well-being and life satisfaction.

Conclusion: Although the mechanism of the effect of using social media on the health of the elderly has been analyzed and most studies have shown that social networks can have a positive effect on important aspects of mental health, but the results of this study only prove that the use Social media is significantly associated with healthy people. Due to the lack of controlled

trials, this study could not determine whether the use of social media has a significant impact on the health of the elderly.

Keywords: Social Media, Health, Elderly

Investigating the impact of the Covid-19 pandemic on the vaccination coverage of children under 6 years old in Qom province (Review)

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Introduction: Background and porpose: With starting of the sars-cov-2 (Covid-19) disease in the world, the issue of routine vaccination of people, became to a very important challenge, especially children. According to the World Health Organization reports, the Covid-19 epidemic has challenged the provision of routine vaccination and the number of children who receive routine vaccines worldwide has decreased. The present study was designed and implemented to determining the impact of the covid-19 pandemic on the vaccination coverage of children under 6 years old (12 and 18 months old) in Qom province in two time periods before and after the covid-19 pandemic.

Methods: Materials and Methods: The present study is of quantitative type and cross-sectional descriptive analytical in applied type. Vaccination coverage data in 2020 and 2021 (before starting and during of the epidemic) was extracted based on the information of children's documents in the Sib database. The rate of non-vaccination and delay in vaccination in the two periods were compared. Data analysis was conducted in SPSS software by paired t-tests, Wilcoxon, independent t, Mann-Whitney, one-way analysis of variance, Kruskal-Wallis and Spearman's correlation tests. The significance level of the tests was considered less than 0.05.

Results: Results: The mean of delay in the first (MMR1) and second (MMR2) doses of measles vaccine was estimated 14.48±26.95 and 20.67±28.74 days, respectively, and the mean delay time of MMR1 and MMR2 vaccine was obtained equal to 6 and 11 days, respectively. Measles vaccination coverage decreased from 87.6% before the Covid-19 pandemic to 74.7% during the pandemic. In addition, the prevalence of non-vaccination rate increased form 12.4% for MMR1 before of starting pandemic to 25.3% for MMR2 during the pandemic which indicates a 12.9% increase in non-vaccination of MMR.

Conclusion: Conclusion: The Covid-19 pandemic has caused a disruption in the routine vaccination of children. After the Covid-19 pandemic the prevalence of vaccination coverage reduced and the delay time in receiving the vaccine in vaccinated children increased. Although higher education of mothers, non-employment of mothers and Iranian nationality have shown a positive relationship with higher and on-time immunization, but the fear of disease transmission in health environments and vaccination centers, as well as some cultural factors, have caused vaccine phobia in the society.

Therefore, appropriate interventions to promote and expand routine immunization coverage and provide safe services in special conditions is essential.

Keywords: Key Words: Covid-19 pandemic, Vaccination coverage, Immunization, vaccination delay, measl

Investigating the Impact of Violence Against Women and Its Consequences on Reproductive Health: A Systematic Review (Review)

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Introduction: Violence against women is common and leads to costly problems for both society and women's reproductive health. Worldwide, one in three women has experienced domestic violence, and very few studies speak of violence and its consequences for women's health. Gender-based violence against women and girls is pervasive and has negative consequences for sexual and reproductive health. Therefore, the aim of this study was to investigate the consequences of violence on women's health in terms of adverse outcomes of pregnancy and reproductive health.

Methods: To achieve this goal, a systematic review without time limit was searched by searching for keywords in the title and abstract of studies in the reputable scientific databases Scopus, Web of Science, PubMed and Google Scholar on June 15, 2022. Titles and abstracts were screened independently based on eligibility criteria. Inclusion criteria included studies in English focusing on the two main terms violence against women, reproductive health, access to the full text of the article, and studies that provided possible answers to questions based on title and content. Exclusion criteria included a text without a full text, no keywords in the title or text of the article, and studies that did not provide any scientific, theoretical, laboratory, or statistical evidence. A total of 9 articles were included in the study.

Results: The results of studies show that violence is higher among a group of illiterate women who have had multiple marriages. There are many forms of violence against women, including partner violence, sexual coercion, exploitation and rape. Injuries that affect women's health from sexual violence include: pelvic pain (<80%), genital infections (<50%), irritable bowel syndrome (<50%), miscarriage and termination of pregnancy, irregularity Menstruation (53.5%). Unfavorable birth outcomes in sexual violence include: low birth weight, 10.5%; Preterm delivery 26.5%; And infant mortality is 2.9%.

Conclusion: The findings of this study may increase our understanding of the impact of violence against women and their reproductive health and thus highlight the importance of measures to prevent spousal violence.

Keywords: Violence against women, Reproductive health, Rape, Depression

Investigating the inhibitory effect of flavonoid compounds on the neuraminidase enzyme of swine influenza virus (Research Paper)

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Introduction: Acute respiratory infectious diseases are one of the most important medical problems of societies, and swine flu, which causes damage to the upper and lower respiratory system, is one of the most important types of these diseases. Influenza virus usually infects a large group of people in two ways, seasonal and pandemic. The outbreak of seasonal diseases with the beginning of the winter season causes more high-risk groups such as children and the elderly to become infected, and in a pandemic, about 25% of the world's population is affected, and it affects all age groups and causes a high number of deaths. At the same time as influenza occurs, other complications may also occur in the patient's body, which can prolong the course of the disease or, in some cases, lead to death; One of the most important complications is primary viral pneumonia, which in most cases causes secondary bacterial pneumonia. The neuroaminidase enzyme of the H1N1 influenza virus breaks down the terminal sialic acid of the glycoconjugates on the surface of the target cells in the upper respiratory tract of mammals. Research has shown that drugs that are made against hemagglutinin and neuraminidase can improve the symptoms of influenza. The drug resistance observed against the treatment has caused the need to introduce alternative and more effective inhibitory treatments.

Methods: In this study, which was carried out in a computer environment and by bioinformatics method, the neuroaminidase enzyme crystallography file was received from the NCBI database, and after selecting the A chain, it was optimized and reduced with Gromax software. The file with the extension .sdf of the compounds used in this research was downloaded from the Pubcam database and converted to .pdb format with the OpenBabel software. Molecular docking was done in the HEX8.0.0 software environment and the binding position of the studied compounds on the protein was obtained using Argoslab software. The analysis of the obtained results was done with WebLab Viewer, Piemol, Excel and Leagueplot software.

Results: The researched compounds from the flavonol class include myristin, murine, fistin, quercetin, kaempferol and galangin and from the flavon class including disometin, luteolin, apigenin, chrysin, catechin, hesperitin, genistein,

nobiltin, naringin and hispidolin and the studied antiviral compounds include were oseltamivir, zanamivir, amantadine and rimantadine. From this study, it was found that the antiviral drug rimantadine binds to amino acid proline 431 of the enzyme by hydrogen bonding; Also, myristin, quercetin and fistin from the flavonol class were bound to tryptophan 189 and galangin, kaempferol and murine all three were bound to the amino acid arginine 371 in the binding pocket of the enzyme.

Conclusion: It was also observed that chrysin, genistein, hesperitin, naringin and luteolin from the flavone class were bound to the amino acid arginine 371 of the active site of the enzyme, and catechin, hispidolin and nobiltin were bound to three different sites in the binding site of the enzyme.he results of this study showed that the three flavonoid compounds galangin, murine, and kaempferol from the flavonol class and chrysin, genistein, hesperitin, naringin, and luteolin from the flavone class flavonoids, by binding to arginine 371 of the enzyme's active site, inhibit the enzyme's function; From this study, it was found that naringin is a stronger inhibitor due to its greater affinity for the active site of the enzyme.

Keywords: Neuroaminidase, Molecular Docking, H1N1 influenza, Flavone, Flavonol

Investigating the interaction between the BIRC5 gene as a biomarker and its associated miRNA in breast cancer through bioinformatics analysis (Research Paper)

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Introduction: Almost every year, tens of thousands of women worldwide die from breast cancer (BC), one of the most aggressive malignant tumors. With about 17 million cases occurring annually, its prevalence is alarming. Bioinformatics analysis was conducted to identify the genes differentially expressed in carcinogenesis and progression of BC.

Methods: The GSE21422 was selected from GEO datasets to identify the differentially expressed genes (DEGs) between 5 tumor and 5 healthy samples in a breast cancer microarray experiment. The GEO2R analysis was performed on DEGs from BC samples compared to noncancerous samples. The adjusted P-value < 0.01 and log2FC (fold change) >5 were considered as statistical significances. Gene functional categories were determined by using the DAVID database as a Gene Functional Classification Tool. The analysis of the DEGs pathways was done in the Kyoto Encyclopedia of Genes and Genomes (KEGG). The associated microRNA (miR) with Baculoviral IAP Repeat Containing 5 (BIRC5) gene was found in the miRDB online database. The miRWalk online database was used to find the interactions between selected miR and associated genes.

Results: A total of 23 DEGs were identified, and GO analysis revealed the role of the BIRC5 gene in the anti-apoptosis of breast cancer. The KEGG database showed that the BIRC5 gene is a member of the inhibitor of apoptosis (IAP) gene family, which encodes negative regulatory proteins that prevent apoptotic cell death. The inhibition of this gene plays an essential role in the apoptosis of breast cancer. The results also showed that has-mir-548t-3p could have a suppressive impact on the inhibitory activity of the BIRC5 gene through apoptosis.

Conclusion: It was found that BIRC5 could act as a biomarker and play a role in anti-apoptotic processes in breast cancer cells based on bioinformatics research. The has-mir-548t-3p can be used as a treatment strategy to lead these cells to apoptosis in treating such patients.

Keywords: has-mir-548t-3p, GEO, anti-apoptosis, DEGs, treatment strategy

Investigating the level of interleukin-6 in ovarian cancer malignancy: a meta-analysis study (Research Paper)

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Introduction: Ovarian cancer (OC) is the second most common cause of death in women with gynecologic cancers. OC is the main cause of cancer-related deaths in the female reproductive tract. Considering the limited prognosis of OC, many efforts have been made to determine new predictive biomarkers that can help physicians approach the treatment of patients with OC. Recent studies have shown that various cytokines are secreted by cancer cells in OC. The tumor environment in which OC develops has been described as an environment enriched with a wide range of proinflammatory cytokines and chemokines. In particular, some of these cytokines such as Tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6) are produced by the tumor itself and by active immune cells that stimulate cancer cell growth. IL-6 is a multifunctional cytokine with multiple biological functions that can be produced by a variety of normal and malignant cell types and can also serve as an autocrine growth factor in malignancies. Previous studies have shown that significant amounts of IL-6 are produced by cancer cells (OC) and that IL-6 increases tumor cell survival. With this in mind, the main aim of this meta-analysis is to investigate the level of IL-6 as a biomarker to diagnose the malignancy of tumors in OC.

Methods: In the present study, a data search was performed in the Pubmed and Scopus databases using the keywords "ovarian cancer" (ovarian cancer) and "interleukin-6" (interleukin-6). In the next step, 5 articles were included in the meta-analysis study based on the reviews. Data analysis and evidence synthesis by The calculated pooled effect size [Standardized mean difference (SMD) and Difference in means (MD) and 95% confidence intervals (95% CI)]; to assess the difference between groups was quantified using a fixed effects model Data heterogeneity was assessed with the I2 index and data were analyzed with Comprehensive Meta-Analysis V3 software.

Results: Finally, five studies with 591 participants were identified. Cases with malignancy in ovarian cancer had a significant increase in IL-6 levels compared to the control group (SMD= 0.501; 95% CI: 0.312-0.690; P< 0.001).

Conclusion: The results of this meta-analysis study show that IL-6 levels are higher in patients with ovarian cancer who are more malignant and advanced than in the group of patients who are in the early stage of the disease. In addition, IL-6 can be used as a marker to detect the progression and malignancy of ovarian cancer.

Keywords: interleukin-6, ovarian cancer, biomarker, malignancy, meta-analysis.

Investigating the mechanisms of thrombosis caused by the injection of Covid 19 mRNA vaccines (Review)

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Introduction: COVID19 infection has become the world's major concern from 2019, and no fully effective medicine has been introduced to treat this disease. Therefore, vaccination is the best strategy to deal with this disease, and so far, a large number of vaccines have been designed and produced on different platforms. Of these, mRNA vaccines have made a significant contribution to vaccination because they have advantages such as high safety, efficacy, and easier production. Unfortunately, one of the commonly reported side effects of this type of vaccine is thrombosis in some people. This study aims to investigate the possible mechanisms of thrombosis.

Methods: By searching the term" intitle: "mRNA vaccine" AND thrombosis AND coronavirus OR SARS-CoV-2" in the Google Scholar search engine. Numerous articles were reviewed and screened, and 11 articles were finally carefully investigated.

Results: Many studies have reported different mechanisms for clot formation due to the injection of vaccines containing mRNA. The vaccine based on ribonucleic acid contains mRNA that produces Protein S. Protein C and S work together to inactivate two important coagulation factors, V and VII. Also, A-II (Angiotensin II), which normally should be deactivated by binding to ACE-2, in another mechanism, due to the binding of Protein S1 subunit to ACE-2 and its inactivation, remains active and by releasing aldosterone and raising blood pressure participates in the formation of clots. Another mechanism is the contamination of platelets with mRNA. In this case, Protein S that is inside the platelet starts multiplying intensely. Faced with this amount of Protein S, the body orders the production of anti-platelet antibodies, which leads to the death of platelets and ultimately the formation of clots. On the other hand, if the person's body has a high level of antibodies or is infected with SARS-CoV-2 during that vaccination period, after the injection, if a strong immune response is created and the complement system is activated, resulting in the death of the vaccinated cell, a large quantity of Protein S and its fragments

are released into the blood, in addition to increasing the probability of clot formation, it also leads to abnormal glycosylation of IgG. Another path of clot formation is the presence of antibodies that are produced against spike glycoproteins and cross-react with myocardial contractile proteins. Due to the increased incidence of clots in men, research has shown that testosterone can inhibit anti-inflammatory immune cells and induce a powerful immune response of the T helper lymphocyte type. In contrast, estrogen has inhibitory effects on pro-inflammatory T cells, thereby reducing the cellular immune response. Also, the immune system may recognize the mRNA contained in the vaccine as an antigen, which leads to the activation of inflammatory cascades and immune pathways.

Conclusion: Since mRNA-based vaccines are considered a new platform, knowing and understanding the mechanisms of clot formation in mRNA-based vaccines allows scientists to continue their research to eliminate the side effects of these vaccines. The current study has investigated the mechanisms involved in causing thrombosis by injecting this vaccine platform.

Keywords: mRNA vaccine, Covid 19, thrombosis, and protein S

Investigating the possibility of using ureB and hcpD genes in the production of recombinant DNA-based vaccine against Helicobacter pylori (Review)

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Introduction: Helicobacter pylori located in the human stomach is the cause of diseases such as gastritis, peptic ulcers and cancer of lymph nodes and digestive system. However, despite the major problems of H. pylori, a medical vaccine against this bacterium has not yet been developed. The best way to prevent infections is vaccination, and so far research has been done on recombinant subunit vaccines and gene vaccines. The production and purification of recombinant proteins is one of the most expensive stages of antibody production, and therefore, the use of DNA-dependent vaccines due to the ease of mass production of recombinant plasmids compared to the production and purification of recombinant proteins and the increase in the duration of immunity due to the continuous expression of antigens and the occurrence of immune response Humoral and cellular can significantly reduce these processes. The purpose of this research is to collect the fastest research results related to the production of recombinant nucleic acid vaccines based on Helicobacter pylori antigens to stimulate the humoral and cellular immune response.

Methods: In this research, SID, ISI and Google Scholar databases were used and the content was collected using the keywords of recombinant vaccine against Helicobacter pylori. In the articles, methods and results were further investigated and the methods of gene extraction from DNA, gene cloning in plasmid vector, transformation of recombinant vector in prokaryotic expression system and subcloning of the final recombinant construct in eukaryotic systemic expression were investigated. Finally, the methods of analyzing the accuracy of the activities were examined and the best method was chosen.

Results: Diagnostic tests for Helicobacter pylori infection include tests that require endoscopy, such as rapid urease test (RUT) and PCR, and non-endoscopic tests, including antibody tests and urea breath tests. Due to the breakdown of urea molecules and the production of ammonia and carbon dioxide by Helicobacter pylori, which creates a sheath of ammonia around the bacterium that protects it from stomach acid, the production of large amounts

of urease enzyme is necessary for the survival and pathogenicity of H. pylori. H. pylori active urease depends on the presence of ureA/B gene constructs to form a 550 kDa holoenzyme. Also, sub-genes ureL/E/F are necessary for the high expression of urease activity and ureB/G/I for the establishment of bacteria in the stomach. ureB is the most effective immunogen of all H. pylori strains that can create a protective immune response in the body against this bacterium. Therefore, ureases, especially ureB, are considered suitable candidates for making a vaccine against H. pylori. Also, recent analyzes indicate active penicillin binding in the HCP protein structure, and more specifically in hcpA, hcpB and hcpD. H. pylori infection can be diagnosed with the immunological assay of this protein, and considering that the hcpD gene in this protein group is able to stimulate the host's immune system, this gene is also considered as a candidate for vaccine production. In all studies, a DNA extraction kit was used to extract genomic DNA, and then the extraction product was electrophoresed on agarose gel. In one of the studies, the concentration test was also done with a nanodrop device, and then the gene product was amplified by PCR. In the most successful studies, the T/A method was used for cloning, which is a fast method without the requirement for restriction enzymes, and the genes were transformed in the pTZ vector. Different strains of E.coli bacteria were used for transformation, and E.coli Top10F strain was used more than other strains. In all studies, LB-Agar growth medium containing ampicillin was used, and the correctness of cloning was confirmed by enzymatic digestion, PCR, and sequencing. Due to the lack of a promoter in the upstream of the cloned gene in the pTZ vector and the inability to reproduce and express the gene in eukaryotic cells, pcDNA3.1(+) vector was used. The two vectors were cut and the gene was removed from the pTZ vector; Also, the vector was linearized. T4 DNA ligase enzyme was used for binding and 2 studies were similar in using CHO cells. Electroporation was used for this cloning. The most important analyzes used were electrophoresis in different stages, enzymatic digestion, RT-PCR, SDS-PAGE and western blotting.

Conclusion: According to the results of the studies based on the successful cloning of the final recombinant structure in eukaryotic cells and changing part of the behaviors of rats, as well as the possibility of multiplying these structures, Helicobacter pylori genes including ureB and hcpD can be used in vaccine production.

Keywords: ureB, hcpD, Recombinant DNA, Helicobacter pylori, vaccine

Investigating the Potential Impact of Variables in nontranslocational Regions of key Genes in Amyotrophic lateral sclerosis and Their Relationship with Disease Progression (Research Paper)

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Introduction: Amyotrophic lateral sclerosis (ALS) is an irreversible neurodegenerative disorder characterized by the selective and progressive loss of upper and lower motor neurons of the cerebral cortex, brainstem, and spinal cord. Leptin has been suggested to play a role in amyotrophic lateral sclerosis (ALS), a fatal progressive neurodegenerative disease. This adipokine has previously been shown to be associated with a lower risk of ALS and to confer a survival advantage in ALS patients. Genome-wide association studies (GWAS) are the most common approach to detecting relationships between genetic variants (frequently, a singlenucleotide polymorphism—SNP) and disease occurrence. One of the possible cause is single-nucleotide polymorphisms (SNP) in the untranslated region (UTR) of active genes in CNS.

Methods: The literature review was used to collecting the ALS -related most susceptible genes. Then, using miRNASNP database, the miRNA-related SNPs located on the 3'UTR of genes were identified. Finally, the pathway enrichment analysis was performed by the KEGG database.

Results: Our results demonstrated that plasminogen activator inhibitor type 1 (PAI 1), gastric inhibitory peptide (GIP), glucagon-like peptide 1 (GLP-1), insulin and glucagon are critical genes in ALS progression, in which on their 3'UTR there are some high-frequency polymorphisms located within the miRNAs target site. These variants may result in an expression blockage of mentioned genes during ALS. The pathway analysis resulted to found that miRNAs in genes (PAI-1 rs1436918 G/A with miRNA: hsa-miR-499a-3p, GIP rs16984239 C/T with miRNA: hsa-miR-551b-5p/3p, GLP-1 rs10459680 T/G with miRNA: hsa-miR-3126-5p/3p) have interfering effects on same of the cancers and hepatitis genes.

Conclusion: Upon the fact that any changes in SNP alleles cause mutations in the vital genes for the normal functioning of the nervous system, it can be stated that these SNPs may play role in development and progression of ALS.

These results may open the new route to develop molecular controlling of Cancer, Hepatitis and ALS in future.

Keywords: Amyotrophic lateral sclerosis, SNP, MiRNA

Investigating the presence of racepinephrine drug in Nepeta medicinal plant subspecies (Research Paper)

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Introduction: With the progress of science, medicinal plants entered the industry, and their effective ingredients became available in the form of medicine after purification and refinement.

Methods: Nepeta, which grows in the foothills of Kerman province, was chosen as a medicinal plant with significant uses. GC-MASS analysis in two subspecies confirms the presence of the medicinal compound Racepinephrine. is a vasodilator effective in the treatment of asthma.

Results: Racepinephrine is a vasodilator effective in the treatment of asthma.

Conclusion: It is hoped that the production of this drug can be increased with the mass production of this plant and its successful formulation.

Keywords: Racepinephrine , nepeta , kerman medical plants

Investigating the probiotic characteristics and anticancer properties of Lactobacillus fermentum isolated from breast milk on breast cancer cell lines (Research Paper)

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Introduction: Lactic acid bacteria have been categorized as probiotics and play a crucial role in human health by stimulating the supply of nutrients, shaping the immune system, and preventing the colonization of pathogenic microbes. Breast milk contains many bioactive compounds such as oligosaccharides, immune cells, and a wide range of different bacteria and their metabolites. Studies have shown that breast milk has 700 different types of bacteria, which include types of probiotics such as Lactobacillus, Streptococcus, and Bifidobacterium. In this study, a lactic acid bacteria, was isolated from human breast cancer, and was identified by using Basic Local Alignment Search Tool search of its amplified 16S rRNA gene sequences. Several primary tests were conducted on isolated bacterium, including Gram staining, catalase assay, low pH and high bile salt concentration tolerance to prove the probiotic properties of isolates. The present study characterized the probiotic potential of an isolated stain, originally isolated from human breast milk. The acid tolerance, bile tolerance, antibiotics susceptibility, and antioxidant activity of these strains was evaluated. The MCF-7 and MDA-MB-231 breast cell lines were used to test the anticancer potential of the heat killed and cell free supernatant of this strain.

Methods: 2.1 Subjects and cultivation of samples Twenty milk samples of healthy women (aged 25 to 34 years old) were collected. All participants signed an informed consent prior to study enrollment. The participants were enrolled according to the following criteria: (1) healthy and without present or past underlying conditions; (2) no antibiotics prescription for at least three months prior to the study; (3) did not taken any probiotics prior to study; (4) normal pregnancy. The milk samples were filled in a sterile container and processed immediately upon receipt. 2.2 Isolation and screening of lactic acid bacteria isolates The samples were diluted in phosphate buffffer saline (PBS) (0.1 M, pH 7.2) and spread on de Man-Rogosa-Sharpe agar plates. The plates were aerobically incubated at 37 °C for 72 h. Pure colonies were

isolated and sub cultured for further experiments. Each selected LAB strains was subjected to tests of morphology, catalase, and Gram's reaction. The isolates of Gram's positive, catalase negative and rod shape were suspected to be lactobacilli and then maintained in MRSc supplemented with 20% glycerol at −80 °C. 2.3. Identification of lactic acid bacteria Molecular identification was used to identify the obtained strain. The total genomic DNA of selected strain was extracted using the Genomic DNA purification kit (Addbio®, Korea) following the manufacturer instructions. The primers used to amplify the 16S rDNA sequences of these strains were forward 5″-AGAGTT TGATCC TGG CTC AG-3″ and reverse 5″-CCGTCA ATT CCT TTGAGT TT-3″. The fragment was amplified using a T100 thermal cycler (Bio-Rad, Hercules, USA) under the following conditions: 94 °C, 30 cycles of 94 °C for 1 min, 58 °C for 45 s, 72 °C for 1 min and finally 72 °C for 10 min. The amplified fragment was screened on an agarose gel (1%) and sequenced by Automated DNA Sequencer (ABI 3500 Genetic Analyzer). The obtained sequence was searched by using the Basic Local Alignment Tool (BLAST) program Conventional lab techniques for analysis of LAB 2.4.1 Gram Staining The Gram staining of the isolate was determined by light microscopy using Gram staining reagents. It is known that LABs are gram-positive. This means that these cultures will produce blue-violet color for Grampositive bacteria and vice-versa. The cultures were grown in MRS media at 37 °C for 24 h under micro-aerophilic conditions. Fresh cultures were used for gram staining. After incubation, the cultures were aseptically transferred into 1.5 ml of eppendorf tubes and centrifuged for 3 min at 9000 rpm. The cells were resuspended in sterile water by removing the supernatant.

Results: 3.1 Conventional lab techniques The isolated strain was subjected to Gram staining and examined under a light microscope (100X magnification). The strain showed blue-purple color staining. Hence the isolated strain was found Gram-positive bacterium. According to our result the strain was recorded as catalase negative. Absence of hemolytic activity was also observed. The result of Arginine hydrolysis test showed that the isolated stain did not produce ammonia from arginine. 3.2 Identification of Lactobacillus stain The result showed that the isolated strain belonged to genus Lactobacillus. The 16S rDNA gene sequence result showed that isolate had 99% homology with L. fermentum. 3.3 Low pH and high bile salt concentration tolerance test The results of acid tolerance test revealed that isolated strain tolerated acid conditions and the residual cells were more than 50% (68%) of the initial cells even after 2 h of incubation at the pH 2.5. According to the results, Cinh for this strain was bigger than 0.4 (0.9). It means susceptibility of this strain to oxgall. 3.4 Antibiotic resistance test The antibiotic resistance of the strains was assessed toward six antibiotics via the disk diffusion method. According to the results, the isolated strain was sensitive to tetracycline, cephalexin, ampicillin, penicillin, and

trimethoprim/sulfamethoxazole. This strain was only resistant toward gentamicin.

Conclusion: In the present study, the probiotic characteristics and anti-tumor activity of a human breast milk isolated Lactobacillus was investigated. Our results demonstrated that Lactobacillus strain exhibited many typical probiotic characteristics such as Gram staining (Gram-Positive Bacilli), higher survival rate under gastric conditions (lower pH), catalase-negative, L-Arginine test, Lack of hemolytic activity, Lack of Arginase activity. Despite the fact that this strain had most of the properties of probiotic bacteria, it did not show resistance to bile salts, and among the 6 antibiotics that were examined in this study, this strain was only resistant to gentamicin and sensitive to 5 other antibiotics. In the investigation of the effect of cell-free supernatant and killed cells of the isolated strain on the viability of two breast cancer cell lines, it was found that the cell-free supernatant of this strain had no effect on the viability of MCF7 cell line but decreased the viability of MDAMB237 cell line in concentration of 100 µg/ml after 72 hours. The heat killed cells of this strain (in concentration of 25 100 µg/ml after 2 h and 100 µg/ml after 48 hours) significantly reduced the viability of MCF7 cell line. In investigating the effect of killed cells on MDAMB237cell line in all three concentrations (25, 50, and 100100 µg/ml) after 2h the viability) significantly decreased.

Keywords: cancer-breast cancer -probiotic-brest milk-anti cancer

Investigating the relationship between mental health and patience in pregnant women admitted to the maternity department of Shiraz hospitals (Research Paper)

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Introduction: Mental health is necessary to maintain the durability of social, occupational and academic performance of people in the society and its provision is the main goal of implementing mental health programs in the society. Patience is one of the moral concepts that is emphasized a lot in Islamic ethics. What comes to mind from this word is an emotional state that happens to certain people during hardships, calamities and troubles. Therefore, the aim of the present study is to determine the relationship between mental health and patience in pregnant women admitted to the maternity department of Shiraz hospitals.

Methods: This research is a descriptive-analytical study that was conducted cross-sectionally in 2019. The study population consisted of 82 pregnant women admitted to the maternity department of hospitals in Shiraz city, who were included in the study through easy and accessible means. Data were collected through demographic information, standard mental health questionnaire (GHQ) which has 28 questions and includes 4 subscales of physical symptoms, anxiety and insomnia. Disruption in social function, symptoms of depression. Also, a standard questionnaire for measuring the amount of patience was designed by Khormai et al. This questionnaire contains 25 questions, which include transcendence, patience, satisfaction, endurance, and persistence. After collecting, using descriptive statistics, mean, standard deviation and range of changes and inferential tests of independent T-test, ONOVA, Pearson's correlation coefficient were analyzed in spss version 21 software.

Results: The results showed that the average age of the participating pregnant women was 26.23±2.4. 36.58% of them were primiparous women. 24.39% of them mentioned a history of abortion. Also, 41.64% of them had undergraduate education. The average duration of hospitalization in these patients is 2.31. The average mental health score is 104.87±5.42 and the average patience score is 64.03±6.54. There was a significant relationship between age and endurance sub-component (p<0.005). Length of hospitalization with anxiety and insomnia, there was a significant relationship (p<0.005). Also, there was a significant relationship between abortion

history and the sub-component of depressive symptoms (p<0.005). Also, there was a direct relationship between the mean score of mental health and patience. (p<0.005)

Conclusion: The results of the present study showed that the score of mental health and patience was good. Also, age was related to the sub-component of endurance. So that the endurance of pregnant women increases with age. Also, the duration of hospitalization was related to anxiety and insomnia. Doubt that with the increase in the duration of hospitalization, the anxiety and insomnia caused by it increases. Pregnant women who had a history of abortion had more depression than other women. Also, pregnant women who had a higher mental health score were also more patient. Therefore, it is possible to increase the level of mental health of these people with appropriate measures in the form of training workshops for pregnant women at the time of receiving prenatal care in health centers so that pregnant women can use its effects during the stages of childbirth and after.

Keywords: Mental health, patience, pregnant women, maternity department

Investigating the Relationship between rs6983267 Single Nucleotide Polymorphism Variants Located in CCAT2 Gene and Susceptibility to Thyroid Cancer in the Azeri Population of Iran (Research Paper)

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Introduction: Genetic is always one of the most effective factors in the occurrence of cancers, and thyroid cancer is no exception. Single nucleotide polymorphisms or SNPs are one of the most common forms of genetic variation in the population that are present in at least 1% of the population. Presence of SNPs within the gene sequence may affect the final products of the corresponding genes. Especially, SNPs in the genes that are participated in fundamental cellular processes can affect the cellular outcome remarkably. Long non-coding RNA molecules (lncRNAs) play a great role in a variety of important cellular processes, and their role in various disease conditions has been demonstrated frequently. These molecules are RNAs with a length of more than 200 nucleotides that are not translated into protein products. CCAT2 (Colon Cancer Associated Transcript 2), a lncRNA molecule related to Colon Cancer, has recently been found to be overexpressed in thyroid cancer. The rs6983267 SNP in CCAT2 gene with two allelic variants (G (ancestral) and T) has been introduced to be associated by some structural and functional properties of the CCAT2 transcript and susceptibility of several diseases. The aim of this study was investigating the allelic (G and T) and genotypic (GG, GT and TT) distribution of rs6983267 SNP of CCAT2 gene in the Azeri population of Iran as well as their relationship with the incidence of thyroid cancer.

Methods: Genomic DNAs were extracted from peripheral blood of 102 individuals affected by thyroid cancer (including 72 females, 26 males and 4 people with unknown gender) and 103 healthy individuals (including 73 females and 30 males), as controls, by salting-out method. The genotype of each DNA sample was determined using TETRA ARMS PCR followed by agarose gel electrophoresis. One sample of each genotype (GG, GT and TT) was sequenced through Sanger's method to ensure the accuracy of the results. The significance of the data was evaluated using the chi-square test

(X2), and the odds ratio (OR) was calculated for the genotypes (using binary logistic regression models) in three genetic models; dominant, recessive and codominant.

Results: Among 102 thyroid cancer patients in this study, 31 individuals (30.4%) represented the GG genotype, 42 individuals (41.2%) GT genotype and 29 people (28.4%) TT genotype. The age range of patients was between 14 and 77 years, with an average of 39.19 years. On the other hand, in the control group, 25 people (24.3%) showed GG genotype, 45 people (43.7%) represented GT pattern, and 33 people (32%) had TT genotype. Then, the frequency of G allele in patients was estimated 51% and the frequency of T allele was estimated to be 49%. The allelic frequencies of control group were 46.1% for G allele and 53.9% for T allele. Based on the chi-square test results, no significant relationship was found between GG, GT and TT genotypes with susceptibility to thyroid cancer occurence (X2=1.000, P-value=0.607). As well, the chi-square test did not show a significant relationship between G and T alleles with thyroid cancer susceptibility (X2=0.971, P-value=0.324). The results of examining the odds ratios in three models of dominant (GG+GT vs. TT: OR=1.187, 95%CI=0.653-2.156, P-value=0.574), recessive (GG vs. GT+TT: OR=1.362, 95%CI=0.735-2.525, P-value=0.326) and codominant (GT vs. GG+TT: OR=0.902, 95%CI=0.518-1.570, P-value=0.716), and for alleles (G vs. T: OR=1.215, 95%CI=0.825-1.791, P-value=0.325) did not stablished any significant relationship.

Conclusion: In this study, the frequency of genotypes (GG, GT and TT) and alleles (G and T) in the rs6983267 single nucleotide polymorphism locus in patients was obtained to be different from control individuals. However, statistical analysis showed no significant association between genotypes and/or alleles with the occurrence of thyroid cancer in the Iranian-Azeri population (P-value>0.05). It is assumed that investigating more subjects from each patients and controls group may lead to further determine the genotypic and allelic frequencies of this SNP locus in Iranian-Azeri population.

Keywords: Thyroid Cancer, SNP, rs6983267, lncRNA, CCAT2

Investigating the relationship between vegetarian diet and its effect on dental health: a systematic review (Review)

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Introduction: Nowadays, the number of people who are interested in vegetarian diet has been risen. Vegetarianism is a diet that follows some roles like not eating animals or anything that is their product, such as milk or honey. A well-planned vegetarian diet can provide all the nutrients that human body needs, but there are still some concerns about uptaking some nutrients like protein, omega-3 fatty acids, vitamin B12, vitamin D and calcium. Studies till now didn't show if there is a relation between vegetarian diet and dental health but since it's been proven that there is a strong link between dental health and acidic foods and lacking of some nutrients and duo to the high prevalence of toothache in about 2.5 billion people around the world, this field of study needs more attention.

Methods: For this research, existing articles in PubMed, Web of Science, Sid, and Google Scholar databases that have been published till 2022 are systematically selected, and 5 articles are included in this study. This research is done in English considering the following keywords: vegetarian, toothache, dental health, nutrients, diet.

Results: There are some pore evidences that vegetarian diet is associated with dental erosion. In a study between a vegetarian and control group, there was no significant difference in tooth erosion. Comparison between vegetarian groups and non-vegetarian groups showed that vegetarians have an upper degree in tooth wear.

Conclusion: According to studies we reviewed, there was no direct link between vegetarian diet and dental erosion but, duo to highly consume of acidic foods by vegetarians, there was higher occurrence of non-carious cavities in teeth in vegetarians. Based on studies, it can be guessed that better dental hygiene among raw vegans comes from their chosen lifestyle.

Keywords: vegetarian, toothache, dental health, nutrients, diet.

Investigating the synthesis of iron nanoparticles from Brevibacterium Casei and drug delivery through folate receptors in brain cancer (Review)

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Introduction: The use of bacteria for the synthesis of nanoparticles has many advantages, including the high compatibility of nanoparticles with the environment and the ability to produce them on an industrial scale. Green synthesis is a simple and fast method and has recently received much attention. Iron oxide nanoparticles are physically and chemically stable and safe. Brevibacterium Casei is one of the microorganisms capable of producing nanoparticles. Folate receptors, which are expressed in different types of cancer cells, can be used in targeted treatments for cancer. Nanoparticles conjugated with folic acid can help in targeted delivery of drugs used in brain cancer and crossing the blood-brain barrier.

Methods: In this synthesis method, after bacterial culture, the suspension is combined with iron nitrate solution and iron nanoparticles are synthesized. After the conjugation of nanoparticles with folate and drugs, its experimental effects can be investigated and observed in cancer cells.

Results: Metal nanoparticles produced by the green method from microorganisms are promising compounds for future biomedical research. Nanoparticles produced by this method, besides being safe and highly biocompatible, also have the capability of mass production and can be more economical than other methods.

Conclusion: Traditional methods such as radiotherapy and chemotherapy as well as conventional drugs have been ineffective for the treatment of brain cancer. Using nanoparticles produced from microorganisms for targeted drug delivery in cancer treatment can be a new perspective for drug design in the future.

Keywords: green synthesis, folate receptor, blood brain barrier

Investigating the titer of IgG and IgA antibodies caused by the injection of Covid-19 vaccines in breast milk. Systematic review (Review)

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Introduction: Breastfeeding is an optimal way to provide nutrients needed by babies and shape their immune systems. Breast milk-derived immune components are associated with a wide range of enteric and respiratory pathogens that the infant will encounter. Immune cells such as B and T lymphocytes, monocytes, macrophages, neutrophils, natural killer (NK) cells, and antibodies such as IgA, IgG, and IgM can be found in breast milk. Novel coronavirus disease 2019 (COVID-19), a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a major threat to global health. Until August 17, 2022, the number of people who injected at least one dose of vaccine in the world was 5,333,933,998 people. This study aims to investigate the level of immunogenicity of breast milk caused by the injection of covid 19 vaccine for covid 19 disease.

Methods: In this systematic review study, a search was conducted using keywords: breast milk, covid-19, corona vaccine and by extracting similar words from the MeSH database in the Google Scholar, and Pubmed databases until August 20, 2022. The inclusion criteria were articles that measured IgA and IgG antibodies caused by the injection of two doses of AstraZeneca, Pfizer, and Moderna Covid-19 vaccines in breast milk, and the study must be published in English. The exclusion criterion was the lack of access to the full file of the articles.

Results: In this study, a total of 7 articles were extracted according to the selected conditions. The total number of people in these 7 articles was 405. The average age of the mothers was 34.2 years when they participated in the study and they were breastfeeding their babies. The average of IgG antibodies attached to breast milk was 97 and the average of IgA antibodies attached to breast milk was 30.2. Immunoglobins isolated from breast milk showed microneutralizing activity against SARS-CoV-2. No special side effects were recorded in the mother and her child. 18 babies developed a fever after the mother injected the vaccine.

Conclusion: As mentioned, in addition to meeting the baby's nutritional needs, breast milk helps to form their immune system. Although the immunoglobulins caused by the injection of the vaccine are low in breast milk, it gives the baby the ability to fight the corona disease. According to the

statistics of one of the studies, in the worst-case scenario, 0.667% of the original vaccine dose is transferred in 100 ml of human milk given to the baby after vaccination. Our suggestion to the managers of the health and treatment system is to follow up and supervise as much as possible on the completion of vaccination of mothers who have infants.

Keywords: Breast milk, Corona vaccine, Covid 19 disease

Investigation and analysis of KPNA2 gene in liver cancer cells (Research Paper)

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Introduction: Primary liver cancer is a life-threatening illness and one of the fastest growing cancer types. Most primary liver cancer is cancer in your liver and cancer in bile ducts in your liver. Both cancer types have common causes, risk factors, symptoms and treatments. Healthcare providers focus on identifying who might be at increased risk so they can catch and treat primary liver cancer as early as possible. Research has been moving from being strictly conducted in a real-life lab environment to a ‘virtual lab’ environment where data management and analysis are done. . This investigation aimed to find a novel differentially expressed gene in the LIHC patients compared to control samples.

Methods: Expression analysis of GSE174570 achieved from GEO2R online software and validation of expression analyses performed by GEPIA2 database. ENCORI and GEPIA2 performed survival, expression, and correlation analyses. The desired gene to miRWALK to find the target miRNA. Target miRNA was searched in lncBase, and appropriate lncRNAs were found. At last, Cytoscape software was used to show the interaction between the components of the CeRNA network.

Results: Through analysis of the GEO dataset, a gene named KPNA2 was found to be considerably upregulated (|logFC| = 1.012, adj. P. Value <0.0001) in LIHC samples. GeneCards Summary for KPNA2 Gene is KPNA2 (Karyopherin Subunit Alpha 2) is a Protein Coding gene and is a specific biomarker for the diagnosis of liver cancer. The connection with this gene includes RNA binding and statistical methods. Among the pathways associated with the KPNNA2 gene are Calmodulin induced events and Homology Directed Repair. Gene Ontology (GO) annotations related to this gene include RNA binding and histone deacetylase binding. An important paralog of this gene is KPNA2. In the survival analysis, the increase in gene expression is directly related to the death rate. By analyzing possible protein interation,P52292 was selected, and By analyzing possible miRNA-mRNA interactions, hsa-miR-3619-5p was selected.

Conclusion: This miRNA was then searched in LncBase and XIST, the strongest interaction.

Keywords: KPNA2; Cancer; mirwalk

Investigation and analysis of MYH11 gene in Bladder cancer cells

(Research Paper)

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Introduction: Transitional cell carcinoma, cancer begins in cells in the innermost tissue layer of the bladder. These cells can stretch when the bladder is full and shrink when it is emptied. Most bladder cancers begin in transitional cells. Bladder cancer (BCa) is the most common malignancy of the urinary tract and one of the most prevalent cancers worldwide. Research has been moving from being strictly conducted in a real-life lab environment to a ‘virtual lab’ environment where data management and analysis are done. This investigation aimed to find a novel differentially expressed gene in the TCC patients compared to control samples.

Methods: Expression analysis of GSE166716 achieved from GEO2R online software and validation of expression analyses performed by GEPIA2 database. ENCORI and GEPIA2 performed survival, expression, and correlation analyses. The desired gene to miRWALK to find the target miRNA.Target miRNA was searched in LncBase, and appropriate lncRNAs were found. At last, Cytoscape software was used to show the interaction between the components of the CeRNA network.

Results: Through analysis of the GEO dataset, a gene named MYH11 was found to be considerably upregulated (|logFC| = -6.14, adj. P value =2.03e-14) in TCC samples. GeneCards Summary for MYH11 Gene MYH11 (Myosin Heavy Chain 11) is a Protein Coding gene. Among its related pathways are EPH-Ephrin signaling and Integrin Pathway. Gene Ontology (GO) annotations related to this gene include calmodulin binding and cytoskeletal motor activity. An important paralog of this gene is MYH10. In the survival analysis, the increase in gene expression is directly related to the death rate. By analyzing possible miRNA-mRNA interactions, hsa-miR-125a-3p was selected.

Conclusion: This miRNA was then searched in LncBase and LINC02605, the strongest interaction.

Keywords: MYH11; Cancer ; CeRNA ; mirWALK ; LncBase

Investigation and bioinformatic analysis of the effect or lack of effect of FABP7 gene on trachea, bronchus and lung cancer (Research Paper)

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Introduction: Trachea, bronchus and lung cancer is a type of disease characterized by uncontrolled cell growth in the lung tissues. If the disease is not treated, the cell growth can spread outside the lung to nearby tissues or other organs in a process called metastasis. Most cancers that start in the lung, called primary lung cancers, are carcinomas that arise from the lining tissue.[1] Across the developed world, 90% of lung cancer deaths in men during 2000 were attributable to smoking (70% for women). We pay in this GEO disease.[2]

Methods: First, gene expression was measured compared to normal samples with GSE36820 obtained from the GEO database[3] and then by GEO2R [4] and then from the GEPIA2 database [5] to investigate gene expression (decrease or increase) and the effect of the gene on Death was analyzed. The death rate of patients was measured from the Over survival section.[6] After that, gene ontology was checked using Enrich R database.[7] The resulting data were put into KEEG for pathway enrichment. [8] Based on the String database, the interactions were investigated [9] and also in the Mir walk database, possible miRNA_mRNA interactions were analyzed. [10] The microRNA selected for search was checked in [11] the gender card of lncRRisearch and LncBase databases [12]

Results: Based on the microarray analysis and analysis, FABP7 was associated with an increase in the target sample (p_value>0.000945, log fc=6.85) and in examining the effect on the mortality rate with data such as HR=0.61 We found the PPAR signaling pathway in the EnrichR database; this gene is also involved in pathways such as triglyceride catabolic process, acylglycetol catabolic process, triglyceride metabolic process, and nervous system development.Among the proteins that have interacted with the desired gene, we can mention things like: MAML1, RBPJ and KAT2B.Then, the micro RNA confirmed by the Mirwalk database (has_miR_197_3p) has the characteristics of score=1, which is effective in the discussed cancer.

Conclusion: The lncRNAs resulting from the has_miR_197_3p search, which were XIST and PTENP, were confirmed in the Gen card database.[8]The desired lncRNAs and miRNAs are not without influence in the discussed cancer.

Keywords: lung cancer,gene expression,smoking ,death rate,microarray analysis

Investigation of gene lmo2 expression in Acute lymphoblastic leukemia (Research Paper)

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Introduction: In recent years, an increasing trend in the incidence of acute lymphoblastic leukemia (ALL) has been reported. However, the molecular mechanisms involved are not fully understood. The aim of this study was to evaluate the expression of LMO2 gene in patients with Acute lymphoblastic leukemia for the identification of the gene expression changes so that the role of the gene in diagnosis and treatment of the disease could be determined

Methods: This case-control study was performed on 40 ALL patients and 40 healthy controls in the years 2020-2021. For this purpose, total RNA was extracted from blood samples and after cDNA synthesis, LMO2 expression was measured using Real-Time PCR. Statistical analysis of the results was performed using SPSS software and appropriate tests

Results: The results of the gene expression study showed that in patients with ALL, LMO2 expression compared to controls had significant increases. These expression changes were not significantly different in age, sex, MRD, and T-ALL and B-ALL categories

Conclusion: In conclusion, downregulation or upregulation of LMO2 may be of importance in the biology of ALL .Other studies are also required to elucidate the exact function of this gene in cancer

Keywords: Acute lymphoblastic leukemia, LMO2 , Case-control studies, Gene expression

Investigation of amino acid profile in prostate cancer patients by liquid chromatography equipped with tandem mass detector (Research Paper)

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1.

Introduction: Cancer disease is one of the causes of death, and the diagnosis of its early stages has greatly affected the survival of patients. Prostate cancer is the second most common cancer in men and the fourth most common cancer. Prostate cancer is an aggressive disease and usually manifests itself in the advanced stage of the disease. The present study aims to analyze and analyze the metabolic amino acid profile as a strategy to identify biomarkers for the diagnosis and early screening of prostate cancer.

Methods: The present study aims to analyze the metabolic amino acid profile as a strategy to identify biomarkers for the diagnosis and early screening of prostate cancer. Biological samples are provided from patients in the early and often asymptomatic stages of cancer. What is important is the observed changes in the amino acid profile of these patients. Among several analytical methods, LC-ESI-MS/MS is a promising tool. In this pilot study, we are dealing with complex biological samples, so a sample prpration method namly magnetic dipersive solid phase extraction is used to purify and concentrate amino acids. The synthesized magnetic adsorbent and the effective factors on the extraction method are investigated and optimized one by one. In the same way, a device analysis method is also launched to determine the amino acid profile. The parameters affecting the device analysis method are optimized one parameter at a time and are used in the next experiments in an optimized way.

Results: The present study was devoted to synthesizing Fe3O4@SiO2 nanocomposites via silica nanoparticles obtained from rice husk waste and then its functionalization using ammonia solution to get Fe3O4@SiO2-NH2 nano-hybrid as a new sorbent by improving selectivity in aminoacids sorption. The structure and morphology of the synthesized sorbent were characterized by X-ray diffraction (XRD), field emission scanning electron microscopy (FE-SEM), and Fourier transform infrared spectroscopy (FT-IR). As-prepared nano-sorbent was successfully used in magnetic solid phase extraction setup with no hazardous solvents and extraction was performed in 9 min. Some important parameters affecting the extraction of the aminoacids were optimized. Under the optimized experimental conditions, the method provided a linear range of 10-1000 ng mL-1 with the correlation coefficients (R2) of 0.998. The intra-day (n=3) and inter-day precisions (n=3 working days) calculated in the form of percent relative standard deviations (%RSDs) were below 10%. The proposed method was successfully practiced for analyzing

aminoacids in several human plasma samples, with recoveries in the range of 84.0–109.5% for the spiked samples.

Conclusion: This study obtains and analyzes the profile of free amino acids in the plasma of prostate cancer patients and healthy men. Considering the contradictory results in changing the characteristics of amino acids in cancers and the high prevalence of prostate cancer in Iran and the lack of epidemiological studies on the level of plasma amino acids in patients with prostate cancer, this study can provide the basis for further studies. Determining amino acid profile using non-invasive HPLC-Tandem MS and new extraction method based on magnetic adsorbent helps in simple separation of amino acids from complex environment and their rapid determination. The developed method is a reliable method for prostate cancer screening, diagnosis and pathogenesis.

Keywords: Biomarker - Prostate cancer - Amino acid profile - Magnetic solid phase extraction

Investigation of antibacterial and antifungal effects of aquatic, ethanolic and methanolic extracts of Acroptilon repens against on E. coli (ATCC 25922) and Malassezia furfur (ATCC 96810) compared by ciprofloxacin and fluconazole (Research Paper)

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Introduction: is the plant belongs to the Asteraceae family, various chemical compounds in its are responsible for the characteristics of the plant. Introduced invasive weeds are a serious problem in grasslands globally (Baker, 1986). These species can have adverse economic impacts by reducing crop yields or the quality of grazing lands and can have negative ecological impacts including reducing biodiversity, endangering rare communities and altering processes such as nutrient cycling (Vitousek, 1990, Young and Longland, 1996, Higgins et al., 1999, Stohlgren et al., 1999). At least 57 000 km2 of public rangelands in the western United States have been invaded by noxious weeds. The total geographic range of these species has quadrupled from 1985 to 1995 (Westbrooks, 1998). Introduced perennial species are particularly important, as they have the capability to dominate native vegetation for extended periods of time. There are a number of factors that influence invasion dynamics, including life history traits of native and exotic species, and physical characteristics of the site, such as soil texture and climate. We have a limited understanding of the relative importance of these different processes and environmental conditions on invasion dynamics. Most studies of invasive perennials have focused exclusively on management methods and have met with limited success (Donald, 1990, Fay, 1991, Rosenthal et al., 1991, Benz et al., 1999). A broader understanding of the ecological processes underlying the invasion and spread of exotic perennial weeds can contribute to our understanding of plant ecology as well as improve our ability to control and eliminate weed infestations (Cousens and Mortimer, 1995, Sheley et al., 1996, Sheley et al., 1999).

Methods: In this study antibacterial and antifungal effects of aquatic, ethanolic and methanolic extracts of Acroptilon repens against on E. coli (ATCC 25922) and Malassezia furfur (ATCC 96810) compared by ciprofloxacin and fluconazole were investigated. Disk diffusion (10, 20, 30, 40 & 50 µl) and well diffusion (100, 110, 150 & 200 µl) strategies to screen antimicrobial activity of Acroptilon repens extracts against E. coli and Malassezia furfur, Then MIC and MBC/MFC of extract were determined

Results: Results showed that there was no any microbial sensitivity against extracts in disk diffusion and well diffusion methods. E. coli was resistant

against extracts and had no MIC and MBC next to the extracts, but MIC of Malassezia furfur against ethanolic and methanolic extracts of Acroptilon repens was 10.66 and 17.66 mg/ml respectively and the MFC 18.65 and 33.32 mg/ml respectively. Inhibitory zone of E. coli next to the ciprofloxacin was 23.33 mm and Inhibitory zone of Malassezia furfur next to the fluconazole was 19.66 mm.

Conclusion: based on results, Acroptilon repens extracts had no antimicrobial effect against gram negative bacteria, but had antifungal effect. However, fluconazole was stronger than Acroptilon repens extracts.

Keywords: Malassezia furfur, E. coli, Acroptilon repens extract, Antimicrobial effects, ciprofloxacin and fluc

Investigation of cisplatin nano-delivery systems for the treatment of breast cancer (Research Paper)

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Introduction: Breast cancer is one of the most common malignancies worldwide, leading to high mortality. Current treatment strategies for breast cancer, which include surgery, chemotherapy, and radiotherapy, may not be practical due to the increased risk of recurrence, poor patient response, and the emergence of drug resistance. Intensive research is being conducted to develop new molecules and technologies to apply more effective and safer therapeutic strategies to overcome this disease. One of these effective drugs for cancer treatment is cisplatin and its derivatives. Cisplatin and its derivatives are essential drugs for treating various human cancers, including breast cancer. Cisplatin currently accounts for about 50% of the anticancer drugs in clinical use. However, low solubility, serious side effects, and the development of resistance to cisplatin limit its continued use in the clinic. The interaction and reaction of cisplatin with other proteins are also associated with cellular damage. Therefore, effectively controlling the delivery and release of cisplatin at the target site is a useful way to overcome these undesirable side effects of cisplatin. Nanoparticle delivery systems for cisplatin have been developed for effective cancer chemotherapy. Compared with cisplatin, cisplatin nanoparticles showed specific tumor-targeting ability, redox effect-responsive drug release method, and more effective antitumor activity with fewer side effects and systemic toxicity than cisplatin, which is of great significance for drug chemistry. It has treatment in the clinic. In this article, the effect of different cisplatin nanoparticle systems in the treatment of breast cancer was studied.

Methods: By searching the keywords "cisplatin", "breast cancer" and "nanoparticle delivery system" in the Pubmed, Scopus, and Google scholar databases, studies on cisplatin and nanoparticle delivery systems in the treatment of breast cancer were examined.

Results: In the first study, by using a liposome formulation and loading cisplatin particles into lipid nanoparticles, it was found that this compound, which has an average diameter of 119.7 ± 2.1 nm and entrapment efficiency of 96.65 ± 3%, causes the release of stability and increased cellular uptake. And showed that these cisplatin-containing nanoparticles play an important role in improving the efficacy of the drug and reducing its dose. In the second study, disulfide-switchable smart nanoparticles complexing cisplatin (NPS-cisplatin switch) were used. The results showed that the NPS-cisplatin switch

had a size of 150 nm and a drug entrapment efficiency of more than 90%. It showed good release and targeting in resistant breast cancer cells and also showed a significant killing effect in vitro in a population of mice with resistant breast cancer cells. In the third study, a tumor-targeted nano delivery system was prepared using branched polyethyleneimine (BPEI) and hyaluronic acid (HA). This cisplatin-polyethyleneimine conjugate (BPEI-SS -Pt) has a drug loading efficiency of 32.66 ± 0.06%, demonstrating the specific tumor targeting ability and redox-responsive drug release method. Moreover, more effective antitumor activity with fewer side effects and systemic toxicity was achieved in vivo cancer treatment compared with cisplatin, which is of great significance for chemotherapy in the clinic.

Conclusion: Based on the studies conducted and the results obtained, cisplatin particles in the form of complexes or nanoparticle carriers have a stronger active effect than free cisplatin. And among the studied and existing nanoparticles, liposome formulation (or loading of cisplatin particles in lipid nanoparticles) has shown the most lethal effect and the least toxicity so far.

Keywords: cisplatin, breast cancer, nanoparticle delivery system

Investigation of diazepam and lorazepam drugs on calnexin protein by molecular docking method (Research Paper)

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1.

Introduction: Multiple sclerosis or MS is one of the diseases that have been seen in many countries of the world, including Scandinavian countries, North America, and Iran, in the last two decades. The aim of this study is the effectiveness of drugs that play a role in reducing anxiety (diazepam and lorazepam) on the Calnexin protein involved in MS.

Methods: This research was done by descriptive-analytical method. In the first step, the desired development was extracted from the PDB site. Important points such as high protein resolution, more number of nucleotides, less number of chains were given effect in protein selection. At the same time, the three-dimensional structure of two drugs, diazepam and lorazepam as ligands, was extracted from the pubchem site. Then the protein preparation step was done in the Chimera 1.15 program, which includes: 1) Selection of a chain, 2) Removal of additional items, including ion removal, water removal,... 3) Protein storage in pdb format and protein preparation for docking process were done. The docking process was done with the pyrx program. First, diazepam drug and then lorazepam drug entered the docking process as a ligand to bind to the receptor (protein). The x, y, and z coordinates of the area were removed from deepsite.

Results: It was observed that these drugs, especially diazepam, have created an acceptable level of binding, and according to the above results, the effectiveness of diazepam is better.

Conclusion: The result of diazepam docking calnexin Binding Affinity(kcal/mol) RMSD/upperbound RMSD/lowerbound Conformation1 -7.4 0 0 Conformation2 -6.9 31.027 29.919 Conformation3 -6.7 23.2 22.096 Conformation4 -6.4 3.519 2.519 Conformation5 -6.4 30.176 29.211 Conformation6 -6.3 26.887 24.894 Conformation7 -6.1 27.331 25.273 Conformation8 -6.1 27.284 25.694 Conformation9 -5.9 26.626 24.691 calnexin Binding Affinity(kcal/mol) RMSD/upperbound RMSD/lowerbound Conformation1 0 0 -6.4 Conformation2 2.617 5.316 -6.3 Conformation3 2.74 5.021 -6.4 Conformation4 2.863 3.877 -6 Conformation5 3.747 4.774 -5.9 Conformation6 17.095 18.937 -6.2 Conformation7 17.716 19.424 -6.1 Conformation8 17.781 19.39 -6.1 Conformation9 17.834 20.031 -6.4 The Result of lorazepam docking calnexin Binding Affinity(kcal/mol) RMSD/upperbound RMSD/lowerbound Conformation1 0 0 -6.4 Conformation2

2.617 5.316 -6.3 Conformation3 2.74 5.021 -6.4 Conformation4 2.863 3.877 -6 Conformation5 3.747 4.774 -5.9 Conformation6 17.095 18.937 -6.2 Conformation7 17.716 19.424 -6.1 Conformation8 17.781 19.39 -6.1 Conformation9 17.834 20.031 -6.4

Keywords: Docking ،Bioinformatics ،Lorazepam ،diazepam ،calnexin

Investigation of herbal compounds in the prevention of breast cancer (Review)

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Introduction: Breast cancer is the main cause of death in women and the second most common type of cancer. The adverse effects of common treatment strategies such as chemotherapy and radiotherapy increase the challenges in treating these patients. In addition, multidrug resistance (MDR) is an additional obstacle to current conventional treatment strategies. The purpose of this study is to investigate herbal compounds in the prevention of breast cancer.

Methods: In this systematic review, we extracted the required articles using keywords and also citing databases such as PubMed, Scopus, Google Scholar and ProQuest. The statistical population of this study is all articles published until 2022. We checked the quality of the data and then reviewed 17 articles.

Results: Zhu-xiang is a herbal concoction mainly used to treat breast cancer, and a herbal formula was used in its production. However, its effectiveness in medical treatments has not been proven. Also, some of its components induce apoptosis when used alone or in combination with other plant components. Use of menopausal hormone therapy (HT) is a risk factor for breast cancer. As a result, an increasing number of women are using herbal remedies (HEP) to manage their menopausal symptoms. Many HEPs are offered for this purpose, including phytoestrogens (flavonoids, stilbenes) and other polyphenolic substances mixed with more unknown medicinal agents from plant species [Actaea racemose. Promotes hormone-independent antioxidant activities and apoptosis. Resveratrol was revealed to prevent tumor initiation, promotion and also to prevent cancer. Ocimum sp is a traditionally used medicinal plant that has antioxidant, anticancer, radioprotective and free radical properties. So far, no detailed studies have been reported on its effects on human cancers. Triterpenoids are metabolites of isopentenyl pyrophosphate oligomers and have been reported as the

largest group of phytochemicals. It is estimated that there are more than 20,000 triterpenoids in nature. They are mainly found in various plants. An increasing number of triterpenoids have been reported to exhibit cytotoxicity against a variety of cancer cells without showing any toxicity in normal cells. Herbs and spices can provide an alternative solution for breast cancer treatment with bioactive components such as alkaloids, flavonoids, anthocyanins, phenylpropanoids and terpenes that can inhibit biological processes related to the growth of breast cancer cells. Spices such as ginger (ginger), Crocus sativus (saffron), cinnamon (Cinnamomum), Elettaria cardamom (cardamom), Piper nigrum (black pepper), black seed (black cumin), Allium cepa (onion), Mentha (leaves), and others In traditional Ayurvedic treatments, they are used to prevent/inhibit the growth of cancer cells.

Conclusion: Nature provides sufficient and appropriate resources for effective cancer treatment. Using the herbs and treatment options discussed above, we can ensure a safe, cost-effective and complete treatment for cancer without the significant physical side effects that appear with other treatment options for cancer treatment. Reducing physical side effects can significantly reduce psychological and emotional side effects such as anxiety, fear, depression, etc. The proposed treatment options are very useful for newborns and elderly cancer patients. The various natural cancer treatments mentioned above suggest changes in lifestyle and eating habits so that the symptoms of cancer can be detected at the earliest opportunity and its progression can be prevented.

Keywords: Breast Neoplasms, Plants, Medicinal

Investigation of miR-185 downregulation and its regulatory correlation with competing endogenous long non-coding RNA MIR155HG in breast carcinoma patients (Research Paper)

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Introduction: Abstract The aim of this study was to evaluate the down-regulation of miR-185 and its regulatory relationship with non-coding competitive endogenous RNA MIR155HG in breast carcinoma patients and to determine its relationship with pathological indicators such as stage, grade, metastatic involvement of lymph vessels and HER activity status. -2. So far, few studies have been performed to evaluate the down-regulation of miR-185, especially its regulatory association with non-coding competitive endogenous RNA MIR155HG in breast carcinoma patients. In the present study, the expression of an lncRNA called MIR155HG in patients with breast cancer was compared with healthy individuals and the results showed a significant increase in its expression in patients. In the present study, miR-185, which was studied, had a tumor suppressant role and as it was observed, its expression in exosomes showed a significant decrease. The results indicate a regulatory relationship between these two non-coding RNAs. Introduction Breast cancer is one of the most common cancers in women. More than 5.1 million women (25% of all women with cancer) are diagnosed with breast cancer each year [1]. The genetic factors involved in causing cancer have been significantly studied. However, evidence has shown that a significant proportion of cancer predisposing factors can not be attributed to changes in protein coding sequences [2]. The identification of a large number of long non-coding RNAs (lncRNAs) with a length of more than 200 bp in humans has helped to unveil the position of these molecules in cancer pathology and their role as important components in thrombosis. [3]. Recently, biological prophylaxis, mainly known as monoclonal antibodies to breast cancer, has been developed to improve the quality of life in patients with breast cancer [4]. One of the main targets of these monoclonal antibodies is HER2 [5]. Early detection of the disease can lead to a good prognosis and a high survival rate. Breast cancer is the most common malignancy in women, causing high mortality. miRNAs are secreted by exosomes and are highly diverse

microRNAs act as oncogenes or tumor inhibitors by inhibiting the expression of cancer-related target genes [6]. Early detection of breast tumors is one of the most important challenges in cancer management. Due to the importance of non-coding RNAs in the pathogenesis of breast cancer, this study determined the expression levels of the long non-coding RNA MIR155HG, which functions as a ceRNA, and its associated microRNA, miR-185.

Methods: Methods Serum samples were selected from patients with breast carcinoma and serum samples from healthy individuals without any disease. The serum is a fluid part of the blood that lacks the coagulation proteins provided by the project [7]. Exosomes were isolated from serum using Exoquick kit. Then complete RNA extraction steps, quantitative evaluation of the extracted RNA, cDNA synthesis, real-time quantitative polymerase chain reaction, data analysis using threshold cycle comparison method. Normalization of changes in miRNA expression levels was performed in comparison with endogenous U6 snRNA expression levels [8]. [(Control) mCT reference gene - (control) mCT gene] = ΔCT: control [(Test) mCT reference gene - (Test) mCT gene] = ΔCT: Test (Test) ΔCT- (control) ΔCT = ΔΔCT Data on average ± Standard deviation (SD) was presented and analyzed using Graph Pad software. Due to the normality of data distribution, the comparison between the treatment group and the control group was analyzed using T-test and p-value was calculated [9].

Results: Results Determining the specificity of real-time PCR reaction using melting curve In this study, SYBR Green dye and its ability to bind to double-stranded DNA formed in PCR reaction were used. This dye is attached to it by replacing it in a small DNA groove. One of the advantages of this method is that it is cheap, convenient and sensitive. One of its major disadvantages is that it connects to double strands such as Primer dimer and other non-specific bands, the results are estimated to be higher than the original concentration and therefore optimization should be done in such a way that the dimer primer and non-specific product is minimized. , Each strand of DNA in the product is single-stranded based on the length and content of GC bases at its own specific melting temperature of 3, and this state change is displayed by the system as a peak. By examining the resulting peaks, it can be seen that the peaks formed at low temperatures are directly related to the amount of nonspecific products formed at the end of the PCR process to confirm the results of the analysis. Melt Curve Analysis is used. Figure 1- As shown in the figure, each gene studied has a unique melting temperature, indicating that the product of amplification was real-time PCR. Evaluation of MIR155HG regulatory RNA expression and miR-185 secretory microRNA in serum extracellular vesicles of breast carcinoma patients Figure 2 In the first step to investigate the possibility of biomarkers of non-coding RNAs selected in this study, their expression levels were examined in exosomal samples of patients and healthy individuals. As shown in the figure, the expression of MIR155HG

lncRNA in the samples of breast cancer patients was significantly higher than normal samples (** P <0.01) and also the expression of miR-185 in the samples of breast cancer patients was significantly higher than the sample. Normals were lower. (** P <0.01) The results suggest an inverse regulatory relationship between these two non-coding RNAs. These results are consistent with the function of MIR155HG ceRNA in regulating miR-185 expression. The figure below shows the gene amplification curve in the Real-time PCR reaction. Evaluation of long non-coding regulatory RNA expression of MIR155HG and regulatory secretory microRNA miR-185 in patients in different stages of the disease Figure 3 Since one of the objectives of this study was to determine the relationship between the expression levels of selected noncoding RNAs and the clinical parameters of breast carcinoma, we found that the expression of miR-185 and MIR155HG lncRNA among patients in different groups based on disease stage Were checked. As can be seen in the figure, the expression level of MIR155HG in Stage III showed increased expression compared to the group of patients in Stages I and II (** P <0.01). In the case of miR-185, the results showed that its expression level in advanced stage III of the disease showed reduced expression compared to the lower stages I, II (** P <0.01). Evaluation of expression levels of long non-coding regulatory RNA of MIR155HG and regulated secretory microRNA of miR-185 in breast carcinoma patients with different Her-2 activity status Because the expression status of Her2 in breast carcinoma patients is directly related to metastasis, the expression levels of long non-coding regulatory RNA MIR155HG and regulated secretory microRNA miR-185 in serum extracellular vesicles of breast carcinoma patients with Her- activity status We paid 2 differently. Figure 4 As can be seen in the figure, MIR155HG lncRNA expression levels showed higher expression in patients with Her-2 (Her-2 positive) expression than in patients with Her-2 (Her-2 negative) expression (* P <0 . 05). In contrast, the microRNA regulated by this ceRNA, miR-185, showed lower expression levels in patients with Her-2 (Her-2 positive) activity than in patients with Her-2 (Her-2 Negative) inactivity (* P < 0. 05). These results are consistent with the function of MIR155HG ceRNA in regulating the expression and function of miR-185 as well as the oncogenic function of MIR155HG lncRNA and the role of miR-185 tumor-expression. Assessing the biomarker potential of non-transfecting RNAs MIR155HG lncRNA and miR-185 in the diagnosis of breast carcinoma Due to the fact that the expression of miR-185 and MIR155HG lncRNA in the two groups of patients and healthy showed a significant difference and inversion with each other and the relationship between their expression with some clinical pathological features of the disease such as disease stage and activity status of Her-2 It was identified, then by examining the ROC (Receiver Operating Characteristics) curve to determine the biomarker capability (biomarker) of these two non-coding RNAs. In this study, miR-185 had decreased expression and MIR155HG lncRNA had increased expression in serum extracellular vesicles compared to the healthy sample.

Area under curve (AUC) was 0.81 for miR-185 and 0.87 for MIR155HG lncRNA Calculated. These numbers suggest biomarker potential for these two ncRNAs. Figure 5 Heatmap analysis of MIR155HG lncRNA and miR-185 expression in breast tumor serum and healthy controls Heat map analysis was used to visualize the expression changes of non-coding RNAs between tumor samples compared to healthy individuals. As can be seen in the figure, green indicates higher expression levels and red indicates lower expression levels. Figure 6 In the present study, the expression of an lncRNA called MIR155HG in patients with breast cancer was compared with healthy individuals and the results showed a significant increase in its expression in patients. In the present study, miR-185, which was studied, had a tumor suppressant role and as it was observed, its expression in exosomes showed a significant decrease. The results indicate a regulatory relationship between these two non-coding RNAs.

Conclusion: Conclusion Therefore, according to the results of this study, the following can be mentioned: The results showed that the expression ratio of MIR155HG in the serum exosome of breast carcinoma was significantly higher than the normal serum exosome. MIR155HG expression levels at higher stages of expression disease are somewhat higher than at lower stages. MIR155HG expression levels in patients who were HER2 positive showed higher expression than in patients who did not express HER2. The results showed that the normalized expression ratio of miR-185 in the serum of patients was significantly lower than that of healthy individuals. MiR-185 expression levels in the higher stages of the disease show somewhat lower expression than in the lower stages. MiR-185 expression levels in patients who were HER2 positive showed less expression than in patients who did not express HER2.

Keywords: Key words Decreasing adjustment -miR-185-Non-coding RNA-MIR155HG

Investigation of the effect of antibacterial nano-lipid system containing Rosemary essential oil (Research Paper)

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Introduction: The aim of this study was to investigate the antibacterial effect of nano-lipid system containing Rosemary essential oil. For this purpose, the lipid system containing Rosemary essential oil has been synthesized for gram-positive (Staphylococcus aureus) and gram-negative (E.coli) antibacterial methods.

Methods: The type of study is laboratory research. The nanoparticle synthesis method is Mozaffari method. Particle characterization has been performed in terms of size and charge with DLS and morphology with the Atomic Force Microscope (AFM) and the amount of loading and release with the spectrophotometer. MIC tests were then performed to evaluate the performance of nanoparticles containing Rosemary essential oil on Staphylococcus aureus and Escherichia coli.

Results: The average particle diameter was 63 nm and its zeta potential was -16.7 mV. The loading rate in nanoparticles was 63%, which was calculated by reading the absorption of light from the standard Rosemary curve. The minimum inhibitory concentration (MIC) of Staphylococcus aureus and E.coli for nanoparticles was 15.625 and 31.25 mg / ml.

Conclusion: Nanoparticles containing Rosemary essential oil kill gram-positive (Staphylococcus aureus) and gram-negative bacteria (E.coli) and can be used as antibacterial nano-systems.

Keywords: Rosemary, Antibacterial, Staphylococcus aureus, Escherichia coli

Investigation of the effect of liposome containing oregano essential oil on Pseudomonas aeruginosa and Escherichia coli as nosocomial infections (Research Paper)

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Introduction: The aim of this study was to investigate the antibacterial effect of liposome containing oregano essential oil. For this purpose, the lipid system containing oregano essential oil has been synthesized for nosocomial infections Pseudomonas aeruginosa and Escherichia coli antibacterial methods.

Methods: The type of study is laboratory research. The nanoparticle synthesis method is Mozaffari method. Particle characterization has been performed in terms of size and charge with DLS and morphology with the Atomic Force Microscope (AFM) and the amount of loading and release with the spectrophotometer. MIC tests were then performed to evaluate the performance of nanoparticles containing clove essential oil on Pseudomonas aeruginosa and Escherichia coli.

Results: The average particle diameter was 46 nm and its zeta potential was -13.5 mV. The loading rate in nanoparticles was 71%, which was calculated by reading the absorption of light from the standard Trachyspermum Copticum curve. The minimum inhibitory concentration (MIC) of Pseudomonas aeruginosa and E.coli for nanoparticles was 15.625 and 31.25 mg / ml.

Conclusion: Nanoparticles containing oregano essential oil kill nosocomial infections Pseudomonas aeruginosa and Escherichia coli and can be used as antibacterial nano-systems.

Keywords: Oregano, Antibacterial, Pseudomonas aeruginosa, Escherichia coli

Investigation of the effect of stem cells on cure of brain ischemia (Review)

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Introduction: Stem cells are cells which have high ability to divide and differentiate, and in response to specific stimuli can differentiate into different types of cells in the body. A brain ischemia occurs when the blood flow to a part of the brain is interrupted or severely reduced, and the tissue of that part of the brain is deprived of oxygen and other nutrients. Neurons and glial cells, depending on their sensitivity to lack of oxygen, begin to die within a few minutes to a few hours. Since nerve tissue cells do not have the ability to divide, stem cells are considered a promising method for treating brain tissue damage and treating diseases related to the death of brain neurons.

Methods: Bone marrow stem cells, fetal umbilical cord blood stem cells, and peripheral blood stem cells are important sources to obtain stem cells.

Results: Among the positive effects of brain ischemia treatment with stem cells, we can mention angiogenesis, neurogenesis, modulation of immune responses, modulation of inflammation, etc. Therefore, stem cells can be used in the treatment of brain ischemia, but should pay attention to the complications caused by this treatment, such as small blockages in the blood vessels, and excessive production of immune cells, etc. With strategies such as the positioning of these cells, the safety and protocol of cell transplantation, the amount of use, the time range, etc., the occurrence of adverse side effects can be prevented. Studies have shown that when stem cells are injected intravenously into rats, these cells move to the damaged areas and differentiate into neurons and astrocytes there. Also, the scientists observed that these animals had a motor-behavioral improvement compared to the control group.

Conclusion: Therefore, it can be concluded that there is enough evidence about the effectiveness of stroke treatment with stem cells, but more studies are needed (including the positioning of these cells, the safety and protocol of cell transplantation, the amount of use, and the time frame) to be able to use these cells clinically for treatment of brain ischemia.

Keywords: Keywords: Stem cell, Brain Ischemia, Neuron

Investigation of the frequency of resistance to Fluoroquinolones and the presence of PMQR genes (qnrA, qnrB and qnrS) in Klebsiella pneumoniae isolated in Tabriz hospitals. (Research Paper)

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Introduction: Klebsiella pneumoniae is one of the important clinical pathogens and responsible for some nosocomial infections; especially pneumonia, septicemia, and urinary tract infection (UTI). Fluoroquinolones are highly effective antibiotics with many advantageous pharmacokinetic properties including high oral bioavailability, large volume of distribution, and broad-spectrum antimicrobial activity. With widespread use, antimicrobial resistance to fluoroquinolones has grown Multiple drug resistance among Klebsiella pneumoniae isolates is one of the most important challenges for treating of such infections worldwide. This study was conducted with the aim of determining the resistance of Klebsiella pneumoniae isolates collected from Tabriz hospitals against fluoroquinolone antibiotics and the presence of the PMQR genes (qnrA, qnrB and qnrS) in them.

Methods: In this cross-sectional descriptive study, 250 gram-negative bacterial isolates obtained from patients Sina, and Al-Zahra hospitals in Tabriz were studied. Samples were processed for microbial and biochemical characterization. Antibiotic susceptibility test was carried out to Commonly used antibiotics in the treatment of infections caused by gram-negative bacteria by using disc diffusion method. The distribution of Plasmid-Mediated Quinolone Resistance (PMQR), qnrA, qnrB, qnrS in isolates were detected by PCR.

Results: 97 isolates of Klebsiella pneumoniae were identified by biochemical tests. The highest antibiotic resistance of Klebsiella pneumoniae isolates to Ampicillin with 100% and the lowest resistance with 11% to Ciprofloxacin was observed. 29% of the isolates showed showed multiple drug resistance (MDR). Resistance to nalidixic acid was observed in 40% isolates and to ciprofloxacin in 11% isolates. qnrb gene was observed in 37% of isolates. qnrA was detected in 14% of isolates. qnrS Gene no detected in isolates.

Conclusion: High resistance to most of the studied antibiotics, especially fluoroquinolones, in the studied isolates should be consider as a vital factor and must rigorously take into account. Antibiogram and selection of appropriate antibiotic is recommended before starting treatment.

Keywords: Antibiotic resistance pattern; Klebsiella pneumonia, qnrb, qnrA,qnrS genes

Investigation Of The Histological Effects Of Phytoestrogen in Cuminum cyminum L . On Ovarian Tissue of Three-Spot Gourami (Trichogaster trichopterus) (Research Paper)

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Introduction: Different types of plants produce compounds that can mimic or interfere with the effects of estrogen hormones in animals. These compounds, called phytoestrogens, are weaker than normal estrogens and are found in medicinal plants. Phytoestrogens are non-steroidal compounds derived from plants that have biological activity similar to estrogen. Studies indicated that phytoestrogens in Cuminum cyminum L could have affected on ovarian tissue. The aim of this study was to investigate the effects of Cuminum cyminum L. of methanolic extract on ovarian tissue of Trichogaster trichopterus.

Methods: In this study, sixty pieces of Trichogaster trichopterus were randomly divided into 6 groups, including two control groups and treatment group were divided into 4 groups. All fish injected with 10, 20.30 and 50 mg/kg doses of the extract of Cuminum cyminum L to IM under every other day for 20 days. After the exposure period, the fish were anesthetized with extract of clove flower . The length and weight of fish were measured and the ovarian tissues of fish have been histology studied. Then, ovarian tissue compared with control and treatments groups.

Results: The administered of Cuminum cyminum L plant extract with different doses have not increasing effect on body weight and ovarian structure. Administration of the extract was not significant change in volume and size of ovarian and follicles in the treated group compared to the control group. Ovarian weight of treated group was indicated a slightly decrease. Histologic studies showed morphological changes in the ovarian tissue. The results showed that using of Cuminum cyminum L plant extracts with conventional doses had significant adverse effect on the ovarian tissue of Trichogaster trichopterus.

Conclusion: The analysis of the results obtained from the comparison of the mean percentage of gonadosomatic index between different treatments and also the histological changes from different groups in terms of the dominant developmental phase of oocytes in each group showed that the use of Cuminum cyminum L plant extract can cause maturation oocytes in three spot gourami fish.

Keywords: Cuminum cyminum L., Trichogaster trichopterus, Ovarian tissue

Investigation of the relationship between polymorphism in the methylene tetrahydrofolate reductase gene (A1298C) and thrombophilia in the Iranian population. (Research Paper)

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Introduction: Thrombophilia is defined as tendency to thrombosis, and the combination of deep vein thrombosis and pulmonary embolism is called venous thromboembolism.Various acquired and genetic factors are known as risk factors for this disease, whose acquired causes include pregnancy, childbirth and surgery. Genetic causes also include mutations in several coagulation factors, one of the most important of which is mutation in the methylene tetrahydrofolate reductase (MTHFR) gene. The purpose of this study is to determine the mutation in the methylene tetrahydrofolate reductase gene (A1298C) using molecular methods in the field of thrombophilia diagnosis.

Methods: At first, sampling was done from 109 people suspected of thrombophilia who referred to medical centers in different cities of Iran. Then DNA was extracted from the samples. The quality and quantity of extracted DNA was determined using electrophoresis on agarose gel and nanodrop device. Finally, by using specific primers and with the help of Allele-specific PCR and tetra- ARMS PCR methods, the desired mutation was investigated.

Results: The results of electrophoresis on agarose gel and nanodrop device showed that the extracted DNA has good quality and quantity. In terms of MTHFR A1298C polymorphism, 43 people were homozygous wild (AA), 50 people were heterozygous (AC) and 16 people were homozygous mutant (CC).

Conclusion: According to the obtained results, the MTHFR A1298C polymorphism can be used as a genetic marker in the diagnosis of thrombophilia.

Keywords: thrombophilia, methylenetetrahydrofolate reductase A1298C, allele-specific PCR, tetra- ARMS PCR

Investigation of the relationship between polymorphism in the methylene tetrahydrofolate reductase gene (C677T) and thrombophilia using molecular techniques (Research Paper)

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Introduction: Thrombophilia, which is one of the most common causes of death in societies, is caused by defects in the coagulation system and is characterized by the predisposition to the development of thrombosis in veins, arteries or both. The clinical symptoms of this disease include superficial or deep vein thrombosis, heart attack, pulmonary embolism, frequent miscarriage, and pregnancy complications. Among the hereditary factors of thrombophilia, mutation in methylene tetrahydrofolate reductase (MTHFR) is of great importance. The purpose of this study is to determine the mutation in the methylene tetrahydrofolate reductase gene (C677T) using molecular methods in the field of thrombophilia diagnosis

Methods: At first, sampling was done from 109 people suspected of thrombophilia who referred to medical centers in different cities of Iran. Then DNA was extracted from the samples. The quality and quantity of extracted DNA was determined using electrophoresis on agarose gel and nanodrop device. Finally, by using specific primers and with the help of Allele-specific PCR and tetra-primer ARMS PCR methods, the desired mutation was investigated.

Results: The results of electrophoresis on agarose gel and nanodrop device showed that the extracted DNA has good quality and quantity. In terms of MTHFR C677T polymorphism, 70 people were homozygous wild type (CC), 29 people were heterozygous (CT) and 10 people were homozygous mutant (TT).

Conclusion: According to the obtained results, the MTHFR C677T polymorphism can be used as a genetic marker in the diagnosis of thrombophilia.

Keywords: thrombophilia, methylenetetrahydrofolate reductase C677T, allele-specific PCR, tetra- ARMS PCR.

Investigation of the role of encapsulated miR-372 in chitosan on induction of apoptosis in MCF-7 cancer cells (Research Paper)

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Introduction: In recent years, various efforts have been made to improve the functional potency of cancer drugs. Due to the fact that Micro RNA in the cell can act as a tumor inhibitor, it can be used as a suitable treatment in most cancers.

Methods: In this study, chitosan coating is considered as a factor that enhances the effect of Micro RNA function and effectiveness. MCF-7 cell line was divided into 4 experimental groups, including untreated MCF-7 cell group, MCF-7 cell group with miR encapsulated with chitosan, MCF-7 cell group with chitosan, and MCF-7 cell group with doxorubicin drug as positive control group. The effect of different concentrations of miR-372 was first evaluated, and the optimal dose was selected to evaluate the following parameters: the induction of cell death by applying flow cytometry, the cell survival by MTT, and the level of P53 protein by Immunocytochemistry.

Results: The results showed that the dose of 1500 ng / µl of miR-372 coated with chitosan could induce cell death up to 50% in 24 and 72 hours of treatment. In addition, the rate of induction of cell death in the group treated with miR-372 coated with chitosan for 72 hours was statistically significant compared with the control group. In addition, the expression level of P53 protein in the same group was statistically significant compared with the control group.

Conclusion: According to the results, the use of cell proliferation cycle regulators such as miR-372 can control the process of proliferation and thus improve the treatment of cancer.

Keywords: Chitosan nanoparticles, Breast cancer , miR-372

Is breastfeeding reduce the endometriosis? A systematic review (Review)

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Introduction: Endometriosis is a common gynecological disease that is defined by the growth of endometrial tissue outside the uterus, and it seems that hormonal factors play an important role in its development. Breastfeeding due to the effect on the hypothalamus-pituitary axis through the prolactin, can have an important effect on endometriosis. The aim of the current review is to comprehensively evaluate the studies conducted regarding the effect of breastfeeding on the prognosis of endometriosis

Methods: In this systematic review, the researchers systematically searched in electronic databases such as Google Scholar, PubMed, Scopus, and Web of Science using the MeSH strategy and the keywords of endometriosis, breastfeeding, and pelvic pain. After the initial screening and evaluation of the searched sources, 12 English studies (8 case-control and 4 cohort studies) were included in the systematic review

Results: Reviewing the results of the studies indicated that breastfeeding reduces the symptoms of endometriosis such as dysmenorrhea, dyspareunia and pelvic pain. According to the results of8 studies conducted on infants who were breastfed, endometriosis was reduced in these infants, but the results of two studies were not significant in this regard. Also, the rate of disease recurrence after the operation in women who breastfed was lower than in women who did not breastfeed. The results of two studies showed that amenorrhea caused by breastfeeding in women with endometriosis caused a decrease in the size of the ovarian endometrioma and also caused a delay in the development of endometriosis. Based on the review of the studies, it can be concluded that amenorrhea caused by breastfeeding through reducing the number of ovulations and the prolactin hormone caused by breastfeeding through its effect on the hypothalamus-pituitary axis, causes a decrease in the production of LH-FSH hormones and ultimately lead to a decrease in the risk of developing endometriosis, reducing symptoms, the possibility of recurrence after surgery and reducing the progression of the disease.

Conclusion: The results of most conducted studies in this regard showed that breastfeeding and amenorrhea caused by it lead to a decrease in the risk of endometriosis in women. Therefore, healthcare providers, especially midwives, should emphasize on the importance role of breastfeeding on mother's health

Keywords: breastfeeding,endometriosis,pelvic pain

Isolation and Identification of Halophilic Bacteria Producing Asparaginase Enzyme from Howz-Sultan Salt Lake (Research Paper)

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Introduction: Because of its anti-neoplastic characteristics, the L-asparaginase enzyme is crucial to the chemotherapy process. Microbes are a useful source for extracting this enzyme even though it is found in several animals, microorganisms, and plants. The purpose of this study is to isolate and characterize the bacteria that produce the L-asparaginase enzyme in Hoz Sultan Lake.

Methods: Samples were cultivated in M9 specific culture medium to separate the enzyme-producing strains from the isolated bacteria. The enzyme activity of the strains was evaluated by colorimetric method. To identify microorganisms in the beginning, biochemical tests were used. With the aid of the PCR approach, the bacteria were further identified using 16S rRNA gene analysis. The sequences of the 3 robust strains, including Brevibacillus laterosporus strain, Brevibacillus laterosporus strain B9, and Paenibacillus dendritiformis strain S10-R2A-10—were immediately released publicly in the NCBI databases with the assigned accession numbers.

Results: This study indicates that the L-asparaginase enzyme may be produced by marine microorganisms. Brevibacillus laterosporus strain B9 is a very productive strain that can be used to make L-asparaginase.

Conclusion: In light of this findings, it is therefore reasonable to consider the Howz-Sultan Salt Lake as a potential bioresource for strains that generate L-asparaginase that could be advantageously used in future large-scale gene cloning for the food and medicinal industries.

Keywords: Halophilic Bacteria, L-asparaginase, Howz-Sultan Salt Lake, Isolation, Identification

Isolation and Structural and Molecular Identification of Phages against Antibiotic Resistance Gram Negative Bacteria Isolated from Burn Wounds and Study the Efficacy and Cytotoxicity of them on Skin Fibroblast Cells (HFSF-PI 3) and Skin Epithelial Tumor Cells (A-375)

(Research Paper)

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Introduction: Invasive bacteria find a special place for their rapid growth and multiplication in burn wounds. The presence of resistance of gram-negative bacteria to common antibiotics in patients with burn wounds has become a serious and controversial challenge in hospitals.

Methods: In this study, gram-negative bacteria were isolated from specialized hospitals for various accidents and burns from several cities in Iran and bacteriophages were isolated from municipal wastewater and hospital wastewater in Isfahan. To confirm the sex and species of bacterial isolates, biochemical identification along with molecular identification was performed using 16S rRNA and universal primers F27 and R1492, and designed primers FT1, RT1, FLAMB and RLAMB were used to confirm bacteriophages. In the present study, observe the morphology of isolated phages, study the antibacterial activity of phages, determine the host range, evaluate the rate of phage uptake, determine the stability of phages at different temperatures and different pHs, evaluate the frequency of infection, evaluate the bactericidal rate of phage, draw a single growth chart Phage stage and .... Molecular identification of phage with determination of approximate size of phage genome, study of enzymatic digestion pattern, identification of proteomics pattern, sequencing of part of genome of one of bacteriophages and their cytotoxic effects on two categories of normal human skin fibroblast cells (HFSF-PI 3) and cells Human epithelial tumor tumors (A-375) were presented.

Results: In this study, a total of 9 specific bacteriophages were isolated for 50 clinical strains of burn wound. Based on the results of host range and morphological observations of bacteriophage Pϕ-Bw-Ab specific to Acinetobacter baumannii strain 101IAU_FAL belonging to the siphoviridae

family, bacteriophage 1-VbϕAB specific to Acinetobacter baumannii BAH_Glau strain Plasmaviridae, bacteriophage BwϕP-Ec01 Specific to Escherichia coliADB_66-1 Bacteriophage ϕ PAVb-1 Bacteriophage Pseudomonas aeruginosa NEG_RA1300 Belongs to the family MyoViridae, EnϕP-HO bacteriophages specific to Enterobacteriaceae Hormachi EHO-Iau100 strain belonged to the Inoviridae family, bacteriophages PϕBw-Kp1, PϕBw-Kp2 and PϕBw-Kp3 were specific to Klebsiella pneumoniae strains belonging to the family Iaufa_ladu, respectively. Bacteriophages at pH 7 or neutral had the highest percentage of stability and antibacterial activity and lytic phage activity was significantly reduced at acidic pH 4, 5 and 10. What is certain is that phages at pH with high acidity are not able to survive . In the thermal stability test, the stability of the desired phages decreased with increasing temperature. According to the results, the rate of phage uptake increased with increasing time, and the rate of uptake of bacteriophages also increased. The phage genomes were sensitive to most restriction enzymes. All isolated bacteriophages had different proteomics patterns in SDS. However, protein fragments were observed in the range of 25 to 90 kDa for each phage. Overall LDH results showed that the isolated bacteriophages had no toxic effect on normal human skin fibroblast cell line (HFSF-PI 3) and a relative cytotoxic effect on human skin epithelial tumor cell line A-375. Overall MTT results showed that isolated bacteriophages had no toxic effect on normal human skin fibroblast cell line (HFSF-PI 3) and human skin epithelial tumor cell line A-375.

Conclusion: With various considerations in the field of potential ability of phages and safety studies, the phages studied in this study can be a good choice and a suitable proposal for control and treatment of such resistant pathogens in burn wounds of hospitalized patients.

Keywords: Gram Negative Bacteria/Phage therapy/ Burn Wounds/cell culture/ Antibiotic Resistance

Isolation of lactic acid bacteria from local dairy products with the ability to inhibit the growth of some gastrointestinal pathogens (Research Paper)

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2.

Introduction: Isolation and identification of lactic acid bacteria from local products can play an important role in introducing unique types of probiotics. The aim of this study was to isolate lactic acid bacteria from local dairy products in Yazd city with the ability to inhibit the growth of some digestive pathogens.

Methods: In order to isolate lactic acid bacteria, culture samples were cultured on specific agronomic culture media of Agar, M17 agar, KAA and MRS + Vancomycin. The isolates were then identified based on common morphological features and biochemical tests and sugar fermentation. Evaluation of the antibacterial activity of the topsoil culture solution against four gastrointestinal pathogenic bacteria was performed by well method.

Results: Out of 29 samples of doogh and local cheese and 7 industrial samples, a total of 76 isolates were identified, among which Lactobacillus casei had the highest frequency with 41.54%. Lactobacillus casei and Lactobacillus acidophilus isolated from doogh and sheep's cheese, and Lactobacillus delbrocci and lactobacillus ramenosus isolated from sheep's butter against all pathogenic bacteria studied, namely Escherichia coli, Candida, and Staphylococcus aureus. Also, lactic acid bacteria isolated from industrial samples showed less antibacterial activity compared to local sample isolates.

Conclusion: In general, due to the antagonistic activity of lactic acid bacteria isolated from local dairy products, it is recommended to evaluate their use as probiotic bacteria.

Keywords: Lactic Acid Bacteria, Local Dairy Products, Antibacterial Activities, Digestive Diseases

Isolation, and identification of Thermophilic protein degrading Bacteria from traditional whey sample (Research Paper)

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Introduction: Extremozymes are highly valuable in a variety of industrial processes, including those in the chemical, pharmaceutical, and agricultural industries. Researchers have become interested in the isolation and characterization of extremophiles since the available enzymes are insufficient to supply the majority of industrial demands. Thermophilic enzymes often exhibit strong catalytic activity at high temperatures due to great thermal stability, but their activities are lower at moderate temperatures than those of their mesophilic counterparts. Due to their diverse biochemistry and numerous uses in the tannery and food industries, pharmaceutical formulations, detergents, and processes like waste treatment, silver recovery, and resolution of amino acid mixtures, thermophilic proteases of microbial origin have significant industrial potential. In household laundry, where over 13 billion tons of detergent are produced annually, thermophilic proteases are most commonly used. Industrial enzymes were produced from plants, animals, and microorganisms' sources. For a number of reasons, microbial sources of proteases are favored to those from plants and animals. These enzymes are known to be produced by a wide range of microorganisms, including bacteria, fungus, yeast, and Actinomycetes. The single most common application of this enzyme is as an active component in laundry detergent. Isolation and characterization of new promising strains is a constant procedure for the synthesis of enzymes for industrial usage. Whey, a milk-derived protein complex, is promoted as a functional food with several health advantages. Whey's biological constituents, including as lactoferrin, betalactoglobulin, alpha-lactalbumin, glycomacropeptide, and immunoglobulins, exhibit a variety of immune-stimulating qualities. Due to the release of a heat-resistant protease, psychrotrophic bacteria can have unfavorable effects on dairy goods like precipitation, gelatin, bitterness, and fat floating on top. Pseudomonas fluorescens is a representative of the genus Pseudomonas, and it is capable of secreting the common heat-resistant protease AprX, an alkaline metalloprotease of the serralysin family with a molecular weight of roughly 40–50 kDa. The aim of this research was identification of Thermophilic protein degrading Bacteria from whey and optimize the protease activity.

Methods: This study employed whey sample as a biologic sample that has several types of bacteria that degrade protein molecules. The whey bacteria were enriched in Luria-Bertani (LB) medium at first. The samples were cultivated for overnight with 120 rpm shaking at various temperatures (30, 40, and 50 °C). Then samples were isolated using cultured LB plate media and subsequently screened on casein- liquid medium, with casein consumption measured using a UV-VIS spectrophotometer after precipitation of intact proteins by using the trichloroacetic acid precipitation. Tyrosine is released into the environment when casein is digested by a protease enzyme, and tyrosine absorbs at a wavelength of 280 nm. In this study, the amount of produced tyrosine as a result of protein degradation was calculated as M of tyrosine liberated/g of protein. The typical tyrosine curve is shown in Fig.1. Ammonium sulfate and protease enzyme from the sample were the materials used for precipitation. The enzyme was created and refined utilizing ammonium sulfate precipitation in a liquid media. The medium was placed on shaker overnight at 50 °C at a speed of 120 rpm. Medium color was changed to the yellow color at the following days which refer to protease enzyme reaction. Centrifugation at 3,500 rpm for 30 minutes at 4 °C was used to separate the precipitate from supernatant. Supernatant and pellet were separated during centrifugation. The pellet was eliminated because it was contained a Bacterium cell wall, whilst the supernatant is regarded as a crude enzyme and may be subjected to additional testing. Ammonium sulfate was used at different concentrations (50, 60, 70, and 80 %) to precipitate crude microbial enzymes during the optimization process. On the precipitate and supernatant of each level of treatment with ammonium sulfate, the specific activity of the protease enzyme and the protein content were seen. SDS-PAGE protein patterns are used for protein content determination. The Laemelli method for sodium-dodecyl sulphate polyacrylamide gel electrophoresis was used. With the help of sodium dodecyl sulfate, the total proteins were separated. The relative mobility of the common protein markers was used to estimate the molecular weight of the bands found in the sample. Based on the 16S rDNA gene sequence, bacteria with the best protease activity were finally found (Fig.2).

Results: Protease ability of bacteria was confirmed by UV-VIS spectrophotometer the method on Casein medium as substrate. The released of tyrosine by Samples in different temperatures were compared with each other. The most content of tyrosine liberated occurred in 50 °C which resulted to 389µM tyrosine liberated. The sample with the best protease activity was selected for 16S rRNA analysis. 16S rRNA gene amplified by PCR reaction and universal primers to sequencing and phylogenic analysis. The PCR product was analyzed by agarose gel electrophoresis Figure 2. Once a pure PCR product of the 16S gene was obtained, it was sequenced and aligned with the bacterial DNA database, thus identifying the bacteria. The sample with the best protease activity was Bacillus. Subtilis strain SAB6. A 70%

ammonium sulfate level treatment had the highest specific enzyme activity (76.245 U/mg) and highest protein content (2.359 mg/mL), according to the measurement of these two factors. In comparison to the specific enzyme activity before to purification treatment (21.42 U/mg), this specific enzyme activity was three times higher. The purified protease by B. Subtilis was also confirmed to be single purified protein molecule by using SDS-PAGE and its molecular weight was determined as 22 kDa by using proteins of known molecular weight (Fig. 3).

Conclusion: In conclusion, the strain isolated in this work (Bacillus Subtilis strain SAB6) contains protease enzyme that extracts to out of the cells and could be cloned in further studied. The purification of Bacillus Subtilis strain SAB6 enzyme by ammonium sulfate purification can increase the specific enzyme activity.

Keywords: Thermophilic Protease – Tyrosine – Casein - Bacillus subtilis - whey

Key Inflammatory biomarkers as COVID-19 severity predictors (Review)

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Introduction: The ongoing global pandemic of Covid-19 (Coronavirus disease 19) caused by SARS-CoV-2 infection, has caused severe disruptions in the economy and healthcare systems in every country. The clinical spectrum of SARS-CoV-2 infection is broad. Most COVID-19 patients exhibited mild or moderate disease and almost 15% of patients showed severity status. It was found that 5% of patients were led to critical conditions with various complications such as pneumonia, multiple organ failure, acute respiratory distress syndrome associated with dysregulated immune response, systemic inflammation, and cytokine storm. The management of patients depends on early identification and hospitalization, risk classification, and selection of appropriate treatments. Identification of laboratory markers or biomarkers can promise the rapid prediction of disease severity which significantly affects patient care. Biomarkers are biochemical substances that can be used to objectively measure the presence and severity of disease and drug responses to a therapeutic intervention. In addition, help to decrease the risk of mortality. In this study, a number of immunological and inflammatory biomarkers are discussed that could guide the treatment of COVID-19 patients.

Methods: We navigated the literature search using the terms of "COVID-19" and "inflammatory biomarkers" in the databases (PubMed, Scopus, Science Direct, and ProQuest) until September 1, 2022. A total of 14 studies from 20 articles were included in this review.

Results: Several studies have recognized increased neutrophilia, lymphopenia, T-helper (CD4+) and T-cytotoxic (CD8+) lymphocyte depletion, and neutrophil: lymphocyte ratio (NLR) as biomarkers to prognosis the disease severity. Moreover, interleukin-6 as cytokine secreted by stimulated monocytes and macrophages-and other pro-inflammatory cytokines (TNFα, G-CSF, GMCSF, IL-1β, IL-2, IL-8, IL-17, IP-10, MCP-1and CCL3,) are significantly increased in severely COVID-19 patients. The higher serum C-reactive protein (CRP), a non-specific acute-phase protein induced by IL-6 in the liver, and procalcitonin (PCT) levels (the precursor of calcitonin), which is typically synthesized and released by thyroid parafollicular C cell, are susceptible to progress the disease severity stages. Another risk factor for COVID-19 severity is a high level of ferritin. Also, it has been shown that impaired type I IFN responses (non-IFN or low-level production) and exaggerated type I IFN responses should be associated with the severity of COVID-19 infection.

Conclusion: In the pandemic of Covid-19, biomarkers as measurable indicators could provide acknowledgment of pathological processes to early recognize disease severity and choose the appropriate treatment strategies. Some laboratory biomarkers including neutrophilia, lymphopenia, elevated CRP, PCT, ferritin, pro-inflammatory cytokines especially IL-6 and TNFα and impaired type I IFN response are significantly associated with inflammatory response. These biomarkers could be used as personalized treatment based on patient responses. Future prospective trials could be demonstrated how the treatment protocols based on these biomarkers may affect the consequence of viral infection severity.

Keywords: SARS-CoV-2; Coronavirus disease 2019; Biomarkers

Key processes which differ in AML and ALL: a bioinformatics approach (Research Paper)

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Introduction: Leukemia is a cancer of white blood cells characterized by increasing in the number of hematopoietic cells. Acute lymphoblastic leukemia (ALL) is the foremost common childhood threat among childhood cancer type, Whereas AML is more common in grown-up(80%) than in children(20%). ALL and AML can be caused by mutations, chromosome translocations and aneuploidy in genes which play role in the white blood cells development.

Methods: In this study suitable microarray dataset was chosen from the GEO database and was analyzed with R, resulted in 54676 genes. Using Cytoscape 82 down and 108 up-regulated genes were obtained. These genes were submitted in g:Profiler, EnrichR and KEGG databases for pathway and GO analysis. At last, pathways were to validate by literature review.

Results: A total of 1225 DEGs (1048 up- and 177 down-regulated genes) were identified. With Degree as basis of comparison, Top ten up-regulated genes including HNRNPC, SMAD4, XPO1, DICER1, SRSF11, PIK3C3, RBM25, RPS27, PTPRC and BCL2L11, which were involved in pathways such as “TGF-beta signaling pathway”, “FoxO signaling pathway” and “Transcriptional misregulation in cancer”. And top ten down-regulated genes including TP53, CYCS, CALR, H2AFX, CD74, BCL2L1, MRTO4, YWHAE, AP2A1 and AP1M1, were involved in pathways such as “Epstein-Barr virus infection”,” Human T-cell leukemia virus 1 infection” and “Synaptic vesicle cycle”.

Conclusion: This study clarified the pathways which significantly differs between AML and ALL. Microarray analysis and recognition of similarities and

differences between biological pathways among different diseases and cancers can be useful for designing further studies and experiments which hopefully lead to a comprehensive and precise definition of these cancers, drug discovery and drug repurposing.

Keywords: Acute Myeloid leukemia, Acute Lymphoblastic leukemia, Microarray analysis, Pathway analysis, cancer

Knowledge, Attitudes, and Practices Surrounding Breast Cancer and Screening in Iranian women (Research Paper)

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Introduction: Introduction: Breast cancer is the most common type of female cancer in most countries, and is the leading cause of death among women. reports about breast cancer indicate that every three minutes a woman is diagnosed with breast cancer, and every 2 minutes a woman dies because of breast cancer. breast cancer is one of the important health issues that threaten the health of women and is considered one of the country's most important research priorities. This study aimed to evaluate the knowledge, attitude, and practice of women on breast cancer and its screening as a step towards health system reform.

Methods: Methods: This descriptive cross-sectional study was conducted on 185 non-pregnant women selected from the population covered by urban health centers in Neishabour, Razavi Khorasan, Iran, using the cluster sampling method in 2017. The necessary data were collected by a researcher-made questionnaire and analyzed in SPSS software (version 17) using the Pearson correlation coefficient, one-way ANOVA, Tukey's test, and independent t-test.

Results: The mean age of the subjects was calculated at 35.77±8.44. Moreover, in this study, the mean score of knowledge, attitude, and practice toward breast cancer was obtained as 20.22±12.51, 177.1±42.27, and 1.67±1.73. The results of the Pearson correlation coefficient indicated that there was a significant positive relationship between the subjects' knowledge and practice (P<0.001).

Conclusion: Conclusion: This study aimed to investigate the level of awareness, attitude, and function of women with breast cancer and screening. Of the participants, 41/1 % had a poor level of awareness of breast cancer

and screening. 57/7 % of participants had a neutral attitude. The performance score was 73 % weak. knowledge and performance were statistically significant .

Keywords: Attitude, Breast cancer, Knowledge, Practice, Women

KRAS and GSK Critical Kinases Biomarkers in Astrocyte and Oligodendrocyte Derived Amyotrophic Lateral Sclerosis (Research Paper)

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Introduction: Amyotrophic Lateral Sclerosis (ALS), a degenerative illness that can lead to death, begins with the loss of motor neurons in the brain and spinal cord. Medical researchers are still trying to figure out molecular mechanisms in neurological diseases like ALS. Both astrocytes and oligodendrocyte dysfunction can hasten the progression of the disease in this case.

Methods: A bioinformatics approach was used to look at the molecular mechanisms and discover important elements between these two cell types in ALS. In this study, we looked at genes, protein products, and miRNAs in astrocytes and oligodendrocytes utilizing integrated and continuous bioinformatics analytics via multiple tools and databases.

Results: Cellular senescence, actin cytoskeleton, and cell cycle signaling pathways were all involved in the findings acquired. When all the information was analyzed, TP53, MDM2, KRAS, PTPRC, and GSK proteins were identified as possible targets of hsa-miR-496-5p, hsa-miR-396-5p, and hsa-miR-4258-3p miRNAs, respectively.

Conclusion: Finally, in this investigation of ALS produced from astrocytes and oligodendrocytes, the four genes had a more robust and better association.

Keywords: Kinases, Astrocyte, Oligodendrocyte, Amyotrophic Lateral Sclerosis

L-carnitine Improves Function and Follicular Survival in Mice Ovarian Grafts through Inhibition of Oxidative Stress and Inflammation: A Stereological and Biochemical Analysis (Research Paper)

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Introduction: Transplantation of ovarian tissue is a fertility restoration technique in patients undergoing chemotherapy and radiotherapy. A major issue associated with ovarian transplantation is ischemia/reperfusion injury that leads to depletion and apoptosis of follicles. L-carnitine has antioxidant and anti-inflammation properties and can therefore be used to improve follicular survival and ovarian structure following transplantation.

Methods: Naval Medical Research Institute (NMRI) mice (at the age of 4–5 weeks) were divided into 3 groups: control, autograft and autograft + L-carnitine (200mg/kg daily intraperitoneal injections). Seven days after ovary autografting, the serum levels of malondialdehyde (MDA), total antioxidant capacity, tumor necrosis factor alpha (TNF-α), interleukin (IL)-6 and IL-10 were measured. Ovary histology, serum concentrations of progesterone and estradiol were also measured 28 days after autotransplantation. Data were analyzed using one-way analysis of variance (ANOVA) and Tukey's test, and the means were considered significantly different at P<0.05.

Results: In the autografted + L-carnitine group, the total volume of the ovary, the volume of the cortex, the number of follicles, the serum concentrations of IL-10, estradiol and progesterone significantly increased compared to the autografted group. In the autografted + L-carnitine group, serum concentrations of IL-6, TNF-α and MDA were significantly decreased compared to the autografted group.

Conclusion: Our results indicated that L-carnitine can ameliorate the consequences of ischemia-reperfusion on the mice ovarian tissue following autotransplantation.

Keywords: Ovary, Transplantation, L-carnitine.

LAMA3 Overexpression as a Potential Contributor to Development of OC and LC and Its Predictive CeRNA Networks (Research Paper)

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Introduction: Laryngeal cancer(LC) and oral cancer(OC) are types of head and neck squamous cell carcinoma(HNSC). HNSC usually begins in the squamous cells that line the mucosal surfaces of the head and neck(for example, inside the mouth and larynx). These cancers are known as squamous cell carcinoma of the head and neck. HNSC, usually diagnosed in elderly patients in association with heavy tobacco and alcohol use, is declining in part due to the decline in tobacco use worldwide. In this study, we focused on finding a common gene between LC and OC to finally find a CeRNA.

Methods: Initialy, OC dataset GSE19089 and LC dataset GSE143224 were obtained from NCBI Gene Expression Omnibus (GEO) and then analyzed by GEO2R; finally, the LAMA3 gene was selected for further work (Log FC > 1, adj. p value < 0.05).

Results: Based on microarray analysis, LAMA3 is significantly increased in patient samples(GEPIA2, ENCORI). Gene ontology and pathway analysis were performed by ENRICHR and KEGG databases to strengthen the relationship of this gene with OC and LC. Analysis of miRNA-mRNA interactions(miRWalk V.3) revealed hsa-miR-2681-5p to be a novel repressor for our gene(score = 1). We analyzed possible lncRNA-mRNA interactions using lncRRisearch and selected LINC01215, which was taken to GENECARDS for lncRNA verification. By analyzing lncRNA-miRNA interactions(lncBase V.3), we found that hsa-miR-2681-5p has a significant interaction with MALAT1 and NEAT1.

Conclusion: As a result, the LAMA3 gene may be a ceRNA along with MALAT1 and NEAT1. Also, the mentioned lncRNAs(MALAT1, NEAT1) may act as transcriptional regulators for numerous genes, including some involved in cancer metastasis and cell migration, and they are involved in cell cycle regulation.

Keywords: Laryngeal cancer, Oral cancer, HNSC, Microarray analysis, Bioinformatics analysis

Laryngeal reflux among bariatric surgery patients (Review)

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Introduction: Laryngeal reflux disease (LPRD) refers to the return of contents from the stomach to the larynx. A person with LPRD usually has symptoms such as throat clearing, hoarseness, excessive mucus production, chronic cough, and globus pharyngeus. Bariatric surgery provides effective management of obesity and obesity-related diseases. This "metabolism-changing" surgery is not without complications. However, gastroesophageal reflux disease (GERD) is the most common complication. Gastric bypass (GB) and sleeve gastrectomy (SG) are common bariatric surgery methods. According to the findings, bariatric surgery, especially SG, can lead to new onset of GERD in many patients, meanwhile, LPR symptoms in GERD patients can be up to 40%, excluding silent reflux.

Methods: In the upcoming review article, data were collected using keywords and using valid databases such as PubMed, Google Scholar, Scopus and ProQuest. In this study, our statistical population includes all the articles that have been published until 2022.

Results: RSI and RFS were adopted to evaluate and investigate LPR among obese patients, as we realized the importance of symptomatic definition of LPR rather than pH-based assessment. The difference in RSI and RFS examination trends shows the complexity of LPR diagnosis. Therefore, the assessment of LPR using one method may be inaccurate. For this reason, it is very appropriate to use RSI and RFS as a combined tool to evaluate LPR in obese patients. The findings also showed that several patients who were well before surgery had a new onset of LPR endolaryngeal symptoms after surgery. Therefore, bariatric surgeons should discuss the risk of de novo LPR with bariatric surgery candidates. Patients who develop de novo LPR may also be started on appropriate therapy, such as proton pump inhibitors, to minimize the effects of reflux. In the presence of non-specific symptoms of the

larynx, it is very necessary to examine endolaryngeal evaluations before and after surgery in candidates for bariatric surgery. We believe that the improved reflux profile among GB patients is due to the following factors: 1. The presence of rare parietal cells in the lesser curvature of the newly formed gastric pouch reduces the exposure of acid to the hypopharynx. 2. Because the small intestine is valveless, a gastrojejunostomy creates a low-pressure luminal system. 3. In GB, gastrojejunostomy and a long loop help reduce subsphincteric pressure (compared to SG) because it bypasses the action of the strong pyloric sphincter mechanism. Therefore, GB may be the method of choice in obesity-related LPR compared to SG.

Conclusion: Obesity is a global health epidemic with considerable economic burden. GB has a better LPR endolaryngeal profile in postsurgery patients. We believe that a thorough evaluation of reflux symptoms as well as esophageal anatomy and pathology should be systematically undertaken in all patients considered for bariatric surgery. This should be followed by an informed and open discussion with the patient about risks and benefits of different bariatric surgical options, leading to optimal shared decision-making.

Keywords: Keywords: Laryngopharyngeal Reflux; Bariatric surgery; Obesity; Gastric bypass; gastrectomy

LESS CONSIDERED GUIDELINES TO PREVENT HBS IN DENTAL CLINICS (Review)

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Introduction: Epidemiological researches reveal that 350 million people (6% of world population) are infected with Hepatitis B virus. Dentists exclusively dental surgeons are exposed to aerosol, mucosa, blood, and sharp instruments regularly. Dental clinics are said to be at the highest risk of contamination. Previous studies have shown the modes of transmission and protocols to minimize the infection risks. The aim of this study was to determine the considerations that are less regarded.

Methods: In order to find relevant studies to the research question, an electronic search using the keywords hepatitis, dentist, liver disease, and infection control, and language (English) restrictions was conducted using PubMed and Medline. Most recent studies including case control studies, original research and review articles were selected. Analysis was done and data were synthesized and compiled in a sequential and presentable paradigm.

Results: According to the data gathered, despite the availability, contribution of dentists and dental surgeons in receiving the Hepatitis B vaccine is considerably low. In addition, using one-handed scoop technique for recapping needles, not bending needles, and removing burs before the handpiece disassembling from the dental unit should be more practiced.

Conclusion: Dental professions can play an important role in the prevention of Hepatitis B by considering every patient as an infected and potential carrier. Proper infection protocol will lead to diminish the risk of HBS.

Keywords: HBS, Dental clinics, Infection control

level of GSK3B expression level is regulated by TSIX as a significant low-expressed gene and potential biomarker in breast cancer patients: integrated systems biology and bioinformatics investigation (Research Paper)

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Introduction: Recently, breast cancer is recognized as a second death factor for women among other cancer-related diseases, and prevention treatments for this cancer are extremely challenging (1). Besides, uncontrolled growth and division of breast cells lead to making a huge number of tissues which are called tumors (2). Accordingly, this cancer can be categorized based on its presence or absence of molecular markers for estrogen or progesterone receptors and human epidermal growth factor 2 (ERBB2; formerly HER2) (3). Due to the existence of a wide range of information in the field of biomedical technologies, this research is performed in a virtual lab instead of real-life-based experiments (4). In this experiment, RNA isolated from human MDA-MB-436 cells and HCC1954 cells from human mammary epithelial cells were studied.

Methods: Expression analysis of GSE1299 was achieved from GEO2R online software and validation of expression analyses was performed by GEPIA2 (5). For supporting the possibility of a correlation between GSK3B and breast cancer, GEPIA2 and ENCORI databases were used and they evaluated the correlation between the gene and patients' survival. Gene ontology information and biological pathway and molecular function were processed by ENRICHR, KEGG, and REACTOME databases. Initially, for exploring the effects of single nucleotide polymorphisms (SNPs) of GSK3B on the 3`UTR miRNA SNP database was used, and for finding out the coding SNPs dbSNP database was used. Also, SIFT was used to find out the deleterious SNPs. HOPE database also was used for recognizing the changing of amino acid chains that are made by SNPs, and for extracting the accession code of the gene UNIPROT database was used. In addition, STRING database was used to demonstrate the protein-protein interactions, and the importance of each protein can be achieved depending on their node degrees. For exploring the microRNA interactions, miRWALK database was used, then for more finding out the co-expression and survival of each microRNA with the target gene (GSK3B), ENCORI was explored. Furthermore, the LncRRIsearch database for the interaction of each

microRNA with LncRNA was searched, but GeneCard had to be used to make sure that those RNAs are the exact LnsRNAs. Finally, lncRNA with microRNA interactions were examined by LncBase database.

Results: According to the analysis of the GEO dataset, a gene named GSK3B was found to be considerably downregulated (|logFC|= 1.505, adj. P value = 0.00300252, P Value = 2.78e-05). This gene plays an important role as a serine-threonine protein kinase that was originally identified as the kinase that phosphorylates and inhibits glycogen synthase. GSK3B plays a role as a tumor suppressor for mammary tumors, and it is able to make breast cancer cells sensitive to chemotherapy drugs (6). Also, relating to the information of ENCORI, Gepia2, and Reactome datasets, GSK3B gene plays a function in some pathways such as Hedgehog signaling, Prolactin signaling, B cell receptor signaling, and IL-17 signaling. Moreover, this gene is a part of some diseases such as Endometrial cancer, Colorectal cancer, and Prostate cancer. To the data from the STRING, the interaction of GSK3B has been shown with other proteins such as MAPT, AKT1, CTNNB1, MYC, APC, AXIN2, LRP6, TP53, CSNK141, and AXIN1. Studying on the miRWALK has revealed has-mir-7160-5p (energy = -28.5), and has-mir-6775-5p (energy = -34.6) has illustrated significant interactor to GSK3B. Then, both those microRNAs were examined in LncRRIsearch and LncBase to show lnsRNAs that have interactions with those microRNAs, so GSK3B had interactions with three important lncRNAs : TSIX (energy = -41.98), HELLPAR(energy = -31.85), and KCNQ1OT1 (energy = -34.96).

Conclusion: To conclude, the expression of GSK3B was decreased in the breast cancer samples, and has-mir-7160-5p and has-mir-6775-5p worked as an inhibitor of microRNA factors on GSK3B. Also, rs201010589, rs201010589, etc. were recognized as deleterious SNPs.

Keywords: bioinformatics, Microarray, breast cancer, Biomarker analysis, GSK3B

LILRB5, has-miR-22-3p, H19,MALAT1 ceRNA axis influences Kaposi Sarcoma cancer development by supervising " Immune regulatory interactions between a Lymphoid and non-Lymphoid cell pathway" bioinformatics gene expression profiling and RNA interaction analyses. (Research Paper)

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Introduction: Kaposi sarcoma (KS) is a low-grade vascular tumor associated with Kaposi sarcoma Herpes virus/Human herpes virus 8 (KSHV/HHV8) infection is the etiologic agent underlying Kaposi sarcoma[1]. Kaposi sarcoma lesions predominantly present at mucocutaneous sites, primary effusion lymphoma, and multicentric Castleman's disease but may involve all organs and anatomic locations. This human gamma herpesvirus was discovered in 1994 by Drs. Yuan Chang and Patrick Moore. Today, there are over five thousand publications on KSHV and its associated malignancies[2]. In this investigate we concentrate on recent expression profiling by array about the genome-wide localization of the Kaposi sarcoma-associated Herpes virus and Murine gamma Herpes virus to find a gene with differentially expressed gene (DEG)that regulated to Kaposi sarcoma and find ceRNA and protein interaction.

Methods: Initially database GSE153601 were acquire NCBI Gene Expression Omnibus GEO and then analyzed byGEO2r to find differentially expressed genes and validation of expression analyses performed by GEPIA2 and ENCORI databases. Through GeneCard and ENrichr gene ontology information and biological pathway involvement were understood .Furthermore , Mirwalk was utilized to find significant miRNA-mRNA interactions.And selected miRNA was searched in Lncbase V.3 to find strong interactions with LncRNAs and contrust a predictive ceRNA network.

Results: eventually the LILRB5gene was selected for further exploration[3] .(log FC<0) (adj.p<.05) . Based on microarray analysis LILRB5is significantly reduction expression host chromatin Gepia2 and Encori[4] [5]. Gene ontology and pathway analysis were accomplished by the Enrichr database to strength association of the LILRB5[6] .Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell. A number of receptors and cell adhesion molecules play a key role in modifying the response of cells of lymphoid origin (such as B-, T- and NK cells) to self and

tumor antigens, as well as to pathogenic organisms [7] [8]. Survey of miRNA and mRNA interactions (mir walk v.3) exhibit has-miR-22-3p to be a novel repressor for our gene [score=1] [9]. We searched possible lncRNA–mRNA interactions using(LncBase) and select H19 , MALAT1 which taken to gene card for lncRNA verification and also we analyzed miRNA -lncRNA interaction by(LncBase)[10].

Conclusion: We announced that has-miR-22-3p has significant interaction with MALAT1and H19 and may be these are ceRNA along for LILRB5 gene[11]. Eventually the mentioned lncRNA (MALAT1and H19) may act as transcriptional regulators for enormous gene.

Keywords: Kaposi sarcoma -Herpes virus/Humanherpsvirus8 (KSHV/HHV8), expression associated, interaction,

Lipid-based Nanocarriers as New Approach to Malaria Chemotherapy (Review)

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Introduction: Malaria as an intraerythrocytic parasite is till now the most severe tropical disease and one of the burdens of humankind throughout the world that cause much debilitation and morbidity. There is a challenge in the treatment, however, the good biological activity success in vitro and in vivo studies, most drugs fail in the clinical stage. However, many antimalarial compounds have low efficacy levels, drug resistance, poor water solubility, and suffer from the lack of suitable delivery systems, which seriously limits their activity. For the fighting parasitic malaria diseases the enhancement of drug absorption by facilitating diffusion through the epithelium, safeguarding of drug from degradation, adjustment of the pharmacokinetics of drug and tissue distribution profiles, and improvement of penetration and distribution into the cell has shown via nano-biotechnology strategies as the ultimate solution. The purpose of this review article was to summarize, highlight, and emphasize lipid-based Nanocarriers as a new approach to Malaria chemotherapy.

Methods: In this research study, the required data were collected using keywords: Malaria, Chemotherapy, Nanocarriers, Lipid-based, and citing valid databases such as PubMed, and Google Scholar. The study's statistical population includes studies conducted up to 2022 in Lipid-based Nanocarriers as a new approach to Malaria chemotherapy.

Results: Nanotechnology is able to reduce the toxicity of drug molecules. For example, encapsulated beta-artemether and lumefantrine co-loaded into small lipid nano-drops (liposomes) have higher efficacy, reduced dose, and can easily access the target site. On the other hand, a reduction in drug cardiotoxicity in the case of polyethylene glycol-coated halofantrine loaded poly-D, L-lactic acid nano-capsules was illustrated. In the experiment, a higher increased life span index for primaquine-loaded nanoparticles on poly (diethylmethylidene malonate) was demonstrated against P. berghei. Another study illustrated that Transferrin-conjugated solid lipid NPs had significantly enhanced brain uptake of quinine compared with the unconjugated forms or

drug solutions for cerebral malaria treatment. The nanoemulsion including encapsulated azacarbazole and polyunsaturated fatty acids ethyl esters as delivery vehicles enhanced stability, and influence against Plasmodium falciparum, without cytotoxicity in comparison with non-encapsulated. Nanostructured lipid carriers can potentiate the antimalarial effect of artemisinin and its derivatives in the heme synthesis pathway of Plasmodium. The advantages were relatively stable in simulated gastrointestinal fluids and plasma, specifically and efficiently internalized into intraerythrocytic parasites, antimalarial effect, and inhibitory activity increasing against Plasmodium.

Conclusion: The rapid advancement of nanotechnology has raised the possibility of using lipid nanocarriers that interact within biological environments to treat infectious diseases. Thus, lipid-based nano-delivery systems (e.g., liposomes, solid lipid nanoparticles, and nano and microemulsions) and polymer-based nanocarriers (nanocapsules and nanospheres) offer a platform to formulate old and toxic antimalarial drugs thereby modifying their pharmacokinetic profile, biodistribution, high biocompatibility, and biodegradability, more efficient for the treatment and targetability. Further, there is a need to develop new chemotherapy-based approaches for inhibiting parasite-specific metabolic pathways.

Keywords: Malaria, Chemotherapy, Nanocarriers, Lipid-based

liposomes technology-based siRNA and miRNA for treatment of breast cancer (Review)

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Introduction: The most frequent type of cancer in women worldwide is breast cancer. Resistance to chemotherapy and radiation therapy is one of the disease's treatment challenges. As a result, a new method for increasing survival and managing this disease is required. Using siRNA and miRNAs to silence particular genes in mammalian cells is one of these methods. Since miRNA and/or siRNA have large molecular weights (more than 10 kDa) and negative charges that make it difficult for them to enter cells, their use for the treatment of breast cancer is only possible when these genetic materials are successfully delivered to the cells. For their transfer, liposomes, a non-viral carrier with low toxicity and high efficiency, maybe a good option. The aim of this study was to evaluate liposomal formulations containing siRNA or miRNA in the treatment of breast cancer.

Methods: In this systematic review, required data were collected by searching the following keywords selected from Mesh: 'breast cancer', 'liposome', 'siRNA' and 'miRNA'. The following databases were searched: PubMed, Scopus and google scholar, articles were evaluated according to the inclusion and exclusion criteria.

Results: There are 23 articles that are related to our topic. In order to investigate the therapeutic potential, 10 articles have used miRNA, 13 articles have used siRNA, and one article has used both. eight articles have used miRNA to target the genes responsible for cell growth and metastasis, which, by downregulating these genes, have stopped the growth and metastasis of cancer cells. One miRNA study induced apoptosis in cancer cells and in one study, it was used as a method to inhibit the growth of cancer cells by targeting the PI3K signaling pathway. Targeting the angiogenic gene with siRNA has been used to stop cancer metastasis in four articles and in one article, cyclooxygenase was targeted to prevent the metastasis of breast cancer. In addition, four articles wanted to stop the growth of cancer cells by using siRNA to induce apoptosis in cancer cells. A study that combined the use of siRNA and miRNA prevented cancer cells from proliferating and migrating.

Conclusion: siRNA and miRNA can be used as potential therapies in the treatment of cancers. liposomes can deliver these substances to cancer cells much more successfully. Therefore, liposomal platforms of siRNA and miRNA can be used as an appropriate platform in research investigated cancer therapy.

Keywords: breast cancer, liposome, siRNA , miRNA

Long non coding RNA as novel biomarkers for early diagnosis of Alzheimer's disease (Research Paper)

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Introduction: Long non-coding RNA (LncRNA) have been reported to be involved in the pathogenesis of neurodegenerative diseases, but whether it can serve as a biomarker for Alzheimer disease (AD) is not yet known. Alzheimer's disease (AD) is neurodegenerative disease with the highest incidence and the most common dementia among the elderly. we investigated the role of lncRNAs in Alzheimer's disease and focus on some specific lncRNAs that may underlie Alzheimer's disease pathophysiology and therefore could be potential diagnostic targets

Methods: The present study aimed to selected specific LncRNA as possible biomarkers for early diagnosis of Alzheimer's disease by using both meta-analysis and bioinformatics methods. . Transcriptomic data were assessed from GEO and Array Express after systematic searches. The differentially expressed LncRNA from both DNA microarray and RNA sequencing datasets were analyzed and corroborated by met analysis. Statistically significant differentially expressed LncRNA were used for enrichment analysis based on KEGG and protein–protein interaction network analysis based on STRING.

Results: We found that the plasma LncRNA was significantly differentially expressed in of AD patients

Conclusion: LncRNAs have been discovered predominantly by high-throughput sequencing technologies,including microarrays and next-generation sequencing (NGS). lncRNAs are differentially expressed in AD patients, therefore can serve as biomarkers even potential treatment target for AD patients.

Keywords: Long non-coding RNA, Biomarker, Diagnosis, Alzheimer disease

Long non coding RNAs and COVID-19; AVAN as a potential biomarker (Research Paper)

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Introduction: Long noncoding RNAs (lncRNAs), a large class of non-coding RNAs, are identified as crucial transcriptions that play active roles in a wide range of biological pathways, such as the regulation of innate and adaptive immune responses. lncRNA AVAN was characterized from Influenza A virus (IAV)-infected patients' neutrophils by RNA-Seq for the first time. RNA viruses can stimulate this lncRNA which leads to boost neutrophil activation and Type I interferon (IFN I) production and consequently, defenses against IAV infection, through promoting the interaction between two major immune response factors; TRIM25 and RIG-I. COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread entirely over the world, and host immune responses against this infection have become the most attractive topic among scientists for molecular research. Moreover, the type I IFN pathway is also an essential immune response that produces interferon-stimulated genes (ISGs) in protection against SARS-CoV-2, according to recent studies. In this study, we hypothesized that blood level of AVAN has a probable association with SARS-CoV-2 infection.

Methods: In this case-control study, we collected blood samples from 14 COVID-19 patients in comparison with 14 healthy controls who were referred to Taleghani Hospital, Shahid Beheshti University of Medical Science. RiboEX™ total RNA extraction solution (GeneAll, Seoul, South Korea) was used for total RNA isolation. After cDNA synthesis of isolated RNA, we

detected the level of lncRNA AVAN by quantitative real-time PCR. GraphPad Prism app and 2-ΔΔCt method were our analytic instruments in this study. Also, diagnostic accuracy was evaluated through ROC curve analysis.

Results: Based on the result, the lncRNA AVAN levels in COVID-19 patients' buffy coat, showed a significant up-regulation in comparison to the control group (Fold change=399.208, P-value <0.0001). The area under the curve (AUC) of AVAN for diagnosing COVID-19 compared to controls was 0.9898 (95% CI= 0.9633 to 1.000, P-value<0.0001), and the optimal cut-off value was calculated to be >-9.121(Sensitivity 92.86%; Specificity 100.0%).

Conclusion: According to this finding, there is a strong correlation between lncRNA AVAN expression levels and SARS-CoV-2 infection. Also, it can be known as a potential biomarker for COVID-19 diagnosis.

Keywords: SARS-CoV-2, lncRNA, Biomarker, interferon I, innate immunity

Long Term Resistance Training has positive effects on Cardiac, Forceps Striated Muscles, microscopic changes in the liver and Kidney of male rats (Research Paper)

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Introduction: Background and Aims: Resistance exercise, known as stretching and weight training, is a special method designed to increase traction and muscle endurance. In response to this type of exercise, skeletal and cardiac muscles adapt and beneficial physiological changes occur in other tissues. This study was conducted to evaluate the effects of Long Term Resistance Training on Pathological and Ultrastructural changes of Cardiac, Forceps Striated Muscles, Microscopic Changes of Liver and Kidney.

Methods: Twenty adult male Wistar rats were randomly divided into control and exercise groups. The exercise group performed Long Term Resistance Training for 4 months. At the end of the course, the animals were first anesthetized and then autopsied and isolated tissues such as heart muscle, Forceps muscle of the right leg, liver, and kidney are performed and the isolated tissues are stabilized in 10% neutral buffer in formalin solution. After tissue preparation and preparation of paraffin blocks, sections with a thickness of 5 microns are prepared and transferred to the slide and after staining by the hematoxylin-eosin (H&E) method are studied by light microscopy.

Results: Histopathological changes in liver tissue in the control group included mild hyperemia. The liver also showed mild degrees of reactivity, with an increase in the size and number of kupffer cells. The infiltration and settlement of neutrophils were visible in the disse space. The liver tissue in the exercise group showed mild hyperemia, the severity of hyperemia was slightly higher than the control group. In exercise group, the liver also showed mild degrees of reactivity, with an increase in the size and number of Kupffer cells. Also, the infiltration and settlement of neutrophils in the disse space was visible. Sinusoid dilation and mild fat change were also observed. In the control group, no complications were seen in cardiac tissue except hyperemia. In the cardiac tissue of the exercise group, mild hyperemia, mild degeneration of the cardiac muscle cells, mild lesions with a transverse cross-section of the muscle cells, and greater staining and hyaline of these cells were seen. Compared with the control group, muscle cell hypertrophy was observed in this group. The Forceps muscle tissue in the control group

showed hyperemia. The Forceps muscle tissue of the exercise group showed mild hyperemia, mild damage lesions with loss of transverse muscle cell translocation, and greater staining and hyaline depletion of these cells. Compared with the control group, muscle cell hypertrophy was highly observed in this group. In the renal tissue of the control group, no complication was observed except mild hyperemia. Also, In the histopathological study of kidney tissue, mild hyperemia was seen in the exercise group. No increase in renal glomerular diameter (renal body) was observed in the four-month group.

Conclusion: In general, long-term exercise in male rats had positive effects on body tissues.

Keywords: Long-term exercise, Cardiac tissue, liver tissue, Forceps Striated Muscle, kidney tissue.

Long-term impact of the covid-19 vaccine on human health and disease control (Review)

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Introduction: Viral diseases are derived from unknown factors that cause very significant consequences and complications for humanity, and these diseases put a lot of pressure on people physically, psychologically, culturally and socially. In the last few decades, the coronavirus disease has caused some behavioral and cultural changes. Although many behavioral changes such as information transmission, staying away from human populations such as home quarantine, avoiding crowds and participating in antiviral treatments have had positive effects to some extent in different countries, but these changes, despite having an effect on physical health, have generally not been able to eliminate the psychological consequences of diseases. Therefore, to prevent the consequences of social and emotional distances, scientists made a vaccine to prevent corona disease. The side effects of all corona vaccines are not the same. Some develop more side effects after the first dose. And others cause more side effects after extra doses. The side effects of the vaccines are the same and short-term. In this study, the long-term effect of the Covid-19 vaccine on human health and disease control was investigated.

Methods: This article was done in a library method. Current relevant information on the long-term effect of the covid-19 vaccine on human health and disease control was searched from databases using the keywords corona, covid-19, vaccination, long-term effects. Data analysis was done qualitatively. Finally, 20 articles in English were used to prepare the article.

Results: The short-term adverse effects of vaccines are moderate in frequency and mild in severity. The short-term effect of side effects is greater in people who have already been infected with corona. In general, Covid-19 vaccines have a significant impact on human health and the control of this type of disease.

Conclusion: Covid-19 vaccines can have a significant effect in preventing this type of disease. So far, no long-term adverse effects have been reported, but short-term complications that occur within 1-2 days of injection have been reported in women and those who have already been infected with corona.

Keywords: Corona, covid 19, vaccine, vaccination

Lower Respiratory Tract Infections in Pediatric Patients with Severe Neurological Impairments (Review)

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Introduction: Severe Neurological Impairments (SNIs) in youngsters can reason many respiration problems. A scientific feature of youngsters with SNIs is inborn encephalopathies, an ischemic or anoxia mind injury, modern metabolic disease, or neuromuscular ailment. Despite its importance, the superiority of LRTIs amongst this populace is unknown, so in this study, we discovered the considerable presence of LRTIs in this organization of youngsters. Pediatric palliative care (PPC) sufferers with an intense neurologic impairment (SNI) go through significant morbidity and elevated mortality from decreased respiratory tract infections. The motor ailment that defines cerebral palsy can also additionally impair fitness, respiratory mechanics, powerful coughing, and reason scoliosis in people with intense impairments; therefore, interventions have to maximize physical, and musculoskeletal functions. Airway clearance strategies assist in cleaning secretions.

Methods: The required data were collected in the forthcoming systematic study using keywords and citing valid databases such as Scopus PubMed, Google Scholar, and ProQuest. The study's statistical population includes all studies conducted up to 2022 in the field of Lower Respiratory Tract Infections in Pediatric Patients with Severe Neurological Impairments. After reviewing the relevant findings and evaluating the data quality, a total of 17 articles were analyzed.

Results: Recurrent LRTIs in youngsters with SNIs are multifactorial, the top essential reasons are Recurrent aspiration, Gastroesophageal reflux, bad dietary fame, impaired airway clearance, and deformity of the backbone and chest wall. Pseudomonas aeruginosa, Escherichia coli, and Klebsiella pneumonia had been the maximum not unusual place and Bronchiectasis is the maximum feasible end result of recurrent aspiration. Adequate remedy for acute airway infections is crucial to saving you headaches. In youngsters with CP, intercurrent respiration infections must be dealt with antibiotics and an extending direction of three to four weeks can be required. Which antibiotic to apply is preferably guided through the end result of a (previous) sputum

culture. Overall, variations in pathogen detection in youngsters with neurologic problems had been in large part age-unique however a decreased share of youngsters with neurologic problems had a respiration pathogen detected in comparison with the ones without neurologic issues.

Conclusion: Lower Respiratory Tract Infections' pathophysiology continues to be uncertain, probably brought on in large part through aspiration of food, saliva, and gastric content, with the extra contribution of the motor ailment that offers CP its definition. The respiration fame of sufferers with CP is encouraged through recurrent aspiration, impaired airway clearance, deformity of the backbone and chest wall, impaired lung function, bad dietary fame, and recurrent respiration infections. These elements must all be addressed while being concerned for sufferers with CP. For the sake of lifestyle exceptional and decrease recurrent LRTIs and reduce morbidity and mortality in this populace, each child, without interest in the diploma of dysfunction, must vaccinate Annually for influenza and uses prophylactic Antibiotic. Patients with CP are vulnerable to pulmonary infections, however, respiration problems aren't usually effortlessly identified and diagnosed. Sometimes, this could be due to: (1) oblique conversation with the affected person through a figure or carer, (2) the fact that investigations are hard to perform, and (three) that preliminary signs and symptoms can also additionally be very diffused. This can also additionally reason postpone in analysis and remedy, growing the threat of headaches on this susceptible populace, even though experienced dads and moms commonly do not diffuse symptoms and symptoms early. The series of specimens from the decreased respiration tract-for example, through acquiring precipitated sputum may want to improve the diagnostic fee of the findings in pediatric sufferers with bacterial LRTIs, however, might not be possible in sufferers with an SNI.

Keywords: lower respiratory tract infection, severe neurologic impairment, pediatric, SNIs

Magnetic nanoparticles as a multifunctional theranostic nanoplatform against brain cancer (Review)

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Introduction: Therapeutic and imaging agents can be delivered to tumor microenvironments at higher concentrations via nanoscale particles. In addition, if the drug or radiation is delivered precisely and subtly to the cancerous tissue margins, it will not adversely affect normal cells adjacent to the cancerous tissue. As well as improving image quality by reducing noise that would otherwise be present, precise delivery of the contrast agent can also increase the background imaging signal. The background imaging can also be improved as a result of collateral damage. Nanomaterials can be used in molecular imaging techniques to improve the contrast and dispersion of different tissues, improving the sensitivity of the diagnostic tests. Consequently, nanoparticles (NPs) can be defined as tiny, colloidal particles with nanometers. Iron oxide nanoparticles (IONPs) and magnetic NPs (MNPs) have been unveiled as new target-specific contrast agents for magnetic resonance imaging (MRI).

Methods: Using the keywords " magnetic NPs", "theranostic", "cancer" and " imaging", we searched PubMed, Web of Science, Google Scholar, and Scopus databases for published studies. Reviews were conducted on articles published.

Results: The size of MNPs ranges from 10 to 100 nm. Their retention in the blood is usually long-lasting. Because of their size, the mononuclear phagocytic system cannot recognize them, and they are too large to be removed by the kidney, their extraordinarily long half-life may be the result of their size. Magnetic NPs can be used for many different purposes that extend beyond the generation of hypointense areas on T2/T2*-weighted MR images. Additionally, intravenous administration of these agents can cause their accumulation in tumor tissues, making them antitumor agents. An application of magnetic fields results in a generation of heat or mechanical pressure. As a result of the alteration of the relaxation time of T2, IO-derived contrast agents are frequently used as T2 contrast agents. There are distinct slopes corresponding to r2 and r1 relaxivities in the 1/T2 and 1/T1 relaxation rate

plots against Fe concentration. A higher r2*/r1 ratio indicates a better T2* contrast. It is observed that superparamagnetic iron oxide nanoparticles (SPIONs) are almost devoid of magnetism at certain temperatures in the absence of an external magnetic field. As a consequence of their highly elevated magnetism inclination, magnetite and maghemite are considered to be sublime magnetic platforms because of the fact that they can become significantly magnetized when exposed to a magnetic field. A further application of these nanoparticles involves using Fe2O3@Au core and shell nanoparticles as a theranostic agent for brain cancers, such as Fe2O3@Au core–shell nanoparticles designed exclusively for the selective targeting of tumors and real-time guidance of photothermal therapy (PTT). By combining the surface plasmon resonance of au with the magnetic core, a fairly effective contrast agent can be formed under external magnetic fields to serve as a magnetic drug targeting platform. Furthermore, in vivo studies demonstrated that systemic administration of Fe2O3@Au core–shell NPs combined with Magnetic Targeting (MT) and NIR irradiation resulted in complete tumor remission. As a result of the research presented here, Fe2O3@Au core–shell NPs may be an effective and safe approach to developing a targeted PTT strategy for eradicating tumor cells under the guidance of MRI.

Conclusion: In the fight against cancer, it has been possible to develop and apply imaging contrast agents and nanovectors for therapeutic purposes. Among the leading approaches under development are magnetic nanoparticles as a way to detect precancerous and malignant lesions and provide concomitant treatment. As a diagnostic tool in both research and clinical settings, magnetic resonance imaging has become a versatile and powerful technique. The use of passive as well as active targeting has shown significant positive results in introducing these agents to tumor cells.

Keywords: Magnetic NPs, theranostic, Cancer, imaging,

MALE FACTOR INFERTILITY AND ORAL DISEASE (Review)

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Introduction: Male factor infertility (MFI) is defined as alterations in sperm morphology, concentration, and/or motility in one sample of at least two sperm analyses, collected between 1 and 4 weeks. The etiology of MFI is considered multifactorial, and several risk factors have been associated with this condition. A bidirectional linkage between oral disease (OD) and several systemic conditions such as infertility have been reported. The aim of this study is reviewing MFI and OD literatures.

Methods: This review has been conducted based on analysis of available literature indexed in PubMed database between 2015 and 2022. Specific keywords including “male factor infertility” and “oral disease” have been used. Experimental and review articles on the mentioned theme were included.

Results: A significant association between sperm motility, low sperm count and periodontal parameters, such as probing depth (PD) and clinical attachment loss (CAL) has been reported in previous studies. One study reported that an Escherichia coli filtrate obtained from 200 extracted teeth with open necrotic pulp resulted in a 25% reduction in sperm motility in vitro. Two mechanisms have been proposed; the increased bacterial load associated to chronic infections originated from OD can result in bacteriospermia impairing sperm mobility, and proinflammatory cytokines associated to OD, such as TNF- alpha could lead to a chronic systemic inflammation inducing sperm apoptosis and lower sperm count.

Conclusion: Within the limits of the current available evidence there seems to be a positive association between MFI and dental health status; however, further longitudinal studies and well-designed randomized control trials assessing confounders are needed.

Keywords: Male Factor Infertility, Oral Disease, Infertility.

mbp protein (Research Paper)

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1.

Introduction: The purpose of this study is to investigate which of the two drugs, tecfidera and mitoxantrone, has a better effect on the MBP protein.

Methods: In this descriptive-analytical study, we first downloaded the most appropriate three-dimensional structure of MBP protein from www.uniport.ir in pdb format. Then the protein chains were analyzed using Chimera software. The most suitable chain was chain E, which had more amino acids than other chains and the largest chain of MBP protein. This software removed all the solvents and water molecules and added hydrogen to it and subjected the protein to charge induction and finally saved in pdb format.

Results: according to the docking results of these two drugs, the binding affinity of mitoxantrone is more negative, compared to Tecfidera, it has better performance and effectiveness

Conclusion: As a result, mitoxandrone drug is more effective for treatment.

Keywords: Mitoxantrone - mbp protein - Tekfidra -

mbp protein in MS (Research Paper)

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Introduction: Myelin basic protein or "MBP" for short is a protein that is important in the myelination process of peripheral nerves. The myelin sheath is a unique multilayered membrane in the nervous system that plays the role of an insulator (insufficient to the outside) and greatly increases the speed of the action potential along the nerves. MBP protein maintains the correct structure of myelin and interacts with the lipid in the myelin membrane. Tecfidera: Dimethyl fumarate or Tecfidera is a prescribed brand name drug used to treat relapsing forms of MS. Mitoxantrone: Mitoxantrone (Nvantron) is a drug that is used to treat secondary progressive (acute) MS - progressive relapsing - or relapsing-remitting MS that gets worse over time. The purpose of this study is to investigate which of the two drugs, tecfidera and mitoxantrone, has a better effect on the MBP protein.

Methods: In this descriptive-analytical study, we first downloaded the most appropriate three-dimensional structure of MBP protein from www.uniport.ir in pdb format. This protein has five A chains. B. C. D. E is. Resolution=3/ 50 A° Then the protein chains were analyzed using Chimera software. The most suitable chain was chain E, which had more amino acids than other chains and the largest chain of MBP protein. This software removed all the solvents and water molecules and added hydrogen to it and subjected the protein to charge induction and finally saved in pdb format. In the next step, we downloaded the three-dimensional structure of mitoxantrone and tecfidera from the Pubchem website in sdf format. The information about mitoxantrone and tecfidera is as follows: Molecular formula of mitoxantrone : C22H28N4O6 Molecular weight of mitoxantrone :444/481 g.mol-1 The molecular formula of Tecfidera :C6H8O4 Molecular weight of Tecfidera : 144/127 g.mol-1 PyRx software was used to perform the docking process. In this software, after entering the protein as a receptor and the drugs mitoxantrone and takfidra as ligands, we obtained the binding site through this software. Mitoxantrone : Center x= 25 Center y = 25 Center z = 25 Tecfidera: Center x= 25 Center y = 25 Center z = 25

Results: After docking with PyRx software, 9 models were proposed, the first 3 models were the best docking modes,Considering that in the binding energy of mitoxandrone drug, the number obtained is more negative, which is -6 and that of Tekfidra drug is -4, as a result, mitoxantrone is more effective.

Conclusion: As a result, mitoxandrone drug is more effective for treatment.

Keywords: Mitoxantrone - mbp protein - Tekfidra -

Mechanisms and prospects of circular RNAs and their interacting signaling pathways in colorectal cancer (Review)

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Introduction: Colorectal cancer is one of the most common malignant tumors of the gastrointestinal tract. Colorectal cancer factors and their molecular mechanisms are an important part of diagnosis and treatment. Based on the collected evidence and information, circular RNA can be used as a biomarker for tumor confirmation. Therefore, our aim in this study is to investigate the mechanisms of circular RNAs and their signaling pathways in colorectal cancer.

Methods: For this research, existing articles in PubMed, Web of Science, Sid, and Google Scholar databases that have been published till 2022 are systematically selected, and 17 articles are included in this study. This research is done in English considering the following keywords: Colorectal cancer, circular RNA, Mechanisms

Results: Since there is a significant decrease in the 5-year survival rate of CRC, it is very important to find some effective and available biomarkers that help early detection and treatment of CRC. Studies show that circular RNA molecules such as circ_3823, and circ-MYH9 can be used as biomarkers in colorectal cancer. Each of these may contribute to prognosis in CRC patients or even be a factor in treatment methods.

Conclusion: The multifactorial CRC has the multiplex step and stag that the accurate and detailed pathogenic mechanism is not obvious. The various physiological and pathophysiological processes as biological functions of circular RNAs (a new class of ncRNAs) included aberrantly expression in CRC and associating with the prognosis and the pathological trait of CRC. Hereupon circular RNA is used as a different biomarker in colorectal cancer, but more studies are still needed.

Keywords: Circular RNAs, signaling pathways, colorectal cancer

Medicinal use of enzymes (Review)

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Introduction: Enzymes are important in therapeutic and commercial procedures because they accelerate a chemical reaction to produce a useful effect or product. The total number of pharmaceutical enzymes used worldwide is probably more than 3000 enzymes, counting tens of thousands of formulations containing different combinations of these substances. Most of the industrial enzymes, including the enzymes used in the pharmaceutical industry, are produced by fermentation of suitable microbial strains, mainly bacteria and fungi, due to their easy handling, fast growth rate, and appropriate scale in large vessels. Enzymes used as drugs have 2 important features that distinguish them from conventional drugs. 1) Unlike drugs, they bind and act on their targets with high affinity. 2) are highly specific and act as catalysts to convert multiple target molecules into desired products. These two properties turn enzymes into special and powerful drugs that can perform biochemical treatment in the body that the synthetic active ingredient cannot do. Several enzymes are used to prevent and treat common diseases such as heart attack and stroke, for example, collagenase enzyme is used to heal burn wounds and chondroitinase enzyme is used to treat spinal cord injury. Lysosomes are naturally used as an antibacterial agent in foods and consumer products, due to their ability to break the carbohydrate chains in the bacterial wall. It has also been shown that they have anti-HIV activities because they have RNaseA and RNaseU and selectively destroy viral RNAs, and they have presented exciting possibilities in the treatment of HIV infection.

Methods: Chemical immobilization of proteins and enzymes was first performed in the 1960s and is an emerging approach for new drug therapies. Immobility means enzymes that have limited mobility or become less mobile due to chemical or physical treatment. The industrial use of enzymes is very limited, because they are very unstable, have a high purification cost, and after the completion of the catalytic process, they have a laborious process of recovering the active enzyme from the reaction mixture. Immobilized enzymes are more stable against pH, temperature stress and are less sensitive to denaturing agents. In addition, an immobilized (immobilized) enzyme should have long-term stability and unchanged biological activity and sensitivity compared to the free enzyme after binding to the matrix if used as a therapeutic target. Immobilization was used for studies with enzymes such as

cytochrome P-450, UDP-glucuronosyltransferases, glutathione S-transferases, S-methyltransferases and N-acetyltransferases.

Results: New strategies for the synthesis and stabilization of new enzymes are constantly emerging to increase their role and efficiency for the treatment of various diseases. In particular, recent advances in biocatalysis combined with novel process engineering have provided improved methods for the production of valuable chemical intermediates.

Conclusion: Enzymes with antioxidant properties are still an intensive research area in the pharmaceutical industry. Superoxide desmutase, which converts highly toxic superoxide anion into relatively toxic hydrogen peroxide, has been of interest to the pharmaceutical industry for some time and is still under research. Advances in biotechnology in the last 10 years have allowed pharmaceutical companies to produce safer and cheaper enzymes with high potency and specificity. Recently, the identification of drug activities based on the understanding of how enzymes work at the molecular level has enabled the industry to discover new classes of successful drugs. Along with these advances, changes in orphan drug laws and new initiatives adopted by the FDA, the United States has been instrumental in facilitating enzyme drug development efforts.

Keywords: Pharmaceutical, Enzyme, Enzyme immobilization, Lysosome

Metabolic potential of human gut microbiome in human nutrition (Review)

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Introduction: the gut microbiome ordinary of numerous microorganisms suchlike bacteria, viruses, protozoa and fungus gift with inside the big gut. Gut microbiome organizes a wrapped assembly that interrelate with together and the host to adjust natural strategies critical for safety. The microbiome in addition too has some duty containing digestion, metabolic synthesis and relevance with the immune tool to resource it and adjust inflammatory response. Our percipience the natural roles of the gut microbiome, which encompass adolescent's boom, maturity of the immune tool and adjust glucose and lipid metabolism has expanded during the last decade. Numerous studies have display that weight-reduction plan has an outstanding effect on the gut microbiome. The motive of this assessment is to provide a defined of the metabolic cap ability of the human gut microbiome in human vitamins.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Metabolic potential of human gut microbiome in human nutrition. After reviewing the relevant findings and evaluating the data quality, a total of 25 articles were analyzed.

Results: studies have display that food and vitamins have become an important center in human lifestyles. This is especially right in patients with beneficial gastrointestinal (GI) disorder, as a result, patients will look for opportunities to dealing with their disease. Presenting attractive election through nutritional interventions and gives patients a grade of self-effectiveness in treatment in addition to delaying or restricting aspect effects of medical treatment and long-term health very last effects in addition to specific enteral vitamins (BEEN) has an outstanding effect on the gut microbiome and is said specific enteral vitamins will lower bacterial variety

and redesign metabolic competencies on the community Further to this, ongoing evidence has display that key and beneficial people of the gut microbiome have an outstanding effect on host metabolism and health, in addition to dietary intake influences the microbiome, microbiome-related pathology has acquired developing hobby with a defined the past century, suggesting that modifications in manner of lifestyles and weight-reduction plan can also disrupt the symbiosis of gut microbiomes due to the dearth of beneficial and shielding microbes, in fact, weight-reduction plan can irreversibly reduce microbial variety and consequently motive the dearth of amazing species of bacteria the digestive Based on this result, modifications in manner of lifestyles ad weight loss software program can prevent disturbances with inside the gut microbiome. With inside the gut, because of this a high-fiber weight-reduction plan is idea to be one of the most powerful strategies to Synthesis the gut microbiome, and extrude boom in health.

Conclusion: gut microbiome's play an outstanding characteristic in improving fat disposition and strength hemostasis, in addition to a host's verbal exchange with circumference agents. Contemporary assessment display that dietary fiber has the with indoors to adjust gut microbiomes and exchanges host metabolic adjustment; with the resource of the usage of and big, the ones data element to new achievements in connection with weight-reduction plan and gut microbiome in addition studies will supply a mile's broader notion of the gut microbiomes and host metabolic

Keywords: Gastrointestinal Microbiome‹metabolic potential ‹human nutrition ‹ Intestinal Microbiotas

Metabolism in Alzheimer's disease (Review)

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Introduction: Alzheimer's disease (AD) is the most common cause of dementia, affecting more than 10% of people over 65. It could be concluded that up to date, we know many mechanisms that could affect the setup and progress of AD pathogenesis. It seems like AD is not only one or two types of disease, but it could be a group of diseases with similar APP and Tau pathologies triggered by different mechanisms. Genetic disposition to AD would play an important role in the mechanisms of Alzheimer's disease initiations. Also, Aging, head injuries, vascular diseases, infections, Changes in metabolism, and environmental factors play a role in this disease

Methods: The human brain requires a significant amount of energy to function normally and accounts for about 20% of the body's total energy expenditure at rest, even though the brain makes up only 2% of the total body weight in addition to energy. Other cellular processes, such as cytoskeleton remodeling, phospholipid synthesis, and axonal transport, require ATP for neural signaling. Therefore, an adequate and continuous energy supply is essential to maintain brain cellular function. Furthermore, today, research focuses on understanding AD pathology by targeting mechanisms such as energy changes resulting from metabolism, amyloid β, and inflammatory response. In this review, we want to check if Alzheimer's disease affects on metabolism. What are these effects?

Results: Overproduction or reduced clearance of Ab peptides in the brain plays a central role in the pathogenesis of AD. Understanding the changes in body metabolism that can affect brain AB levels is critical to developing treatments to reduce the incidence of AD. Almost every aspect of lipid metabolism, especially cholesterol, is related to Ab production, Ab clearance, or AD risk. Also, changes in the energy level related to glucose, ketogenesis, etc. are effective in Alzheimer's disease

Conclusion: Alzheimer's disease (AD) is initially characterized by the deposition revealed in patients with AD, characterized by the presence of nerve cells and loss of synaptic cells in this disease. The death of nerve cells is because of a peptide of 40-43 amino acids called peptide (AB) beta-amyloid, which causes the nerve cells to die. The toxicity is high. Now the question arises, what is the reason for their resistance? It was observed that these cells do not respond to high concentrations of AB in amyloid toxicity by

inhibiting growth or by accumulating peroxides. These resistant cells express a much higher level of antioxidant enzymes catalase and glutathione peroxidase (GPX). A change in ROS metabolism is a significant component of AB toxicity. AB-resistant cells have been shown to have high levels of G6PDH and NADPH, increased glucose flux through the shunt pathway, and elevated glycolysis and pentose activities. These AB-resistant clones also strongly reduce ROS levels. For example, laboratory studies showed that Aβ activates the hydrolysis of sphingomyelin and causes the accumulation of ceramide. Ceramide, in turn, affects the production of Aβ by releasing beta and promoting the amyloidogenic pathway. Also, during Alzheimer's, there are changes in the energy level of cholesterol and other lipids, which causes a change in the level of ROS and increases the incidence of AD.

Keywords: Alzheimer's disease ,glutathione peroxidase ,enzymes catalase ,beta-amyloid,toxity

Microbes and spontaneous heart disease, endocarditis (Review)

Aliasghar GHasemi,[1,*]

1.

Introduction: Ever since microbes were discovered, the most common of which are bacteria, viruses, and fungi, mankind also realized that these organisms are the causes of diseases, such as cardiac endocarditis, which is an infectious disease. The internal parts of the heart are damaged. Sometimes this injury is so severe that a person has to undergo surgery.

Methods: This information has been collected in the form of a search on the Internet and biomedical sites, as well as a review of various articles in this field, and is presented in the form of a review article.

Results: Endocarditis is an inflammation of the inner lining of the heart that targets the heart valves. This disease is usually caused by an infection caused by bacteria, fungi and other microbes. The bacteria that most cause this disease are streptococcal or staphylococcal. These infections sometimes spread in the blood from different parts of the body such as the mouth and the upper part of the respiratory system and enter the heart. In this infectious disease, due to the formation of a coating of bacteria on the heart valve, the function of the heart is disturbed. This causes an abscess to form on the valves and heart muscles. The symptoms of this disease are different for each person. And it occurs in both acute and semi-acute forms. It is difficult to diagnose this infectious disease and its symptoms are also variable. This disease is more severe in people with underlying heart diseases. Among the most important factors that increase the incidence of this disease are surgical procedures that lead to infection, such as dental procedures, as well as congenital heart defects and having an artificial valve. The ways to diagnose this disease are: blood culture test. Erythrocyte sedimentation rate. Electrocardiogram and CT scan. After the diagnosis of this disease, until it does not damage the heart, antibiotics are prescribed. But if the damage to the valve is so great that the blood returns to the heart, surgery becomes necessary.

Conclusion: We found that microbes are very dangerous and the cause of some infectious diseases. A disease that damages the heart, such as endocarditis. A disease that has fainting symptoms and always changes color. We can prevent it by taking care of health.

Keywords: endocarditis. Heart. infection Sickness. bacteria Gate

Microbiome and gastric cancer: a review (Review)

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Introduction: With the discovery of Helicobacter Pylori (H. pylori) in 1982, the theory that the gastric is sterile was refuted, leading to a period of gastric microbial research. In addition, advances in nucleic acid sequencing techniques indicated that a complex community of microbes might coexist with H. pylori in the gastric.

Methods: Numerous studies have examined the crucial function of H. pylori in gastric cancer, particularly strains that harbor the Cag A and Vac A genes; this bacteria contributes to carcinogenesis by altering gastric acidity and, consequently, the organization of the gastric microbiota. While there is increasing evidence that microorganisms other than H. pylori and their metabolites play a significant role in gastric carcinogenesis, The function of the viral and fungal microbiome in gastric cancer has gotten less consideration. Investigating the microbiome's effect on the development and progression of gastric cancer can contribute to substantial improvement in preventing, diagnosing, and treating this disease.

Results: It is crucial to note that the complex interactions of bacteria are not limited to the gastric microbiome; the oral microbiome and intestinal microbiome also potentially affect gastric cancer.

Conclusion: This review article surveyed the carcinogenic role of the gastric microbiome, which is caused by complex communities of bacteria, viruses, and fungi in this organ.

Keywords: Gastric cancer, Gastric microbiome, Intestinal microbiome, Microbiota

MicroRNA biomarkers and identification of infectious agents (Review)

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Introduction: Non-coding microRNAs are 18-22 nucleotides and evolutionarily conserved. They control gene expression after transcription by degrading mRNA or inhibiting it's translation. They are involved in control of physiological and pathological processes and act as oncogenes or tumor suppressors. About 2,600 miRNAs have been identified in the human genome, of which 2,000 types are found in biofluids. The amount of miRNA in plasma is 9000-134000 copies/µl. They are used as diagnostic biomarkers in a wide range of non-infectious diseases such as cancers, autoimmune diseases, Alzheimer's, etc., but their use in infectious diseases is relatively weak, while infectious diseases contribute to 15% of deaths and due to the rapid and simple spread of the factors epidemic infections such as Covid-19 require a quick, accurate, specific and early identification so that health and treatment interventions can be carried out as soon as possible.

Methods: Traditional methods for identifying pathogens include in vitro culture, isolation, protein-based evaluations such as ELISA and serology, microscopic evaluations (histology, pathology, morphology), mass spectrometry, immunofluorescence, nucleic acid-based evaluations such as qPCR, sequencing, Nested RT-PCR, etc, but microRNAs can be identified with lateral flow test device, electrochemical biosensor, µPAD, colorimetric, Microarray, Northern blot, etc.

Results: Many of these methods require large amounts of sample size, high time and cost, high technician expertise and technical limitations, and are sometimes associated with false positive and negative results. Due to their small size, they are stable in biofluids, multiple freeze-thaw cycles and pH changes. Some pathogens such as Rabies and CMV have played a role in escaping and changing the immune system and are difficult to detect in early stages with conventional methods. This leads to low sensitivity and specificity because in many cases the infectious agent is located in a specific area or a special cell, but the advantages of miRNA markers include identifying the infectious agent or infection in the early stages of disease, accurate and sensitive identification of the pathogen, predicting host responses, better guiding treatment choices, diagnosis hidden infections as well as personal medicine with little cost and time.

Conclusion: In order to identify many infectious diseases, the current diagnostic methods are incomplete and insufficient. Many rely on the appearance of symptoms or the presence of pathogen-specific antibodies to detectable titers, but microRNA markers have a high potential to detect infectious agents separately or in the form of expression profiles. They are changed in biofluids due to infections such as bacterial, fungal, parasitic, viral and even prion and they can be used in diagnosis, prognosis and even checking the treatment process. Their application is not without challenges, such as increased expression of miR-146a, which occurs in patients with HBV, HCV, schistosoma, malaria, JEV, HeV, prions and heart disease and therefore it is not a specific microRNA and is related to the activation of the NF-κB signal transduction pathway but their use can be standardized with analytical and validation methods. When infected with Hendra virus, HIV, Tuberculosis, Malaria and Ebola, changes in the miRNA profile of a person can be seen in the early stages of the disease, which indicates the importance of examining changes in the ratios of miRNAs compared to examining them individually.

Keywords: MicroRNA, Infectious agents, Molecular diagnostics, Expression profiling.

MicroRNAS Role as glutamate receptor 5 inhibitor in PI3K/Akt/mTOR Pathway in Huntington's disease (Research Paper)

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Introduction: Huntington's disease (HD) is an adult-onset, inherited autosomal dominant neurodegenerative disorder caused by a polyglutamine (CAG) repeat expansion in exon 1 that encodes the amino-terminal of the huntingtin protein. Recently, microRNAs (miRNAs) have emerged as a novel class of gene regulatory elements with conserved roles in development and disease .so the purpose of our study is to investigate the relationship between microRNAs and CREB in PI3K/Akt/mTOR pathway.

Methods: The feature of microRNA was archived by using miRBase, HMDD and miRdSNP. Valid target genes and predict one were identified by miRTarBase, MIRWALK2.0, TargetScan and DIANA Tools. Venn diagram used to identify common target genes between MiRNAs .Gene expression in brain was obtained from The Human Protein Atlas. Finally, the pathway enrichment analysis was performed by the KEGG, David path. GENEMANIA used to find gene network.

Results: The result indicated that hsa- miR-1324, hsa-miR-185-5p, hsa-miR-199a-5p, hsa-miR-199b-5p, hsa-miR-24-3p and hsa- miR-573 inhibit MAPK3 by blocking RAS which active ERK5 and MEK5 by phosphorylation. Mentioned microRNAs activate NF-κβ by inhibiting AKT, PDPK1 and PIK3CD in neurotrophin pathway and prevent Huntington development. Metabotropic glutamate receptor 5 (mGluR5) which is inhibited in PI3K/Akt/mTOR signaling resulting in ULK1 activation and the initiation of autophagy. Canonical mTOR signaling is initiated following receptor- dependent activation of PI3K to phosphorylate PDK1.

Conclusion: the inhibition of mGluR5 using CTEP, a selective negative allosteric mGluR5 modulator, can delay disease progression. Finally hsa-miR-1324, hsa-miR-185-5p, hsa-miR-199a-5p, hsa-miR-199b-5p, hsa-miR-24-3p and hsa-miR-573 by acting as NF-κβ activator, prevent Huntington progression.

Keywords: Huntington's disease, PI3K/Akt/mTOR Pathway, MicroRNA, Metabotropic glutamate receptor 5 (mGluR5)

MicroRNAs-199a-5p, 3120d, 215,194-1,664a prevent development of cancer cell and tumor spread by directly targeting oncogenic genes in Esophageal squamous cell carcinoma (Research Paper)

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Introduction: Esophageal squamous cell carcinoma (ESCC), is the most common type of esophageal cancer worldwide, mainly occurring in the Asian esophageal cancer. Phosphatidlinositol 3-kinase (PI3K)/protein kinase B (Akt)/mammalian target of rapamycin (mTOR) signaling pathway is one of the most important cellular signaling pathways, which plays a crucial role in the regulation of cell growth, differentiation, migration, metabolism and proliferation. MicroRNAs, are small noncoding RNAs which regulate gene expression primarily at the posttranscriptional level and their expression profile improve classification diagnosis and prognostic information of malignancies including ESCC cancer as oncogene or tumor suppressor. Here in, this study investigates the communication between mir-199a-5p, 3120d, 215, 194, 664a and ESCC cancer in cellular pathways.

Methods: By using mirbase, miRNA properties were obtained. The mirtarbase and MIRWALK2.0 target genes were identified. Through NCBI, the expression of target genes in the normal and ESCC tissue was obtained. Using DAVID, signal paths were obtained and the pathways associated with ESCC were interpreted. The gene network was obtained through GENE MANIA.

Results: The result demonstrated that mir199a-5p, 3120d, 215, 194 and 664a inhibit ERK by blocking Ras, SOS which active Raf, MEK through phosphorylation. So ERK by blocking ELK, MYC effect on adhesion increasing through preventing cell migration and suppress cancer. Mentioned microRNA by inhibiting EGFR, Ras, SOS, ERK inhibit proliferation of cancer cell and tumor spread. MicroRNAs by inhibiting Ras, PI3K take their stimulation impact of PIP3 and block Act, IKK, NFkB and prevent cell migration and metastasis.

Conclusion: Mir199a-5p, 3120d, 215, 194 and 664a effect on metastasis, proliferation and adhesion of cancer cell. Mentioned microRNAs by effecting on Act, Ras, SOS, EGFR, MAPK1, PI3K in ERB, Non-small cell ESCC cancer, RAS, PI3-ACT pathways, inhibit proliferation and metastasis by

effecting on adhesion increasing and prevent cell migration. Therefore MicroRNAs act as tumor suppressor and destroy cancer by preventing the development of cancer cell and spread of tumor.

Keywords: Esophageal cancer, Signaling pathways, MicroRNA, Oncogenic genes

miR-17-5p might regulate the expression level of RXFP1 in the Neuroactive ligand-receptor interaction pathway in the multiple sclerosis patients: integrated systems biology approach (Research Paper)

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Introduction: Through immune system regulation or suppression, several disease-modifying medications have been developed during the past several decades due to more excellent knowledge of the processes behind relapsing-remitting multiple sclerosis. However, the treatment choices for progressive multiple sclerosis are still mostly unsatisfactory and challenging [1]. In this study, we performed a high-throughput data analysis to find the novel regulatory RNAs (protein-coding and non-coding) in multiple sclerosis (MS) patients.

Methods: The GSE38010 [2] microarray dataset was downloaded and analyzed to find novel possible dysregulated regulatory mRNAs in the MS patients compared to control. Raw data was downloaded by affy package [3], downloaded from Bioconductor (http://bioconductor.org/). Normalization of raw data and differential expression (DE) analysis were performed by the limma package [4]. Pathway enrichment and gene ontology (GO) analysis were performed by Enrichr [5] online database (https://maayanlab.cloud/Enrichr/). microRNA (miRNA)-mRNA interaction analysis was performed by miRWalk [6] online software to find novel regulatory miRNAs for potentially dysregulated mRNAs (http://mirwalk.umm.uni-heidelberg.de/).

Results: Based on microarray analysis, RXFP1 has a significant up-regulation in the MS patients compared to control samples (logFC: 6.31551, adj. P. Val: 0.00991). miRWalk analysis revealed that hsa-miR-17-5p has significant high-score interaction with RXFP1 (score: 1, position: 3'UTR, number of pairings: 16, binding energy: -20.5). Based on Enrichr pathway analysis, RXFP1 plays a significant role in the Relaxin signaling pathway and Neuroactive ligand-receptor interaction pathway. Based on GO analysis, RXFP1 regulates the activation of adenylate cyclase activity (GO:0007190), is involved in G protein-coupled peptide receptor activity (GO:0008528), and is located integral component of the plasma membrane (GO:0005887).

Conclusion: Based on this integrated systems biology research, hsa-miR-17-5p regulates the Relaxin signaling pathway and Neuroactive ligand-receptor interaction pathway by activating adenylate cyclase activity involved in G protein-coupled peptide receptor activity in MS patients. This miRNA performed mentioned mechanism by regulating the expression level of RXFP1 mRNA. Disturbance of the interaction between miR-17-5p and RXFP1 might be one of the possible causes of MS.

Keywords: Microarray analysis, Systems biology, Multiple Sclerosis, RNA interaction network

miR-520a-5p and lncRNA CRNDE regulates the expression level of ADAMTS5 as the novel up-reglated non-coding RNAs in the Degradation of the extracellular matrix signaling pathway: Integrated systems biology and experimental investigation on breast cacer patients

(Research Paper)

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Introduction: A new gene family of proteins known as a disintegrin and metalloproteinases (ADAMs) has similarities in sequence to the reprolysin family of snake venomases and shares the metalloproteinase domain with matrix metalloproteinases (MMPs). Based on their structural similarity, they are separated into two classes: membrane-anchored ADAM and ADAM with thrombospondin motifs (ADAMTS). The biological processes of membrane protein shedding, proteolysis, cell adhesion, cell fusion, and cell migration are all impacted by these molecules. In this study, we performed an integrated systems biology approach to find the related competitive endogenous RNA network, regulating ADAMTS5 in the breast cancer (BC) patients.

Methods: The RNA interaction analysis tools miRWalk, lncRRisearch, ENCORI, and lncBase3 as well as the protein interaction analysis tool STRING were used in this investigation. ENCORI and GEPIA2 carried out assessments of survival, expression, and correlation. Microarray analysis also carries out expression analysis. Enrichr online software was used to find the gene ontology (GO) and pathways related to selected genes

Results: Based on microarray analysis, GEPIA2, and ENCORI online databases, ADAMTS5 has a significant low-expression in the BC samples (logFC: -3.791881, adj. P. Val < 0.0001). hsa-miR-520a-5p has a significant interaction with the ADAMTS5 in the 5UTR region of mRNA (score: 1). miR-520a-5p has a significant up-regulation in the BC patients (Fold Change: 2.16, FDR: 0.05). lncRNA interaction analysis revealed that lncRNA CRNDE has a significant interaction with ADAMTS5. CRNDE has a significant up-regulation in the BC patients (FC: 1.30, FDR: 0.0001). Based on pathway enrichment analysis, ADAMTS5 regulates the Degradation of the extracellular matrix signaling pathway. Mentioned gene regulates negative regulation of metabolic process in endoplasmic reticulum lumen.

Conclusion: miR-520a-5p might modulate the Degradation of the extracellular matrix signaling pathway in the BC patients by regulation of the

expression level of ADAMTS5. lncRNA CRNDE also regulates the expression of ADAMTS5 as a significantly up-regulated lncRNA. Mentioned RNA could be considered as the novel biomarkers in the BC diagnosis.

Keywords: Bioinfomatics, Systems Biology, RNA interaction, Breast Cancer, Gene Expression Profiling

MiRNA-320 as a novel therapeutic target in Prostate cancer (Review)

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Introduction: Prostate cancer remains the most prevalent noncutaneous cancer, leading to almost 30 000 deaths every year in men. Although risk reduction of prostate cancer has been somewhat successful, effective prevention is still lacking. Immunotherapeutic approaches, although moderately complicated, remain promising in an effort to control the progression and development of the disease. Taken together, the parameters of epidemiological studies and immunotherapeutic regimens might eventually be the most effective and preventive approach for prostate cancer. MiRNAs are endogenous 21–22-nucleotide (nt) noncoding small RNAs. This review highlights some of the events associated with the development and prevention of prostate cancer.

Methods: In this study, The PC3 and DU145 cell lines were maintained in RPMI media 1640 supplemented with 10% FBS and cultured under standard conditions of 95% humidity and 5% CO2 at 37 °C. Transfection of miR-320 mimic and negative control (NC) was established using Electroporation technique. Electroporation is a physical transfection method that uses an electrical pulse to create temporary pores in cell membranes through which substances like nucleic acids can pass into the cells. MTT assay was performed to investigate the cytotoxic effect of miR-320 mimic PC3 and DU145 cell lines. Cytotoxic performed using the MTT method, the optimum of which was determined to be 40.

Results: These findings indicate that transfected miR-320 mimic could suppress PC3 and DU145 proliferation.

Conclusion: As expected, these results confirm the tumor-suppressive effect of miR-320 in the PC3 and DU145 prostate cancer cell lines by reducing proliferation.

Keywords: prostate cancer, microRNA-320, proliferation, electroporation and MTT assay.

miRNAs as Diagnostic Biomarkers for Endometriosis (Review)

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Introduction: Endometriosis is a common disorder, characterized by ectopic endometrial tissue. Despite its high prevalence, the diagnosis is usually delayed for several years, which may be because the gold standard for diagnosis is an invasive surgical assessment by laparoscopy or laparotomy. The recent discovery of microRNAs (miRNAs), make them an attractive biomarker. Various studies on miRNAs in endometriosis have identified their cardinal role in the pathogenesis of the disease and have proposed them as potential biomarkers. The aim of this review is to find out the possible effect miRNA as biomarker of endometriosis.

Methods: A literature search of eligible studies was conducted in the PubMed database from 2017 to 2021. By searching relevant keywords: (“miRNA or RNA”) AND (“endometriosis”) AND (“diagnostic biomarker”) a total of 26 studies (systematic reviews and meta-analysis) were found, 6 of which were finally reviewed in this study.

Results: The sample type was serum and plasma in all studies, but most miRNAs found in one study were harvested from tissue samples, which precludes their use as a non-invasive diagnostic test. At 2 studies MiR-200 family, miR-143, 145, miR-20a, and miR199a miR-17-5p were the most dysregulated miRNAs in endometriosis.

Conclusion: These findings suggest that circulating microRNAs may act as potential non-invasive biomarkers of endometriosis, but no single miRNA has been approved as a diagnostic biomarker so far. Due to incomplete results and low sample studies; More well-designed studies with more samples are needed.

Keywords: Endometriosis, MicroRNA, Diagnostic Biomarker.

Molecular docking study of Cyclin-dependent kinase 2 with natural flavonolignans towards the treatment of colon cancer (Research Paper)

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Introduction: Colorectal cancer is one of the most common cancers worldwide, and it is also one of the major causes of mortality from cancer. Cyclin-dependent kinases (CDKs) are cell cycle regulators, and abnormal activation can accelerate tumor cell proliferation. Therefore, inhibition of CDKs is considered a important therapeutic strategy. This study focused to investigate anti-CDK2 potential of natural flavonolignans using molecular docking approach.

Methods: The molecular docking process was performed using Molecular Operation Environment (MOE) software to predict the mode of interaction between the best possible biological conformations of flavonolignans in the active site of CDK2 enzyme. The 2D structure of flavonolignans including silybin A, silybin B, isosilybin A, isosilybin B, silychristin, isosilychristin, and silydianin were prepared by Chem Draw ultra 8.0 software and converted into PDB format by Hyper Chem7 using AM1 semiempirical method. The flavonolignans were docked into the active site of CDK2 (PDB ID: 2A4L) by MOE software. The best pose of compounds with the higher score was selected for ligand-target interaction analysis by the LigX module in MOE software.

Results: The docking results showed that isosilychristin (−16.71 kcal mol−1) to be the most potent inhibitor of CDK2 as compared to 5-fluorouracil (−6.50 kcal mol−1). Other flavonolignans namely, silybin A (−15.70 kcal mol−1), silybin B (−13.71 kcal mol−1), isosilybin A (−14.50 kcal mol−1), isosilybin B (−15.85 kcal mol−1), silychristin (−14.85 kcal mol−1), and silydianin (−14.90 kcal mol−1) also showed potent inhibition against CDK2, the stability of these molecules with CDK2 was almost more than 5-fluorouracil. According to docking results, flavonolignans bind strongly with some of the amino acid residues in the active site of CDK2 such as Asp86, Lys89, His84, Leu83, Glu81, Lys33 and Leu134.

Conclusion: These results can provide a lead in exploring the flavonolignans in treatment of colon cancer after further studies.

Keywords: CDK2, Flavonolignans, Molecular Docking

Molecular docking study of hinokiflavone with RNA dependent RNA polymerase (NSP12) of SARS-CoV-2 (Research Paper)

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Introduction: SARS-CoV-2 is caused a major outbreak of coronavirus disease 2019 (COVID-19) and threatening global health safety [1]. COVID-19 is an enveloped virus having four different structural proteins, N (nucleocapsid), M (membrane), E (envelope) and S (spike), whereas, non-structural proteins (NSPs) comprise of RNA dependent RNA polymerase protein (RdRp) that is coded by NSP12 gene [2]. The Nsp12 RNA-dependent RNA polymerase (RdRp) constitutes highly conserved regions in non-structural proteins among coronaviruses which can be targeted [3]. In this work, we present molecular docking of the potential hinokiflavone compound that specifically target vital protein of Nsp12 RNA polymerase of SARS-CoV-2.

Methods: The molecular docking process was performed using Molecular Operation Environment (MOE) software to predict the mode of interaction between the best possible biological conformations of hinokiflavone in the active site of NSP12 protein. The 2D structure of hinokiflavone was prepared by Chem Draw ultra 8.0 software and converted into PDB format by Hyper Chem7 using AM1 semiempirical method. The hinokiflavone was docked into the active site of NSP12 (PDB ID: 6m71) by MOE software. The best pose of compound with the higher score was selected for ligand-target interaction analysis by the LigX module in MOE software.

Results: The docking result showed a high potency of hinokiflavone with binding energy of −11.59 kcal mol−1. According to docking result, hinokiflavone binds strongly with some of the amino acid residues in the active site of NSP12 such as Ala550, Ser549, Ser682, Glu811 and Lys551.

Conclusion: Molecular docking analysis of the hinokiflavone showed that this compound could be significant in treatment of COVID-19. However, these finding may be further supported by experimental data for its possible clinical application.

Keywords: NSP12, molecular docking, hinokiflavone

Molecular docking study of the analgesic effect of 17-β estradiol by AMPA receptor (Research Paper)

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Introduction: Molecular modeling is a powerful tool for studying structure-activity relationships in the research-based pharmaceutical industry. Pharmacodynamic data such as strength, affinity, effectiveness, and selectivity are studied by applying these methods. Before performing experimental experiments, the interaction of chemical compounds with proteins can be investigated using computational methods, and after making sure that the compounds are more likely to bind to the target, they can be tested in the laboratory or in living systems. According to the results of our previous research, the analgesic effect of intra-paragigantocellularis lateralis 17β-estradiol on formalin-induced inflammatory pain might be mediated via AMPA receptors in Male Rats. This study investigated the antinociceptive role of 17β-estradiol and its interaction with the AMPA receptor by molecular docking.

Methods: MPA receptor PDB file was downloaded from Protein Data Bank (PDB) with the code 6NJN. Also, 20 SDF files for 17β-estradiol were downloaded from the ZINC database. The active site was delimited based on reported residues at PDB and complemented with searching of close residues until 6 Å far crystallized protein supported by Molegro Virtual Docker Tools. Thus, active site was constituted by following residues: 6NJN (chain A); Val-484, Leu-483, Glu-487, 6NJN (chain D); Gln-766, Lys-762, Leu-763, Leu-761, Lys-734, Leu-748, Leu-742, Glu-731, His-735, Asn-747, Ala-744, Val-746, Val-760, Ala-749, Ala-745, IIe-732, Cys-736, Gly-737. All molecular docking assays were carried out using flexible residues. Ligand and protein were docked employing Molegro Virtual Docker. In the strongest docked pose, residual interaction maps were obtained with Molegro Molecular Viewer for compounds that exhibited the highest affinity energy.

Results: The results of molecular docking were first analyzed in terms of affinity energy. 20 compounds of 17β-estradiol were tested via molecular docking. From docked compounds, the eleventh top pose of 17β-estradiol with the code ZINC000028107020 was found strongest docked pose, which demonstrated an important strong affinity with AMPA (–64.253 kcal/mol).

Three hydrogen bondings (His-435 D, Ala-745 D, and Cys-436 D) and four steric interactions (His-435 D, Ala-745 D, Cys-436 D, and Lys-752 D) between amino groups of AMPA and this pose were found.

Conclusion: In conclusion, AMPA could constitute an efficient and unexplored target for antinociceptive drug discovery research.

Keywords: Molecular docking study, Analgesic, Estradiol, AMPA receptor

Molecular immunology using nutrition and its association with cancer (Review)

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Introduction: The natural immune system composed of different cells including neutrophils, eosinophils, monocytes, macrophages, basophils, dendritic cells, and natural killer cells (NK). The complement system is activated and numerous cytokines are secreted as an inflammatory response to infection and inflammation. Immunity consists of extremely integrated cells susceptible to surrounding factors [1]. The lymphoid system is widely localised in the gut and those cells are particularly sensitive to metabolites induced from nutrients and products induced from microbiota and they also modulate the activation and function of the cells. Approximately 70% of the cells in the immune system and over 90% of the Ig producing cells in human body are localised in the intestines. 2.5*1010 lymphoid cells are seen in bone marrow, spleen and lymph nodes while 8.5* 1010 Ig producing cells were described in the gut-related lymphoid tissue. For these reason gut is the largestimmune organ where nutrients have the first contact with immunecell receptors and their effects occurred on the immune system [2].Nutritional immunology was identified for the first time in theearly 19th century by the identification of an atrophy of thethymus in a malnourished patient. Progressive developments inmolecular studies in the field of nutritional immunity or immunonutritionaldiscipline have been observed during the lastdecade [1,3].

Methods: we use articles.

Results: After investigations, we found thatcellular stress may be of pathogenic, nutritional, oncogenic or physical origin. Cellular stress includes principal reflection, such as response to DNA damage, tumor suppressor genes and activation of aging. In contrast, the secondary response to cellular stress is the activation of immune system, and natural killer cells (NK) may indirectly activate the immune system. However, intrinsic responses can directly activate the immune system; and it was also demonstrated that some chemotherapies could not be effective without the presence of an immune system.

Conclusion: In conclusion, cellular stress may be of pathogenic, nutritional,oncogenic or physical origin. Cellular stress includes principalreflection, such as response to DNA damage, tumor suppressorgenes and activation of aging. In contrast, the secondary responseto cellular stress is the activation of immune system, and naturalkiller

cells (NK) may indirectly activate the immune system. However,intrinsic responses can directly activate the immune system;and it was also demonstrated that some chemotherapies could notbe effective without the presence of an immune system. This raises a question: to approach more specific and morereliable treatments for the activation of intrinsic and extrinsic responses,how can we use the effectiveness of therapeutic agents? Inaddition to these therapeutic agents, positive roles played by nutrientsin the immune system should not be forgotten. However,one should consider that the positive effect of nutrients is producedat the correct dose, in the correct form, and through the correctdelivery of the condition. A better understanding of the mechanisms related to nutrientsand the immune system is an exciting and promising field for thefuture. The development of broad spectrum of studies in this fieldand improvement of clinical results with medical diet models maysupport the development of further strategies related with microbiotaand immunity.

Keywords: Nutrition, molecules, cancer, immunology.

Monkey pox virus (Review)

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Introduction: Monkeypox is a rare smallpox-like disease caused by the monkeypox virus. It is mostly found in African regions, but it has also been seen in other regions of the world. It causes flu-like symptoms such as fever, chills, and a rash that may take weeks to resolve. Like the more well-known virus that causes smallpox, it is a member of a family called orthopoxviruses. Poxviridae viruses isolated from various animals are large, enveloped, double-stranded DNA viruses. The main hosts of smallpox viruses are rodents, rabbits and non-human primates, which can occasionally be transmitted to humans and facilitate human-to-human transmission. The virus is surrounded by a dumbbell-shaped core with lateral bodies, slightly pleomorphic. There are two distinct genetic clades for monkeypox virus: the Central African (Congo Basin) clade and the West African clade. Of the two genetic clades, historically, the Congo Basin clade has caused more severe disease and is thought to be more malignant. A higher degree of morbidity, mortality, human-to-human transmission, and viremia was associated with Congo Basin human monkeypox than the 2003 United States outbreak. The clinical manifestations of monkeypox virus are similar to smallpox. Monkeypox is less lethal than smallpox, with a mortality rate of approximately 10%.

Methods: Monkeypox was discovered in 1958 when two smallpox-like outbreaks occurred in groups of monkeys used for research. The first human case was observed in 1970 in a 9-month-old boy from the Democratic Republic of Congo. Monkeypox virus has several routes of transmission, all of which involve direct contact with infected animals or humans. The exact mode of transmission of monkeypox is still under investigation. Animal-to-human transmission is direct contact or exposure to infected animals and is usually due to body fluids such as saliva, breathing frequency, or can be secretions from skin or mucosal lesions. Although human-to-human transmission is less common than animal-to-human transmission, it usually involves respiratory droplets with prolonged face-to-face contact or contact with the waste matter of an infected person. Contaminated surfaces, such as sleeping in the same bed, living in the same house, or eating or drinking from the same utensils as an infected person, are considered risk factors for transmission of the virus among family members. Amid the ongoing epidemic of monkeypox, it has also

been observed that the disease is more common in men who have sex with men. According to the World Health Organization (WHO), it is not yet known whether monkeypox is sexually transmitted, however, transmission can be attributed to close contact. The initial symptoms of this disease include the following: Fever. shake Headache. Muscle pains tiredness Swollen lymph nodes. Common and non-specific symptoms begin one to two weeks after a person is infected with the monkeypox virus. These symptoms include fever, lymphadenopathy, myalgia, etc., and due to the non-specific nature of these initial symptoms, the affected person may mistake this disease for a seasonal cold. After a few days, a rash often develops. The rash starts as smooth, red bumps that can be painful. These bumps turn into blisters that are filled with pus. Eventually, the blisters will peel and fall off—the entire process can take two to four weeks. You may also develop sores in your mouth, vagina, or anus. To diagnose monkeypox, a doctor takes a tissue sample from an open sore (lesion). It is then sent to a laboratory for polymerase chain reaction (PCR) testing (genetic fingerprinting). You may also need to give a blood sample to check for the monkeypox virus or the antibodies your immune system makes to defend against it.

Results: The current spread of MPX in non-endemic areas is a risk that shows that the spread of this virus in endemic areas has not been given much attention.

Conclusion: It should also be remembered that in an interconnected and globalized world, no region or country is immune to zoonotic pathogens such as MPXV, unless the virus is endemic. Global health response strategies should prioritize MPX outbreaks in endemic areas of sub-Saharan Africa.

Keywords: Monkeypox, viruses, Poxviridae viruses, DNA, PCR

Monkeypox and prevention of its epidemic spread: a systematic review (Review)

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Introduction: Outbreaks of emerging infectious diseases shared by humans and animals, such as Ebola virus, highly acute avian influenza (H7N9), and Middle East respiratory syndrome, have occurred in recent years, causing the infection of these relatively rare diseases among countries. Another emerging zoonotic disease is monkeypox, which was first identified in the Democratic Republic of the Congo (DRC) in 1970, but since 2010 has spread to seven other African countries causing human outbreaks. and the frequency and volume of its prevalence in the human population has increased steadily.

Methods: The current research is a systematic review that was searched using the keywords smallpox, monkeypox, epidemic in PubMed, Google Scholar, sid, Elsevier and the desired articles.

Results: Two main strains of human monkeypox virus (MPXV) have been identified: the West African (WA) strain and the Congo Basin (CB) strain, the latter of which has been associated with greater morbidity, mortality, and human-to-human transmission. The smallpox vaccine is estimated to be 85% effective against monkeypox, and residual immunity from past vaccinations significantly reduces the frequency and severity of clinical signs and symptoms. It is difficult to distinguish between monkeypox and smallpox skin lesions, but lymphadenopathy is usually one It is one of the prominent features of monkey pox, recorded symptoms include vomiting and diarrhea, inflammation of the conjunctiva and corneal ulcer, sepsis, encephalitis and pneumonia.

Conclusion: Try to make the smallpox vaccine available before the peak of the epidemic and explain to the general public the necessary training to recognize this disease, the ways to prevent its spread and spread, considering the lack of specific treatment, try to find the necessary supportive drugs to reduce the side effects. Due to this disease, masks and personal protection items should be produced and stored.

Keywords: smallpox, monkeypox,, epidemic

More accurate brain activation maps using Spatiotemporal models (Research Paper)

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Introduction: Precision and accuracy of the statistical analysis methods are essential for brain activation maps. Spatiotemporal correlation adjustment for considering this property that is embedded in fMRI data may increase their accuracy. The present study aimed to apply and assess the two fast spatiotemporal models to assess their accuracy.

Methods: We applied the spatiotemporal Gaussian process (STGP) and fast, fully Bayesian models as spatiotemporal classical and Bayesian, fast models for both simulated and experimental memory tfMRI data and compared the findings with General Linear Model (GLM). The models were fitted to the simulated data (1000 voxels,100 times points for 50 people) to assess their accuracy and precision. Functional and activation maps for all models were calculated in experimental data analysis.

Results: STGP and Bayesian models resulted in a higher Z-score in the whole brain, in the 1000 most activated voxels, and in the frontal lobe as the approved memory area. Based on the simulated data, these two models showed more accuracy and precision than the GLM models. However, their computational time was more than the GLM, as the price of model correction.

Conclusion: Spatiotemporal correlation consideration in the statistical models further improved the accuracy of models compared to the GLM model. This can result in more accurate activation maps.

Keywords: Brain mapping, fMRI data analysis, Accuracy Assessment, Spatiotemporal Correlation

Morphological and molecular characteristics of glioblastoma and the hopes of its treatment (Review)

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Introduction: The most frequent primary brain tumor, glioblastoma multiforme (GBM), is classified as a grade IV astrocytoma by the World Health Organization (WHO), and it has a median survival time of roughly one year with current multi-modal therapies. Recent data reveal that the general category of gliomas accounts for about 30% of all primary and 80% of all malignant brain tumors, whereas 54% of all malignant brain tumors are GBM and arise at a rate of 3.20 per 100 000 person-years. The clinicopathological aspects of GBM exhibit significant variation, and recent research has raised the possibility that the existence of a cancer stem cell (CSC) population may both explain this heterogeneity and offer a mechanism for tumor recurrence and therapy resistance. The aim of this study was investigating Morphological and molecular characteristics of glioblastoma and the hopes of its treatment.

Methods: This study with the Morphological and molecular characteristics of glioblastoma and the hopes of its treatment by, Google Scholar, scientific databases including Science Direct, Springer, and PubMed.

Results: Results revealed severe dysregulation of PDGFRA's downstream molecular signaling pathways and copy number changes in the protein. Chromosome 1q gains were more common in HGG (30%) compared to adult GBM (9%) but chromosome 7 gains were more common in adult GBM (13% vs. 74%). Chromosome 10q losses were more prevalent in adult GBM (35% vs. 80%). Furthermore, HGG did not exhibit any IDH1 alterations. In HGGs exposed to radiation, chromosome 1q gain and PDGFRA amplification were more prevalent. Newly discovered key genes that play a role in HGG formation have brought attention to the distinct ways that this tumor develops in contrast to adult GBM. In a recent groundbreaking study, 48 HGGs with matched germline tissue were subjected to whole-exome sequencing, which revealed 80 somatic mutations in tumors. Two single-nucleotide polymorphisms in H3F3A, which encodes the variant of the histone H3.3 protein involved in DNA organization, were found. 36% (32/90) of HGGs and just 3% (11/318) of young adult GBMs had H3F3A mutations. Interestingly. The majority of HGG also had mutations in p53, ATP-dependent helicase (ATRX), death-associated protein 6 (DAXX), which is involved in chromatin remodeling, and these mutations largely overlapped with H3F3A mutations.

Conclusion: The histological, clinical, and molecular understanding of GBM and its variants have advanced significantly. Impressive data regarding probable new variants and their differentiating characteristics have also been presented by recent studies. Nevertheless, in order to distinguish real variants from histopathological differentiation signs, new diagnostic and prognostic indicators of GBM variants are required. Finally, future investigations will require the use of uniform diagnostic criteria to define these developing variants. Understanding these GBM variations may help to clarify the mechanisms underlying the significant heterogeneity and therapeutic resistance of this disease. Last but not least, GBM continues to be an aggressive disease with a dismal prognosis and therapeutic options. Few effective treatments or biomarkers have been created, despite the large number of randomized studies that have been done to guide standard therapy for different illness presentations. A method to more effectively assess intriguing candidate medicines and biomarkers is required. New incentives for scientific discovery and investment in the disease are also required.

Keywords: glioblastoma, tumor, signaling, molecular characteristics

Multifunctional matrix metalloproteinases; targets for cancer treatment (Review)

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Introduction: Cancer is the most important death cause in both industrial and developing countries, and metastasis is the major cause of cancer morbidity and mortality. Matrix metalloproteinases (MMPs) or matrixins are a family of calcium- and zinc-dependent endopeptidases with extra and intracellular functions. Based on domain organization, sequence similarity and substrate specificity, MMPs are classified as collagenases, gelatinases, stromelysins, matrilysins, transmembrane type I, transmembrane type II and glycosylphosphatidylinositol-anchored MMPs. MMPs orchestrate metastatic events including modulation of tumor microenvironment (by disruption of basement membrane and extracellular matrix molecules), secretion and activation of chemokines, cytokines, growth factors, adhesion molecules and cytoskeletal proteins, production of angiogenic factors, recruitment of myeloid populations and inhibition of immune surveillance. The present review considers current therapeutic strategies that inhibit MMPs.

Methods: Recent reports included key words matrix metalloproteinases, target therapy, cancer metastasis were extracted from databases PubMed, Web of Science and Scopus.

Results: As understanding of MMPs' function in cancer metastasis has greatly improved in recent years, safe and effective agents have been developed to regulate the expression and activity of these enzymes. Current strategies target MMPs at transcription level (via transcription factors like HIF-1 and NF-κB or and signaling pathways such as MAPK and ERK), translation level (by antisense strategies), inactivation of pro-MMPs (using monoclonal antibodies) and blocking the proteolytic activity by MMP inhibitors (MMPIs). MMPIs are divided as the following; Peptidomimetics that are pseudopeptide derivates simulating the structure of a peptide sequence identified by MMPs (drugs like Batimastat and Marimastat); Non-peptidomimetics that are designed according to the 3D X-ray crystallography structures of MMPs' active site (drugs such as Prinomastat, Rebimastat and Tanomastat); Chemically modified tetracyclines with no antibiotic activity (drugs like Doxycycline and Minocycline) and Off target inhibitors that diminish MMPs enzymatic activity (such as Zoledronic acid and Letrozole).

Conclusion: Therapies designed to interfere with expression and activation of MMPs may be useful in the control of metastatic disease, and thus, improve the overall survival of cancer patients.

Keywords: Matrix metalloproteinases, Target therapy, Cancer metastasis.

Mycobacterium tuberculosis review article (Review)

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Introduction: Tuberculosis is an infection disease caused by Mycobacterium Tuberculosis which is first appeared roughly 2000 years ago and it's transmitted from person to person via droplets. MTB mixed infection is described as a disease state in which patient harbors more than one MTB strain at the same time either as a result of a single transmission involving multiple distinct strains or as result of multiple transmission events. These strains are largely categorized in to eight distinct genetic lineage. The different lineages are not only associated with particular geographical area , but they also have distinct pathogenic characteristics that influence disease transmission , treatment outcomes and antimicrobial drug.

Methods: Virulence factors of MTB can generally be divided in to two groups : Proteins and cell wall components. Rather than rashly inducing acute inflammation, MTB takes compromised countermeasures to enter into a quiescent latency status to elude host immune clearance. During the latency period, MTB employs a range of effector proteins to reinforce its living niches and counterbalance host immune defense.

Results: MTB possesses an arsenal of protein and lipid effector that influence macrophage functions and inflammatory responses. Tuberculosis modulates intracellular trafficking, undermines macrophages effector functions, control cell death way, impair antigen presentation and survives in diverse intracellular environment. MTB reduces the mitochondrial dependency to glucose and increases the mitochondrial dependency to fatty acid. Iron is essential for MTB but is severely limited in the human host. Secretion of protein tyrosine phosphatase ,ptpA, is essential for MTB inhibition of host macrophage acidification and maturation and it is a substrate of the protein tyrosine kinase ,ptkA, encoded in the same operon. There is evidence that MTB pathogens interact with Golgi-derived vesicles that contain enzymes implicated in innate immunity. MTB is able to subvert or neutralize host defenses early in the phagosome maturation pathway using wide variety of molecules and strategies. The most notable of MTB secreted protein is the protein tyrosine phosphatase (PtpA) which is essential for the growth of MTB within human macrophages. It inhibits macrophage V-ATPase staling phagosome acidification. Deletion of PtpA gene showed no effect on MTB growth nor its ability to initiate infections in human cells. Neutrophils are the

most widely present cell population in patient with active TB. The immune response of T lymphocytes begins at the moment that MTB spreads inside the lymph nodes. . T lymphocyte are critical for prevention of primary disease from initial MTB and loss of CD4 T-cell through infections greatly exacerbate Tuberculosis susceptibility and reactivation of latent infection memory response is more effective if it's positioned at site of pathogen infection. The role of humoral adaptive immunity in TB is extremely uncertain. Complementmediated opsonization does not alter MTB survival. . There is an interaction between other disease and TB such as Covid19 or Diabetes . Covid19 decreases the number of TH1 and other immune cells which leads to TB infections. Diabetes is a major risk factor for the development of active and latent TB increased susceptibility to TB in patients with diabetes has been endorsed to several factors including direct effect related to hyperglycemia, Insulin resistance, indirect effect related to macrophage and lymphocyte function

Conclusion: TB drugs are administered in different combinations of four first line drugs (Rifampin , Isoniazid , Pyrazinamide and Ethanbutol) which form the core of treatment regimens in the initial treatment phase of 6-9 months. Several reasons account for the failure of TB therapy such as (i) Late diagnosis, (ii) Lack of time and administration of effective drugs, (iii) Lower availability of less toxic, inexpensive and effective drugs, (iv) Long treatment duration, (v) Nonadherence to drug regimen and (vi) Evolution of drug resistant TB strains.

Keywords: Mycobacterium tuberculosis, Infection, Drug resistance

Nano-robots & cancer treatment (Review)

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Introduction: Today, cancer is one of the biggest problems in the health sector of modern societies. The use of nano science and nano robots in medical science has created new ways to diagnose, image and treat cancer in humans. Our article is an overview of the application of nanoscience and nanorobots in cancer diagnosis and treatment.

Methods: To collect and summarize the information, 78 articles were selected from 11 international websites and 8 Iranian websites. By looking at their titles, 48 articles were removed and by studying the summary of the remaining articles, we reached 20 articles.

Results: The application of nanoscience in medical sciences is very wide, but with the help of designing nanorobots, cancer cells can be identified and treated. Although there are still challenges and limitations for the use of nano robots in medicine, it is hoped that in the near future nano robots will create a great revolution not only in oncology but also in medicine.

Conclusion: As we mentioned in the previous chapters, in the last decade, cancer is known as the second cause of death, which is known as a hard-to-treat disease. On the other hand, scientists turned to nanoscience to treat this disease, and by designing nano-robots, They went to the treatment and identification of cancer cells. In addition to the significant uses that can be made of nano-robots in the treatment of cancer, we must know that we need to commercialize this product (nano-robots) for widespread use in the world. Chen and Hu (2019) believe that despite all the progress made, there are still challenges in the final commercialization of nanomedical robots. One of the most important challenges is their recognition by the body's immune system as a disturbing factor that can cause problems in their functioning. In addition, the ingredients of these nano-robots must be degradable and at the same time have enough strength to carry drug doses that are somewhat contradictory. Finally, the big challenge of nano-robots is to move against the body's blood flow, which requires a strong force. To solve these challenges, scientists have resorted to a variety of electromagnetic, chemical, and even bacterial and viral methods, and every day there are news from some parts of the world about the development of a new technology. We will have to wait and see in the end this difficult yet transformative commercialization path.

Keywords: nano - robot. Nanopano technology. Medical progress. Cancer.use of DNA

Nanobioglass in tissue engineering (Review)

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Introduction: Bioglass® is a bioactive implant that promotes bone regeneration. This substance undergoes a sequence of surface reactions in an aqueous environment, resulting in the production of a hydroxycarbonate apatite (HCA) surface layer.

Methods: The attachment and proliferation of osteoblasts on the glass surface, as well as the release of soluble silica, are caused by the creation of this layer and the release of soluble silica. Particulate Bioglass® has been demonstrated to have a significant antibacterial effect on oral microorganisms, particularly those linked to caries and periodontal disease.

Results: When Bioglass® is used in periodontal applications, its antibacterial property may help to lower the risk of bacterial colonization. By inserting nano-bioceramic particles such as nano bioglass (nBG) into the scaffold, a biomimetic scaffold that closely mimics the extracellular matrix of the bone was created.

Conclusion: According to several studies, scaffolds with nBG are better options for orthopedic and periodontal tissue engineering applications.

Keywords: Tissue Engineering, Nanobioglass, Nano-bioceramic particles, Biomimetic, Nano-bioceramic

Nanocarriers based on bacterial membrane materials for cancer vaccine delivery (Review)

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Introduction: Nanocarriers primarily based totally on bacterial membrane substances for optimum cancers' vaccine transport New vaccines primarily based totally normally on recombinant proteins and DNA, are extra solider than conventional vaccines, however they'll be much less immunogenic. Therefore, there may be a pressing want for the improvement of powerful and solid adjuvants and transport structures that may be used with new era of vaccines. Currently, a few promising Nano companies with intrinsic immune adjuvant residences, together with polymeric and lipid nanoparticles with stimulator of interferon genes (STING) pathway activation capacity, were evolved. These Nano companies can make certain that immune activation and antigen transport rise up withinside the same APCs, it simply is essential for powerful antigen presentation. Inspired through way of the body’s herbal immune defenses withinside the course of bacterial invasion, our group has evolved exclusive sorts of Nano company primarily based totally on bacterial membrane substances for optimum cancers' vaccine transport. Owing to the massive quantities of pathogen-related molecular patterns (PAMPs), the bacterial membrane substances can act as terrific Nano companies with intrinsic immune adjuvant residences Cancer vaccines primarily based totally on resected tumors from sufferers have received brilliant hobby as an individualized most cancers' remedy technique. However, eliciting a robust healing impact with custom designed vaccines stays a venture due to the susceptible immunogenicity of autologous tumor antigens. Utilizing exogenous prokaryotic elements that act as adjuvants to enhance immunogenicity is a promising technique to conquer this limitation. However, nonspecific stimulation of the immune gadget can also furthermore elicit an unwanted immunopathological state.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Nanocarriers based on bacterial membrane materials for cancer vaccine delivery. After reviewing the relevant findings and evaluating the data quality, a total of 20 articles were analyzed.

Results: Nanocarriers offer many advantages, most significantly their ability to have interaction with natural boundaries and shipping the bioactive molecule without changing its antigenicity. Previously, we evolved automatic glide peptide synthesis era that notably hurries up the manufacturing of synthetic peptides. Herein, we display that this era lets in the synthesis of high-brilliant peptides for custom designed medicine. This portrays illustrates how automatic glide synthesis era can allow custom designed peptide treatment flowers via way of growing synthesis and growing purity. We envision that enforcing this era in medical settings will notably growth ability to generate medical-grade peptides on demand, it simply is a key step in carrying out the entire capacity of custom designed vaccines for the remedy of most cancers and exclusive diseases. As the notable majority of most cancers mutations are particular to the person patient, custom designed techniques are needed.

Conclusion: From the destiny perspective, improvement of vaccines using combined strategic technique like Nano companies brought via way of mucosal course of transport can play an essential feature withinside the remedy of infectious diseases. Our efforts display that automatic glide peptide synthesis can growth the rate and brilliant of peptide synthesis for IMP and ASP manufacturing. Flow synthesis produced IMPs with similar or better purity than every microwave or batch synthesis. Flow synthesis furthermore legal the manufacturing of an entire set of neoantigen immunizing peptides, similarly to an entire set of assay peptides which might be of enough brilliant to be used in immune tracking assays. The identity of really powerful tumor neoantigens despite the fact that is primarily based totally on the verification of immunogenicity, which calls for assessment of synthetic vaccines in the aesthetic immune cell. Pressing tumor Nano vaccines normally encapsulate the neoantigen into the Nano company, it simply is an inefficient technique and now not able to efficiently grow to be privy to a massive variety of tumor neoantigens

Keywords: nanocarriea ‹bacterial membrane ‹cancer ‹vaccine

Nanodelivery applications in the management of Alzheimer`s disease (Review)

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Introduction: Alzheimer's disease (AD) is the most frequent neurodegenerative disease, which is characterized by an age-related progressive loss of brain neurons. Bringing neuropsychiatric and cognitive alternations and impaired behavior, AD is the most common cause of dementia, affects 50 million people worldwide each year, and places a tremendous burden on the medical community. Nanomaterials are microscopic particles with at least one dimension less than 100 nm. Having the advantage of a huge specific surface area for loading large amounts of drug and protecting the drug from enzymatic degradation, they improve drug stability and potency. Since conventional drug delivery systems cannot provide actual recovery in AD by sufficient resilience to the cellular architecture and critical connections, our aim in this study is to investigate the applications of nano delivery in the management of Alzheimer's disease.

Methods: This study is a systematic review with the keywords: Alzheimer`s disease, Nanomedicine, Nanostructures. Reliable scientific databases, and sites, including PubMed, Google Scholar, Scopus, Science Direct, Sid was conducted till 2022 and 17 articles related to the research selected.

Results: Regarding the multifactorial nature of Alzheimer`s disease, numerous clinical data suggest that AD patients have severe impairment of the cholinergic neurotransmitter system, possibly due to suppression of acetylcholine by acetylcholinesterase (Ache) activity and activation of the glutamatergic system increase. Accordingly, researchers have developed several approved drugs such as tacrine, donepezil, rivastigmine, glutamine (Ache inhibitor), and memantine (N-methyl D-aspartate, NMDA, receptor

antagonist). Although these drug candidates have been successful in preclinical trials, they have not shown the expected efficacy in human trials. Possible reasons for this failure are poor pharmacokinetics or low bioavailability and chemical properties (absorption across the biological blood-brain barrier) in biological systems. Drug-filled nanomaterials can travel through the blood-brain barrier (BBB) and can be targeted to accumulate in damaged cells and tissues but not in normal cells and tissues, after modifying the surface molecules, thereby increasing target specificity and reducing off-target effects. Liposomes, dendrimers, micelles, nanoemulsions, nanosuspensions, etc., are some of the nanoformulations used in efficient drug delivery. Besides, using phytochemicals_ such as quercetin, catechin, myricetin, anthocyanins, ferulic acid, tannins, resveratrol, curcumin, turmeric, and dietary lipids_ combined with nanotechnology enhances the therapeutic effect.

Conclusion: Nanomaterials are nano-sized materials capable of drug delivery, surpassing BBB, denaturable, non-toxic, non-reactive with high affinity for the target, and potentially high efficiency. Thus, nanoencapsulation of drugs is a promising biocompatible strategy for the management of neurodegenerative diseases such as Alzheimer's disease.

Keywords: Alzheimer`s disease, Nanomedicine, Nanostructures

Nanomaterials for nucleic acid delivery in cancer immunotherapy: A systematic review study (Review)

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Introduction: Cancer is an important cause of death worldwide and many efforts have been made to design chemotherapy drugs, but only some of them have shown significant effects in destroying cancer cells, which has created challenges. Nanotechnology has been widely studied and exploited for cancer treatment, as nanoparticles can play an important role as a drug delivery system. Compared with conventional drugs, drug delivery based on nanoparticles has certain advantages such as improved stability and biocompatibility, increased permeability and long-lasting effect, and precise targeting. Hybrid nanoparticles incorporate the combined properties of different nanoparticles, this type of drug carrier system has reached the next level. In addition, drug delivery systems based on nanoparticles play a role in overcoming drug resistance associated with cancer. Due to the size and surface characteristics of nanoparticles and their performance in increasing permeability and retention, nanocarriers can increase the half-life of drugs and also induce their accumulation in tumor tissues. Meanwhile, the targeting system protects normal cells from the cytotoxicity of drugs, which reduces the adverse effects of cancer treatment.

Methods: In the following article, data were collected by using keywords and searching in valid databases such as Google Scholar, Scopus, ProQuest and PubMed. The statistical population of this study includes all articles published until 2022. In this research, after checking the findings and data quality, we analyzed a total of 11 articles.

Results: NPs have shown certain advantages when it comes to antitumor multidrug resistance (MDR), as they provide platforms for drug combination therapy as well as inhibiting the function of certain drug resistance mechanisms, such as efflux transporters on cell membranes. Nanoparticle-based therapy has been reported to have potential in overcoming MDR in several types of cancers, including breast cancer , ovarian cancer , and prostate cancer. Nanoemulsions are usually formed using oil-in-water (O/W)

or water-in-oil (W/O) techniques, when two immiscible liquids are mixed, they are typically 20 to 200 nm in size. Nanoemulsions have been shown to contain drugs with poor water solubility, so their bioavailability can be increased. Also, nanoemulsions can also be utilized in bioimaging. Nanofibers are another class of NPs.They can be inorganic, organic or a mixture of the two materials.Their large surface areas, , low density and large pore volume allow them to load a many drugs.

Conclusion: Compared to traditional drugs, NP-based drug delivery systems are associated with improved pharmacokinetics, biocompatibility, tumor targeting, and stability, while simultaneously playing a significant role in reducing systemic toxicity and overcoming drug resistance. These advantages make NP drugs particularly useful in chemotherapy, targeted therapy, radiotherapy, hyperthermia, and gene therapy. Moreover, nanocarrier delivery systems provide improved platforms for combination therapy, that are involved in overcoming mechanisms of drug resistance, including efflux transporter overexpression, defective apoptotic pathway, and hypoxia in tumor microenvironment. Although nanoparticles have raised exciting expectations for cancer diagnosis and treatment, challenges continue to exist and arise, especially in achieving practical application inliving organisms. For new nanomaterials, gene delivery techniques and approaches continue to be developed, the main challenge will be the balancetransfection efficiency, targeting specificity, particle size, biodegradability and cytotoxicity, as well as their short- and long-term fate in the environment.

Keywords: Nanoparticle; Chemotherapy; Drug Delivery Systems; Neoplasms

Nanomedicine based strategies for managing leishmaniasis (Review)

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Introduction: Leishmaniasis, a tropical disease, is an ecting around 12 million people and 350 million people are under the risk of infection in 98 developing countries. Leishmaniasis has recently earned more attention due to its infection and morbidity rate. The obligate protozoan parasite Leishmania species causes leishmaniasis. There are almost 51 species of parasites, out of which 21 are cause Leishmaniasis. The disease comprises 3 groups namely visceral leishmaniasis (VL), cutaneous leishmaniasis (CL), and mucocutaneous leishmaniasis (MCL); CL has the most prevalent rate. Nanotechnology is effective treatment for protozoan infections. Nanocarriers can penetrate the macrophages' cells and reach the infectious parasite, enabling targeted delivery. A group of nanocarriers serve as a method of enhancing ecacy, regulating pharmacokinetics, and reduced drug toxicity with sustained release of the drug. One of the reasons for progress in the field of pharmacology is nanotechnology. In this review, an attempt has been made to compile based on the combination of nanomedicines and nanotechnology with emphasis on the use of different techniques in nano dimensions and recent reports on the treatment of leishmaniasis.

Methods: In this review article, the required data was collected by using keywords, referring to reliable databases such as ProQuest, Scopus, PubMed and Google Scholar. Our statistical population consists of all studies conducted until 2022.

Results: In order to treat or increase drug delivery in CL, the green synthesis of zinc oxide nanostructure by extract of natural sweetener (Stevia) from nanosilver and nanogold has been used. In anti-leishmania treatments, nano DDS based formulations are an advanced approach. The killed parasite has been used as an antigenic component to produce Leishmania immunization vaccine, but its efficiency was low. Delivery of AMB via NLCs is preferable to the use of amphotericin B alone. Nanotubes are actually excellent nanocarriers. In a study, the antileishmanial effect of AmB associated with carbon nanotubes has been investigated. The researchers found that this

formulation performed better targeted killing of L. donovani than free AmB. Functionalized carbon nanotubes (f-CNTs) are lesson the drug-induced toxicity and inhibit parasite growth. In single and triple doses of SODB1 nanoparticles, IgG2a and IgG2a/IgG1 were significantly higher than the other groups($p<0.05$), which shows the efficiency of chitosan nanoparticles in developing a nano vaccine for leishmaniasis. MSNPs aided in the healing of skin lesions when applied topically daily for 21 d. MSNPs treated CL better than Pentos tam and CNPs. Finally, MSNPs synthesized by C. molmol have the potential to be considered as a nanotherapeutic approach against leishmaniasis.

Conclusion: Chemotherapeutic drugs are expensive and the parasite has developed resistance against them. To prevent leishmaniasis, there is no effective vaccine available to society. In the treatment of Leishmania, peptide vaccine can be considered a promising approach, which is associated with challenges such as degradation by the immune system. The most cost-effective drug currently in the treatment of leishmaniasis is AmB. Many researches show that the factors that have a potential effect in the treatment of Leishmania can be carbon nanotubes, PLGA nanoparticles, liposomes and SLNs. The mentioned cases increase the targeted drug delivery of the parasite. However, more studies are needed to produce effective drugs at a low cost. Nano vaccines are emerging as a novel approach to the methodology of vaccination, having shown promising results in inducing both humoral and cell-mediated immune responses.

Keywords: nanomedicine, leishmaniasis, drugs

Nanoparticles and Their Therapeutic Potential Against Bacterial Infections (Review)

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Introduction: One of the most significant worldwide health problems is the growth of antibiotic resistance in bacteria, and new research is required everywhere to create antimicrobial chemicals that are more potent. Nanotechnology has emerged as one of the most significant and pervasive fields of science in the twenty-first century. Structures with at least one dimension on the nanoscale scale are known as nanomaterials (1-100 nanometers). Nanoparticles have demonstrated effects against both gram-positive and gram-negative bacteria across a broad spectrum. Investigating the value and potential of nanoparticles in preventing bacterial infections is the study's main goal the significance of nanoparticles and their potential for treating bacterial infections was the focus of this investigation.

Methods: Using the databases from PubMed, Scopus, Science Direct, and Google Scholar, the following search terms were used: "Bacteria," "Nanotechnology," "Antibacterial," and "Nano." Additionally, keyword searches and searches of additional pertinent journals were done. The following subjects were covered in the articles we selected: articles examining the antibacterial effects of nanoparticles on bacteria, articles exploring the advantages and uses of nanoparticles in the fight against bacteria, and studies looking at variables influencing the antibacterial effects of nanoparticles.

Results: Results indicated Nanoparticles' antibacterial defense mechanisms include blocking bacterial protein and DNA synthesis. Regulation of Metabolic Gene Expression by Nanoparticles. Nanoparticle Inhibition of Bacterial Biofilm Formation. The Impact of Nanoparticles on Various Bacterial Components Nanoparticle interactions with bacterial cell walls and cell membranes. In contrast, factors impacting nanoparticles' antibacterial mechanisms were observed. Size, charge, zeta potential, surface shape, and crystal structure of nanoparticles are just a few of the physicochemical characteristics that have a significant role in how well they interact with bacterial cells. The antibacterial effects of nanoparticles are also influenced by ambient factors and the length of exposure to other elements. According to recent studies, a nanoparticle's

size has a significant impact on how antibacterial it is. Compared to larger nanoparticles and polymers, smaller nanoparticles have more focused surface areas and are more likely to come into contact with bacterial cell membranes.

Conclusion: Antibiotic resistance has increased recently, making it harder to treat patients and combat infectious infections, which can result in fatal complications. Since nanoparticles either have no cytotoxicity or often have extremely low toxicity, they appear to be a good replacement for antibiotics and could potentially address the issue of the growth of resistant bacteria. Additionally, their production processes don't require any delicate or risky procedures. Green chemistry has made it possible to create nanoparticles that are smaller, more effective, and have acceptable antibacterial capabilities.

Keywords: bacterial resistance, Antibiotic, Biofilms, nanoparticles

Nanoparticles as a new approach to improve the neuroprotective effects of quercetin (Review)

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Introduction: Quercetin is a flavonoid presenting potential protective effects against neurodegeneration, including antioxidant, metals chelating, anti-inflammatory, and anti-apoptotic effects. Numerous studies have designed various nanoparticles (NPs) to improve quercetin properties.

Methods: Here, the protective properties of quercetin against neurodegeneration is reviewed and then, new nanoparticles and their effects on quercetin properties is reported.

Results: NPs prepared by different researchers improved biological effects of quercetin. In addition to enhancing the quercetin solubility and bioavailability, the NPs could ameliorate the antioxidant and anti-inflammatory properties of quercetin.

Conclusion: This study reviews efficiency of quercetin NPs (QNPs) and quercetin-carrier NPs and suggests the NPs can be effective to improve the neuroprotective effects of quercetin.

Keywords: Inflammation, nanoparticles, oxidative stress, quercetin

Nanorobots, tiny biological machines - the most promising medical tools (Review)

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Introduction: Robotic systems have especially expanded the attain of human beings in detecting, interconnecting, transforming, and manipulating the universe around us. Specifically, the conflux of various technologies has enabled a solstice in medical applications of robotic technologies toward meliorating health care. With the continual improvement of micro-nanomaterial synthesis technology, numerous micro/nanorobots have been expanded in depth and have expansive application visions, particularly in the biomedical field. Biomedicine basically comprises diagnosis and treatment. From an engineering perspective, diagnosis is the evaluation of numerous abnormal phenomena in the human body, and treatment is to change the current condition of human cells. With the improvement of medicine to the cellular and molecular stages, diagnostic techniques should be decreased to micron and nanoscale scales, detecting at the cellular molecular scale, and supplying new diagnostic techniques. The appearance of robots is the innovation of modern biomedical methods, supplying new ideas, which can enter the human body in negligibly invasive ways, and none of the traditional medical technology is able to attain this technology.

Methods: In this review, we studied more than 30 articles from 2000 to 2022 from valid databases. clearly, we describe the medical applications of nanorobots as tiny biological machines and then discuss the future advances and their potential properties.

Results: Richard Phillips Feynman originally recommended that micro/nanorobots can be utilized in biomedical applications, and he foresaw that the micro-machines can attain microscopic treatment. Also, the first person that used nanorobots for single-cell analysis and manipulation was Toshio Fukuda. Notwithstanding little design and controlled navigation ability, micro/nanorobots have been generally utilized in many fields, such as drug delivery, negligibly invasive surgery, cell capture, and separation, nano printing, analysis and detection, and environmental purification.

Conclusion: Micro/nanorobots have made some advances in various fields of precision medicine throughout the last 10 years due to their extremely little size, opportunity, and unconstrained and controllable ability to control movement and achieve several in any little environment. Looking to the future, the improvement and utilization of micro/nanorobots in medicine are supposed to become a powerful research area. To understand the maximum potential of the micro/nanorobots in the medical field, nanorobotic researchers ought to work more closely with medical scientists for thorough examinations of the behavior and usefulness of the robots, including studies on their biocompatibility, maintenance, therapeutic affection, and biodistribution.

Keywords: micro/nanorobot, medical diagnosis, disease treatment, targeted drug delivery

Nanotechnology and COVID-19: Potential application for treatment (Review)

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Introduction: The novel coronavirus (2019-nCoV) emerged in China at the end of 2019 and then spread worldwide, particularly to Italy, Spain, USA, and Iran. Currently, Coronavirus Disease 2019 (COVID-19) is a main public health issue. As of April 9, 2020, more than a million confirmed cases of COVID-19 with more than 90,000 deaths have been reported in 202 countries by WHO. The 2019-nCoV can be spread by direct contact or droplets between humans and shows great potential for a pandemic. At present, there is no particular antiviral therapy for 2019-nCoV-infected persons, however, a wide range of therapeutic agents are being examined. The capabilities inherent to nanotechnology hold a large guarantee in presenting innovative approaches in the field of COVID-19 prevention, diagnosis, and cure.

Methods: Reviewing and evaluating the researches that have been done in the past and the materials that have been published.

Results: We in this article discuss how nanotechnology can improve the treatment of persons infected with COVID-19 virus.

Conclusion: As shown in this review, remarkable works have been done in nanoformulation therapeutics for treatment of the lung infections. Nanotechnology presents an excellent opportunity for the basic improvement of current treatments and development of novel therapeutic options for lung infections formerly thought impossible or difficult to treat. Nonetheless, we are yet in the primary stages of nanomedicine in respiratory infections care, which requires physicochemical and nanotoxicological analysis for possible human applications. At present, we are entering a modern world where nanotherapeutics will change the way we practice respiratory medicine. Nanotherapeutics offer improved clinical efficacy for patients, especially to those patients who are currently treatment-resistant to conventionally administered therapeutics. According to the above content and the potential applications of nanotechnology to delivery of anti-infection drugs to the lungs, current and potential therapeutics of COVID-19 can be encapsulated into nanocarriers and delivered to the lungs through the respiratory tract.

Keywords: 2019-nCoV, COVID-19, Coronavirus, Nanotechnology.

Necroptosis signaling pathways in Alzheimer disease: from mechanisms to therapies (Review)

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Introduction: Alzheimer disease (AD) is a progressive neurodegenerative disease and the most common cause of dementia, accounting for 60% to 80% of cases. AD is clinically characterized by cognitive impairments and neuropathologically by the presence of extracellular amyloid beta (Aβ) plaques and intracellular neurofibrillary tangles. The extensive neuronal loss and atrophy have been detected in the cortex and hippocampus areas of the brains with AD. There is increasing evidence suggesting that activation of necroptosis signaling pathway plays an important role in AD-related neuronal loss. Necroptosis, the most characterized regulated necrosis, is mediated by TNFα binding to TNFR1 followed by assembly of the necrosome complex composed of RIPK1, RIPK3 and MLKL. MLKL then translocates to the plasma membrane and forms pores, leading to membrane rupture and release of intracellular content into the microenvironment. Increased immunoreactivity for pRIPK1, pRIPK3, and pMLKL was observed in AD transgenic mice as well as in AD patients, which were associated with decreased neuronal density and cognitive deficits. Moreover, preclinical studies have shown that genetic or pharmacological inhibition of necrosome components can exert protective effects against learning and memory deficits in several models of AD through reducing Aβ burden, hyperphosphorylated tau protein level, inflammation, and neurodegeneration. More interestingly, clinical studies are designed to assess the efficiency and effectiveness of necroptosis inhibitors in healthy subjects and AD patients. A clinical investigation conducted in the US and the Netherlands have proven that the RIPK1 inhibitor (DNL747) is safe, tolerable and effectiveness in AD patients.

Methods: This abstract is a review type and does not include materials& methods and results section.

Results: This abstract is a review type and does not include materials& methods and results section.

Conclusion: Taken together, targeting necroptosis may provide a promising strategy for the treatment of AD.

Keywords: Alzheimer disease , Necroptosis, Neuronal loss, Cognition

Neuronal pathways involved in operant learning (Review)

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Introduction: Animal's survival and reproduction depend on two different learning processes which are studied experimentally applying classical or Pavlovian conditioning and operant or instrumental conditioning.

Methods: The paper has been written based on published articles relevant to operant learning.

Results: In Drosophila, the inhibition of operant learning system by classical learning system prevents direct modification of the behavior and keeps the memory flexible. After extended periods of time in this situation, a mushroom body (MB) mediated inhibition is overcome and the behavior is modified by operant learning system, which may improve efficiency but also leads to habitual responses and inflexibility.

Conclusion: Certain MB output neurons (MBONs) are specialized for world and operant conditionings using visual stimuli. Flies can learn specific visual patterns by forming associations between punishment and color as a visual stimulus. Complex learning behaviors can be observed in flies and a great deal of effort has been devoted to understand the neural circuits that underlie operant learning behaviors. Evidence shows different levels of divergence of postsynaptic connections of MBONs throughout the brain. The major input from the MB onto fan-shaped body (FSB), protocerebrum, and lateral accessory lobe (LAL) , suggest these brain regions as main candidates for descending information from the MB to the motor centers.

Keywords: Drosophila, MBONs, LAL, FSB, MB, Learning

New recent advances of biosensors in nano field (Review)

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Introduction: Nano biosensors which based on nanomaterial are used in analytical determination through a specific circumstance. It is also boost by nanomaterial existence. These biosensors are DNA-based with electrochemical and FET-based transduction which have diverse kinds of nanomaterial like metal nanoparticles, nanowires, etc. affinity-based biosensors (ABBs) is compelling devices for affordable and early recognitions. SARS-COV2 appear to be linked with milder infections but it is rapidly spread to become global pandemic problem. Cov family is enveloped, positive-sense, singlestandarded RNA viruses that could spill over the mammals and birds. The biosensor's fast response time, high specify, etc, permit them for POC use and accomplishment of current process of screening and monitoring. This article tries to illustrate new recent advances of biosensors in nano field.

Methods: In this systematic review, the data required for this study were collected using keywords and based on reliable databases such as Google Scholar, PubMed, Scopus and ProQuest. In this study, our statistical population includes all articles registered until 2022. After reviewing the relevant findings and evaluating the quality of the obtained data, 17 articles were analyzed.

Results: According to the sources there are two type of nanobiosensores: 1- bottom-up nanostructures (lithography 51, 58) 2- top-down nanostructures (lithography 47-50, 44). First one usage are in clinical application especially in places where no storage facility exist, being balancer factors, colloidal plasmatic nanoparticles (NPs) synthesize is in same with bottom-up approach, for enhancing the stability extensive endeavor apply toward PNP synthesis, etc. In contrast top-down benefits are long shelf-life, effortless portable, also used for detection, etc. This variety of differences caused researches to be done in fabrication technique for high performance nanoplasmonics such as e-beam, mask lithography, etc. As long as performing nanofabrication technique began to count as sensor transducers.

So these nanostructures illustrate capable advantages against SPR, for instance handling need for complex light coupling system, etc. Nowadays a few nanobiosensors available in streets but it is not used for laboratories or clinics for routine tests. Even researches is continued to merge nanotechnology provided assets which could beat SPR biosensors.

Conclusion: Plasmonic materials and nanostructures have incomparable potential for comprehension of noble enabling biosensor technologies. Plasmonic biosensors can suggest analytics label-free recognition of any type with sensitivities and real-time one-step format. Plasmatic and Nanoplasmonic could be used in portable and user-friendly devices at needed occasions. For developments and designs several factors may be considered, include metal selection of plasmatic, the particle geometry, biorecognition interface, etc. after take account all aspects these techniques could be used in fast detection of cancer, screening huge amount of population or routine tests of food or water contaminant.

Keywords: biosensors, advances, Nanostructures

New techniques for diagnosis and treatment of Cervix Cancer (Research Paper)

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Introduction: Cervix cancer is caused by the human papillomavirus (HPV). HPV is one of the most important sexually transmitted viruses in the world. Cervix cancer is the second leading cause of death among women after breast cancer. Also, this cancer is the 10th rank among all cancers of women and men.

Methods: In this research, the original English and Farsi articles in the databases Google Scholar Direct, Scopus Cochrane Library, PubMed Science and in Iran's database including SID and IranMedex since the year 2018-2020 were searched. To find HPV diagnosis articles, in the database Searching medical titles (MeSH) from the words: "human_risk high papillomavirus "HPV16" or "HPV18" and biosensor "piezoelectric method" or "optical method" or "electrochemical". "detection" and "colorimetric method" or "fluorescent method" or "diagnosis" was used together with the prepositions AND and OR.

Results: Cervix cancer diagnosis methods are colposcopy, biopsy,Ultrasound or intravaginal ultrasound, CT scan, IPV, PET, MRI and the new method of biosensors. To treat the method Surgery, radiotherapy, hormone therapy and chemotherapy are used.

Conclusion: Considering the high prevalence of Cervix cancer and the risks of contracting the virus HPV, early diagnosis and timely treatment of this disease to reduce the death rate And it is essential. The best diagnostic method is to use a Pap smear test It is for early detection of cancer and the best treatment method is surgery.

Keywords: Cervix cancer , human papillomavirus , death , CT scan

New treatment of intestinal cancer (Review)

Fatemeh Ahmadi,[1,*]

1. Kharazmi

Introduction:
LymphomacanceriscommonafteresophagealcancerinWestAsiaBasedonthisarticle,itispossibletopreventthespreadoflymphomaintheintestine,digestivesystem,sideeffectscausedbychemotherapytreatment.Suggestionofthearticle:Afterdiagnosingthetypeofcancerandthecenterofspread,thegenetodealwithitisinjectedintothestemcellandenteredintotheplacewherethelymphomaaccumulatesinthepatient'sbodyInthiscase,thestemcellislocatedaroundthecanceroustumorandthepossibilityofmetastasisislostforthecancerAtypeofgrowthstimulantisaddedtothestemcelltocontrolcellproliferationFinally,thecancerouscellwillturnintoahealthycellandifitneedstoberepairedthestemcellwillrepair

Methods: 1- The pluripotent stem cell found in umbilical cord blood and fat tissue or a suitable donor cell 2- Immune system gene to fight cancer 3- a type of growth regulation protein 4-Freezing stem cells 5- Entering the patient's body And there is no need to prescribe high-dose and expensive chemotherapy drugs

Results:
ChemotherapyorsurgerythesehavedangeroussideeffectssuchasanemiainfertilitykidneyrespiratoryproblemsandhighcostsStemcelltransplantationisinthelaststageWhenthelymphomahasrelapsedorbecomeresistant,thesuggestedmethodisusedafterknowingthetypeandseverityofthecancerThepatientnolongersufferstheppainandsufferingofthepreviousstreatmentmethodsthecostsareverylowithasfewersideeffectsthanthepreviousones,itonlyrequiresanallogeneicstemcelltransplant,itseemsthatusingthismethodtotreatintestinallymphomaCanbetreatedatanystageInvestigatingtheuseofthismethodcanbeeffectiveforlymphomainotherpartsofthebody,suchasbrainlymphomaandgastriclymphoma

Conclusion: Immunotherapy focuses on the site of cancer cells, but there is a possibility of cancer recurrence or immune system defense response against healthy cells. In radiation therapy, to destroy cancer cells, it has many side effects and costs a lot. There is also a possibility of cancer recurrence

Keywords: Cancer

New treatment options against Carbapenem Resistant Acinetobacter Baumanii isolates (Review)

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Introduction: Acinetobacter baumanii is a gram negative and opportunistic nosocomial pathogen that cause nosocomial infection such as Bacteremia, Ventilator Associated Pneumonia Surgical Site Infections, Secondary Meningitis and Urinary Tract Infections. Because of its ability to resist again almost antimicrobial agents including carbapenems, so the World Health Organization (WHO) identified this pathogen as a critical bacterium. Frequency of CRAB isolates have been reported increasingly so the problem of treating Acinetobacter baumannii infections has became a challenge. The emergence of CRAB isolates left several active antimicrobials including colistin, tigecycline, and sulbactam as β-lactamase inhibitor, but reported resistance to thess drugs. Colistin is consistently used as rescue therapy, but monotherapy with COL often leads to suboptimal clinical outcomes, which are attributed to uncertain dosing parameters as well as nephrotoxicity. The present study aimed to explore new treatment options against Carbapenem Resistant Acinetobacter Baumanii isolates

Methods: In this study various databases used to select articles in both Persian and English languages. Targeted databases were Google Scholar, PubMed, Scopus, Web of Science. The applied keywords included Carbapenem resistant Acinetobacter baumannii, CRAB isolates and treatment

Results: Studies showed that colistin combined with other antibiotics including sulbactam, meropenem and tigecyclin may be suitable combination for treatment carbapenem resistant A. baumannii infections. The results revealed that combined treatment of colistin with other antibiotics have shown superior clinical outcomes compared to colistin alone so to limit nephrotoxicity side effect and reduce resistance to this drug, combination therapy is suggested

Conclusion: In Conclusion, some of these studies were conducted in invitro conditions, so for better conclusions and clinical use of these drugs, need further trials and more investigations in invivo conditions to confirm this findings

Keywords: Carbapenem resistant, Acinetobacter baumannii, treatment

Niosome hesperidin decreased the level of lipid peroxidation and improved memory function in depressed rats (Research Paper)

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Introduction: Major depressive disorder (MDD) is a heterogeneous disease triggered by biological, psychological, genetic, social, and family factors. Oxidative stress parameters are involved in the formation of the pathogenesis of depression. Depression can also affect memory function and cause malfunction. Hesperidin is a natural antioxidant and Niosome hesperidin is new in Nano drug delivery. This study aims to effects of hesperidin and Niosome hesperidin on neurobehavioral activity and levels of malondialdehyde (MDA) in the hippocampal area of rats in depression rats.

Methods: In this study, we used 36 adult male rats. The animals were divided into six groups. The control group received saline for 14 days. The depressed group received reserpine (0.5 mg/kg) for 14 days to induce depression. The treatment group with hesperidin first received reserpine for 14 days to induce depression and then received the antioxidant hesperidin (20 mg/kg) for 14 days. The hesperidin group received hesperidin (20 mg/kg) for 14 days. The niosome hesperidin group received niosome hesperidin (20 mg/kg) for 7 days. The treatment group with niosome first received reserpine for 14 days to induce depression and then received niosome hesperidin (20 mg/kg) for 7 days. The Behavioral tests included the Passive avoidance test (shuttle box) was performed on days 7 and 14 to assess showed improvement in memory retrieval and recognition memory consolidation. 24 hour after the last injection, animals sacrificed and their brain is dissected. The level of MDA was measured in the hippocampus. The basis of the tissue MDA measurement method is based on reaction with thiobarbituric acid (TBA), and extraction with butanol. Data analyzed by using repeated measure of One-Way ANOVA

Results: The results showed that there was a significant difference between the groups in passive avoidance test and the level of malondialdehyde (MDA) in the hippocampal area in depression rats. In the Passive avoidance learning test, treatment with Niosome hesperidin in depressed rats significantly increased the amount of memory function ($p<0.05$) compared with depression group without treatment. Interestingly Niosome hesperidin improved the function of memory compared to control group ($p<0.05$). Administration of

niosome hesperidin significantly ($p< 0.05$) decreased the level of hippocampal MDA compared to the control group.

Conclusion: It seems that niosome hesperidin as a Nanoparticle can decrease the level of MDA as a lipid peroxidation factor in the hippocampus of depressed rats and also can improve the memory function of these rats.

Keywords: Depression, Niosome hesperidin, Nanoparticle, Memory, Lipid peroxidation

Noninvasive and invasive techniques in the prenatal screening of Down syndrome: a review (Review)

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Introduction: Down syndrome is a chromosomal disorder that is attributed to the extra genetic material of chromosome 21. This is included a portion or total of this chromosome. Down syndrome is the most common cause of mild to moderate intellectual disability. As well, patients present characteristic facial features and growth problems. Different methods have been used in prenatal screening for Down syndrome (DS) which developed significantly over the recent years with the upgrading the serum screening in the first- and second trimester and the introduction of cell-free fetal DNA. In this review, we discuss the various methods of prenatal screening and diagnosis and their importance in down syndrome.

Methods: This review article has been written by gathering information from articles published in Pubmed about Down syndrome and prenatal screening methods.

Results: The focus of prenatal screening has been on the detection of trisomy 21 (Down syndrome) since the 1980s. Multiple markers are used for risk screening of DS including pregnancy-associated plasma protein (PAPP)-A, inhibin A, human chorionic gonadotrophin (hCG), the free-β subunit of hCG, unconjugated estriol (uE3), inhibin A and AFP, ultrasound nuchal translucency (NT) and more specialized studies with molecular methods, including non-invasive and invasive sampling, respectively, including NIPT and CVS, amniocentesis, etc. More studies on the sensitivity and specificity of these screening techniques, and knowing the optimal time to perform each of them will be beneficial for the effective use of these methods.

Conclusion: This review presents all currently accessible noninvasive and invasive techniques for the screening and diagnosis of Down syndrome. By introducing these methods and the probable alternatives, the health care providers will be able to provide their patients with all the information essential to make an informed decision about their medical management.

Keywords: Down syndrome, prenatal screening, Noninvasive, invasive

Nursing Trainees' Health Communication Investigation after Curriculum Revision (Research Paper)

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Introduction: Health communication (HC), the process of exchanging emotions and information between patients and healthcare workers, plays an influential role in providing positive physical and mental outcomes in patients and nurses' professional success(1-2). However, results of various studies indicate the weakness of nurses in establishing HC with patients(3-4). According to healthcare reforms, since 2013, the "professional ethics and communication course" has been integrated into the nursing curriculum to train competent nurses(2). Therefore, it seems necessary to investigate the nursing trainees' HC using psychometric tools.

Methods: In this descriptive, analytical research, the study population included all undergraduate nursing students (different grades) of Tehran University of Medical Sciences (TUMS), Tehran, Iran, in 2020. The minimum sample size was 234 (n=〖Z^2*S〗^2/d^2) at a 95% confidence interval and 10% attrition rate (d=0.67)(2). Two instruments were used to gather data, including a demographic questionnaire and a nursing student health communication questionnaire (NSHCQ). The first questionnaire was used to collect the students' background information, such as gender, age, and semester. The second tool was a valid and reliable questionnaire consisted of 35 items and five subscales: "cooperation attraction" (6 items), "maintaining dignity" (6 items), "preparedness" (9 items), "empathic understanding" (7 items), and "responsiveness" (7 items). The items were rated on a five-point Likert scale, ranging from one ("never") to five ("always"). Cronbach's alpha and intra-class correlation coefficient of NSHCQ were 0.75 and 0.85, respectively. The students' HC was categorized based on their score (sum of item scores) into three categories of weak (<50%), moderate (50-75%), and desirable (>75%)(2). The study was accepted by TUMS ethics committee (IR.TUMS.REC.1394.807). The second researcher attended selected TUMS hospitals for three months and distributed the questionnaires after explanations regarding the voluntary participation and data confidentiality. A convenience sample of 234 students passing at least one clinical rotation was recruited and asked to sign a consent form. To analyze the data, SPSS Version 22 was used. After appraising the normal distribution of data using Kolmogorov-Smirnov test, descriptive statistics were measured to compare the frequency of nominal variables. Inferential statistics were also measured

for evaluating the students' demographic characteristics and semester distribution with regard to HC domains.

Results: The majority of nursing students in this study were female (59.17%) with mean age of 22.13±3.02. Also, most of the students (88.3%) were in the pre-internship period (semesters 2-6). The results showed that the HC of students was moderate and desirable. The score of "cooperation attraction" was the lowest (24.55±2.92), this may be related to the fact that most students did not have enough knowledge to educate patients and give them feedback for modifying their health behaviors(3). Results showed a significant difference between males and females in the domain of "empathic understanding" (P<0.005), based on the Chi-square test. It seems that intrinsically compassionate female students were more successful in HC because of their patience, flexibility, good listening skills, and understanding of the patient's bad condition and problems both verbally and non-verbally(3). Also, in the present study, there was no significant correlation between age and HC. This finding is in contrast to the results of Mirhaghjou et al. in which the majority of older students were experienced practical nurses, and therefore, obtained higher HC scores(4). Moreover, the results demonstrated a significant correlation between all five domains of HC and the individual's semester, based on the Chi-square test (P<0.01). Since senior students have more knowledge and experience in performing HC, they have higher interactional skills, compared to other students(4).

Conclusion: To conclude, the added course has been effective in promoting the HC of nursing trainees. However, applying simulation-based workshops can make students more successful in relating and educating patients.

Keywords: nursing, students, health communication

Nutritional Assessment for malnutrition in Pediatric Chronic Kidney Disease (CKD) (Review)

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Introduction: Children with chronic kidney disease (CKD) had problems in growth and development. Malnutrition and undernutrition are common in CKD children. This study aims to investigate nutritional assessment methods for children with CKD.

Methods: To accomplish this narrative review, we searched 4 Databases (PubMed, Web of Science, Scopus and google scholar) based on the search strategy from 2012 to 2022 with the high sensitivity on September 2022 by following MeSH keywords: " Chronic Kidney Disease ", " Pediatrics ", " Nutritional Assessment ", " Malnutrition ", " Undernutrition ".

Results: Most studies indicated that growth assessment and management parameters must be included: Anthropometric data, nutritional status, and Caloric Intake. Protein intake is critical for muscle and skeletal growth. Route of feeding is essential; a few sufferers may also require supplementation remedy or enteral feeding. Monitoring fluid balance through comparing blood pressure and weight gain earlier than and after dialysis, or the use of bioimpedance spectroscopy is necessary. Protein (positive nitrogen balance). The maximum recommendation of sodium is 1500–2400 mg/day. Serum potassium must be in the normal range of 3.5–5 mmol/L. Phosphate recommends varies according to age for first month's child is 5.2–8.4 mg/dl and then reduces with age and personal needs. The need for calcium for children is 100-200% of DRI.

Conclusion: Based on the date of our study, close monitoring for children with CKD is necessary for better growth and prevention of comorbidities.

Keywords: Chronic Kidney Disease, Nutritional Assessment, Pediatric

Occupational Therapy And Speech Therapy For Children With Cerebral Palsy (Review)

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Introduction: Cerebral palsy is a permanent and non-progressive childhood syndrome that occurs in two to three cases out of every 1000 live births and originates in the prenatal period, perinatal period, or the first few years of life and negatively affects brain development. It affects and causes movement disorders, body posture, and imbalance, which severely limits activity. Muscle hypertonicity due to brain damage is the most common symptom observed in cerebral palsy patients along with other motor problems such as impaired balance, coordination, hand function, etc. Patients with cerebral palsy often experience non-motor problems that must be managed into adulthood, including cognitive dysfunction, seizures, pressure sores, osteoporosis, emotional or behavioral problems, and hearing and speech disorders. To control the situation, there must be a balance between a person's complex interactions with the environment and tasks. Balance involves a complex interaction between the musculoskeletal and nervous systems.

Methods: This study is a systematic review with English keywords Cerebral Palsy, Treatment, Occupational Therapy, Speech Therapy, Children in reliable English and Farsi scientific databases and sites, including Pubmed, Google Scholar, Scopus, Sciencedirect, Magiran, Sid in the period from 2002 to 2022. It was done and 50 articles were found in the initial search, after removing duplicates and evaluating the title and abstract, 18 articles were selected with the necessary conditions to participate in the present study, and general conclusions were made based on the information in the various selected articles.

Results: Studies show that the treatments performed improve motor activities. Treatments such as physical, occupational, speech, and behavioral

therapy help with therapy and caregiving, while family-centered therapies can be provided. Some of the techniques used include hippotherapy, neurodevelopmental therapy, sessions of 30 to 45 minutes twice a week for 8 to 12 weeks, deep brain stimulation and electrical stimulation, serial casting, robot-assisted walking training, Body Weight Support Treadmill Training, virtual reality, and biofeedback, vestibular intervention. The most common movement disorders observed in cerebral palsy are muscle spasms and dystonia with problems with coordination, strength, and selective movement control. Spasticity is a major challenge in the management of children with cerebral palsy. It causes the bone and joint deformities due to spasms, pain, and loss of function. Common medications found in the literature to relieve spasticity include baclofen, diazepam, clonazepam, dantrolene, and tizanidine. Baclofen and diazepam help relax muscles but have many side effects. The first line of treatment for spasticity is physiotherapy, occupational therapy, botulinum toxin injection, selective dorsal rhizotomy, and intraspinal baclofen. Combined use of active vestibular interventions and occupational therapy can improve functional balance in children with spastic cerebral palsy. One of the most common speech problems in children is cerebral palsy, which includes problems such as drooling, swallowing, and feeding, which affects half of the children. Speech therapy for such conditions helps improve motor skills, anesthesia problems, and communication skills and includes oral care, feeding techniques, food modification, and oral muscle movement. Excessive drooling can be controlled by controlling the problem, Mouth control, tongue control, behavioral therapies, intraoral appliances, and medications such as cholinergic and onabotulinum toxin (Botox) injections into the salivary glands and surgery on the ducts and salivary glands, and managed biofeedback. Speech therapy and the use of computer synthesizers can help improve communication.

Conclusion: Deciding on the most effective and efficient amount of treatment services for children with cerebral palsy and how to provide them is complex. However, any severe disorders associated with this disease should be managed carefully. Occupational therapy helps children with cerebral palsy improve their ability to perform daily tasks. Interventions that include specific exercises of child-initiated movements, environmental modifications, and parent education provide the best response. Family-centered rehabilitation treatments are positively associated with greater participation in family/recreational activities and walking tolerance. Occupational therapists help children work on improving their impairments. The parental perception that rehabilitation treatments meet the child's needs is associated with greater participation in family/recreational activities. Speech therapy teaches children to communicate successfully. Intensive speech therapy focuses on creating a stronger voice that improves the clarity of children's voices and speech. Treatments such as physical, occupational, speech, and behavioral therapies help strengthen patient-caregiver interactions while providing family support.

Keywords: Cerebral Palsy, Treatment, Occupational Therapy, Speech Therapy, Children

Optimizing blood vessel decellularization process to create biological scaffold for vascular tissue engineering (Research Paper)

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Introduction: For decades researchers have employed different types of biomaterials for tissue engineering. However, finding a biomaterial with the exact properties of natural tissues remains a formidable challenge. In tissues like blood vessel, these challenges become more apparent due to low thickness and delicate structure. Any minor defect in this structure causes serious dump in mechanical properties and pathological consequences like aneurysm. Moreover, direct contact with blood has forced researchers to prepare perfect hemocompatible surfaces for this tissue. Besides these problems, geometrically we need a cylindric shape for vascular tissue engineering which makes it worse. Controlling cell growth inside the cylinder is not easy, and overgrowth of cells like smooth muscle cell (SMC), and fibroblast causes intimal hyperplasia followed by hypertrophy, fibromuscular dysplasia and etc. In this research, we decellularized the ovine blood vessel to reach a biological scaffold (BS). This BS has the most similar properties to the natural blood vessel. Evaluating the BS's mechanical strength, viability and cellular adhesion revealed a promising future for blood vessel tissue engineering.

Methods: After cleansing the vessels tissue, they were immersed in 70% ethanol for 5 min to sterilize. Then osmotic pressures were exerted on the tissue for physical disruption of the cells without hurting the extracellular matrix (ECM). Finally, 0.025% trypsin and 1% Triton X-100 were employed to remove the cell debris. All the steps have been done at 4˚C. After washing the obtained BS, smooth muscle cell was grown on it for up to 4-day.

Results: The BS showed no cytotoxicity, and SEM images revealed appropriate cell attachment. Histological studies proved cell migration to the BS's pores has done after 4-day culture. In addition, the optimized decellularized process didn't have any harmful effects on the mechanical properties of the BS.

Conclusion: Reducing the concentration of the reagents and the temperature of the reactions gentled the kinetics of the decellularization process. It enhances the process control and the quality of the ECM.

Keywords: Blood vessel; Tissue engineering; decellularized scaffold; cellular adhesion; mechanical properties

Optogenetics Is a New Star For The Treatment of Parkinson's (Review)

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Introduction: Optogenetics is a technology that combines optics with genetics to induce a precise gain or loss-of-function in cells or tissue by applying light. This biological technique involves: 1) engineering a gene that must be delivered in a cell specific manner and expressed at adequate levels, 2) developing a mode to deliver light for in vitro and in vivo studies, 3) detecting the effect of optogenetics. This light-sensitive technology has revolutionized the study of neuroscience with single-cell and millisecond precision control of neurons. Accurate spatial and temporal control is especially important to a system as complex as the nervous system, containing a network of billions of cells. Parkinson disease (PD) is the second most common neurodegenerative disorder after Alzheimer disease. PD is a common and slowly progressive neurodegenerative disease caused by the gradual loss of dopaminergic (DAergic) neurons in the substantia nigra pars compacta (SNc). The cardinal motor symptoms of PD are tremor, rigidity, bradykinesia/akinesia and postural instability, but the clinical picture includes other motor and non-motor symptoms. Movement disorders including Parkinson's disease is caused by neurological dysfunction, typically resulting from the loss of a neuronal input within a circuit. Neuromodulation, specifically deep brain stimulation (DBS), has proven to be a critical development in the treatment of movement disorders. Continuing efforts aim to improve DBS techniques, both in how they exert their effects and in the efficacy of the mechanism involved in eliciting those effects. We review the benefits of cell-type specific manipulations in understanding the root cause of movement disorders and how DBS might optimally combat those causes. research employing optogenetics provides the specificity and feasibility to uncover the mechanisms that will help realize these gains in patient care.

Methods: All experiments were conducted in accordance with the guidelines of the National Institutes and the protocols approved by the The Rockefeller University Institutional Animal Care and Use Committees. Mice were housed in a 12-h light–dark cycle (lights on at 7:00) with ad libitum access to food and water. Male mice were used for all the behavioral and histological studies; both male and female mice were used for tracing studies. Mice were at 8–16 weeks old at the time of surgery. All mouse lines were in a wild-type background. The following mouse lines were used: Pitx2-Cre , Gabrr3-Cre , Sapap3 KO. The subthalamic nucleus (STN) plays a key role to control

movement functions. The relationship between STN modulation with deep brain stimulation (DBS) and Parkinson's disease was investigated.

Results: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective therapy for the motor symptoms of Parkinson's disease (PD). However, the neural elements mediating symptom relief are unclear. A previous study concluded that direct optogenetic activation of STN neurons was neither necessary nor sufficient for relief of parkinsonian symptoms.

Conclusion: The term “optogenetics” cannot be reduced to a single method or technique but can be broken down into a number of components that could be used independently of assembled in various combinations leading to a very broad spectrum of exciting therapeutic perspectives. A bright future for such applications can be foreseen. Optogenetics thus appears as a challenge well worth the substantial research effort that it stillrequires. While optogenetic stimulation is currently infeasible in human patients, opto-DBS research provides an indispensible avenue to understand the mechanisms of DBS therapeutic and adverse effects.

Keywords: Optogenetic, Parkinson's disease, DBS, STN

ORAL DISEASE AND POLYCYSTIC OVARY SYNDROME (Review)

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Introduction: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women of reproductive age that not only is the leading cause of infertility but also shows a reciprocal link with oral health. Studies showed that women with PCOS have increased levels of pro-inflammatory cytokines, groups of proteins that help regulate immunity and inflammation. This chronic inflammation can lead to several oral health problems. The aim of this study was to evaluate the association between PCOS and oral disease.

Methods: In order to find relevant studies to the research question, an electronic search with time (recent five years, up to 2022) and language (English) restrictions was conducted using PubMed. Most recent studies including case control studies, original research and review articles were selected. Analysis was done and data were synthesized and compiled in a sequential and presentable paradigm.

Results: Several studies reported a strong association between periodontal disease and PCOS with a high level of systemic inflammatory markers, including adhesion molecules, TNF-α, IL-1β, and IL-6. In a cross-sectional study is found that serum C-reactive protein levels were higher in females with newly diagnosed PCOS. In women with PCOS, salivary Porphyromonas gingivalis, Fusobacterium nucleatum, Streptococcus oralis and Tannerella forsythia levels were higher than healthy women.

Conclusion: From the mentioned results, there seems to be a positive relation between oral disease and PCOS. However, multicenter studies, with larger sample sizes, are to be conducted to establish a clearer and stronger association.

Keywords: Polycystic ovary syndrome, Oral disease, Inflammation.

Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia (Review)

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Introduction: One of the vital problems in unit (intensive care units) is Lack of oral hygiene. as a result of poor oral hygiene directly will increase the danger of ventilator associated pneumonia (VAP). VAP is that the second most common healthcare facility infection and additionally is AN bronchopneumonia largely caused by bacterium that colonize the rima oris and dental plaque19. AN oral care intervention that specialize in removing the number of bacterial plaque and rising oral cleanliness among automatically vented patients ought to be often enforced to boost the oral health condition and probably forestall VAP development.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. After reviewing the relevant findings and evaluating the data quality, a total of 17 articles were analyzed.

Results: The most basic and economical methodology is Mechanical plaque management or Mechanical biofilm removal. In unit they use tiny and soft brushes. tiny for having the ability to succeed in posterior components of oral cavity and soft so as to reduce traumatization of soft tissues. Another physical method which is a smaller amount efficient in mechanical plaque control is victimization Foam swabs. generally, Foam swabs are referred to as another for toothbrush. Another useful method is tongue cleanup which reduces the entire variety of harmful microorganism. In general, any method during which harmful microorganisms will be physically destroyed is enclosed in our review list. There also are chemical strategies like using CHX (Chlorhexidine Mouthwash). Among the variability of artificial gargles within the market, antiseptic (CHX) is that the handiest anti-microbial. Experiments show that victimization the CHX when brushing will increase the potency of the method. Another sort of mouthwashes are Mouthwashes containing binary compound answer of metal bicarbonate cut back secretion consistence and so make removal of fabric alba easier. Some folks use Oxidizing antiseptic as a mouthwash in concentrations of 1%-3%Due to its irritating effect, protocol is

increasingly emphasized. One of the impactive factors within the field of VAP sickness is xerostomia. Dry mouth has been related to a coated tongue and VAP. thus it's necessary for us to search out the most effective ways that to unravel the matter of dry mouth and analyze them. Plain water is used for membrane dampening and symptomatic treatment of xerostomia. Also scouring with acid and glycerol answer stimulates salivation, thereby quickly relieving the symptoms of xerostomia.

Conclusion: VAP (ventilator-associated respiratory disease) is that the commonest kind of health facility pneumonia and a number one cause of morbidity and mortality notably among medical care unit (ICU) patients when knowing concerning this illness Our main goal was finding the ways in which of treatment or interference of VAP in every state of affairs and so comparing them to search out the simplest ones.

Keywords: immunoinformatics ،Coxiella burnetii Infection ،Q Fever Vaccine ،multi-epitope vaccine

Ostrich oil as a treatment for chronic anal fissure: a randomized clinical trial (Research Paper)

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Introduction: Introduction: Chronic Anal fissure is a rupture in the anal canal for duration of more than 8 weeks. Due to the recurrence of the disease, researchers are always in search of new medicines for medical therapy. Ostrich oil has anti-inflammatory and analgesic effects on wounds. It has angiogenesis and re-epithelialization effects, too. In this study we investigated the effect of ostrich oil on the treatment of chronic anal fissure.

Methods: Material and methods: In this clinical trial, 150 patients with chronic anal fissure were randomly divided into intervention and control groups. The intervention group received Glyceryl trinitrate (GTN) 0.2% -Ostrich oil 50% and the control group received 0.2% GTN ointment until the disease recovered and meant 4 and 5 weeks, respectively. Patients were follow up for symptoms of recurrence. The collected data were analyzed by SPSS 24.

Results: Results: Most of the patients in this study were women. The interaction between group and time showed that the slope of decreasing the mean pain score at the time of intervention in the intervention group was significantly higher than the control group ($P < 0.001$). Wound grade ($P = 0.620$) and bleeding grade ($P = 0.719$) in the two groups showed the same response to treatment. In the first two months after cessation of treatment, patients in the control group experienced a recurrence of the disease 2.63 times more than patients in the intervention group ($P = 0.001$) and up to 4 months after cessation of intervention 1.90 times more than patients in the intervention group ($P = 0.003$). At the end of the intervention, the effect of the intervention on the pain score disappeared, wound grade relapsed with $p = 0.004$ and $p = 0.004$ and bleeding grade relapsed with $p = 0.001$ and $p = 0.013$ in 2-months and 4-months follow-up, respectively.

Conclusion: Discussion: The results of this study showed that ostrich oil can possibly reduce pain in patients with chronic anal fissure during treatment, accelerate healing and reduce the course of treatmen and prevent recurrence of the disease, especially early recurrence after healing and it can be used as a complementary treatment.

Keywords: Chronic anal fissure, Ostrich oil, Glyceryl trinitrate, Healing, Recurrence, Anal fissure

overexpression of SOX11 and its possible ceRNA network in patients with small cell lung cancer tissue (Research Paper)

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Introduction: Mortality from small cell lung cancer worldwide has made this disease a significant health care problem.[1] The microarray technique is used for environmental and/or clinical studies. Although microarray is an accurate and sharp diagnostic tool, the expertized bioinformaticians were able to minimize the outcome biases and maximize the flexibility and accuracy of the technique.[2]

Methods: First of all, Microarray expression data of 18 pairs of small cell lung cancer (sclc) and tumor and adjacent lung tissues(GSE149507) was collected from NCBI Gene Expression Omnibus (GEO)[3] and then GEO2R analysis was used to find differentially expressed genes in small cell lung cancer tumor and adjacent normal lung tissues.GEPIA2[4] was used to confirm the accuracy of gene expression and the correlation between the target gene and lung cancer. In addition, from the ENCORI[5]database obtained survival analysis which handles time-to-event outcomes.[6] Gene ontology and biological pathway plus molecular function were obtained by Enrichr[7] and KEGG[8] .furthermore, String[9] database was searched to find significant interactions between proteins. additionally, miRwalk[10] was operated to find miRNA-mRNA interaction based on the 3'UTR region. then, target miRNA was investigated in lncbased.3 [11] to find miRNA-lncRNA Significant interaction and create a predictive ceRNA network.

Results: Based on the GEO analysis, a gene named SOX11 was found to be an upregulated gene (logFC= 3.92831595, adj. P value= 3.17E-06) In tissue lungs with small cells of lung cancer.then,GEPIA2 provided Boxplot which was match with first obtained datas.Survival analysis from ENCORI confirms the data obtained from GEO again(log-Rank p=0.0055 in 235 low number and 234 high number,Hazar ratio:0.76). The transcription factor SOX11 (SRY-related high mobility-group (HMG) box 11), a member of the SOXC group, is expressed during embryogenesis but largely absent in most adult differentiated tissues. SOX11 regulates progenitor and stem cell behavior and often acts together with the other two SOXC group members, SOX4 and SOX12, in regulating developmental processes, including neurogenesis and skeletogenesis. [12] searches on KEGG revealed SOX11 is participating in signaling pathways regulating pluripotency of stem cells which is related to lung cancer.in addition,Investigated of possible miRNA-mRNA interactions

showed hsa-miR-6727-3p as a significant interactor to SOX11 mRNA. Lncbase v3 searches indicated that selected miRNA had significant interaction with TCL6 and HNF1A-AS1.

Conclusion: By way of conclusion ,SOX11 is overexpressed in small cells lung cancer and constructs a Predictive ceRNA network among hsa-miR-6727-3p ,TCL6 and HNF1A-AS1. All in all, it can be said that SOX 11 is a possible biomarker for lung cancer and it would be suggested to conduct more research on this gene.

Keywords: lung cancer,SOX11,ceRNA

oxidative stress diabetic retinopathy (Review)

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Introduction: Diabetes is a metabolic disease that can cause neuropathy, retinopathy and nephropathy. Diabetic retinopathy is one of the main causes of blindness in adults in the world. In this disorder, due to the activation of biochemical pathways related to hyperglycemia and ultimately the increase of oxidative stress factors, inflammation and nerve damage, defects are created in the capillaries of the retina, which will cause vision loss and eventually blindness. Oxidative stress is the result of an imbalance between the production of free radicals and the body's antioxidant defense. Considering the vital role of mitochondria in aerobic metabolism, the function of this organelle is significantly related to the pathophysiology of diabetes. In addition, mitochondria produce reactive oxygen species as a result of fuel oxidation, and these radicals and the oxidative stress caused by them are very important in the pathophysiology of diabetes and its complications. as a result of reducing free radicals and protecting mitochondrial function and using various vitamins and drugs such as angiotensin-converting enzyme inhibitors and sulfonylureas and lipoic acid as well as antioxidant effects in various plants including flavonoids found in plant sources which have been observed in recent years, all of them indicate the very prominent role of oxidative stress in diabetes and its complications.

Methods: Diabetes retinopathy is the cause of blindness among people. Oxidative stress is a phenomenon that is an imbalance between the formation and elimination of free radicals, and we can say that oxidative stress and the production of free radicals as a result of hyperglycemia are involved in the development and complications of diabetes. Although chronic hyperglycemia is an important factor in the development of diabetes complications. There are mechanisms that cause organ dysfunction. One hypothesis is that intracellular glucose causes the production of the final product of glycosylation through non-enzymatic glycosylation of proteins and cells. The second hypothesis is that the cause of chronic complications of diabetes is that hyperglycemia increases glucose metabolism through the sorbitol pathway. The third hypothesis states that hyperglycemia increases the formation of diacylglycerol, which in turn activates protein kinase C. Important growth factors play a role in causing diabetes complications. Vascular endothelial growth factor is increased in diabetic retinopathy. Free radicals play an important role in both health and disease. Free radicals are divided into three types. Hydroxyl, superoxide and peroxide. Most of the radicals are produced by mitochondria and the most radical damage is on the membrane and DNA

of mitochondria. Most of the free radicals in the biological system are derived from oxygen (ROS), but there are also derivatives of nitrogen. It has been shown that hyperglycemia, hyperinsulinemia and insulin resistance increase free radical production and oxidative stress in type 2 diabetes. Hyperglycemia can be involved in the development of neuropathy due to oxidative stress through autoxidation of glucose to the formation of AGES, disruption of the polyol pathway, change in eicosanoid metabolism, and reduction of antioxidant defense.

Results: The role of oxidative stress caused by imbalance in the production of free radicals in diabetic retinopathy. ROS such as superoxide radical, hydroxyl radical and hydrogen peroxide radical are very unstable or even very reactive. Excessive production of superoxide radicals, altered mitochondrial electron transport chain reactions, destroys various cell structures.

Conclusion: The purpose of this review is to provide a better understanding of the complex molecular mechanisms and pathogenic roles of oxidative stress in the development of diabetic retinopathy, one of the most common complications of diabetes. Oxidative stress is a cytopathic consequence caused by an imbalance between the production and removal of ROS and seems to play a major role in it. A series of metabolic abnormalities caused by hyperglycemia, including polyol, AGE formation, metabolic pathways accordingly form a vicious cycle that causes cell mitochondrial damage, retinal cell apoptosis, lipid peroxidation, dysregulated epigenetic modification on genes. antioxidant defense system and structural and functional damages in the retina.

Keywords: Key words: diabetic retinopathy, oxidative stress, antioxidants

Oxytocin and Social Behavior; From research to usage (Review)

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Introduction: Over the past decade, oxytocin has transferred from a peptide hormone that regulates birth-related processes to a neurotransmitter with magical abilities. Various behaviors and cognitive skills have been linked to oxytocin, among which social behavior and cognition have received the most attention. Also, various clinical applications of oxytocin are under development and are expected to be available soon. Numerous clinical trials are being conducted to investigate the effects of this hormone.

Methods: This article provides a brief review of the latest findings on the role of oxytocin in various types of social behaviors. PubMed and google scholar databases were used to gather this information using these keywords: oxytocin, social cognition, relationships, and cognitive neuroscience.

Results: It has been documented that oxytocin regulates certain social behaviors such as parturition, lactation, parental nurturing, perception and the processing of facial expressions, empathy, cooperation, trusting behaviors, etc. Oxytocin works by improving the salience of social stimuli, mitigating the signal-to-noise ratio, and modulating synaptic plasticity. The effect of oxytocin on trust has been well documented. First, it was argued that it causes the promotion of trust in human subjects. Later, these findings were supported by neuroimaging studies indicating that oxytocin reduces the activation of the amygdala and dorsal striatum. Another argument for explaining the effect of oxytocin on trust is that it increases social cohesion by facilitating conformity to other members of groups we trust. It is suggested that oxytocin uses the amygdalo-fronal-striatal to mitigate motivation to respond to social clues. Administering oxytocin as a treatment for improving social cognition due to its few adverse effect, availability, and the fact that it is easy to use has been widespread. Clinical trials administering oxytocin have risen significantly in the last few years, both in psychiatric populations and others with social deficits. However, many aspects still have been neglected, such as neuroendocrine biomarkers and standardized evaluation of social behaviors. These factors must be addressed in future clinical trials and research.

Conclusion: The new emphasis on the effect of oxytocin on social behavior has been a favorite topic of research in the last ten years. Researchers have discussed that oxytocin can regulate prosocial behaviors and has been considered a treatment for several disorders with social deficits. However, there are still many unknowns on its procedures of action and efficiency.

Keywords: oxytocin, social cognition, relationships, and cognitive neuroscience.

Pathophysiology and Genetic of Cardio-oncology (Review)

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Introduction: Cardio-oncology is a multidisciplinary field, established to find and manage patients (prevention, diagnosis, and treatment) with adverse cardiovascular effects of anticancer treatments. For the first time, cardiotoxicity of thoracic radiation was described in patients who exhibited pathological alternations in their myocardium. Both traditional cancer therapies including chemotherapies, radiation and new treatments like targeted therapies via monoclonal antibodies, kinase inhibitors and immune checkpoint inhibitors, have demonstrated mild to severe cardiovascular complications.

Methods: This review provides a summarized overview of pathophysiology and genetic base of cardio-oncology discipline through searching databases, PubMed and Scopus.

Results: Pathophysiology Cancer therapies affect the interaction between cancer and the endothelium, resulting in vascular and metabolic perturbations. Cardiotoxicity is the most serious side effect of chemotherapy. Anthracyclines are used to treat patients with different childhood and adult-onset cancers. They cause cardiotoxicity in a dose-dependent manner in some patients. cardiomyopathy process initiates with single-cell myocytolysis and finally leads to disruption of myocardial structure and heart failure. Various mechanisms are proposed comprising, oxidative stress, mitochondrial injury, topoisomerase 2-ß, impaired DNA synthesis, deregulated gene expression, inhibited calcium release from the sarcoplasmic reticulum, defective mitochondrial creatine kinase function and activity, cardiac stem cells depletion and titin in sarcomeres. Immune checkpoint inhibitors like atezolizumab (PD-L1), ipilimumab (CTLA-4), nivolumab (PD-1), durvalumab (PD-L1), permbrolizumab (PD-1), avelumabn (PD-L1) cause vasculitis and myocarditis through activation of immune Tcells. Patients who consume therapeutic agents targeting tyrosine kinases: ABL directed, nilotinib, dasatinib and ponatinib may suffer from myocardial ischemia, systemic hypertension, cerebrovascular complications and venous thromboembolic disease. Suggested mechanisms for these abnormalities are, decrease of endothelial cell cAbl signaling and cell survival, reduction in VEGF-R2 signaling with attenuated endothelial proliferation, function and survival. Cancer development and progression itself, can lead to cardiac wasting, fibrosis and vasculature thromboembolic events. Hence, tumor cells and their microenvironment express inflammatory cytokines, procoagulant factors,

hormones, autophagy and ubiquitin-proteasome enzymes. Besides, cancer patients develop tumor lysis syndrome specially in leukaemia and lymphomas. Cancer and cardiovascular disease (CVD), share risk factors comprising, smoking, sedentary lifestyle, obesity, hypertension, diabetes mellitus and pathophysiological mechanisms like oxidative stress, chronic inflammation and genetic contributors. Cardiac dysfunction may also facilitate angiogenesis, tumor growth and invasiveness by increasing oxidative stress and secretion of pro-inflammatory factors and cardiokines. Genetic Recent studies emphasize that genetic factors have crucial role in the development of cardiotoxicities, resulting from cancer and its treatment and may illustrate why occur only in a subset of patient. cancer and CVD share genetic risk factors. patient with BRCA1/2 mutations also have coagulating problems. Altered levels of IGF-1 increase the risks of insulin resistance, contributing to CVD. Low levels of IGF-1 in individuals having only BRCA1/2 mutations, while high-level IGF-1 in breast cancer patients with BRCA1/2 mutations were observed. mutations of TTN are frequent in dilated cardiomyopathy and also demonstrated in 30% of solid tumors. researchers recruited TTN mutations to predict responses to immune checkpoint inhibitor immunotherapy. Through investigating shared genetic contribution for both disorders, an extremely interconnected network with a single subnetwork comprising 56 nodes and 146 edges were detected. TTN, ATM, JAK2, TET2 showed the highest number of disease interactions. The pathway enrichment analysis indicated that studied genes were significantly enriched in DNA damage repair pathways. cardiotoxicities relevant to anthracycline have genetic basis. Various single nucleotide polymorphisms have demonstrated associations like, ABCC1 (rs3743527TT, rs246221TC/TT, rs3743527TT), SLC28A3 rs7853758, FMO2 rs2020870, SPG7 rs2019604, SLC10A2 rs9514091, SLC22A17 rs4982753, SLC22A7 rs4149178. Genotypes of rs2232228 in HAS3 showed different effects on anthracycline-induced cardiomyopathy risk. cardiomyopathy in patients with GG genotype, was uncommon and was not dose-dependent. When patient exposed to high dose anthracyclines, AA genotype demonstrated an 8.9-fold higher cardiomyopathy risk. Non-coding RNAs also affect cardiotoxicities of cancer therapies. knockdown of lncRNA NEAT1 in human gastric cancer cells, which are resistant to doxorubicin, promoted apoptosis of doxorubicin-resistant cells. miR-22 is expressed in cardiac and skeletal muscles and is upregulated in doxorubicin treated cells. Inhibition of miR-22 reduces oxidative stress and apoptosis in cardiomyopathies. Therefore, targeting miR-22 may reduce doxorubicin cardiotoxicity.

Conclusion: Cardio-oncology revealed that molecular processes of cancer and cardiovascular diseases are intertwined and have improved our understanding of both disorders. However, identifying predictors of diseases risk, finding safer cancer therapeutics or cardioprotective drugs are the challenges in cardio-oncology.

Keywords: Cardio-oncology, Cardiovascular diseases, Cancer therapies, Genetic

Pediatric and adolescent COVID-19 vaccination side effects: A retrospective cohort study of the Iranian teenage group in 2021 (Research Paper)

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Introduction: On February 19, 2020, the first case of COVID-19 was announced in Iran, and COVID-19 development was reported in 8.5 million cases since the beginning of pandemic about 125,000 deaths. Hence, the need for medical, social and economic response to COVID-19 epidemic led to the rapid development and production of a large number of vaccines. Recent studies have all documented the immunogenicity of the vaccine in adults and the elderly, and only a handful of studies have examined the efficacy of these vaccines in children. Therefore, one of the most controversial issues is the vaccination of people under 18 years of age. Regarding the start of vaccination of children in Iran, we examined the safety and possible side effects of vaccination under 18 years to provide a safe and effective vaccine. This study is one of the national studies with large sample size aimed to evaluate safety and efficacy (regarding the break-through infection) of COVID-19 vaccination in Iranian children and adolescents.

Methods: In this retrospective cohort study, contact numbers of parents of teenagers under 18 years of age referred to a teenager vaccination centers in Tehran-Iran to receive the corona vaccine were collected and following

information were obtained via the phones:demographic information, type of vaccine and number of doses received, and additional information,like complications, required treatments.

Results: 11,042 subjects aged 10-18 years, mean age 14.55±1.83 years, including 5374 boys and 5768 girls were investigated. 88.1% received the Sinopharm and 11.9% the Soberana vaccine. General side effects, including fatigue, fever and chills, injection site pain and dizziness, etc. happened in 2978 cases, 7421 children presented with at least one general or organ-specific side effect following vaccination, including potentially critical side effects,such as vascular injuries, respiratory complication, etc.0.1% of the subject needed hospital admission. The breakthrough infection happened in 200 individuals.

Conclusion: Our study shows that Sinopharm and Soberana (PastoCoVac) COVID-19 vaccine are generally safe with no serious side effects in fewer than 18 years old. COVID19 infection and reinfection can occur after vaccination, but the incidence is actually tolerable and significantly lower than in the unvaccinated group.

Keywords: Safety, Efficacy, Vaccination, COVID-19, Children

PERIODONTAL DISEASE AND ENDOMETHRIOSIS (Review)

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Introduction: Endometriosis affects 6-10% of reproductive-age women. The immunobiology of endometriosis represents a paradigm shift in theories of the pathogenesis of endometriosis. Periodontal disease is a chronic inflammatory disorder as well. Since both endometriosis and periodontal disease are chronic, inflammatory processes, the aim of this review was to investigate whether an association exists between endometriosis and periodontal disease.

Methods: This review has been conducted based on analysis of available literature indexed in PubMed database between 2015 and 2022. Specific keywords including “endometriosis”, “periodontal disease” and “inflammation” have been used. Experimental and review articles on the mentioned theme were included.

Results: Higher proportion of severe periodontitis among women with endometriosis has been reported. There was a commonality of altered levels of immune modulators in patients with endometriosis and periodontal disease. Increased levels of cytokines and interleukin-1beta, IL-6, IL-8 and tumor necrosis factor-alpha have been demonstrated in patients with endometriosis. In addition, chronic periodontitis is linked to a chronic systemic inflammatory burden secondary to the systemic dissemination of periodontal pathogenic bacteria, their products (e.g., lipopolysaccharides), and locally produced inflammatory mediators (i.e., IL-1β, IL-6, TNF-α).

Conclusion: The immune dysregulation seen in periodontal disease can be the reason for the local immune deficiency propagating endometriosis, and oxidative stress of the periodontal disease may enhance the stress for endometriosis. However, further studies among larger cohorts of endometriosis may provide more evidence about the association.

Keywords: Endometriosis, periodontal disease, inflammatory processes.

Pharmacogenomics and Implications for Nursing Practice (Review)

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Introduction: This article aims to introduce the nurse to pharmacogenomics and its implications for clinical practice with regard to drug therapy.

Methods: Reviewed literature, websites, and professional guidelines related to pharmacogenomics and nursing practice were reviewed.

Results: This information is now being translated into practice with regard to the patient's genetic profile and the impact on drug therapy, which is pharmacogenomics.

Conclusion: The utilization of the patient genetic-genomic profile is beginning to have an impact on patient drug therapy in clinical practice.

Keywords: advanced practice nursing; genomics; Pharmacogenetic nursing

Phylogenetic Analysis and Antimicrobial Resistance Profiles of Attaching and Effacing E. coli isolated from pet birds as a possible reservoir for human diarrheagenic E. coli (Research Paper)

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Introduction: Diarrhea in humans is caused by a wide variety of agents such as viruses, bacteria, and parasites. Among bacterial pathogens, Diarrheagenic Escherichia coli is one of the important causes of diarrhea. Escherichia coli (E. coli) is a gram-negative, rod-shaped, non-sporulating, and facultative anaerobic bacterium of the genus Escherichia and the family Enterobacteriaceae. Diarrheagenic strains of E. coli are divided into four main categories: 1) Enterotoxigenic E. coli (ETEC) that cause diarrhea due to enhanced intestinal secretion, 2) Enteroinvasive E. coli (EIEC) that invade intestinal cells and cause diarrhea like Shigella spp., 3) Enterohemorrhagic E. coli (EHEC) produce intestinal disease by intimate adherence to the intestinal epithelium and the development of SLT, and 4) Enteropathogenic E. coli (EPEC) are characterized by intimate adherence between the bacterium and intestinal epithelial cell membranes. Furthermore, Captive wildlife animals (such as birds) are highly susceptible to opportunistic diseases and they may be considered as a reservoir of pathogenic bacteria. Escherichia coli can be considered the most common opportunistic enterobacteria in captive animals and is associated with systemic disease in birds. The pathogenesis of enteritis by E. coli in birds is still unclear, but the presence of diarrheagenic strains may represent a public health risk. Shiga toxin-producing E. coli (STEC) and enteropathogenic E. coli (EPEC) represent two of at least six pathotypes of human diarrheagenic E. coli (EPEC, EHEC, ETEC, EAEC, EIEC, and DAEC) that affect birds and may be considered as zoonotic pathogens. E. coli strains (EHEC and EPEC) that cause characteristic attaching and effacing (A/E) lesions in the intestinal mucosa are classified as attaching and effacing E. coli (AEEC). Our study aimed to determine attaching and effacing E. coli, evaluate their antibiotic resistance, as well as investigate their phylogroups.

Methods: In total, 200 fecal samples were collected from pet birds (belonging to 22 different species and 5 orders) referred to the avian specialty unit of the faculty of veterinary medicine hospital, University of Tehran. UspA, eae, bfpA, stx1, and stx2 gene-specific primers were utilized in PCR techniques to identify AEEC. The agar disk diffusion and MIC techniques were used to

evaluate the recovered isolates' antibiotic susceptibility. Based on the Clermont phylotyping techniques, their phylogroups were examined.

Results: Nine of 26 (13%) isolated E. coli strains harbored the eae gene (three Cockatiel, two Mynah, two White-eared Bulbul, one Rose-ringed parakeet, and one Duck). The White-eared Bulbul had the highest percentage of isolated E. coli (60%), followed by Duck (37.5%), Canary (20%), Mynah and Rose-ringed parakeet (18.2%), Budgerigar (14.2%), African Grey Parrot and Lovebirds (12.5%), and Cockatiel (10.1%). None of the eae positive samples carried the bfpA gene, but five samples had both stx1 and stx2, and four samples had stx2. So, all AEEC isolates were classified as STEC based on the absence of the bfpA gene and the presence of stx1 and/or stx2 genes. All but two (duck and cockatiel) of the AEEC isolated strain phylogroups were identified by Clermont et al.'s (2019) upgraded phylogroup approach. Four B2 (Cockatiel, Mynah, Rose-ringed parakeet, and White-eared bulbul), and three D phylogroups (Cockatiel, Mynah, and White-eared bulbul) were identified. Our findings indicated that seven of the nine AEEC discovered strains exhibited multi-drug resistance (MDR).

Conclusion: Shiga-toxin-producing E. coli is one of the most significant diarrheagenic E. coli with zoonotic potential, and it should be regarded as a serious concern for the public's health. In addition to the isolation of these strains from companion birds (4.5%), as a popular pet in our country, the significant isolation of STEC from patients suffering from gastroenteritis indicates the importance of paying more attention to this agent as a risk to public health, particularly children and those people who suffer from immunosuppression diseases. Furthermore, the high rate of resistance to a wide range of antibiotics used in human medicine establishes AEEC as a considerable public health threat.

Keywords: Attaching and Effacing E. Coli, E. coli, Phylogrouping, Shiga toxin, STEC

Phylogeny of metalloproteases form Hemiscorpius lepturus scorpion venom (Research Paper)

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Introduction: Hemiscorpius lepturus is a dangerous scorpion and referred to health concern issue in Khuzestan, Iran. The venom of H.lepturus is cytotoxic and its effect is similar to spider Loxosceles reclusa. Metalloproteinases are the important class of enzymes in the venom that has hemorrhagic activity. The early fi nding suggests the existence of metalloproteases in the transcriptome of venom gland of H.lepturus.

Methods: Phylogenetic analysis was accomplished to reveal the evolutionary relationship of identifi ed metalloproteases. The phylogenetic tree was constructed by Molecular Evolutionary Genetics Analysis software and neighbor-joining method.

Results: Results showed among three sequences, two metalloproteinases named HLMP1 and HLMP3 of H.lepturus were most close to spider P. tepidariorum. The third sequence named HLMP2 was different and formed an independent clade in the phylogenetic tree.

Conclusion: The results suggest that the sequence of metalloproteases in the venom component of H.lepturus is similar to the spider than the scorpion.

Keywords: Phylogeny; metalloproteases; Hemiscorpius lepturus

Physical activity, obesity and cancer mechanisms (Review)

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Introduction: Obesity is a major risk factor for developing cancer. The number of cancers caused by obesity is estimated at 20% with the increase risk that malignancies are influenced by diet, weight change and body fat distribution as well as physical activity. These results are alarming, as the world experiences a pandemic of obesity and, therefore, insulin resistance. Obesity can increase the risk of various types of cancer through several mechanisms, including increased sex and metabolic hormones and inflammation. Despite this knowledge, knowledge of the existence of these associations remains limited. The purpose of this review article was to summarize the epidemiological evidence related to the contribution of physical activity, sedentary behavior and obesity to cancer etiology and to provide insight into the biological mechanisms that may mediate between these factors and cancer incidence.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Physical activity, obesity and cancer mechanisms, a total of 17 articles were analyzed.

Results: Strong and consistent evidence exists that higher levels of physical activity reduce the risk of six different tumor sites (bladder, breast, colon, endometrium, esophageal adenocarcinoma, gastric cardia), while moderate evidence inversely associates physical activity with lung, ovarian, pancreatic and kidney cancer and limited evidence inversely correlates physical activity with prostate cancer. Sedentary behavior independent of physical activity has been shown to increase the risk of colon, endometrial and lung cancer. Obesity is a consistent risk factor for 13 different tumor sites (endometrial, postmenopausal breast, colorectal, esophagus, kidney/kidney, meningioma,

pancreas, gastric cardia, liver, multiple myeloma, ovary, gallbladder, and thyroid).The association between obesity and increased cancer risk is mainly due to anthropometric parameters and lifestyle factors that activate different biological mechanisms. The anthropometric parameters are BMI, weight gain and the amount of body fat, especially visceral. Lifestyle factors include sedentary habits and dietary parameters, such as a high-calorie and/or low-quality diet. The most important biological mechanisms that mediate the adverse influence of the above factors are hyperinsulinemia and insulin resistance, the activities of IGFs and IGF binding proteins, sex hormones and SHBG, general and adipose tissue low-grade inflammation, changes in adipose tissue production of adipokines and vascular growth factors, oxidative stress, endocrine disruptors, and alterations in immune function. We still don't have clear scientific evidence that avoiding or gaining weight significantly reduces cancer risk.

Conclusion: In conclusion, physical inactivity and obesity independently increase the risk of multiple cancers, and some evidence that sedentary behavior has a similar effect. High BMI is a main risk factor that continues to increase in prevalence, even in developing countries. Increases in urbanization, sedentary jobs, and leisure-time spent at the computer or watching television have further led to inactive lifestyles and increase the risk of multiple noncommunicable diseases. Knowledge resulting from this research may be used to identify an obesity phenotype that is particularly strongly associated with cancer risk, and thus pave the way for targeted prevention of cancer morbidity and mortality. Additional research is needed to increase the depth and scope of knowledge pertaining to these associations.

Keywords: Metabolism; Obesity; Physical activity

Physicochemical stability of reconstituted trastuzumab under freeze-thaw stress (Research Paper)

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Introduction: Trastuzumab is a recombinant humanized immunoglobulin G1 monoclonal antibody that is directed against human epidermal growthfactor receptor 2. Its action against CD20 leads to the death of CD20-positive cells, which is a desirable outcome. Because of the proteic nature of its structure, trastuzumab is vulnerable to a wide variety of chemical and physical degradation processes when subjected to a variety of various kinds of stress.

Methods: In this study, the stability of reconstitued trastuzumab was investigated when subjected to a number of different freeze-thaw cycles using a variety of orthogonal techniques, such as cation-exchange chromatography, size exclusion chromatography, attenuated total reflectance-Fourier infrared spectroscopy, and dynamic light scattering.

Results: According to the findings, reconstituted trastuzumab that had been kept in polyolefine bags remained stable after going through one cycle of freezing and thawing. There was no indication of either physical or chemical instability that was discovered. The hydrodynamic diameter of trastuzumab was found to be unaltered in the observations made. When compared to the profile of the control sample, the charge heterogeneity profile of the samples that were stressed did not change as a result of the freeze-thaw cycles. By using cation exchange chromatography, it was possible to determine that there was neither a new peak nor a reduction in the area under the curve. The protein's secondary structure did not undergo any changes as a result of the experiment.

Conclusion: In order to ensure the physicochemical stability of mAbs in addition to their biological stability, additional research is required to test the bioactivity of the stressed sample using an appropriate bioassay method. This is necessary in order to guarantee that mAbs will remain stable over time.

Keywords: stability, Therapeutic proteins, Monoclonal antibody, Trastuzumab, Freeze-thaw, Stress

Physiological Modulators Of Hematopoietic Stem/Progenitor Cells Mobilization (Review)

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Introduction: Peripheral blood hematopoietic stem and progenitor cells (HSPCs), are widely used for both autologous and allogeneic stem cell transplantation as a widely procedure to treat malignant and nonmalignant diseases of the blood and bone marrow (BM). HSPC mobilization involves a multifaceted and complex interaction of HSPCs and stromal and hematopoietic niche cells, as well as an array of proinflammatory cytokines (such as granulocyte colony-stimulating factor(G-CSF), TNFα, IFNα, IL-1, IL-6), chemokines, and small molecules. In addition, BM contains various types of hematopoietic cells (such as neutrophils, macrophages, osteoclasts, and red blood cells) and non-hematopoietic cells (including MSCs, ECs, and osteoprogenitors) that contribute to HSPC mobilization. There is a complex interaction between hematopoietic and non-hematopoietic compartments in BM, which leads to the maintenance and support of HSCs in the BM niche through chemokines and adhesion molecules, such as CXCL12 and SCF.

Methods: Agents such as G-CSF, granulocyte-macrophage colony-stimulating factor (GM-CSF), SCF, and AMD3100 have been approved for HSPC mobilization in the clinical setting, as well as other agents, such as inhibitors of IL-8, FL, VCAM-1/VLA-4, S1P agonists , and Hyperbaric oxygen therapy have been tested mainly in experimental animal studies. Over the past two decades, the use of HSPCs mobilized with G-CSF has increased and has largely replaced BM as a source of stem cells for transplantation, and the development of this method facilitates transplantation. Although the administration of G-CSF to It is generally safe and serious side effects are rare, but it also has limitations, including the necessity for prolonged parenteral administration and suboptimal efficiency in certain groups of patients.

Results: Identifying methods that can collectively affect the many mechanisms underlying HSPC mobilization may lead to significant improvements in HSPC mobilization methods and subsequent transplantation outcomes. Ideally, collective HSPC-stimulating agents can be titrated to the required dose of peripheral blood HSPCs, have an excellent safety profile, can be administered as a single dose, and are inexpensive.

Conclusion: All in all, as presented, there are wide variety of mobilization inducers with different potencies that can provide the stem cells needed for bone marrow transplantation.

Keywords: HSPCs, G-CSF, HSPC Mobilization, Stem cell transplantation

Positron Emission Tomography in nuclear cardiology and detection of coronary artery disease (Review)

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Introduction: Early detection and treatment of coronary artery disease (CAD) remain paramount, given its morbidity, mortality, and economic consequences. Over the past few years, we have witnessed a rapid evolution of PET instrumentation, which now offers higher sensitivity and hybrid scanners integrating PET and computed tomography (CT). Hybrid PET-CT scanners account for approximately 80% of the new PET units installed.

Methods: Different terms explored in PubMed and Google Scholar databases: Nuclear cardiology, Coronary artery, and Positron Emission Tomography. The obtained results were selected for the title and abstracts. Finally, 21 relevant papers were selected and reviewed in full text.

Results: Experience with radionuclide assessments of myocardial perfusion can be measured over decades. Single-photon emission computed tomography (SPECT) myocardial perfusion scintigraphy (MPS) has been validated for the diagnosis and prognosis of cardiac disease, and the technique is embedded in national and international guidelines. Positron emission tomography (PET) has been used to assess myocardial viability, but it is now used increasingly to detect flow limiting CAD. Although previously used mainly to assess myocardial viability, PET is now more commonly used to assess myocardial perfusion, and it is generally considered the non-invasive gold standard for this. Although cyclotron-produced radiotracers, such as N-ammonia or O-water, are regularly used, recent efforts have also focused on the use of rubidium-82. This tracer is produced by a generator, compares favorably with other PET tracers for myocardial perfusion and perfusion reserve measurements, and is an attractive option for hospitals without easy access to a cyclotron. PET offers higher resolution images and provides quantification of perfusion in absolute terms (ml/g/min). PET may have better sensitivity and specificity than SPECT MPS for detecting CAD, particularly where there is a severe multi-vessel disease and in obese patients. Two meta-analyses with PET demonstrated 90–93% sensitivity and 81–88% specificity for CAD detection, superior to myocardial perfusion SPECT.

Conclusion: Myocardial perfusion in absolute units measured by PET further improves diagnostic accuracy, especially in patients with multi-vessel disease, and can be used to monitor the effects of various therapies. The method also has significant prognostic value. Despite the demonstration of cost-effectiveness in high-throughput centers, the clinical utility of PET is still constrained by high upfront cost and low availability compared with SPECT.

Keywords: Nuclear cardiology, Coronary artery, Positron Emission Tomography

Post-irradiation induces abscopal effect, how does it occur? (Review)

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Introduction: For more than a century, radiotherapy has been utilized to treat local tumors. Radiation therapy(RT) breaks the DNA and causes cancer cells to die. Radiotherapy often affects uses to Impact the proliferation of tumors at the targeted spot. Nevertheless, there have been instances of cell death outside of the targeted areas. The ability of concentrated radiation to trigger an anticancer response across the body at locations that were not exposed to directed RT is known as the abscopal effect. This phenomenon was introduced by R.H.Mole in the early 1950s. The exact mechanisms of the abscopal effect are not fully understood. The goal of this article is to shed light on possible mechanisms and pave the path for future research (1, 2).

Methods: To conduct this review, we searched Pubmed, Scopus, and Google scholar databases using the keyword "Abscopal effect" AND" Radiotherapy" and selected the latest related articles.

Results: Historically, RT was thought to suppress the immune system because lymphocytes are some of the radiosensitive cells. Although, several pre-clinical and clinical research backs the idea that the immune system is involved in the spontaneous shrinkage of tumors beyond the irradiated region. Pre-clinical experiments have now demonstrated that RT can improve MHC class I levels and the antigen-processing and presentation pathway.MHC class I is involved in the activation of CD8+ T cells, which are the most important tumor-killing cells. Apparently, RT's abscopal effects depend on CD8+ T cells. It has been shown that radiotherapy can cause DNA damage in almost two ways:1- direct DNA break which is due to the high energy electrons and 2-development of free radicals that can result in indirect DNA damage. The most fatal kind of DNA damage is double-strand breaks (DSBs), which are brought on by RT. DSBs can reveal double-stranded DNA (dsDNA) to the cytoplasmic dsDNA sensor cyclic GMP-AMP synthase (cGAS) which in

turn, cGAS induces type I interferon production by the downstream stimulator of IFN genes (STING). Type I IFN released by irradiated cells is necessary for RT to elicit the abscopal effect effectively. According to recent investigations, particular types of programmed cell death, like necroptosis and immunogenic cell death (ICD), are induced by RT. Both ICD and necroptosis can lead to the release of damage-associated molecular patterns (DAMPs) from irradiated cells. DAMPs such as HMGB1, HSP, membrane-exposed calreticulin, and glucose-regulated protein 96(GP96) can enhance antigen presentation by dendritic cells and induce phagocytosis of tumor cells. These events cause the maturation of dendritic cells and lead to boosted T CD8+ cell-mediated tumor lysis. The adaptive anti-tumor immune response can function both independently and in conjunction with the innate immune system. For instance, human neutrophils can secret neutrophil elastase to particularly kill tumor cells (3, 4). It is believed that mechanisms through which RT improves ICI are either or both proliferation and differentiation of naive T cells or the revitalization of exhausted intra-tumoral CD8+ T cells. Nowadays, monoclonal antibodies (mAb) that stimulate the immune system have already been coupled with RT and, in some cases, had an abscopal effect (4).

Conclusion: As mentioned above, both RT alone and RT in combination with immunostimulatory monoclonal antibodies (such as anti-CTLA-4 mAb, and anti-PD-1 mAb) generated an abscopal effect. Pre-clinical research demonstrates that in a range of animal models, ICI compounds, and RT changes lead to a range of responses. The best radiation dosage to elicit the abscopal effect has generated debate; some support single, ablative radiation doses, while others advocate for fractionation plans. Barsoumian et al. showed that the RadScopal methodology, which combines high-dose and low-dose radiation therapy with immunotherapy, can be used to produce the abscopal effect. In this technique high-dose RT is administered to primary tumors to kill cancerous cells, reveal neoantigens, and stimulate T lymphocytes, while delivering low-dose RT to secondary tumors modifies the tumor stroma by inhibiting TGF-ß, allowing the infiltration and growth of effector T cells and natural killer cells. However, the abscopal effect is not just limited to RT.especialy in renal cancer, the abscopal effect has been seen after surgical resection of the primary tumor. Although the main reason for this is not fully understood, the possible reasons are that Surgery to remove the primary tumor lowers the tumor burden and makes it possible for the immune system to successfully remove any leftover cells or Surgery may systemically expose tumor antigens, exposing T lymphocytes to the appropriate antigen repertoire. Despite the promising results obtained from the studies, the abscopal effect is a complex and unpredictable phenomenon, and more research is needed to fully understand the mechanisms involved in this phenomenon (1-4).

Keywords: abscopal effect – radiation therapy - immunotherapy – immune response

potential inhibitory effect of lycopene on prostate cancer (Review)

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Introduction: Prostate cancer (PCa) is one of the most common urological malignancies in adult men. There are several risk factors such as genetics and environment for PCa. Nutrition plays an important role in causing cancer. Lycopene is a bright red carotenoid hydrocarbon found in red vegetables (such as red carrots), some fruits (such as tomatoes). In addition, dietary lycopene was associated with a reduced risk of PCa. Therefore, the important role of lycopene has made it necessary to develop it as a therapeutic agent for PCa. There is still no conclusive evidence to support an anti-cancer effect. The aim of this research is to investigate the potential effect of lycopene on prostate cancer

Methods: In this systematic review, we collected the data we needed by using keywords and also by referring to reliable databases such as PubMed, Scopus, google scholar and ProQuest. The statistical population of this study includes all studies conducted until 2022 after reviewing relevant findings and evaluating data quality, we analyzed 15 articles

Results: Most studies have shown that lycopene inhibits cell proliferation, stops the cell cycle at different stages, and increases apoptosis in human PCa cell lines. Several studies have shown that lycopene have no significant effect on PSA levels. Due to the limited number of available studies, there is heterogeneity regarding the source and dose of lycopene, participants' health status, baseline PSA, and circulating lycopene. Some studies have shown that consumption of canned and cooked tomato-based products is inversely associated with prostate cancer risk, but the association between prostate cancer risk and raw tomatoes, were not statistically significant.

Conclusion: In conclusion, the present study supports the suggestion that lycopene extracted from food products may have a protective effect on PCa.

These findings further support current dietary recommendations to increase intake of dietary sources of lycopene to reduce prostate cancer risk

Keywords: lycopene, prostate, Prostatic Neoplasms

Predicting metastasis of cancer by complex systems and artificial neural networks (Research Paper)

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Introduction: Accurately understanding the stages of cancer progression has a great impact on choosing the treatment method and the possibility of the patient's recovery, and predicting the time of metastasis is one of the most important factors in choosing the treatment method. In this research, using the periodic tests database of more than 5000 patients with colon and liver cancer, we have investigated the relationships between the results of these tests by using the machine learning method and optimizing the learning algorithm by using complex systems. In this method, we used image processing and linear regression to analyze the results of the patient's medical images and statistically analyzed the results of biochemical tests. The result of this work was the correct prediction of the start of metastasis with a rate of 53% among 50 test samples. It should be noted that the result of our prediction estimated a period of 38 days

Methods: Our method for the analysis of medical images (MRI) was to use image processing using regression and combining supervised learning methods and modifying the neural network using the equations obtained in the data analysis by unsupervised learning method. Also, the results of biochemistry experiments were done by statistical analysis method using unsupervised learning and network optimization using Lotka-Volterra equation.

Results: By using a neural network trained to check the information of periodical tests and MRI images of 50 patients whose test results and the date of the beginning of metastasis were known in the patient records, we successfully predicted the time of the beginning of metastasis with 54% success. Then with optimal Creating the algorithm and using Lotka-Volterra equation, we re-examined these patients, and the prediction results were successful up to 76%.

Conclusion: The use of statistical data, image processing and the combination of machine learning methods along with optimization using Lotka-Volterra equation can help predict the metastasis time of new patients from the records of previous patients. As the number of data increases, our artificial neural network can improve and train itself with higher accuracy and help predict the time of metastasis with much higher accuracy. In this case, the doctor can choose a more appropriate treatment method using the

resulting information. Also, our investigations show that by using this artificial neural network, it is possible to predict the possibility of cancer in susceptible patients.

Keywords: Artificial neural network, cancer, predicting the start of metastasis, complex systems

Prediction of miRNAs Targeting KIF11, a Probable Therapeutic Approach in Treatment of Breast Cancer (Research Paper)

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Introduction: By expanding the range of information in biological fields, bioinformatics tools provide researchers with the possibility of using and analyzing data easily. Today, the use of bioinformatics tools has significantly reduced the time and cost of molecular studies in the field of diseases. MicroRNAs (miRNAs) are a relatively new class of functional small RNAs with diverse functions that have attracted the attention of many researchers in recent years. These small RNAs play a role in many metabolic and signaling pathways, and we see their dysregulation in many diseases including cancer. therefore, the study of these RNAs will be beneficial in finding treatment methods. It has been previously reported that KIF11 (Kinesin Family Member 11) is upregulated in breast cancer and is related to increased cell viability and proliferation, colony formation, migration and invasion; As a result, KIF11 as an Oncogene plays a key role in promoting breast cancer, hence new therapeutic pathways can be found by identifying its regulatory network through miRNAs.

Methods: Using the GENE section in the NCBI database, the number of nucleotides in the 3'UTR region of KIF11 was determined. Afterward, in the nucleotide section of the same database, the sequence of KIF11 was obtained in FASTA format and its 3' UTR region was highlighted on the sequence. 72 miRNAs that interact with KIF11 were predicted using miRTargetLink 2.0 database. The sequence of these miRNAs was obtained from the miRbase database. With the help of RNAHybrid, the interaction of each of the predicted miRNAs and the 3'UTR of KIF11 was analyzed bioinformatically. Eventually, Diana miRpathv3 was used to study metabolic and signaling pathways related to these miRNAs.

Results: After data analysis, among the 72 predicted miRNAs related to KIF11, all of which were analyzed by RNAHybrid, 7 miRNAs that showed a stronger relationship with KIF11 were selected; These 7 miRNAs are hsa-miR-432-5p, hsa-miR-296-3p, hsa-miR-145-5p, hsa-miR-1237-3p, hsa-miR-154-5p, hsa- miR-659-3p and hsa-miR-122-5p respectively. The data obtained from Diana miRpath show a strong relationship between hsa-miR-154-5p, hsa-miR-432-5p, hsa-miR-145-5p , hsa-miR-122-5p and ECM-receptor interaction pathways. Also, the heatmap designed by Diana tool showed that hsa-miR-296-3p, hsa-miR-145-5p, hsa-miR-432-5p and hsa-miR-122-5p are involved in transcriptional mis-regulation in cancer.

Conclusion: Considering the oncogenic role of KIF11 in progression and development of breast cancer and its upregulation in this disease that disrupts the natural balance of cell viability, proliferation, colony formation, migration and invasion, the reduction of its expression due to the overexpression of any of listed miRNAs above can inhibit the proliferation of breast cancer cells and as a result can be used as a new therapeutic approach in treatment of breast cancer.

Keywords: KIF11 , Breast cancer , miRNA , Bioinformatic analysis, microRNA

Prenatal screening tests for chromosomal abnormalities (Review)

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Introduction: The health of the fetus is the main concern of all parents, and chromosomal abnormality in the fetus is one of the main causes of stillbirths and the birth of infants with abnormalities. Since it is possible for every pregnant woman to give birth to a child with birth defects, performing screening tests before birth makes it possible to be aware of chromosomal health. Over the past years, different methods and procedures have been used to identify the chromosomal status of the fetus before birth. These procedures are divided into two groups: invasive and non-invasive. Amniocentesis and chorionic villus sampling (CVS) are invasive procedures, while non-invasive methods include ultrasound, first-trimester screening, second-trimester screening, and non-invasive prenatal testing (NIPT). In ultrasound, performed between weeks 11 and 14 of pregnancy, factors such as nuchal translucency (NT), crown-rump length (CRL), and the presence or absence of a nasal septum are of paramount importance. Typically, the screening of the first trimester of pregnancy is performed between weeks 11 and 13 of pregnancy. The free beta-human chorionic gonadotropin (β-hCG) and pregnancy-associated plasma protein A (PAPP-A), which are produced during pregnancy, are measured in the blood. Finally, through NT ultrasound information and other important factors such as mother's age, diabetes, other children's history of chromosomal abnormalities, twin pregnancy, and smoking, a numerical risk is obtained based on which, we can decide for the next step. In the screening of the second trimester, which is best performed between weeks 15 and 18 of pregnancy, the levels of four substances of alpha-fetoprotein (AFP), unconjugated oestriol (UE3), inhibin-A, and β-HCG are measured in the blood, and combined with the factors mentioned in the first trimester, the risk of chromosomal abnormalities is obtained. NIPT, also known as cell-free DNA, can be performed from 10 weeks of pregnancy. In this test, which is performed on the mother's blood, parts of the fetal DNA that entered the mother's blood circulation from the placenta are examined. NIPT test has higher sensitivity and specificity in detecting trisomies compared to other pregnancy screening tests. Non-invasiveness and quick response are other advantages of this test, leading to the growing use of this test around the world. However, it also has some drawbacks, causing NIPT not to be still considered as a diagnostic test, and if its results turn out to be positive, administrating such diagnostic tests as aminosynthesis and CVS will be necessary to confirm it. One drawback of NIPT is that it is possible that the DNA circulating in the mother's blood develops from the placenta and not from the fetus, and the chromosomal abnormality is related to the placenta

that does not affect the fetus. Further, it is also likely to get false positive or negative results where the mother has a tumor, has a low fetal fraction in the blood, is pregnant with multiples (more than twins), and is overweight.

Methods: this article is a literature review

Results: To get information regarding the chromosomal status of the fetus, non-invasive tests such as first-trimester screening, second-trimester screening, or NIPT are used. Among these, NIPT has the highest sensitivity and specificity, but it is not considered a diagnostic test due to due to its limitations. Amniocentesis and CVS are accurate prenatal diagnostic tests, which are invasive and carry the risk of miscarriage.

Conclusion: Performing aminosynthesis and CVS tests requires sufficient experience and high expertise in this field. The growing use of NIPT in many countries has reduced the need to use invasive tests (e.g., aminosynthesis and CVS), leading to a decrease in the number of experienced specialists performing diagnostic tests. Therefore, researchers are trying to overcome the disadvantages of the NIPT test by expanding the science and technology so that it can be applied as a non-invasive diagnostic test in the future.

Keywords: prenatal screening, prenatal diagnosis, aneuploidy

Preparation and antibacterial evaluation of chitosan hydrogel containing crocin for wound dressing application (Research Paper)

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Introduction: Hydrogels with biomimetic characteristics and minimal invasiveness have been proposed for tissue regeneration and the wound healing, they can provide good oxygen permeability, a moist wound site and absorb excess tissue exudate which facilitate the release of bioactive factors under controlled conditions. Among biopolymers chitosan derivatives have attracted great interest due to their potent wound healing properties including biodegradable, antimicrobial, and biological activity effect. Aim: The purpose of this study was to design a chitosan hydrogel contain crocin as an antioxidant agent and investigate its potent wound healing properties.

Methods: The prepared hydrogels were characterized by visual examination and scanning electron microscopy (SEM) and FTIR. Also the physical properties including porosity, swelling, WVTR, density, and mass loss were examined. In vitro cell proliferation, cell viability and cell migration potential of the synthesized hydrogels were analyzed by MTT assay and wound healing scratch assay respectively in L292 cell line

Results: The results showed that the prepared hydrogel has appropriate physical and structural properties such as porous structure, high water absorption and provided suitable conditions for cell adhesion, migration, and proliferation. Also, rigidity and stability seemed proper to wound healing. But hydrogels revealed no antibacterial activity.

Conclusion: hydrogel systems are promising wound dressing because of their ability to combinations with various natural materials and drugs for therapeutic purposes. This study suggested a hydrogel structure for wound healing dressing application in future.

Keywords: hydrogel, chitosan, crocin, wound healing

Prevalence Of Acute Depression Of Pregnancy Before And During The Covid-19 Pandemic (Review)

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Introduction: Depression is the most common psychiatric disorder during pregnancy and even after pregnancy. With the emergence of COVID-19 pandemic, the mental health status of the whole society has been thought to be threatened due to COVID-19 associated changes in daily life and even biological effects of the disease itself. In this study, we aimed at reviewing the trends of the pregnancy depression before and after the COVID-19 pandemic.

Methods: This was a narrative review study that quarried literature for pregnancy depression before COVID-19 pandemic in studies published on data before 2020 and compared those with studies during the pandemic.

Results: Research has indicated that depression spiked during the Corona epidemic and quarantine and that this was impacted by a multitude of reasons. Now, in addition to pregnancy raising the risk of depression, the COVID-19 pandemic from late 2019 has raised the risk of depression. According to research, those who had a history of mental illness before the pandemic era experienced worsening symptoms during the epidemic. The fear of sickness, the death of loved ones, and the virus's influence on the neurological system were the main concerns of individuals during this era.

Conclusion: In addition to more research on the problem, strategic plans to control and screen pregnant women should be developed. Because the signs of depression may not be visible, and COVID-19 may decrease the visits and screenings for this mental condition before and during the pregnancy.

Keywords: COVID-19, SARS-Cov-2, pandemic, pregnancy, pregnancy depression.

Prevalence of latent hepatitis B infection transmission among hemodialysis patients in Mashhad in 2022 (Review)

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Introduction: Hepatitis viruses cause liver involvement and inflammation. Currently, six types of viruses are known as hepatitis viruses (A, B, C, D, E, G), only five of which cause hepatitis. Hepatitis B virus infection is a major public health problem worldwide. Approximately 30% of the world's population shows serological evidence of current infection. Hepatitis B virus is a partially double-stranded DNA virus with several serological markers. The virus is transmitted through contact with infected blood and semen. A safe and effective vaccine has been available since 1981, and although variable, the implementation of universal vaccination in infants has led to a sharp decline in prevalence. Overall, 40% of men and 15% of women with perinatal acquired hepatitis B virus infection will die of cirrhosis or liver cancer. A study has shown that low anti-HBs neutralization capacity may be ineffective when a high viral load prevails. Anti-HBc blood units appear relatively infectious without detectable anti-HBs, except in immunodeficiency receptors. Elderly people with immunodeficiency and patients receiving immunosuppressive therapies may be less susceptible to infection at lower doses, even in the presence of anti-HBs. Extensive blood transfusions have also been used in various clinical settings, and some extensive transfusion protocols improve patient outcomes. This study aimed to determine the prevalence of latent hepatitis B infection transmission among hemodialysis patients in Mashhad in 2022.

Methods: This is a secondary study with a narrative approach, in 2022 by searching for keywords such as Hemodialysis, Infestations, Hepatitis B, Virus Infection, and Serologic in Mesh and reputable databases such as Science Direct, PubMed, And the Web of Science was conducted, and finally, 15 articles were found, of which 10 articles were included in the study.

Results: According to the studies obtained from the articles, the results show that hepatitis B virus (HBV) is still a major risk for infection is transmitted through blood transfusions. OBIs carrying detectable anti-HBs (approximately 50%) are essentially non-infectious by injection. Recent data, however, indicate that OBI is an undetectable status of serum hepatitis B surface

antigen (HBsAg) but that serum and/or intrahepatic hepatitis B virus (HBV) DNA are detectable. OBI may be due to acute self-limiting hepatitis, or in patients with chronic hepatitis B who have acquired HBsAg serocirculence, who lose the ability to detect serum HBsAg with or without antibodies to HBsAg (anti-HBs) in Refers to chronic hepatitis B (CHB). Clinical consequences of OBI include cirrhosis and HCC, liver transplantation, blood transfusion, hemodialysis, and more.

Conclusion: OBI is the most common cause of hepatitis B following blood transfusions in India. Remaining high, in addition to RR, the prevalence of latent HBV or anti-HBc infection also indicates a risk of HBV infection in donated blood.

Keywords: Hemodialysis, Infestations, Hepatitis B, Virus Infection and Serologic

Prevalence of SARS-CoV-2 in sport clubs in 2021, Tehran, Iran

(Research Paper)

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Introduction: Acute respiratory tract infections (ARTIs) are infectious diseases caused by various pathogens such as bacteria. however, more than 80% of ARTIs are due to viruses (1). In most cases, it starts in the nose, trachea, and lungs. ARTIs account for more than75% of all acute morbidities in developed countries (2). Upper respiratory tract infections (URTIs) and lower respiratory tract infections (LRTIs) are two types of acute respiratory tract infections (ARTIs). The upper respiratory tract consists of the nose, larynx, paranasal sinuses, and middle ear. Nasopharyngitis, laryngitis, and pharyngotonsillitis (3). Several respiratory viruses have been responsible for URITs, for instance, Rhinoviruses, Human coronaviruses, Adenoviruses, Parainfluenza viruses, Human metapneumo viruses, and Influenza viruses are the most common viruses causing URTIs (4). Besides, Respiratory syncytial virus, Influenza A and B, Parainfluenza 1, 2, 3, and Adenovirus have been identified as common viruses for LRTIs in numerous investigations (1). Coronaviruses are a group of viruses belonging to the Coronaviridae, which are divided into four genera including α-CoV, β-CoV, δ-CoV, and γ-CoV. moreover, it has 22 subclasses, and 40 species (5). Among these species of the coronavirus, seven species have been identified that have been transmitted to humans and can cause a variety of colds in humans. hCOV-2229E, hCOVOC43, hCOV-NL63, and hCOV-HKU1 are responsible for pneumonia in children and adults (6). However, SARS, MERS, and SARS-CoV-2 are other types of coronaviruses with more severe symptoms such as fever, dry cough, sore throat, and respiratory problems (7). COVID-19 is caused by SARS-CoV-2 (Severe Acute respiratory syndrome coronavirus-2) which belongs to β-CoV. In this genera, viruses are enveloped with a single-stranded RNA genome (8). COVID-19 has come to be the most threatening

issue to all populations around the world. According to the United Nation as of April 28, 2022, over 512 million verified cases and over 6 million deaths have been reported worldwide (9). well known that different kinds of exercises including indoor and outdoor conditioning are essential for health (10). Exercise has been found to maintain physical processes namely, respiratory, circulatory, muscular, neurological, and cadaverous systems. Regular training performs a fundamental role in the forestallment and administration of cardiovascular and metabolic health conditions (11,12). During this epidemic, several scientific studies have been done to find out whether it's safe to go back to the health clubs. Due to athletes high commuting and the kinds of activities that take place there, fitness installations have been linked as a high threat for acquiring COVID-19. Various threat factors including, the average amount of time spent in the fitness club, the viral load of an infected person, and ventilation, play a part in viral transmission in fitness centers. According to the review and meta-analysis ‘has been published in the Sports Medicine journal, exercises strengthen the first line of protection of the immune system and contribution to related cells. The U.S. Centers for Disease Control and Prevention and WHO instructions would be essential for the protection against COVID-19 spread among individuals who attend gymnasiums and fitness clubs. A well-maintained and operating system, adding the rate of air change, having a mask, maintaining social distancing exceeding two meters, ventilation and filtration to adulterate contagion aerosols, hygiene, including handwashing, which removes the chance for direct and circular transmission and washing bottoms and shells are important actions during the epidemic (13). Therefore, we tried to study the prevalence of COVID-19 among athletes in sport clubs in Tehran, Iran. We looked at 124 cases from 3 age groups, the 58 (47%) cases aged between 18 – 25, 30 (52%) were female and 28 (48%) were male. 46 (37%) cases aged 25 – 50, consisting 20 (43%) female, 26 (56%) male and 20 (16%) cases were over 50 years old,7 (35%) were female and 13 (65%) were male. In each case, nasal swab samples were taken. The High Pure Viral Nucleic Acid ROJE kit was used to extract ribonucleic acid (RNA). Real-time PCR was used to identify SARS-CoV-2 RNA. Among all cases, 6 (10%) of SARS-CoV-2 positive cases were between 18 – 25 years old, consisting of 5 (83%) males and 1 (17%) females. 3 (6%) were between 25 – 50 years old which 2 (67%) cases were male and 1 (33%) case was female and finally, 2 (10%) positive cases were male and over 50 years old. Cough, sneezing, and rhinorrhea were the most common clinical symptoms of cases.

Methods: This study evaluated the possible existence of SARS-CoV-2 infection in 124 throat and nasal swab samples using Real-time PCR. All samples were collected from patients with respiratory symptoms in sport clubs, Tehran, Iran.

Results: From 124 people selected as the study sample, 11 samples (8.87%) tested positive using Real-time PCR. The results of the sample testify to the positive effect of sports clubs on the prevalence of SARS-CoV-2.

Conclusion: This study was performed to Investigate the risk of transmission in society among symptomatic athletes. Our study showed that SARS-CoV-2 can spread easily in society by this group of patients and all sport clubs should measure PCR negative results mandatory for entry into these sports clubs.

Keywords: Respiratory Tract Infection , SARS-COV-2 , ARIs , Prevalence , COVID-19

Preventing the progression of spinal muscular atrophy in children and adults with gene therapy and herbal extracts (Review)

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1.

Introduction: Spinal muscular atrophy (SMA) is a rare neuromuscular disorder that results in the loss of motor neurons and progressive muscle wasting.It is usually diagnosed in infancy or early childhood and if left untreated it is the most common genetic cause of infant deathIt may also appear later in life and then have a milder course of the disease. The common feature is progressive weakness of voluntary muscles, with arm, leg and respiratory muscles being affected first. Associated problems may include poor head control, difficulties swallowing, scoliosis, and joint contractures. In the treatment method for people with the disease (children and adults), we use gene therapy and extracts of complementary medicinal plants that have a lot of protein to treat this disease. Among these plants, we can mention (spirulina algae, elderberry, hemp seed, walnut, Irish moss, whey protein, etc.). In this method, which is for children and adults, we use gene therapy, which is the main and basic method of this type of treatment, and its complementary method, which is the use of medicinal plant extracts. This extract of medicinal plants contains the protein gene related to smn1 protein.

Methods: This study is an interventional (experimental) clinical study that will be carried out in vivo and in genetics, pathology and biomolecular research laboratories. levels 1- Performing preliminary tests 2- Isolation of healthy smn1 gene from eukaryotic organisms (one patient or Drosophila) 3- Injection of healthy smn1 gene into the target tissue in the spinal canal 4- Using the treatment method (combination of complementary medicinal plant extracts) 5- Conducting tests to get the results and performance of motor neurons

Results: Medicinal plant extracts can compensate for the lack of this protein in the human body and can be used as an adjunct to gene therapy and also have a positive effect on gene therapy. Also, using this method for treatment will cost much less than other drugs and this method can be used to treat all ages.

Conclusion: By using this method, the progress of the disease in the patient will be stopped and it will not cause any side effects to the body. Also, this extract of medicinal plants is great for the proper functioning of the human body system and will prevent the symptoms of the disease.

Keywords: 1-Spinalmuscularatrophy 2-Motorneurons

Probiotics as alternatives to antibiotics, A Review (Review)

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Introduction: The use of antibiotics to control and prevent diseases requires very high costs every year, and their continuous use causes drug resistance. On the other hand, from the point of view of human health, the issue of drug residues in food products has also been raised, and there are reports of some diseases. Antibiotics are not the answer to their treatment, so creating bacterial competition use probiotics is a new strategy for health, prevention, and treatment of various gastrointestinal, urinary-genital, and skin infections in humans and animals. Also, nowadays, probiotics are suitable substitutes for antibiotics for Coping with pathogenic agents in humans and animals has been introduced and the popularity and use of probiotic products and medicines have become widespread. Another important problem is the transfer of antibiotic residues from animal meat to the human body, which are widely used to fight infectious agents and also as growth promoters in animal husbandry. The infections of different rivers, especially the establishment of different strains of salmonella in the human intestine, are not only caused by food contamination, but probably the exposure of livestock and poultry to antibiotics and finally, the consumption of their meat by humans also contributes to this. Therefore, it is necessary to use probiotics as a suitable alternative to antibiotics in the control of infectious and bacterial diseases in both humans and livestock. Also, probiotics can be used as improvers of food digestion and vitamin production, and they can be used as an alternative to growth-promoting antibiotics in livestock and poultry farming. This study aims to review the key role of probiotics as a suitable replacement for antibiotics in our fight against infectious disease.

Methods: This study is reviewing data accumulated from literature and prestigious case studies which are in connection with our subject.The search words were:" Probiotics," "Antibiotics," "Antibacterial," "effective effects of probiotics," using PubMed, Scopus, Science Direct and Google Scholar databases. Furthermore, manual searches of other relevant journals and keywords searches were performed. We have focused on published papers from 2010 to 2022.

Results: The role of probiotics in the prevention and treatment of infectious diseases and the strengthening of the body's immune system is of great importance, and this role has been proven in numerous studies, and it has been repeatedly emphasized that these microorganisms can be considered as a suitable alternative to antibiotics.

Conclusion: Several studies have been conducted on probiotics and their beneficial effects. Probiotics are one of the newest and most effective targeted products, which are used both as super-specialized food products and as targeted drugs in human and animal breeding, and as a suitable substitute for antibiotics and growth stimulants. Lactobacillus and bifidobacteria are the most important bacteria found in most fermented products and the digestive system, which were used in the form of foods such as yogurt and kefir since ancient times to treat some diseases and digestive disorders, and it is even believed that some of these foods Like kefir, they also cause longevity in humans. With these observations, we can understand the important role of these beneficial microorganisms in the prevention and treatment of infectious diseases and consider them as suitable substitutes for antibiotics, although this statement may be weak in some infectious diseases, but the role of these microorganisms should not be underestimated. It was neglected in strengthening the immune system and helping to cure many diseases. Despite the safety of consuming products containing this type of probiotics it should be given more attention and study so that the probiotic product that reaches consumption has a safety standard and then becomes available to the general consumers. another important problem is the transfer of antibiotic residues from animal meat to the human body, which are widely used to fight infectious agents and also as growth promoters in livestock breeding, which ultimately affects Excessive use causes antibiotic resistance in humans. Therefore, it is important to replace antibiotics with probiotics in livestock and poultry breeding.

Keywords: Probiotics, Antibiotics, Antimicrobial activity, Infectious diseases

Production of Herbal Nanosuspensions from Cynodon dactylon (L.) root by Rapid Expansion of Supercritical Solution into Aqueous Solutions (RESSAS) (Research Paper)

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Introduction: The present study sought to stabilize the nanosuspension of potent antioxidant such as Vitexin, Petunidin as well as Tricosane from the root related to Cynodon dactylon by utilizing the RESSAS process. These compounds include low efficacy and bioavailability since are rarely soluble in aqueous media. Thus, producing stable nanosuspensions can solve the related problem by decreasing the size of the particle. In addition, central composite design (CCD) was used for analyzing the impact of oven temperature, pressure, CO2 flow rate, and modifier volume on the antioxidant activity index (AAI) in the outcome of RESSAS process. Further, DLS, FE-SEM, and LC-MS techniques were implemented for evaluating the features of nanosuspension. Based on the results, the behavior of the particles after forming particle was emphasized, which indicated that the RESSAS process results in decreasing the agglomeration of the particle and enhancing AAI for the extract. Thus, the bioavailability of the products related to herbal medicinal can be dramatically increased in biological media.

Methods: Traditional herbal medicines have been extensively used all over the world as the oldest source of drugs and has attracted a lot of attention in today's medical practice. Most of the natural compounds used in plants consist of some forms of biological activities which are implemented to treat different diseases and can positively affect human health. In addition, during the last decades, the natural bioactive compounds have less been emphasized after the creation of molecular biology and combinatorial chemistry, which plays a role in discovering new drugs and structures. However, natural compounds and their role have been supported more as a formidable skeleton for producing drugs (Pollio et al., 2016). Further, some of the phyto-compounds and nutrients in foods are normally insoluble or include insignificant solubility in biological media. Therefore, a decrease occurs in using these kinds of drugs due to their poor solubility features, which results in creating a low bioavailability, along with its threshold concentration of toxicity which is approximately near the therapeutic dosage (Müller et al., 1999; Xu and Luo, 2014). In this respect, nanoparticles manufacture can be regarded as a good choice for increasing the dissolution rate of such bioactive compounds, along with their related bioavailability (Chai et al., 2020; Huang et al., 2010; Momenkiaei and Raofie, 2019). Nano dispersions formulation is considered as an appropriate method for solving the problems related to

bioavailability since an increase in the accessible surface areas can lead to an increase in the volume dissolution related to low soluble compounds available in water (Ahire et al., 2018; Merisko-Liversidge and Liversidge, 2008). Furthermore, the process of rapid expansion of supercritical carbon dioxide solution results in creating strong solvating force of the supercritical fluid (Eckert et al., 1996) and fragmenting the heat-sensitive compounds without producing any damage and creating particles less than 500 nm in diameter (Türk, 2009; Young et al., 2000). In addition, high rapidity of supersaturation leads to the speedy precipitation of the extracted substance as micro or nanoparticles because of reduction in pressure related to the expansion chamber (Karimi and Raofie, 2019; Pessi et al., 2016; Türk, 1999). The main challenging issue is related to the behavior of the particles after it is created based on nanoparticle reports. Nanoparticle may be improved through condensating, agglomerating, and coagulating in the period of residence in the collection vessel. However, it is worth noting that dispersing most of the systems again is approximately inoperative because theoretical framework of expanding supercritical solution process can predict the formation of primary particles with a diameter of smaller than 50 nanometers (Weber and Thies, 2007). Regarding water-insoluble substances, spraying RESSAS outcome straightly into an aqueous media encompassing a surfactant via heating the capillary jet is regarded as a satisfactory method for obtaining the fine particle (Sane and Thies, 2005; Uquiche and Martínez, 2016). RESSAS technique has been used in some studies in the pharmaceutical field and the results represented the preparation of successful submicron particle with stabilizing factors and various pharmaceutical compounds (Lee et al., 2018; Pathak et al., 2006; Sane and Limtrakul, 2009; Türk and Lietzow, 2004). Manipulation on particle size, size distribution, and possible polymorph can be achieved through altering the operating conditions in RESSAS process. Based on the results of the previous studies, an aqueous solution encompassing emulsifier at the expansion chamber avoids growing particle, coagulating, and agglomerating of the herbal extract (Liu et al., 2006; Ya-Ping et al., 2005).

Results: 3.1. Optimization of RESSAS process for the antioxidant activity In this study, pressure (A), oven temperature (B), modifier volume (C), and CO2 flow rate (D) were taken into consideration. In addition, a design by five levels (rotatable CCD, α = 1.68) was utilized for optimizing the factors playing a role in the antioxidant capacity of bioactive compounds in the Cynodon dactylon root. Based on the results, DPPH tests represented a decrease in intensity of absorption at 517 nm in the visible region to measure the AAI related to the extracted Cynodon dactylon root by focusing on RESSAS process at 200 µg/mL concentration in every sample (DPPH 0.2 mM). Table 1 indicated the plan matrix of the parameters related to the CCD. To this aim, 29 spaced runs (24 + (2 ×4) + 5) were used for performing the CCD for A, B, C, and D factors, including a (24) factorial plot enhanced with (2 ×4) star and 5 central points. This plan makes the reply possible for modelling by inserting a second-order

polynomial as shown in Eq. (4): AAI = -4.4675 + 0.0150917 A + 0.0952222 B + 0.0106875 C + 0.742083 D - 0.000008125 A2 - 0.000065 AB - 0.0000096875 AC - 0.0006375 AD - 0.000827778 B2 + 0.0000354167 BC 0.000916667 BD - 0.0000275391C2 - 0.000609375 CD - 0.0753125 D2 (4) Based on the ANOVA results, the model had a well proficiency in R2 regulated 0.82 (Table S2). As indicated in Table 1, the superlative AAI is 2.61 and maximum extracted yield of Cynodon dactylon root flour is 41.12 mg oil/g Cynodon dactylon root and as the Pareto chart is shown in Fig. 2, the pressure and modifier volume had a positive effect on this outcome. Further, a wide gain of the extract is not often related to a wide gain with respect to antioxidant capacity. 3.2. The effect of RESSAS process parameters on the antioxidant activity As displayed in Fig. 2, Pareto diagram analyzes in the CCD related to RESSAS indicates the estimated impact of factors and their interplays on the antioxidant activity. The negative or positive mark on the plot represents a decrease or increase while crossing off the nethermost to uppermost area set for the specific parameter, respectively. Similar studies were reported that extraction yield and antioxidative activity increased remarkably by an increment of pressure at constant other parameters, owing to an increment of the solubility. In the present study pressure plays the most effect on the results. The extraction efficiency and antioxidant activity increased by raising the pressure because increasing the extraction pressure results in decreasing intermolecular mean distance of CO2 molecule and a higher fluid (CO2) density. Thus, it causes an increment in the specific interaction between the solute and solvent molecules, which results in enhancing the solubility of the target compounds. By increasing the temperature, the herbal compounds' vapor pressure improves the outgrowth before the optimal point. As regards, since an optimal temperature, enhancement in the temperature decreases the congestion of the supercritical CO2, which plays a negative efficacy on the outcome (Oliveira et al., 2011). Based on the outcome, all of the antioxidant activity growth by apply ethanol for pure CO2, as a modifier. Further, extracting polar herbal compounds with pure carbon dioxide at supercritical area quantitatively cannot be successful because of the confined solubility of supercritical CO2 as a non-polar solvent (Veggi et al., 2011). Of course, the addition of ethanol to the extraction chamber affects the weight of the final product and in this way apparently increases the extraction yield (mg/g), but this residual solvent has no efficacy on the amount of absorbance and AAI. Additionally, ethanol can play a role in forming and creating stability for nanoparticles. Thus, adding a polar pharmacological modifier to supercritical CO2 can growth the extraction efficiency of natural compounds so that it cannot create disorder supercritical fluid (Bhargavi, 2011). Based on the results, an increase in the flow rate of CO2 can positively influence the AAI in the produced extract. In fact, a high supercritical CO2 flow rate leads to a high AAI. The consequence can be normally logical as a tradeoff among a thermodynamic equilibrium state and mass transfer (Kuś et al., 2018; Yousef et al., 2001). In fact, a superior mass

flow rate equals to concise residence time, which prohibit agglomeration the particles in the collection vessel, leading to the creation of smaller particles and an increase in their the absolute bioavailability in an aqueous solution. However, excessive flow rate results in decreasing the stay time more. Thus, it causes the how to deviate of equilibrium and leave the extractor by the incomplete extraction solvent. The specimen response is conformed versus two experimental factors based on the CCD, while other factors are placed in its central surface area. Fig. 3 displays the response surface that representing the impact of (A) pressure and CO2 flow on the AAI at constant oven temperature value and modifier volume in its center value, and (B) oven temperature and modifier volume on the AAI at the fixed value of pressure and CO2 flow rate in its center value. Based on the ANOVA results in Table S2, a change taken place in the modifier volume and pressure could significantly influence extracted AAI (p <0.05). 3.3. Characterization of nanosuspension The DLS results indicated the post-expansion conditions play a role in the RESSAS process, which prevents from growing and agglomerating nanoparticles when it is used as an appropriate surfactant at a good concentration. Thus, it caused the stable and uniform suspension about 100 nanometers. Fig. 4 displays the calculations related to the particle and distribution size after one day (A), one week (B), and one month (C). In addition, FE-SEM technique was implemented to determine the surface of nanoparticle, along with the morphology and dimensions and of the sampled nanoparticles. Based on the FE-SEM image results in optimized mode of the RESSAS process, the initial particle size was circa 30-100 nm diameter range (Fig. 5). In other words, the process can produce nanoparticles of extratced Cynodon dactylon root. Fig. 6 illustrates the total ion chromatogram (TIC) of the herbal extract that identified by the component LC-MS produced in optimized mode by RESSAS method. Based on the LC-MS analysis results, diagnosis of antioxidant compounds with the suitable amount in the extract from the RESSAS process was confirmed. Table 2 indicates some of the potent antioxidant compounds with their acquisition time. Finally, the extracted ion chromatogram (EIC) and mass spectra of some detected potent antioxidant compounds are shown in Fig. S1.

Conclusion: In the present study, the RESSAS process was implemented successfully for producing stable and uniform nanosuspensions of the negligible soluble herbal compound in the extracted Cynodon dactylon root. The optimization of the operative conditions with 350 bar pressure, 45 °C oven temperature, 132 µL modifier volume, and 2.6 mL/min CO2 flow rate allowed potent antioxidant nanosuspensions by a particle size about 100 nm so that it can be produced with an increased bioavailability. Tween 80, as the stabilizer, created stable nanosuspension by preventing from growing and agglomerating the particle after being sprayed into an aqueous solution. Based on the AAI results related to the processed extracts, potent antioxidant activity was observed in Cynodon dactylon root by decreasing the particle

size. Thus, RESSAS process is considered as an appropriate method for producing stable nanosuspension and enhancing the bioaccessibility of insoluble or negligible soluble natural compounds related to pharmaceutical plants.

Keywords: Supercritical CO2; Nanosuspension;Herbal medicine; Antioxidant Activity; Cynodon dactylon root

Progress in nanomaterial-based biosensors for pathogenic bacteria (Review)

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Introduction: Pathogenic bacteria infections cause health threats and financial concerns.Rapid, sensitive, specific and reliable detection of pathogenic bacteria is essential. Conventional methods for detecting bacteria largely such as culturing techniques and biochemical analysis are time-consuming and laborious.PCR and PCR-based methods are unable to distinguish between live and dead bacteria, which could be a potential gap to limit the future development of PCR. Organic/inorganic nanomaterials (polymers, lipids, metal oxides, nanoparticles, etc.) have been widely studied for biological infection problems, because of their flexibility, functional modification, and controllable drug targeting/releasing. The purpose of this review article was to summarize progress in nanomaterial-based biosensors for pathogenic bacteria.

Methods: In this review article, we collected the required data using keywords and using databases such as Google Scholar, PubMed, Scopus and ProQuest. In this study, the statistical population includes all the studies whose articles have been published until 2022. After reviewing the findings and evaluating the quality of the obtained data, 13 articles were analyzed.

Results: Developed CRISPR-Cas12a-powered dual-mode is able to used as a nanomaterial biosensor consisting of gold nanoparticles (AuNPs) with DNA endonuclease-targeted CRISPR trans reporter. DNA Pom-Pom like nanostructure with a diameter of ~50 nm, and successfully achieved DNA PP-N based multifunctional platform. To utilize this PP-N assembly as an amplifies signal probe and aptamer as bacteria recognition element. Other biosensors include: Aptamer as an oligonucleotide selected by repeated screening in vitro or systematic evolution of ligands by exponential enrichment(SELEX) in aptamer-based biosensors, electrochemical biosensors, Paper-based analytical devices (PADs) emerged as critical POC tools.

Conclusion: DNA nanomaterials as biological analysis tools can be attributed to their unique structure and property features: simple and quick producing process; being environment-friendly; good chemical and thermal stability; easy for chemical conjugation and modification. In general, using highly specific Watson-Crick base pairing capability through the formation of hydrogen bonding, several 2D/3D DNA nanostructures of varying size and complexity have been successfully assembled. The aptamer-functionalized and antibiotics-loaded PP-N platform demonstrates excellent merits of high antibiotic's molecule loading capacity and negligible cytotoxicity to targets. The amplicons of Salmonella (used as a model)-specific invA sequence trigger CRISPR-Cas12a-based indiscriminate degradation of single-stranded DNAs that are supposed to link two gold nanoparticles (AuNP) probe pairs, inducing an aggregation-to-dispersion change, so the advantages of this method can be mentioned that, this generated observable color changes that became even more apparent after centrifugation. The color changes can be discerned by the naked eye and recorded using a portable colorimeter.PADs due to their simplicity, low fabricating costs, easy storage, portability, and disposability, particularly in resource-limited areas, emergencies, and in-home healthcare, without relying on external devices and reagents are important for medical diagnostics and among them, colorimetric paper-based biosensors are in demand and are the most attractive because the presence of a specific pathogen can be conveniently monitored by a simple change in color, which can be distinguished easily with the naked eye without expensive and complex but the major limitation of colorimetric assays is low sensitivity since it is often difficult to transform detectable signals into a color readout. Disadvantages of using viruses and bacteria as a sensing element include poor selectivity, low sensitivity, and slow response, which limits the interest in expanding biosensors to detect pathogens in the market. The future perspective is to develop, smart contact devices consisting of hundreds of biosensors and nanomaterials, for early detection of cancers or other malignancies.

Keywords: nanomaterial, biosensor, pathogen detection

Protective effect of folic acid on the deltamethrin-induced toxicity on sperm quality and testosterone in mice (Research Paper)

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Introduction: Deltamethrin (DM) as one of the most widely used agricultural pesticides, is one of the environmental factors that can have destructive effects on the male fertility. According to studies, folic acid is one of the effective factors in increasing the quality of male fertility.

Methods: In this experimental study, 25 adult NMRI male mice were divided in to five groups (n=5/each). The control group received only normal saline. Sham received 0.2 ml corn oil. Folic acid group 0.08 mg/kg, DM group 0.6 mg/kg and DM+FA group received both of them. After 28 days of treatment, the mice were anesthetized and blood samples were taken from the heart to extract serum. The mice were then operated on and the left tail of the epididymis was removed to extract adult sperm. Hormonal analysis was performed by ELISA and CL methods.

Results: The results showed that in DM group sperm count, motility, testosterone and free testosterone significantly decreased. (p<0.001) treatment with FA in the DM treated mice significantly improved these changes.

Conclusion: With these findings it was concluded that folic acid can protect against deltamethrin induced damage and improve epididymal sperm parameters and increase fertility in male mice.

Keywords: Sperm ،Infertility ،Testosterone ،Reproduction

Protein glycosylation in cancers and its potential therapeutic applications in neuroblastoma (Review)

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Introduction: Neuroblastomas (NB) is the most now no longer unusual place area of pediatric malignancy identified earlier than the number one birthday, which represents approximately 6% of all cancers in children, is more now no longer unusual place area in boys than in girls. This most now commonplace area, greater cranial teens robust tumor, has a presumable molecular starting area with withinside the sympathoadrenal lineage of the neural crest subsequently of development. Cells and tissues are continuously monitored through a manner of way of an ever-alert immune device. In the tool of maximum cancers' progression, however, robust tumors have tailor-made to the selection strain exerted through manner of way of the immune device and characteristic superior the potential to avoid it. Glycosylation is the enzymatic tool responsible for the attachment of glycan to proteins, lipids, or exquisite saccharides. Glycan and glycoproteins have been significantly used withinside the hospital as each stratification and evaluation of maximum cancers biomarkers. Given the essential characteristic of glycan in tumor biology, together with its microenvironment and the immune response regulation, it has emerged as apparent that glycosylation modifications taking area in maximum cancers want to have a high-quality impact on maximum cancers' treatment.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Protein glycosylation in cancers and its potential therapeutic applications in

neuroblastoma. After reviewing the relevant findings and evaluating the data quality, a total of 17 articles were analyzed.

Results: Changes in glycosylation on proteins or lipids are one of the hallmarks of tumorigenesis which can also furthermore need to modulate inflammatory responses, permit viral immune escape, promote maximum cancer's mobileular metastasis or alter apoptosis. Functionally, glycans control or have an impact on several factors of maximum cancer's mobileular biology, starting from mobileular adhesion, extracellular matrix interactions, mobileular signaling and proliferation, and proximal and distal communication. These natural techniques underlie essential maximum cancers hallmarks which incorporates invasion, angiogenesis, and metastasis formation, along the development of allowing maximum cancer's abilities together with the modulation of the immune response. Identification of glycan structures at unique sites, and its abundance in a protein. Apart from these, the development of effective synthetic machine for analyzing the effect of glycosylation on shape and abilities of biomolecules is as an opportunity tough due to the fact multiple isoforms of glycosyltransferases can encode an unmarried glycan epitope.

Conclusion: Maximum cancers-associated glycoforms and glycotransferases associated with the synthesis of such glycans have capability use for drug discovery glycosylation research come upon several challenges, which incorporates identifying unique natural results of expression patterns and levels of glycosyltransferases/glycosidases; While research on this area stays in its early levels, many studies have illustrated that Protein glycosylation has emerged as a promising cause for max cancers treatment and each in treatment and withinside the biomarker area unfold out a cutting-edge manner of thinking for treatment of the 1/3 most not unusual place area teens maximum cancers. Further investigations of most cancer's unique glycans are hoped to boom more beneficial prognostic, diagnostic, and recovery goals withinside the fight withinside the path of maximum cancers.

Keywords: Protein glycosylation, cancer, neuroblastoma, treatment, Protein Disulfide-Isomerases

Protein nanoparticles as targeted drug delivery systems, a novel combination of nanotechnology and biology (Review)

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Introduction: A drug delivery system generally includes the selection and delivery of medicinal and therapeutic compounds to a desired tissue or cell in the body in a targeted manner. to create a successful treatment, it is necessary to maintain the concentration of the drug at the appropriate level in the blood and to release the desired medicinal substances at a certain rate. in recent years, there has been considerable interest in the development of drug delivery systems using nanotechnology. various nanomaterials such as polymers, liposomes, magnetic nanoparticles, and dendrimers can be used as carriers for drug delivery. today, protein nanoparticles are very valuable in drug delivery, which comes of the desirable properties of proteins. Such as the capacity to bind to water molecules, easy control of particle size, less toxicity, stability, and biodegradability. protein nanoparticles can be used together with biodegradable polymers in the structure of microspheres as a targeted drug delivery system. different methods are used to prepare protein nanoparticles, which three different methods include chemical, physical, and self-assembly. All of them lead to the formation of bonds or cross interactions between nanoparticles and drug molecules.

Methods: In this review, we studied more than 30 articles from 2000 to 2022 from valid databases. clearly, we describe the protein nanoparticles as novel drug delivery systems and then focus on the different kinds of proteins that can be used as protein nanoparticles.

Results: Different proteins are used to produce protein nanoparticles, which include animal and plant proteins. Animal proteins such as elastin, collagen, gelatin, albumin, silk protein, and milk proteins (including casein and whey proteins). Plant proteins include lectin, gliadin, zein, and soy protein. Each has significant advantages. For example, gelatin has an arginine-lysine-glycine sequence in its amino acid sequence, which plays a notable role in cell connections and cell signaling by binding to integrin receptors on the cell surface. Likewise, collagen nanospheres are used as stable excipients for various drugs due to their thermal stability and the ability to form a clear colloidal solution. In addition, caseins are not sensitive to temperature, while whey proteins are significantly denatured at temperatures above 70 degrees. Zein, due to its high hydrophobicity, is used as a drug delivery system for

hydrophobic drugs. Soy protein nanoparticles are quite stable in near-neutral pH conditions, while some other nanoparticles are rapidly degraded in acidic conditions, and this fact can be of interest for pharmaceutical applications such as skin treatments or drug delivery through the skin.

Conclusion: Targeted drug delivery is one of the new fields of science, among which protein nanoparticles are used in the delivery of anticancer drugs, hormones or growth factors due to their favorable characteristics such as fewer side effects and possible toxicity. drug delivery efficiency can be improved by controlling properties such as size, shape, and surface charge of protein nanoparticles. in addition, the loading and release of drugs are also regulated according to the characteristics of nanoparticles or the concentration and type of drug. Although the application of protein nanoparticles is already evident, it is hoped that we will see more developments in the future.

Keywords: Protein nanoparticles, drug delivery systems, targeted drug delivery

Protein Requirements for Children with Advanced Chronic Kidney Disease (CKD): A Clinical Recommendations (Review)

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Introduction: Since children with chronic kidney disease (CKD) often have low growth, it is significant for them to get sufficient protein, particularly for children on peritoneal dialysis (PD) and hemodialysis (HD). In this study, we need to reveal sufficient protein for children with chronic kidney disease.

Methods: To accomplish this narrative review, we searched 4 Databases (PubMed, Web of Science, Scopus and google scholar) based on the search strategy from 2010 to 2022 with the high sensitivity on September 2022 by following MeSH keywords: " Chronic Kidney Disease ", " Children ", " Protein requirements ", " Peritoneal dialysis ", " Hemodialysis ".

Results: Some studies suggest that the protein required in children with chronic kidney disease stages 2–5 and those on hemodialysis (CKD2-5D) is higher than in healthy children. It was recommended that dietary protein intake be maintained at 100% of the Dietary Reference Intakes (DRI) for the ideal body weight, plus an allowance for dialytic protein and amino acid losses. So, the protein requirement for children on peritoneal dialysis is 0.15–0.3 g/kg/day and for children on hemodialysis is 0.1 g/kg/day. Nitrogen balance can be used to estimate the amount of protein required. Dietary protein reduction, which increases the risk of malnutrition and stunted growth in children in the early stages of CKD, should be avoided. However, reducing protein intake can help improve metabolic control in some cases, provided the nutritional status is maintained.

Conclusion: Recent studies have recommended that adequate protein intake is essential for children with CKD. Although protein reduction, in some cases, is necessary, more clinical studies are required.

Keywords: Children; Protein requirements; Chronic Kidney disease; Peritoneal dialysis; Hemodialysis

PTEN gene therapy induces apoptosis in tumor cells and enhances sensitivity to oxaliplatin in colorectal cancer. (Research Paper)

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Introduction: Colorectal carcinoma (CRC) is the most common malignancy of the gastrointestinal tract and the third most common cancer worldwide (1). Nowadays, surgical resection and systematic chemotherapy are applied for CRC treatment. Oxaliplatin is the first platinum derivative that is effective in the treatment of CRC (2). However, due to drug resistance, advances in chemotherapy for CRC are limited. A tumor suppressor gene on chromosome 10q23, PTEN, has been reported to be mutated or deleted in a variety of tumors, including colon cancer (3). The initial identification of PTEN as a phosphatase suggested its functional role as a regulator of mitogenic signaling pathways. Specifically, PTEN acts as a phosphatidylinositol phosphatase with a possible role in phosphatidylinositol 3 -kinase (PI3-K)-mediated signal transduction. Activation of the proto-oncogene Akt, a serine-threonine kinase downstream in the PI3-K pathway, promotes cell survival by inhibiting the function of pro-apoptotic proteins. In the nucleus, PTEN-mediated PPIs enhance the activity of numerous protein substrates such as the E3 ubiquitin ligase APC/C and p53 (4). In general, these nuclear interactions have been shown to benefit chromosomal stability and healthy cell-cycle progression (4). Introduction of PTEN into PTEN deficient cells inhibits the activation of Akt (5). Activating mutations, amplifications and rearrangements in the upstream members of the pathway, e.g. RAS and PTEN are the most common events in cancers (6) . In the present study, we show that PTEN gene therapy of human colorectal cancer cells inhibit tumor growth and exhibits increased efficacy when combined with oxaliplatin.

Methods: SW480 Cell lines were cultured in DMEM with 10% heat-inactivated FBS. The cells were cultured in 5% CO2 and 37 °C. PTEN was cloned into pCMV-Tag2 plasmid, purchased from Addgene. When the confluency of SW480 cells reached to 80%, they were transfected by calcium phosphate method. Neomycin was used for the selection of transfected cells.

Cells were treated with 2μM oxaliplatin 24h post transfection and harvested 48h post treatment.

Results: Cells transfected with PTEN show 33% more cell death in flowcytometry, compare to cells transfected with control plasmid. Similar comparison was conducted between cells transfected with PTEN and treated with oxaliplatin and cells with control plasmid and oxaliplatin treatment which indicate 60% increase in cell death in the PTEN-transfected cells. In cells transfected with PTEN, real-time PCR data reveal an increase of the caspase 9 gene, demonstrating the protein's function in the intrinsic route of apoptosis.

Conclusion: First reported by Tanaka et al. in 2000, PTEN was exogenously introduced via an adenoviral vector into PTEN-null human bladder cancer cells where it was found to suppress tumor cell growth through the abrogation of AKT signaling (7). Subsequent studies involving human colorectal and prostate cancer cells yielded similar results (8,9). This research demonstrates that forced expression of PTEN can provide effective therapy for some colorectal cancers. It enhanced the sensitivity to oxaliplatin in SW480 cells by promoting apoptosis. Combining PTEN gene therapy with oxaliplatin can result in greater efficacy.

Keywords: PTEN; cancer; apoptosis; gene therapy; colorectal

Purification and performance evaluation of polyclonal antibody against the SARS-CoV-2 (Research Paper)

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Introduction: SARS-CoV-2 is amongst the human coronaviruses which cause severe pneumonia or even death. Due to the importance of its rapid identification/treatment and with the regard to this fact that pAbs are relatively cheap, maybe able to neutralize antigens, this study was done with the purpose of production/purification of anti-SARS-CoV-2 polyclonal antibodies (pAb) in rat.

Methods: The purification of viral antigens was done by PEG/NaCl precipitation. Immunization was done by the purified antigen and ammonium sulfate precipitation (33%) was utilized for the purification of primary antibody. Following the final purification by ion-exchange chromatography, the the antibody's specificity was verified by ELISA and western blotting (WB). All data were analyzed by SPSS software.

Results: The results showed that increase of PEG concentration, will increase the amount of concentrated virus. Besides, high-titres of pAb were induced in rat and a good antibody-antigen interaction was indicated in ELISA/WB results.

Conclusion: Herein, we presented a cheap and simple protocol for purification of relatively high quality of whole viral particles. The results verified that these antigens elicit a good immune response and have a good specificity against the CoV's antigens.

Keywords: SARS-CoV-2; western blotting; polyethylene glycol; ELISA.

QSAR modeling of a Ligand-based pharmacophore derived from Hepatitis B virus surface antigen inhibitors (Research Paper)

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Introduction: Functional cure for Hepatitis B virus (HBV) by inhibiting HBV surface antigen (HBsAg) is crucial. Therefore, it was aimed to develop a predictive quantitative structure-activity relationship (QSAR) model on a ligand-based pharmacophore (LBP).

Methods: LigandScout v3.12 was used for LBP modeling. The best model with the highest score was used for high throughput screening (HTS) screening. A QSAR model was developed by a stepwise multiple linear regression (MLR) with a confidence interval (CI) of 95%. The goodness of fit statistics evaluated the fitness of the model. A comparable R2 and adjusted R2 were considered as the lack of overfitting. Further RMSE and Q2 statistics were measured for testing the model on the validation set.

Results: 34 active anti-HBsAg compounds were used to develop an LBP model. 9/34 of compounds with higher clustering pharmacophore-fit scores were tagged as the training set, and the rest of the inhibitors were used as the test set. The best model had a 0.8832 fit score. HTS resulted in 10 potential hit compounds with a fit score of 101.44±0.65. A QSAR model was developed with two response variables, including Yindex and GATS8m, with substantial variance information (p < 0.05). The model was well fitted (R2 = 0.9563, MSE = 0.0023).

Conclusion: A reliable well-fitted predictive QSAR model was developed. The model can be applied to the chemical libraries fitted to the LBP model, and the QSAR equation would estimate the biological activities of the hit compounds with 95.63% accuracy with only two Yindex and GATS8m descriptors.

Keywords: Hepatitis B virus - QSAR - Ligand-based pharmacophore

Radioimmunotherapy application in Glioblastoma multiforme Treatment (Review)

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Introduction: The incidence of brain tumors is increasing slightly each year and patient prognosis remains disappointing. The lower Karnofsky performance score and older age are associated with poorer prognosis. Standard therapy for the management of brain tumors in routine clinical practice consists of debulking surgery, radiation therapy, and chemotherapy. Therefore, researchers are looking for ways to improve the therapeutic index as an important therapeutic goal. Gliomas, cancer cells derived from glial progenitor cells, account for approximately 75% of all adult primary malignant brain tumors (about 30% of all brain tumors) and are characterized by poor outcomes. In children, primary brain tumors are the second leading cause of cancer death after leukemia and the most common solid tumor. Glioblastoma multiforme (GBM) is a rapidly growing glioma that arises from astrocytes and oligodendrocytes. GBM often referred to as grade IV glioma, is the most lethal primary brain tumor. The standard treatment of GBM consisting neurosurgery, followed by radiotherapy. Nonetheless because of its invasive and aggressive growth pattern GBM cannot be completely controlled. To improve local tumor control, considerable research was implemented into new GBM therapies, one of the promising techniques being radioimmunotherapy (RIT). RIT is a nuclear medicine modality that uses a radionuclide component combined with a monoclonal antibody(mAb) which is targeted against surface tumor antigens or antigens in the tumor microenvironment. This approach has the advantages of selective delivery of antibodies and cell-killing characteristics of radionuclides. RIT is based on the presence of specific antigens within the tumor that are able to bind with MAbs after local or systemic administration. For a successful RIT, it is essential to select surface antigen present on the majority of tumor cells and of a specific targeting antibody. Furthermore, this surface antigen should have a low expression (ideally no expression) on

normal cells. Targets and Radionuclides that have shown potential results in radioimmunotherapy of GBM are going to be discussed in this paper.

Methods: To conduct this article we searched Scopus, PubMed, and google scholar databases in the period from 2018 to 2022 using "Radioimmunotherapy", "Glioblastoma multiforme", "Glioma" and "Radionuclide" keywords. Duplicated titles were removed by endnote software and after checking abstracts related articles were reviewed.

Results: Epidermal growth factor receptor (EGFR) and tenascin are targets that have shown therapeutic potential in literature and for brain disorders. Furthermore, some preclinical and clinical trials were implemented with promising results. EGFR expression has been identified in 19-85% of primary malignant gliomas, especially in GBM. However, its expression is low in normal brain tissue. Probably the most investigated target for brain tumors is Tenascin, which is expressed all over the extracellular matrix of gliomas. There are other molecular targets that have shown promising results to treat tumors like the extra domain B of fibronectin (EDB), human neural cell adhesion molecule (NCAM) and disialoganglioside GD2. Solid tumors like GBM can be treated with radionuclides that emit α and β –particles. More than 95 percent of clinical trials have used 131I and 90Y as a standard to which all other radionuclides are compared. Availability, favorable emission properties, and flexible radiochemistry have led to the use of these β-particle-emitting radionuclides in RIT. The treatment of GBM α- and β-emitting radionuclides have some advantages and disadvantages because of their radiobiological and physical characteristics. Half-life, range in tissue, mean energy, and linear energy transfer (LET) are important parameters that can affect targeted cells. Furthermore, effective half-life which can match the properties of the tumor when choosing a suitable radionuclide for clinical use is a highly valued parameter in the context of RIT.

Conclusion: Despite advances in surgery radiotherapy and chemotherapy approaches GBM relative survival is below 7% within 5 years. RIT has proven successful in clinical results in hematological malignancies. However, because of several reasons which are mostly related to the different biological properties of solid tumors and hematological cancers, RIT has not indicated significant success in solid tumors. Numerous powerful tools for GBM therapy have been provided by recent advances in nuclear medicine and biotechnological technologies that are related to molecular knowledge and new clinical opportunities have been created by the development of innovative radionuclides. Furthermore, A better understanding of the tumoral microenvironment and radionuclides properties is needed to optimize GBM treatment using RIT approaches.

Keywords: Radioimmunotherapy, Glioblastoma multiforme, Glioma, and Radionuclide

Radiomics application in precision radiotherapy (Review)

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Introduction: Precision medicine aims to increase the quality of healthcare by tailoring the healthcare process to each patient's uniquely evolving health condition. This work spans a wide range of scientific disciplines, including drug discovery, genetics, radiomics, etc... Imaging plays a vital role not only in diagnosing and staging cancer but also in planning radiation therapy and assessment of treatment response. Furthermore, the role of imaging in precision medicine cannot be ignored. Radiomics is a quantitative approach to medical imaging that aims to relate large-scale extracted imaging information to biological and clinical endpoints. Disease detection, diagnosis, prognosis, and therapy response assessment/prediction are its applications. the possibility of translating data science research into more personalized cancer treatments has been opened up by the expansion of quantitative imaging methods along with machine learning. As radiation therapy aims for more personalized treatment, radiomics can play a key role at various stages before, during, and after treatment.

Methods: To conduct this article Scopus, PubMed, and google scholar databases have been searched in the period from 2018 to 2022 using "Radiomics", "precision medicine" and "radiotherapy" keywords. Duplicated titles were removed by endnote software and after checking abstracts related articles were reviewed.

Results: Radiation therapy offers unlimited possibilities for cancer treatment. There is a growing and urgent need to implement individualized radiotherapy strategies thus, radiomics has been extensively studied in radiotherapy and clinical studies have shown the role of radiomic features analysis as a source of information with the potential to impact the radiation oncology practice. These features can be used as a biomarker to predict patient prognosis, treatment response, and underlying genetic changes. precise and robust

machine learning, deep learning algorithms, or statistical techniques by creating classification or predictive models make radiomic features more useful for clinical applications.

Conclusion: Radiomic can be used by Artificial intelligence to develop individualized radiotherapy. The trend of many clinical studies has shown that the future is the era of precision medicine using artificial intelligence. Despite the progress in precision medicine, there is still a long way to achieve a precisely personalized treatment of cancer. Furthermore, radiomic are able to be linked with genomic, metabolomic, and other information to improve the ability of precision medicine

Keywords: Radiomics, precision medicine, and radiotherapy

Recent advances in drug delivery system for hepatocellular carcinoma (Review)

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Introduction: Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer in adults and is currently the most common cause of death in people with cirrhosis. HCC is the third leading cause of cancer-related deaths worldwide. Therefore, it is very important to develop an efficient treatment method. Drug delivery system (DDS) is a new way of administration of drugs or, more accurately, therapeutic substances into the body. Altering the time, place, and rate of the drug release, helps us improve the drug's efficacy. Therefore, our aim in this study is to review recent advances in drug delivery systems in hepatocellular carcinoma.

Methods: For this research, existing articles in PubMed, Web of Science, Sid, and Google Scholar databases that have been published till 2022 are systematically selected, and 16 articles are included in this study. This research is done in English considering the following keywords: Drug delivery systems, Hepatocellular carcinoma, Therapeutics

Results: Studies show that recently the drug delivery system has made good progress in the field of nanocarriers. DDS used in the treatment of HCC is mainly nanoparticles, which include: organic nanoparticles, inorganic nanoparticles, polymers, and lipids, which accumulate in the site of cancer cells due to anatomical or pathophysiological characteristics, and by using particles with ligands, they can be effectively bound to cancer cell receptors. Polybutylene cyanoacrylate nanoparticles (DHAD-PBCA-NPS) with dihydroxy anthracenedione nanoparticles can have a good inhibitory effect on the development of HCC. On the other hand, Zp has the highest absorption rate in the liver, which can be very effective in the field of smart drug systems. Dual reactive liposomes under MRI guidance (GNSPLD) can release the drug at the tumor site and also increase the antitumor effect of the drug. These liposomes can be a new development in the field of smart drug delivery systems. Combination therapy has also been reported as a new method for cancer treatment. The combination of doxorubicin (DOX) and DNA (shAkt1) in a coating of poly ethyleneimine, decorated with GA (glycyrrhetinic acid) (PEI-

GA) and the gene of cancer cells. The liver has a good effect in delivering drugs to HepG2 cells, autophagy, and apoptosis of these cells.

Conclusion: Generally, Drug delivery systems are capable of offering physicians new options for better destruction of cancer cells, especially in biopsy-proven unresectable hepatocellular carcinoma. The drug delivery system, as a new interface between the patient and the drug, increases drug efficacy and provides us with new means to cure Hepatocellular carcinoma.

Keywords: Drug delivery systems, Hepatocellular carcinoma, Therapeutics

Recombinant human erythropoietin and cancer (Review)

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Introduction: Patients with developed cancer often undergo clinically significant anemia that occurs through myelosuppressive chemotherapy. In more detail, severe anemia, defined as a hemoglobin level less than 8g/dL, is usually treated, whereas on another side mild-to-moderate anemia (hemoglobin level of 8–11 g/dL) is left untreated in most patients undergoing treatment with chemotherapy and radiation therapy. Another notable point is that the serum concentration of erythropoietin (EPO) is lower in cancer patients than in patients with iron deficiency, which suggests that the anemia observed in cancer patients is at least partially due to EPO deficiency. In the past, blood transfusion was the only treatment option for severe cancer-related anemia and the fastest means to alleviate symptoms associated with anemia, however, there are short-term and long-term effects associated with this treatment like the transmission of infectious agents, transfusion reactions, etc. which have prompted oncologists to develop more safe and efficient treatments like recombinant human erythropoietin (rHuEPO) therapy. Until now, various scholars working on investigating the efficiency of this therapy and also shedding light on different aspects of its utilization in the patient's life level improvement.

Methods: This study has been performed by searching various texts, authoritative scientific articles, and several keywords such as anemia, cancer, erythropoietin, rHuEPO and so on to find all relevant publications on the role of recombinant human erythropoietin in cancer disease.

Results: According to the findings, more than half of cancer patients have a low serum level of erythropoietin. The introduction of recombinant human erythropoietin (RHuEPO) has revolutionized the treatment process for patients with anemia of chronic renal disease. The initial results demonstrated that RHuEPO could restore the packed cell volume, decrease the necessity of regular blood transfusion in patients, and improve overall well-being. The results of these trials were so impressive that RHuEPO was granted a license as a therapeutic agent in 1988 for patients with anemia of chronic renal

failure, only three years after its discovery. Other studies have demonstrated that recombinant human erythropoietin (rHuEPO) has been used safely and effectively to treat anemia, it is shown that RHuEPO therapy corrects 50% of cancer anemia in general. The results of rHuEPO therapy in chronic anemia of cancer are far more than laboratory values. The quality of life after treatment with recombinant human erythropoietin (rHuEPO) often have been reported in patients with end-stage cancer disease. Different studies present that the patients treated with erythropoietin had a statistically significantly lower risk of blood transfusion and, on average, received statistically significantly fewer blood transfusions, and cancer patients treated with erythropoietin had an increased hematologic response compared with untreated patients. In general, RHuEPO therapy improves both treatment outcomes and the survival of cancer patients.

Conclusion: The above results suggest that r-HuEPO may be a proper agent to alleviate the consequences of the anemia that is usually found in association with advanced cancer. The rHuEPO therapy also enables the patients with response to lead a physically and socially more active life with less anxiety, brighter moods, and an increased general feeling of well-being.

Keywords: rHuEPO, Erythropoietin, Cancer, Anemia, Recombinant Protein

Regulation of HIF-1 by microRNAs in various cardiovascular disease (Review)

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Introduction: Today, we see an increase in death due to cardiovascular diseases all over the world, which has a lot to do with the regulation of oxygen homeostasis. Also, hypoxia-inducing factor 1 (HIF-1) is considered a vital factor in hypoxia and its physiological and pathological changes. HIF-1 is involved in cellular activities including proliferation, differentiation, and cell death in endothelial cells (ECs) and cardiomyocytes.

Methods: Pubmed, Google Scholar

Results: The molecular regulation of HIF-1 is considered to improve therapeutic approaches in clinical diagnoses of cardiovascular diseases.

Conclusion: In this review, we studied the collected data on HIF and the complex molecular network under its control in hypoxic conditions. Understanding the mentioned molecular pathways can be used in applying more efficient treatment methods for cardiovascular diseases.

Keywords: Hypoxia-Inducible factor 1(HIF-1), miRNAs, Cardiovascular diseases

Regulation of the Cell Cycle and role of Ink4 Family in cancer (Review)

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Introduction: The Ink4 family of proteins consists of four members: p15Ink4b, p18Ink4c, p19Ink4d, p16Ink4a, and p19Ink4d. The only D-type cyclin-dependent kinases that the Ink4 family of proteins bind to and block are CDK4 and CDK6. In co-immunoprecipitation tests, a protein that interacted with CDK4 and was later identified as MTS1 was determined to be the first member of the Ink4a family. This study's goal was to learn more about how the Ink4 Family affects cancer and how the cell cycle is regulated.

Methods: This study was the regulation of the cell cycle and role of the ink4 family in cancer from scientific databases such as science direct, springer, google scholar, and PubMed.

Results: Results have indicated the key structural similarities amongst ink4 proteins include the presence of four or five ankyrin repeats, which mediate protein-protein interactions with cdk4/6. each repetition consists of an extended strand joined to the following extended strand by a helix-loop-helix (hlh) motif. the p19ink4d-cdk6 complex's crystal structure has been determined, and this information has been extremely helpful in understanding how ink proteins block cdk. the p19ink4d ankyrin repeats form a "cap" over cdk6's n-terminal domain and cause it to migrate spatially away from the c terminus. while it prevents effective at binding, this event has little effect on CDK-cyclin complex formation. all four ink proteins have similar pharmacological actions toward cdk4 and cdk6, as would be predicted from their structural similarities. the ability of a short peptide generated from one of the ankyrin motifs to bind and inhibit cdk4 is intriguing and suggests the significance of these domains in ink4 functioning.

Conclusion: Ink proteins have comparable tertiary structures and similar biochemical activity, but their regulation is different. Most tissues do not express p16Ink4a. Instead, it is brought on by the production of transforming or oncogenic proteins as well as by cellular senescence. The expression of p16Ink4a is controlled by numerous oncogenes and tumor suppressors. For instance, p16Ink4a levels are elevated in primary rodent cells when Ras is overexpressed. The tumor suppressor p53 or the retinoblastoma susceptibility protein, Rb, can both be inactivated to increase p16Ink4a expression. TGF-, on the other hand, is one example of a growth-inhibitory factor (anti-mitogen) that controls p15Ink4b expression. Only the expression of p18Ink4c and

p19Ink4d appears to be controlled throughout the cell cycle, peaking during the S phase. During development, Ink4 protein expression patterns are also variably controlled.

Keywords: Ink4 Family, cancer, tumor, tumor suppressor

Relationship between cytokine storm and the causes of corona disease with severe symptoms (Review)

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Introduction: The virus's cytopathic effects and ability to evade the host defense system are thought to play a role in the severity of COVID-19 disease .The host immune system can lead to a fatal inflammatory condition known as CRS in COVID-19 individuals. This is a phenomenon of an excessive inflammatory response, as the name implies, in which inflammatory cytokines are swiftly and massively released in response to infective stimuli. This uncontrolled inflammatory cytokine storm is a serious condition that is seen in patients who need to be admitted to the intensive care unit (ICU). This study sought to determine whether there was any connection between cytokine storm and the underlying causes of corona illness with its severe symptoms.

Methods: This study was conducted to Relationship between cytokine storm and the causes of corona disease with severe symptoms based on scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: The findings indicated that CRS is one of the potential triggers for the fatal and progressive types of COVID-19. Clinical criteria for CRS are difficult to define, however current research suggests several characteristics, including clinical symptoms and test results, to support this status. Although there are many theories, it is still unclear what causes inflammatory substances to be released without restriction. The first is a result of viral replication, which triggers pyroptosis, a particularly inflammatory type of lytic-programmed cell death (apoptosis). Pyroptosis disrupts macrophage and lymphocyte activities, releases pro-inflammatory cytokines, and results in peripheral lymphopenia in COVID-19 patients. Interferon (INF)-1 may modify innate immunity, according to mounting evidence. INF-1 has a critical role in supporting adaptive immune systems and viral proliferation. It is true that COVID-19 affects the host's innate immune response and reduces INF-1's ability to operate in response to infection. As the body's initial line of defense after a virus infection, macrophages, dendritic cells, and neutrophils initiate the immunological response. Moreover, recent studies suggest that excessive production of some cytokines, such as IL-6, may be the primary cause of the inflammatory response in COVID-19. The second hypothesis is related to adaptive immunity and the production of neutralizing antibodies against the surface antigen of the virus. Lung autopsies from patients who died from COVID-19 showed a high infiltration of macrophages into the bronchial mucosa. Immunoglobulin (Ig) Gs were reported to attach to the S protein and

initiate inflammatory cascades in some animal investigations. Through the production of IL-8 and monocyte chemoattractant protein (MCP)-1, this binding can increase the number of pro-inflammatory macrophages and monocytes in the lungs. The virus anti-S-IgG complex interacts with the Fc receptor (FcR) on the surface of monocytes and macrophages to cause an inflammatory response. The fact that pro-inflammatory cytokine levels dropped when macrophage receptors were blocked lends credence to this idea. Additionally, many pieces of evidence show that the development of severe respiratory disease in COVID-19 patients coincides with the presence of anti-viral IgGs.

Conclusion: Conclusion and views the cytokine storm in COVID-19 may be caused by dysregulated acquired immune system and hyperinflammatory innate immune responses. In this article, we first examined putative pathways underlying the COVID-19-induced CRS before outlining potential treatment options. In fact, in critically ill COVID-19 patients, the CRS is directly related to catastrophic outcomes. The survival rate of infected patients may increase with the use of immunomodulatory drugs and cytokine antagonists to control the cytokine storm. The therapeutic efficacy of antiviral medication in COVID-19 patients can be improved by focusing on inflammatory cytokines in this regard. On the other hand, because the inflammatory network is so complicated, focusing on a single inflammatory signaling pathway can trigger later compensatory immune responses. Therefore, it is important to weigh the advantages and disadvantages of using anti-inflammatory medications. According to the data presented here and the authors' point of view, inflammatory cytokine-targeting antibodies continue to be a popular therapeutic strategy. As a result, combination therapy using inflammatory inhibitors and other COVID-19 modalities may be more effective than either strategy used alone. To comprehend the fundamental mechanism of cytokine storms in COVID-19, highly credible evidence is needed. To clarify the significance of anti-inflammatory therapies to control excessive inflammation, more research is required.

Keywords: cytokine storm, corona disease, symptoms, COVID-19

Relationship between health and awareness of timely screening test (Review)

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Introduction: Screening which is one of the most important ways of prevention and prevention of cancer is proposed and made in almost all over the world in order to reduce the cancer burden The main purpose of this study is to examine the relationship between the perception of cancer screening and making and the perception of health

Methods: Two questionnaires were used in the study The first questionnaire included questions on demographic characteristics and canser screenings. The second survey was Health Perception Scale The study was analyzed with three hundred and twenty two participants

Results: The mean age of the study group was forty two and sixty five percent of the study group was female. When examined according to the knowledge of cancer screening done; eighty three percent In a community of two hundred and sixty seven people stated that he knew. When these two hundred and sixty seven people were asked what cancer screening they were aware of seventy seven percent reported that they had breast cancer Forty seven percent had colon cancer and Seventy four percent had been screened for cervical cancer thirty nine percent at least once said he had the scan sixty three percent of women aged forty years and older had mammography fifty eight percent of women aged thirty and over had pap smear twenty two percent of individuals aged fifty and over had a hidden blood test in the stool fourteen percent stated that he had colonoscopy. The mean health perception score calculated based on the health perception scale of the study group was fifty There is a significant correlation between health perception screening and cervical and breast cancer screening.

Conclusion: There is a limited limited age range between health perception score and cancer screening, and more information and training studies especially for colorectal cancer screening are recommended to increase the awareness of cancer screening

Keywords: cancer colorectal cancer breast cancer

Relationship between Helicobacter pylori infection and its severity with eating habits (Research Paper)

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Introduction: Gastric cancer is the most common malignancy in Iran. Helicobacter pylori and some components of the diet are among the risk factors for this disease, but there are few studies on the relationship between these two factors in the world. The aim of this study was to investigate the relationship between Helicobacter pylori infection and its severity with diet in Yazd.

Methods: This study was a cross-sectional descriptive study. The samples were 77 people who underwent upper endoscopy in Yazd Gastroenterology and Liver Research Center. A questionnaire containing demographic information and a food frequency questionnaire for individuals was filled out and a sample of anther was sent for pathological examination. Data analysis was performed by non-parametric tests.

Results: The rate of Helicobacter pylori infection was 40.8% based on pathological examination (hematoxylin-eosin). Positive HP infection was inversely related to weekly consumption of fish (P = 0.009), green pepper (P = 0.01) and water (P = 0.019) and weekly consumption of tuna (P = 0.013) and tea (P = 0.048) was directly related. The severity of HP infection was inversely related to weekly consumption of fish (P = 0.001), green pepper (P = 0.045) and water (P = 0.001) and with weekly consumption of tuna (P = 0.011) and sugar (P = 0.044) was directly related.

Conclusion: The results indicate the possibility of the effect of some foods such as fish (except tuna), green pepper and water on HP and the severity of this infection. Due to the limitations of this study, more comprehensive and accurate studies are necessary to prove the findings and achieve more details.

Keywords: Helicobacter pylori, Eating habits, Gastric cancer, Risk factors

Relationship between miRNA polymorphism and brain tumours (Review)

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Introduction: Brain tumor refers to a collection of brain neoplasm that either originates from the central nervous system or presents as a metastasis from other neoplasms. Primary malignant tumors of the nervous system constitute 2.3% of all human malignant tumors and cause the death of more than thousands of people in the world every year. Therefore, efficient methods for rapid diagnosis of brain tumors are vital. MicroRNA (miRNA) are non-protein-coding RNAs that regulate gene expression at the post-transcriptional level, and they mostly include 19–24 nucleotides. These molecules are an important regulator of gene expression, and they are considered to have an important role in pathological processes like cancer. Therefore, our aim in this study is to investigate the relationship between different miRNA polymorphisms and brain tumors.

Methods: For this research, existing articles in PubMed, Web of Science, Sid, and Google Scholar databases that have been published till 2022 are systematically selected, and 10 articles are included in this study. This research is done in English considering the following keywords: Brain Neoplasms, microRNA, and polymorphism.

Results: Studies show that there is a significant relationship between some miRNA and tumor grade. Deregulation of miRNA in the cerebrospinal nervous system (CSF) is considered to be a factor in brain tumors. Some miRNAs can be anti-apoptotic agents, and some of them can act as silencers of anti-apoptotic agents. MiR-21 roles as an oncogenic agent in glioblastoma multiform (GBM) by blocking genes that induce apoptosis. The GG genotype of miR-146a shows a higher risk of developing brain tumors in comparison with the GC genotype. CC genotype of the pir-miR-34b/c rs4938723 shows a lower risk of glioma compared to the TT genotype of this miRNA. On the other

side, the CC genotype of the TP53 Arg72-Pror has proved to be at a higher risk of glioma than the GG genotype. On the other hand, it's been proven that some miRNAs such as miR-129 have been increased and other miRNAs such as miR-142-5p and miR25 have significantly decreased in brain tumor samples. Some miRNAs such as miR-302-367, miR-Cdh4, miR-378a-3p, miR-342, miR-153, miR-940, miR-7-5P, miR-101, and miR-338 can inhibit growth of glioblastoma. Some miRNAs such as miR-183, miR-135b, miR-221, miR-222, miR- 4443, miR-422a, miR-494-3P, miR-502-5P, miR-520f-3p, miR-549, and miR-223 are shown to be a factor of glioblastoma.

Conclusion: In general, there is a significant relationship between some miRNAs and the development of brain tumors. Changing RNA-based biomarkers can help to diagnose different types of brain tumors, but more studies are needed in this field.

Keywords: Brain Neoplasms, MicroRNAs, Polymorphism

Relationship between serum Vitamin D and Adipokines in diabetes type 2 (Research Paper)

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Introduction: Diabetes is one of the metabolic diseases in which various factors play a role. The role of adipokines in causing inflammation in adipose tissue and subsequent brief inflammation in the body is known, which can be the cause of diabetes and increase the speed of disease progression and its serious complications. Research has shown that adipokines and vitamin D may be associated with the onset or progression of type 2 diabetes. Objective: The aim of this study was to investigate the relationship between serum vitamin D and adipokine levels in type 2 diabetic patients.

Methods: This case-control study was performed on 30 patients with type 2 diabetes in Mashhad hospitals in 2020 and 30 healthy individuals. The lipid profile, creatinine, uric acid, fasting blood sugar, HbA1c, and blood pressure were registered. Insulin resistance was measured using the HOMA-IR formula. Serum levels of vitamin D, Adiponectin, and Resistin were measured by ELISA method. The software used in this study is SPSS v.24, and the significance level of the tests is considered less than 5%.

Results: Thirty patients with a mean age of 52.90±10.38 years including 16 women and 31 healthy individuals with a mean age of 48.53±10.36 years including 16 women were studied. BMI level (P=0.002), systolic blood pressure (P=0.034), fasting blood sugar (FBS) level, HbA1c, insulin, insulin resistance, and resistin levels in diabetic patients were significantly higher than the control group (P<0.05). Vitamin D and adiponectin levels were significantly different between the two groups which the control group was significantly higher than the case group (P<0.05).

Conclusion: Our results showed that resistin and adiponectin had a significant inverse relationship with vitamin D. In addition, resistin has a significant direct relationship with HbA1C and FBS, while adiponectin has a significant inverse relationship with insulin resistance, insulin, and creatinine levels. Therefore, controlling these parameters can help improve diabetes.

Keywords: Type 2 diabetes, Adiponectin, Resistin, Vitamin D

Relationship of Cognitive Emotion Regulation and Meaning in Life With Health Anxiety (Review)

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Introduction: The history of anxiety disorder research exemplifies how an emphasis on empirical research can facilitate theoretical and practical developments. The purpose of this review is to explore how data derived from emotion regulation studies might similarly advance existing anxiety including health anxiety disorder theory. Emotion regulation can be defined as all of the external and internal processes that an individual uses to monitor, evaluate, and modify the nature and course of an emotional response. It is the ability to direct spontaneous reactions and the ability to delay spontaneous reactions in a way that is sufficiently flexible and socially tolerable. Health anxiety is when someone spends so much time worrying about its ill, or about getting ill, when there are no signs of illness or any health problem and it starts to take over their life. Represents a dimensional and multifactorial construct consisting of cognitive, behavioral, affective, and perceptual components. The construct of emotion regulation has been increasingly investigated in the last two decades, and this work has important implications for advancing anxiety disorder theory. Depending on the type of emotion regulation strategy used, movement regulation can reduce or increase fear.

Methods: In this systematic review, the data required for this study were collected using keywords and based on reliable databases such as Google Scholar, PubMed, Scopus and ProQuest. In this study, our statistical population includes all articles registered until 2022. After reviewing the relevant findings and evaluating the quality of the obtained data, 17 articles were analyzed.

Results: regulation of emotion and anxiety can be distinguished at the neural, conceptual and behavioral levels of analysis. It is a defensive response against potential sources of anxiety, which includes obvious behavioral,

physiological, and cognitive indicators, and is also neurologically located around the amygdala. According to neurobehavioral research, the amygdala may mediate cognitive, behavioral, and physiological indicators of fear. Studies have shown that emotion regulation techniques have an effect on these verbal-cognitive, behavioral and physiological indicators. Cognitive coping processes have long been involved in the expression of feelings and experiences. Recently, a new instrument, the cognitive emotion regulation questionnaire was developed to measure nine different cognitive coping strategies people often: self-blame, other blame, rumination, catastrophizing, acceptance, putting into perspective, positive refocus, refocus on planning, and positive reappraisal. Results supported the convergent and discriminant validity of the research. In the research, it was found that there is a difference between the results of the cognitive strategies of emotion regulation. Adaptive strategies have a negative relationship with anxiety symptoms. While maladaptive strategies were found to be positively associated with depressive symptoms. Neuroimaging studies indicate that emotion regulation and fear involve distinct neural regions, and that neural regions mediating fear are negatively correlated with neural regions mediating emotion regulation during reappraisal. Therefore, emotion regulation appears to be a distinct construct that may causally influence anxiety including health anxiety expression. Results of Studies revealed significant and consistent associations between the dimensions of health anxiety and dysfunctional coping and emotion regulation strategies. And the associations between health anxiety and strategies of coping. In other studies there is a significant relationship between positive and negative emotional regulation strategies and health anxiety with the mediating role of emotional ataxia. On the other hand, other significant coefficients were observed between emotion regulation strategy with health anxiety attitude and disaster emotion regulation strategies, rumination with emotional distress

Conclusion: The results suggested a significant relationship between cognitive emotion regulation and health anxiety, especially in the subscale of rumination in terms of negative cognitive emotion regulation. Also, Results show that meaning in life has significant negative relationship with health anxiety Also it has been showed that higher presence of meaning in life, as a coping skill, was associated with less health anxiety. Having meaning in life is a useful coping skill that enables people to enjoy good times and endure bad time and Purposeful work. Even when constructs of emotional reactivity, such as depression and generalized anxiety, are controlled for, there is a significant association between difficulties in emotion regulation and anxiety disorder symptoms. Emotion regulation can strengthen the effect that emotional response has on symptoms. Accordingly, these data compliment experimental research demonstrating that emotion regulation techniques can augment or diminish anxiety and related psychopathology.

Keywords: health ,anxiety, emotion ,regulation, life

Relative expression analysis of CXCL8 mRNA in colon cancer: a study based on gene expression omnibus (GEO) and bioinformatics analysis. (Research Paper)

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Introduction: In most cases, colon cancer originates from intestinal polyps, which usually do not cause any specific clinical symptoms in the body, but turn into cancer over time. Colon polyps are lumps of flesh that originate from the inner lining of the colon. A person with an intestinal polyp may not have any symptoms or discomfort. But these polyps may turn into cancer if not treated. Colon cancer almost always originates from polyps or premalignant lesions of the intestine. Therefore, polyps should be removed from the colon to prevent cancer.Treatments for colon cancer can include a combination of surgery, radiation, chemotherapy, and targeted therapy. colorectal Cancer(CRC) is on of the most common malignant diseases in the world,and it's incidences increased with age.The signs and symptoms of this disease can include things such as blood in the stool (hematochezia), changes in bowel movements and bowel movements, weight loss, and constant fatigue.

Methods: First GSE(185770) were downloaded from NCBI GENE Expression omnibus(GEO). GEPIA2 and ENCORI analyzed the data sets to find out differentially expressed genes in patients.Pathway enrichment was performment KEGG.We usedfor the probability cause of increased expression SNPs located on the 3'UTR region.from the STRING site for interaction pro-pro and intraction miRNA-MRNA from mirwalk database and intraction LncRNA-miRNA from the LncRRisearch and intraction mRNA-LncRNA from the Lncbase3 search it.

Results: CXCL8 had a significant high expression in the tumor samples.(logFc=2.79 ,adj=1.537e_02).Also in databases GEPIA2 and ENCORI expression increase in cancer cells was significant.CXCL8 is in Malaria pathway. This has-MIR 374a-3p suppresses the CXCL8 gene.and we found by blacing diffrent genes HELLPAR Lnc RNA. HELLPAR Lnc RNA intraction was observed in CeRNA.rs769138009 in gene 3'UTR cause target loss.

Conclusion: As a result of this study, concluded that HELLPAR LncRNA act as a tumor suppressor in colorectal cancer(CRC) by inhibiting the function of

the has-mir-374a-3p mirRNA so it blocks miRNA sponging and eventually represses the CXCL8 gene which is an important gene for metabolism and biosynthesis.therefore,this result may be considered as potenial therapeutic purpose for CRC patients.

Keywords: Biomarker, Microarray analysis, RNA interacton, Systems Biology

Relative expression anglysis of COl1A1 mRNA in Clear Cell Renal Cell Carcinoma(ccRCC),Bioinformatics gene expression profiling and rna interaction analysis (Research Paper)

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Introduction: Clear cell Reual Cell Carcinoma(ccRCC) is a type of Kidney cancer that causes tumors to grow in side your Kidneys.ccRCC is also called coventional renal cell .RCC arises from the renal cortex or the renal tubular epithelial cells.In adult,ccRCC is the most common type of kidney cancer,and makes up about 80% of all renal cell carcinoma cause. currently,it is the 7th most common cancer amang men.The purpose of this research,is how it to express a specific Gene and analysis it in various databases to target novel biomarkers for diagnosis and treatment of ccRCC.

Methods: Gena expression data of ccRCC patients (GSE 105261) was obtained From the NCBI Gene Expression Omnibus (GEO) and then analyzed by ENCORI and GEPIA2 to Find differentially expressed genes.We Found evidence based on signaling pathways with REACTOM and KEGG From ENRICHR database. Then the miRNA SNP site was used For the possible cause of increased expression of SNPs located on the 3'UTR region. One to the most significant gene was taken to miRWalk to Find target miRNA.Target miRNA was search in LncRRIsearch , and appropriate LncRNA was Found. At last,LncBasev.3 was used to show the interaction between the componets of the CeRNA network.

Results: Based on microarray analysis COl1A1 have a significant up_regulation (|log FC|=2/987 , adj.P value=5/71e-04)in the kidney cancer. According to the data we obtained From ENCORI and GEPIA2 sites, we came to the conclusion that the studied gene is significant and has caused an increase in the expression in cancer. COL1A1 is in Extrancellular matrix organization Homo sapiens and AGE _RAGE signaling pathway in diabetic complications. rs 1219390329 in gene 3'UTR cause target loss.miR_10a_5p is a noval suppressor For COL1A1(score:1.00),and this miRNA have RNA interaction with NORAD LncRNR.HEIH LncRNA interaction was observed in CeRNA network.

Conclusion: in conclusion this finding could be suggested novel interactions among lncRNA, mRNA, and miRNA (NORAD , COL1A1 , hsa-miR-10a-5p) for

the candidate diagnostic and prognostic markers associated with KIRC by bioinformatics analysis. We believe that, without any severe negativeside effects, this ceRNA network could be used as a potential tool for both preventative and adjuvant treatment techniques in KIRC patients.

Keywords: Biomarker,Microarray,COL1A1,Bioinformatics cancer,RNA interaction.

Remodeling of extracellular matrix during cancer metastasis (Review)

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Introduction: Metastasis of cancer cells accounts for about 90% of patient mortality, as spread of neoplastic cells to organs such as liver and lung makes their eradication challenging. Cancer cells grow in a dynamic tumor microenvironment consists of various types of stromal cells, lymphatic network and extracellular matrix (ECM). Beside serving as a scaffold, ECM undergoes vast remodeling during different stages of tumorigenesis that influences migration, adhesion, survival, proliferation and differentiation of cancer cells. In present review, we focused on biochemical modifications of ECM associated with migration and invasion of cancer cells.

Methods: Recent review articles included key words extracellular matrix, metastasis, ECM remodeling, cellular deposition and protein composition were extracted from databases Google Scholar, Web of Science, PubMed and Scopus.

Results: Remodeling of ECM, which affects abundance, structure and organization of its components, can be divided into ECM deposition, chemical modifications and proteolytic degradation. Stromal cells are major depositors of ECM components that secret various growth and inflammatory factors such as TGF-α, TGF-β, FGF-2, PDGF and EGF, as well as matrix metalloproteinases (MMPs) and chemokines. Chemical modifications of ECM components, which affect their complexity and three-dimensional topology, include hydroxylation, glycosylation, carbamylation and isomerization of collagen, phosphorylation of fibronectin, MMPs and laminin, sulphation of glycosaminoglycans and cross-linking between collagen, fibronectin and elastin. Degradation of ECM components are mediated by target-specific proteases, such as MMPs, and proteases that specifically cleave at serine, cysteine and threonine residues. The proteolytic enzymes secreted by cancer and stromal cells serve multiple roles during tumor progression; they allow progressive destruction of normal ECM and its replacement with tumor-derived ECM, they release ECM-bound growth factors and thereby increase their bioavailability, and more importantly, they pave the way for cell motility.

Conclusion: Remodeling of ECM not only supports tumor growth, also promotes migration of cancer cells and modifies the ECM in distant organs to

allow for metastatic progression. Deeper understanding of ECM remodeling and its underlying mechanisms would lead to developing therapeutic approaches for cancer patients and/or prevent malignancy.

Keywords: Extracellular matrix, Remodeling, Metastasis, Chemical modification, Proteolytic degradation.

Restoration of Ovarian Tissue Endocrine Function and Estrous Cycle in Mice After Autografting Using Platelet Lysate (Research Paper)

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Introduction: Ovarian tissue transplantation is performed to preserve fertility in cancer patients. However, one of the major problems associated with this procedure is ischemia/reperfusion (IR) injury which leads to apoptosis and serious loss of the follicular reservoir within the first few days after transplantation. Platelet Lysate (PL) as a potent anti-oxidant, anti-apoptotic and anti-inflammatory agent, can prevent graft damages due to IR. The aim of this study was to investigate the effect of PL injection on the endocrine function of the transplanted mouse ovarian tissue.

Methods: In this experimental study, Naval Medical Research Institute (NMRI) mice were divided into following groups: Control, autograft and autograft + PL (5mg/kg daily intrapritoneal injections). After 28 days, blood samples were collected and levels of progesterone (P4) and estradiol (E2) in serum samples were analyzed. In order to evaluate the resumption of cyclic ovarian activity following transplantation, daily vaginal smears were taken, starting on day 7 post-transplantation. Data were analyzed using one-way analysis of variance (ANOVA) and Tukey's test, and the means were considered significantly different at p < 0.05.

Results: The serum level of progesterone and estradiol were significantly lower in the autografted group compared to the control counterpart, whereas in the autografted + PL group, the mentioned parameters were significantly higher when compared to the autografted group. In addition, the estrous cycle recovery was more rapid in the autografted + PL group than the autografted group.

Conclusion: PL can restore the endocrine function of the transplanted ovaries through reducing oxidative stress and inflammation.

Keywords: Platelet Lysate, Mice, Ovarian graft, Endocrine function.

Review of Genetic Profile of Recurrent Implantation Failure (Review)

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Introduction: Introduction: Successful implantation is a complex and imperative process in which a mature blastocyst-stage embryo attaches and invades the receptive endometrium for placentation and achieving an ongoing pregnancy. Implantation can occur during a short and restricted period, known as the window of implantation (WOI) (days 20–24 of the cycle, during the secretory phase), depends on high endometrial receptivity. During WOI, a synchronization between embryo development and endometrial status, as well as a proper two-way interaction between them are critical that depend on many molecular, physiological and genetic factors involved in this process. Compared to other mammals, human implantation success is quite inefficient. According to studies, 75% of women that suffer from recurrent pregnancy loss are diagnosed as recurrent implantation failure (RIF) and among patients under infertility treatment, 15% experience RIF. Regarding to the complexity of the implantation process, there are some causes for RIF, which one of most important of them is genomic and epigenomic factors that could be also divided into uterine and embryo genetic factors. This review tries to summarize these genomic factors involved in RIF. Regarding evidence has demonstrated a role for genetic and epigenetic regulation in endometrial function and embryo development and survival both in physiological and pathological conditions so, many genomic factors involved in the embryo implantation and various single-nucleotide polymorphisms (SNPs) have been reported to be associated with RIF. Several studies have analyzed some epigenetic modifications, focusing on long non-coding RNAs (lncRNAs) or microRNAs (miRNA) in RIF. Revel et al. (2011) first showed a different miRNA expression profile in the secretory endometrium from women with RIF in compared with fertile women. Then investigations indicated that some miRNAs regulating molecular pathways and target genes crucial for implantation (endometrial receptivity and embryo development and survival) are dysregulated in patients with RIF. Polymorphisms of microRNAs such as miR-449bA>G, miR-27a rs895819 and miR-449b rs10061133 involved in the expression of several implantation genes might be related to RIF pathogenesis. Also, according to several analyses, it was revealed that inherited thrombophilia could be a risk factor of RIF. It was observed that the presence of factor V Leiden and mutation of methylene tetrahydrofolate reductase (MTHFR) were associated with RIF and 68.9% of patients with RIF after the first IVF-embryo transfer cycle had inherited thrombophilia. However, there were some analysis that did not reveal this relation. Moreover, some variants of p53 gene, as regulator of cell growth and inducer of angiogenesis,

are linked with RIF. Furthermore, some recent studies have shown an association between p53 rs1042522 (R72P, G/C) and p53 rs17878362 (Ins16bp, N/D) polymorphism and the risk of implantation failure. In addition, it was also investigated that polymorphism of human leukocyte antigen (HLA)-G, an important factor of the immunomodulatory system and implantation, such as rs1632947, rs1233334, rs371194629 HLA-G, as well as, HLA-G 14-bp polymorphism were significantly correlated with RIF occurrence. Also, several variants of VEGF, an angiogenetic factor involved in implantation process, such as –1154A>G were indicated as a significant risk factor of RIF. Finally, another genetic factor associated with RIF is several variants of the estrogen receptor 1 (ESR1) gene such as ESR1/AA (rs12199722) genotype, which was common in the RIF group compared with women who became pregnant on their first cycle of IVF/intracytoplasmic sperm injection.

Methods: Method: In this literature review, publications available in PubMed and Scopus databases, as well as in Google Scholar were taken into account. Eligibility criteria included studies on genomic and epigenomic factors of recurrent implantation failure.

Results: Genetic and epigenetic polymorphisms of all genes involved in embryo development and survival, as well as endometrial receptivity could lead to impossibility of embryo nesting and recurrent implantation failure occurrence that is a great challenge for human reproductive medicine.

Conclusion: Conclusion: Genetic and epigenetic polymorphisms of all genes involved in embryo development and survival, as well as endometrial receptivity could lead to impossibility of embryo nesting and recurrent implantation failure occurrence that is a great challenge for human reproductive medicine.

Keywords: Keywords: implantation, recurrent implantation failure, genetic factor, polymorphism

Reviewing the nature of virtual education and its challenges during the covid-19 pandemic in Iran's university system (Review)

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Introduction: Education systems play an important role in economic and social development. The technological advances have changed the university teaching and student learning. Virtual education as a new attitude has developed in the field of learning. The first time virtual education was revealed in the UK, but Americans executed it for the first time. This education has been developed and applied in different countries for many years, but the real development was due to the Internet globally spread. The development of virtual education in Iran is related to the last two decades in Tehran University. The COVID-19 pandemic changed all social mechanisms, including education. Staying at home and quarantine, closure of offices and organizations, telecommuting, distance learning were the consequences of this virus for the whole world.

Methods: The present study is a comprehensive review that was conducted in order to identify the nature and challenges of virtual education in university education. International and national databases including Scopus, PubMed, Science Direct, ISC, SID, and Magiran were used for searching. Keywords included virtual education, university education, teaching, and learning. The search was done without time limit and the findings were presented in text format.

Results: Virtual education is mentioned to as the method of training where the teacher and student are divided by time, space or both. In compare to the traditional methods where training is offered face to face in classrooms, laboratories, etc., in virtual education, technological tools like internet, video conferencing, multi-media, mobile phones, tablets, etc. support the instruction. The challenges of the traditional system, the rapid development of the web as a potential underlying factor in online courses, the benefits of e-learning and budget constraints have provided significant incentives for universities to grow and develop virtual education. Flexible learning, choose the time, place, and duration of learning, speed of learning, attention to learners' learning styles, saving on educational expenses including travel costs to cities where universities are located, and holding courses by important universities have made virtual education courses popular in world. Many countries have been taking virtual education seriously for years ago and have provided the necessary context. Therefore, they were ready to deal with the crisis. Iran was used virtual education in a limited way previously. However, the mandatory

use of this type of education provided a transformative opportunity for higher education system in Iran. Virtual education system was launched in almost all Iranian universities including public and private after COVID-19 pandemic. Due to the global use, there was an opportunity to identify education problems. The access to the internet and related costs, lack of planning and therefore non-presentation of practical courses, unwillingness of some professors to technology using were some observed problems in the field of virtual education in Iran.

Conclusion: Based on studies, the shortage of necessary software and hardware infrastructures, limit in bandwidth, the costs of Internet, organizational and cultural obstacles were seen as main barriers of the development of virtual education in developed countries at the beginning. Considering the uncertainty of the end of COVID-19, the benefits of virtual education and the desire to continue it in the post-corona, it seems necessary to identify weaknesses and obstacles and provide solution and infrastructure by education planners and policymakers in Iran.

Keywords: Virtual education; university; COVID-19; teaching; learning

Role and relevance of NFκB signaling pathway in cancer (Review)

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Introduction: Cell signaling is where the cell responds to the stimuli of molecules leaving the cell that reaches the cytomembrane or binds within the cell cytoplasm. This binding to receptors transmits signals to the nucleus and induces the corresponding natural phenomenon, thus producing biological effects and cellular responses. The nuclear factor-kappa B (NFkB) signaling pathway may be a multicomponent pathway that regulates the expression of the many genes and organismal processes. Currently, the role of the NFκB signaling pathway in cell biogenic activities could also be a hot spot in cancer research. NFκB signaling is involved in cellular immunity, inflammation, and stress, additionally with the regulation of cell differentiation, proliferation, and apoptosis. The NFκB pathway is commonly altered in both solid and hematopoietic malignancies, promoting tumor cell proliferation and survival. NFkB is constitutively active in most tumor cell lines, whether derived from hematopoietic or solid tumors. However, recent evidence suggests that NFκB plays a tumor suppressor role in certain cancers through the transcriptional activation of the Fas ligand.

Methods: In this article, the role of NFκB signaling pathway in cancer has been investigated, and the articles from 2015 to 2022 have been reviewed from Pubmed and Science Direct databases.

Results: The nuclear factor kappa B (NF-κB) family of transcription factors plays an essential role as stressors in the cellular environment and controls the expression of important regulatory genes such as immunity, inflammation, cell death, and proliferation. NF-κB protein is located in the cytoplasm and can be activated by various cellular stimuli. There are two pathways for NF-κB activation, canonical and non-canonical pathways, which require complex molecular interactions with adapter proteins and phosphorylation and ubiquitinase enzymes. Accordingly, it increases NF-κB translocation into the nucleus and regulates gene expression. Two signaling pathways lead to NFkB activation, known as the canonical (classical) pathway and the non-canonical pathway (alternative pathway).

Conclusion: Cancer is a group of cells that grow malignantly and multiply uncontrollably. Currently, cancer treatment methods mainly include surgery, chemotherapy, radiotherapy, molecular targeted therapy, gene therapy, and immunotherapy. However, the therapeutic effects of these treatments have so far been limited by the specific characteristics of tumors. Abnormal activation of signaling pathways is involved in tumor pathogenesis and plays an important role in cancer growth, progression and recurrence. Targeted therapies against factors affecting oncogenic signaling have improved the outcomes of cancer patients. NFκB is an important signaling pathway involved in the pathogenesis and treatment of cancer. Overactivation of the NFκB signaling pathway has been documented in various tumor tissues, and studies on this signaling pathway have become a hot topic for targeted cancer therapy. Nuclear factor kappa B (NFκB) is a key regulator of immune development, immune responses, inflammation, and cancer.

Keywords: NFκB signaling pathway, cancer,

Role miR-21 as a potential biomarker in Diffuse large B-cell lymphoma (DLBCL) (Review)

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Introduction: Diffuse large B-cell lymphoma (DLBCL) is classified as a subtype of non-Hodgkin's lymphoma, accounting for 30-40% of all non-Hodgkin's lymphomas. Based on gene expression profiling (GEP), DLBCL is divided into two molecular subgroups, active b-cell-like (ABC) and the germinal B-cell-like (GBC) (1), (2), and (3). The miRNAs (microRNAs) are a class of non-coding RNAs that participate in the post-transcriptional control of target gene expression that makes cellular identity. miRNAs are the 19-23 nucleotide RNAs that play a critical role in regulating cell proliferation, invasion, and migration in tumors (4) and (5). Overexpression of miR-21 has been well characterized in association with some of tumor types including lung, breast, stomach, prostate, colon, and pancreatic tumors. For example, the miR-21 level increased in glioblastoma, and also miR-21 had antiapoptotic properties. In addition, some studies have shown the correlation between overexpression of mir21 and poor outcomes in cancer treatment (6), (7), (8), and (9). The purpose of the current review study was to investigate the role of miR-21 as a potential biomarker in Diffuse large B-cell lymphoma (DLBCL).

Methods: We assessed the most recent studies on miR-21 in different lymphoma types. The publications were identified by searching PubMed. Then studies were selected based on keywords ((“Diffuse large B-cell lymphoma” OR “DLBCL”) AND “miR-21”).

Results: Increasing evidence has shown that miR-21 as an oncomiR play an important role in lymphoma. knocking down miR-21 has demonstrated that miR- 21 is increased under inflammatory conditions. Therefore, miR-21 could be helpful in the diagnosis, prognosis, and treatment of DLBCL.

Conclusion: Mir-21 could be suggested as a potential biomarker for DLBCL diagnoses or a prognostic factor. Moreover, the mentioned microRNA may also be promising therapeutic targets. However, it is necessary to do some cohort studies in the future.

Keywords: Biomarker, DLBCL, miR-21, miRNA

Role of miRNAs in Hepatocellular Carcinoma: Tumor suppressor, oncogenic, Carcinogenesis, Progression, and Therapeutic Target (Research Paper)

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Introduction: The liver is one of the most important organs of the human body and any disorder in this vital organ causes acute problems for the patient. Because the liver plays an important role in eliminating and excreting natural and artificial toxins from the blood . MicroRNAs, on the other hand, have significant properties in controlling cancer cells and can be considered as key targets for understanding the pathways that lead to cancer. miR-101 is one of the Tumor suppressor microRNAs that is associated with decreased expression in hepatocellular carcinoma, this prevents the cells from dividing and metastasizing abnormally to the surrounding tissues and prevents abnormal cell death, so miR-101 targets the Mcl1 gene, which is a suppressor gene. Tumor in the TGF_B molecular pathway of the liver prevents the spread of tumorigenesis in the liver and adjacent tissues. Therefore, the aim of this study was to evaluate the bioinformatics of miR-101 in inhibiting tumorigenesis of liver carcinoma cells by acting on the tumor suppressor gene Mcl1 in the TGF_B molecular pathway and preventing its metastasis to other organs using databases and algorithms. To further investigate the role of this microRNA as a metastasis suppressor and inhibitor of tumorigenesis, as well as its effect on the Mcl1 gene as a diagnostic / prognostic biomaker in the treatment of liver cancer.

Methods: In this study, using bioinformatics algorithms, first to investigate the role of microRNA-101 in liver cancer, to look for changes in the expression of microRNA-101 in this disease at OncomiR site and then to investigate the role of microRNA-101 in pathways Interfering signaling in liver cancer pathogenicity, miR-101 is examined in the bioinformatics site mirPath v.3. Then, by entering the full name of microRNA-101 in the window related to the KEGG database and selecting the TarBase V.7 algorithm, we will examine the molecular paths and thermal map of the miR-101. Finally, to ensure the accuracy of the results and prevent false positive results, 11 known online gene target prediction databases are used in the miRWalk 0.2 database. R software is also used in further interaction studies (first to control the existing raw data using the Limma package, available in the Graph prism and R software by PCA) and then to normalize the microarrays using It is done by LOESS method and between samples by several methods. Criteria for gene identification are evaluated by differential expression and significance of Fold Change> 2 and Pvalue <0.05.

Results: The relationship miR-101 with HCC from bioinformatic data in HCC was mined. Using bioinformatics algorithms and statistical analysis with R and Graph prism software Information profiling uncovered that when By reducing the expression of miR-101 gene, it has tumor suppressive properties.

Conclusion: The value of miR-101-3p and miR-101-5p has been evaluated as biomarkers for early diagnosis of HCC; Because it reduced the expression of PTEN and Mcl1 genes in the TGF-B signaling pathway, and in addition, their molecular mechanisms provide the results of a deeper understanding of the role of miR-101-3p/5p in HCC.

Keywords: Liver Cancer - Biomarker - Algorithm-HCC

Role of Ultrasound in Predicting Tumor Invasiveness in Follicular Variant of Papillary Thyroid Cerci… (Review)

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Introduction: In contemporary years, the superiority of thyroid maximum cancers has been at Therese, making it the most now no longer unusual place malignant tumor of the endocrine tool with inside the world. chance element for recurrence and awful PTM Cs Therefore, early detection of cervical metastasis. Currently, sonography is the modality of choice for supplying steering for fine-needle aspiration biopsy and for imaging of cervical lymph nodes in patients with PTC, for every preoperative and postoperative surveillance.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Role of Ultrasound in Predicting Tumor Invasiveness in Follicular Variant of Papillary Thyroid Cerci. After reviewing the relevant findings and evaluating the data quality, a total of 19 articles were analyzed.

Results: According to the World Health Organization elegance tool, according micro carcinoma (PTMC) is defined as a thyroid maximum cancer measuring ≤1.0 papillary thyroid in its exceptional dimension. Reportedly, a thyroid maximum cancer account for approximately30% of all papillary thyroid cancers PTC Thyroid maximum cancers, together with PTMC, Lymph coin is the most crucial. In some patients with early metastasis overall survival of distinguishing features, the presence or absence of number one lymph node lets to determine the surgical plan for a procedure and carefully related to the evaluation and survival of PTC patients. Certain features of thyroid nodules on

ultrasound (US)are usually predictive of malignancy and are and alack requirements for FNA. These requirements have numerous lymph node specificity, but regrettably none of them determine sufficient to discard or come across malignancy efficiently. Furthermore, there may be large PCs Andes in the assessment and reporting of some of Certain patterns. Used as the most crucial requirements for nodule desire is thyroid sensitivity and. The largest diameter in most of the studies have come to be at the least 2 cm. However, one has a look at included nodules with duration from 1 cm, alohas be described via evolving approach with greater experience. Other studies used nodule amount as requirements for inclusion, Furthermore, variability from 4 to 12 ml in published studies. Based on the fact according slow amount to reduce charge is used due to the fact in its of effectiveness after RFA, it might be, Lymph to use amount as an inclusion criterion as well. To been discussions about how initial nodule duration or in the treatment effects, and its miles been considered that RFA Used effective effects if nodule amount is a lot an entire lot ton much less than 20 ml. Patients with big nodules also can moreover require a couple of inclusion, if it's far possible, preferably surgical treatment due to the fact the first – line that nodule. Three-dimensional imaging, and the necessities, permitting more correct provide a much greater unique assessment. Improved discrimination There had, and malignant nodules can help determine which nodules need to undergo quantity impacts aspiration biopsy (FNA), and numerous malignant it has been defined, together with micro calcifications, hypo echogenicity, an odd margin, lack of the halo, gives more

Conclusion: Micro calcification and an abnormal form are predictors of LNM in thyroid carcinoma sufferers. In addition, avionics' evaluation has promising fee in screening significant ultrasound functions in thyroid most cancers sufferers with LNM. Therefore, the prediction of LNM primarily based totally on ultrasound functions and radio mic features is beneficial for making suitable selections concerning surgery and interventions earlier than thyroid carcinoma surgery. Ultrasonography turned into proved to be a treasured technique for preoperative analysis of PCs. Hypo echogenicity and abnormal margins had been strongly related to PCs. Therefore, the cervical lymph nodes ought to be cautiously tested via way of means of ultrasonography in sufferers with PCs

Keywords: Papillary thyroid carcinoma ‹Ultrasonography ‹Lymph node metastasis ‹Thyroid Cancer

Rs94142948 modulates the neurodegeneration signaling pathway by regulating the expression level of FAM90A in the retinoblastoma patients: integrated systems biology and bioinformatics investigation (Research Paper)

Saba Hojjati,[1,*] Mohammad Rezaei,[2]

1.
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Introduction: Retinoblastoma is a rare type of eye cancer that usually develops in early childhood, typically before the age of 5. This form of cancer develops in the retina, which is the specialized light-sensitive tissue at the back of the eye that detects light and color.In children with retinoblastoma, the disease often affects only one eye. However, one out of three children with retinoblastoma develops cancer in both eyes. The most common first sign of retinoblastoma is a visible whiteness in the pupil called "cat's eye reflex" or leukocoria . Retinoblastoma is diagnosed in 250 to 350 children per year in the United States. It accounts for about 4 percent of all cancers in children younger than 15 years.

Methods: First of all, GSE208143 raw data was selected from Gene Expression Omnibus (GEO) and analyze by R studio to obtain differentially expressed genes(DEGs). The limma package was used for the statistical analyses and finding the novel DEGs. Protein-protein interaction analysis was performed by STRING online software. Pathway enrichment analysis was performed by ENRICHR. Single nucleotide polymorphism (SNP) analysis was performed by miRNASNP v3.

Results: Based on the microarray analysis, FAM90A1 (logFC: 4.37 , adj. P. Val: 8.942507e-05) has a significant uo-regulation in the retinoblastoma patients, compared to control. ALG1, USP31, RFPL4A, ZNF329, FAM90a26, and ZNF195 has a significant protein interaction with FAM90A1. Based on the pathway enrichment analysis, FAM90A1 and its interactome has a significant contribution in the regulation of Endocytosis and Pathways of neurodegeneration signaling pathway. miRNASNP analysis revealed that rs941412948 (A/G) regulates the expression level of FAM90A1 by reducing the binding affinity of hsa-miR-7-2-3P, hsa- miR-495-3P, hsa-miR-5688, hsa-miR-1323, hsa-miR-5480-3P, hsa-miR-7-1-3P, and hsa-miR-607 miRNAs to this mRNA. miRWalk online database validates the interaction of mentioned microRNAs with FAM90A1.

Conclusion: Rs941412948 has a significant novel role in the modulating the Endocytosis and Pathways of neurodegeneration signaling pathway by

regulating the expression level of FAM90A1 in the retinoblastoma patients. Mentioned region of DNA could be a novel therapeutic target for the prognosis, diagnosis, and possible treatment strategies for retinoblastoma patients.

Keywords: Systems biology, Bioinformatics, Retinoblastoma, Nervous system, Network analysis

Salivary Biomarkers Of Myocardial Infarction: A Review (Review)

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Introduction: Myocardial infarction is one of the presentations of the acute coronary syndrome(ACS). Myocardial infarction could be fatal and it can also cause long-term complications that decrease the patient's lifelong survival. According to the World health organization (WHO), the leading cause of death in 2019 was ischemic heart diseases, being responsible for 16% of the world's total death. As we know, in diagnosing myocardial infarction “time is muscle”; Routinely, serum levels of cardiac biomarkers such as cardiac troponin (cTn), creatine phosphokinase (CK), and its MB isoenzyme are used for the diagnosis of myocardial infarction. Whole saliva, produced by salivary glands, consists of more than 1000 proteins and 19000 peptide sequences. Using MI-related biomarkers in saliva as a diagnostic method has been a trending topic over the past several years. This method has several advantages such as being noninvasive and safe to collect, it’s affordable and serial monitoring is quite simple. In this review, we went go through articles that focused on the salivary level of cardiac biomarkers in course of myocardial infarction and discuss the advantages and disadvantages of this method against the routine use of serum levels of the so-mentioned biomarkers.

Methods: Myocardial infarction is one of the presentations of the acute coronary syndrome(ACS). Myocardial infarction could be fatal and it can also cause long-term complications that decrease the patient's lifelong survival. According to the World health organization (WHO), the leading cause of death in 2019 was ischemic heart diseases, being responsible for 16% of the world's total death. As we know, in diagnosing myocardial infarction “time is muscle”; Routinely, serum levels of cardiac biomarkers such as cardiac troponin (cTn), creatine phosphokinase (CK), and its MB isoenzyme are used for the diagnosis of myocardial infarction. Whole saliva, produced by salivary glands, consists of more than 1000 proteins and 19000 peptide sequences. Using MI-related biomarkers in saliva as a diagnostic method has been a trending topic over the past several years. This method has several advantages such as being noninvasive and safe to collect, it’s affordable and serial monitoring is quite simple. In this review, we went go through articles that focused on the salivary level of cardiac biomarkers in course of myocardial infarction and

discuss the advantages and disadvantages of this method against the routine use of serum levels of the so-mentioned biomarkers.

Results: After reviewing 9 articles we went through each of these markers. Salivary cardiac troponin as a myocardial infarction biomarker was reported to be elevated significantly in three different studies. However, a study in 2013 reported that levels of salivary troponin could have a variety of patterns. Ischemia-modified albumin is another biomarker that was reported elevated in a study specifically on the first day after myocardial infarction. Moreover, a study reported that evaluating salivary biomarkers such as CKMB, TnI, and BNP in combination with symptoms and ECG resulted in better sensitivity and specificity in the diagnosis of MI. There is also a study regarding the use of salivary CKMB. It suggested that salivary CKMB could be used as an alternative to serum CKMB. An article in 2011 suggested that Salivary CPK can be used for the diagnosis and monitoring of myocardial infarction patients. Using cathepsin L as a cardiac biomarker was reported in a study however it was concluded that salivary levels of this biomarker would not help in the diagnosis of the acute coronary syndrome.

Conclusion: In this article, we conducted a brief review regarding the use of salivary cardiac biomarkers for diagnosis of myocardial infarction. The use of this method for the diagnosis of MI has several mentioned advantages such as ease of use, being noninvasive, and could be performed in a quick manner. Also these markers could be used in other fields such as evaluation of post-myocardial infarction complications, although further studies are required in these subjects. Overall it can be concluded that the use of these salivary biomarkers has a strong correlation with myocardial infarction and specifically combined together could yield a better result, however using this method as a routine for diagnosis of myocardial infarction in a clinical setting and specific and detailed technique for collection and interpretation of these markers in saliva requires further investigation.

Keywords: Myocardial Infarction, Salivary, Biomarker, Diagnosis

Sapovirus isolates in untreated and treated wastewater; A serious public health issue (Review)

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Introduction: Waterborne enteric viruses are the emerging cause of acute gastroenteritis outbreaks and a major threat to global public health. These enteric viruses may originate from human sewage and are rapidly transmitted in aquatic environments. Sapoviruses (SaVs) and Noroviruses are the most common agents of gastroenteritis which are members of the Caliciviridae family. In general, SaV has 19 genogroups, which genogroups GI, GII, GIV, and GV are only found in humans. The clinical symptoms of SaV infection are similar to those of other enteric viruses, which include diarrhea, nausea, vomiting, and abdominal pain, and usually disappear within a week. SaVs can spread from person to person through sewage infiltration into drinking water sources and in contaminated food.

Methods: We searched for articles that were related to the presence of SaVs in water matrices in Scopus, ScienceDirect, and PubMed databases.

Results: The presence of SaV varies from 48% to 100% and 4% to 58% in treated and untreated wastewater, respectively. This suggests that wastewater treatment plants (WWTPs) are failing to completely remove the virus before discharge. This reaffirms the inefficient operation of several WWTPs around the world, which has an effect on water sources downstream of the WWTPs. According to prior studies, genogroup I (GI) was the most prevalent genogroup. GI.1 and GI.2 were also the most predominant genotypes.

Conclusion: This study has provided useful information on the presence of SaVs in water sources affected by deficient WWTWs in various nations. Furthermore, it has been demonstrated that clinically relevant SaV strains may be circulating in various water sources. Due to the low infectious dose of enteric viruses, high titers of pathogens such as SaV in insufficiently treated discharged wastewater may have a significant impact on the health of those who use the water for household, recreational, or agricultural purposes. For precise risk management, it is crucial to monitor and identify the source of enteric viruses in ambient waters.

Keywords: Sapovirus, Wastewater, Enteric viruses, Diarrhea, Acute gastroenteritis

Screening of key biomarkers and biological processes in liver cirrhosis: Evidence based on systems biology analysis (Research Paper)

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Introduction: Liver cirrhosis develops as a result of chronic hepatitis. At present, there are not effective strategies to treat liver cirrhosis, partially due to a poor understanding of the molecular mechanisms leading to cirrhosis. The present study aimed to screen key biomarkers and biological processes involved in liver cirrhosis based on systems biology analysis.

Methods: Microarray dataset GSE164760 was downloaded from the Gene Expression Omnibus (GEO) database, which including 8 cirrhotic samples and 6 healthy samples. The differentially expressed genes(DEGs) (adjusted p-value<0.05) was computed using R studio software. Protein-protein interaction network(PPI) was constructed by STRING database. Hub genes were selected by Geghi software. Gene ontology (GO) and KEGG pathway enrichment analysis of DEGs were performed with Enrichr web server.

Results: Seven key hub genes were identified with degree>=14, which were FETUB, FTCD, AMBP, AGXT, COL3A1, F2 and CXCL8. GO analysis showed that DEGs (304 genes) were mainly enriched in biological processes such as extracellular structure organization (GO:0043062, combined score=949.3), negative regulation of blood coagulation (GO:0030195, combined score=10681.5), positive regulation of neutrophil chemotaxis (GO:0090023, combined score= 3855.5) and cellular amino acid catabolic process (GO:0009063, combined score=2962.4). KEGG pathway analysis showed that up-regulated genes were mainly enriched in Focal adhesion(combined score= 677.2), Cytokine-cytokine receptor interaction (combined score=704.7) and Antigen processing and presentation(combined score=2535.3). Down-regulated genes were mainly enriched in Glycine, serine and threonine metabolism(combined score=6651.8), Complement and coagulation cascades(combined score=4718.09) and arachidonic acid metabolism(combined score=775.2).

Conclusion: In liver cirrhosis the genes involved in amino acid and fatty acid metabolism and coagulation were under-expressed and genes related to collagen synthesis and inflammation were over-expressed that can be noticed as diagnostic and therapeutic targets.

Keywords: liver cirrhosis, Hub genes, Gene ontology, systems biology

Second Primary Cancer Occurrence after Colorectal Cancer: A Systematic Review and Meta-Analysis (Research Paper)

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Introduction: Introduction: Colorectal cancer (CRC) is the third most frequent cancer diagnosis and the second leading cause of cancer-related death. There is evidence of an increased risk of developing a second primary colorectal cancer in CRC patients. This systematic review and meta-analysis aims to provide a pooled relative risk of second primary cancer after colorectal cancer (SPCAC) in CRC patients based on available evidence.

Methods: Search Method: Medline (via PubMed), Web of Science, and Scopus databases were searched for English cohort studies that reported standard incidence ratio (SIR) of SPCAC up to 10 Aug 2020. This study was performed based on the PRISMA guideline. Heterogeneity across included studies was determined using the I2 statistic. We used the random-effect models for pooled Standard Incidence Ratio (SIR) and 95% confidence intervals (CIs). Studies included if they met the following criteria: original studies with cohort design in the English language; studies that investigated and reported the SIR of second primary cancer after colorectal, colon, and rectum cancer. The pooled SIR of SPCAC based on the primary site of cancer was measured. Statistical analysis was performed using STATA version 11.0 (Stata Corp., College Station, TX)

Results: Results: A total of 6676 citations were identified through electronic database searches. After excluding 3507 duplicated papers, 3169 records were included after the screening. Through 30 extracted papers, 142429 confirmed SPCAC adult patients (more than 19 years old) were included in this meta-analysis. The SIR of SPCAC was 1.27 (95% CI 1.16-1.37) and was

reported by 12 studies. The SIR of SPCAC for digestive, reproductive, and urinary organ's involvement was 1.31 (95% CI 0.89-1.72), 1.45 (95% CI 0.99-1.90), and 1.27 (95% CI 1.10-1.45), respectively. In comparison to general populations, small intestine, endometrial, colon, and ovary cancer are most common in individuals with previous CRC and will surge in Colorectal cancer survivors (CCSs). Findings of this meta-analysis indicated that people with a history of CRCs are three times more likely prone to subsequent uterus and endometrial cancers (SIR: 3.03).

Conclusion: Conclusions: CCSs are more vulnerable to SPCAC of the small intestine and endometrium. The result of this study might be helpful for both clinicians and policymakers. Further investigations on etiologic factors for prevention and early diagnosis of SPCAC are suggested. Unavailable confounding characteristics such as smoking, alcohol intake, physical activity, food, and lifestyle, may restrict the findings.

Keywords: Secondary Cancer, Incidence, standard incidence ratio, Colorectal Cancer

Selection strategies for efficient enrichment of CHO cells in CRISPR-Cas9/RMCE hybrid system (Review)

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Introduction: Recombinant Chinese hamster ovary (CHO) cell line development (CLD) is a critical step for producing complex therapeutic glycoproteins. It is mainly based on random integration of the transgene of interest into the host genome followed by extensive screening to find stable high-producing clones. With the availability of the CHO genome and the advent of CRISPR/Cas9 technology, site-specific integration has been proposed as a potential method to address some drawbacks of the RI method. An intriguing method for accelerating CLD is the combination of CRISPR/Cas9 technology with recombinase-mediated cassette exchange (RMCE) technology. In the first step of this approach, platform cell line harboring a landing pad into a predefined locus of the host genome are generated utilizing the CRISPR/cas9 system. Then, employing the RMCE technology, any gene of interest can be inserted into the fully characterized platform cell line (1–3). In addition to the effectiveness of integration in both stages, selection strategies—which should effectively select cells that contain landing pads and enrich cells undergoing RMCE—are a key factor in achieving on-target clones quickly. Here we reviewed the selection methods applied to this end.

Methods: This study was a review and information were extracted from Google Scholar, PubMed, Science direct, and ProQuest databases by entering the desired keyword.

Results: The primary selection strategy for the first stage (platform cell line development) relies on positive selection utilizing antibiotics including puromycin, hygromycin, blasticidin, and G418 that are suitable for mammalian cell selection. Cells can be chosen with the appropriate antibiotic by including an antibiotic resistance gene in the landing pad design (4). The second strategy might involve using fluorescent activated cell sorting and including

the genes for reporter proteins like GFP or mCherry into the landing pad. This method offers a selection approach devoid of antibiotics, which is very valuable for the creation of commercial cell lines (5–7). In the second stage, cells with successful landing pad exchange with the gene of interest (GOI) should be enriched. Negative selection with ganciclovir (GCV) is one strategy provided that the thymidine kinase (TK) gene is incorporated into the landing pad to convert ganciclovir prodrug to its active form. Using this approach, it is anticipated that cells undergoing RMCE will survive after GCV selection (4,7). However, it has been noted that GCV counterselection does not completely eliminate all TK-positive cells (8,9). Therefore, it is crucial to take into account a variety of selection procedures for the second step. This step may also benefit from the aforementioned inclusion of the reporter gene into the landing pad. Indeed, cells with successful RMCE would be negative for the reporter protein and can be enriched using FACS system (5–7). Another selection strategy that has been reported as an efficient method to increase the enrichment of desirable cells is the promoter trap or poly (A) trap approach. With the promoter trap technique, the desired promoter is positioned outside of the landing pad, so that if the RMCE is accurate, a promoterless antibiotic resistance gene in the donor vector is inserted under the promoter, and desired cells survive after antibiotic selection. (7). There has also been report of using a combination of promoter and poly (A) trap. In this instance, a promoterless GOI RMCE donor vector was employed, ensuring that the GOI would only express upon the proper RMCE. In conjunction with the FACS enrichment method, this strategy can be an effective method for rapidly enriching cells that express a GOI (5).

Conclusion: The development of CHO cell lines using the CRISPR/Cas9 and RMCE combination is a two-step process that calls for an effective selection approach to enrich desired cells. Even if the effectiveness of targeted integration is low in the CRISPR or RMCE steps, stringent selection can compensate for this and eliminate any unwanted cells. As a result, combining selection options such as FACS enrichment and the promoter/poly (A) trap method could significantly shorten the CLD timeline. This work was financially supported by Pasteur Institute of Iran (grant no. BD-9579) and National Institute for Medical Research Development (NIMAD’s project no. 978694)

Keywords: CRISPR/Cas9, recombinase-mediated cassette exchange (RMCE), antibiotic selection, FACS enrichment

Self-powered biosensors (Review)

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Introduction: Today, various sensors are used to obtain various information about physiological indicators and body movements. Sensors can play a role in facilitating diagnosis and health care monitoring; So that they help the health workers in checking heart rate, temperature, breathing rate and other necessary things. Biosensors are one of the most widely used sensors in the health field, which generally has the task of converting body chemical data into an analytical signal to evaluate chemical and physiological analytes; They can measure electrons, photons or other physical properties. Due to the many applications that these self-powered biosensors can have, we decided to investigate them in this abstract.

Methods: In this review study our search based on the keywords biosensors, self-powered biosensors and Self-powered was done. We have reviewed several databases (including Google Scholar, PubMed and Scopus) since 2019. After evaluating the quality of the data, the most relevant articles were examined.

Results: Since many self-powered biosensors are available, studies have shown that enzymatic biosensors use glucose analyte as cellular fuel; After completing the investigations, this concept was used to measure glucose, fructose, cholesterol, lactate, oxygen, ethanol, acetylcholine and ascoric acid. Organelle Self-Powered Biosensors were another group of sensors; Because of the sensitivity of the organelles to different toxins, the type based on their inhibition were studied more than other types. Therefore, they are used to detect mitochondrial toxicity resulting from various drugs and pesticides. Another biosensor we examined was microbial biosensors, which, despite being less specific than enzymatic biosensors; Their development can provide the possibility to obtain microbial fuel cell (MFC). It has been seen that the presence of different concentrations of toxic and organic compounds that

reduce or inhibit the activity of microbial cells can affect the energy production by MFC.

Conclusion: According to the studies, in the evaluation of different automated electrochemical biosensors, the general advantages of higher sensitivity in many samples and the lack of need for power supply and circuits were seen as disadvantages such as more noise. More specifically, automatic enzymatic biosensors have high sensitivity and selectivity and fast response time. On the other hand, microbial biosensors had low specificity and long lifetime. For this purpose, more comprehensive research is needed to better understand the stability, response time and specificity of each biosensor. Our proposal is to further investigate cell designs, raw materials and new engineered biological catalysts.

Keywords: Biosensors, Microbial fuel cell, Self-powered

SEMA6A-AS1/miR-148a-5p/RYR2 ceRNA axis regulates the insulin secretion signaling pathway in cancerous renal patients: integrated bioinformatics and systems biology investigation (Research Paper)

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Introduction: Clear cell renal cell carcinoma (ccRCC) is the most common type of kidney cancer, comprising approximately 75% of all kidney tumors.[1]. This investigation aimed to find a novel differentially expressed gene (DEG) in the ccRCC patients compared to control samples.

Methods: Initially, gene expression data of ccRCC patients (GSE168845) was obtained from the NCBI Gene Expression Omnibus (GEO) and then analyzed by GEO2R to find differentially expressed genes (DEGs). A gene was selected for further study. Survival and expression were performed by GEPIA2[2] and ENCORI[3]. gene ontology information and biological pathway involvement were understood by using Enrichr[4], KEGG[5], and GENECARDS[6]. RYR2 was taken to miRWalk[7] to find miRNA. miRNA was searched in LncBase v.3 [8], and appropriate lncRNAs were found.

Results: Through analysis of the GEO dataset, a gene named RYR2 was found to be considerably upregulated (|logFC| = 4.24, adj. P value =1.19e-07) in ccRCC samples. RYR2 has a significantly high expression, based on ENCORI (Fold Change: 2.72, FDR: 0.027). The survival has shown that the death rate was higher in people with high expression compared with low expression (Logrank p=3.7e−06, HR(high)=2.1, p(HR)=6e−06). lncRNAs and hsa-miR-148a-5p interaction with RYR2.Analysis of hsa-miR-148a-5p revealed that Increasing the expression of hsa-miR-148a-5p is one of the factors that increase the expression of RYR2. Pathway analysis expressed that RYR2 is involved in the secretion of insulin.

Conclusion: In conclusion, RYR2 is overexpressed in ccRCC and forms a possible ceRNA network. SEMA6A-AS1 by regulating the expression of RYR2 indirectly can work as a ceRNA and it can affect insulin secretion.

Keywords: Clear cell renal cell carcinoma (ccRCC) ; RYR2; hsa-miR-148a-5p ; lncRNA ; SEMA6A-AS1

Severity and prevalence of COVID-19 infection among patients with respiratory symptoms and history of four doses of vaccination

(Research Paper)

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Introduction: Acute respiratory infection (ARI) is a severe infection that affects a person's respiratory system and causes breathing problems. Coronaviridae is one of the viral families that cause respiratory infections in birds and mammals. The efficiency of vaccination against COVID-19 infection is undeniable so this study aimed to evaluate the symptoms of SARS-CoV-2 in people who received four doses of the Sinopharm vaccine

Methods: This study evaluated the prevalence and severity of COVID-19 infection in vaccinated people with four doses of sinopharm vaccine. All samples were collected from patients with respiratory symptoms who were referred to Besat hospital, Tehran, Iran

Results: From 290 patients with respiratory symptoms, 109 patients were positive for COVID-19 infection with a history of four doses of Sinopharm vaccine and the most common clinical symptom of infection were cough, runny nose, and fever but the hospitalization rate was very low.

Conclusion: Although vaccination can’t prevent infection with SARS-CoV-2, but against COVID-19 infection seems to be beneficial in reducing symptoms and hospitalization rate, especially if they have received a forth booster dose.

Keywords: Respiratory Tract Infection, COVID-19, Vaccination, Sinopharm

Sinopharm vaccination impact on breast cancer tumors progression

(Research Paper)

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Introduction: In December 2019, a novel coronavirus namely severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection started in China; within a short time, this infection spread all over the world and over 500 million people across 219 countries were infected. Vaccines to prevent SARS-CoV-2 infection are considered the most promising approach to controlling the epidemic. People with cancer or a history of cancer have a higher risk of dying from Covid-19 than the ordinary people; hence, the former population should be considered a high-priority group for vaccination. On the other hand, no appropriate study has performed to evaluate the effect of the Covid-19 vaccination on cancer. This study is one of the first in vivo studies that try to show the impact of the Sinopharm vaccine on breast cancer (the most common cancer among women worldwide).

Methods: Mice 4T1 mammary carcinoma triple-negative breast cancer (TNBC) model by injecting cells subcutaneously. After the tumor reached appropriate size, vaccination performed with 1 or 2 doses of Sinopharm (S1/S2) in relation to dose to the human. The tumor size of mice was monitored every two days. After 30 days, the mice were euthanized with the aid of CO2; their tumors and vital organs (heart, lung, liver, kidney, and spleen) were carefully dissected, and the existence of Tumor-Infiltrating Lymphocytes (TILs) in the tumor site and metastasis to the vital organs assessed by Hematoxylin and Eosin (H&E).

Results: The final tumor size in the control groups (C1 and C2) were 1325.89± 167.36 mm3 and 1231.54 ± 201.77 mm3 respectively; and in the groups that received Sinopharm vaccine (S1 and S2) were 899.21±50.47 mm3 and 524.19±80.79 mm3 respectively (difference between S1 and C1, and C2 and S2 were statically significant (p value< 0.05)). Amongst all groups, S2 showed the most hindrance in the rate of tumor growth, and the highest TILs' count. The group that received one dose of Sinopharm was at the next level and the control groups had the lowest TILs' count. H&E staining results on vital organs showed that the C1 had lesions of metastasis in liver and lung, and the C2 group showed these lesions in the liver but no

metastatic lesions were seen in the vital organs of the mice received Sinopharm.

Conclusion: According to the obtained data, Sinopharm vaccination against corona shows anti-tumor activity that can obstruct tumor growth and metastasis into vital organs. This effect, can be explained partially by the increasing in the existence of immune cells (TILs) in the tumor site. The mentioned effect is better where two doses of the vaccine are received than one dose.

Keywords: SARS-CoV-2, Sinopharm, TNBC, tumor size

social health; Speed and improvement of students' social skills
(Research Paper)

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Introduction: Having social skills and effective communication is necessary to have a successful performance in life. Social skills are influenced by the culture and social groups that a person is in contact with, and the degree of having these skills plays a significant role in the behavioral and social health of people.

Methods: This descriptive-analytical study was conducted in Jahrom province in the year 1400. The studied sample was randomly selected from a list of schools in the 4 education regions of Jahrom city based on the three variables of gender, educational level and type of school based on the distribution of students. The required sample size was calculated based on simple random sampling of 1400 people. Measurement of social skills was done using the standard tool of Gresham & Elliott by conducting an interview. A questionnaire containing demographic characteristics and other background information related to the purpose of the research was also designed.

Results: In total, 1544 parents of students answered the questions of their children's social skills questionnaire and social skills scores were obtained for 1410 of their children. The average age of the students was 15.7 years (±1.3 = standard deviation) and most of them were studying in high school. The average score of social skills was 52.8 (27.8 ± 27.8) and 65% of students in both sexes were equal and below the 50th percentile of social skills. In the study of analytical relationships, the average score of social skills showed a significant relationship with gender and educational level . Also, students' academic performance (absence from school and grade point average) had a significant relationship with the percentile of social skills.

Conclusion: According to the results, the social skills of the studied students were not at an optimal level. This raises the need to review educational and training methods at the family level as well as educational and training programs in order to promote and develop social skills.

Keywords: social health, students, social skills

SOX17 can be used as a biomarker to distinguish rheumatoid arthritis from osteoarthritis (Research Paper)

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Introduction: Osteoarthritis and rheumatoid arthritis both are diseases of joints which associated to falling physical function with very diverse etiologies. The present study aimed to find the differential gene expression in terms of transcription factors in order to distinguish RA from OA patients.

Methods: The expression profiling array of patients, 7 osteoarthritis samples and 10 rheumatoid arthritis patients, were obtained from the GEO database (GEO accession: GSE39340), and the samples were analyzed. Genes with differential expression patterns were isolated with the GEO2R by logFoldchange (logFC) ≠ 1 investigation. In addition, important transcription factors (TFs) of differential expressed genes was analyzed using Enrichr database.

Results: The result demonstrated that 114 genes upregulated and 116 genes downregulated in OA. Of which SOX17, STAT5A, E2F1, IRF1, VDR, CTNNB1 and CEBPA were among the important transcription factors network for differential expression genes which can distinguish RA from OA. Regarding to the amount of interaction, the main TF in this network was SOX17 which probably have important role in the pathophysiology of RA.

Conclusion: All in all, SOX17, STAT5A, E2F1, IRF1, VDR, CTNNB1 and CEBPA TFs might play important role in RA pathology. However, SOX17 can be a good marker to distinguish RA from OA states. Further, more experimental analysis is required to confirm the exact role of the TFs.

Keywords: Osteoarthritis, rheumatoid arthritis, array, SOX17

Spinal cord glioneuronal tumor with rosetted neuropil-like islands in pediatric age group (Review)

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Introduction: Glioneuronal neoplasms are unusual tumors categorized through manner of approach of world health organization (WHO) into three sorts consisting of papillary glioneuronal tumor (PGT), rosetted glioneuronal tumor with neuropil-like islands (GTNI), and rosette-forming glioneuronal tumor (RGNT) of fourth ventricle. Glioneuronal tumors commonly have an impact on children and more youthful adults with a predilection for the temporal lobe but recently, GTNIs happening in extraventricular sites especially spinal cord and those with malignant behaviors were reported. The literature in this novel neoplasm is sparse and confined, very probably for their rarity and variable clinical aggressiveness. Reviews on charactristics of this tumor are fewer and far between with the current as a great deal as a decade old.

Methods: In the forthcoming systematic study, the required data were collected using keywords and citing valid databases such as: Scopus PubMed, Google Scholar and ProQuest. The statistical population of the study includes all studies conducted up to 2022 in the field of Spinal cord glioneuronal tumor with rosetted neuropil-like islands in pediatric age group. After reviewing the relevant findings and evaluating the data quality, a total of 16 articles were analyzed.

Results: These tumors were mainly described withinside the pediatric population, with a median age of five years and a slow growing route with a slight female dominance. The imaging characteristic of spinal GTNI is that of a big intramedullary mass, with MRI findings showing a solid mass without or with cystic components. GNTNI appears with a biphasic histology, including neurocytic cells that surround precise oval neuropil-rich islands and protoplasmic, fibrillary, or gemistocytic astrocytes as part of the glial part. This glial component shows anaplastic features consisting of more frequent mitosis, increased cellularity, and nuclear pleomorphic and high proliferation index. Vascular proliferation and necrosis are unusual. Considering the location of GTNI tumors, most of them were positioned withinside the supratentorial and few were in spinal regions. However, authors describe

disseminated or spinal disease at primary stage of tumor frequently. The most frequent clinical symptoms of spinal GTNI are weakness, numbness, and limb paresthesia. Other symptoms include lumbar, chest, and lower back pain. Scoliosis and urinary incontinence, superior neck pain and dizziness with no dominant neurological change were moreover noticed in a few cases. According to literature reviews, spinal GTNIs are poor in their prognosis. Clinical treatment includes tumor resection combined with chemotherapy and radiotherapy.

Conclusion: In summary, as glioneuronal neoplasms are low grade and nicely manageable, the knowledge of their clinical presentation and histological analysis is essential for treatment. GTNI withinside the spinal cord is unusual and appears to be more aggressive; therefore, it is all-important to distinguish GTNI from exclusive benign glioneuronal tumors. Moreover, the pathophysiologies and biological features of spinal GTNI are not definitely known yet. Further researches with long-time period follow-up based mostly on treatment plans are required to further improve the management of GTNIs.

Keywords: spinal cord tumors, Neuropil-riched islands ‹Neurologic symptoms ‹tumors in Pediatric Age Group

Spinal cord injury and stem cell therapy (Review)

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Introduction: In central nervous system (CNS) disorders, unlike the peripheral nervous system (PNS), neurons have less ability to regenerate and reconstruct neural tissue.

Methods: One of the most destructive neurological disorders is spinal cord injury (SCI) that so far, various therapeutic methods have been tested in SCI treatments, such as physiotherapy, rehabilitation methods, and pharmacological therapy. Over the last twenty years, as our knowledge about stem cell biology has dramatically developed, stem cell therapies for treating CNS injuries and diseases have evolved and provided an alternative approach for neural regeneration and restoring neurologic function after SCI.

Results: The main advantage of stem cells for treating CNS diseases such as SCI is their immunomodulatory activities, neuroprotective effects, and self-renewal potency. They can help the compensation of SCI by modulating the inhibitory environment, re-myelination, formation of new neuronal connections, and limiting secondary injury.

Conclusion: The goal of this study is to review the recent studies about stem cell therapies in SCI treatment. Moreover, the increase in our understanding of stem cells and their therapeutic potential can help to discover new treatment approaches for spinal cord injury.

Keywords: Spinal cord injury, stem cell therapy, central nervous system, regenerative medicine

statistical comparison of a number of new tuberculosis vaccines. (Review)

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Introduction: Tuberculosis (TB) is one of the most dangerous diseases caused by Mycobacterium tuberculosis and is considered a major global and public health problem also TB is an airborne infection caused by Mycobacterium tuberculosis, which affects about 30% of the world's population also TB is the most common cause of death from an infectious pathogen .The high mortality rate increases the need to develop an effective vaccine but due to limit global resources, few vaccines can be upgraded to large-scale efficacy trials and our goal in this study was a detailed statistical comparison of a number of new TB vaccines.

Methods: In the forthcoming systematic review, the required data were collected using keywords and citing valid databases such as Scopus, PubMed, Google Scholar and ProQuest. The statistical population includes all studies conducted until 2022 in the field of statistical comparison of a number of new TB vaccines. After reviewing the relevant findings and evaluating the quality of the data, 17 similar articles were reviewed and analyzed, and the latest information on tuberculosis vaccines was studied from them.

Results: Tuberculosis is a major global problem and the only licensed vaccine is Bacillus Chalmette- Guerin (BCG), however, tuberculosis is still one of the main causes of morbidity and mortality in the world while the BCG vaccine is somewhat effective against severe tuberculosis in children and many new TB vaccines are designed to boost BCG, but the development of improved TB vaccines needs to overcome several challenges and one of the most important challenges is the lack of sufficient assurance in human clinical trials.

Conclusion: In general, the response of the human immune system in the field of vaccination requires the attention of more research to determine how successful the new tuberculosis vaccines will be in inducing humoral and cellular immunity.

Keywords: Tuberculosis _ Vaccine _ Immunity

STC1 downregulation and CRIP1 upregulation associated with inflammatory Osteoarthritis (Research Paper)

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Introduction: Osteoarthritis (OA) is the most common form of arthritis and resulting in joint deterioration. OA synovial tissue typically displays a mild to moderate degree of inflammation. Synovial inflammation is present in the OA joint and has been associated with pain progression. In the present study, we aimed to detect critical genes with differential expression patterns in patients with Synovial inflammation.

Methods: The expression profiling array of patients with synovial cells from inflammatory (12 samples) and normal areas of osteoarthritis synovial membrane (12 samples) were obtained from the GEO database (GEO accession: GSE46750), and the samples were analyzed. Genes with differential expression patterns were isolated with the GEO2R by P.value < 0.05 and logFoldchange (logFC) ≠ 1 investigation. In addition, the biological process (BP) of differential expressed genes was analyzed using PANTHER17.0database.

Results: The result demonstrated that 101 genes upregulated and 149 genes downregulated. Of which stanniocalcin 1 (STC1) was the most downregulated with logFC = -2.544 and P.value = 0.00022177 and cysteine rich protein 1 (CRIP1) was the most upregulated ones with logFC = 1.467and P.value = 0.00065214. Further Biological process (BP) analysis revealed cellular process (GO:0009987) including cellular metabolic process, cellular response to stimulus and cell communication were the important process in pathophysiology of osteoarthritis.

Conclusion: All in all, STC1 downregulation and CRIP1 upregulation might play important role in pathophysiology of inflammatory OA. However, more experimental analysis is required to confirm the exact role of them in OA.

Keywords: Osteoarthritis, Synovial inflammation, array, STC1, CRIP1

stem cell (Review)

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1. Danesh pazhoohan 1

Introduction: Hello . In this article, I want to talk about stem cells. Their types, their types of methods, bone marrow transplantation, etc. Stem cells have many uses in medical science because of their unique characteristics and help to save people's lives.

Methods: Trial . Research and promotion. I have obtained this information by using the internet and articles, as well as going to the stem cell faculty. I have been extensively researching stem cells for almost 8 months

Results: As a result of this research, I was able to learn all stem cell tests and have information about them, I have written articles about stem cells and participated in stem cell competitions and now with the best and newest treatment. I have become familiar with diseases

Conclusion: Bone marrow stem cells are used more often, they have fewer complications, and embryonic stem cells are used less often because some people believe that this will cause the death of a person and an adult will replace it, and stem cells Umbilical cord blood is easily available

Keywords: medicine Biomedical stem cells

Stem cell-based tissue engineering approaches for burn wound healing (Review)

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Introduction: Introduction: One of the skin wound models is the burn wound model. Many people die annually due to burns and tissue damage. One of the causes of this high mortality is the lack of biological and natural compounds compatible with the human body for treatment. Nowadays, stem cell-based tissue engineering therapeutic approaches have been proposed to treat these wounds.

Methods: Method: This study overviews advances of tissue engineering approaches for healing burn wound these approaches and give insights into mechanisms that aid burn wound healing in different clinical scenarios.

Results: Results: Addition to the conventional wound care practices, stem cells and tissue engineering approaches have been recently gained increased importance in healing burn wounds. Skin tissue engineering is a new solution for treating wounds and skin diseases, and its ultimate goal is to replace damaged tissues, to return to the functional state before complications, to overcome the limitations of conventional skin graft methods. Engineered tissues not only close wounds, but also stimulate the regeneration of the dermis, which is very useful for burn wound healing. Tissue engineering is based on the three main pillars of cells, scaffolds and growth factors. Stem cells are also used to treat a wide range of skin injuries and degenerative

diseases. Currently, through the approach of skin tissue engineering and the application of biomaterials, it is used as a platform to improve the grafting of implanted stem cells and facilitate the function of cells by mimicking the tissue microenvironment to regenerate damaged skin tissue.

Conclusion: Conclusion: Stem cell- based tissue engineering strategies for burn wound healing have been developed over the past few decades and successful results have been obtained. However, all through the continual development of tissue engineering in bourn wound repair, a close collaboration between tissue engineers and clinicians is critical to maintain the translational efficacy of this approach.

Keywords: Keywords: : burn, wound, tissue engineering, stem cell

Stem cells and epilepsy (Review)

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Introduction: Epilepsy as one of the most common neurological disorders affects more than 50 million people worldwide with a higher prevalence rate in low-income countries. Although current therapies exist to control the number and severity of clinical seizures, there are no pharmacological cures or disease-modifying treatments available. Nowadays, similar to other diseases, epilepsy also is a candidate for treatment with different types of stem cells. Various stem cell types were used for treatment of epilepsy in basic and experimental researches.

Methods: This study was conducted with the aim of investigating whether the use of stem cells in epilepsy has any effect by reviewing the published articles in this field. That for this, by searching in Google Scholar with the phrase of "stem cells AND epilepsy AND seizure", we randomly checked some of the articles that contained these words and according to the results obtained.

Results: it was found that stem cells can be among the significant cases in the treatment of epilepsy

Conclusion: the potential major roles of stem cell therapy in epilepsy are seizure remission, inhibition of the progression of the epileptogenic process, prophylaxis against the development of chronic epilepsy, and improvement of cognitive function.

Keywords: Seizure, Hippocampus, Anti-Seizure drugs.

Stem cells as carriers for oncolytic viruses in treatment of cancer (Review)

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Introduction: Oncolytic viruses (OV) are considered as a novel class of anti-cancer agents due to their selective ability to infect and destroy cancer cells.

Methods: Currently, the most common way of delivering OV is intratumoral to target metastatic diseases and tumors. The effective methods for the systemic delivery of OVs, is like the use of carrier cells.

Results: Due to the specific migration capacity of stem cells, they can be used as carriers or vectors targeting metastatic cancers.

Conclusion: Promising results have been reported in the use of stem cells and oncolytic viruses as a therapeutic approach to the treatment of metastatic cancer.

Keywords: Oncolytic viruses, carrier cells, stem cells, metastatic cancer

Stereological investigation of the Androgenetic alopecia (AGA) after treatment with Minoxidil solution and conditioned media (Research Paper)

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Introduction: Male-pattern baldness, also known as androgenetic alopecia (AGA), is a dihydrotestosterone-mediated hair loss disorder that is characterized by a shortened anagen hair cycle that occurs when the follicles gradually shrink, resulting in thinning hair. The process of transforming thinning hair into thick hair is important in the development of successful treatment by stimulating and extending the length of the anagen phase, inducing and maintaining the anagen in the hair cycle. This study was carried out to investigate the effect of conditioned media derived from umbilical cord mesenchymal stem cells and minoxidil separately and simultaneously on male-pattern hair loss.

Methods: Testosterone dissolved in the thermo-sensitive gel based on poloxamer 407was injected into 4-weeks-old mice weighing 30 g to induce male pattern hair loss. Then, 5% minoxidil was applied topically daily, then the gel was optimally injected in two stages subcutaneously. Two months later, their skin was placed in formalin for stereology and H&E staining tests.

Results: Treatment of mice models with minoxidil made significant changes such as reduction of volume density of sebaceous glands and volume density of hair follicles compared to the model group, but these changes in treatment with conditioned media and minoxidil were more significant and effective.

Conclusion: Therefore, it was found that treatment with conditioned media could be a more effective method compared to other treatments such as

minoxidil. Also, treatment with conditioned media has the same effect as treatment with conditioned media and minoxidil simultaneously.

Keywords: Androgenic Alopecia, Minoxidil, conditioned media

Strategies for target delivery of RNAi: Review Abstract Article (Review)

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Introduction: In last decades, RNA interference (RNAi) technology has become a powerful tool for clinical approaches. These oligonucleotides, targeted mRNA with high specificity and efficacy and induce degradation of the targeted mRNA by the RISC machinery. Inhibition the expression of protein is the key for the purpose of treatment of diseases. The major challenge for RNAi application is enhance its stability and bioactivity. PEGylated lipid-based delivery system plays an important role for targeting delivery of nucleic acids. In this review, we discuss PEGylated lipid-based RNAi delivery systems and strategies to overcome technical barriers for target delivery of RNAi.

Methods: Many strategies were developed to overcome technical barriers for target delivery of RNAi. Viral vectors, such as adenovirus or lentivirus, chemical methods, physical methods (hydrodynamic injection, particle bombardment, and electroporation and polymer, lipid-based delivery systems, Self-assembled lipid-polymer hybrid NPs, these are strategies, which explain the difficulty of this approach to enhance endosome escaping efficiency and target delivery of RNAi.

Results: Viral vectors are efficient in gene delivery, but they have some contraindication due to many drawbacks such as insertional mutagenesis, immunogenic and inflammatory responses. Non-viral vectors, including Lipid-based nanoparticles were developed as a promising platform to enhance target delivery of RNAi. PEGylated lipid-based delivery system plays an important role for target delivery of RNAi. Key advantages of PEGylated lipid-based delivery system is increase the circulation time, low immunogenicity, ability to deliver large size genetic materials, cost-effective manufacturing.

Conclusion: In recent years, variety of lipid-based nanoparticles were developed as a promising platform to enhance target delivery of RNAi. PEGylated lipid-based delivery system plays an important role for targeting delivery of nucleic acids due to increase the circulation time, low toxicity,

biocompatibility, and facilitating scaled up. RNAi-PEG conjugates, suggesting that they can be potential promising platform for clinical approaches.

Keywords: RNAi, RISC machinery, PEGylating

Strategies to improve the oral and dental health of people with diabetes (Review)

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Introduction: Diabetes is the main and growing health problem internationally. It caused an estimated 1.5 million deaths and was the ninth leading cause of death in 2019. Poorly managed diabetes can lead to multiple difficulties, one of them being dental and oral problems, which the most prevalent one of them is periodontal (gum) disease that is often presented as the sixth complication of diabetes. In the past couple of years, substantial attention has been given toward these associations and their implication for people living with diabetes. But People with diabetes often are not informed about the relations between diabetic control and oral or periodontal diseases nor do they receive dental referrals from their diabetes care providers. Also, the study revealed 66. 38% of diabetic patients were never questioned about their oral hygiene by their diabetic educators. Another study focusing on the effectiveness of furnishing oral health information for diabetic patients indicated that participants who received the information, had 2.9 times the odds of maintaining adequate oral health knowledge compared to participants who did not receive the information. Besides certified diabetes educators' (CDEs) time constraints, no related oral health training programs and examination tools exist for them. But with proper training, not only CDEs, but non-dental professionals like nurses have successfully integrated oral healthcare in other settings. Also results of another survey conducted in Iran indicated the moderate level of knowledge and the practice of dental students in Tehran regarding the oral health of diabetic patients.

Methods: In this systematic review, we extracted the required articles using keywords and also citing databases such as PubMed, Scopus, Google Scholar and ProQuest. The statistical population of this study is all articles published until 2022. We checked the quality of the data and then reviewed 17 articles.

Results: Three main themes emerged from reviewed articles regarding CDE's and dental hygienist's perspective on oral health in diabetic patients. Education (educating the people, resources for patients, and professional

practice guidelines), Inter-professional collaborative care (role of medical staff to raise awareness for oral health in diabetes) and Dental insurance. Also, General Practitioners (GPs) reported 20–30% of their patients having oral health inconveniences. Several barriers were identified by GPs including absence of referral pathways, time constraints, and limited knowledge and training in promoting oral health care. GPs suggested that resources such as standardized assessment tool and education/training could assist them in promoting oral health care. In addition, 62% of questioned CDEs in a survey agreed that CDEs need to join forces with dental specialists in disease management and 84% indicated interest in an oral health constituent being added to their ongoing education curriculum. Although, 51% discussed oral health with their patients and 64% said they have referred a patient to a dentist within the past year, but only 20 lt self-confident enough to provide an oral health screening to their patients.

Conclusion: The three emerging themes are interrelated, indicating that strategies to improve oral health for people with diabetes are multifaceted. Important strategic arrangements across patient, general public, and care provider levels, comprising inter-professional collaborative care, dental and diabetes professional organizations is necessary to achieve the objective of improving oral health for people with diabetes,. Local, regional and national initiatives could promote or harmonize the assessment and management of the oral health of patients with diabetes to bridge the gap between medicine and dentistry in this field.

Keywords: diabetes, dental health, Oral Health

Study of Biofilm Formation and Escherichia coli Biofilm Resistance Pattern Isolated from Urinary Culture Infections (Research Paper)

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Introduction: Urinary tract infections are one of the most commonly nosocomial infections that it is cloned by Escherichia coli bacteria and it affects the host's mucous membrane. The increased resistance of bacteria to antibiotics, as well as the biofilm adhesion of infectious bacteria to the glass and plastic surfaces of hospital equipment, is another issue that causes the problem in treating this type of bacterial urinary tract infection. The aim of this study is to study the biofilm formation and bacterial resistance and biofilm resistance to antibiotics.

Methods: In this study, 150 samples of suspected urinary tract infection were collected; cultured on McConkey medium; and finally stained. Catalase test and culture in differential media (TSI, Simon Citrate, SIM, MR and VP) were used for isolation of Escherichia coli bacteria from other gram-negative bacilli from EMB Agar medium; and for completely identification of Escherichia coli bacteria in the positive samples. Routine biochemical methods and Antibiogram tests were performed to detect antibacterial sensivity of the bacteria. Biofilm formation of this bacterium was performed by Microtiter Plate and Tubal methods. Therefore, to study of antibiotical and probiotical resistance patterns on Escherichia coli biofilm, antibiogram discs of ampicillin (AM), ciprofloxacin (CP), cefixime (CFM), co-trimoxazole (STX), and gentamicin (GM) anticotics were used. In the next step, antibiotical resistanc pattern of Nystitin was performed on Escherichia coli biofilm and free Escherichia coli bacteria, and determination of MIC and MBC points. Finally, the effect of Nystitin anticotic on planktonic and biofilm bacteria was determined.

Results: The results showed that of total 150 initial samples, 23 samples (15.33%) were infected; by using conventional biochemical methods and Antibiogram test determined that 18 samples (78.26%) of 23 infected samples contained Escherichia coli bacteria. The staining of bacteria identified the gram-negative bacilli species and then, by cultivate the specimens on the differential medium, the bacteria that had green gloss was isolated as Escherichia coli. The result of catalase test was also positive. The isolated had thses bichemistrial features: citrate-negative, catalase-positive, endol-

positive and motile. Also, it is determined that the bactira within the urinary specimens have the highest resistance (50 %) to co-trimoxazole and the least resistance (5.55%) to gentamicen; and probiotic Lactobacillus acidophilus had no effect on planktonic Escherichia coli bacteria; and also, it was not inffective on the biofilm. During the study of antibiotic resistance pattern of Nystatin on biofilm and free Escherichia coli, it was found that the biofilm of Escherichia coli is much more resistant than biofilm of Planktonic Escherichia coli bacteria. The final test results also showed that Nystatin antibiotic did not affect on the biofilm but in the concentration of 0.02% (125 µL) was effective on Planktonic bacteria. These results were similar to the results of several studies. For example, in a study by Abdollahi Kheirabadi and colleagues (2012), the resistance of Escherichia coli to antibiotics was increased by ciprofloxacin; and in the study of Tajwidi et al. (2013), the highest resistance to co-trimoxazole was observed. Boniadian et al. (2013) reported the low sensitivity of Escherichia coli to cefixime. Zarrinfar (2016) and Fazeli (2004) also confirmed the lack of effect of probiotics on growth of Escherichia coli.

Conclusion: As a result, it can be said that it is better to did not use from co-trimoxazole as an epileptic treatment in the treatment of urinary tract infections caused by Escherichia coli, and it prevented to froming of biofilm at any surface, because bacterial biofilm is more resistant and probiotics do not show antimicrobial effects on biofilm.

Keywords: Urinary infection, Escherichia coli, Biofilm, Probiotic, Lactobacillus.

study of the effect of levodopa on BPAN protein using molecular docking method (Research Paper)

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Introduction: levodopa remains the gold standard for the treatment of Parkinson disease. However, some doctors prescribe this drug for NBIA disease. In this descriptive-analytical study, we investigate levodopa and its effect on Beta-propeller Protein-associated Neurodegeneration using molecular docking method.

Methods: we used molecular docking method, which is both faster and cheaper compared to laboratory methods. Also from the software ViewerLite, AutoDockTools-1.5.6, Chimera 1.15 and PyRx were used.

Results: conformation1 of levodopa has negative binding affinity(-4/9kcal/mol) and RMSD is zero

Conclusion: According to Docking studies, we found that none of the conformations can be effective in affecting the BPAN, because their binding affinity is more than what we expected (more than -5kcal/mol), despite of suitable RMSD lower bound and RMSD upper bound.

Keywords: NBIA , BPAN , Molecular docking , Levodopa

Studying the expression levels of two P53-associated lncRNAs under hyperglycemic conditions in bone marrow mesenchymal stem cells (Research Paper)

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Introduction: Diabetes mellitus is the most common metabolic disease in humans that is characterized by chronic hyperglycemia and alteration of cellular homeostasis. Increased oxidative stress is a key factor in the pathogenesis of this disease. Recent studies demonstrated that elevation of glucose metabolism causes DNA double-strand breaks and activation of p53. Long non-coding RNAs (lncRNAs) are involved in the regulation of the DNA damage/repair network. LincRNA-RoR (RoR) is a strong negative regulator of p53 while DINO is required for p53-dependent gene expression, cell cycle arrest and apoptosis in response to DNA damage. Still, the role of lncRNAs in hyperglycemic condition is not known. In this study, the expression level of ROR and DINO were evaluated in mesanchymal stem cells after exposure to hyperglycemia.

Methods: Cells were treated with 30 and 40 mM glucose for 3 days followed by DNA damage evaluation through comet assay. The gene expression of p53 and lncRNAs were evaluated using Real-Time PCR.

Results: The results of commet assay showed increased in DNA olive tail moment as an indicator of DNA damage after exposure to different concentration of glucose. P53 was increased in expression in hyperglycemic condition. Also, there was a notable increase in the expression of DINO and reduction in ROR expression in response to 30 and 40 mM glucose compared to control group ($p<0.0001$).

Conclusion: This finding showed a detrimental effect of hyperglycemia on DNA integrity of bone marrow derived mesenchymal stem cell and suggest a role for DINO and ROR as masters regulator of P53 signalling in hyperglycemia induced-DNA damage. Further studies are still needed to dissect the precise role of these lncRNAs.

Keywords: Diabetes, MSC, DNA damage, ROS, LncRNAs, ROR, DINO

Studying the expression of the SLC25A4 gene in the development process of Kidney Renal Clear Cell Carcinoma and its forecast in the ceRNA network (Research Paper)

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1. Zist Fanavari Novin
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Introduction: Kidney Renal Clear Cell Carcinoma (RCCs) is a glandular (adeno) carcinoma of the kidney, and it includes 85% of kidney cancers [1]. Importantly, RCC is a disease of increasing incidence. By using genomic data and genomic observations, an important step can be taken in the process of prevention and development of treatment methods [2]. The investigation aims to investigate gene expression SLC25A4 by measuring hsa-miR-370-3p at the cellular level of kidney Renal Clear Cell Carcinoma patients.

Methods: At the First, the gene expression data of RCC patients (GSE148795) was obtained from NCBI Gene Expression Omnibus (GEO), and then the expressed genes were searched by GEO2R and analyzed differently (GEPIA2) and (ENCORI). Then the Enrchr database was used to analyze the signaling pathway. Also, the complete form of the signaling pathway was obtained in the KEGG database. Through UniProt [3] and GeneCards [4], gene ontology information and biological pathway involvement were apprehended. In addition, miRWalk was used to find significant miRNA-mRNA interactions in the 3'UTR region. In addition, the selected miRNA was searched in LncBase v.3 [5] to find strong interactions with lncRNAs and complete a predictive ceRNA network.

Results: Through analysis of the GEO dataset, a gene named SLC25A4 was found to be considerably upregulated (logFC = -0.1913039, adj. P value =2.83E- 01) in RCC samples. The SLC25A4 gene provides the instructions for making a protein called adenine nucleotide translocase type 1 (ANT1). ANT1 functions in mitochondria, which are structures within cells that convert the energy from food into a form that cells can use [6]. Analysis of possible miRNA-mRNA interactions revealed hsa-miR-370-3p as a significant interactor to SLC25A4 mRNA. This miRNA was then searched in LncBase v.3, and AD000090.1, KCNQ1OT1, NAMPTP1, and SAR1AP1 had the strongest interactions.

Conclusion: Thus, SLC25A4 is overexpressed in RCC and Forms a possible CeRNA network among hsa-miR-370-3p, and AD000090.1, KCNQ1OT1, NAMPTP1 and SAR1AP1.

Keywords: Kidney Renal Clear Cell Carcinoma, Gene Expression Omnibus, miRNA-mRNA interactions

Studying the inhibitory effect of flavonoid compounds of the flavonol class on the influenza virus neuroaminidase enzyme (Research Paper)

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Introduction: Millions of people in the world suffer from various types of acute respiratory infectious diseases every year as one of the most important medical problems of today's human societies. Influenza is one of the most important diseases that causes damage to the upper and lower respiratory system. The outbreak of the influenza virus in 1918 infected more than 500 million people worldwide, which was the largest pandemic in the history of this disease and killed more than 20 million people; Also, in 1956 and 1968, other pandemics caused by this deadly virus occurred, which caused the death of more than one million people in the world; And before the outbreak of the Covid-19 disease, which spread all over the world since the end of 2019, it was considered as the biggest threat to human health. The first pandemic outbreak of H1N1 swine flu disease in the 21st century occurred in early April 2008 equivalent to March 2009 in Mexico and caused a large number of people around the world to be infected and caused high mortality and economic damage. It spread all over the world and was known as the swine flu disease early on, and due to the rapid spread of the disease in more than 200 countries, it was named the new H1N1 flu by the World Health Organization that year. Researchers' research has shown that drugs made against hemagglutinin and neuraminidase can improve the complications caused by influenza virus. In recent years, drug resistance has been observed, which is due to the high consumption of drugs; Therefore, it is necessary to introduce a more effective inhibitor to inhibit the neuroaminidase enzyme, which is one of the effective enzymes in the pathogenesis of the swine flu virus.

Methods: In this study, which was carried out by bioinformatics simulation method, the structural file of neuroaminidase protein was downloaded from the NCBI database, and since this protein has 4 identical chains, chain A was selected, and using Gromax software package, energy optimization and minimization steps were performed. It was done. The drugs used in this study were downloaded from the Pubcam database and converted to .pdb format with the OpenBabel software. Molecular docking was done with HEX8.0.0 software and the binding position of each drug on the protein was obtained

with Argoslab software; The results were analyzed using WebLab Viewer, Piemol, Excel and Leagueplot software.

Results: The herbal compounds studied in this research were from the flavonol class, including myristin, murine, fistin, quercetin, kaempferol, and galangin, and the antiviral compounds studied included oseltamivir, zanamivir, amantadine, and rimantadine. In this study, it was observed that the antiviral drug rimantadine binds to amino acid proline 431 of the enzyme by hydrogen bonding; Also, myristin, quercetin, and fistin were bound to tryptophan 189 in the active site of neuroaminidase enzyme, and galangin, kaempferol, and murine were all bound to arginine 371 amino acid in the binding pocket of the enzyme.

Conclusion: Arginine 371 is located in the active site of the enzyme;This study showed that galangin, murine and kaempferol from the flavonol class of flavonoids by binding to arginine 371 of the active site of the enzyme inhibit the catalytic function of the enzyme.

Keywords: Neuroaminidase, Molecular Docking, H1N1 influenza, Zanamivir, Plant Flavonoids, Flavonol

Subliminal and root regrowth Using stem cells (Research Paper)

zakiyeh khosravi,[1,*]

1.

Introduction: Stem cells are the body's natural reservoirs to replace damaged specialized and non-specialized cells. These cells have a very high potential and have the ability to transform and differentiate into most or we can say all the cells and tissues of the body. Stem cells with their differentiation can become cells. including muscles, red blood cells, brain cells, etc. Here, we want to examine a sample of mesenchymal stem cells, which are an important population of multipotent stem cells with high growth and recovery capabilities. These cells can differentiate into all the cell lines that are the basis of mesenchyme or connective tissue and cause the repair or regeneration of such tissues. Also, as mentioned, these cells retain the characteristics of stem cells and tissue regeneration capacity. These findings suggest that periodontal ligament stem cells may be used to create a biological root that can be used in a similar way to metal implants. According to the findings and tests, it was found that even the teeth have a reserve of stem cells that are found in both milk and permanent teeth. These cells have the ability to fully regenerate themselves. Due to their compatibility with the body's immune system, these cells can be used in many fields of medical science. Pulp cells of human deciduous teeth show high proliferation and differentiation ability, and by differentiating these cells into pseudo-odontoblast and osteoblast cells, it is possible to help rebuild the lost structure of the tooth. Different methods can be used to track cells. This growth, due to the recognition of the potential of stem cells, led to surprising results, such as the possibility of rejection of the transplant after the transplantation of these cells is less, and there is no need to use immunosuppressive drugs. Of course, in relation to the potential of mesenchymal cells of children and adults, it can be mentioned that according to the clinical features of the pulp of children's milk teeth, it was observed that these cells have a high proliferation and differentiation ability compared to the pulp cells of adults. Attention to the many results obtained can be found that the use of mesenchymal cells from children's milk teeth leads to greater efficiency, and these cells can be differentiated into a complete set of teeth after growth and passage in a laboratory environment, as well as determining the number of dental canals by using the expression of affected genes find.

Methods: Investigation in 18-25 year olds 14 samples from the pulp and 6 samples from the dental follicle of the third molar of adults between 18 and 25 years old were collected. The collected samples were extracted due to impaction or orthodontic treatment with expert diagnosis and with the prior consent of the patients. These teeth had no caries or previous restorations,

and the patients were all healthy and did not have any systemic disease.After being drawn into the tubes containing Gibco, RPMI 1640, containing 2x antibiotics (2 times the strength of penicillin and streptomycin, Gibco), the tooth samples were transferred to the molecular cell laboratory at a temperature of 4 degrees Celsius, and to reveal the pulp chamber of the teeth. , were cut from the enamel-cement connection by carbide disc and handpiece. And after that, the pulp was separated from the teeth, from the pulp chamber by means of a fine file; Then, for cell culture of the pulp tissue and follicle, these cells were divided into smaller pieces by surgical blade number 10, and then they were placed in Falcon containing 4 mg/ml collagen type (sigma I) solution, 104 mg/ml Dispase solution (Gibco) with a ratio of 1.1 was placed for 45 minutes at a temperature of 37 degrees Celsius After that, they were added to the culture medium and centrifuged at 600 g for 10 minutes. The resulting cell plates were cultured with mixed culture medium and after being transferred to the appropriate zvt in an incubator with a temperature of 37 degrees Celsius, 5 atmospheres and 2% CO2. This culture medium was changed every two days until 70% of the bottom of the plate was filled with cells. When the bottom of the plate reached 70%, the samples were passaged with the help of trypsin-EDTA. And finally, flow cytometry analysis was used to investigate the phenotypic profile of surface markers and the nature of stem cells from the pulp and follicular tissue of the third molar tooth. For this purpose, the cells were suspended in one milliliter of PBS (Phosphate Buffer Saline) in the third passage of trypsin. They were placed with a concentration of 1,000,000. Then the cells were divided into 6 tubes and 5µl of antibody was added to each PE tube and the tubes were then placed in a dark environment at 4°C for 30 minutes and after this period the cells were washed with 1ml of washing buffer. and centrifuged at 1200 MPR for 5 minutes, after which each cell sample was suspended in 300 µl to 500 µl washing buffer and analyzed by flow cytometry.

Results: According to the mentioned cases, it can be said that there are mesenchymal stem cells of the dental pulp in the mature cells of the adult because after a dental injury, the dental pulp undergoes dentination in order to repair the damaged area by building and depositing the dentin matrix. This repair process takes place throughout a person's life, which indicates the presence of mesenchymal cells in the dental pulp of adults and the ability to create odontoblasts under the influence of appropriate signals ‹But in general, the potential of adult stem cells is not as much as that of fetal and childhood stem cells, for this reason, it is better to extract or use embryonic tooth root mesenchymal cells (from the gums, especially the posterior gums) for the reconstruction and repair of teeth. From the mesenchymal stem cells of milk teeth, these cells, as mentioned, are not limited to any category and age group, and even the ability to donate these cells from one person to another is possible, and the condition of donating teeth:The complete genomic and systematic health of the donor person, with this work, even in adults who often

have lost their milk teeth (except for latent milk teeth), the gene of mesenchymal stem cells of children or fetuses can be used to repair and regenerate teeth do . In the laboratory method, mesenchymal stem cells in adults, although they have the possibility of repair or regeneration, but after they are separated from the patient, they must first go to the laboratory environment, and after their amplification and differentiation, they are injected into another person as an allograft or xenograft recipient, but with Paying attention to the many problems that may arise during the strengthening, injection, long time and potential and less adaptation of these cells, such as early tooth decay, tooth loss, immune system attack on these cells through immune response, etc. In this regard, it can be said that the use of a secondary method (experiment: laboratory cultivation of mesenchymal cells of milk teeth) is more effective and efficient in this field. And due to the problem-causing factors that exist in adult mesenchymal cells, this ideal protocol for humans is relatively far away from its application. Recently, with the discovery of a gene called DIK1, with the discovery of a gene called DIK1, it is possible to learn about the activation of stem cells and tissue regeneration in teeth repair and to undergo a shorter treatment period in tooth repair using stem cells. (restoration and reconstruction of teeth have gone through a relatively long period) With the activation of stem cells, these cells can send messages to the main cells that help to activate the repair and reinforcement cells (this is also possible by using low power lasers) as a result of these cells forming dentin. the(hard tissue of the tooth) helps a lot.

Conclusion: Therefore, it can be said that tooth regrowth is a reality, not an ideal, and considering that the tooth is made up of two different types of tissue, logically, making a tooth requires communication and cooperation with epithelial cells and odontogenic mesenchyme. The recombination of epithelial tissue and dental mesenchyme to create teeth both in the laboratory and in the living environment leads to the fact that the combined cells can organize and form individual layers and are also able to differentiate into odontoblasts and amyloblasts. In order to make a complete tooth that has enamel and dentin, epithelial and mesenchymal cells are respectively introduced into the collagen gel solution and then implanted inside the oral cavity, and with this technique, the presence of all dental structures such as odontoblasts, amyloplast, pulp, Blood vessels, crown, root, periodontal ligament and alveolar bone can be seen, so the implantation of this dental mass (mesenchyme + epithelial cells) leads to the development of maturity and regrowth of teeth. So, it can be said that by using engineering and modern methods, mesenchymal stem cells extracted from the pulp of mature teeth and milk teeth can be used to repair dental tissues, especially sub-tissues that have mesenchyme and connective tissue, and with this Humans at any age are able to re-grow their teeth using the mesenchymal stem cell gene, and it is worth noting that the use of the mesenchymal gene is not restricted from one person to another (no age limit) and one of the challenges which makes

this different from other methods: the use of this method, if the mesenchyme gene used is healthy, unlike the implant, does not have any limitations or harm ،And replacing this method instead of today's methods, dentists can use it more economically and optimally.

Keywords: Mesenchymal stem cells_tooth pulp _tooth follicles

Sulfated Carboxymethyl Cellulose and Carboxymethyl κ-Carrageenan Immobilization on 3D-printed Polycaprolactone Scaffolds Differentially Promote Preosteoblast Proliferation and Osteogenic Activity (Research Paper)

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Introduction: Lack of bioactivity of three-dimensional (3D)-printed polycaprolactone (PCL) scaffolds limits cell-material interactions in bone tissue engineering. This limitation can be overcome using surface-functionalization by glycosaminoglycan-like anionic polysaccharides, e.g. carboxymethyl cellulose (CMC), a plant-based carboxymethylated, unsulfated polysaccharide, and κ-carrageenan, a seaweed-derived sulfated, non-carboxymethylated polysaccharide. Sulfation of CMC and carboxymethylation of κ-carrageenan critically improve their bioactivity, but how sulfated carboxymethyl cellulose (SCMC) and carboxymethyl κ-carrageenan (CM-κ-Car) affect the osteogenic differentiation potential of preosteoblasts on 3D-scaffolds is still unknown. Here we aimed to assess the effects of surface-functionalization by SCMC or CM-κ-Car on physicochemical and mechanical properties of 3D-printed PCL scaffolds, as well as the osteogenic response of preosteoblasts. MC3T3-E1 preosteoblasts were seeded on 3D-printed PCL scaffolds either or not functionalized by CM-κ-Car (PCL/CM-κ-Car), or SCMC (PCL/SCMC), and cultured up to 28 days. The scaffolds' physicochemical and mechanical properties and preosteoblast function were assessed experimentally and by finite element modeling.

Methods: Sulfation of CMC: CMC was allowed to react with SO3/pyridine complex to prepare SCMC. Carboxymethylation of κ-carrageenan: CM-κ-Car was synthesized by alkalization of κ-carrageenan to form alkoxy-κ-carrageenan, followed by etherification with monochloroacetic acid. Characterization of SCMC and CM-κ-Car: The chemical structure of CMC, SCMC, κ-carrageenan, and CM-κ-Car was studied using FTIR spectrophotometry, and NMR spectroscopy. 3D-printing of PCL scaffolds: PCL scaffold (l×w×h:10×10×10 mm; volume: 1000 mm3) strands (diameter: 0.7 mm) were printed layer-by-layer with a 0º/90º lay-down pattern. Surface-functionalization of 3D-printed PCL scaffolds by SCMC or CM-κ-Car: SCMC and CM-κ-Car were immobilized on aminolysed 3D-printed PCL scaffolds using EDC/NHS as crosslinker. Scaffold characterization: Physicochemical properties of 3D-printed PCL, PCL/SCMC, and PCL/CM-κCar scaffolds, i.e. surface elemental composition (EDS), hydrophilicity, surface topography and morphology (SEM), void size and strand diameter, surface roughness, surface charge, surface chemical composition (ATR-FTIR), total protein adsorption, and as well as mechanical properties, i.e. compression modulus, and ultimate compression strength were determined. Finite element (FE) modeling: FE modeling was used to quantify the mechanical behavior, von Mises stress distribution and magnitude, under uniform 2% compression strain deformation. Cell culture and scaffold bioactivity: MC3T3-E1 preosteoblasts were seeded at 5x105 cells/cm3 on the scaffolds, and cultured up to 28 days. Preosteoblast seeding efficiency, cell morphology and spreading (SEM), expression of osteogenic genes (RT-PCR), proliferation, and alkaline phosphatase (ALP) activity, collagen production, and calcium deposition were determined. Statistics: Differences in mean values were tested using one-way ANOVA. Two-way analysis of variance with pairwise comparison was used to assess differences between groups and over time. Differences were considered significant if p<0.05.

Results: Surface-functionalization by SCMC and CM-κ-Car did not change scaffold geometry and structure, but similarly increased surface roughness (PCL/CM-κ-Car: 6.62-fold), hardness, as well as decreased water contact angle and elastic modulus. Finite element modeling showed that maximal von Mises stress for 2% compression strain did not exceed yield stress for bulk material in all scaffolds. Surface-functionalization by SCMC and CM-κ-Car increased protein adsorption, and improved cell spreading, resulting in well-spread cells with a natural spindle-shaped morphology on the surface of PCL/SCMC and PCL/CM-κ-Car scaffolds. Surface-functionalization by SCMC decreased Runx2 and Dmp1 expression, while surface-functionalization by CM-κ-Car increased Cox2 expression at day 1. Surface-functionalization by SCMC most strongly enhanced preosteoblast proliferation and collagen production, while CM-κ-Car most significantly increased alkaline phosphatase activity and mineralization after 28 days.

Conclusion: In conclusion, surface-functionalization by SCMC or CM-κ-Car of 3D-printed PCL-scaffolds enhanced preosteoblast proliferation and osteogenic activity, likely due to increased surface roughness and hydrophilicity. Surface-functionalization by SCMC most strongly enhanced cell proliferation, while CM-κ-Car most significantly promoted osteogenic activity, suggesting that surface-functionalization by CM-κ-Car may be more promising, especially in the short-term, for in vivo bone formation.

Keywords: Carboxymethylated κ-carrageenan; Polycaprolactone; Preosteoblast; Sulfated carboxymethyl cellulose

Suspected to be affected with stickler syndrome type 1 (Research Paper)

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Introduction: Stickler syndrome, or hereditary progressive arthro-ophthalmopathy, is an autosomal dominant connective tissue disorder that can affect the eyes and the joints. The prevalence and incidence of this syndrome are 1 to 3 per 10,000 and 1 per 7,500-9,000 births, respectively. Has known in six different types according to their genetic origin, the most common of which is type 1, which accounts for approximately 80 to 90 % of cases. This syndrome is caused by a mutation in the COL2A1 gene located on chromosome 12q13.11. This study was conducted with the aim of determining the clinical manifestations of patients suspected with stickler syndrome type 1 in Iran.

Methods: This cross-sectional, descriptive-analytical study was carried out on patients referring to a cranial deformity clinic in Isfahan, Iran. The medical records of all eligible patients admitted between 2009 and 2022 (over 6000 individuals) were assessed. Totally, 24 patients suspected with stickler type 1 were identified and their clinical manifestations were examined. Then, the data were analyzed in SPSS v.26 using descriptive tests (independent sample T-test and chi-squared test) at the significance level of0.05.

Results: The mean age of patients was estimated to be 12.8 ± 6.2. Notably, the common complications in the patients included: cleft palate (orofacial abnormality; 95.8%), ocular abnormalities (79.2%), hearing abnormalities (54.2%), cleft lip (orofacial abnormality; 45.8%), heart abnormality (29.2%), abnormality of muscle tone (25%), and nasal regurgitation (25%). There was no significant relationship between age and clinical manifestations (p-value > 0.05). However, a significant relationship was observed between gender and cleft palate (p-value < 0.05), such that 82.6% of men and 17.4% of women have had these condition.

Conclusion: According to the findings, most of the patients had cleft palate abnormalities, and fewer showed abnormalities of muscle tone and nasal regurgitation. There are mixed reports concerning the prevalence rate of abnormalities associated with stickler syndrome. It is also recommended that researchers in other countries evaluate the frequency (percentage) of clinical manifestations of patients with stickler syndrome type 1.

Keywords: stickler syndrome type 1, clinical manifestations, cleft palate

Synthesis of silver nanoparticles Using pistachio skin extrac (Review)

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Introduction: The green synthesis of silver nanoparticles is an environmentally friendly approach that should be considered for its potential Different plants are further investigated for the synthesis of nanoparticles. In this review Green synthesis of silver nanoparticles using green skin of pistachio and the role of plant metabolites in it We describe the synthesis process Despite the abundance of pistachio cultivation land in Iran, access to Pistachio skin is easy to throw away. The use of plant extracts due to the elimination process complex cell culture and not using pressure, temperature, high energy and toxic substances as well The stability of the produced products is very useful for the synthesis of silver nanoparticles on a large scale Is. silver nanoparticles in different aspects such as antimicrobial, biomedical, environmental We describe life and agriculture. Plants contain phenolic compounds that are molecules Simple like phenolic acids to highly polymerized molecules like tannins Pistachio kernel and skin as a rich source of phenolic compounds with antioxidant properties, anti It is known to be anti-inflammatory and anti-microbial. Silver nanoparticles due to their antiviral properties They are known by themselves. Cellular absorption, biological distribution, penetration of biological barriers of prokaryotes or eukaryota to evaluate these parameters from very sensitive and specialized methods of analysis They are used quantitatively and qualitatively. Plant chemicals including terpenoids, flavonoids and amides They are directly involved in the reduction of ions and the production of silver nanoparticles

Methods: Pistachio shell synthesis) for The production of silver nanoparticles has a beneficial effect on the environment. With a review of NC sites BI, Google Scholar and PubMed found out: with the DLS device, the amount of light scattering and The SIM device measures the size of silver nanoparticles By using SEM and DLS, it is determined that pistachio skin extract is used It is prepared from a rotary device to detect and check the silver nanoparticles used Placed

Results: The purpose of this research is to produce nanoparticles with silver value using Pistachio skin extract has antibacterial properties and antioxidant properties Through investigation and research, we found that the synthesis of

nanoparticles in different conditions causes a change in the size of Nanoparticles will be synthesized

Conclusion: Sigun kadagiti nabasa nga artikulo, babaen ti pannakaaramid ti kudil ti pistachio, nabigbigmi a posible ti mangpataud kadagiti pirak a nanopartikulo nga addaan iti kudil ti pistasio New forms of products with silver for sure in future treatment Many complex and difficult diseases will be used. Hopefully the results from This article aims to advance biological science and medical science

Keywords: silver nanoparticles, DLS device, device Rotary, green synthesis, antibacterial properties,

Targeted delivery of doxorubicin chemoreagent to breast cancer cells using chitosan-folic acid micelles (Research Paper)

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Introduction: Using nanoparticles for anticancer drug delivery can increase drug circulation time and decrease the effective drug concentration, leading to reduced side effects. It is well known that tumor capillaries develop malformation in their structure, leading to increased permeability. As a result, nanoparticles can be accumulated in the tumor area. In addition, cancer cells overexpress some receptors, such as folic acid receptors on their surface, which can be used for active targeting. In the present study, we have used amphiphilic polymeric micelles decorated with folic acid to deliver chemoreagent doxorubicin to the breast cancer cells. For optimum drug delivery, nanoparticles must be able to keep their cargo in the circulation, but also capable of releasing the drug in the tumor site. pH-sensitive delivery systems can maintain the drug in the physiologic pH; however, they discharge it in the acidic tumor environment. Therefore, in our study, we have used chitosan as a pH-sensitive polymer for micelle fabrication.

Methods: Micelles were fabricated using a high-speed homogenization method. Ninhydrin and DLS assays were used to determine the characterization and size of fabricated nanoparticles. To assess the cell viability, MTT assay was used. Fluorescent microscopy used to show the uptake of nanocarriers into the treated cells. Also hemolysis test was used to show the effect of obtained nanocarriers on red blood cells. At last, the effect of drug-loaded nanoparticles was assessed in tumor-bearing mice.

Results: First, we have proved the presence of chitosan and folic acid in our fabricated micelles using ninhydrin assay. Also, the DLS results confirmed that our micelle size was around 150 nm. The drug release assay showed the sustained release of doxorubicin with the maximum release after 80 hours. In vitro experiments indicated that doxorubicin-loaded nanoparticles could effectively reduce the cell viability of breast cancer cells in 48 and 72 hours. Also, fluorescent microscopy images confirmed the uptake of doxorubicin in the nanoparticle-treated cancer cells. Additionally, hemolysis study demonstrated the biocompatibility of the nanoparticles for in vivo application.

At last, in vivo experiment revealed that systemic injection of doxorubicin-loaded nanoparticles could effectively decrease tumor volume.

Conclusion: To conclude, our data showed that sustained drug release from our nanoparticles makes them a suitable and practical option for the suppression of breast cancer cells growth.

Keywords: Cancer, Nanocarriers, Doxorubicin, Micelle

Targeting miRNAs with CRISPR/Cas System in Cancer (Review)

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Introduction: Cancer is a fatal disease that requires multiple gene mutations and alters epigenetics throughout the genome. In a cancer cell, oncogenes are activated and tumor suppressors are inactivated, as well as dysregulation of the epigenome, which regulates normal gene expression, happens. MicroRNAs (miRNA) are short, small, and non-coding protein RNA molecules with a length of 20–24 nucleotides. These tiny RNAs can function as oncogenes or tumor suppressors in cancerous cells. CRISPR (clustered regularly interspaced short palindromic repeats) and Cas (CRISPR-associated) proteins are crucial elements of an ancient bacterial adaptive immune system. The Cas proteins are divided into two main classes. Mostly the class 2 systems (type II Cas9 and Cas12a) have been adopted for gene editing applications. The main difference between these two Cas is the ability of Cas12a to process the pre-crRNA (CRISPR RNA) itself so this Cas protein can be used for multiplex editing. Furthermore, Cas12a has only one nuclease domain (RuvC domain) and induces breaks in double-stranded DNA (dsDNA) or single-stranded DNA (ssDNA). Cas12 can be guided by its processed-crRNA to recognize complementary ssDNA or dsDNA with protospacer-adjacent motif (PAM) sequences and cleaves target DNA. The CRISPR-Cas system with the target-specific binding and cleavage has been applied in various fields such as genetics, gene therapy, and molecular diagnosis. Glioblastoma is the most widespread and lethal primary tumor of the central nervous system. Several studies have shown aberrant expression of miR-21 in many cancers including glioblastoma with a high expression of miR-21. In a survey, the knocking out of this important miRNA in glioma caused decreased proliferation capacity of these cells.

Methods: For studying the knocking-out function of CRISPR-Cas12a on miR-21 in glioma cells, animal models, and cell cultures were used. A combination of encoding plasmids with different sgRNAs for miR-21 and a plasmid expressing Cas12a were transfected to glioma cultured cells. Cell sorting was done using different fluorescence dyes, and cells with both Cas12a and sgRNA plasmid were selected. miRNA levels were analyzed using the TaqMan qRT-PCR. In the following steps, DNA and RNA sequencing, and western blotting were carried out to validate the CRISPR activity and to verify the miR-21 knock-out in mouse and human glioma lines. Then for imaging, immunofluorescence staining using anti-GFP was accomplished. Moreover, different assays were applied for evaluating the amount of cell proliferation, migration, and invasion.

Results: Following a comparison of expression levels of miR-21 in wild-type (WT) and CRISPR-edited human and mouse cells, it was shown that miR-21 levels of the miR-21 knockout (KO) of mouse and human glioma cells were significantly lower than the WT cells. Next, the CRISPR-edited clones were aligned to the WT sequences to analyze the CRISPR-induced insertion-deletion (INDEL). There were no changes outside of the intended target. NGS results represented that miR-21 KO cell lines showed INDELs around the cut site compared with no INDELs in the WT sequence. Moreover, RNA-seq analysis of downstream miR-21 targets showed that the lack of miR-21 resulted in enhanced levels of several miR-21-regulated anti-proliferation mRNAs. Proliferation was significantly decreased in miR 21 KO mouse and human glioma cells, as compared with miR-21 WT cell lines. Also, animal experiments showed that the mice injected with miR-21 KO cells indicated a reduction in tumor growth and an increase in survival compared with the mice injected with miR-21 WT cells.

Conclusion: CRISPR-Cas system is a reliable and powerful gene modifier technology by taking advantage of the sequence-specific target binding and cleavage. It provides an incredible method for genome analysis, regulation, and editing which impacts the treatment and prognoses of patients with cancer. Disruption in the regulation of miRNAs expression in cancer cells can act as either a tumor suppressor or oncogene, resulting in inhibition or promotion of tumor development, respectively. In many cancers, including glioma, miR-21 is highly expressed and functions as an oncogene regulating many various downstream mRNA targets. Knocking out of miR-21 in glioma using the CRISPR technique was confirmed by non-detectable miR-21 expression levels and NGS. This deletion resulted in reduced proliferation, migration, and invasion of these cells in vitro, as well as increased survival of tumor-bearing mice in vivo.

Keywords: CRISPR/Cas, miRNA, Cancer, Glioblastoma

Tetrahydrobiopterin responsiveness in Phenylalanine hydroxylase deficient patients from North-east of Iran: genotype-phenotype correlation, identification of a novel mutation and seven new responsive genotypes (Research Paper)

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Introduction: Phenylalanine hydroxylase enzyme defects result in a hereditary metabolic disorder called phenylketonuria. Sapropterin (tetrahydrobiopterin) is one of the treatment strategies for this disorder. Even though a correlation between genotype and BH4 responsiveness was established by earlier studies, a subset of mutations often presented inconsistent responses and/or phenotypes. Different genetic background is one of the potential reasons for this fact.

Methods: In this study, the genotype of a total of 34 PAH deficient patients from Khorasan-Razavi providence in the north-east of Iran was obtained. Among this patients, 21 individuals took the 24h and 48h BH4 loading test and if the result was positive, their Phenylalanine tolerance was assessed. It is the first study of its type in patients from Iran to evaluate genotype role in predicting the most probable responsive individuals.

Results: The known pathogenic variant p.R169P and the novel variant p. Leu72_Asp75delinsTyr were first classified as responsive .Seven genotypes were reported as responsive for the first time. All patients carrying at least one pathogenic variant, which was previously reported as BH4 responsive, respond to BH4. Three patients with p.L48S, p.R261Q and p.A309V pathogenic variants were exceptions. There was no certain statistical correlation between genotype and response. Genotype and phenotype were significantly correlated and majority of patients with mild phenotype carried at least one non-null pathogenic variant

Conclusion: In Khorasan-Razavi province of Iran, patients with at least one non-null mutation are most probable to demonstrate mild phenotype and respond to BH4 phenotype.

Keywords: Phenylketonuria, BH4 response, Phenotype, Genotype, mutation

The effect of cigarette smoke on the growth of oral stem cells (Review)

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Introduction: Stem cells are cells capable of creating any type of cell in the body. Under the influence of different growth factors in the culture medium, they can be converted into cells with specific functions such as heart muscle cells or insulin- producing cells, pancreas, etc. These cells also have their own renewal capability, meaning they are able to perform mitosis divisions in order to preserve their population. An epithelial cell is a specialized cell that forms a thin tissue barrier, which can be on the surface or inside a tissue. Different types of epithelial cells, including epithelial tissue, skin, mouth, respiratory tract, etc. can be found throughout the body. Oral mucosa is constantly exposed to environmental forces and must be constantly renewed. Accordingly, oral mucosal epithelium contains a large reservoir of epithelial stem cells, which is essential for tissue homeostasis. If stem cells change, they can become cancer cells. The only difference between cancer stem cells and stem cells is they also have tumorigenic power. Some environmental factors can turn them into cancer cells by affecting stem cells. Cigarettes are one of these cancer-causing substances, accounting for 22 percent of all cancer deaths annually. Cigarette smoke in terms of physical nature has two parts: gas (95%) and particles (5%), which contains substances such as droplets, which is the most important known carcinogen in nature. More than 5000 elements have also been found in cigarette smoke, among which at least 150 compounds contain free radicals, which can cause systemic disorders such as heart disease, cancer and lung disease. Recently, it has been proven that imbalances in the level of free radicals and reactive oxygen species along with antioxidants may play a key role in the onset and development of several inflammatory oral injuries. When smoking, smoke from cigarettes has direct contact with most stem cells (epithelial) of the palate, which can cause oral cavity cancer. Oral cancer is a cancer that occurs as a result of the growth of malignant cells. This cancer, which occurs in the area of mouth, tongue, foam, palate, mouth and gums, is more common in smokers. Oral cavity cancer is often caused by abnormal division of stem cells (epithelial). In a healthy body, there are thousands of billions of cells that are divided according to the body's needs. Healthy cells have life cycles, reproduction and death based on their type. With the death of old or damaged

cells, new cells replace them. they will be One of the environmental factors that disrupts this process and alters stem cells is oxidant or oxygen free radicals in cigarette smoke, which changes epithelial stem cells to cancer stem cells that eventually lead to tumors and cancer. The main reason for the oxidant damage is that free radicals lack a whole pair of electrons, take electrons from other molecules and damage those molecules in the process. Antioxidants neutralize free radicals by losing some of their electrons, thereby no longer harming the body and improving the general health of the body. Vitamin C is one of the substances with high antioxidant properties and studies have shown that vitamin C consumption can have a great impact on preventing cancer.

Methods: In this review article, searches were conducted in electronic and scientific databases, Magiran, SID, PubMed, Google Scholar and other valid databases and 50 valid articles related to the subject were used.

Results: The results show that the damage caused by smoking is caused by substances called oxidants. These substances affect them by disrupting stem cell niches and turning them into cancer cells and can eventually cause cancer. To prevent damage caused by oxidants to the body, antioxidants can be used. Vitamin C is one of the examples of unnecessary antioxidants and people who smoke can first avoid smoking to prevent cancer and if unable to, Use vitamin C to maintain your health.

Conclusion: The oxidant in cigarette smoke causes oral cavity cancer and other cancers that can reduce the oxidant effect by using antioxidants, especially vitamin C.

Keywords: Stem cells, cancer, cigarette smoke and antioxidants.

The Analysis of expression level of UBE2B and CX3CR1 in sperm cell of infertile patients (Research Paper)

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Introduction: Male infertility is one of the most prevalent Health problems around the globe which affects millions of people. Evaluation of semen sample is most common used test for evaluation of male infertility but there is a significant overlap between semen parameters of fertile and infertile men which makes the characterization of male infertility difficult and the significate part of male infertility is called “unexplained infertility”. So, the researchers in the field of infertility tried to find new molecular markers for better characterization and understanding of male infertility.

Methods: In current study sperm samples of 80 infertile male were recruited. 24 samples were asthemoteratospermia (AT), 18 asthenospermia (AS) and 17 numbers were Teratospermia (TS). 21 numner of semen samples were choosen to be normospermia (NS). Using Real-time PCR technique, expression level of three genes including UBE2B and CX3CR1were evaluated.

Results: No significant alteration was observed in expression level of CX3CR1 gene compared to the control group. Also, using Real-time PCR no expression was observed in UBE2B gene in sperm samples.

Conclusion: This study showed that alteration in expression level of genes can be used as proper molecular markers for male infertility in the future. We didn’t observe significant alterations in expression level of CX3CR1 and still more studies are required to correlate expression level of this gene with sperm characteristics.

Keywords: Male infertility, Asthenospermia, Asthenoteratospermia, Asthenoteratospermia, teratospermi

The anatomy of the liver in traditional medicine and comparsion with modern medicine findings (Review)

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Introduction: Introduction: The science of anatomy is one of the important bases in both traditional and modern medicine, and a physician cannot treat diseases without knowledge the anatomy and physiology of the organ. Hakim Seyed Ismail Jorjani wrote in his book, "If a doctor does not know how to do a good dissection, he will make a lot of mistakes in diseases. The doctor must first dissection the same organs, and the combination of compound organs, the neighborhood, and the participation of each organ with the other, and the properties and he should know the action and strength of each one and know the form and organization of each one to achieve his purpose. Therefore, the aim of this study was to investigate the anatomy of the liver from the perspective of ancient medicine and compare it with modern medicine.

Methods: Method: In this descriptive-comparative study, first, authentic texts such as Akbari's Medicine, Khwarizmshahi's collection, Mansouri's Tashrih and Abdolvahab Tafreshi book have been noted. Then a comparison of the materials was made and the commonalities and differences were categorized and compared in the form of tables.

Results: Results: The descriptions include the liver location, nerves, vessels, ligaments and anatomical Adjacents. In the ancient books, the liver is dark red and its location is mentioned on the right side (right hypochondrium). Its convex side is towards the diaphragm and its concave side is the portal vein. The impressions of the liver are related to the diaphragm, colon, right kidney, fundus, and gall bladder. Ancient medicine considered the liver to be insensitive, but the membrane covering it was considered to have a lot of sensation. A branch of the descending aorta is mentioned in the book of liver descending aortae, which is in line with modern medicine. Liver ligaments include falciform ligament, coronary ligament, and triangular ligament.

Conclusion: Conclusion: The consistent of the anatomical descriptions about the liver shows the knowledge of traditional medicine physician about the science of dissection without facilities such as CT scan and MRI is excellent. In addition, the review of ancient medical texts shows that the basis of modern anatomy is the information that has reached the hands of todays years ago.

Keywords: Liver, ancient, medicine, comparative

The anticancer effect of Malva sylvestris extract on human glioblastoma U87 cell line (Research Paper)

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Introduction: Glioblastoma is a rapidly growing and aggressive brain tumor that attacks the tissues near the brain and spinal cord and in many cases does not respond well to various drug treatments. Malva sylvestris is a medicinal herb and its flowers, leaves and seeds have been used for many years. extract of this plant is used in traditional medicine to treat inflammatory and infectious diseases and heal wounds.

Methods: In this study the effects of Malva sylvestris hydroalcoholice extract were searched by MTT assay on human glioblastoma U87 cell line . The MTT assay is a colorimetric assay for assessing cell viability and metabolic activity in different treatments. NAD(P)H-dependent oxidoreductase enzymes are capable of reducing the tetrazolium dye, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, to an insoluble formazan, which has a purple color with appropriate absorption in 570 nm. As a scale, IC50 was determined for this extract and this cell line. In cellular researches, IC50 is a quantitative measure that indicates how much of an inhibitory substance (for example a herbal extract) is needed to inhibit cell growth by 50%.

Results: The results of this investigation after two days compared to the control and with three repetitions, showed that the death of cancer cells when exposed to concentrations of 0.005 to 0.8 miligrams/ml of the extract of this plant has an almost concentration-dependent trend. By drawing a graph of cell viability percentage in different concentrations of the extract, IC50 was determined, and the optimal concentration was 0.24 mg/ml.

Conclusion: The aerial parts of this plant are composed of several compounds, including mucilage polysaccharides, tocopherols, carotenoids,

and various flavonoids such as anthocyanin, luteolin, kaempferol and similar compounds. It is still not possible to say that the observed anticancer effect is related to which of the compounds of this plant, but further research and isolation of compounds and treatment of glioblastoma cells with each of the constituent compounds of this plant will clarify this issue.

Keywords: cancer Malva sylvestris glioblastoma U87 herbal medicine

The antimicrobial activity of nanoparticles: upcoming hope to overcome antibiotic resistance crisis (Review)

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Introduction: Bacterial infections still represent a serious and increasing therapeutic problem despite exponentially increasing knowledge in all fields of medicine and considerable improvements in both diagnostic and therapeutic medicine. In the 21st century, nanotechnology has become one of the most important and influential technologies in science worldwide. Nanomaterials are structures that have at least one dimension on the nanometer scale (1-100 nanometers). an option to overcome biofilm formation and bacterial resistance is restoring the antibacterial effects of antibiotics by their combination with novel nanostructured antibacterial substances. The nanostructured antibacterial materials include metal or nonmetal nanoparticles (NPs) such as silver, gold, copper, bismuth, and selenium, and metal oxide NPs such as ZnO or Al2O3 NPs. Most of these nanostructured materials show antibacterial effects themselves through nonspecific activity, which can limit the development of bacterial resistance. one of the outstanding advantages of nanotechnology in antimicrobial treatment is the potential of this technology to deal with existing microbial resistance and also to prevent its further development. These results can be achieved by designing different strategies, including simultaneous targeting of multiple pathways using multiple antimicrobial nanomaterials. There are two main approaches in nanomedicine applications in antimicrobial therapies. The first approach is the expansion of organic and inorganic nanomaterials with antimicrobial properties and the second approach is the release of antimicrobial drugs with nanoparticles. this study focuses on the mechanisms of bacterial resistance and antibacterial activity of nanoparticles, because investigating the antibacterial mechanisms of these particles is very important for the production of more effective antimicrobial agents.

Methods: To select the used documents, first the titles found by the search engine were checked in terms of thematic relevance. The found materials were divided into three groups: internet, books, and articles. The search words were: "Bacteria," “Nanotechnology,” “Antibacterial,” “Nano”, ”Narrative Review article(s) ” ‘”Review article(s) ” review of the literature, narrative review, title, abstract, authorship, ethics, peer review, research methods, medical writing, scientific writing, using PubMed, Scopus, Science Direct, Google Scholar databases and Scientific Information Database. in addition, manual searches of other relevant journals and keywords searches were performed. We have focused on published papers from 2010 to 2021.

Results: Antibacterial effects of nanoparticles are created due to the presence of special physical and chemical properties in nanoparticles, because unlike common antibiotics, nanoparticles have specific dimensions of about 100 nm. Their small and unique size leads to the creation of new properties, among these properties is greater interaction with cells due to the creation of a larger surface, increasing the surface-to-mass ratio and controlling their acceptance. Nanoparticles have a high ability to be used as a carrier and adjuvant, and they also have the ability to strengthen the immune system and fight bacteria using several mechanisms at the same time. Nanoparticles attack microbes through multiple mechanisms that are active simultaneously. Simultaneous mechanisms greatly reduce the probability of multiple mutations in different genes, so it becomes very difficult to create resistance against nanoparticles. Nanoparticles can fight against microbes and the resistance mechanism in bacteria, they can also act as a carrier for antibiotics. Combining nanoparticles with antimicrobial substances, such as antibiotics, peptides or various biological molecules, is one It is one of the new and suitable methods to eliminate antibiotic resistance. The most important characteristics and advantages of nanoparticles as carriers of antibiotics are: small size of nanoparticles, protection of nanoparticles from drugs, accuracy in drug targeting, ability to control drug release, and the ability to combine and transport several antibacterial drugs.

Conclusion: Today, antibiotic resistance in bacteria is the most important crisis in global public health, and new research should be done worldwide for the development of more effective antimicrobial compounds. Nanoparticles are among the agents that have been given much attention to target bacteria as an alternative to antibiotics, so that they are beneficial in the treatment of bacterial infections. According to the studies, nanoparticles have a high potential to solve the problem of the emergence of resistant bacteria; Because nanoparticles either do not have cytotoxicity or usually their toxicity is very low and their production methods do not include risky and complex processes.

Keywords: Nanoparticles, antimicrobial resistance, Antimicrobial activity, Antibiotic

The Antiviral effect of Selenium on the Replication of Herpes Simplex Virus Type 1 (Research Paper)

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Introduction: Herpes simplex virus-1 (HSV-1) is an enveloped double-stranded DNA virus that infects about 70% of the world population. Selenium as a cofactor for glutathione peroxidase has a key role in antioxidant defense for cells. Several studies have reported that selenium deficiency promotes viral mutations, replication, and the emergence of more pathogenic forms of viruses. Selenium can be an antiviral, but its direct effect on HSV-1 is unknown. The present study was designed to evaluate the antiviral effect of selenium (Se) against HSV-1.

Methods: After determining cytotoxicity by MTT assay, selenium (0.5 uM, 1 uM) was added to HeLa cells 24 h before (pre-infection treatment) and 24 h after (post-infection treatment) HSV-1 inoculation. After 47 h of incubation at 37°C, the viral titer and expression levels of the UL47 gene were determined by tissue culture infectious dose 50 (TCID50) and Real-Time PCR methods, respectively.

Results: Selenium with concentrations of 0.5 uM to 4 uM had cytotoxicity lower than 50% during 24 h and 48 h incubation. HSV-1 titer in all experimental assays was significantly lower than the virus titer in the control group. In general, the reduction of virus titer in post-infection assay was lower than pre-infection assay. Se in concentration of 1 uM could reduce the virus titer about 2.33 Log10 TCID50/ml. Se in concentrations of 0.5 uM and 1 uM decreased UL47 gene expression level about 1.6 and 2-fold, respectively.

Conclusion: Selenium has potent antiviral activity against HSV-1. However, further studies are needed to clarify the antiviral mechanism of selenium.

Keywords: selenium-herpes simplex virus-Antiviral

The application of shape memory polymers in the treatment of various diseases,today and future: a narrative review (Review)

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Introduction: Expensive and dangerous surgeries, the slow process of healing of many diseases and the possibility of their relapse are problems that have become a global concern today. Shape memory polymers (SMP) are materials with a three-dimensional porous structure that can change their geometric shape in response to external stimuli such as heat, moisture, and pressure, and can be used as foam, scaffold, patch and other polymer substrates. Generally, the structure of SMPs consists of two phases, called basic phase and reversible switching phase. In the basic phase, SMPs are in their original form, while in the switching phase, the secondary form is created and the possibility of changing the form is provided. In tissue engineering, porous SMPs can be designed as self-regulating scaffolds that are used to stimulate the growth or regeneration of various tissues. The use of SMPs has the potential to replace current medical procedures with much less invasion. This review aimed to synthesize evidence on the benefits of application of SMPs in treatment of various diseases.

Methods: This is a narrative review study conducted in September 2022, and the authors searched PubMed, Embase, Web of Science, Google Scholar search engine, and Scopus databases (from 2010 to 2022) using the keywords "shape memory polymer", "Tissue engineering", "self-regulating", "biofunctionality", "minimally invasive delivery" and "personalized treatment". After the initial search, screening was done in two stages. In the first stage, the title and abstract were checked in terms of relevance to the study objectives, and 132 related articles were selected. In the next step, 25 articles that met the inclusion criteria (English-language studies, original, intervention and observation articles) were selected and finally, we independently extracted and combined the data from the selected articles.

Results: The results of this study showed that the benefits of using SMPs in the treatment of various diseases include: improving the effect of treating bone defects as a result of diseases such as osteonecrosis and a suitable replacement for arthroplasty, improving the effect of treating vascular aneurysm by filling the expansion of vascular aneurysm, eliminating thromboembolism in stroke brain, intra-intestinal stents to transfer the prosthesis to the intestinal canal, reconstruction of congenital defects in the rat's stomach, recovery of heart attack using SMP scaffold with stem cells and growth factors as a patch of the injury site and placing them in the heart tissue with the help of Needle (the transfer of tissue pieces is not limited to one tissue, because the transfer can be done under the skin, heart, liver and around the aorta). SMPs can also be used in dialysis to reduce arterial pressure, control fertility and temporary and permanent sterilization in the form of stents, open or close the urinary and genital tracts in the form of stents, reduce intraocular pressure in the form of implant and healing Astroglial lesions in the brain injury.

Conclusion: This study stated benefits of application of SMPs According to the reviewed studies, we concluded that in the near future, a strong focus on SMP will enable recovery and activation of scaffold forms independent of body temperature and without the need for direct access. In addition, they can be used for personalized patient care. Also, degradable SMP stents are considered a very attractive future strategy that may overcome treatment-related complications such as late thrombosis and also provide a way to deliver SMP materials to the heart via angiography. This study has tried to have a comprehensive and comparative review of the benefits of SMPs in the treatment of various diseases, and more studies are needed to examine the benefits and challenges of each of the mentioned cases in a more specialized manner.

Keywords: Shape memory polymer(SMP), Tissue engineering, Biofunctionality, minimally invasive delivery, person

The association between ARNTL expression and metabolic syndrome (Review)

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Introduction: Due to the importance of early diagnosis and its effectiveness in the treatment of head and neck cancer, we identified and validated ten lncRNA as a biomarker for diagnosing head and neck cancer. The circadian clock, which is affected by fluctuating changes in the conditions of light, darkness, and temperature, is effective in all aspects of human life despite being independent of the sun. Many periodic and daily behaviors such as blood pressure and digestive activities that increase during peace or melatonin production in the evening are regulated and occur with food and sleep. This cell-independent oscillator, which exists in almost all cells of the body, is called the circadian clock. 4 This molecular clock is maintained by a master pacemaker that resides in it. The superior asthmatic nuclei (SCN) of the hypothalamus receive signals by the dawn-dusk light cycle, which pass through the photosensitive retinal ganglion cells (ipRGCs) and then are transmitted to the SCN by synaptic connections. Finally, the ling factor directs the transcriptional response mediated by per genes. Because exposure to light adjusts the SCN and the environmental clocks are synchronized with it when the geographical conditions change and the body travels, it takes approximately 24 hours to adapt to the new phase of darkness and light. Because the circadian clock is relatively stable against these extracellular changes and it is possible to match the physiological and behavioral hub cycle. Today, one of the biggest threats to our health, which every ethnic group and society is facing, is a sleep disorder, which more than 22 million Americans suffer from. Its many complications include major metabolic syndrome, arteriosclerosis, high blood pressure, dyslipidemia, obesity, diabetes mellitus, cardiovascular diseases, several cancers, and certain types of brain diseases such as Alzheimer's disease.

Methods: In this review, relevant studies were searched in scientific databases fusing Based on their title, keywords associated with ARNTL, metabolic syndrome and circadian clock from 2010 to march 2022. Out of 356studies, 27 articles related to our aim according to the inclusion criteria of this review article, were studied.

Results: Changes in circadian clock function have been linked to metabolic disorders in genome-wide association studies. Epidemiological studies have shown that a loss of nocturnal decline in blood pressure increases the risk of cardiovascular morbidity and mortality and end-organ damage. Looking at clock genes, however, there is no obvious association between symptoms of diabetes or metabolic syndrome and clock gene expression.

Conclusion: Studies clearly show that circadian disruption is important a risk factor for developing metabolic disorders, while obesity feedback and its Metabola-physiological consequences in circadian clock function in central and peripheral tissues, Creating a vicious cycle while cardiovascular complications like As high blood pressure is often seen in type 2 diabetes and in patients with metabolic syndrome, and circadian regulation disorder Rhythm in blood pressure regulation may or may not occur. This variety is another strong case for outpatient blood

Keywords: ARNTL, metabolic syndrome , circadian

The beneficial effects of combination herbal therapy (zayesh booalidaroo®+ Safoof-e hefz + Royal jelly) on semen quality of oligo-astheno-teratozoospermic men (Research Paper)

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Introduction: Male infertility is defined as a man's inability to conceive a child from a fertile woman. It has been shown to be responsible for 30-50 percent of infertility in humans and affects about 7% of all men. In the world today, several factors such as genetics, exposure to toxins, and aging have resulted in significant levels of male infertility. Semen quality is utilized as a criterion of male fecundity whereas male infertility is frequently caused by defects in the semen parameters including sperm concentration, appearance, and motility. Since infertility as a health-care issue has the potential to cause substantial psychological problems, as well as a difficult and depressing life for parents, its treatment has become a major pharmaceutical and medical industry concern, with products ranging from fertility hormones and other medications to in vitro fertilization procedures. In the meantime, traditional medicine is a very important discipline of pharmacy and medicine, and the plants employed in this medicine are considered as the main sources for the pharmaceutical industry's research into pharmacologically active medications. Furthermore, worldwide public interest in the use of this sort of treatment is steadily increasing. A variety of plants has been used to treat specific facets of male infertility, including sexual inability, libido (sexual desire), erectile and ejaculatory problems, and sperm abnormalities (azoospermia, oligospermia). It seems that the antioxidant, anti-inflammatory, anti-oedematous, and vagotonic properties of medicinal herbs can be considered as their probable mechanism to improve sperm parameters. They may also contain precursors for sperm production and raise serum testosterone (T) levels. Most of the investigations on the use of medicinal herbs in treating male infertility are conducted on experimental animals, with only a few clinical trials being published. Therefore, further investigation of the therapeutic effects of herbal medicine in humans seems to be necessary. The aim of this study was to

evaluate the effects of compound herbal medicine (zayesh booalidaroo®+ safof-e hefz+ royal jelly) on improving abnormal sperm parameters and the hormonal level (LH, FSH, and T) of oligo-astheno-teratozoospermia (OAT) patients.

Methods: This study was conducted as a phase 3 randomized clinical trial. Totally, among infertile men referring to the highly specialized Rooya infertility treatment center, ACECR, Qom branch, 50 men with OAT were enrolled in this study, in 2020. All individuals gave informed consent prior to participation in the study. Patients were recruited with the following inclusion criteria: infertile couples with no previous report of pregnancy, normal female partners, and male partners defined as having OAT based on World Health Organization (WHO, 2010) criteria (24). Exclusion criteria were: History of receiving chemotherapy drugs, corticosteroids, anticoagulants, testosterone, and anti-androgens two months before the start of the study. Genital infections, anatomical abnormalities, chromosomal abnormalities, history of genital surgery (varicocele), alcohol or drug use, patients with ejaculatory disorders, systemic diseases (malignancy, thyroid disease, liver, and gallbladder). All the participants were selected based on the results of semen analysis by a urologist. The patients orally received combined herbal medication including zayesh booalidaroo®+ Safoof-e hefz+ Royal jelly- which is produced in Booali Daroo Company, Iran- for 3 months. Variables including seminal parameters, sperm DNA fragmentation (SDF), chromatin maturity, total antioxidant capacity, lipid peroxidation, and hormonal parameters (LH, FSH, T, Prolactin, and Estradiol) were measured before and after the interventions.

Results: According to the obtained data, improved total and /ml count ($p=0.0001$ and $p=0.007$, respectively) along with increased progressive and total motility (0.02 and $p= 0.043$, respectively) were shown after the herbal intervention. Also, herbal therapy decreased SDF significantly ($p= 0.000$), while couldn't change the percentage of protamine deficiency ($p= 0.49$). In hormonal assessment, except in the case of the T hormone which showed an elevated amount ($p= 0.00$), there was no significant change after the intervention ($p>0.05$). The increase in testosterone level, which subsequently leads to the improvement of sperm parameters, as well as the amelioration of sperm chromatin quality, in turn, are derived from the antioxidant properties of the ingredients contained in the herbal complex, whereas the concentration of seminal plasma antioxidant including malondialdehyde (MDA), total antioxidant capacity (TAC) and superoxide dismutase (SOD) revealed significant increase ($p= 0.000$, $p= 0.005$, $p= 0.013$, respectively).

Conclusion: Our herbal complex improves male infertility in an efficient manner and can be regarded as an alternative option for ameliorating semen quality.

Keywords: Oligoasthenoteratozoospermia, Herbal therapy, Semen parameters, Antioxidant enzymes

The bioinformatics role of Mir-203 in the PI3K / AKT / MTOR / ERK signaling pathway involved in prostate tumorigenesis (Research Paper)

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Introduction: The prostate is a small gland located below the bladder and covers the upper part of the urethra. Prostate cancer is the most common adenocarcinoma of men in the United States and the fourth most common cancer in the Iranian male population. MicroRNAs are small single-stranded RNAs that, by degrading the target strand or inhibiting its translation, play a key role in regulating the post-transcription of multiple biological processes and molecular pathways involved in cancer. The pathway is regulated by microRNAs and eventually causes cancer; Studies over the years have shown that miR-203 has been shown to increase its expression by acting on its target genes in prostate cancer, leading to disruption of the intracellular signaling pathway and metastasis to other tissues Followed. Therefore, the aim of this study was to bioinformatically evaluate the role of miR-203-3p and miR-203-5p and predict its role in the intracellular signaling pathways of PI3K / AKT / MAPK / ERK in the development of prostate cancer, as a biomaker. The diagnosis / prognosis is examined.

Methods: In this study, using bioinformatics algorithms, first to investigate the role of microRNA-203 in prostate cancer, to look for changes in the expression of microRNA-203 in this disease at OncomiR site and then to investigate the role of microRNA-203 in pathways Interfering signaling in the pathogenesis of prostate cancer, miR-203 is examined in the bioinformatics site mirPath v.3. Then, by entering the full name of the microRNA-203 in the window related to the KEGG database and selecting the TarBase V.7 algorithm, we examine the molecular paths and the thermal map of the miR-203. Finally, to ensure the accuracy of the results and prevent false positive results, 11 known online gene target prediction databases are used in the miRWalk 0.2 database, and finally the results of mir-203 are used using the DIANA TOLLS-miRPath v database. .3 is shown. . Data analysis will be scored using the results extracted from the databases and the significance of Pvalue <0.05 will be considered by Mann-Whitney test.

Results: In the present study, several bioinformatics databases were investigated to predict miR-203 in prostate cancer in order to initially predict the possible interaction of genes and pathways involved with miRNAs, which reduced costs and wasted time.

Conclusion: Highly sensitive bioinformatic approaches were used to predict miR-203 and showed the value of miR-203-3p and miR-203-5p as a diagnostic marker in prostate cancer with further studies and molecular evaluation in the pathways leading to prostate cancer. It can be used as a diagnostic target in the detection and diagnosis of prostate cancer.

Keywords: cancer-algorithm-parastate

The connection between ace2 and inhibitory ace2 drugs with sars-cov-2 (Review)

Haniye Zafari,[1] Maral Atri,[2,*] naeimeh shibaei,[3]

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Introduction: Corona is a group of viruses that result in respiratory infectious disease in birds, mammals and humans. One of the types of corona virus is Sars-Covid-2 which causes the disease of Covid-19. The main reason of death in patients which suffering from this virus have acute respiratory failure. Among other causes, we can mention the failure of several organs that leads to dysfunction of the heart, kidneys and etc. Sars-cov-2 is a type of enveloped virus with nucleocapsid ,membrane and simple single-stranded RNA. Corona virus has a crown-shaped structure called spike protein (s) which includes s1 and s2 subunits. SARS-CoV-2 uses the receptor of angiotensin-converting enzyme 2(ACE2) and it competes with angiotensin II to bind to the receptor of ACE2. By the initial connection of the S1 domain with the ACE-2 receptor, the S2 part of the virus causes the fusion of the host membrane with the virus membrane then the RNA virus can enter the host cell and motives a disruption in the expression of the enzyme gene and its reduction. This may cause an imbalance of the RAAS, a hormonal system that is responsible for a series of enzymatic reactions that mainly lead to the creation of angiotensin II and the regulation of blood pressure and body fluids. In this article, the relationship between Covid-19 and the renin-angiotensin system has been investigated.

Methods: This article was selected from the PubMed international database. The keywords of Covid-19, coronavirus, angiotensin were utilized. Then off-topic and duplicate sections were removed from the related articles.

Results: Importance of ACE2 in SARS-CoV had been studied by different scientists, Wenhui Li and teammates by testing on angiotensin-converting enzyme 2 and SARS-CoV, found that ACE2 is a functional receptor for SARS-CoV. Daniel Batlle and his teammates concluded by experimenting on mice using soluble recombinant protein ACE2 that it can be a new tool to fight the corona virus by limiting the attachment of the virus to the cell membrane. They also pointed out those studies on animals or humans using this method is not yet available and should be tested. Jun Mori and his teammates, by researching the different strategies to prevent spreading Covid-19, concluded that, the Sars-Covid-2 virus causes disturbances in the metabolism of the RAAS and the functioning of several organs, in addition to respiratory complications. They suggested that by restoring the balance in the RAAS, it is

possible to the severity of the disease and mortality in patients with covid-19. RAAS-blocking drugs are the most common ACE2 inhibitor as an effective drugs for the management of COVID-19 but the effect of RAAS inhibitor for kidney patients are unknown, so for high-risk patients, RAAS inhibitor drugs should be recommended based on the patient's kidney function and clinical stability and doctors should be aware of the sudden discontinuation of RAAS and unwanted consequences based on empirical evidence. ARBs are antihypertensive drugs that block the angiotensin II receptor and affect the renin-angiotensin system. There might be an association between antihypertensive drugs such as RAAS inhibitors, specifically ARBs, inhibitors and angiotensin-receptor blockers and the COVID-19 disease. Some studies have shown that ARBs in patients with acute lung injuries have a positive effect on the patient and may be useful. Mortality due to pneumonia in patients treated with ARBs is lower compared to patients treated with controlled treatment according to 37 meta-analysis studies.

Conclusion: In these studies, the significance of ACE2, RAAS as drugs targets were pointed out and it was found that the renin-angiotensin system, especially the ACE2 receptor, plays an important role in covid-19 and it is recommended to consider the renin-angiotensin system in the therapeutic aspects.

Keywords: Covid-19, coronavirus, angiotensin

The cytoprotective activity of an alcoholic extract of Conocarpus erectus against UVB rays in the skin cell line HSF-PI 17 (Research Paper)

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Introduction: Given the beneficial effects of kenocarpus extract in healing skin wounds, this study looked into the impact of Conocarpus leaf extract in protecting HSF-PI 17 type fibroblast cells from the harmful effects of UVB rays.

Methods: Following cell culture, the MTT method was used to test the cytotoxicity of Conocarpus extract. The cells were divided into the control group, those receiving radiation only, and those receiving radiation and the Conocarpus section. Trypan blue staining was used to determine the number of viable cells. The amount of ROS produced was calculated by measuring the fluorescence colour intensity. Real-time PCR was used to assess gene expression, and Western blotting was used to determine protein expression.

Results: Conocarpus extract had no toxic effect on HSF-PI 17 cells in the doses used. The impact of radiation resulted in a significant increase in ROS production and a substantial decrease in the cell growth rate compared to the control group . In the third group, Conocarpus extract significantly moderated growth reduction and ROS production compared to the second group. TGF-β and SMAD2/3 gene expression and Collagen protein levels were significantly lower in the second group than in the control group (p<0.05). TGF-β and SMAD2/3 gene expression and collagen protein expression increased substantially in the third group compared to the second group.

Conclusion: Conocarpus leaf extract reduces the harmful effects of UVB rays in HSF-PI 17 skin fibroblast cells.

Keywords: Conocarpus erectus, Fibroblast, HFF-PI 17, UVB, Buttonwood

The detection of HBoV, B19 and PARV4 polyomaviruses DNA in Covid-19 patients as possible coinfection agents (Research Paper)

Seyed Amir Mohammad Seyed Mirzajani,[1] Seyed Reza Mohebbi,[2,*] Seyed Masoud Hosseini,[3] Shabnam Kazemian,[4] Mahsa Saeedi Niasar,[5] Hamid Asadzadeh-Aghdaei,[6]

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Introduction: The goal of this research was to detect co-infection of polyomaviruses including polyomavirus B19, human bocaviruses (HBoVs), and human parvovirus 4 (PARV4) with severe acute respiratory syndrome 2 (SARS-CoV-2). Emerging evidence shows that individuals with Coronavirus Disease 2019 (COVID-19) frequently have viral co-infections. Symptoms of COVID-19 resemble those of frequent causes of respiratory tract infections (RTIs). Properly diagnosing the etiologies of patients with RTI symptoms is essential for both disease control and averting the breakdown of the healthcare system, especially during the COVID-19 pandemic.

Methods: Between March 21, 2021, and April 18, 2022, we collected oropharyngeal swab samples from 360 Iranian patients and analyzed them using the Multiplex PCR and Nested PCR techniques for the presence of the mentioned polyomaviruses. Of these samples, 160 (44.44%) tested positive for SARS-CoV-2 and 200 (55.56%) were negative.

Results: Three (1%) SARS-CoV-2-negative samples and seven (2.33%) Covid-19-infected study subjects had polyomavirus DNA (HBoVs, PARV4). Four (1.33%) samples had polyomavirus B19 DNA, including 3 samples from COVID-19-infected individuals and 1 sample from a negative control sample.

Conclusion: According to research conducted during the COVID-19 pandemic, coinfections are prevalent in COVID-19 patients. Furthermore, during the COVID-19 illness course, the coinfecting pathogens may be identified at various periods. However, their role in exacerbating illness symptoms is unknown. Certain research suggests that a number of them may also be able to lower the likelihood of viral co-detection. As a result, it's crucial to monitor the patients throughout the course of the infection and search for any potential coinfection agents, particularly rare viral coinfection agents like polyomaviruses.

Keywords: Covid-19, Coinfection, polyomaviruses, SARS-CoV-2

The dual role of Necroptosis in cancer therapy (Review)

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Introduction: Abstract Introduction Cancers have always been very challenging to beat. Defeating cancer and tumor progression is a big objective and also a great concern in biomedicine area. various means are widely known to defeat cancer and inhibit tumor progression like chemotherapy and radiation. But in cellular and molecular scales, everything is a bit different. Nonetheless, tumors are excessively proliferating cells; therefore, stopping them through inhibition of internal and molecular factors is a better way to remove them from the body. Among cellular and molecular pathways and factors, necroptosis is a promising but controversial way to delete cancerous cells.

Methods: As it may be known, necroptosis is a regulated and programmed inflammatory-mediated necrotic cell death, which is different from autophagy and apoptosis. Necroptosis is an immune cellular response based pathway which can be considered as an immunogenic necrosis for tumor cells. It can be effective in all stages of cancer, including oncogenesis or cancer intiation, tumor progression and also metastasis. Activation and even modification of molecular mechanisms of necroptosis for modulation of different stages of cancer is being discussed to take advantage of this promising and effective way of cell death.

Results: One of the main components of necroptosis are Receptor Interaction Protein Kinases (RIPK), especially type 1 and 3, which play an important role in the mechanism of necroptosis. Activation of these RIPKs can be triggered by various stimuli and subsequently regulate necroptotic pathway in the target cells. Another main component of this pathway is Mixed Lineage Kinase Domain-Like Protein (aka MLKL) which is a substrate to RIPK3. understanding the pathway details is highly essential in order to use this tool in anticancer therapy, although precise pattern of its mechanism is still to be discovered.

Conclusion: With current knowledge, the main mechanism is Caspase independent and generally based on the interaction between RIPK 1 and 3 and MLKL protein. Multiple stimuli can elicit necroptotic pathway including cytokines and Damage-Associated Molecular Patterns (DAMPs), which can evoke inflammatory and immune responses to induce cell death. Cytokines that can trigger necroptosis include Tumor Necrosis Factors (TNFs) and Interferon (IFN) family. The process of necroptosis should initiate with one of

the stimuli such as TNF-α, resulting in activation of TNF Receptor, activation RIPK1 and RIPK3 , phosphorylation and oligomerization of MLKL leading to necrosome formation to disrupt membrane integrity and release microchemicals. necroptosis is also an effective strategy when the cancerous cells are resistant to apoptosis; due to inactivation, inhibition or alteration of caspase activity in them. Hereby, induction of necroptosis would be a solution of omission of these tumor cells. But in general, some of the necroptosis characteristics can cause the dual function of this pathway, making it a so-called two-edged sword in cancer therapy. It can either suppressive or promotive to the tumor cells under certain conditions and circumstances. Targeting the key components and steps of this process can modify the exact function, which is tumor suppression and cancer cells eradication.

Keywords: necroptosis, cancer, cell death, therapy, immuno-oncology

The effect of cigarette smoke on the growth of oral stem cells (Review)

Sana Sivanani,[1,*] Aysa Mohammadi,[2] Narges hedayat,[3] Dorsa Mohammadi,[4] Ayda Mousavi,[5] Golshan Najafian,[6]

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Introduction: Stem cells are cells capable of creating any type of cell in the body. Under the influence of different growth factors in the culture medium, they can be converted into cells with specific functions such as heart muscle cells or insulin- producing cells, pancreas, etc. These cells also have their own renewal capability, meaning they are able to perform mitosis divisions in order to preserve their population. An epithelial cell is a specialized cell that forms a thin tissue barrier, which can be on the surface or inside a tissue. Different types of epithelial cells, including epithelial tissue, skin, mouth, respiratory tract, etc. can be found throughout the body. Oral mucosa is constantly exposed to environmental forces and must be constantly renewed. Accordingly, oral mucosal epithelium contains a large reservoir of epithelial stem cells, which is essential for tissue homeostasis. If stem cells change, they can become cancer cells. The only difference between cancer stem cells and stem cells is they also have tumorigenic power. Some environmental factors can turn them into cancer cells by affecting stem cells. Cigarettes are one of these cancer-causing substances, accounting for 22 percent of all cancer deaths annually. Cigarette smoke in terms of physical nature has two parts: gas (95%) and particles (5%), which contains substances such as droplets, which is the most important known carcinogen in nature. More than 5000 elements have also been found in cigarette smoke, among which at least 150 compounds contain free radicals, which can cause systemic disorders such as heart disease, cancer and lung disease. Recently, it has been proven that imbalances in the level of free radicals and reactive oxygen species along with antioxidants may play a key role in the onset and development of several inflammatory oral injuries. When smoking, smoke from cigarettes has direct contact with most stem cells (epithelial) of the palate, which can cause oral cavity cancer. Oral cancer is a cancer that occurs as a result of the growth of malignant cells. This cancer, which occurs in the area of mouth, tongue, foam, palate, mouth and gums, is more common in smokers. Oral cavity cancer is often caused by abnormal division of stem cells (epithelial). In a healthy body, there are thousands of billions of cells that are divided according to the body's needs. Healthy cells have life cycles, reproduction and death based on their type. With the death of old or damaged

cells, new cells replace them. they will be One of the environmental factors that disrupts this process and alters stem cells is oxidant or oxygen free radicals in cigarette smoke, which changes epithelial stem cells to cancer stem cells that eventually lead to tumors and cancer. The main reason for the oxidant damage is that free radicals lack a whole pair of electrons, take electrons from other molecules and damage those molecules in the process. Antioxidants neutralize free radicals by losing some of their electrons, thereby no longer harming the body and improving the general health of the body. Vitamin C is one of the substances with high antioxidant properties and studies have shown that vitamin C consumption can have a great impact on preventing cancer.

Methods: In this review article, searches were conducted in electronic and scientific databases, Magiran, SID, PubMed, Google Scholar and other valid databases and 50 valid articles related to the subject were used.

Results: The results show that the damage caused by smoking is caused by substances called oxidants. These substances affect them by disrupting stem cell niches and turning them into cancer cells and can eventually cause cancer. To prevent damage caused by oxidants to the body, antioxidants can be used. Vitamin C is one of the examples of unnecessary antioxidants and people who smoke can first avoid smoking to prevent cancer and if unable to, Use vitamin C to maintain your health.

Conclusion: The oxidant in cigarette smoke causes oral cavity cancer and other cancers that can reduce the oxidant effect by using antioxidants, especially vitamin C.

Keywords: Stem cells, cancer, cigarette smoke and antioxidants.

The effect of active and passive pelvic floor muscle preparation technique on pain and rate of episiotomy during delivery: A systematic review (Review)

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Introduction: Pelvic floor muscle pain and episiotomy during childbirth is very common during delivery, especially among primiparous women. It is frequently observed during delivery and can have detrimental effects on a mother's health and quality of life. Having prepared pelvic floor muscle can reduce these negative effects. Pelvic floor muscle preparation techniques can be divided into active and passive. Active techniques need patients voluntary contractions like pelvic floor muscle exercises, while passive techniques are applied by therapist and the patients muscles do not engage voluntarily like perineal massage. The aim of this study is evaluating the effect of active and passive pelvic floor muscle preparation technique on pain and rate of episiotomy during delivery.

Methods: The present study is based on articles extracted from Web of Science, Pubmed and Scopus databases and Google scholar search engine. Initially, 140 articles related to the keywords Pelvic floor muscle exercise, Antenatal perineal massage, perineal tearing, Pregnancy, Physiotherapy and Episiotomy were found during the years 2013 to 2022. Then, with further reviews, 17 completely related articles based on the PRISMA checklist were selected for review.

Results: 11 articles reviewed the passive technique. 2 of them considered the effect of these techniques in the process of reducing pain during childbirth ineffective, and the remaining 9 indicated the positive effect of these methods on reducing pain. It should be noted that all 11 articles expressed the positive effect of passive technique on reducing the rate of episiotomy. 6 other papers reviewed active techniques, all of which reported reduced pain and the rate of episiotomy during delivery.

Conclusion: According to the articles reviewed in this study, it seems that active and passive preparation technique reduces pelvic floor muscle pain and rate of episiotomy during delivery. More research are needed to compare the effectiveness of active and passive techniques.

Keywords: Pelvic floor muscle pain, Labor phase, Active and Passive pelvic preparation technique

The effect of arsenic on the body (Review)

Fatemeh jafari,[1,*]

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Introduction: Arsenic is one of the most dangerous elements in the world and it is combined in nature and we can find it in the earth's crust, especially in groundwater and soil. Arsenic is also released when coal is burned, but today more arsenic reaches our bodies because the rice we eat now contains arsenic. But what is important is that arsenic is a carcinogenic substance that directly affects DNA and causes skin, bladder, and bladder cancer by induction. Also, arsenic compounds cause dysfunction in some body organs such as the liver, digestive tract, kidneys, and bladder. And the respiratory system and its effect on the pancreas to produce insulin can be mentioned that eventually the person will get type 2 diabetes.

Methods: The effect of arsenic on cancer: Arsenic is involved in the beginning of cancer through the induction of oxidative stress and the production of ROS Methylation of arsenic by adenosylmethionine and glutathione produces highly toxic methylated species, arsenic with strong cytotoxic activity and enzyme inhibitory effect causes epigenetic effects such as histone changes and DNA methylation. Arsenic is able to bind to sulfhydrylcysteine groups of some proteins and inhibit their activity.

Results: During the research conducted, arsenic affects the function of a specific selenoprotein and increases the risk of developing diabetes. It also affects beta cells and metabolism and involves them until it causes changes in polymorphisms in Selenoprotein - and the difference in the DNA code of these proteins.

Conclusion: Today, scientists are investigating the medicinal activities of C. aromatica leaf extract, and the present experiment is planned for it. We hope these tests will give good answers.

Keywords: Arsenic, cancer, diabetes, genetics,treatment

The effect of Ashwagandha on autism (Review)

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Introduction: The NHE6 protein is linked to autism, with mutations in NHE6 leading to a condition called Christian-Sohn syndrome, characterized by unusual facial expressions, involuntary muscle movements, and autistic symptoms(1). Ashwagandha is a small herb is found in India and Southeast Asia. It is used to improve some pregnancy problems and anxiety(2) and reduce cortisol levels(3). In this research, the effect of Ashwagandha plant on autism has been investigated.

Methods: In order to check the effect of Ashwagandha on NHE6 protein, we have downloaded the 3D structure of NHE6 from uniport website and the 3D structure of Ashwagandha drug from Pubchem website in SDF format, Then, using ViewerLite software, we have removed the B chain and water molecules, NHE6 protein and saved the file in pdb format. At the end, the protein is prepared and the drug is entered into the PyRx software and the effect of the drug in the area of x: -2.0090 y: -3.8832 z: -27.1564 proteins have been investigated

Results: After molecular binding, the result showed that the affinity of the drug to the protein NHE6, RMSD lower bound: 0.0 and RMSD upper limit: 0.0 the binding affinity is (Kcal/mol: -11.3).

Conclusion: The result showed that Ashwagandha medicine is effective on NHE6 protein for autism

Keywords: Bioinformatics-molecular docking-NHE6-Ashwagandha -autism

The effect of cell suicide on cancer inhibition (Review)

seyed lafteh fardzadeh,[1,*] Ahmad sovidan,[2] mohamad javad sovidan,[3] Ali reza sokaini,[4] Ali reza nassari,[5] seyed amir ali fardzadeh,[6]

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Introduction: Cancer cells are different from normal cells in various ways. An unusual change in the division cycle of cancer cells has caused a change in the life process of the organism. Sometimes, cancer cells may be so-called benign and will not have many abnormal effects on the body's metabolism. In some cases, cancer cells are malignant and they act as invaders, which will endanger the metabolism of other cells. In recent years, extensive studies have been conducted on cancer. One of the most important unique behavior of cells is when cancer occurs. Cell suicide is one of the most important of these methods. In this mechanism, cells commit cell suicide through molecular pathways

Methods: Library Studies Reading various articles from reliable databases such as SID, Scopus,...

Results: Results obtained from human cancer cells show that inhibition of ERK5 activates "cytotoxic autophagy". Cytotoxic autophagy is a process that initiates the destruction of cancer cells without affecting healthy cells. Combination of ERK5 inhibitors and chemotherapy can improve cancer treatment.

Conclusion: Inhibiting the progression of cancer and helping to cure the disease

Keywords: cancer,autophagy,cells,suicide

The effect of cigarette smoke on the growth of oral stem cells (Review)

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Sana Sivanani,[1] Aysa Mohammadi,[2,*] Narges hedayat,[3] Dorsa Mohammadi,[4] Ayda Mousavi,[5] Golshan Najafian,[6]

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Introduction: Stem cells are cells capable of creating any type of cell in the body. Under the influence of different growth factors in the culture medium, they can be converted into cells with specific functions such as heart muscle cells or insulin- producing cells, pancreas, etc. These cells also have their own renewal capability, meaning they are able to perform mitosis divisions in order to preserve their population. An epithelial cell is a specialized cell that forms a thin tissue barrier, which can be on the surface or inside a tissue. Different types of epithelial cells, including epithelial tissue, skin, mouth, respiratory tract, etc. can be found throughout the body. Oral mucosa is constantly exposed to environmental forces and must be constantly renewed. Accordingly, oral mucosal epithelium contains a large reservoir of epithelial stem cells, which is essential for tissue homeostasis. If stem cells change, they can become cancer cells. The only difference between cancer stem cells and stem cells is they also have tumorigenic power. Some environmental factors can turn them into cancer cells by affecting stem cells. Cigarettes are one of these cancer-causing substances, accounting for 22 percent of all cancer deaths annually. Cigarette smoke in terms of physical nature has two parts: gas (95%) and particles (5%), which contains substances such as droplets, which is the most important known carcinogen in nature. More than 5000 elements have also been found in cigarette smoke, among which at least 150 compounds contain free radicals, which can cause systemic disorders such as heart disease, cancer and lung disease. Recently, it has been proven that imbalances in the level of free radicals and reactive oxygen species along with antioxidants may play a key role in the onset and development of several inflammatory oral injuries. When smoking, smoke from cigarettes has direct contact with most stem cells (epithelial) of the palate, which can cause oral cavity cancer. Oral cancer is a cancer that occurs as a result of the growth of malignant cells. This cancer, which occurs in the area of mouth, tongue, foam, palate, mouth and gums, is more common in smokers. Oral cavity cancer is often caused by abnormal division of stem cells (epithelial). In a healthy body, there are thousands of billions of cells that are divided according to the body's needs. Healthy cells have life cycles, reproduction and death based on their type. With the death of old or damaged

cells, new cells replace them. they will be One of the environmental factors that disrupts this process and alters stem cells is oxidant or oxygen free radicals in cigarette smoke, which changes epithelial stem cells to cancer stem cells that eventually lead to tumors and cancer. The main reason for the oxidant damage is that free radicals lack a whole pair of electrons, take electrons from other molecules and damage those molecules in the process. Antioxidants neutralize free radicals by losing some of their electrons, thereby no longer harming the body and improving the general health of the body. Vitamin C is one of the substances with high antioxidant properties and studies have shown that vitamin C consumption can have a great impact on preventing cancer.

Methods: In this review article, searches were conducted in electronic and scientific databases, Magiran, SID, PubMed, Google Scholar and other valid databases and 50 valid articles related to the subject were used.

Results: The results show that the damage caused by smoking is caused by substances called oxidants. These substances affect them by disrupting stem cell niches and turning them into cancer cells and can eventually cause cancer. To prevent damage caused by oxidants to the body, antioxidants can be used. Vitamin C is one of the examples of unnecessary antioxidants and people who smoke can first avoid smoking to prevent cancer and if unable to, Use vitamin C to maintain your health.

Conclusion: The oxidant in cigarette smoke causes oral cavity cancer and other cancers that can reduce the oxidant effect by using antioxidants, especially vitamin C.

Keywords: Stem cells, cancer, cigarette smoke and antioxidants.

The effect of cigarette smoke on the growth of oral stem cells (Review)

Sana Sivanani,[1] Aysa Mohammadi,[2] Narges hedayat,[3] Dorsa Mohammadi,[4] Ayda Mousavi,[5,*] Golshan Najafian,[6]

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Conclusion: The oxidant in cigarette smoke causes oral cavity cancer and other cancers that can reduce the oxidant effect by using antioxidants, especially vitamin C.

Keywords: Stem cells, cancer, cigarette smoke and antioxidants.

The Effect of Circular RNA on Alzheimer's Disease (Review)

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Introduction: Alzheimer's disease (AD) dementia refers to a particular onset and course of cognitive and functional decline associated with age together with a particular neuropathology. Deficits in the ability to encode and store new memories characterizes the initial stages of the disease. The risk of Alzheimer's disease is 60–80% dependent on heritable factors. This disease is the most common cause of dementia in elderly population characterized by the presence of neurotoxic senile amyloid plaques, hyper-phosphorylated tau tangles, massive neuron death, and neuro-inflammation. Circular RNAs (circRNAs) comprise a large class of non- coding RNAs that are produced by a non- canonical splicing event called backsplicing. CircRNAs are single-stranded, covalently closed RNA molecules that are ubiquitous across species ranging from viruses to mammals. These structures have the 3′ and 5′ ends joined together by covalent bonds giving a circular appearance. prominence of stable circRNAs in the synapse provides both the stability and flexibility of neuronal networks which are vital to all behavior, including learning and memory. In this descriptive-analytical study, we investigate circRNA to be an important player in the development of neurodegenerative diseases such as Alzheimer's disease.

Methods: Parietal cortex RNA-sequencing (RNA-seq) data were generated from individuals with and without Alzheimer disease (AD; ncontrol= 13; nAD= 83) from the Knight Alzheimer Disease Research Center (Knight ADRC). Using this and an independent (Mount Sinai Brain Bank (MSBB)) AD RNA-seq dataset, cortical circular RNA (circRNA) expression was quantified in the context of AD. STAR software was used in chimeric read-detection mode to align the reads from both RNA-seq datasets to the GENCODE-annotated human reference genome . Chimeric reads were further processed and filtered using DCC software to identify backsplice junctions. Finally, the backsplice junction counts were collapsed on to their linear gene of origin to generate a set of highconfidence circRNA counts for downstream analyses. DESeq2 software was used to perform circRNA differential expression analyses for neuropathological AD case–control status as well as for correlation with AD quantitative traits

Results: Significant associations were identified between circRNA expression and AD diagnosis, clinical dementia severity and neuropathological severity. It was demonstrated that most circRNA–AD associations are independent of changes in cognate linear messenger RNA expression or estimated brain cell-type proportions. Evidence was provided for circRNA expression changes occurring early in presymptomatic AD and in autosomal dominant AD. It was also observed that AD associated circRNAs coexpressed with known AD genes. Finally, potential microRNA-binding sites were identified in AD-associated circRNAs for miRNAs predicted to target AD genes. Finally, the AD relevance and potential disease-influencing mechanisms of AD-associated circRNAs were investigated through relative importance, network co-expression and miRNA-binding site-prediction analyses.

Conclusion: circRNA function and their relationships with Alzheimer's disease and other neuropathies remain to be fully elucidated. circRNAs are usually abundant and found to be stable in vivo, which might attribute to their importance in molecular diagnostics. Importantly, the potential role of circRNAs as miRNA sponges can be utilized as an innovative approach to regulate gene expression. Further research on circRNA will enhance our understanding in relation to neuropathies like AD and lead to new diagnostic biomarkers and promising therapeutic.

Keywords: Neurodegenerative , Alzheimer's disease , Circular RNA , miRNAs

The effect of clove extract on streptococcus bacteria (Review)

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Introduction: Tooth decay is one of the common infectious diseases among humans, especially in groups with low social and economic status. Streptococcus mutans and Streptococcus subrinus are considered as the main etiological factors of tooth decay in humans. These bacteria are the most common pathogens isolated from human dental plaque and their prevalence has been reported in epidemiological studies. Various chemicals are commercially available to prevent and treat tooth decay, but these can change the oral microbiome and cause unwanted side effects such as diarrhea, vomiting, and tooth discoloration. Considering the above cases, the use of natural compounds, especially plants, has been considered for the prevention, control and treatment of tooth decay. One of the medicinal plants that have been used in the past to treat oral and dental diseases is the clove plant. Clove essential oil was used as a mouth freshener by Chinese emperors in the 3rd century BC. Hindus used clove extract in dentistry and Ibn Sina used its oil to treat gum and tooth decay. In the 19th century, clove oil was used to treat root canals and serious dental problems. Today, there are many reports confirming the antibacterial, antifungal, and antiviral properties of cloves due to its protective power against free radical fixation. In this article, in the form of analytical research, using library sources and case studies, the effect of clove extract on Streptococcus mutans bacteria has been investigated.

Methods: The buds of cloves were obtained from the large market of medicinal plants in Tehran. In order to ensure that the humidity reaches the minimum possible, the dried clove plant was placed in the oven under vacuum for 2 hours at a temperature of 40 degrees Celsius. In order to extract the extract, the dried samples were turned into powder using a Bamesh 40 grinder. The ethanolic extract of the studied plant was obtained by soaking method. In this method, clove powder was mixed with 70% ethanol at a ratio of 1:10 in an Erlenmeyer flask with an aluminum cover at room temperature, and the sample was placed on a shaker at 130 rpm for 48 hours, and then the mixture was passed through filter paper. (Whatman No. 4), ethanolic extract was obtained. Then the extract was condensed using a rotary evaporator under vacuum at a temperature of 60 degrees Celsius and the solvent was separated. In order to dry the extract, the solvent was evaporated with the

help of an oven under vacuum at a temperature of 45 degrees Celsius and a pressure of 25 ml of mercury. For microbial tests, the obtained extract was filtered using 0.45 micron filters to get rid of microorganisms. The extract was kept in a sterile glass container and closed, in the dark and in a refrigerator at a temperature of 4 degrees Celsius.

Results: the clove plant, due to its antibacterial and pain-relieving properties, can affect Streptococcus mutans bacteria and reduce the pain caused by it.

Conclusion: We conclude that the clove plant, due to its antibacterial and pain-relieving properties, can affect Streptococcus mutans bacteria and reduce the pain caused by it. It is hoped that the results of this article will be effective in advancing biological science and medical science.

Keywords: Streptococcus mutans, tooth decay, medicinal plants, cloves

The effect of coumarin as an active ingradient in Urtica dioica on sperm count and testosterone in mice (Research Paper)

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Introduction: Urtica dioica as a medicinal plant has various active ingradients, one of the most important of which is coumarin.

Methods: In this experimental study, 20 adult NMRI male mice were divided in to four groups (n=5/each). The control group received only normal saline. The experimental groups also received coumarin at doses of 0.25, 0.5, 0.75 (mg/kg) respectively. Daily injections were administered intraperitoneally for 30 days.The mice were anesthetized and blood samples were taken from the heart to extract serum. The mice were then operated on and the left tail of the epididymis was removed to extract adult sperm. Hormonal analysis was performed by ELISA and CL methods

Results: The results showed that in a group of mice that received coumarin sperm count, testosterone and free testosterone significantly decreased. (p<0.001)

Conclusion: With these findings it was concluded that coumarin as an active ingradient of Urtica diouca , contrary to expectations, reduces epididymal sperm parameters, testosterone and free testosterone. As a result, it may have a potential reproductive toxicity in adult male NMRI mice. Further studies, are thus needed to determine its mechanism of action upon spermatogenesis.

Keywords: Sperm ،Infertility ،Testosterone ،Reproduction

The effect of COVID-19 vaccination on fetal outcomes: a review Study (Review)

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Introduction: Pregnant people are at higher risk of severe disease compared with non-pregnant women in reproductive years, due to physiological changes in their cardiopulmonary and immunological system functions. Vaccines have been developed to combat the COVID-19 pandemic caused by the SARS-CoV-2 coronavirus. Although they are considered the best approach for preventing mortality, there are many arguments for the safety and efficacy of COVID-19 vaccines in pregnant women and their babies. The aim of this study is to review the effect of COVID-19 vaccine on fetal outcomes.

Methods: In this review, English studies available in PubMed, Google scholar, Science Direct and Springer databases using the keywords coronavirus, COVID-19, vaccine, vaccination, pregnancy, fetus and infant from 2022-2020 were reviewed and finally according to inclusion criteria 24 articles were selected.

Results: Study results showed that there was no increased risk in adverse pregnancy outcomes including miscarriage, preterm birth, small for gestational age, and neonatal death after vaccination when compared with data before the COVID-19 pandemic. several studies demonstrated that COVID-19 vaccination was not associated with higher incidence of congenital malformation compared with historical rates. There was no significant difference between vaccinated and unvaccinated individuals in terms of mode of delivery, gestational age, Apgar scores, and the incidence of adverse maternal and neonatal outcomes including eclampsia/ preeclampsia, gestational hypertension, thromboembolism, birth trauma, uterine rupture, stillbirth, hypoxic-ischemic encephalopathy, low birth weight, and neonatal intensive care admission. After SARS-CoV-2 vaccination in a pregnant woman, trans placental transmission of antibodies against the spike protein occur. Efficient trans placental transfer of SARS-CoV-2 IgG antibodies was also shown in the majority of seropositive pregnant women after natural infection. The presence of neutralizing antibodies in the fetal/neonatal circulation is potentially an added benefit of vaccination for the protection of the baby, in both fetal and neonatal life, against COVID-19.

Conclusion: These data support the safety of COVID-19 vaccination during pregnancy; so the midwives and nurses should provide counseling to pregnant women to increase their knowledge and correct misconceptions regarding COVID-19 vaccine.

Keywords: coronavirus, COVID-19,, vaccination, pregnancy, fetus

The effect of FGF/FGFR, MAPK/ERK, and NF-kB signaling pathways on multiple sclerosis and the role of tissue engineering strategies in its treatment:A Narrative Review (Review)

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Introduction: Multiple sclerosis (MS) is a central nervous system (CNS) inflammatory disorder that frequently causes impairment in young people. Treatment options are limited and often only somewhat effective. The condition is most likely caused by a complicated interplay between numerous genes and environmental variables, which results in CNS inflammation. In autoimmune illnesses like MS, three main pathways have been shown to play a key role: the FGF/ FGFR and MAPK/ ERK and NF-kB signaling pathways. Recent researches on postmortem tissues suggest that we'll go through some recent advances in the role of FGF signaling pathway in MS, since it modulates inflammation and myelination in MS. The role of MAPK pathways in neurodegeneration, particularly MAPK/ ERK, has previously been indicated in preclinical studies. In MS lesions, activation of the NF-kB induction reservoir in macrophages might improve the inflammatory response by controlling the participation of NF-kB-controlled adhesion molecules and cytokines, implying a cure for MS.

Methods: In this review article, 115 valid articles from PubMed and Google Scholar databases were examined and the best articles were selected. The search keywords includedMultiple sclerosis, FGF / FGFR, MAPK / ERK, NF-kB, Tissue engineering.

Results: specific receptor manipulation of the FGF/ FGFR, MAPK/ ERK, and NF-kB signaling pathways presents a novel therapeutic paradigm that might lead to new insights into MS pathogenesis and significant implications for successful therapy.

Conclusion: specific receptor manipulation of the FGF/ FGFR, MAPK/ ERK, and NF-kB signaling pathways presents a novel therapeutic paradigm that

might lead to new insights into MS pathogenesis and significant implications for successful therapy.

Keywords: Multiple sclerosis, FGF / FGFR, MAPK / ERK, NF-kB, Tissue engineering

The effect of histatin one and honey on wound healing (Review)

Aref Farhadloei,[1,*]

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Introduction: Wound healing is a complex multifactorial process that can be thought of as sequential steps including homeostasis, inflammation, proliferation, and remodeling.It has long been known that oral mucosal wounds heal more quickly and effectively than skin wounds, and several factors contribute to these differences. Wound infection and inflammation have always been one of the important issues. Oral wounds heal faster and with less scar formation than skin wounds. One of the key factors involved is saliva, which heals wounds in different ways. Saliva contains significant amounts of tissue factor that dramatically accelerates blood clotting.Histatins are a type of cationic peptide from protein. Histatin one has thirty-seven amino acids. These proteins are present in the saliva of all mammals. Histatins are usually known as factors involved in mineral homeostasis.Histatins are small molecular weight proteins that are produced by human salivary glands and show antifungal and antibacterial activities, and human histatin has both antimicrobial and wound healing properties. In this family of proteins, histatin one and histatin three are full-length products.On the other hand, honey is a sweet liquid, a supersaturated solution of sugars, mainly glucose and fructose. Honey contains many other components such as vitamins and minerals, antioxidants, proteins and hydrogen peroxides and other unknown components. Honey has a high inhibitory level against Staphylococcus aureus, which is one of the resistant hospital pathogens. Also, honey has an effect on Escherichia coli, Pseudomonas aeruginosa bacteria.According to some researchers, due to the high amount of glucose, honey produces hydrogen peroxide and as a result destroys itHigh concentration of sugar, hydrogen peroxide and low pH are known antibacterial factors in honey, and recently methylglyoxal and antimicrobial peptide bee defensin-one have been identified as important antibacterial compounds in honey. The antibacterial activity of the tested honeys can be largely attributed to the formation of hydrogen peroxide and in some cases to unknown protein compounds. Therefore, according to this information, these two substances can act as complements and play an effective role in healing and repairing wounds and burns

Methods: Research method using zinc and basic solvent to purify seventy% of histatin and dissolve it in Manuka honey at Twenty-five degrees. Due to the lack of facilities in the area, two almost identical scratches were made on the left legs of two brothers' cats using a scalper, and on one of them, the desired compound was applied to their wound, and this was done three times at a distance. This was repeated for eight hours. The superficial wound of the

other cat was also bandaged so that the infection would not cause errors in the test.

Results: The results showed that the use of histatin combination with Manuka honey was effective on the superficial wounds of cats and caused the wounds to heal. Honey was combined with histatin, which was applied on the body surface of one of the male cats whose body surface was scratched by a scalper, and this mixture was applied to their wound for three times at an interval of eight hours. It was repeated after that the desired information of the treatments that received the combination of histatin one and honey with the control group that did not apply any substance to their body wounds (cat. two), the results showed that the combination of histatin and manuka honey caused the healing of superficial wounds.

Conclusion: Histatin 1 is a human salivary protein encoded by the HIS1 gene. This protein is the main cause of early healing of wounds in the mouth compared to others, as well as licking of wounds by some animals. This thirty-eight amino acid protein causes angiogenesis and disinfects the wound site. This protein can be separated and purified by a special method of chromatography. Also, honey is an organic substance made by bees and has a higher antibacterial effect than histatin 1. Honey has a high inhibitory level against Staphylococcus aureus, which is one of the resistant hospital pathogens. Also, honey has an effect on Escherichia coli, Pseudomonas aeruginosa bacteria.According to this information, these two substances can act in a complementary way and play an effective role in healing and repairing wounds as well as burns. After protein purification, it can be dissolved in honey and used as an effective medicine with less side effects than other products of this branch.

Keywords: Histatin 1 - Honey - Staphylococcus aureus - Wound healing

The Effect of Hypoxia-Induced Exosomes on Anti-Tumor Immunity and Its Implication for Immunotherapy (Review)

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Introduction: Hypoxia is a common feature of many solid tumors that is associated with tumor growth, treatment resistance, and mortality. Tumor cells in their microenvironment encounter low oxygen levels due to insufficient oxygen flow and physiological abnormalities in tumor vasculature, leading to normoxic, hypoxic, as well as necrotic areas. In most solid tumors, the average oxygen concentration is close to 10 mmHg, while in other tissues it reaches 40 and 60 mmHg. In addition to inducing metabolic reprogramming of tumor cells to adapt to the hypoxia of the tumor microenvironment (TME), hypoxia can also enhance tumor growth by affecting the secretion of exosomes. Exosomes are small vesicles with a membrane and a size of 30 to 100 nm, which are present in blood, urine, saliva, semen, serum, etc. Exosomes play an important role in a variety of important biological processes such as immune response and inflammation, pregnancy, tissue proliferation, blood coagulation and angiogenesis. They are also involved in pathological processes such as disorders of nervous disorders, cancer, infectious diseases, cardiovascular, etc. Cancer-related cells secrete more exosomes than healthy cells due to the need for intercellular communication or nutrient exchange. It is worth noting that hypoxia-induced exosome changes are present not only in tumor cells but also in various TME cells, including stromal cells and immune cells. Studies of these exosome properties in tumor pathogenesis have led to the development of therapeutic and diagnostic approaches using exosomes for cancer treatment. Exosomes have many advantages for the delivery of therapeutic agents such as small interfering RNAs, microRNAs, membrane associated proteins and chemotherapeutic compounds. Therefore, they are considered a prime candidate as a delivery tool for cancer therapy. Because exosomes provide an optimal microenvironment for the effective action of immunomodulatory agents, exosomes containing bioactive molecules have been designed as cancer immunotherapeutic that can effectively activate each stage of the cancer

immune cycle to create cancer-specific immune success. In this review, we focused on the effects of hypoxia on exosome secretion.

Methods: In this review article, we collected the required data using keywords and using databases such as Google Scholar, PubMed, Scopus and ProQuest. In this study, the statistical population includes all the studies whose articles have been published until 2022. After reviewing the findings and evaluating the quality of the obtained data, 13 articles were analyzed.

Results: First, hypoxia-induced exosomes are not vesicles loaded with cellular debris, but key mediators of intercellular communication. Second, exosome cargoes differ in hypoxic and normoxic TMEs. Hypoxia may affect the biosynthesis, metabolic degradation, and post synthetic modification of cargoes and the efficiency of specific cargo sorting mechanisms. Under adverse TME conditions such as hypoxia, high glucose, and drug therapy, the cargo transported and delivered in the exosome is significantly altered, which in turn modulates immune cell function. Third, exosomes are secreted by immune cells such as DCs and chimeric antigen receptor T cells.

Conclusion: In recent years, anti-tumor immunotherapy, representing immune checkpoint inhibitors, has changed the treatment option for various tumor types. As previously mentioned, the infiltration and activation of immune cells in the TME is closely related to successful immunotherapy. Due to the role of exosomes in cancer progression and biological properties, exosomes have promising potential for cancer treatment. Therefore, understanding the effect of exosomes on the anti-tumor immune system can further increase the effect of immunotherapy. To date, several exosome-based cancer therapies have been studied and developed, including the use of natural immune cell-derived exosomes to suppress cancer cells, inhibition of cancer cell-derived exosome activity, and the use of exosomes as gene/drug carriers. However, there are significant challenges to overcome. First, the differences between exosomes from different sources are still unclear. Second, the number of exosome required to obtain a therapeutic effect may vary significantly among different cancers. Third, tumor scalability and heterogeneity may affect treatment outcome.

Keywords: Hypoxia, Exosomes, Anti-tumor immunity, Immunotherapy, Tumor microenvironment

The Effect of IVF (in vitro fertilization) on Heterotopic Pregnancy: A Systematic Review Study (Review)

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Introduction: Heterotopic pregnancy is a condition that occurs simultaneously in intrauterine and ectopic pregnancies. Ectopic pregnancy can occur in the ovaries, cervix, cornea, abdomen, or more commonly in the fallopian tubes. It is less common in the general population. It is from 1 in 30,000 and studies have shown that its incidence has increased in recent years. Reported heterotopic pregnancies often occur in women with a history of assisted reproductive techniques, ovarian stimulation, and pelvic inflammatory disease. As a result, heterotopic pregnancies increase to 0.1-2% in pregnancies using the methods. Reproductive assistance includes intrauterine insemination of semen and in vitro fertilization and embryo transfer with or without intra-cytoplasmic fertilization. Cervical pregnancy (CP) is a rare form of ectopic pregnancy (EP) in which the fetus implants and grows inside the endocervical canal. Heterotopic cervical pregnancy is an even rarer form of EP in which at least two embryos are implanted simultaneously in different locations and only one embryo is implanted in the uterine cavity. Although many treatment approaches are available, ideal management remains unclear. Here, we describe two cases of CP resulting from assisted reproductive technologies (ART). One case was fertilized by intracytoplasmic sperm injection (ICSI) for male factor infertility, and another was frozen-thawed embryo transfer (FET) followed by in vitro fertilization (IVF). This study aimed to evaluate the effect of IVF (in vitro fertilization) on heterotopic pregnancy

Methods: This is a secondary study (Systematic Review - 2022) looking for preferential reports for systematic reviews and meta-analysis recommendations (PRISMA) that we searched in the PubMed, Embase, and Ebsco databases for published studies on IVF and Heterotopic Pregnancy. There were no restrictions based on language, age, or country of origin. The first search was conducted on May 1, 2022, followed by an additional search on May 12, 2022. The three authors independently screened all search results from three databases at the title and abstract level, and if any, the discrepancies were resolved. We retrieved all available resources in the studies provided for additional resources. The following keywords were used

to identify the reports, respectively: “IVF” [Mesh] AND “Heterotopic” [Mesh] OR “Pregnancy” [Mesh] OR “Cervical Pregnancy” [Mesh] “Ectopic Pregnancy” [Mesh] OR “intracytoplasmic sperm injection ”[Mesh]

Results: Rapid diagnosis of heterotopic pregnancy with no symptoms and the presence of a live intrauterine fetus is a challenge. Measurement of BHCG and a transvaginal ultrasound may aid in diagnosis Serial measurement of BHCG often complicates interpretation of Sacral uterine ligament (USL) Ectopic is abdominal. This is the first case of USL heterotopic pregnancy after in vitro fertilization (IVF). The patient presented 6 weeks after double embryo transfer with acute onset of abdominal pain and suspected ectopic pregnancy and was diagnosed with live tubes with live intrauterine pregnancy on ultrasound. Was removed. This highlights the importance of considering non-tubular heterotopic pregnancies in the context of risk factors, including IVF with double embryo transfer presented with abdominal pain. Transvaginal ultrasound is reduced. Therapies include surgery, expectant therapy, and fetal aspiration with or without the use of lethal drugs. Due to the rarity of heterotopic pregnancies, treatment experience is limited and it is difficult to determine which treatment is preferred. Fallopian tube closure, previous ectopic pregnancies, pelvic inflammatory disease, and previous surgery due to endometriosis or myomectomy are risk factors for heterotopic pregnancies. is.

Conclusion: Transvaginal ultrasound is the main diagnostic tool because the ectopic fetus is mostly located inside the wall of the fallopian tubes, fallopian tubes, or ovaries. Laparotomy or laparoscopy are the main treatment options with appropriate perinatal outcomes.

Keywords: IVF, Heterotopic, Pregnancy, Cervical Pregnancy, Ectopic Pregnancy

The effect of marijuana on the spatial learning and memory at different ages: the role of BDNF protein (Research Paper)

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Introduction: Cannabis or marijuana is the most common psychoactive substance used by 183 million people worldwide. Some studies suggest that the effect of cannabis on performance behavior depends on the age of use initiation. Few animal studies have examined the effects of the life-long use of marijuana. This study evaluated the role of BDNF in the effects of marijuana (M) spatial learning and memory of young and old female rats

Methods: Young (5-7 months) and old (22-24 months) female rats received an intraperitoneal injection (i.p) of M (every day), for 28 days. One hour after the last injection, the Morris water maze (MWM) test was conducted. Moreover, the density of BDNF (brain-derived neurotrophic factor) was assessed by the ELIZA method

Results: Marijuana impaired spatial learning and memory in young female rats, while improved in old rats. we did not observe the change in the BDNF protein levels in this study.

Conclusion: There are age-related differences in the effects of marijuana on spatial learning and memory BDNF plays no role in these differences, probably.

Keywords: Cannabis, cognition, age, BDNF

The Effect of Nano-Chitosan Particles on Candida Biofilm Formation

(Research Paper)

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Introduction: Candida species are the most common pathogenic fungus and have the ability to form biofilms and represent an essential virulence factor. Candida biofilm formation is clinically important which can be the reservoirs of candidiasis. Nano-chitosan particles has an extensive antimicrobial scale against various pathogenic microorganisms. Nano-chitosan particles reveal eminent antibiofilm conducts versus multidrug-resistant pathogens and are contemplated a potential substitution to common drugs. The aim of this study was to evaluate the effect of nano-chitosan particles on candida biofilm formation.

Methods: In this in-vitro study, nano-chitosan particles were synthesized. These nanoparticles are approved by transmission electron microscope. Candida albicans were collected from the oral cavity of patients with oral candidiasis. Nano-chitosan particles with concentrations of 0, 1%, 10%, and 20% were exposure with suspension of Candida albicans isolates. Then biofilm formation was measured with crystal violate staining method.

Results: Nano-Chitosan Particles showed strong antimicrobial activity against Candida strain. The observed differences between untreated Candida strain (control) and treated Candida strain with nano-chitosan particles in terms of biofilm formation were significant (P<0.05).

Conclusion: The finding shows that nano-chitosan particles can have a significant impact on Candida biofilms. These substances are estimated to become conceivable candidates for the treatment of fungal disease caused by candida species due to their excessive effect on biofilm. However, cytotoxicity testing is also required.

Keywords: Nano-chitosan Particles; Biofilm; Candida species; Antifungal drugs; Resistance

The effect of Nano-curcumin on Cyclin D1 and DILA1 gene expression in breast cancer cells (Research Paper)

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Introduction: Breast cancer is the leading cause of cancer worldwide. It accounts for 22% of invasive cancers and 18% of all cancers in women. Breast cancer is a heterogeneous disease and there are differences in the response to various treatments, the risk of disease progression, and metastatic sites. About 20% of breast cancers have CCND1 gene amplification, and many irregularities in signaling pathways can lead to overexpression of CyclinD1 in about 50% of breast cancers, which are more of the ER + type. This project, study the expression of Cyclin D1, which is one of the most important oncogenes in breast cancer. There is also an LncRNA called DILA1, which interacts with Cyclin D1 and is overexpressed in breast cancer cells.DILA1 specifically binds to Ther286 of Cyclin D1 protein and inhibited its phosphorylation, leading to decreased ubiquitination and degradation of Cyclin D1. Recent investigations in cancer treatment have revealed curcumin anti-cancer properties through different pathways. Nanotechnology has been employed to overcome this barrier. Nano-formulated curcumin (Curcuden) has been shown to provide a significantly higher bioavailability for oral consumption.

Methods: MCF-7 cells were cultured in DMEM, supplemented with 10 % fetal bovine serum and 1% Pen-Strep. 2×105cells were planted per well in a 6-well plate in duplicate. After 24h cells were treated with nano-curcumin(17μM). Next, in 24h and 48h total RNAs were extracted with Trizol Reagent. The quality of RNA was measured by gel electrophoresis. cDNAs were synthesized using the manuscript's protocol. Expression of Cyclin D1, DILA1, BAX, and BCL2 genes were measured by qRT PCR in treated and untreated MCF-7 cells.

Results: Results: To compare the expression level of Cyclin D1 and DILA1 in untreated, 24h and 48h nano-curcumin treated cells qPCR was done. Expression of Cyclin D1 and DILA1 was decreased at 24h and 48h after being treated with nano-curcumin compered to untreated cells. As expected the reduction of these genes was much higher in 48h than 24h after treatment. To study the effect of nano-curcumin on the apoptotic pathway, the expression

level of apoptotic genes was determined by qRT PCR. The results confirmed that nano-curcumin is apoptosis inducer by downregulation of BCL2 and upregulation of BAX gene.

Conclusion: These results indicate that nano-curcumin was able to significantly reduce the DILA1expression leading to destabilizing of the Cyclin D1 protein. Therefore, reducing DILA1 expression induces apoptosis in breast cancer cells.According to these results, nano-curcumin induces apoptosis in breast cancer cells by downregulation of Bcl2 and upregulation of BAX gene. Nanocurcumin has a relatively cytotoxic effect on MCF-7 breast cancer cells, suppressing the expression of Cyclin D1, a critical gene in the development and metastasis of breast cancer.

Keywords: MCF-7,Nano-nancurcumin, Cyclin D1,DILA1

The effect of nanoparticles and stem cells in the treatment of burn wound. (Review)

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Introduction: Burn is an injury to the skin or other tissues. Destruction of the skin barrier and health in burn injuries and suppression of the immune system are the most common causes of death in these patients. Wound healing is a complex and dynamic physiological process that involves various cells, mediators, extracellular matrix components, growth factors and proteinases. Research on burns has gained special importance in the past few decades and several advances and studies in the field of treatment with stem cells and nanoparticles are underway to stabilize the patient's condition and improve the performance of the treatment. Treatment of burns with nanoparticles and stem cells is reviewed in this article.

Methods: Pubmed and Oxford academy databases were utilized and keywords such as burns, burn treatment, stem cells in burns, nanoparticles in burns were searched. Then their abstracts were read and the relevant topics were selected. Again, the articles have been checked in full text then the irrelevant parts have been removed. By collecting this information, the use of stem cells, nanoparticles in burns healing has been investigated.

Results: Nanotherapies have been widely used to diagnose and treat various diseases, including skin and inflammatory diseases such as burn wounds. Some nanomaterials can act as antibacterial agents to prevent infection of burn wounds because these materials have an antibacterial effect and they can increase the interaction between drugs and bacteria or change the route of the drug to improve its antibacterial effects and they can improve drug penetration into tissue barriers and bacterial biofilms. Nano-treatments can include drugs, bio-macromolecules and therapeutic substances such as some metals and chitosan which at least one dimension of the structure is nano. This causes the interaction between drugs and bacteria to increase. Silver, zinc oxide nanoemulsions and chitosan nanoparticles that act as antibacterial agents can be mentioned among useful nanomaterials in accelerating burn wound healing. The mechanism of action of nano metallic materials such as silver is through to break down biofilms and destroying bacterial DNA or producing reactive oxygen species(ROS) which leads to the inhibition of bacterial growth. Chitosan is a cationic polymer nanomaterial that has antibacterial properties due to the positive charge of the polymer. These substances stick to bacterial surfaces and damage their membrane wall which

prevents microbial growth. To care for burn wounds, stem cells can secrete all the necessary growth factors stably and respond to local stimuli. The use of stem cells in burn repair is through the rapid improvement of better skin regeneration and the modulation of the inflammatory response and the reduction of fibrosis and infection. Stem cell products such as exosomes and their conditioned media have also been used to treat burns. Also, mesenchymal stem cells play a role in inducing collagen production by fibroblasts and help heal wounds. Stem cells with anti-inflammatory effect and stimulation of angiogenesis can heal the wound. Faubert and colleagues were able to accelerate re-epithelialization of wounds by using stem cells derived from fat. Direct injection of stem cells into the wound or Intravenous, both can be helpful for wound healing. Using epidermal stem cells, Yang et al can stimulate fibroblasts to proliferate and migrate which can lead to accelerated wound healing. By using stem cells derived from fat, Belili et al concluded that these cells increase blood vessels and increase collagen mRNA expression and collagen deposition in wound treatment.

Conclusion: By assessing articles, It was concluded that the treatment of burns with the assistance of nanotherapy and stem cells can be effective in the process of regeneration of burned and damaged skin. It is recommended to pay special attention to nanotherapy and stem cells along with other treatments.

Keywords: burn infection, Nanotherapies, stem cell

The effect of nuclear localization signal tagging of recombinases/ integrases in recombinase-mediated cassette exchange efficiency in eukaryotes (Review)

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Introduction: Chinese hamster ovary (CHO) cells host over 70% of recombinant glycoproteins (1). CHO cell line development is mainly based on random integration (RI) of a gene of interest (GOI). Due to the uncontrollable integration sites, RI-generated cell pools are extremely heterogenous, requiring extensive screening to find stable and high-producing clones. Targeted integration of the GOI into a predefined locus has been introduced as a promising strategy to mitigate some limitations of the RI approach. Two main strategies have been used to achieve this goal. The first type involves the use of site-specific recombinases such as Cre/loxP and Flp/FRT in a technique known as recombinase-mediated cassette exchange (RMCE). The second type employs programmable nucleases, which CRISPR/Cas9 technology regards to be a breakthrough due to its efficiency, ease of use, and low cost. The generation of a platform cell line harboring a landing pad with a recombinase recognition site is a prerequisite of the RMCE technique (2,3). CRISPR/Cas9-mediated targeted integration of the landing pad into a predetermined locus of CHO cells has been proposed as a potential method for rational CHO platform cell line generation (4,5). Once the platform cell line has been established, it can be used to introduce any gene of interest using the RMCE technique. However, the low efficiency of the recombination event has remained an impediment to this approach. In this study, we reviewed several approaches that have been introduced to improve RMCE efficiency and therefore streamline the process of cell line development.

Methods: This study was a review and information was extracted from Google Scholar, PubMed, Science direct, and ProQuest databases by entering the desired keyword.

Results: Enhancing the nuclear transport of RMCE components, such as recombinase and donor plasmids, has been described as a potential way for improving RMCE efficiency. Shin et al. studied the effect of several types of nucleus localization signals (NLSs) and DNA nuclear-targeting sequences (DTSs) on recombinase and donor plasmid, respectively. Nucleoplasmin (NP) N-terminal NLS tagging of Cre recombinase and NP C-terminal NLS tagging of Bxb1 integrase showed approximately 4 times higher RMCE efficiency than that of the control group. On the other hand, NF-κB 5′/3′DTS was the most effective DTS in both Cre and Bxb1 RMCE systems (6). In another study, Andreas et al. investigated the effect of NLS on the performance of PhiC31 integrase and showed the strong enhancement of PhiC31 activity by the addition of C-terminal NLS (7). Xue et al investigated the effect of NLS addition in fourteen serin integrases in Saccharomyces cerevisiae and demonstrated the presence of NLS had little effect on most integrases' efficiency except for TP901 and the φC31 integrases with slightly increased activity (8). Duportet et al. reported no improvement in integration efficiency upon NLS fusion to Bxb1 recombinase, albeit N-terminal NLS negatively impacts efficiency due to steric hindrance with catalytic domain (9).

Conclusion: In conclusion, reports of how fusing an NLS to recombinases affects RMCE efficiency have been contradictory. C-terminal NLS tagging may be advantageous for high-molecular-weight serine integrases like φC31 integrase that are unable to cross nuclear pores through passive diffusion.
Acknowledgment: This work was financially supported by the Pasteur Institute of Iran (grant no. BD-9579) and National Institute for Medical Research Development (NIMAD's project no. 978694)

Keywords: recombinase-mediated cassette exchange efficiency, nuclear localization signal, CHO cell line

The effect of one month of fasting and regular physical activity on hematology and blood biochemistry indicators (Research Paper)

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Introduction: Fasting in the month of Ramadan is a religious obligation and belief that is obligatory for all healthy and mature Muslims. The purpose of this study is to compare the effect of one month of fasting and regular exercise on biochemical and hematological indices of active and inactive men.

Methods: In this study, 40 healthy men between the ages of 15 and 35 were divided into two inactive fasting groups (20 people) and active fasting groups (20 people). Two blood samples were taken from both groups for biochemical and hematology tests on the first and 30th day of Ramadan. The data were analyzed using repeated analysis of variance test.

Results: In both groups, the average indices of hematocrit, number of red blood cells, TC, LDL, HDL, LDL/HDL, TC/HDL and VLDL at the end of Ramadan have decreased significantly compared to the beginning of Ramadan. HDL values increased significantly during fasting in active fasting group (P=0.023) and passive fasting group (P=0.042) at the beginning and end of the study. The decrease in FBS levels was significant only in the active fasting group (P<0.05).

Conclusion: Fasting in the holy month of Ramadan combined with regular sports activities can produce positive changes in serum hematological-biochemical indicators, which can be due to changes in the diet and biological reactions of the fasting people's body to hunger and physical activity during the month of Ramadan

Keywords: Fasting, physical activity,hematology, blood biochemistry indicators

The effect of personnel's knowledge in controlling the infection (Review)

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Introduction: Nosocomial infection refers to infections that occur while hospitalized patients are affected, and the disease manifestations may occur during hospitalization or after discharge. Nosocomial infections are undoubtedly the most critical problem in the health centers of the world, and their occurrence in each country is different. Due to the effects of losses in hospital infections on the individual and society, it is necessary to measure and control these infections. Since the health care team members have a unique role in preventing infections, they should be aware of the correct scientific and sufficient information on the types of hospital infections and follow-up methods. Therefore, this study investigated the effect of personnel's knowledge in controlling the infection.

Methods: Articles related to the subject of this review are extracted from Google scholar, PubMed, Scopus, and Science Direct from 2015 to 2022. to do this, the words hospital infection, infection control, hospital staff, and hospitalization were among the words that were searched.

Results: In all similar studies conducted on the effect of personnel's knowledge in controlling the infection, there is a consensus that there is a positive correlation between the prevalence of hospital infections and the level of the personnel's knowledge. The more knowledgeable the personnel are, the more uncomplicated controlling hospital infections would become.

Conclusion: From significant points, the personnel's knowledge is the basis of infection control. Since the personnel plays an essential role in preventing infections, their knowledgeableness significantly affects the reduction of these infections.

Keywords: hospital infection, infection control, hospital staff, hospitalization

The Effect of Pro-/Synbiotic Supplementation on Brain-Derived Neurotrophic Factor: A Systematic Review and Meta-Analysis of Randomized Controlled Trials (Review)

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Introduction: There is a growing interest in supplementation with pro-/synbiotics for brain and mental health. Animal studies have reported that pro-/synbiotic administration can increase brain-derived neurotrophic factor (BDNF), a key regulator of neuronal function. Nevertheless, the results obtained from human studies are inconsistent and conflicting. Therefore, we aimed to conduct a systematic review and meta-analysis of randomized controlled trials (RCTs) to investigate the impact of pro-/synbiotic supplementation on BDNF levels.

Methods: Scopus, Medline, Web of Science, Cochrane Library, and Google Scholar were searched up to July 10, 2022 to find eligible RCTs. The following Medical Subject Headings (MeSH) and non-MeSH terms were searched within keywords, abstracts, and titles: ("probiotics" OR "probiotic" OR "synbiotics" OR "synbiotic" OR "prebiotics" OR "prebiotic" OR "symbiotics" OR "symbiotic" OR "psychobiotics" OR "psychobiotic" OR "fermented" OR "Lactobacillus" OR "Bifidobacterium" OR "Saccharomyces" OR "Streptococcus" OR "Lactococcus" OR "Enterococcus" OR "Pediococcus" OR "Bacillus" OR "Leuconostoc" OR "Escherichia") AND ("brain-derived neurotrophic factor" OR "brain derived neurotrophic factor" OR "BDNF"). The weighted mean difference (WMD) and 95% confidence interval (CI) were computed for BDNF using a random-effects model.

Results: In the present study, 10 RCTs with 12 treatment arms consisting of 652 participants were included. The meta-analysis revealed that supplementation with pro-/synbiotics significantly increased BDNF concentrations in comparison with placebo (WMD: 0.20 ng/mL, 95% CI: 0.06 to 0.34, I2 = 86.6%). Moreover, subgroup analysis showed that target population, ethnicity and mean age of participants, number and type of probiotic strains, administration form, and dose and duration of pro-/synbiotic supplementation were potential sources of heterogeneity between RCTs.

Conclusion: In conclusion, pro-/synbiotic administration can be considered as a BDNF enhancer and possible brain booster.

Keywords: Probiotics, Synbiotics, Brain-derived neurotrophic factor, Systematic review, Meta-analysis

The Effect of Probiotic on Liver Enzymes and Lipid Profile in Animal Model of Breast Cancer (Research Paper)

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Introduction: Probiotics have beneficial effects in liver protection and modulating of serum lipid profile. Therefore this study assessed levels of liver enzymes and lipid profile in an animal model of breast cancer following administration of probiotics.

Methods: In this study, 48 animals of Balb/C mice were divided into 6 groups: 1-the healthy control, 2-the cancer control, 3-the healty group receiving 0.5 g of probiotics, 4-the cancer group receiving 0.5 mg of probiotics, 5-the cancer group receiving 1 g of probiotics and 6- the cancer group receiving 1 g of probiotics for 3 weeks. 4T1 cell line was used to induce cancer. Blood samples were used for evaluation of levels of lipid profile and liver enzymes by calorimetric methods. Data were analyzed using SPSS-Ver-18 and one-way ANOVA, T-test, Kruskal-Wallis and Mann–Whitney U tests methods ($p < 0.05$).

Results: The results of this showed that probiotics resulted in a non-significant increase in HDL, and significanr decrease of LDL,TG and cholestrol levels (p=0.01, 0.006 and 0.02 respectively). and non-significant decrease of ALP,AST and ALP in the treatment group compared with untreated cancerous group.

Conclusion: The use of probiotics resulted in improvement of liver enzymes and lipid profile abnormalities in animal breast cancer model.

Keywords: Probiotics, liver enzymes, lipid profile, Breast cancer

The effect of salivary biomarkers in the diagnosis of oral cancer (Review)

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Introduction: Cancer as a disease is associated with changes in gene expression and function due to genetic and epigenetic changes and is associated with strong genomic instability. Oral cancer is a malignancy that affects both the lips and the oral cavity and ranks as the 16th most common cancer. Oral squamous cell carcinoma (OSCC) accounts for about 90% of these tumors. Some patients develop OSCC from a clinically detectable precancerous stage. These conditions are collectively known as oral potentially malignant disorders (OPMD). A biomarker (DNA, RNA, proteins, and metabolites) is defined as a characteristic measured as an indicator of normal biological processes, pathogenic processes, or responses to exposure or intervention. The resulting disease is the treatment of advanced disease and the reduction of the economic burden of disease management. However, the current approach to OSCC diagnosis, which involves visual examination of the oral cavity followed by biopsy, is sometimes ineffective. Biomarkers for the diagnosis of OSCC can greatly improve the early detection of OSCC. For this purpose, the salivary proteome of OSCC patients was quantitatively investigated in this study.

Methods: In the following article, data were collected by using keywords and searching in valid databases such as Google Scholar, Scopus, ProQuest and PubMed. The statistical population of this study includes all articles published until 2022. In this research, after checking the findings and data quality, we analyzed a total of 11 articles.

Results: The biomarkers reported in the studies were classified according to the molecular type. 52% of studies reported protein biomarkers, followed by DNA (12%), RNA (8%), metabolites (3%) and microbial (2%) biomarkers. Early detection of OPMD lesions allows the application of secondary preventive measures, thereby reducing the incidence of malignant transformation. Accumulating evidence shows that the measurement of oral-specific miRNAs and cytokines in saliva is a very promising technique for the

diagnosis and prognosis of OSCC. The analysis of these salivary biomarkers together with the study of other histopathological markers such as the presence of eosinophils and the immune phenotype can be a key factor in the development of new strategies in the treatment of OSCC. The main limitation of this review is that the included studies show a high heterogeneity with regard to the methods and protocols used for the analysis of miRNA and cytokines. Saliva also has disadvantages, including rapid biofouling on the surface of biosensors, the effect of interferents present in saliva at different concentrations, and the presence of a highly dynamic oral environment.

Conclusion: The importance of saliva as an available and continuously regenerated biological fluid for further stimulation has been emphasized. However, the origin of these molecules needs to be confirmed before classifying them as candidate biomarkers. The abundance of salivary biomarkers that have been proposed for cancer screening or early detection in the last decade shows the intense interest of the medical community. However, validation of findings obtained in pilot studies among larger population groups is essential in order to establish meaningful correlations between outcomes. Rapid advances in electronics and nanotechnology now allow the fabrication of advanced biosensor systems at a fraction of the cost of complex laboratory equipment. Given that the concentration of salivary biomarkers is usually lower than that of other biofluids, typically in the ppb-ppt range, highly sensitive biosensors are required for reliable detection of the analyte of interest. As a non-invasive specimen for liquid biopsy, human WMS is expected to play an important role in uncovering the mysteries of the diagnosis and pathogenesis of oral cancers. It will have additional advantages such as non-invasive, painless, simple and easier to administer. The emergence of new technologies with higher sensitivity for detection purposes can be expected in the near future. Access to these highly sensitive techniques (next-generation sequencing, mass spectrometry, microarray technologies) makes even smaller amounts of salivary analytes possible for accurate detection.

Keywords: Biomarkers, Oral, saliva, Neoplasms

The effect of sexual health in people with cystic fibrosis on fertility (Review)

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Introduction: Cystic fibrosis (CF), a genetic disorder that can shorten people's lifespan. It can also occur in people of any race or ethnicity. This disease was first described as a clinical and pathological entity in the 1930s. The number of people with cystic fibrosis (pwCF) has increased, with more than half of people with CF being adults. As life expectancy and quality of life improve, sexual and reproductive health (SRH) has become an increasingly important aspect of patient-centered care.

Methods: In the forthcoming systematic review, the required data were collected using keywords and citing valid databases such as Scopus, PubMed, Google Scholar and ProQuest. The statistical population includes all studies conducted until 2022 in the field of The effect of sexual health in people with cystic fibrosis on fertility. After reviewing the relevant findings and evaluating the quality of the data, 17 articles were analyzed.

Results: Pregnancy in women with cystic fibrosis is more likely to be successful if planned because poor maternal outcomes are more common in conditions of unstable respiratory health. Puberty is associated with worsening health status in CF. A few years after puberty, the rate of pulmonary exacerbations (PEx) increased in adolescent girls and boys, but was observed to a greater extent in females than in males. The interplay of disease-specific risk factors, such as drug interactions, gastrointestinal absorption, CFRLD, CFRD, bone health, and frequent use of intravenous access devices for antibiotics, may complicate contraceptive decisions for women with CF. Men with CF are at risk for hypogonadism due to frequent illness, stress, lower nutritional status, and medications such as glucocorticoids or opioids. Studies have reported the prevalence of hypogonadism in women with CF. There are aspects of CF that are directly related to CFTR dysfunction and its downstream consequences that may impair sexual function in people with CF, such as dyspareunia related to

vaginal dryness, body image caused by testosterone deficiency, low body weight. , and cough and shortness of breath during sexual intercourse.

Conclusion: Identifying relevant SRH specialists with experience with people with cystic fibrosis can be difficult. Education of primary care providers about cystic fibrosis is often neglected, and cystic fibrosis physicians see themselves as providing comprehensive care to their patients. Multidisciplinary teams should optimize the SRH of people with cystic fibrosis, whether they want to become pregnant or not. Regardless of age, this is enhanced by engaging and educating primary care providers about the SRH needs of individual patients. It will also benefit from the development of specialized networks that include urology, medical genetics, gynecology and IVF, obstetrics and gynecology, and genetics. The CF care team now has increasing responsibility for diagnosing and managing issues related to sexuality and fertility, such as menstruation and fertility, sexual activity, contraception, planning, and menopause. Other registries and clinical trial data are urgently needed to inform better care related to these issues. CF providers should coordinate sexual and reproductive health care with general gynecologists and relevant specialists in reproductive endocrinology, maternal-fetal medicine, and family planning to maximize the reproductive health of women with CF.

Keywords: sexual health, cystic fibrosis, fertility

The Effect of Silibinin on Apoptosis and PTEN in Human Breast Cancer Cell Line (Review)

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Introduction: Breast cancer is the most frequent malignancy in females. Amongst several naturally-occurring flavonoids, Silymarin is extracted from the seeds and fruits of milk thistle plant Silybum marianum which consists of main biologically active component as silibinin. It is known to inhibit cell proliferation, induce apoptosis, and curb angiogenesis. SB has demonstrated activity against many cancers, such as skin, liver, lung, bladder, and breast carcinomas. The PTEN gene acts as a tumor suppressor found in almost every tissue of the body. loss of function of the PTEN tumour suppressor is one of the most common events observed in many types of cancer.

Methods: 1. Cell lines and culture The human T47D breast cancer cell line was cultured in Medium DMEM. 2. MTT cell viability assay in T47D The human T47D breast cancer cell line was treated with different concentrations of silibinin (50- 250 µg/mL) for 24, 48 and 72 hours. The cytotoxic effect of silibinin on T47D viability was determined using Methyl-Thiazolyl-Tetrazolium (MTT) assay by IC50 determination. 3. Flow cytometric analysis for apoptotic Apoptosis was evaluated by Annexin V/propidium iodide staining. 4. Real-time PCR To assess the alterations of PTEN transcriptions, the real-time PCR reactions were performed using the Power SYBR-Green PCR Master Mix according to the manufacturer protocol. The relative gene expression levels were calculated using the $2^{-\Delta\Delta CT}$ method.

Results: IC50 concentrations of SB was144.6 % ± 9.41 for T47D cell after 48h treatment which demonstrated that SB cytotoxic activity on T47D was strong. Flow cytometry results illustrated that SB induced significant apoptosis cell death in T47D cell in comparison to untreated ones. mRNA expression levels demonstrate that SB significantly increased PTEN expression in T47D cell line, as compared to control groups.

Conclusion: Our results suggest that the apoptotic activity of SB in T47D cells. Our results have also revealed that SB can decelerate cancer cell progression and growth by targeting PTEN.

Keywords: Breast cancer, Silibinin,, Apoptosis, RT-PCR

The Effect of Sperm k + and SLO3 Channels on Sperm Motility in Male Infertility (Review)

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Introduction: SlO3 channels are regulated by pH, which may be expressed in mammalian sperm and may play a role in its alkalization. While growing evidence supports the vital role of potassium (K +) channels in somatic cells. Little is known about the localization and regulation of these channels in mammalian sperm. Previous studies have reported that SLO channels are the major K + channels in humans and mice. The sperm of these channels belong to the SLO gene family. It plays a vital role in regulating sperm volume and has also been shown to play a role. The sequence of changes that occur during capacity. Notably, such a regulatory role is mainly performed by SLO3 in mice, which includes SLO1 and SLO3 in human sperm. Be. The SlO3 channel is very important for male fertility.

Methods: This study is a secondary study (review) with a narrative approach in 2022 that searches for keywords such as K + channels, SLO3 channels, Spermatozoon, Male infertility, Sperm Motility in reputable databases including , Science Direct, Web of Science, Scopus. In this study, the relevant studies were entered based on the inclusion and exclusion criteria. A total of 15 articles were reviewed, of which 10 articles were included in the study.

Results: According to studies from various articles, the results are that, in order to be successful in fertilization, sperm must decode environmental signals that require a set of ion channels. Recent findings suggest that K + and Cl- channels are involved in some of the major functions of sperm. This study examines the evidence for the involvement of K + and Cl- channels in motility, maturity, acrosome reaction, and progress in identifying molecular identities and their regulatory states. Improving our insights into how these channels work strengthens our ability to overcome some infertility problems, improve animal husbandry, preserve biodiversity, and develop selective and safe contraceptive tools for men. The observed effects of TEA are consistent with its high capacity to block K + channels. Regardless of whether they open or close. Due to the decrease in sperm motility, we also saw a significant decrease in sperm velocity (VCL, (VSL) and VAP) parameters and in cross-frequency pulse (BCF). Consistent with these findings, non-selective blockage

of K + channels has also been shown to inhibit progressive movement in human sperm. In addition, our data also demonstrate the importance of K + conductivity for sperm motility during in vitro capacity building.

Conclusion: According to the results, high-power screening methods can accelerate the identification of new factors that enhance sperm motility. In addition, it is important to confirm that these locomotives do not have any adverse effects on the developing fetus.

Keywords: K + channels, SLO3 channels, Spermatozoon, Male infertility, Sperm Motility

The effect of stem cells in the treatment of intestinal lymphoma (Review)

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Introduction: Intestinal lymphoma cancer is one of the common cancers in our country, which has a relatively high prevalence. This disease is an aggressive disease that is currently treated with a combination of chemotherapy and surgery. Forty percent of lymphomas occur in areas other than lymph nodes, and the digestive system is the most common. Stem cells are cells which have high ability to divide and differentiate, and in response to specific stimuli can differentiate into different types of cells in the body. By using stem cells, it is possible to prevent the spread of intestinal lymphoma and complications caused by chemotherapy (anemia, infertility, respiratory and kidney problems, risk of infection, etc.) and surgery.

Methods: Bone marrow stem cells, fetal umbilical cord blood stem cells, and peripheral blood stem cells are important sources to obtain stem cells.

Results: New studies on gastrointestinal lymphoma in the intestine suggest a solution to destroy and destroy cancer cells using chemotherapy and then using stem cells. The given solution is that after knowing the type of cell involved in cancer and finding the center of this cell, the protein gene that controls the proliferation of cancer is placed in the stem cell (umbilical cord blood stem cell, fat stem cell, etc.) and then enter the place of accumulation of lymphoma. In this case, the stem cell surrounds the cancer cell and there is no opening left for the cancer cell to metastasize. It is also possible to add a type of Grb2 protein to the stem cell to control cell proliferation. In this case, the cancer cell, which is trying to escape from this stem cell protection, becomes weak, and at this time, the use of low doses of medicine is enough to destroy it. In addition, there is no need for surgery and the long-term use of chemotherapy drugs, and the healthy cells around the cancer cell also remain healthy.

Conclusion: This method, that is, the treatment of cancer cells using stem cell transplantation, can be used in the treatment of gastrointestinal lymphomas, including intestinal lymphoma. For this, we need multipotent stem cells that can be taken from the individual or preferably donated cells. It seems that using this method to treat intestinal lymphoma can treat lymphoma at any stage.

Keywords: Keywords: Stem cell, Intestinal lymphoma, Cancer

The effect of the flipped classroom on the learning of medical sciences students compared to the traditional teaching method; A systematic review (Review)

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Introduction: Using the traditional teaching method (teacher-centered) is a passive method.. One of the problems of teacher-centered teaching is the large amount of content that the teacher must present to the students during the classroom hours, but usually, due to the limited time in face-to-face classes, it is not possible to present a complete lesson content. Flipped classroom is one of the student-centered teaching methods that can have a significant impact on medical sciences students by providing the course content to the learners at an appropriate time interval before each face-to-face class session, gives them enough time to study the course content carefully and patiently before starting the class. And then during the face-to-face classroom, the teacher deepens their learning by doing supplementary educational activities, such as question and answer, group discussion, problem solving, etc. The aim of this review study is to investigate the effect of the flipped classroom compared to the traditional teaching method among medical sciences students.

Methods: This review study conducted through an advanced search of reputable scientific databases including Pubmed, Scopus, ERIC, and Google Scholar search engine from 2016 to September 2022 using keywords “Flipped Classroom”, “Inverted classroom”, “Medical Students”, “Medical education”. After the initial search, only the title and abstract of interventional and qualitative studies were examined for relevance to the study objectives and the unrelated articles were excluded. We included publications relevant to the education of medical sciences students such as medical students, residents,

nursing students, etc. The articles related to the study were also evaluated through the Mixed Method Appraisal Tool (MMAT).

Results: Students can use modern methods, especially the flipped classroom, in teaching courses. The results of this review identified positive outcomes among medical sciences students after a flipped classroom experience in terms of knowledge, attitudes, and practices. It improves students' problem solving ability. In comparison to traditional lecture-based method, flipped classroom led to greater students satisfaction. Students belived that the worksheet provided before the class makes a better understanding of the subject, and learning key foundational content before coming to class enhanced the learning of course material in class. Also, there was a significant difference between the scores of the students before and after the test and the final test scores of the students. The scores were improved significantly. Most of graduate and undergraduate medical sciences students agreed that the flipped classroom is more engaging and interesting than the traditional classroom. Those students who believed traditional lecture-based classes are better than flipped classroom, were of the opinion that they have to spend more time for learning than traditional classes. Some studies mentioned limitations like limited electronic content available.

Conclusion: Flipped classroom is one of the educational methods that makes students learn better. It also leads to greater student satisfaction and better student performance in comparison to traditional teaching methods. It should be noted that several factors including course factor can be determining factors for choosing this method. However, more studies are needed to make a certain conclusion

Keywords: Flipped Classroom, Inverted Classroom, Medical students, Medical Education

The Effect of the Frequency of Hereditary Thrombocytopenia and Its Modulating Factors on Bone Marrow (Review)

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Introduction: Hereditary thrombocytopenia (ITs) are a heterogeneous group of disorders characterized by low platelet counts and often present as hemorrhagic diathesis, which in turn leads to impaired homeostasis. Hereditary thrombocytopenia (IT) includes a group It is an inherited disorder characterized by a decrease in platelet count as the main feature and often with abnormal platelet function, which in turn can lead to impaired homeostasis. Hereditary thrombocytopenia is caused by genetic mutations in genes involved in the differentiation of megakaryocytes and/or platelet formation and clearance. Protect the integrity of blood vessels. They play an important role in normal homeostasis to prevent excessive bleeding at the site of blood vessel damage. Causes of secondary or reactive thrombocytosis include reactive responses to systemic infection, chronic inflammatory conditions, hypovolaemia, malignancy, iron deficiency, bleeding, surgery, and trauma. False platelet counts can also occur when other cellular factors, including microspherocytes, schistocytes, or infectious organisms, are mistaken for platelets. This study aimed to determine the frequency of hereditary thrombocytopenia and its modulating factors on bone marrow.

Methods: This research is an initial observational study, an experimental study with an intervention approach that in 2022 by searching for keywords such as Thrombocytopenias, Heterogeneous, Megakaryocyte, Bone Marrow, Thrombopoietin gene in the MeSH database and reputable databases such as Science Direct, Pub Med and Science Direct were performed. Finally, 15 articles were extracted and 10 of them were included in the study.

Results: According to studies from the articles, the results are that the inherited pattern of IT disease was first discovered in a disorder called Bernardsulie Syndrome (BSS). Since then, advances in clinical and scientific research have led to an increase in patients' understanding of molecular defects. Has been affected by IT. They appear in women with various symptoms including epistaxis, mild bruising, petechiae, prolonged bleeding from the incision, bleeding gums, excessive postoperative bleeding, hematuria, and menorrhagia. Since bleeding is considered to be the main

clinical complication for patients with IT, some patients with common IT tend to develop other disorders such as blood malignancies and kidney failure. Although there are other causes for thrombocytopenia. Like infections and immune disorders, IT is mainly caused by mutations in genes involved in megakaryocyte differentiation, maturation, and platelet release. To date, 40 genes and their mutations have been implicated in many different forms of inherited thrombocytopenia. The human THPO gene contains seven exons and six introns. With a location of more than 6 KB. The THPO gene encodes a humoral growth factor (332 amino acids with a molecular mass of ~ 70 kDa) that exerts profound stimulatory effects on megakaryopoiesis and thrombosis.

Conclusion: The process of megakaryopoiesis and thrombosis involves a series of complex biological events. Megakaryocytes, like all blood cells, are derived from hematopoietic stem cells (HSCs) in the bone marrow during the lineage commitment process. The process of hematopoietic stem cell differentiation involves committed precursors, including common myeloid precursor (CMP) and megakaryocyte-erythroid precursor (MEP).

Keywords: Thrombocytopenias ،Heterogeneous ،Megakaryocyte ،Bone Marrow ،Thrombopoietin gene

The effect of thyroid drugs on laminin protein by molecular docking method (Research Paper)

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1. -

Introduction: Laminin is one of the main proteins of the basement membrane, and they are the most important and active part of the basement membrane, which play a role in cell differentiation, cell migration, cell attachment, and their survival . (According to research, laminin protein is a target for thyroid cancer treatment). Sorafenib is used in the therapy of advanced renal cell, liver and thyroid cancer . . Liothyronine is used for prevention and treatment of thyroid cancer. Levothyroxine is a medicine for hypothyroidism . Methimazole is a drug that is used in the treatment of hyperthyroidism . The purpose of this research is to investigate the effects of thyroid drugs on laminin protein .

Methods: material and method : First, prepared the three-dimensional structure of the laminin protein by using the Uniprot site . Then, we obtain the three-dimensional structure of Sorafenib-Liothyronine-Levothyroxine and Methimazole drugs through the Pubchem site. In the next step, using the Chimera 1.10.2 program, we include changes such as removing ions, adding hydrogen, removing extra chains, etc. in the original protein . Finally, with the PyRx program, we start docking by loading the modified protein file as macromolecule and the drug file as input . Docking location was as follows : Center-x : 189.747 Center-y : 163.775 Center-z : 155.2557 Size-x : 25.0 Size-y : 25.0 Size-z : 25.0

Results: Result : At the end of docking, the results are as follows : Protein : Laminine (LAMC1) RMSD bound Binding Affinity (kcal/mol) Drug 0 -10 Sorafenib 0 -6.7 Liothyronine 0 -6.3 Lithroxine 0 -4 Metamazole

Conclusion: According to the investigations, sorfanib has the most effect on laminin protein, and liothyronine -levothyroxine and metamazole have the most effect, respectively .

Keywords: Tyroid-cancer-laminin protein-gland

The effect of vitamin C supplements on sperm health (Review)

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2.

Introduction: Sperm health is very effective in male fertility, and therefore changes in concentration, morphology, and sperm mobility can cause infertility in men. Diet, environment and genetics, and the production of intracellular oxygen species (ROS) can change sperm factors and affect sperm generation and quality.the imbalance between ROS levels and physiological antioxidants can lead to oxidative stress, and oxidative stress is one of the main causes of reproductive failure .scorbic acid, best known as vitamin C, is the most important semen antioxidant and 65 % of the semen's antioxidant capacity belongs to this vitamin.

Methods: In this systematic review, the PubMed and Google Scholar and Scopus database reviewed the key words used in this study were sperm, vitamin C and infertility.

Results: Oral administration of Vitamin C is associated with a daily basis with increasing level of expression of the Protamine gene in men. vitamin C therapy In addition to improving sperm properties and DNA integrity, the MRNA level of Protamine 1 (PRM1), Protamine 2 (PRM2), as well as the Prm1/PRM2 ratio.treatment with vitamin C supplements increases sperm count, sperm analysis improves and fertility increases. Therefore, higher doses of vitamin C may be helpful in the treatment of infertility. Increasing the dose of vitamin C to 1000 mg daily also significantly improves sperm properties in smokers. Vitamin C, in addition to enhancing sperm quality, prevents its accumulation and increases sperm motility.

Conclusion: In this study, the positive effect of vitamin C on sperm functional properties examined. We believe that these results are of high scientific value for future research. Based on these findings, we found that further studies are needed to evaluate the effect of vitamins and minerals on sperm properties, so that supplements can be used as therapeutic recommendations in the treatment of male infertility.

Keywords: sperm, vitamin C, male fertility, antioxidant

The effect of zinc oxide nanoparticles on bacterial resistance in gram-negative and positive bacteria (Review)

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Introduction: Antibiotic resistance in bacteria has now become a worldwide issue. Today Antimicrobial misuse has led to the creation of multidrug-resistant bacteria, resulting in a rise in infectious illness and mortality. Nanomaterials, such as metal oxide nanoparticles, have emerged as viable candidates in the last several years as researchers looked into different solutions to this challenge. As a result of its widespread applicability, nanotechnology science has advanced substantially. Zinc oxide (ZnO) nanoparticles (NP) have showed promise in inactivating bacteria at a time when the number of new antibiotics in development is dwindling and, more concerning, the incidence of bacteria resistant to presently used antibiotics is rising. ZnO NPs have already been successfully incorporated into a number of biomedical applications due to their ability to inactivate germs. The goal of this study is to see how zinc oxide nanoparticles affect bacterial resistance in both gram-negative and gram-positive bacteria.

Methods: The current study was conducted by scanning scholarly resources such as Google Scholar, Science Direct, Springer, and PubMed for information zinc oxide nanoparticles and bacterial resistance.

Results: The current study was conducted by scanning scholarly resources such as Google Scholar, Science Direct, Springer, and PubMed for information zinc oxide nanoparticles and bacterial resistance.

Conclusion: The end outcome revealed in general, surface changes of ZnO NPs boost antibacterial activity, lowering the MIC of these NPs against the microbes studied. This is due to ZnO NPs' better size distribution and increasing resistance. ZnO had a stronger effect against Gram-negative E. coli than it did against Gram-positive S. aureus. Bacterial cells were more easily damaged by ZnO particles. They have a tendency to penetrate bacteria's membranes, which appears to be more efficient against larger oval-shaped E. coli than tiny spherical S. aureus

Keywords: ZnO Nanoparticle, bacterial resistance, Antibiotic

The Effects of Conditioned Medium from Adipose Tissue-derived Mesenchymal Stem Cells on Differentiation of Spermatogonial Stem Cells (Research Paper)

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Introduction: Spermatogenesis is a biological process essential for the male germline's continuity by which haploid spermatozoa are produced. Throughout the male's life, spermatogenesis is a continuous and coordinated process of cell proliferation and differentiation that results in the development of unrestricted numbers of spermatozoa. Spermatogonial stem cells (SSCs), which have the remarkable ability to self-renew and produce differentiated daughter cells that will eventually form spermatozoa, are at the heart of this scheme. In seminiferous tubules, SSCs are highly rare stem cells found in niches surrounded by Sertoli cells and differentiating spermatogonia. In vitro differentiation of stem cells into male or female germ cells has recently been proposed as a new strategy to the treatment of infertility by researchers. The use of mesenchymal stem cells (MSCs) is gaining popularity since they face to no ethical problems of embryonic stem cells and can be collected from a variety of sources such as adipose tissue, bone marrow, and menstrual blood which all have a strong ability to develop into various tissues. The adipose tissue-derived mesenchymal stem cells (AD-MSCs), as almost easy access and well characterized source of MSCs, have been widely employed for therapeutic purposes. In vitro effects of conditioned medium (CM) from MSCs on germ cell regeneration has been shown. The aim of this study was to compare and evaluate the proliferation and differentiation of spermatogonia stem cells using their co-culture with Sertoli cells and supernatant from fat-derived mesenchymal stem cells.

Methods: This experimental study was conducted on Wistar Rats from Medical Sciences Animal Lab (Iran, Qom), under standard conditions with free access to Food and water. The testicular tissues were separated from 2-7 days old neonate Wistar Rats and transferred into the laboratory. After

mechanical and 2-step enzymatic digestion with collagenase I and 0.25% trypsin enzymes, the SSCs and Sertoli cells were isolated and cultured in DMEM with 10% FBS, 1X antibiotic, bFGF, and GDNF and incubated in 95% humidity, 5% CO2 and 34°C. The isolation of SSCs and Sertoli cells was confirmed with immunocytochemistry (ICC) for CD49f and Vimentin, respectively. The cells were treated with the conditioned medium from adipose tissue-derived MSCs for 12 days and then the genes related to differentiation were measured with Real-Time PCR. Also, the expression level of two major spermatogenic markers of DAZL and DDX4 was calculated with ICC and Western Blotting (WB).

Results: CD49f and Vimentin were positive for SSCs and Sertoli cells, respectively (Fig. 1). The expression level of Scp3, Dazl, and Prm1 genes was significantly increased after treatment compared to the control group. However, no significant difference was observed in Stra8 expression between the group treated with conditioned medium and the control group (Fig. 2). The ICC results showed that DAZL and DDX4 were positive in the experimental group compared with the control (Fig. 3). Also, WB revealed that both DAZL and DDX4 were higher in the treated group than the control group, however, no significant difference was observed (Figure 4).

Conclusion: Given that SSCs are essential sources for male germline continuity, maintaining and restoring their differentiation potential sounds critical. In this study, we concluded that the conditioned medium obtained from adipose tissue-derived MSCs could be considered as a suitable biological material to induce the differentiation in spermatogonial stem cells.

Keywords: Spermatogonial stem cells, Mesenchymal stem cells, Conditioned medium, Differentiation

The effects of mothers' knowledge on the health of babies and fetuses during pregnancy (Research Paper)

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Introduction: The most important guarantor of maintaining the health of the mother and the fetus during pregnancy is to be aware of the cares during this period and to act on them. Health literacy is an important and modifiable factor to improve the achievement of this awareness. For this purpose, the present study was conducted with the aim of determining the level of health literacy of pregnant mothers and its relationship with prenatal care in Shiraz city in 2019.

Methods: This research is a descriptive analytical cross-sectional study that was conducted in 2019 on 205 pregnant women who referred to health centers in Shiraz city. People were selected by simple random sampling and the data collection tool was the MHLAPQ Maternal Health Literacy and Pregnancy Outcomes Questionnaire. Data analysis was done with spss software version 19 and statistical tests, T-test, ANOVA, correlation and chi-square. In all tests, 0.5 was considered as a significant level.

Results: The findings of the research show that 69% of the pregnant women studied were employed and 91% had higher than bachelor's education. The average health literacy score of pregnant mothers was 94.9±07.57; Also, there was a significant relationship between mothers' health literacy and job education level > 0.05, 0.1000. But there was no significant relationship between the use of multivitamin supplement 0.261>0.05 and the use of iron supplement 0.507>0.05.

Conclusion: The results showed that the state of health literacy among pregnant mothers in Shiraz is in a favorable state. Considering that there was a significant relationship between the health literacy of mothers, occupation and education, this issue shows the need to pay more attention to improving the education of women in the society and their occupational status in order to improve the health literacy of this segment of the society.

Keywords: mothers' knowledge , health , fetuses , pregnancy

The effects of plant oils intake on Gallstone Disease: A systematic review (Review)

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Introduction: Gallstone disease (GD) is a relatively common health challenge in developed and developing countries. The role of plant oils intake has been researched in some studies. The purpose of this systematic review is to investigate the effect of plant oils intake on GD pathogenesis.

Methods: Pubmed (Medline), Embase, and Scopus were searched for the existing literature up to December 2021. All clinical trials, cohort, cross-over, case-control, and animal studies that investigated the effects of dietary plant oils on the occurrence of GD were included. Studies containing incomplete information were excluded.

Results: 7 of the 3771 articles that we found had inclusion criteria. In one animal study, corn oil intake significantly increased cholesterol levels in serum and bile, cholesterol saturation index, cholesterol monohydrate crystals formation and gallstones formation. In two animal studies, safflower oil consumption caused a higher incidence of cholelithiasis, and in another research, safflower oil fed animals has a lower incidence of lithiasis. Consumption of olive oil and corn oil in one animal study, significantly reduced gallstones formaition. In another animal study by six oil groups (butter, palm stearin, coconut oil, rapeseed oil, olive oil, sunflower seed oil), no cholesterol gallstones were observed with the butter, coconut oil, rapeseed oil, olive oil and sunflower seed oil groups. In one animal study by three oil groups (coconut oil, olive oil, safflower oil), olive or safflower oil consumption caused a similar low concentrations of free cholesterol in liver and plasma. Coconut oil resulted in a slightly higher levels of free cholesterol in both hepatic and plasma.

Conclusion: Due to the different effects of plant oils consumption, recommendations should be based on the choice of adequate amounts of fats as well as following a healthy diet and lifestyle.

Keywords: Plant oil, Gallstone disease, Pigment gallstone

The effects of silver nanoparticles on the expression of TNF-α genes in infected Staphylococcus aureus Balb/C mice (Research Paper)

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Introduction: Methicillin-resistant Staphylococcus aureus strains are one of the most important clinical and epidemiological problems in hospitals. Currently, antibiotic resistance in bacteria is a major concern among physicians who are the main cause of treatment of patients and increased mortality. Nowadays, with the advancement of nanotechnology, nanoparticles have many capabilities in approaches to diagnosis, and medical treatment, especially drug delivery and gene therapy systems. The present study aimed to investigate the effect of silver nanoparticles on the expression of TNF-α genes in Balb/C mice infected with Staphylococcus aureus.

Methods: The microbial species used in this study was Staphylococcus aureus. The number of 35 Balb/C were purchased with 22 ± 5 g and all sexes and divided into five groups of seven. On the first day in the morning, the control and nano-control groups were injected intraperitoneally with saline so that the effect of shock induced by injection was similar in the groups. The third, fourth, and fifth groups received an intraperitoneal microbial suspension. Three hours later, the first control group received saline, the second group received nano-silver, the third group received saline, the fourth group received nano-silver, and the fifth group received vancomycin. Finally, after a 1- day and 5 - day period, samples of spleen preparation, RNA extraction, and Real-time were evaluated for TNF-α gene expression.

Results: The results of the study of different treatments with control samples indicated both in the 5 - day period and in the 1- day period after vancomycin, the use of nano-silver increased TNF-α gene expression.

Conclusion: Finally, by examining the treatments, nano - silver can be concluded that nanoparticles can be used to replace common antibiotics against the aforementioned bacteria.

Keywords: Staphylococcus aureus _ Nano silver _ gene TNF-α _ Balb/C

The effects of siRNA-mediated gene silencing of alpha-7 nicotinic acetylcholine receptors on drug resistance to oxaliplatin in colorectal cancer cell line (Research Paper)

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Introduction: Colorectal cancer (CRC) is one of the most common cancers worldwide. Oxaliplatin (OXA) is one of the chemotherapy drugs used in this cancer. On the other hand, the alpha-7 nicotinic acetylcholine receptor (α7nAchR), which is one of the members of the nicotinic receptors family, has a crucial role in different types of cancers and the resistance to chemotherapy. The role of α7nAchR in CRC chemoresistance, especially in OXA-resistant cells, has not yet been identified. Therefore, this study was designed and performed to evaluate the impact of suppression of α7nAchR by siRNA on OXA-resistant cells.

Methods: OXA-resistant SW-480 cells were established by raising the concentration of OXA and exposing cells repeatedly. Then, the electroporation method was used to transfer siRNA sequencing to cells to inhibit α7nAchR expression. IC50 values of OXA and the combination of α7nAchR-siRNA and OXA were determined using the MTT assay. qRT-PCR was used to evaluate the expression of α7nAchR, MDR-1, Bcl-2, and Caspase-3 genes.

Results: The results indicated that suppression of α7nAchR expression could cause sensitization in OXA-resistant cells. This study also showed significant induction in α7nAchR mRNA expression in OXA-resistant cells compared to naïve cells. α7nAchR-siRNA transfection significantly reduced the expression of α7nAchR simultaneously with IC50 values. Also, following transfection with α7nAchR-siRNA, decreased expression of MDR-1 and Bcl-2 genes was observed along with increased expression of the Caspase-3 gene.

Conclusion: According to the findings of this study, α7nAchR has an important role in OXA chemosensitivity. Thus, α7nAchR may be considered a clinical marker in CRC drug resistance, and its suppression may be a potential therapeutic approach for CRC therapy.

Keywords: Colorectal cancer; siRNA; α7nAChR; Oxaliplatin; SW-480

The effects of ZnO nanoparticles on the expression of TNF-α genes in infected Staphylococcus aureus Balb/C mice (Research Paper)

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Introduction: Methicillin - resistant Staphylococcus aureus strains are one of the most important clinical and epidemiological problems in hospitals. Currently, antibiotic resistance in bacteria is a major concern among physicians who are the main cause of treatment of patients and increased mortality. Nowadays, with the advancement of nanotechnology, nanoparticles have many capabilities in approaches to diagnosis, medical treatment, and especially drug delivery and gene therapy systems. The present study aimed to investigate the effect of ZnO nanoparticles on the expression of TNF-α genes in Balb/C mice infected with Staphylococcus aureus.

Methods: The microbial species used in this study was Staphylococcus aureus. The number of 35 Balb/C were purchased with 22 ± 5 g and all sexes and divided into five groups of seven. On the first day in the morning, the control and nano-control groups were injected intraperitoneally with saline so that the effect of shock induced by injection was similar in the groups. The third, fourth, and fifth groups received an intraperitoneal microbial suspension. Three hours later, the first control group received saline, the second group received nano-ZnO, the third group received saline, the fourth group received nano - ZnO, and the fifth group received vancomycin. Finally, after a 5 - day and 1- day period, samples of spleen preparation, RNA extraction, and Real-time were evaluated for TNF- α gene expression.

Results: The results of the study of different treatments with control samples indicated that at 5 days after vancomycin, the use of nano- ZnO can increase the expression of the TNF- α gene. While during the 1- day period just vancomycin TNF- α gene expression.

Conclusion: Finally, by examining the treatments, nano - ZnO was observed to increase the expression of TNF- α as compared to nano - copper and ZnO, which is the most significant effect of the gene. This shows its greater effect

during the increase in the length of the treatment. Therefore, it can be concluded that nanoparticles can be used to replace common antibiotics against the aforementioned bacteria.

Keywords: Staphylococcus aureus _ Nano ZnO _ gene TNF-α _ Balb/C

The efficiency of titanium dioxide nanoparticles as contrast agents in radiotherapy of tumor (Review)

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Introduction: Conventional non-nanoparticle image contrast agents such as iodine have been validated for radiotherapy enhancement applications. Ionizing radiation is used to treat tumors during radiotherapy. This causes damage to DNA and other biomolecules in the tumor, leading to cell death. Radiation therapy has the inherent drawback of inflicting radiation on the surrounding healthy tissues of the treated tumor. Some tumors are unsuitable for radiotherapy since the dose required to destroy the tumor may harm the surrounding healthy tissue. In radiation therapy applications, titanium dioxide nanoparticles (TiO2-NPs) have been found to have absorptive properties and a higher refractive index, which can be beneficial for the treatment of cancer.

Methods: We searched Google Scholar, Web of Science, PubMed, and Scopus databases for published articles related to titanium dioxide, diagnosis, cancer, and radiotherapy using the keywords titanium dioxide, diagnosis, cancer, and radiotherapy. Reviews were conducted on articles published.

Results: As a radio-sensitizer for radiotherapy of triple-negative breast cancer (TNBC), hybrid anisotropic nanostructure is composed of gold-doped titanium dioxide (TiO2). Sonodynamic therapy (SDT) with ultrasonic activated TiO2 for increased quantum yield. According to Yang et al., when titanium dioxide was exposed to ultrasound, carbon-doped titanium dioxide generated ROS, eliminating tumor cells. A cancer catalytic internal radiotherapy (CIRT) system that utilizes auger electrons (AEs) to construct an active site is reported by Su et al. Radiation therapy using contrast agents and kilovoltage X-rays (contrast-enhanced radiotherapy or CERT) is called contrast-enhanced radiotherapy. Consequently, a high Z content in materials can affect the distribution of absorbed doses because they have different absorption properties from healthy tissues. A localized dose increase can be achieved in areas containing contrast agents without affecting healthy tissues. Since photo-absorbing properties change with kilovolt energy, the kilovolt range is ideal for CERT. Medical linear accelerators (Linacs) also provide X-ray energy in the megavolt range, improving contrast. Cell membranes can be penetrated by TiO2-NPs with a size under 100 nm, causing them to accumulate in cancer cells. Furthermore, it can be used as a contrast agent. In order to monitor NPs

synthesized for radiotherapy and ionizing radiation with CT scanners, the standard imaging tool for planning and diagnosing treatment, it would be useful to monitor them with CT scanners. These CT scanners are gradually replacing radiotherapy treatment planning simulators. Iodine CERT can also be used to deliver therapeutic doses of X-rays to a conventional CT scanner. A similar dose distribution can be generated by this method so that simulations, hybrid imaging, and treatment can be performed on the same basis as with 10 MV therapy. An alternative that is similar to this would be highly desirable in the case of more advanced contrast agentsThese TiO2-NPs are not only contrast agents, but can also be used as radiotherapy enhancement agents and cancer-fighters.

Conclusion: As a contrast agent, TiO2-NPs are effective in diagnosing and treating cancer in these studies. Unmodified TiO2-NPs have not mainly been studied in imaging studies, whereas chemically modified TiO2-NPs have been studied in imaging studies.

Keywords: titanium dioxide, radiotherapy, cancer

The epigenetic effects of the combination of diesel exhaust exposure and excess nutrition in development of insulin resistance (Research Paper)

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Introduction: Numerous investigations have been conducted to disclose risk factors for type 2 diabetes. Overnutrition is the most well-known contributor to its development. Meanwhile, exposure to air pollution (PM) has recently been shown to trigger insulin resistance, leading to diabetes; however, its underlying mechanisms are not fully understood. Nutrient-induced insulin production is aided by incretin hormone receptors (GLP-1R and GIPR) working in tandem with transcription factor7-like 2 (TCF7L2). We hypothesize that insulin resistance may be triggered as a result of PM tampering the modulators of the nutrient-induced insulin secretion. Thus, focusing on pancreas malfunction, we examined the mechanism by which PM exposure in conjunction with high-fat feeding may induce insulin resistance.

Methods: The experiment involved four groups of C57BL/6 mice, namely (N/F, H/F, N/P, and H/P). The mice were fed a control/high-fat diet and exposed to PM/filtered air for 10 weeks to examine pancreatic Gipr, Glp-1r, and Tcf7l2-E4 gene expression. Fasting blood glucose and insulin sensitivity were evaluated via insulin surrogate indices. Pancreatic concentration of TCF7L2 was also assessed.

Results: High-fat-fed mice displayed lower Gipr and pancreatic TCF7L2 protein expression associated with impaired glucose tolerance despite preserved insulin tolerance. PM exposure led to a downward trend in Gipr, Glp-1r, and Tcf7l2-E4 expression, while their glucose tolerance and insulin sensitivity state were steady. Moreover, pancreatic TCF7L2 protein level increased significantly in response to PM.

Conclusion: Present findings suggest that sub-acute exposure to diesel exhaust PM can disrupt the normal gene expression in the pancreas, which due the importance of the genes might cause susceptibility to the development of insulin resistance.

Keywords: Air pollution; High-fat diet; Gipr; Glp-1r; Tcf7l2

the evaluation of LYL1 gene in Acute lymphoblastic leukemia in children (Research Paper)

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Introduction: In recent years, an increasing trend in the incidence of acute lymphoblastic leukemia (ALL) has been reported. However, the molecular mechanisms involved are not fully understood. The aim of this study was to evaluate the expression of LYL1 gene in patients with Acute lymphoblastic leukemia for the identification of the gene expression changes so that the role of the gene in diagnosis and treatment of the disease could be determined

Methods: This case-control study was performed on 40 ALL patients and 40 healthy controls in the years 2020-2021. For this purpose, total RNA was extracted from blood samples and after cDNA synthesis, LYL1 expression was measured using Real-Time PCR. Statistical analysis of the results was performed using SPSS software and appropriate tests

Results: The results of the gene expression study showed that in patients with ALL, LYL1 expression compared to controls had significant increases. These expression changes were not significantly different in age, sex, MRD, and T-ALL and B-ALL categories

Conclusion: In conclusion, downregulation or upregulation of LYL1 may be of importance in the biology of ALL .Other studies are also required to elucidate the exact function of this gene in cancer

Keywords: Acute lymphoblastic leukemia, LYL1 Gene, Case-control studies, Gene expression

The global crisis of antimicrobial resistance, A Review (Review)

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Introduction: Antibiotics, either are cytotoxic or cytostatic to the bacteria and other microorganisms, allowing the body's natural defenses, to eliminate them. They often act by inhibiting the synthesis of a bacterial cell, synthesis of deoxyribonucleic acid, ribonucleic acid, proteins, by a membrane disorganizing an agent, or other specific actions. Also, antibiotics can enter the cell walls by binding to the cell walls of bacteria (using energy transfer mechanisms in ribosomal sites) and lead to the inhibition of protein synthesis. Antimicrobial resistance is a serious threat to public health that causes unfavorable effects clinical and economic effects. Antibiotic resistance develops in a short time and is a worrying crisis. With the improvement of technology, more people are now aware of the ill-effects caused by resistance to the available drugs, however, very few take pro-active steps to curb the resistance by not over using the antibiotics. In the developing world, almost all the antibiotics are available over the counter and can be bought without any medical prescription which is one of the most important factors in causing the resistance. Human behavior governs the speed and extent at which antimicrobial resistance arises and develops, thus appropriate antimicrobial stewardship incorporating a 'One Health' approach is required to help manage the problem. Therefore, if the resistance to the antibiotics needs to be curbed, the only way shall be to educate the patients and the general public. Researches about the resistance of microbes to antibiotics and the ineffectiveness of emerging antibiotics have been started in the world and Iran for years. These surveys indicate the need for more research in this field.

Methods: This study is reviewing data accumulated from literature and prestigious case studies which are in connection with our subject. The search words were: antibiotic resistance," "Antibiotics," "Antibacterial," using PubMed, Scopus, Science Direct and Google Scholar databases. Furthermore, manual searches of other relevant journals and keywords searches were performed. We have focused on published papers from 2010 to 2022.

Results: Many solutions have been reported to prevent antibiotic resistance. One of the basic and effective solutions to deal with the phenomenon of antibiotic resistance is to prevent the lateral transfer of genes, which can easily prevent the transfer of bacteria between people and accelerate this process by observing personal hygiene. Also, in the investigations that have been done in hospitals to prevent broad-spectrum antibiotic resistance. Respecting the health of patients, changing the strategy of antibiotic use,

completing the course of antibiotic use and creating sterile conditions in the departments where patients are hospitalized for a long time, as well as preventing the use of antibiotics and prescribing them when necessary are among the main and important solutions. Which play a key role in preventing infections caused by emerging antibiotics.

Conclusion: Antibiotic resistance is a challenge facing today and future generations, and with the passage of time, this concern is felt more than before. Antibiotic resistance is increasing in humans, animals and agriculture, despite measures taken by some WHO member countries. The cost of treatment in infection control as well as the lack of response to treatment in the health care sector (due to long stays in hospitals and isolation wards, and strict measures) have become a major challenge. The World Health Organization should establish a coordinated system with continuous review of mandatory reports (for antibiotic resistance) at the national and international levels. Both domestic and global policies need to be conventional and adhered to stop the overuse and misuse of antibiotics.

Keywords: Antibiotic resistance, Antibiotics, bacterial resistance

The gut microbiota as a potential treatment for liver cancer (Systematic review) (Review)

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Introduction: Liver cancer is a life-threatening malignancy due to its high incidence and mortality worldwide. The imbalance of gut microbiota plays an essential role in the occurrence and progression of liver cancer. The aim of this study is to investigate gut microbiota-mediated therapy as a potential option for liver cancer treatment.

Methods: This review article was performed within articles published at PubMed, Science Direct, Google Scholar, SID, and Cochrane until September 2022. The keywords were liver cancer, gut microbiota, probiotics, and treatment. By searching this database; 79 articles were found, 35 of them by Reading titles and abstracts were removed. 44 articles were selected under the inclusion criteria. All articles were chosen from English and Persian articles.

Results: Finally, 44 articles were included in the study. Gut microbiota could present a non-invasive biomarker for early liver cancer diagnosis. Bacillus subtilis, Lactobacillus casei, and Candida utilis could degrade aflatoxin and had a positive effect on the prevention of hepatocellular carcinoma (HCC). Prevotella and Oscillibacter were known as producers of anti-inflammatory metabolites, which reduced the Th17 polarization and promoted the differentiation of anti-inflammatory Treg/Tr1 cells in the gut. Probiotics modulated host gut microbiota, to prevent pathogen-associated-molecular patterns (PAMPs)-mediated hepatic inflammation. The gut microbiota could modulate host responses to chemotherapeutic drugs for liver cancer and the mechanisms were translocation, immunomodulation, metabolisms, enzymatic degeneration and reduced diversity. Modified FMT could bring the gut microbiota of HCC patients closer to normal people. Immunotherapy targeting CTLA4 and PD-1 could improve the immunosuppressive environment shaped by harmful species of gut microbiota. Farnesoid X receptor (FXR) agonists like obeticholic acid and TLR4 inhibitors such as eritoran might inhibit HCC development by altering the gut microbiota indirectly. Sodium butyrate treatment reduced inflammation and by enriching Christensenellacease, Blautia, Lactobacillus and bifidobacterium. Synbiotics that consisted of Lactobacillus paracasei B21060 plus arabinogalactan could reduce hepatic inflammation.

Conclusion: Targeting the gut microbiota has a vital function in the diagnosis, prevention, and treatment of liver cancer. However, need to be more research done on this topic.

Keywords: Liver cancer, gut microbiota, treatment, probiotics

THE IMPACT OF CONSULTATION ON INFERTILITY TREATMENT AND OUTCOME (Review)

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Introduction: Infertility is a major crisis in life which exerts a stress effect on both personal and interpersonal areas. The effect of consultation on infertility treatments and marital and sexual functioning and health related quality of life is not well defined. The present study aimed to review the effects of consultation on infertility outcome.

Methods: This review has been conducted based on analysis of available literature indexed in MEDLINE and PubMed databases between 2015 and 2022. Specific keywords including “infertility” and “Consultation” have been used. Epidemiological, experimental and review articles on the mentioned theme were included.

Results: Accumulating evidence from studies suggests behavioral, cognitive and emotional consultation can decrease the negative aspects of infertility. Moreover, psychological consultation increased the life satisfaction in infertile women. One clinical trial revealed providing people undergoing in vitro fertilization with emotional and mental support will increase their chances of pregnancy and this kind of support will be helpful for patients if it is given in the form of midwifery consultation. However, findings from another study indicated that the collaborative infertility counseling did not improve treatment success.

Conclusion: As far as our study concerns findings suggest that still firm evidence does not exist to support that consultation could improve fertility outcomes. It seems there is need for multi-center studies with bigger sample size or even a collaborative study including samples from different countries to provide solid evidence for policy and practice.

Keywords: Fertility, Infertility, Consultation

The Impact of Serious Games on Nutritional Knowledge of Children: A comprehensive review (Review)

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Introduction: The term "Serious Game" refers to a type of game which its main purpose is more than entertainment. As choosing healthier foods and reducing the consumption of processed foods lead to a healthier life, having accurate information about nutrition can improve the nutritional knowledge and practice of target populations, such as children. In this term, serious games can be defined as promising and innovative games using modern information technologies to increase nutritional knowledge among individuals. Therefore, the present study is designed to review the impact of serious games on children's nutritional knowledge.

Methods: The present study was a brief review study designed in 2022. The search was conducted through electronic databases including PubMed, Scopus, and google scholar with the keywords “Serious Games”, and “Nutrition”. Inclusion criteria included articles that examined the impact of serious mobile games on developing nutrition knowledge and healthy eating habits after 2013.

Results: According to the study inclusion and exclusion criteria, 364 articles were included and finally, 8 studies were reviewed to achieve the goals of the present study. As an overview, the studies indicated that digital nutrition information was commonly sent to the population through social media and television, and non-digital information was mainly sent through schools and parents. Beyond the role of any technologies in nutritional education, studies showed the impact of serious games on more informed food choices and increased fruit and vegetable consumption in the target group. In general, serious games by influencing children's nutritional knowledge can play a significant role in promoting healthy eating behavior among them. And be used as an effective tool for learning nutrition knowledge and forming healthy eating habits.

Conclusion: According to the importance of healthy nutrition for children, having accurate nutritional knowledge and practice is a necessary issue. In this field, serious games seem a useful tool; however, further investigations are required to determine this educational method's features, benefits, barriers, limitations, and disadvantages.

Keywords: Serious Game, Knowledge, Nutrition Education, Children

The Importance of Exosomes in The Occurrence of Breast Cancer (Review)

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Introduction: Exosomes of almost all cell types secrete into the extracellular spaces. They include active genetic material in the form of messenger RNA (mRNA), micro RNA (miRNA), DNA, and active peptides that are representative of the original cell in their lumen, which may be isolated from various physiological fluids. The aim of this study was to investigate the importance of exosomes in the occurrence of Breast cancer.

Methods: The current study, which looked through academic databases like Google Scholar, Science Direct, Springer, and PubMed, investigated the importance of exosomes in the occurrence of Breast cancer.

Results: According to the findings, there are three types of transport that occur across the cell membrane: vesicular, passive, and active (exosomes). Exosomes are tiny vesicles that various cell types discharge. According to accumulating evidence, exosomes are significant in cancer. By transporting proteins and nucleic acids between cancer cells and the stroma, exosomes aid in communication. It has been demonstrated that exosome quantities and composition change in response to the emergence of cancers. The role exosomes play in the development of breast cancer, the most dangerous type of cancer in women, has drawn more attention over the past ten years. Breast cancer may cause salivary glands to emit certain exosomes, and these exosomes may act as biomarkers for the early diagnosis of breast cancer. Exosomes carry proteins and nucleic acids that help breast cancer metastasize, develop tumors, and become resistant to treatment. Drug resistance is more likely to develop as a result of exosomes' potential to disseminate anti-cancer drugs outside of breast cancer cells. However, exosomes are effective anti-cancer drug delivery systems with lower immunogenicity and toxicity. This strategy for developing a drug delivery system appears promising. Breast cancer is the most prevalent cancer that can be lethal and the primary cause of cancer-related fatalities in women. Due to late diagnosis, the majority of breast cancer patients have poor prognoses. Serum, tissue, and gene markers are currently used in diagnosis; nevertheless, they are inefficient for identifying breast cancer at an early stage. New research indicates that a number of factors, including proteins and microRNA (miRNA), contribute to the onset or progression of breast cancer. The two main causes of death in the clinic are regionally recurring malignancies and distant metastatic disease. De novo and acquired

resistance to anticancer medicines continue to be key challenges in the treatment of breast cancer. Signaling pathways, growth factors, and miRNA all have a role in distant metastasis of breast cancer. Active, passive, and vesicular methods of transportation exist between cells and the outside world. Extensive research has been done on vesicular transport, particularly exosome-mediated transport, which is essential for cellular transport. Proteins, nucleic acids, and other materials are sent to the microenvironment via cell-secreted exosomes in order to connect with it. Exosomes play a variety of roles as diverse promoters in the carcinogenesis, metastasis, and drug resistance of breast cancer. Deregulation of exosome-mediated transport results in the development of illness.

Conclusion: Nanosized vesicles called exosomes facilitate intracellular and intercellular communication. Exosomes are increasingly being shown to be crucial to the development of pathogenic conditions, according to available data. Exosomes may serve as biomarkers for different tumors, such as breast cancer. Compared to healthy breast cells, breast cancer cells release different amounts and types of exosomes. Exosome dysregulation in bodily fluids suggests that diseases might not be sensitive or specific. Drugs aimed at breast cancer cells could be transported through exosomes.

Keywords: exosomes, Breast cancer, inter-cellular, intra-cellular

The Importance of SOMAscan in Investigating Serum Biomarkers (Review)

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Introduction: The power to assess people with different abnormalities and, more specifically, those most noteworthy hazard adverse health outcomes remains a vital neglected requirement in most ailments. So that a perfect solution should involve a test, such as a blood sample test, that can specifically be conducted in a primary care setting. In this manner, a population of interest, as they are most likely to advantage from effective mediations. The proteomic analysis allows the simultaneous assessment of numerous proteins within a biological sample. The SOMAscan proteomics approach was utilized to recognize biomarkers that differentiate disease stages, in a population of patients with multiple abnormalities.

Methods: We selected the characteristic SOMAscan keyword from Mesh in NCBI. Then we search SOMAscan in Scopus and PubMed databases to publish a specific subject about SOMAscan. Assay. In the following, the gained and related articles are summarized and discussed.

Results: The SOMAscan method was used to quantify the expression of more thousand proteins biomarkers in each serum sample. SOMAscan information underwent quality control and transformation based on bioinformatics standards. SOMAscan involves a specific protein measurement system using Slow Off-Rate Modified Aptamer (SOMAmer) molecules that bind to proteins with high affinity and specificity.

Conclusion: SOMAscan has been used to identify diagnostic signatures of Serum Proteins Associated With multiple diseases, Biomarker Clustering Analysis, Hormonal Pathways Dysregulation in Patients, and Machine Learning.

Keywords: SOMAscan, Serum, Biomarker

The inhibition of Panc1 cancer cells invasion by hAMSCs secretome through suppression of tyrosine phosphorylation of SGK223 (at Y411 site), c-Src (at Y416, Y530 sites), AKT activity, and JAK1/Stat3 signaling (Research Paper)

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Introduction: SGK223 is a scaffolding protein involving in the oncogenic tyrosine kinase signaling. SGK223 was phosphorylated at Y411 by c-Src and in response to the Epidermal growth factor receptor (EGFR). Tyrosine phosphorylated SGK223 at Y411 enables to interact with CSK resulting up regulation of c-Src activity and promotion of the cell migration. Human amniotic mesenchymal stromal cells (hAMSCs) are a population of multipotent cells that it was considered to be as a potential platform in cancer therapy.

Methods: Herein, we employed a co-culture system to clarify the effects of hAMSCs secretome through tyrosine phosphorylation of c-Src, SGK223, AKT activity, and JAK1/Stat3 signaling in Panc1 pancreatic cancer cells. By using the 0.4 µm pore sized transwell membranes, both cell lines were firstly co-cultured for 72 h. Next, c-Src activity (tyrosine phosphorylation levels at Y530 and Y416), tyrosine phosphorylation level of SGK223 (at Y411), AKT activity, and JAK1/Stat3 signaling in Panc1 cells after treatment with hAMSCs were evaluated.

Results: Our results showed that hAMSCs have the inhibitory effects on Panc1 pancreatic cancer cells invasion.

Conclusion: It suggests that the suppression of c-Src activity, SGK223 expression, AKT activity, and JAK1/Stat3 signaling may be as critical targets in pancreatic cancer therapy.

Keywords: Stem cells, pancreatic cancer cells, AKT, SGK223, JAK1/Stat3 signaling

The inhibition of tumor migration through down regulation of Fibronectin in MDA-MB-231 breast cancer cells by hAMSCs secretome (Research Paper)

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Introduction: More than 200 cases of cancer have been diagnosed and breast cancer is the most common invasive cancer and the second leading cause of cancer mortality in women. There are several treatments for breast cancer. The failure of many therapeutic options is referred to drugs resistance and side effects of drugs and therefore, identify new tools and specific platforms with the lowest side effects and high effectiveness remains a main challenge among interested researchers. Stem cells are a multipotent population of cells with unique biological characteristics and thereby, it was demonstrated to be a potent tool for cancer therapy. Focal adhesions play key roles in cell motility and migration. Of note, overexpression of focal adhesions in many human cancer types was reported. The aim of this study was the evaluation of the therapeutic effects of human amniotic mesenchymal stromal cells (hAMSCs) on MDA-MB-231 breast cancer cells migration through down regulation of Fibronectin.

Methods: we employed a co-culture system using 6 well plates transwell and after 72h, hAMSCs-treated MDA-MB-231 breast cancer cells were analyzed by using western blot method. Also, the cell shape and motility of cells were analyzed.

Results: Our results showed that the hAMSCS secretome has therapeutic effects on cancer cells migration through down regulation of Fibronectin.

Conclusion: Our present study revealed that Fibronectin may be considered as a potential target by hAMSCs secretome in breast cancer therapy. However, the molecular mechanisms are not clear and thereby, more experiments will be required.

Keywords: MDA-MB-231 breast cancer cells, hAMSCs, Fibronectin expression, Cell migration

The MALAT1/has-mir-149-5p/FAT1 CeRNA network: a diagnostic biomarker for head and neck squamous cell carcinoma (Review)

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Introduction: Head and neck squamous cell carcinoma (HNSC) originating from the mucosal epithelium of the mouth, throat, and larynx is the sixth most common cancer worldwide and has mortality rates approaching 50%. Cancer biomarkers are biological molecules that have a clinical utility in the screening, diagnosis, and treatment of cancer. Competing endogenous RNAs (CeRNAs) such as long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs) play an important role in cancer initiation, progression, metastasis, and recurrence. Using CeRNA networks as a biomarker to early diagnose cancer presents new opportunities for decreasing cancer complications. This study aims to identify ceRNAs as diagnostic biomarkers for head and neck squamous cell carcinoma.

Methods: The 20 genes with the highest mutation frequency in HNSC were downloaded from the cosmic database and the FAT1 gene was selected as a possible biomarker for HNSC using the GEPIA2 database (Log2FC>+1, p-value <0.05). Using the Venny 2.1 tool, we got the intersection between the down-regulated miRNAs in HNSC from the dbDEMC 3.0 database (LogFC<-1, adjusted p-value<0.05), and the NRG1 targeting miRNAs from the starBase v3.0 database, as well as the intersection between the miRNAs corresponding lncRNAs from the starBase v3.0 database and the up-regulated HNSC lncRNAs from the Lnc2cancer database. Then, we used the Cytoscape software version 3.9.1 to visualize the lncRNA-miRNA-mRNA network and determine the hub lncRNAs and miRNAs that have key roles in regulating the FAT1 gene.

Results: We determined that hsa-miR-23b-3p, hsa-miR-149-5p, MALAT1, and H19 lncRNAs and FAT1 mRNA have the highest scores in the maximal clique centrality (MCC) ranking method.

Conclusion: The MALAT1/has-mir-149-5p/FAT1 CeRNA network can be used as the novel diagnostic biomarker for the early detection of head and neck squamous cell carcinoma.

Keywords: MALAT1, FAT1, Biomarker, Head and neck squamous cell carcinoma

The microbiota as a promising target for lung cancer treatment (Systematic review) (Review)

Mahya Najjari,[1,*]

1.

Introduction: Lung cancer is one of the most serious types of cancer with high rates of incidence and mortality. The gut microbiota has clinical implications on regulating the efficacy of natural anticancer agents. The aim of this study is to investigate the gut microbiota-mediated therapy as a helpful treatment for lung cancer.

Methods: This review article was performed within articles published at PubMed, Science Direct, Google Scholar, SID, and Cochrane until September 2022. The keywords were lung cancer, microbiota, and treatment. By searching this database; 53 articles were found, 19 of them by Reading titles and abstracts were removed. 34 articles were selected under the inclusion criteria. All articles were chosen from English and Persian articles.

Results: Finally, 34 articles were included in the study. Microbiota-derived antigens participated in pulmonary immune homeostasis. Ruminococcus gnavus stimulated secretion of IL-25, IL-33, and thymic stromal lymphopoietin (TSLP) by colon tissues, those cytokines activated DCs and ILC2 to produce cytokines IL-4, IL-5, and IL-13 that traveled through the bloodstream to the lungs and could lead to infiltration of the lung parenchyma by eosinophils and mast cells. Butyrate-producing gut bacteria dampened lung group 2 innate lymphoid cell (ILC2) function, thus weakening the development of airway hyperreactivity. A reduction of intestinal microbial diversity and metabolic-related biological activities manifested in the intestinal flora of patients with lung cancer compared with healthy subjects. The enrichment of Bifidobacterium longum, Alistipes putredinis and Prevotella copri could lead to better immune checkpoint inhibitors efficacy. Parabacteroides and Methanobrevibacter predicted better lung cancer control. Bifidobacterium enhanced dendritic cell (DC) function and intensified accumulation of CD8(+) T cells in the tumor beds; thus, they exhibited antitumor capacity to the same degree as PD-L1 inhibitor, that combination treatment eliminated tumor outgrowth. Lactobacillus plantarum CIRM653 reduced the counts of lung innate immune cells, such as macrophages and neutrophils, TNF-α and IL-6, as well as triggering an immunosuppressive Treg cell response in the lungs that alleviated the lung inflammatory response in mouse models infected with Klebsiella pneumoniae . Clostridium butyricum, Lactobacillus rhamnosus GG, Bifidobacterium longum, Saccharomyces cerevisiae UFMG A-905 and Akkermansia muciniphila played a major role in lung health.

Conclusion: The microbiota components and metabolites affect host immune homeostasis locally and systematically. Manipulating the intestinal flora is a potential option for enhancing the efficacy of lung cancer treatment. However, need to be more research done on this topic.

Keywords: Lung cancer, microbiota, treatment

The ovarian stimulation effects on Muc1 expression of the mouse endometrium before implantation (Research Paper)

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Introduction: The implantation process involves complex and synchronized molecular and cellular events between the uterus and the implanting embryo. Implantation occurs only during a certain time in pregnancy referred to as the window of implantation. The opening of this window and process of implantation are known to be controlled by ovarian steroid hormones. The receptive status of the Endometrium in embryonic implantation is a balance between the activation of adhesion molecules and the presence of a barrier that the embryo may encounter on the endometrial epithelium. The nonreceptive uterus maintains a thick glycocalyx on the apical surface of luminal epithelial cells. Within this carbohydrate mixture is a transmembrane mucin, mucin-1 (Muc1). Muc1 is an extremely large (>200 kDa), heavily glycosylated molecule that is proposed to extend much farther from the luminal surface than other components of the apical glycocalyx. Sex steroids can be involved in the regulation of Muc1 transcription either by directly interacting with the Muc1 promoter or indirectly by stimulating or repressing of the transcription factors.The purpose of this study was to investigate the alterations on Muc1 expression of the mouse endometrium after hyperstimulation using HMG and HCG injections. Therefore, a careful evaluation of the regulation of Muc1 at the endometrial surface is necessary.

Methods: The paraffin-embedded tissues were sectioned to a thickness of 5 µm. Sections were then deparaffinized in xylene, dehydrated in a series of ethanol solutions and stained using standard immunohistochemistry procedures. Tissue sections were pretreated by boiling in 10 mmol/L citrate buffer (pH 6.0) for 15 min as recommended by the supplier. For immunohistochemical detection of Muc1, CT1 polyclonal antibody (sigma, USA) at dilution of 1:200 was used, then incubated with alkalin phosphatas conjugated secondary antibody (abcam, ab5746) (1:100 dilution in TBS) for 1 hour. The antibodies were visualized by incubating with NBT/BCIP cromogen (Roche) for 10 min. Staining intensity of tissue sections was evaluated and graded. The sections were then counterstained with hematoxylin rinsed in tap water and mounted. The positive controls were used by breast cancer samples.

Results: In this study, Immunoreactivity was scored according to the tensity of staining and statistic analysis didn’t perform. Immunoreactivity was graded as – (negative), ± (trace positive), + (positive), ++ (moderately positive) or +++ (strongly positive).The samples were scored by two independent observers,

and slides with discordant interpretations were examined by both observers together until a consensus was reached. As expected, staining was restricted to the apical aspects of luminal and glandular epithelial cells. Our data showed that the levels of Muc1 associated with the uterine epithelia are reduced by the time of implantation of the blastocyst. Ovarian hyperstimulation didn't alter the Muc1 expression markedly in surface and glandular epithelium, which could affect on its receptivity.

Conclusion: In the present study we demonstrated, in the control and hyperstimulation groups the Muc1 expression is markedly reduced in the luminal uterus epithelium at the time of implantation. Our results are consistent with the existing viewpoint that endometrial expression of Muc1 positively correlates with endometrial receptivity and embryonic implantation. This loss of Muc1 protein is potentially due to the action of steroid hormones. In addition, our results showed that ovarian hyperstimulation didn't alter the Muc1 expression markedly in surface and glandular epithelium, which could affect on its receptivity.

Keywords: Endometrium, Muc1 expression, Ovarian stimulation

The potential role of tea in preventing and reducing cancer (Review)

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Introduction: In recent years, the number of cancer patients has increased, and it has even become the first cause of death in developed countries. Many studies have been conducted to investigate the effect of various types of tea on various types of cancer, including colon, lung, stomach, esophagus, breast and prostate cancer in humans and animals, in which the protective effect of teas, especially green tea, has been suggested. Tea is made from the Camellia sinensis plant and is the second most popular non-alcoholic beverage in the world. This drink contains more than 450 types of organic compounds, more than 15 types of minerals and essential nutrients. Among these compounds, there are catechins such as epigallocatechin gallate (EGCG) and taflavin (TF) and a variety of natural polyphenols that are responsible for anti-inflammatory and anti-cancer effects, and their action is through reducing of Wnt/β -catenin and Hh/Gli1 signaling pathways to delay cancer progression. In general, tea is considered as a prophylactic agent that destroys cancer cells and promotes cancer cell apoptosis by improving antioxidant activity, thereby increasing cancer resistance. Therefore, in this review, an attempt has been made to investigate the potential role of tea in preventing and increasing cancer.

Methods: In this review study, the required data were collected using keywords such as biosensors, self-powered biosensors and self-powered and citing valid databases such as Google Scholar, PubMed and Scopus. After evaluating the quality of the data, the most relevant articles from 2019 to 2022 were investigated.

Results: The evidence obtained from cell, animal, clinical and epidemiological studies showed that tea consumption has benefits such as prevention of

cancers, chronic inflammation, heart and liver diseases, diabetes, neurological diseases such as Alzheimer's and bone fractures. In the study conducted by Beynon,Rhona A.,et al which recommended drinking green tea, there was evidence of a reduction in the ratio of polyunsaturated fatty acids to total fatty acids. Green tea consumption is inversely related to the risk of breast cancer, and drinking at least five cups of green tea per week is associated with a reduced risk of breast cancer. Similar research has shown that there is no connection between drinking tea and bladder cancer. In an animal study, it was shown that tea consumption prevents squamous cell skin cancer caused by inorganic arsenic, and the combination of this substance with green tea destroys liver cancer cells by preventing cell proliferation, cell migration and induction apoptosis of cancer . Therefore, tea increases PL3K/AKT signaling and even green tea plays a role in reducing Bcl-2/Bax ratio to regulate apoptosis of infected cells. The results showed that TF, TR present in tea and their compounds do not change the G1 and S phases of the cell cycle, but they can cause significant cell arrest in the G2/M phase. Therefore, the results showed that TF, TR have a significant effect on cell viability in a concentration-dependent manner .

Conclusion: According to the studies, the consumption of various types of tea by people has been associated with pathological changes in cancer cells in different stages of their growth, proliferation and metastasis. However, comprehensive research is needed to better understand the effects of each type of tea on people's health.

Keywords: Tea, Cancer, Anti-cancer effect, Health

The prevalence of gastrointestinal disorders and their association with lifestyle habits in medical students of Mashhad University of Medical science (Research Paper)

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Introduction: Medical student well-being is affected by multiple stressors. Also, there is growing literature in the area of highly prevalent functional gastrointestinal disorders (FGIDs) among medical students around the world. Up to the moment, there are no reports on the combined association of lifestyle factors and gastrointestinal symptoms with quality-of-life issues. We have therefore investigated the links between aspects of the quality of life, lifestyle-related factors, and gastrointestinal symptoms in medical students.

Methods: A self-administered questionnaire survey was carried out among the students recruited from the Faculty of Medicine at Mashhad University of medical sciences, in February 2021. The gastrointestinal disorders among students were assessed through the Gastrointestinal Symptom Rating Scale (GSRS) questionnaire including symptoms of five categories: reflux, abdominal pain, indigestion, diarrhea, and constipation. And employing the Short Form 36 Health Survey (SF-36), both mental functioning subjective health status were measured. We studied the influence of demographic characteristics, physical activity, and quality of life scales on the prevalence of FGIDs among these students. Comparisons were performed according to gender, BMI, and level of physical activity.

Results: Of all the eligible students, 498 (52.2% men) aged 20.7±1.9 years old on average, had completed the surveys and were enrolled in the study. The mean BMI of the subjects was 22.6±3.6 kg/m2. And the majority of the students (39.0%) were categorized in the group with a low level of physical activity. The mean scores for quality of life were significantly poorer in girl

students compared to boys, 75.7±11.1 and 72.5±12.9, respectively (P < 0.01). A between-group comparison also revealed significant lower scores in Physical functioning (PF), Role physical (RP), and Role emotional (RE) in female students. The mean GSRS scores for participants were notably different between groups(P=0.03), as higher scores in hunger pain and constipation reported by female students (P < 0.01 and P =0.02, respectively). Hunger pain was reported the most in both, however, male students yielded higher GSRS indigestion scores second to hunger pain, whereas, in female students, constipation was in second place in scores. Functional gastrointestinal disorders were significantly associated with quality of life, and several domain scores of mental and physical functioning, in both boy and girl groups. Having gastrointestinal symptoms was significantly associated with lower mental and physical functioning, except for mental functioning in male students with experience of diarrhea and physical functioning in females with diarrhea (all P < 0.01). Moreover, boy students with indigestion symptoms and girls with hunger pain had lower scores in all domains of the SF-36 (r= -0.334, P < 0.01 and r= -0.329, P < 0.01, respectively).

Conclusion: Notable impairments in mental and physical functioning health status were observed among medical students. Health-related quality of life was impaired especially in girl students and those with GI upsets such as indigestion and hunger pain. The results from this research can be dedicated to raising awareness and helping medical schools to institute efforts in ensuring the students' nutritional, lifestyle habitual, and emotional support, particularly during critical phases of medical training.

Keywords: functional gastrointestinal disorders, quality of life, mental and physical health, medical student

THE RELATIONSHIP BETWWEN BDNF GENE THERAPY AND GLAUCOMA BLINDNESS (Review)

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Introduction: Brain-derived neurotrophic factor (BDNF) is a predominant neurotrophic factor in the brain that plays an important role in the mechanisms of differentiation, regeneration, and plasticity. BDNF inhibits ischemia-induced neuronal death, oxidative stress, glutamate toxicity, and proteins such as amyloid B. Glaucoma is the second most common cause of blindness, affecting 70 to 80 million people worldwide. The death of retinal ganglion cells (RGC) is the main cause of blindness associated with this disease. A new opportunity for glaucoma treatment is the use of technologies related to stem cells and gene therapy. Previous studies have shown that intravitreal delivery of brain-derived neurotrophic factor (BDNF), by injection of recombinant protein or by gene therapy can reduce retinal ganglion cell (RGC) loss after optic nerve injury. BDNF gene therapy. It can improve RGC survival in experimental models of glaucoma, which is the leading cause of irreversible blindness worldwide. Increased concentrations of neurotrophic factors in ganglion cells to prevent cell death were seen in glaucoma.

Methods: In this article, the relationship between BDNF gene therapy and glaucoma has been investigated. The articles from 2015 to 2022 have been reviewed from PubMed and science direct databases.

Results: Glaucoma is the leading cause of irreversible blindness worldwide and is characterized by progressive and permanent damage to the optic nerve, leading to the loss of retinal ganglion cells (RGC). BDNF levels in the serum of patients with POAG and tears of normotensive glaucoma patients are significantly lower than those of controls, suggesting that BDNF may be a biomarker for glaucoma. BDNF gene expression in the retina promotes robust RGC survival in various experimental glaucoma models, including optic nerve transaction and elevated IOP. Overexpression of the BDNF receptor TrkB in RGCs can stimulate RGC survival after optic nerve transfection. These findings suggest that BDNF-TrkB signaling is another good therapeutic target for glaucoma.

Conclusion: Several studies have shown that intravitreal delivery of BDNF by recombinant protein injection or through gene therapy methods can reduce RGC loss after optic nerve injury. BDNF is produced from a precursor protein called pre-pro-BDNF, which is cleaved into proBDNF. After that, pro-BDNF is cleaved to mature BDNF. TrkB begins to dimerize upon binding to mature BDNF. This cascade activates the signaling in the target cell with at least three different transmission pathways to maintain the survival, growth, and synaptic and plasticity of neurons. TrkB activation is a potential therapy for glaucoma relief. Considering the role of BDNF in three signaling pathways that lead to neural growth, survival, and plasticity, it seems that BDNF is the most important substance in maintaining neural health in the brain. Scientists have accumulated a large amount of information about the biology of BDNF-TrkB and the role of BDNF in synaptic plasticity and synaptic growth. In addition, BDNF is known to be a neuroprotective agent that can repair synaptic defects.

Keywords: GENE THERAPY,BDNF,RGC,SIGNALING PATHWAY

The restorative effects of platelet rich plasma and stem cells-derived exosomes on the genes involved in spermatogenesis of non-obstructive azoospermia Rat models (Research Paper)

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Introduction: A significant portion of male infertility is caused by azoospermia, which comes in two types: obstructive (OA) and non-obstructive (NOA). Adoption or the use of donated sperm are the two choices available to NOA patients who do not respond to medical therapy and are unable to conceive on their own. These patients still have a chance to become pregnant despite significant abnormalities in spermatogenesis. The only ways to conceive biological offspring in NOA patients are through testicular biopsy and assisted reproductive techniques since the impairment to spermatogenesis in these people is irreversible. In patients with NOA, these techniques have a limited rate of success, though. Furthermore, these relatively expensive and unavailable for azoospermic spermatogenesis failure technologies may use genetically impaired sperm in fertilization through natural barrier crossing techniques. However, despite the promising survival rates for children with cancer who may have undergone specific radiotherapy and chemotherapy, when they reach reproductive age, their fertility is impaired. As a result, the current target is to improve either their ability to produce sperm in their ejaculate or the probability that sperm can be successfully retrieved from the testis for ICSI. In this way, scientists are currently working to create azoospermia treatments based on stem cell transplantation. Extracellular vesicles (EVs), such as exosomes derived from mesenchymal stem cells (MSCs), have been found to have biological properties similar to those of stem cells while also providing important advantages over the cells from which they were made in the field of regenerative medicine. Unlike transplanted cells that cannot be recovered, EVs can get around most of the safety concerns related to direct cell transplantation. Additionally, unlike treatments involving transplanted cells, EVs are temporary and can be terminated quickly if negative effects appear. One of the most significant

blood derivatives is platelet-rich plasma (PRP). More than 20 growth factors and other protein molecules, such as binding molecules and chemokines, are present in this bioactive substance, and they are involved in activities including cell proliferation, differentiation, and regeneration. These biological components and elements have given PRP therapeutic promise.

Methods: In this study which was conducted on 30 male Wistar rats 8-12 weeks old, we compared the effects of human PRP and exosomes released by adipose tissue-derived MSCs (AD-MSCs) on the restoration of in vivo spermatogenesis (Intra testis injection in NOA rat models). In the cell culture laboratory, AD-MSCs were isolated and cultured up to passage 3. After that, the exosomes were separated from their conditioned media. Peripheral blood from volunteer donors was obtained, and PRP was isolated in accordance with the manufacturer's instructions. In order to induce NOA in rats, they were injected with two doses of busulfan (10 mg/kg body weight intraperitoneally) at a 21-day interval. The rats received the following treatment at the time points of three days and two weeks: intratesticular injection of 100 microliters of exosome (500 mg/mL), 100 microliters of PRP, and 100 microliters of PBS in the AD-Exo, PRP, and sham groups, respectively. The rats were euthanized for future investigations two months after their last treatment.

Results: Based on the results of analyzing the expression of genes in various experimental groups, it was found that, with the exception of the SCP3 gene, which is involved in the late differentiation of spermatogonial cells, the expression of the other studied genes was significantly lower in the NOA and SHAM groups than in the control group ($p \leq 0.05$), indicating that NOA had been successfully induced, while significantly increased expression was reported in the treatment groups with AD-Exo and PRP ($p \leq 0.05$). Therefore, it appears that these therapies were successful in restoring the expression of spermatogenic genes including DAZL, DDX4, Miwi, and meiotic genes like stra8 and cyclin A1.

Conclusion: The ameliorating effects of PRP and exosomes secreted from AD-MSCs on the genes involved in spermatogenesis were confirmed in this study. It is obvious that additional research in histological, anatomical, plasma seminal antioxidant enzymes, the protein level of the genes studied in this study, etc. are required to determine the therapeutic impact of these treatments on patients with NOA.

Keywords: Non-Obstructive Azoospermia (NOA).Platelet Rich Plasma (PRP).Exosomes. Mesenchymal Stem Cells (MSCs)

The role of CIN in cancer with cGAS/STING pathway (Review)

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Introduction: Chromosomal instability (CIN) is a hallmark of human cancer and is associated with poor prognosis, metastasis, and treatment resistance.CIN in cancer cells has been reported to activate the cGAS-STING innate immune pathway through micronuclei formation. Thus, it affects tumor immunity and tumor progression. In addition to their well-characterized cellular mechanisms of action, their effect on chromosome segregation implicates the contribution of the cGAS-STING pathway leading to antitumor immunity. For this purpose, Zierhut et al. have shown that STING is an essential determinant of mitotic cell death in breast cancer cell lines treated with Taxol in vitro.cGAS can recognize dsDNA inside ruptured micronuclei that have fragile envelopes. This recognition leads to activation of downstream signaling, suggesting that CIN activates the cGAS/STING pathway mainly through micronuclei formation.

Methods: In this review article, we studied and analyzed the articles published from 2018 to 2022 using PubMed and Science Direct search engines and the desired keywords.

Results: Theoretically, the cGAS/STING pathway may affect chromosomal stability through actions during interphase that induces CIN during mitosis or direct effects on mitotic progression. These results indicate that STING activation regulates cGAS chromosomal stability. Furthermore, identifying a means to prevent tumor cell adaptation to cytosolic DNA will be critical to our ability to target a lethal characteristic of cancer for a therapeutic benefit.

Conclusion: Our findings provide the first evidence for the role of the cGAS/STING pathway in maintaining chromosomal homeostasis as a cell undergoes division. Our results suggest the first mechanism by which the cGAS–STING pathway directly regulates CIN without the involvement of the immune system and demonstrate that all components of the cGAS/STING/TBK1/IRF3 signaling pathway function together to maintain chromosomal stability. Given the widespread nature of CIN in human cancer, CIN-based therapies have the potential to profoundly impact clinical outcomes, including minimizing the onset of treatment resistance, treating

advanced and metastatic disease, and enhancing systemic antitumor immunity.

Keywords: CIN,cGAS/STING,cancer

The role of circular RNAs in thyroid cancer (Review)

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Introduction: Introduction: The incidence rate of thyroid carcinoma (TC) has increased significantly during the last decade and has become the fourth tumor in women. Thyroid cancer (TC) is the most common widespread endocrine malignancy, especially in women. A large number of circRNAs in cancer tissues have been identified and investigated. Circular RNAs (circRNAs) are covalently linked single-stranded RNA molecules that have unique properties and very powerful biological functions. A large number of studies have reported circular RNAs (circRNAs) as potential novel diagnostic and prognostic biomarkers for thyroid cancer. Thousands of circRNAs have been identified as oncogenes or tumor suppressors that mediate tumorigenesis, metastasis, and chemotherapy resistance in several cancers (such as TC, colorectal cancer, and kidney cancer). Most of the circRNAs that promote the proliferation of thyroid cells fulfill their role by acting as miRNA sponges.

Methods: Search method: In the upcoming systematic review, the required data were collected using keywords and also by using reliable databases such as PubMed, Scopus, ProQuest and Google Scholar. In this study, the statistical population includes all studies that have been conducted until 2022. After reviewing the relevant findings and also evaluating the quality of the data, 16 articles were analyzed.

Results: Findings: CircRNAs have a great diagnostic and therapeutic value in cancer and also play a role in the initiation of thyroid carcinoma. Many circRNA-miRNA-mRNA axes have been reported to be associated with the development of malignant diseases. Currently, the activities of circRNAs are mainly recognized as sponging specific and unique miRNAs that act as tumor suppressors or promoters. PI3K-AKT-mTOR signal transduction is increased in patients with primary cancer. Several studies have reported that circRNA activates the PI3K-AKT channel and promotes TC progression. evaluated the

association between circRNA expression and clinical features in PTC, and some dysregulated circRNAs were associated with BRAFV600E mutation, capsular invasion, advanced T stage, and lymph node metastasis. The expression patterns of circRNAs are related to the progression and prognosis of TC, so they have great value as biomarkers in the management of TC patients. Exosomes have been reported to participate in intercellular communication by transporting their cargoes, including miRNAs, lncRNAs, proteins, and even circRNAs, to recipient cells, thereby regulating tumor progression. Exosome modification clarifies a new path for the diagnosis and treatment of TC and thus brings the great potential of exosomal circRNA as an important biomarker and therapeutic tool for TC.

Conclusion: Conclusion: In summary, circRNAs constitute an emerging class of ncRNAs that play an important role in gene expression regulation by controlling miRNA and protein functions. The results indicated that those dysregulated circRNAs may act as miRNA sponges and lead to PTC progression, but the specific underlying mechanism needs further investigation. Our review pointed out and summarized the growing statistics and development of studies on TC-related circRNAs, and similarly highlighted male or female circRNAs that could play an oncogenic, anticancer or chemosensitivity role within tumorigenesis, metastasis and TC treatment resistance. This review highlights the expression of circRNAs in TC and increases the potential of circRNA as a regulatory molecule, diagnostic, prognostic and therapeutic tool in TC research. Taken together, circRNAs with their distinct properties are more stable in cells and can even induce drug resistance, thus suggesting that they may be used to diagnose and treat malignancies. Research on circRNA and thyroid cancer is still ongoing. Indeed, the ability of circRNA to function by binding to DNA or proteins as well as modifying methylation is also very promising.

Keywords: Keywords: Thyroid Neoplasms, RNA, Circular, Neoplasm Metastasis

The role of cyclin and cyclin-dependent kinases in the occurrence of cancer (Review)

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Introduction: Several human cancer cell types exhibit unchecked proliferative behavior, which is related to the dysregulation of Cdk/Cyclins. Mutations that hyperactivate Cdk activity, in contrast to those that inactivate checkpoint regulators, tumor suppressor genes, or CKIs, specifically enhance cell proliferation. Chemicals involved in the G1/S phase transition of the cell cycle are frequently altered in cancers. The majority of the time, it has been found that the Cdk4/6-cyclinD/INK4/pRb/E2F pathway is disrupted by mutations in the genes encoding these proteins or in its regulators. In medulloblastomas, squamous cell carcinomas, lymphomas, leukemias, and squamous cell carcinomas, Cdk6 gene amplification and overexpression have been shown. In some leukemias, Cdk6 overexpression can result in Cdk6 translocation, and in medulloblastoma, it may connect the TP53 and RB1 tumor suppressor pathways. Uncontrolled cell growth is caused by an imbalance between mitogenic stimuli and the control of the cell cycle, which is linked to the hyperphosphorylation of Rb brought on by the deregulation of Cdk4 and Cdk6/D-cyclins. The Cdk4/cyclin D/p16INK4a/pRb axis exhibits genetic changes in the majority of malignancies, according to research. Several malignancies, including melanoma, breast carcinoma, refractory rhabdomyosarcoma, osteosarcoma, glioma, and neuroblastoma, have been linked to dysregulations of Cdk4 as a result of gene amplification or overexpression. The goal of this study was to investigate the role of cyclin and cyclin-dependent kinases in the occurrence of cancer.

Methods: This study was on the role of cyclin and cyclin-dependent kinases in the occurrence of cancer from scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: Cdks have important functions in the control of cell cycle and gene expression. Members of a distinct group of Cdks that regulate transcription depending on RNA polymerase II include Cdk7, Cdk8, and Cdk9 (RNA Pol II). Cdk8 and cyclin C are components of the Mediator complex, a transcriptional repressor. The Mediator complex suppresses the development of the pre-initiation complex by phosphorylating cyclin H to inhibit transcription factor II H (TFIIH) activity and RNA Pol II's carboxyl-terminal domain (CTD) to prevent it from binding to promoter DNA. The Cdk7/cyclin H holoenzyme, on the other hand, is a transcriptional activator. As part of TFIIH, Cdk7/cyclin H is brought to the proximal promoter during transcription initiation and phosphorylates

RNA Pol II's CTD at the serine position to facilitate the capping enzyme's subsequent binding. In order to cause a change from transcription initiation to elongation, Cdk7/cyclin H, acting as a CAK, phosphorylates and activates Cdk9, the catalytic subunit of the positive transcription elongation factor b (P-TEFb). NELF and DSIF are phosphorylated by the active Cdk9/cyclin T to release the elongation complex from its paused state, and the CTD of RNA Pol II is phosphorylated at serine 2 sites to encourage progressive elongation of the transcript. In essence, Cdk-mediated phosphorylation of the CTD of RNA Pol II is what propels the sequential transition from pre-initiation to initiation to elongation. Cyclin D overexpression, genetic amplification, polymorphism, translocation, and alternative splicing are frequently linked to Cdk4 hyperactivity. One of the most prevalent tumor suppressor mutations in human malignancies, p16INK4a genetic inactivation leads to poor Cdk4 inhibition. Proteins involved in DNA replication, cell cycle progression, histone synthesis, and centrosome duplication are phosphorylated by Cdk2/cyclin E.

Conclusion: The combination of Cdk inhibitors and well-known cytotoxic drugs entered human trials based on the preclinical data that Cdk inhibitors can generally augment the anti-tumor actions of these agents in a dose- and sequence-dependent way. Prospective studies can aid in determining the best parameters for combination therapy, as well as determining whether highly selective versus pan-selective CDK inhibitors represent more effective treatments.

Keywords: cyclin-dependent kinases, cancer, Cdk inhibitors

The role of endoplasmic reticulum stress in diabetes and its complications (Review)

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Introduction: Diabetes is a complex metabolic disease characterized by increased levels of blood glucose as a result of insulin resistance or impaired insulin secretion from pancreatic β-cells. Recent studies have suggested that endoplasmic reticulum homeostasis is involved in diabetes. Glucose-regulated protein 78 (GRP78) is an ER stress protein that is overexpressed under ER stress conditions. In this review study, the role of endoplasmic reticulum stress, especially GRP78, is investigated in diabetes.

Methods: In this review article, the studies conducted using the keywords of diabetes, ER stress, GRP78 in the databases PubMed, Science direct, Scopus, Google Scholar.

Results: The level of GRP78 increases in the tissue and serum of diabetic patients. Increased CRP78 causes apoptosis of pancreatic beta cells and inhibition of the insulin receptor. Also, the increase of csGRP78 (cell surface) causes the production of proteins (like collagen and fibronectin) in the extracellular matrix (ECM), which leads to the accumulation of ECM in the glomerulus and causes nephropathy. On the other hand, the increase of GRP78 in the retinal cell inhibits ATF4, which plays an important role in inhibiting oxidative stress.

Conclusion: GRP78 contribute to the pathogenesis of diabetes and its complications. Therefore can be considered as a therapeutic target for the treatment of this disease.

Keywords: Diabetes, Endoplasmic Reticulum Stress, GRP78

The role of iPSCs-based models and PSEN1 gene in understanding and developing a treatment for Alzheimer's disease (Review)

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Introduction: Alzheimer's disease (AD) is a neurodegenerative disease responsible for 60–70% of the 50 million cases of dementia worldwide. It is caused by synaptic failure and excessive accumulation of misfolded proteins. This disease is associated with complications such as neurodegeneration, shrinking of brain tissue, and progressive cognitive, motor, and behavioral disorders which often are fatal. Some failures and ambiguous results of anti-tau and anti-inflammatory treatments and significant progression in the field of cell therapy have inclined the scientific community to new methods such as stem cell therapy. In recent years, with the improvement and maturity of induced pluripotent stem cell technology and direct cell reprogramming technology, the differentiation of human somatic cells followed by their transformation into nerve cells has become possible in vitro and in vivo. Induced pluripotent stem cells (iPSCs) are utilized in two procedures for discovering new therapeutic approaches for neurodegenerative diseases, including Alzheimer's. iPSC-derived cells can be implanted directly to regenerate neuronal subtypes or be used to fabricate constructs for drug testing and AD modeling. In this review, we will discuss the importance of Alzheimer's disease-induced pluripotent stem cell models in analyzing PSEN1 gene mutations' implications over the early stages of Alzheimer's disease pathogenesis throughout neuronal differentiation impairment.

Methods: In the context of these modelings, researchers generated human iPSCs from fibroblasts from a patient with AD harboring a specific mutation in the PSEN1 gene and reprogrammed the cells using viral vectors. iPSCs exhibited the ability to differentiate into neuronal lineage in a 3D environment. These iPSC-derived neurons harbored Aβ oligomers confirmed by Western Blot (WB) and immunostaining

Results: Taking into account that the disturbance in the regulation of neural miRNA may play a role in the pathophysiology of Alzheimer's disease (AD), researchers utilized the neurons derived from iPSCs mutated in the PSEN1 gene. Although miR-124 function may be dependent on the neuronal AD model, data indicate that keeping the miR-124 level strictly controlled is crucial for proper neuronal function. Furthermore, the iNEU-PSEN cellular model stands out as a useful tool for AD mechanistic studies and perhaps for the development of personalized therapeutic strategies. In another recent

study, the potential of the iPSC-based familial AD cell model was evaluated as a platform for drug testing. NPS 2143, a negative allosteric modulator of the calcium-sensing receptor, was used as a potential drug for AD treatment. Maria Lo Giudice et al, in their studies, assessed the potential of their iPSCs-based familial AD cellular model as a platform for drug testing. They found that iPSCs-derived neurons respond to treatment with γ-secretase inhibitor, modifying the physiological amyloid-β protein precursor (AβPP) processing and amyloid-β (Aβ) secretion. Moreover, they demonstrated the expression of calcium sensing receptor (CaSR) protein in human neurons derived from healthy and familial AD subjects. Recently, researchers have looked for the effect of some mutations such as L286V and R278I on PSEN1 gene function, and in this regard, the control and mutation of PSEN1 and the spontaneous differentiation of human neural stem cells into neuron and astrocyte co-cultures were investigated. paper data provides evidence that the PSEN1 mutations L286V and R2781 significantly alter protein expression associated with AβPP processing and cellular redox status, and that study highlights the potential for iPSC-derived neuron and astrocyte co-cultures to be used as an early human model of FAD. Another research indicates that presenilin-1 plays an essential role in neural progenitor maintenance, neurogenesis, neurite outgrowth, synaptic function, neuronal function, myelination, and plasticity. Therefore, an imbalance caused by mutations in presenilin-1/γ-secretase might cause aberrant signaling, synaptic dysfunction, memory impairment, and increased Aβ42/Aβ40 ratio, contributing to neurodegeneration during the initial stages of AD pathogenesis.

Conclusion: iPSCs-based models from AD have and will play a significant role in analyzing mutations, studying the Alzheimer's disease progression process, and screening molecules. iPSCs-based models are very efficient in the study of PSEN1 gene mutations and the physiological processing of protein Aβ, and due to the mentioned links between these two with AD, they could be promising in advancing therapeutic strategies.

Keywords: Alzheimer's disease, Induced Pluripotent Stem Cell, presenilin-1, Amyloid-β

The role of mesenchymal stem cells along with Electric pulse in modulating the human immune system (Especially in corona disease) (Review)

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Introduction: Recent developments and advances in the field of regenerative medicine have led to more uses of stem cells. Human mesenchymal stem cells, which were first obtained from bone marrow, have been used in human clinical trials due to their ease of use. But according to what mechanism do these types of stem cells work? Are they involved in immunity only through secretory factors or not? Do mesenchymal stem cells play an important role in immunity, especially against corona disease? This idea was completely new at the time of its birth (Nowruz 1400), but taking into account the great attention paid by researchers and medical staff to this disease at the global level and the related advances and achievements, sooner or later its novelty (based on the use of MSCS) will lose. Although the nature of this idea is to pay attention to MSCS properties and use them, the presented solutions are different and new. MSCs are derived from various sources such as bone marrow, adipose tissue, skeletal muscle, Wharton's jelly, umbilical cord, and placenta. The suppressive/modulating function of MSCs is carried out by their inhibitory effect on the cells of the innate and acquired immune system. This function is caused by the communication of these cells with immune cells in the form of direct cell-to-cell contact or through paracrine secretory factors. The set of paracrine secretions of these cells includes various components such as growth factors, cytokines, chemokines, mediators. It is anti-inflammatory and exosomes, so that these secretions affect the surrounding cells and cause changes in them. Many studies in animal models consider the ability of mesenchymal stem cells to rebuild and repair tissues, often instead of their proliferative properties, to be caused by their suppressive/modulating function by the same secretory factors. Cytokines play an important role in health and disease. These molecules help the body in inflammatory and infectious reactions, repairing tissue damage and fighting some cancers. Cytokines are a group of small proteins that cause communication between two cells that are made by the immune system and act as a chemical messenger. Cytokines are proteins, peptides or glycoproteins that are secreted by lymphocytes or monocytes and regulate immune responses, hematopoiesis and maturation of lymphocytes. B and T lymphocytes are very important in regulating immune responses. Based on the results of various studies, the effect of MSCs in acquired immune responses is mostly exerted through T lymphocytes, but nevertheless, MSCs can stimulate B lymphocytes through cell-to-cell contact and by releasing soluble factors. to influence The

response of T lymphocytes to MSCs can be expressed in three cases, which include inhibiting the proliferation of T cells stimulated by many stimuli, regulating the production and secretion of cytokines (pro-inflammatory and anti-inflammatory) from these cells, and affecting the differentiation of different subtypes of T cells. In particular, the induction of regulatory T lymphocytes (Treg) type 1 (TR1) and expressing Foxp3 (Foxp3+ Treg). On the other hand, in an inflammatory environment, the response of innate immune cells to MSCs will also lead to an acquired immune response. Therefore, through the modulation of innate immune cells, these cells have indirect regulatory effects on T lymphocytes and especially on B lymphocytes (Hosseini et al., 2019). There is evidence that mesenchymal stem cells, by reducing the expression of MHC-II, CD11 and CD83, stop the activity of macrophages and reduce the secretion of pro-inflammatory cytokines such as TNFα and IL12. Stopping T lymphocytes in the G0/G1 phase of the cell cycle and also reducing the secretion of pro-inflammatory cytokines TNFα, IL6 and IL17 are other effects of MSCS on the human immune system (Weiss and Dahlke, 2019; Golchin et al., 2020). Many studies have been conducted in relation to inhibiting the proliferation of T lymphocytes, because inhibiting the proliferation of these cells is the most important function of MSCs in the laboratory environment. For example, MSCs can inhibit the proliferation of T lymphocytes stimulated by polyclonal mitogens and alloantigens, as well as the activation of T lymphocytes by CD3 and CD28 antibodies. In addition, it has been reported that exposure of Treg cells to MSCs in co-culture significantly increases their immunosuppressive ability. These results indicated that programmed cell death receptor interactions may be responsible for the increased suppressive ability of Treg cells exposed to MSCs. However, it is noteworthy that the depletion of Treg cells from the culture medium has no effect on the suppression of T lymphocyte proliferation by MSCs, because It seems that MSCs prevent the physical contact of T lymphocytes with antigen presenting cells (APCs) in an unknown way. Although a specific molecular mechanism has not been identified in this field, there are hypotheses in this regard. T cells provide For example, it has been suggested that Treg cells strengthen the interaction of T lymphocytes with low affinity to APCs by reducing the probability of T lymphocytes separating from APCs, and thus regardless of whether the cells are tolerant or responsive. Treg stabilizes the immune status (Hosseini et al., 2019). On the other hand, MSCs are involved in regulating the production and secretion of cytokines from T lymphocytes. Many reports in this regard show that MSCs reduce cytokine secretionpro-inflammatory and increased production of anti-inflammatory cytokines IL-10 and IL-4 from activated T lymphocytes play a role. Also, MSCs can produce suppressive molecules such as IDO, PGE2, TGF-β, nitric oxide (NO), heme oxygenase 1 (HO1), leukemia inhibitory factor (LIF), apoptosis, liver growth factor. (HGF) and galectins have a direct effect on T cells. Mesenchymal stem cells can be very important in the treatment of diseases such as multiple sclerosis, colorectal cancer and corona. Multiple sclerosis is an autoimmune disease of

the central nervous system in which progressive destruction of the myelin sheath is observed. In their interaction with the innate immune system, MSCs exert their regulatory effect on the immune system. This type of stem cell secretes anti-apoptotic molecules and neuron growth in order to protect neurons in nerve damage. According to various studies, MSCs apparently play a role in repairing damaged tissues in this disease. B and T lymphocytes play a role in the development of autoimmune diseases, and as mentioned earlier, MSCs have a regulatory effect on these lymphocytes and with their functional mechanisms (secretion of cytokines and direct cell-cell contact) can play an important role in the treatment of MS. Based on the studies, the fourth most common cancer leading to death is colorectal cancer (CRC), and in the targeted treatment of this type of cancer, research is focused on MSCs. MSCs are cells with high division ability that are not completely differentiated, and one of the characteristics of these types of cells is their tendency to form tumors. However, these cells are used as carriers to deliver drugs to the primary site of the tumor, and there are studies that show the potential of MSCs to destroy the tumor by inhibiting tumor cell proliferation and inducing apoptosis. are, of course, taking into account the important point that when MSCs are in contact with pathogenic agents, their secretions, proliferation and differentiation are affected. According to studies, MSCs derived from adipose tissue stimulate and increase tumor growth and cancer metastasis. Also, MSCS can be oncolytic virus carriers. This type of virus has two types of anti-tumor activity, which includes anti-cancer activity and stimulation of the body's immune system. Stimulation of the immune system is done by initiating an acquired anti-tumor response against cancer epitopes (part of cancer antigens). Today, the corona disease has become a global problem that has taken the lives of many people and has had various mutations. As you know, this virus has a great impact on a person's lungs and lungs, and by multiplying in this organ and other parts of the body, it affects the respiratory system and, in some cases, blood circulation, and as a result, they suffer disrupts Due to the speed of mutations of this virus, it is not possible to market a suitable and definite vaccine with the desired expected performance. Because these mutations, over time, can reduce the efficiency and effectiveness of the vaccine, and if during the mutation, a large part of the antigenic form of the virus changes, against the mutated type, the vaccines will be significantly less effective. And they will lose their effect. Therefore, we must look for another solution besides the vaccine. Mesenchymal stem cells can be used to help solve this crisis! Based on the characteristics and effects of these cells on the immune system, they can be used to fight the virus from the moment it enters the body. Regarding the functions of MSCS, Dr. Hossein Baharond, Royan Research Institute and Kerman University of Medical Sciences mentioned the therapeutic properties of these cells and the type derived from the umbilical cord. These centers have announced that MSCS play an important role in improving the complications of Corona and dealing with this disease by improving and repairing the degenerated tissue, and by emitting electric

pulses in the environment, it should be checked whether MSCS is present in the mentioned diseases. They increase the speed of treatment or not?

Methods: In order to investigate the effect of viruses and mesenchymal stem cells on other changes, in each sample (lung tissue cells, T, B lymphocytes and natural killer cells (phagocytes), the test is summarized in six samples. In this way, I found out what effect each one alone would have on lung cells and the mechanism of MSCS effect on zinc. In the experiment in question, the basis was Shiraz, in cooperation with the University of Medical Sciences, in the safety level 3 laboratory and to achieve the results. More precisely, it should be done with three repetitions. But due to the lack of full facilities to work with such a dangerous virus, and high costs, the experiment was not carried out. In this way, the plan to defend the plan was written and presented to the university, and instead, a project on the validity of the collaboration and acceptability of the idea and research carried out by Borji Mohammad Rasulullah of Medical Sciences of Shiraz University was approved. Further, if MSCS has such a feature and mechanism, it should heal naturally without humans, but due to the relatively slow and late action speed, such an event cannot decide whether to increase phagocytes and MSCS. undertook In addition to the above, electrical pulses play a role in cell migration and proliferation. The effect of these pulses can be seen on the cells at a voltage between 0.5 and 2 volts and for half an hour to two hours. Also, based on the research conducted (Cen Chen, Xue Bai,...), movement can be used as a tool to regulate the behavior of cells and tissue engineering, which is important in calling MSCS to the treatment site. gave performs Although they investigated the effect of electrical pulses on the normal function of viruses, cells, tissues and surrounding organs, but in general, this design can be useful in treatment.

Results: Mesenchymal stem cells have diverse and extensive potentials, which with the advancement of science and the increase of people's knowledge and awareness of it, more features are discovered and more uses are made of it in the field of treatment. According to the research, the anti-inflammatory property of MSCS interferes with the activity of the corona virus. As you know, the immune response and inflammation are regulated by inflammatory cytokines (TNF), increasing the secretion of these substances, with positive feedback, can increase inflammation and worsen the patient's condition. Cells infected with the virus secrete a protein called type 1 interferon in response to the entry of the virus they do. In the secretion of this type of interferon, a protein called mitochondrial antiviral messenger protein (MAVS) is involved. Mesenchymal stem cells affect lymphocytes in two ways, cells that are the most important in specific defense and play an important role in fighting viruses and other pathogens. Secretion of paracrine agents and cell-to-cell contact are also among these methods. The paracrine secretory complex includes exosomes, chemokines and the most important of them, cytokines. The most important feature of MSCS is not having a receptor for

corona virus and AIDS. This feature means that the corona virus is able to enter this type of cell and destroy it. During the research and the results obtained, showing the positive effect of MSCS in repairing the tissues damaged by the virus is. Also, these cells control the secretion of pro-inflammatory and anti-inflammatory cytokines and thus control the inflammation caused by the activities of the virus. The presence of a sufficient amount of MSCS can be effective in the process of dealing with the virus, and considering that the mentioned research, due to the lack of possibilities and costs, has changed from an experimental mode to a research and questionnaire in Shiraz University of Medical Sciences. A definite result of MSCS's direct confrontation with the coronavirus cannot be provided. However, with the presence of more and more mesenchymal stem cells in the area infected with the virus, not only the inflammation is controlled and can save the patient from death, but with its secretions, it can indirectly fight the corona virus. also pay For example, one can pay attention to the statistics of deaths caused by Corona; This statistic is higher in adults than in teenagers, and the lower the age, the lower the statistics will be seen. Here, we can mention the continuous and more active presence of MSCS in teenagers and younger ages as one of the factors of reducing mortality. As you know, with increasing age, the successive division of cells will decrease and as a result, the number of mesenchymal stem cells will decrease and old samples will remain. As a result, it can be mentioned that along with other relevant factors, with the decrease in the number of MSCS, the repair and anti-inflammatory activity and the mentioned mechanism have decreased and as a result the death rate has increased.

Conclusion: Acquired or adaptive immune cells that increase stem cells in body blood fluids to accelerate the healing process of tissue damage and infectious diseases are influenced by MSCs. Many innate immune cells, including macrophages, neutrophils, mast cells, suppressor cells derived from myeloid stem cells, and natural killer cells exist in inflammatory sites and can be regulated by MSCs. For example, MSCs, by producing immunosuppressive molecules and metabolites such as prostaglandin E2 (PGE2), a protein called TNF-stimulated gene (TSG6), lactate, kynurenic acid and spermidine, can change the characteristic of macrophages from pro-inflammatory phenotype. change to an anti-inflammatory phenotype, which is a very important mechanism in the processes of corona disease. The functional mechanism of mesenchymal stem cells (MSCs) is carried out by communicating with T, B, and natural killer cells with the help of paracrine secretory factors and direct cell-to-cell contact, and plays a role in the activity of lymphocytes. T lymphocytes are one of the most important agents of the body's immune system, which MSCs affect in three ways, including inhibiting the proliferation of T lymphocytes, releasing pro-inflammatory and anti-inflammatory cytokines, and inducing regulatory and expressing T lymphocytes. is. Also, in autoimmune diseases such as MS, MSCs play an

essential role due to their regulatory effect on T lymphocytes and their secretions, and researchers hope to be able to use these MSCs in the treatment of MS. Mesenchymal stem cells are a very important factor in colorectal cancer (CRC). The function of MSCs has significant effects in both healing and aggravating the cancer. These cells can stimulate and grow cancer tumors (in the type derived from adipose tissue) and against this feature, they can carry drugs and prevent tumor proliferation. Also, mesenchymal stem cells are very important in corona disease. These cells, in addition to treating corona indirectly (with the help of proposed functional mechanisms), play an important role in improving the complications caused by the disease. Also, according to the studies and scientific model, it can be concluded that mesenchymal stem cells will have more continuous activity in the presence of electric pulses and electric pulses play an effective role in calling these cells to a specific tissue of the body. This can have wide-ranging effects and treat various diseases in the field of medicine, including the mentioned diseases and today's global problem, Corona. Finally, with the help of this project, we can have the vision to control diseases and some of today's medical challenges.

Keywords: Mesenchymal stem cells (MSCs), immune balance, immune cells, lymphocyte, Covid19

The role of mir-320 in the Bladder cancer cell line (Review)

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Introduction: Bladder cancer (BC) is one of the most common cancer in both women and men in all over the world. MicroRNAs are involved in multiple processes such as cell differentiation, transcription, inflammation, proliferation, cell signaling, and apoptosis. In molecular biology mir-320 microRNA is a short RNA molecule. Therefore, this study was performed to investigate the biological functions and molecular mechanisms of miR-320 in human bladder cancer cell line.

Methods: The bladder cancer cell line was retained in the RPMI 1640 medium, supplemented with 10% FBS and cultured under standard conditions of 95% moisture and 5% CO2 at 37°C. Transfection of miR-320 mimic and negative control (NC) was established using Electroporation technique. The tetrazolium-based MTT assay has long been regarded as the gold standard of cytotoxicity assays as it is highly sensitive and has been miniaturized for use as a high-throughput screening assay. MTT assay was performed to investigate the cytotoxic effect of miR-320 mimic EJ138 cell line. Cytotoxic and cell viability performed using MTT method, the optimum of which was determined to be 40.

Results: These findings indicate that transfected miR-320 mimic could suppress EJ138 cell line proliferation and Infected EJ138 cell line containing miR-320 mimic administration with MTT assay showed that the proliferation rates of cell line decreased.

Conclusion: These results support the tumor-suppressive effect of miR-320 in the EJ138 Bladder cancer cell line by reducing proliferation, Therefore, miR-320 may be a novel molecular therapeutic target for the treatment of BC.

Keywords: microRNA-320, Bladder cancer, cytotoxicity, electroporation and MTT assay.

The role of PIK3CA gene mutations in breast cancer (Research Paper)

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Introduction: Today, breast cancer is one of the most common cancers among women and at the same time one of the most important diseases in the world. Extensive research is being done to prevent and treat this cancer, which causes many deaths among women every year. Epidermal growth factor 2 (HER2) receptor, a member of the epidermal growth factor (EGF) family , which is highly expressed in a large proportion of breast cancers. Trastuzumab or Herceptin is a monoclonal antibody that acts as an anti-HER2 agent for targeted therapies , Patients treated with HER-2 overexpression are treated, Therefore, for some HER2 + breast cancer patients, trastuzumab is not beneficial and breast cancer in these patients spreads or spreads over time. . The PI3K pathway is a family of lipid kinases that phosphorylates the 3OH group of phosphatidylinositol, PI3K has alpha (α), beta (β) and gamma (γ) subunits. The alpha subunit (PI3KCA) plays a much more important role in the transmission of cancer messages, and various studies have been performed on it. Activation of PI3K activates a message cascade that promotes the growth, survival, and metabolism of cancer cells. The PIK3CA gene encodes the alpha catalytic subunit of the PI3K enzyme. PIK3CA mutations indicate resistance to trastuzumab therapy by activation of the PI3K / AKT pathway. The aim of this study was to evaluate the frequency of mutations in common points of PIK3CA gene, including exons 9 and 20, in HER2 + breast cancer patients resistant to trastuzumab , compared with patients who responded to treatment.

Methods: In this case-control study, a number of control and paraffin-embedded breast tissue samples from HER2 + ductal carcinoma patients who were treated with Transtuzumab for one year. After examining the variables to be studied by the oncologist, samples were collected from the Breast Cancer Research Institute and the tumor bank of Imam Khomeini Hospital in Tehran and examined. The age range of patients was between 27 and 67 years and their mean age was 47 years . These patients were evaluated for age and type, size, grade and stage of the tumor and the number of lymph nodes involved, and Stage 4 patients were not included in the study. Also information about the presence of tumor markers such as HER2, ER, PR . Patients' medication regimens were also evaluated. DNA extraction was performed from the samples and PCR test was optimized using breast cancer tissue samples expressed in exon 9 and exon 20 of PI3KCA gene and positive and negative control along with the size of the marker. Primers were optimized and used. Finally, Sanger method was used to sequence exons 9

and 20 of PIK3CA gene in this study, which was performed by Macrogen Company of South Korea.

Results: Mutations identified in this study include mutations; Exon 9: 67039G>T and exon 20: 86860C>G. The frequency of 67039G>T mutation in the control group was 7.7% but this mutation was not observed in the case group (odds ratio: 0.12, P = 0.1) and the 86860C>G mutation had a frequency of 17.4% in the case group and 20.7% in the control group (odds ratio: 0.8, P = 0.7

Conclusion: Trastuzumab is in fact an effective and essential anti-cancer drug in the treatment of people with breast cancer. A significant number of patients after initial treatment with a diet containing trastuzumab, their disease progresses progressively and requires the addition (continuation) of the treatment process. The results of this study showed a mutation in PIK3CA gene in HER2-positive breast cancer patients treated with trastuzumab, but the study of the presence of these mutations in two groups resistant and sensitive to trastuzumab and calculating the amount of these mutations in both groups, a significant relationship between this Mutations with resistance to trastuzumab treatment were not observed. The mutations found in this study included 67039G>T on exon 9 and 86860CG on exon 20, of which 67039G>T was not observed in the group of sensitive patients with a frequency of 7.7% and in the group of resistant patients.

Keywords: Transtomazob , HER2, PI3K, Breast cancer,PCR

The role of plant metabolites in treating Systemic Lupus Erythematosus (Review)

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Introduction: Systemic lupus erythematosus (SLE) is a typical systemic autoimmune disease, which causes multiorgan disorder. SLE has variable presentation, course and prognosis including skin disease, neuropsychiatric disease (NPSLE), haematological disease, renal disease, and cardiovascular disease. The primary pathological findings in patients consist of inflammation, vasculitis, immune complex deposition, and vasculopathy. The exact aetiology of SLE is unknown. The disease shows a strong familial aggregation, with a much higher frequency among first degree relatives of patients. Moreover, in extended families, SLE may coexist with other organ specific autoimmune diseases. Genetic factors also play an important role in predisposition of the disease. However, most cases are sporadic without identifiable genetic predisposing factors, suggesting that multiple environmental or yet unknown factors may also be responsible. Most of the clinical manifestations are associated with certain pathophysiological cascades, particularly involving the hyperactivation of the immune response and abnormality in the immune regulation system. Hence, both autoantibodies and inflammatory cytokines are responsible for aggravating the pathology of SLE. There is no absolute treatment for this ailment. However, Current therapeutic strategies of this disease are limited to the use of steroids and cytotoxic drugs.

Methods: 1. Pathogenesis and pathology of SLE The loss of immune tolerance, increased antigenic load, excess T cell help, defective B cell suppression, and the shifting of T helper 1 (Th1) to Th2 immune responses leads to B cell hyperactivity and the production of pathogenic autoantibodies. Also, certain environmental factors besides various genetic factors are probably required to trigger the disease. Multiple genes confer susceptibility to disease development. Interaction of sex, hormonal milieu, the HPA axis, and defective immune regulation, such as clearance of apoptotic cells and immune complexes, modify this susceptibility. The loss of immune tolerance, increased antigenic load, excess T cell help, defective B cell suppression, and shifting of Th1 to Th2 immune responses lead to cytokine imbalance, B cell hyperactivity, and the production of pathogenic autoantibodies. Most of the clinical manifestations of the disease are associated with certain pathophysiological cascades, particularly involving the hyperactivation of the immune response and abnormality in the immune regulation system. Proinflammatory cytokines, namely IL6, IL10, IL12, IL17, IL21 and IL23, are

produced in excess as mediated by rho associated protein kinase (ROCK); transcription factors, namely STAT3 and CREMα; nuclear factor NFκB and NFAT, thereby leading to the co-stimulation of B and T cells, ultimately causing the excessive production of autoantibodies. Finally, certain environmental factors are probably needed to precipitate the onset of the disease; such as dietary factors, infectious agents, hormones and environmental oestrogens and chemical/physical factors. 2. Natural plant metabolites as remedial candidates for SLE: Some plant species with: Immunomodulation benefits which suppress the inflammation, inhibit the proliferation and pro-inflammatory cytokines, and down regulate Th1/Th2 cytokines expression are including Argyrolobium roseum, Camellia sinensis, and Tripterygium wilfordii. Besides, there are some other plant species with immunomodulation and signaling regulation benefits which inhibit T cell activation and reduce the level of pro-inflammatory cytokines Allium sativum, Bupleurum falcatum, Clerodendron trichotomum, and Coriandrum sativum are categorized in this group. Berberis aristata and Curcuma longa with signaling regulation benefits, down regulate the expression of STAT3 and ROCK. Moreover, Acacia farnesiana, Andrographis paniculata, Angelica glauca, Arundo donax, Malus domestica, Ocimum gratissimum, Paeonia lactiflora, Picrorhiza scrophulariiflora, Salvia miltiorrhiza,and Uncaria tomentosa have anti-inflammatory benefits and decrease the nitrite level.

Results: The suggested herbal drugs, are devoid of any potential toxicity or adverse drug reactions and are completely harmless and helpful for patients suffering from SLE. There are also evidences published for analyzing toxicological effects of them which represent the safety usage of these herbal medicines.

Conclusion: Systemic lupus erythematosus (SLE), commonly referred to simply as lupus, is a chronic autoimmune disease that can cause swelling (inflammation) and pain throughout your body. The chemotherapeutic drugs used in treating SLE symptoms may have negative effects on some body organs. For this reason, utilizing medicinal plants are rising due to controlling symptoms of the disease in patients. These plants may be represented as immunomodulators such as Camellia sinensis, anti-inflammatory effects such as Acacia farnesiana, and signaling regulator such as Berberis aristata. They may also have effects on helping the patients lower their anxiety because of various side effects of the disease.

Keywords: Systemic Lupus Erythematosus, Autoimmunity, Plant metabolites, Herbal medicines

The role of rs10842262 polymorphism of SOX 5 gene in idiopathic non-obstructive azoospermia . (Research Paper)

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Introduction: Globally, infertility is estimated to be approximately 9-16% .Males are found to be solely responsible for 20-30% of infertility cases and contribute to 50% of cases overall. Many causes and risk factors play a role in increasing the incidence of male infertility, which can be classified as congenital, acquired and idiopathic.The largest group of infertile men are those diagnosed as suffering from ‘idiopathic infertility’. These men constitute about a third of the patients attending infertility clinics . Idiopathic male infertility is a multifactorial heterogeneous disease in which genetic causes can be identified in all major categories of male infertility. In recent decades, we have been faced with a large decrease in sperm count and an increase in infertility in men all over the world. Without genetic diagnosis, doctors cannot give answers to couples about the causes of infertility, possible diseases, potential success of ART, etc. With the advances in genomics, the number of genes related to male infertility has increased in recent years, and one of the candidate genes that has been recently studied and received attention is SRY-box transcription factor 5(SOX5). Recent studies show that the SOX5 gene is related to male infertility and the high expression level of its short transcript (S-SOX5) in the testis shows that S-SOX5 plays an important role in regulating the expression of genes necessary for sperm function and can affect male fertility. Considering the key role of S-SOX5 in the formation and function of sperm motile cilia and the specialized role in spermatogenesis within the testis and the regulatory role on the expression of key genes, polymorphism in this gene can affect the function of this gene and this Disorders may be associated with infertility in men. Identifying the genetic changes in this gene can be helpful in diagnosing the cause of infertility. Considering that no study has been conducted on the relationship between polymorphisms of this gene and idiopathic non-obstructive azoospermia infertility in men in Iran, in this research we concluded to Check the presence of the functional polymorphism of rs10842262, SOX5 gene in idiopathic non-obstructive azoospermia patients and compare with the control group of fertile men. The desired polymorphism status of this gene was checked using the Modified ARMS-PCR method followed by Sanger sequencing in the available DNA samples and then subjected to statistical analysis. Objective: To

determine the relationship between SOX5 gene rs10842262 polymorphism and idiopathic non-obstructive azoospermia.

Methods: Methodology: In this project, in the first stage, the files of azoospermia patients whose samples are available in the Royan DNA Bank were examined and among them the Infertile men who that met our criteria were selected. Then the extracted DNA of infertile patients with idiopathic non-obstructive azoospermia as well as the extracted DNA of fertile men (control group) were obtained from the DNA bank. Then, in the next step, according to the reported SNP (rs10842262) and the relevant clinical significance in this gene (SOX5), the primer was designed for this SNP and this region was amplified by PCR in both control and patient groups. In order to check the presence or absence of variants and check the sample type (heterozygous, healthy homozygous or diseased homozygous), the modified ARMS-PCR technique was used, which is a simple method to detect any mutation that includes base changes or small deletions. ARMS test is based on the use of specific PCR primers and allows DNA replication only when the target allele is present in the sample. Modified ARMS-PCR test is usually widely and accurately used to determine SNP (single nucleotide polymorphism) genotype with the help of special primers. Primer design for mutant (with SNP) and normal (without SNP) alleles allows the results to be easily analyzed after electrophoresis. Finally, a number of samples from each group were sequenced by Sanger method for further confirmation.In order to analyze the data and compare the frequency of genotypes and the frequency of alleles in the two studied groups, Chi – squared(X2 (test and SPSS software were used, and in all cases the error coefficient for reporting statistical differences was considered less than 0.05.

Results: Result: The results of the statistical analysis showed that out of 102 healthy and fertile men, 29 people (28.4%) had the GG genotype, 12 people (11.8%) had the CC genotype, and 61 people (59.8%) had the CG genotype. Among the 94 infertile men with azoospermia Non-obstructive 29 people (30.9%) have GG genotype, 2 people (2.1%) have CC genotype and 63 people (67.0%) have CG genotype. The results of statistical analysis showed that in the population of healthy and fertile men, the frequency of G allele is equal to 119 (58.3%) and the frequency of C allele is equal to 85 (41.7%). In the population of infertile men with non-obstructive azoospermia, the frequency of G allele is 121 times (64.4%) and the frequency of C allele is 67 times (35.6%).

Conclusion: Conclusion: According to the pvalue, the difference in the allelic frequency between the control group and the patient is not statistically significant because the P value is equal to 0.221, which is more than 0.05, but the difference in the genotypic frequency between the groups is statistically significant. P=0.032

Keywords: Infertility-Idiopathic- Non obstructive azoospermia-Polymorphism-SOX5

The Role of Selenium in Male Reproductive Performance (Review)

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Introduction: Trace minerals nutrition have significant impact on reproductive health and performance. Development of male reproductive tissue requires an optimal level of selenium (Se) in testis, and a small deviation, either deficiency or excess, leads to abnormal development. Selenium is a constituent of selenoproteins including GPx1, GPx3, mGPx4, cGPx4, and GPx5 that protect against oxidative damage to spermatozoa throughout the process of sperm maturation. A factor of central importance in male fertility is oxidative damage to spermatozoa, and Se helps to protect from this damage and consequently plays an important role in maintaining male fertility. Thus, Se and selenoproteins ensure viability of spermatozoa as well as providing protection against reactive oxygen species. In this study the role of Se and various selenoproteins in male reproductive performance is reviewed.

Methods: MEDLINE, Cochrane and Google scholar have been searched between Jan 1, 2015, and Jan 1, 2022, with imposing English language restrictions, for observational and clinical trial studies evaluated the impact of selenium in men reproductive performance. “Selenium”, “male reproduction” and “selenoproteins” have been used as keywords in this study.

Results: Previous studies confirmed that spermatogenesis is a Se dependent process regardless of the source of Se. Elevated levels of lipid peroxidation, malondialdehyde, and reactive oxygen species have been observed in male mice consuming both Se deficient (0.2 ppm sodium selenite) and Se excessive (1.0 ppm sodium selenite) diets, which resulted in harmful effects to semen quality by decreasing the fraction of motile spermatozoa, spermatozoa concentration, and number of motile spermatozoa and by increasing tailless and headless spermatozoa. A diet deficient in selenium (0.2 ppm sodium selenite) has been shown to reduce glutathione peroxidase (GSH-Px or GPx) activity in human studies, while its excess (1.0 ppm sodium selenite) intake resulted in increased GPx activity, impairing male reproductive potential.

Conclusion: The mammalian system needs a continuous supply of certain trace element, one of which is Se. Results from this review showed that presence of adequate Se in the male reproductive tract is essential for normal spermatogenesis, and Se has a fundamental role in mammalian sperm maturation. However, further longitudinal studies and well-designed randomized control trials assessing confounders are needed.

Keywords: Selenium; Male reproduction; Selenoproteins

The role of stem cells in endodontics treatment (Research Paper)

zakiyeh khosravi,[1,*]

1.

Introduction: Stem cells are the body's natural reservoirs to replace damaged specialized and non-specialized cells. These cells have a very high potential and have the ability to transform and differentiate into most or we can say all the cells and tissues of the body. Stem cells with their differentiation can become cells. including muscles, red blood cells, brain cells, etc. Here, we want to examine a sample of mesenchymal stem cells, which are an important population of multipotent stem cells with high growth and recovery capabilities. These cells can differentiate into all the cell lines that are the basis of mesenchyme or connective tissue and cause the repair or regeneration of such tissues. Also, as mentioned, these cells retain the characteristics of stem cells and tissue regeneration capacity. These findings suggest that periodontal ligament stem cells may be used to create a biological root that can be used in a similar way to metal implants. According to the findings and tests, it was found that even the teeth have a reserve of stem cells that are found in both milk and permanent teeth. These cells have the ability to fully regenerate themselves. Due to their compatibility with the body's immune system, these cells can be used in many fields of medical science. Pulp cells of human deciduous teeth show high proliferation and differentiation ability, and by differentiating these cells into pseudo-odontoblast and osteoblast cells, it is possible to help rebuild the lost structure of the tooth. Different methods can be used to track cells. This growth, due to the recognition of the potential of stem cells, led to surprising results, such as the possibility of rejection of the transplant after the transplantation of these cells is less, and there is no need to use immunosuppressive drugs. Of course, in relation to the potential of mesenchymal cells of children and adults, it can be mentioned that according to the clinical features of the pulp of children's milk teeth, it was observed that these cells have a high proliferation and differentiation ability compared to the pulp cells of adults. Attention to the many results obtained can be found that the use of mesenchymal cells from children's milk teeth leads to greater efficiency, and these cells can be differentiated into a complete set of teeth after growth and passage in a laboratory environment, as well as determining the number of dental canals by using the expression of affected genes find.

Methods: Investigation in 18-25 year olds 14 samples from the pulp and 6 samples from the dental follicle of the third molar of adults between 18 and 25 years old were collected. The collected samples were extracted due to impaction or orthodontic treatment with expert diagnosis and with the prior consent of the patients. These teeth had no caries or previous restorations,

and the patients were all healthy and did not have any systemic disease.After being drawn into the tubes containing Gibco, RPMI 1640, containing 2x antibiotics (2 times the strength of penicillin and streptomycin, Gibco), the tooth samples were transferred to the molecular cell laboratory at a temperature of 4 degrees Celsius, and to reveal the pulp chamber of the teeth. , were cut from the enamel-cement connection by carbide disc and handpiece. And after that, the pulp was separated from the teeth, from the pulp chamber by means of a fine file; Then, for cell culture of the pulp tissue and follicle, these cells were divided into smaller pieces by surgical blade number 10, and then they were placed in Falcon containing 4 mg/ml collagen type (sigma I) solution, 104 mg/ml Dispase solution (Gibco) with a ratio of 1.1 was placed for 45 minutes at a temperature of 37 degrees Celsius After that, they were added to the culture medium and centrifuged at 600 g for 10 minutes. The resulting cell plates were cultured with mixed culture medium and after being transferred to the appropriate zvt in an incubator with a temperature of 37 degrees Celsius, 5 atmospheres and 2% CO2. This culture medium was changed every two days until 70% of the bottom of the plate was filled with cells. When the bottom of the plate reached 70%, the samples were passaged with the help of trypsin-EDTA. And finally, flow cytometry analysis was used to investigate the phenotypic profile of surface markers and the nature of stem cells from the pulp and follicular tissue of the third molar tooth. For this purpose, the cells were suspended in one milliliter of PBS (Phosphate Buffer Saline) in the third passage of trypsin. They were placed with a concentration of 1,000,000. Then the cells were divided into 6 tubes and 5µl of antibody was added to each PE tube and the tubes were then placed in a dark environment at 4°C for 30 minutes and after this period the cells were washed with 1ml of washing buffer. and centrifuged at 1200 MPR for 5 minutes, after which each cell sample was suspended in 300 µl to 500 µl washing buffer and analyzed by flow cytometry.

Results: Therefore, it can be said that tooth regrowth is a reality, not an ideal, and considering that the tooth is made up of two different types of tissue, logically, making a tooth requires communication and cooperation with epithelial cells and odontogenic mesenchyme. The recombination of epithelial tissue and dental mesenchyme to create teeth both in the laboratory and in the living environment leads to the fact that the combined cells can organize and form individual layers and are also able to differentiate into odontoblasts and amyloblasts. In order to make a complete tooth that has enamel and dentin, epithelial and mesenchymal cells are respectively introduced into the collagen gel solution and then implanted inside the oral cavity, and with this technique, the presence of all dental structures such as odontoblasts, amyloplast, pulp, Blood vessels, crown, root, periodontal ligament and alveolar bone can be seen, so the implantation of this dental mass (mesenchyme + epithelial cells) leads to the development of maturity and regrowth of teeth. So, it can be said that by using engineering and modern

methods, mesenchymal stem cells extracted from the pulp of mature teeth and milk teeth can be used to repair dental tissues, especially sub-tissues that have mesenchyme and connective tissue, and with this Humans at any age are able to re-grow their teeth using the mesenchymal stem cell gene, and it is worth noting that the use of the mesenchymal gene is not restricted from one person to another (no age limit) and one of the challenges which makes this different from other methods: the use of this method, if the mesenchyme gene used is healthy, unlike the implant, does not have any limitations or harm ‹And replacing this method instead of today's methods, dentists can use it more economically and optimally.

Conclusion: According to the mentioned cases, it can be said that there are mesenchymal stem cells of the dental pulp in the mature cells of the adult because after a dental injury, the dental pulp undergoes dentination in order to repair the damaged area by building and depositing the dentin matrix. This repair process takes place throughout a person's life, which indicates the presence of mesenchymal cells in the dental pulp of adults and the ability to create odontoblasts under the influence of appropriate signals ‹But in general, the potential of adult stem cells is not as much as that of fetal and childhood stem cells, for this reason, it is better to extract or use embryonic tooth root mesenchymal cells (from the gums, especially the posterior gums) for the reconstruction and repair of teeth. From the mesenchymal stem cells of milk teeth, these cells, as mentioned, are not limited to any category and age group, and even the ability to donate these cells from one person to another is possible, and the condition of donating teeth:The complete genomic and systematic health of the donor person, with this work, even in adults who often have lost their milk teeth (except for latent milk teeth), the gene of mesenchymal stem cells of children or fetuses can be used to repair and regenerate teeth do . In the laboratory method, mesenchymal stem cells in adults, although they have the possibility of repair or regeneration, but after they are separated from the patient, they must first go to the laboratory environment, and after their amplification and differentiation, they are injected into another person as an allograft or xenograft recipient, but with Paying attention to the many problems that may arise during the strengthening, injection, long time and potential and less adaptation of these cells, such as early tooth decay, tooth loss, immune system attack on these cells through immune response, etc. In this regard, it can be said that the use of a secondary method (experiment: laboratory cultivation of mesenchymal cells of milk teeth) is more effective and efficient in this field. And due to the problem-causing factors that exist in adult mesenchymal cells, this ideal protocol for humans is relatively far away from its application. Recently, with the discovery of a gene called DIK1, with the discovery of a gene called DIK1, it is possible to learn about the activation of stem cells and tissue regeneration in teeth repair and to undergo a shorter treatment period in tooth repair using stem cells. (restoration and reconstruction of teeth have gone through a relatively

long period) With the activation of stem cells, these cells can send messages to the main cells that help to activate the repair and reinforcement cells (this is also possible by using low power lasers) as a result of these cells forming dentin. the(hard tissue of the tooth) helps a lot.

Keywords: Mesenchymal stem cells_tooth pulp _tooth follicles

The role of stem cells in the occurrence of cancer (Review)

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Introduction: Introduction and aim: A group of proliferating cells with high power and great treatment resistance, known as CSCs, are the primary cause of cancer. The purpose of this review is to examine the part stem cells play in the development of cancer.

Methods: Search Method: The current study, which looked through academic databases like Google Scholar, Science Direct, Springer, and PubMed, examined the part that stem cells play in the development of cancer.

Results: Result: The CSCs might be made to adapt to various settings. According to research, the strong proliferative potential with a loss of a normal differentiation program and great efficiency in response to environmental changes determine the CSC self-renewal potential. The proliferative and quiescent states, which are distinguished by symmetric and asymmetric cell divisions, are the two primary phenotypes of CSCs. The primary cause of metastasis that would develop years after surgical removal of a primary tumor may be CSCs with a quiescent phenotype.

Conclusion: Conclusion: It can be deduced that chemotherapy would kill tumor cells without the CSC marker, causing the tumor to retreat, while the CSC-positive cells are resistant to the medication and their number would increase in the tumor. Quiescence, enhanced production of anti-apoptotic proteins, expression of ABC (ATP-binding cassette) drug pumps, and resistance to DNA damaging agents are all ways to protect CSCs from therapeutic agents and boost their resistance to the therapeutic process.

Keywords: Keywords: CSC markers, tumor, chemotherapy, metastasis

The role of the CRISPR technique in the treatment of Acute lymphoblastic leukemia (Review)

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Introduction: Introduction and aim: Acute lymphoblastic leukemia (ALL) is a cancerous condition that develops from hematological B- or T-cell progenitors and is characterized by significant genetic and clinical variability. Powerful animal genetic models that simulate cooperative oncogenic lesions affecting genes with a known involvement in the proliferation and establishment of the leukemic clone have been created thanks to the advent of novel tools for genetic editing like CRISPR-Cas9. The CRISPR-Cas9 technique is based on the Cas9 nuclease producing a guided cut in the double strand of DNA. This technology has the potential for multiplex genome editing. One 20-nucleotide RNA strand, which precisely pinpoints the breakage location, is responsible for this. After DNA cutting, the repair machinery of the host cell leads to repair errors and thereby promotes a modification of the original sequence by a mutation such as an insertion, deletion, or in-version, among others. the aim of this study was to the role of the CRISPR technique in the treatment of leukemia.

Methods: Search Method: The current study was carried out by searching scholarly databases such as Google Scholar, Science Direct, Springer, and PubMed for investigating CRISPR in leukemia.

Results: Results: Results revealed that genome editing techniques have advanced and are now used in therapeutic and clinical settings. Their use has made it easier to create novel treatments like chimeric antigen receptors (CARs) and has made it possible to investigate the genes implicated in the development of pathogenesis. The foundation of the genome editing system is the employment of designed nucleases that have non-specific DNA cleavage modules coupled to sequence-specific DNA-binding domains. These chimeric nucleases cause DNA double-strand breaks (DSBs), which activate cellular DNA processes such as homologous recombination and error-prone non-homologous end joining (NHEJ) (HR). CRISPR interference (CRISPRi) and CRISPR activation (CRISPRa) developed from the CRISPR-Cas9 system. CRISPRi uses a catalytically inactive version of Cas9 (dCas9) lacking endonucleolytic activity in combination with a sgRNA designed with a 20-bp complementary region to any gene of interest to silence a target gene. While CRISPRa uses fusions of dCas9 to activator domains to activate gene expression.

Conclusion: Conclusions: Future efforts to create mouse leukemia models that mirror human malignancies may benefit from the development of genomic editing techniques. In this regard, the disease's multigenic basis presents significant challenges. Murine models of ALL based on a single change have been unable to fully develop the disease, at least in part. We might approach the true clinical settings and create a more effective model for the study of this type of tumor by combining several of the gene changes discovered in patients in a mouse model. Creating an animal model with many genetic modifications used to be a time-consuming and expensive operation, but techniques like CRISPR-Cas9 now make it possible to introduce multiple mutations at once. Thus, it will be possible to produce more complicated animal models in a shorter amount of time, enabling us to more accurately mimic the conditions that exist in patients and providing the necessary framework for researching and creating novel therapeutic approaches. In addition, genome editing tools in the clinic will support the advancement of customized medicine by tying together genomes, disease phenotypes, and treatment objectives. By utilizing these technologies, we will be able to identify novel mechanisms of acquired resistance to pathway target treatments and expand our understanding of the mode of action of these innovative medications. The safety and effectiveness of medicines must be addressed before genome editing technologies can be applied in a clinical context. One of the biggest barriers to this technology is still the off-target effect. In the future, researchers will need to develop better genetic tools to get rid of any off-target effects and boost the effectiveness of gene editing. Despite this, genome editing presents fresh possibilities for treating conditions like ALL that were beyond the scope of earlier treatments.

Keywords: CRISPR technique, Acute lymphoblastic leukemia, cancer

The Role of Thylakoids in Weight Management: A Review (Review)

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Introduction: Overweight and obesity are major epidemic health problems that can bring about some other health issues such as cardiovascular disease, the first cause of mortality worldwide. Thylakoids are disc-like membranes responsible for photosynthetic light reactions in chloroplasts of green plants. In this article, we briefly described thylakoids and reviewed studies which have evaluated their impact on weight management and obesity-related factors. We also looked at the mechanisms of action of thylakoids.

Methods: Multiple databases including PubMed, ScienceDirect, Google Scholar, Scopus, and Web of Science were searched using the following search terms: “thylakoids” and “obesity” or “overweight”. In PubMed, the above search terms were entered as both medical subject headings (MeSH) and text words.

Results: Although a limited number of animal and human studies have investigated the impact of thylakoids on overweight- and obesity-related factors, all of them have resulted in positive outcomes. These outcomes are as follows: increment of satiety response; suppression of hunger sensations, particularly hedonic hunger; reduction of body weight and fat; promotion of glucose homeostasis; decrease in serum lipids; attenuation of oxidative stress and inflammation; and modulation of gut microbiota, notably by increasing beneficial bacteria such as Lactobacillus reuteri. It seems that some of these useful effects are related to retarded absorption of dietary fat and carbohydrate caused by thylakoids.

Conclusion: To sum up, supplementation with thylakoids may have beneficial effects on weight management. Nevertheless, more well-designed studies are needed before a firm conclusion can be drawn.

Keywords: Thylakoids, Overweight, Obesity

The role of vitamin D and serotonin in autism (Review)

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Introduction: Serotonin or 5-hydroxytryptamine is a neurotransmitter that is synthesized by a group of central nervous system neurons and intestinal enterochromaffin cells. Serotonin, which is a type of monoamine neurotransmitter, is activated by vitamin D and is derived from the amino acid tryptophan. It is one of the 22 main amino acids of living cells and one of the essential amino acids in the human diet, the indicator of which is the presence of aromatic rings in its structure.

Methods: During the last ten years, a lot of research has been done in this regard. The results of some of them indicate that We describe a mechanism by which the vitamin D hormone activates TPH2 and represses TPH1 expression, thereby inversely controlling serotonin production in the brain relative to tissues outside the blood-brain barrier. Future studies will directly test vitamin D-mediated regulation of these 2 tryptophan hydroxylase genes. Serotonin (5-hydroxytryptamine), a neurotransmitter and brain morphogen, has been proposed to play a central role in autism based on physiological evidence, genetic polymorphisms, and animal models. Disruption of the serotonergic system is one of the most consistent observations associated with autism. Serotonin in the brain promotes social behavior and the correct evaluation of social-emotional cues. The brains of people with autism show a significantly lower concentration of serotonin compared to the brains of non-autistic people. Low serotonin during early brain development in mice can lead to neuroanatomical defects such as fewer dendritic spines, abnormal dendritic arbors and somatosensory barrels, and reduced synaptic density. In addition, the reduction of serotonin in neonatal mice causes abnormal growth of the cerebral cortex and behavioral features that resemble autism. Such neurodevelopmental defects have been observed in people with autism, which suggests that insufficient concentration of serotonin in the brain prevents normal brain development.

Results: Serotonin deficiency and problems are very important and doctors should be well aware of possible drug interactions. In addition to its well-known effects on emotions, sleep and appetite, serotonin helps with the movement of the digestive system, peripheral and cerebral vessels, and platelet aggregation, but in this text, we discussed the effect of serotonin on autism and the conditions that happen to the body. We found that the use of

vitamin D and tryptophan supplements in the diet is a practical and low-cost way to help prevent and cure autism.

Conclusion: It has been shown in studies that diet intervention with vitamin D, tryptophan and omega-3 fatty acid; Strengthens the concentration of serotonin in the brain and helps to prevent and possibly eliminate some of the symptoms associated with autism spectrum disorders (ASD). Regulation of TPH1 and TPH2 may also be an important clue in understanding the inverse relationship between serotonin concentrations in the blood compared to the brain in children with autism. The growth peak in serotonin synthesis in the brain occurs before puberty and is thought to be involved in the growth and differentiation of neurons throughout the brain, this peak does not occur in children with autism. On the other hand, a high concentration of serotonin in the blood has been observed in 25-50% of children with autism. An inverse correlation between high blood serotonin concentrations and low serotonergic neurotransmission has been demonstrated in young adult males with autism, a phenomenon we refer to as serotonin dysregulation.

Keywords: Serotonin , vitamin D, autism, tryptophan

The Roles of Virtual Reality in Medical Education During the COVID-19 Crisis: A comprehensive review of qualitative studies (Review)

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Introduction: Since the last days of 2019, the novel coronavirus disease 19 (COVID-19) had been affected many aspects of human lives. Medical education was one of the sides that faced major changes while in-person classes shifted to virtual sessions during this pandemic to keep a safe distance to decrease students' interactions; so many types of distance learning, assessment, and virtual teaching methods are being proposed in this case. One of the novel educational tools which used increased is virtual reality (VR) technology in universities and hospitals for training students but it's not very common to use in comparison with video or online classes. Therefore, the present study is designed to determine the role of VR, its benefits, and obstacles, in medical education during the COVID-19 crisis.

Methods: The present comprehensive review was conducted through the electrical databases including PubMed, Scopus, and Web of science by searching with the keywords including "Covid-19", "Medical education" and "Virtual Reality" from 2019 to August 2022 in English. Qualitative studies that investigated the effects of VR on students' learning quality, the advantages, and disadvantages of VR in medical education, and the role of VR in undergraduate medical education theoretical and clinical training were the inclusion criteria. On the other hand, review articles, quantitative studies, and studies that only investigated the role of VR in a specialized field and VR in assessment medical education were excluded from the present review.

Results: Totally, 165 studies were found and according to the exclusion criteria; finally, 4 related articles were reviewed. During the Covid-19 pandemic, various virtual teaching and learning methods were increased in use, but most of the existing platforms were mostly suitable for teaching theoretical issues and could not be used for courses that require practical or clinical training. At this time, VR technology in medical education helped to teach these lessons more effectively. By reviewing the studies during this period and according to the results of all the studies, the use of VR was evaluated positively, even some people considered it more suitable than traditional classes, but the majority preferred the use of this technology along with face-to-face and clinical training. Students found this type of training useful for clinical assessment, diagnosis, and treatment. Among the other advantages mentioned by the students were easy access to training and no time limit for the classes, as well as no limit on the number of classes and not

missing the training due to reasons such as being away from the professors. On the other hand, this technology has made it possible to interact with professors and other students. Another important point that can be mentioned is that students from all over the world can experience special and diverse cases with this technology, which increases the level of scientific literacy of students. Reducing the costs of creating different classes in different places is another advantage of VR in medical education that students from faraway areas can participate in classes and have the same level of education without being limited by location. Besides the positive points of this technology, some students have considered it difficult to access online classes and use this technology due to the lack of a suitable platform and sufficient facilities. Another noteworthy point is that due to the newness of this technology, there are many 360° videos of training courses available, but interactive courses are not available enough for students, and we need equipment and construction for these courses that need the passing of time.

Conclusion: In the last two decades, education has moved towards virtual platforms, but since 2019, due to the change in the teaching process and the distribution of classes, especially the spread of Covid-19, the platform and facilities of virtual education have increased significantly especially in medical education, as a result of this review, VR was able to maintain the quality of education and make it satisfactory and effective for the medical student. According to the results of the review, it seems to increase the use of this technology after Covid-19 and can be more effective in medical education if it adds to traditional medical education. However, more studies are needed to clear gray areas of the impact of VR in medical education.

Keywords: Keywords: COVDI-19, Virtual Reality, Medical Education

The Study of gene expression pattern in osteocyte differentiation of Mesenchymal Stem Cells on polymer nanofiber (Research Paper)

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1.
2.

Introduction: Bone tissue engineering requires a well-designed scaffold that can be biodegradable, biocompatible, and support the stem cells to osteogenic differentiation.Biodegradable polymers, such as polycaprolactone (PCL) and Poly(L-lactide)(PLLA) , are promising materials in the field of tissue engineering and regenerative medicine, which aims at creating viable options to replace permanent orthopedic implants. In this study we evaluate the osteogenic differentiation and gene expression of human bone marrow mesenchymal stem cells (hBMSCs) into PCL and PLLA scaffolds

Methods: MSCs were cultured on PCL and PLLA scaffoled for 21 days. Expression of osteoblast-related genes, including ,Runt-related transcription factor 2 (Runx2), osteonectin and collagen type1 , was assessed by real time-PCR.

Results: The real time PCR showed that the osteogenic gene expression including osteonectin , collagen type 1 and runx2 seeded in the nanfiber culture has higher expression than cells differentiated in control culture.

Conclusion: It can be concluded that PLLA and PCL are suitable substrates to support the proliferation and osteogenic differentiation of MSCs and holds promising potential for bone tissue engineering and regenerative medicine applications

Keywords: PLLA, PCL, Bone tissue engineering, gene expression. scaffold

The Study of the Effect of Nickel Heavy Metal concentrations, Salinity and temperature changes on Production of Alkaloid in Catharantus Roseus Medicinal Plant (Research Paper)

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Introduction: Plants, in their life cycle, are usually exposed to various kinds of environmental stresses including Heavy Metals, salinity and heat shok which affects many physiological parameters of plants. Catharantus Roseus plant, as a rich source of alkaloid chemical compounds consists of more than 130 secondary metabolites. Some of these compounds have pharmacological effects. Vinbelastine which is the most important alkaloid found in the leaves of Catharantus Roseus is used to heal the diseases like: testicle and breast cancers, lymphoma, neuroblastoma, hodgkin and nonhodgkin's lymphoma, Mycosis fungoides, histiocytosis and kaposi's sarcoma. It also controls mitotic activity by stopping the cells in metaphase through nonreturnable connection to tubeline. This alkaloid is the chemical analog of vincristine.

Methods: In this research, the effect of 0, 2.5, 5, 10, 25, 50 mM density of NiCl2 and 0, 25, 50, 100, 200 mM density of NaCl and temperature of 20°C, 25°C, 30°C and 35°C on the amount of alkaloids of Catharantus Roseus's total seeds of pink and white variety was investigated.

Results: The results showed that The total amount of alkaloid noticeably increased in the plant root and shoot.

Conclusion: Investigating the TLC plates/ planes, the increase in the amount of vinbelastine, katharantine, and ajmalicine alkaloids especially in high densities and temperatures was observed.

Keywords: Catharantus roseus, Environmental stresses, TLC, Alkaloids

The study the Effect of Salinity on Some Physiological Parameters of Catharantus roseus (Research Paper)

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Introduction: Plants, in their life cycle, are usually exposed to various kinds of abiotic stresses including salinity which affects many physiological parameters of plants. Studies have shown that change in the planting conditions can affect the qualitative and quantitative features of Catharantus roseus; therefore, creating stressful conditions (e.g., salinity) can be an effective way to investigate the changes.

Methods: In this research, the effect of 0, 25, 50, 100, 200 mM density of NaCl on degree of growth factors, catalase activity, amount of proline accumulation, Na/K content and photosynthetic parameters on seeds of pink variety of this plant was investigated.

Results: The results showed that degree of catalase activity, the amount of proline accumulation increased in plant under NaCl treatment, especially at high densities, while the total protein decreased. The NaCl stress also affected photosynthetic parameters, and decreased the amount of pigments, as well as the photosystem II efficiency.

Conclusion: The length, the wet and dry weight and the amount of Kin the plant shoot decreased while the length and the amount of Na in the root increased.

Keywords: Catharantus roseus, Salinity, Catalase, Photosynthetic parameters, Growth factors

The survey of antibiotic resistance pattern and prevalence of Tetracycline resistance (tetA, tetB) genes in Escherichia coli isolates collected in Ahar Bagheralolum hospital. (Research Paper)

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Introduction: Escherichia coli is the most important member of normal intestinal flora in humans and animals, and can causing opportunistic infections. Tetracyclines are a family of antibiotics that inhibit pro-tein synthesis by preventing the attachment of aminoacyl-tRNA to the ribosomal acceptor (A) site. They are also used to treat Escherichia coli infections. However, the continued widespread use of antibiotics has led to the development of resistant organisms. This study was conducted to investigate the resistance to tetracyclines and investigate the frequency of tetA and tetB genes among Escherichia coli isolated from patients hospitalized in Ahar hospital.

Methods: 120 bacterial samples with initial diagnosis of Gram-negative bacillus (Enterobacteriaceae family) were collected from Ahar Hospital. Samples were processed for microbial and biochemical characterization. Antibiotic susceptibility test was carried out by using disc diffusion method. The distribution of tetracycline resistance (Tcr) genes (tetA and tetB) in isolates were detected by PCR

Results: 76 isolates from 120 samples were recognized as E. coli. The higher resistance rate was 82.19% to Ampiciline, and the lowest resistance rate was 8.21% to Gentamycine. 75% and 72.6% of the isolates, however, were resistant to Doxycycline and Tetracycline respectively.The distribution of tetracycline-resistance genes among isolates included tetB 14% , tetA 36%

Conclusion: The increase in the resistance of tetracycline with high diversification is an indication of antibiotics overuse. Strict enforcement of regulation is urgently needed to control and prevent the spread of tetracycline resistant strains which are detrimental to the environment.

Keywords: Escherichia coli, Antibiotic resistance pattern, tetA, tetB

The therapeutic effects of hAMSCs on pancreatic cancer cells through autophagy activation (Research Paper)

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Introduction: Pancreatic cancer is one of the most lethal cancers worldwide. Poor prognosis and therapeutic resistance is known major barriers to survival of pancreatic cancer patients. Currently, the most common types of cancer treatment are surgery, chemotherapy, immunotherapy and radiotherapy. Off-target effects, toxicity effects on normal cells, and the formation and development of drug resistance are the major limitations on effectiveness of current therapies options. Stem cells have unique features including differentiation into other cell types, simple isolation, secretion of bioactive factors, and low immunogenicity. The niche of stem cells contains secreting products such as cytokines, growth factors, chemokines, bioactive lipids, and microRNA (miRNA) that maintain homeostasis in an autocrine/paracrine-manner. Currently, stem cells and their secretomes for repairing or replacement of damaged tissues or diseased organs seem to be beneficial. Among different types of stem cells, mesenchymal stromal cells (MSCs) exhibit characteristic favorable for tissue regeneration in paracrine manner. Also, stem cell-base anticancer therapy is recently established. Due to drug resistance in cancer therapy and toxicities effects of anticancer agents on normal cells, researchers are always interested to find novel, safe and more effective strategies to design anticancer drugs. Therefore, stem cells approach will be considered as a potential opportunity. Autophagy is a process where cellular components such as macro proteins or even whole organelles are sequestered into lysosomes for degradation. The study of molecular events associated with MSC/tumor cell interactions would be essential for identifying the role(s) of stem cells to suppress or induce the key signaling pathways of tumor cells and it will be critical to design therapeutic approaches.

Methods: Herein, we are interested to evaluate the therapeutic effects of human amniotic mesenchymal stromal cells (hAMSCs) on pancreatic cancer cells, Panc1, in co-culture manner through induction of autophagy pathway

Results: In this regard, hAMSCs and Panc1 cells were co-cultured by using the trans-well membranes. Total cell lysates of cells were prepared and analyzed by using western blot. Our results can be critical to find new anticancer therapy platforms depend on paracrine manner particularly in pancreatic cancers.

Conclusion: In this study, we found that activation of autophagy pathway by hAMSCs secretome is a potential platform in cancer therapy. Also, it can be useful to find more information about interaction between stem cells and cancer cells to extract effective and novel components from stem cells.

Keywords: Stem cells; Pancreatic cancer cells; Autophagy

The therapeutic effects of hAMSCs secretome on tumor invasion through down regulation of SgK269 in HT-29 cells colon cancer cells (Research Paper)

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Introduction: Colon cancer is one of the leading tumors in the world, killing many people each year. Currently, the most common types of cancer treatment are surgery, chemotherapy, immunotherapy and radiotherapy. Due to drug resistance in cancer therapy and toxicities effects of anticancer agents on normal cells, researchers are always interested to find novel, safe and more effective strategies to design anticancer drugs. Stem cells with unique characteristics such as self-renewal, directional migration, differentiation, and modulatory effects on other cells, are considered as a new platform in cancer therapy and repair of damaged tissues. Atypical kinase Sugen Kinase 269 (SgK269) was reported to regulate invasion and cell motility. The aim of present study was to evaluate the therapeutic effects of human amniotic mesenchymal stromal cells (hAMSCs) on colon cancer cells (HT-29) invasion through analyzing SgK269 expression.

Methods: To do so, we employed a co-culture system using 6 well plates transwell with a diameter of 0.4 µm pore sized. After 72h hAMSCs-treated HT-29 cells, the expression of SgK269 was analyzed by using western blot method.

Results: Our results support of the idea that MSCs may be a novel and more effective therapeutic approach to inhibit colon cancer cells invasion by targeting specific gene expression.

Conclusion: It seems that hAMSCs may be a nobel and potential platform in colon cancer therapy. However, more experiments are required to determine the details of related molecular pathways.

Keywords: HT-29 cells colon cancer cells, hAMSCs, SgK269, Invasion

The use of stem cells in the treatment of diabetes (Review)

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Introduction: Diabetes is a common endocrine disease. This disease requires frequent and constant measurement of blood sugar, insulin injection and restriction in diet. In addition to constant insulin injections, people with diabetes suffer from complications such as kidney disease, cardiovascular disease, vision problems, infection, etc., and treating the complications of this disease causes many problems for the affected person. Therefore, we have to find a permanent treatment for this disease. Stem cells have the ability to differentiate into cells of different tissues. Therefore, the use of stem cells has been suggested as a treatment methods for diabetes.

Methods: Various studies have shown that insulin-producing cells can be created and produced from stem cells extracted from bone marrow, fetal umbilical cord, and fat tissue. There are no ethical concerns about the use of these cells and it is expected that they will be used to treat many diseases in the coming years.

Results: Researchers were able to transform stem cells into insulin-producing beta cells and take an important step in the treatment of diabetes. New insulin-producing cells behave like normal beta cells in healthy people when exposed to glucose and show a quick and appropriate reaction. When these new cells were injected into diabetic mice, their blood sugar levels stabilized. Of course, it should be noted that this was only an experiment on animals.

Conclusion: Considering the increasing number of diabetes in the world and the complications it causes for the patient (vision problems, leg ulcers, etc.) and also the high treatment costs that diabetes imposes on the patient's family, stem cells can be a big step for treatment of this disease.

Keywords: Keyword: Stem Cell, Diabetes, beta cells

Therapeutic applications differentiation of stem cells into vascular endothelial cells (Review)

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Introduction: Vascular endothelial cells derived from stem cells have substantial potential for the development of novel vascular therapeutics and cell-based therapies for the repair of ischemic damage. For instance, atherosclerosis is a slowly progressing and multifactorial disease, in which endothelial dysfunction and damage play an initial role. Following endothelial death, the neighboring mature endothelial cells actively proliferate and migrate to heal the wound. Therefore, with the rapid development of stem cell research, it is expected that stem/progenitor cells may serve as a new source for vascular repair. Therefore, this study aims to review the in vitro and in vivo differentiation of stem cells into endothelial cells for therapeutic applications.

Methods: This study is a review article with the use of a systematic search in valid databases such as ScienceDirect, EBSCO, ProQuest, and PubMed which were done in 2012-2022.

Results: It is demonstrated that vascular endothelial growth factor-A (VEGF-A) plays important role in cell differentiation and proliferation since it is an endothelial cell-specific mitogen produced by various cell types such as mesenchymal stem cells (MSCs), Totipotent embryonic stem (ES) cells, and adipose stromal cells. VEGF-A, the most important member of the VEGF family, mediates angiogenesis and cell differentiation. While there is no

conclusive marker for endothelial progenitor cells (EPCs), it is currently believed that the cells could be EPCs if they are double positive for markers including CD34, CD133, or VEGFR2 and murine EPCs as CD34, c-Kit, Sca-1 or Flk-1. Especially that temporal and spatial expressions of both Flk-1 and VEGF correlates with vasculogenesis in the embryo. In the cell culture system, embryonic stem (ES) cells can also undergo hematopoietic differentiation in a similar way to that found in the yolk sac and early fetal liver. Endogenous EPCs have multiple origins including bone marrow, spleen, intestine, liver, adipose tissue, and adventitia. But bone marrow is the most defined source of circulating EPCs. CD133+ Hematopoietic stem cells (HSCs) and CD34+ HSCs isolated from peripheral blood can differentiate into endothelial cells in vitro and contribute to vascularization in animal models. After release from bone marrows, EPCs are mobilized to their destination via cytokines such as stromal cell-derived factor (SDF)-1, nitric oxide, and VEGF, then they are retained on the vascular surface by binding to adhesion molecules. Once attached to the surface of the injured endothelium/vessel, EPCs undergo differentiation into ECs, in which the local micro-environment affects this process. Furthermore, mature ECs co-culture can also direct peripheral blood EPC differentiation toward endothelial phenotype. Besides MSCs, human adipose stromal cells are multipotent cells with pericytic properties that can stabilize vascular assembly in vitro. This reciprocal production resulted in angiogenesis and adipose stromal cell-mediated reduction of EPC apoptosis. additionally, PDGF-BB secretion by ECs and VEGF production by adipose stromal cells play a role in the process. Moreover, miRNAs are known to play important roles in maintaining stem cell pluripotency and regulating endothelial cell function and may play a role in angiogenesis. The last factor is hypoxia which upregulates several genes involved in angiogenesis like basic fibroblast growth factor, VEGF, the VEGF receptors KDR and FLT-1, and components of the plasminogen system.

Conclusion: The isolation of MSCs makes them ideal tools for autologous or allogeneic cell therapy. The use of autologous vascular endothelial progenitor cells seems attractive for the development of engineered vessels as well as for the vascularization of engineered tissues and may also be useful to augment vessel growth in ischemic tissue. The mentioned factors in the study can potentially provide therapeutic benefits in pathological conditions that involve endothelial cells, such as wound repair, angiogenesis in ischemic tissues, microvascular permeability, vascular protection, and hemostasis and these findings may promote the understanding of tissue repair mechanisms and may lead to the development of novel strategies for therapeutic interventions aimed at ischemic diseases.

Keywords: Stem cells, Endothelial cells, Stromal Cells, Endothelium, Differentiation

Therapeutic approaches for DMD disease (Review)

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Introduction: Duchenne muscular dystrophy (DMD) or Xp21 dystrophy is a malady that causes severe proximal leg weakness. Mutation in the dystrophin gene located on the X chromosome is the cause of DMD disease because the protein encoded by it plays an essential role in maintaining skeletal muscle stiffness. Dystrophin protein is located under the basal lamina and extends to the sarcoplasm and acts as a linker between the intracellular skeleton and the extracellular matrix by binding to actin and the DAPC (Dystrophin-associated protein complex) complex. Lack of production of functional dystrophin also will lead to dysfunction of the heart muscle as well as the pulmonary diaphragm. Although some treatment options such as respiratory support have led to the reduction of clinical symptoms and improvement of the quality of life in these patients, there is still no definitive treatment for these patients. However, some features of the dystrophin gene, including its monogenicity and the long lifespan of muscle cells facilitate the use of gene therapy to treat this disease.

Methods: In a study by D.R. Asher and his colleagues, the AAVrh74 vector was used for the transfection of SRP-9001 microdystrophin transgene along with the MHCK7b muscle-specific promoter and α-MHC (α-myosin heavy chain) and MCK (Muscle creatine kinase) enhancers to DMD patients lacking functional dystrophin protein. Since the cDNA of the dystrophin gene is larger than the capacity of the AAV viral vector, a shortened version of the dystrophin gene was used in this study, which includes only the essential parts of the protein, including N-ter (for binding to actin), C-ter (for binding to DAPC), R1-R3 region (to connect with sarcolemma), and hing domains (to maintain protein flexibility) and its middle parts were removed. The design of this transgene is based on shortened dystrophin protein in BMD patients who have milder symptoms than DMD patients. Nicolas Wein et al. used the scAAV vector to deliver four molecules of U7 snRNA (U7 small nuclear RNA) to DMD patients with exon 2 duplication. Duplication of exon 2 leads to disruption of the protein reading frame and non-functional protein production in DMD patients. The U7 snRNA molecules prevent the splicing complex from joining to pre-mRNA by binding to the splicing sites of exon 2 repeats, and thus exon skipping occurs for one of exon 2 repeats. Another common mutation in DMD patients is the exon 44 deletion. Deletion of exon 44 results in a premature termination codon in exon 45 following splicing of exons 43 and 45. In one study, Yi-Li Min and colleagues used the CRISPR/Cas9 system to delete exon 43 or 45 and restore the reading frame of the dystrophin protein. In this study, four sgRNAs (small guide RNA) of 20 nucleotides (G1, G2, G3, G4) were used to connect to the splicing acceptor

and donor regions in the vicinity of exon 43, and another four sgRNAs (G5, G6, G7, G8) were designed to bind to the 5' splicing site of exon 45. In this way, the deletion of each exon 43 or 45 led to the restoration of the protein reading frame and the production of functional dystrophin protein.

Results: In all the mentioned gene therapy methods, the production of functional dystrophin protein has been restored through healthy gene transfection or restoration of the protein reading frame during mRNA translation.

Conclusion: Today, various methods are used to treat DMD, including transfection of adenoviral vectors carrying microdystrophin (which includes the functional sequences of dystrophin protein), exon skipping during pre-mRNA splicing, and genome editing through CRISPR/Cas9 technology. All these methods lead to the production of functional dystrophin protein, although with a shortened length, which leads to a reduction in the clinical symptoms of DMD patients and an improvement in the quality of their life.

Keywords: Duchenne muscular dystrophy, dystrophin, gene therapy, exon skipping, CRISPR/Cas9

Therapeutic approaches in autism spectrum disorders (ASD): A review study (Review)

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Introduction: Autism spectrum disorder or ASD is a neurodevelopmental disease with disability in social and emotional communications, anxiety, restrictive and repetitive behaviors. The prevalence of autism is almost 0.37% in Asia. The etiology of autism is vary heterogeneous, both environmental and genetic factors are involved in autism. Some of the environmental factors such as parent's age, asphyxia-related birth complications and preterm birth. The genetic factors such as SNPs, Copy Number Variations, Single mutation genes, Epigenetic factors. It has been showed that almost 800 genes involving in Synapse function, Chromatin remodeling and cortical development are associated with ASDs. Current autism treatments can mostly be divided into behavioral and medicine approaches. Behavioral treatments mostly include some activities to encourage social communications, self-awareness and increase attention. The medicine approaches improve some specific activities associated with autism prescribing medication. Generally, it has been recommended several treatment strategies, but none of them were effective to cure and eradicate the autism. Some in vivo and ex vivo gene therapy using CRISPR have been done for autism and neurodevelopmental disorders to the aim of therapy or made an animal model for study about autism. The CRISPR method can be a promising therapeutic approach for ASDs. The purpose of this review article is to summarize some of the effective treatment approaches for ASDs.

Methods: In behavioral therapy the Intensive Behavioral Intervention method providing significant profit for core ASD symptoms is a potential technique to treat younger children with autism; especially in premature ages. It has been reported that to improving social interaction, social skills' groups can be effective. The method of Cognitive Behavioral Therapy can help adults with autism disorder in the context of treating anxiety and Obsessive Compulsive

Disorder. Some studies has reported that pharmacological treatments; such as risperidone; fluvoxamine; fluoxetine; divalproex sodium, and placebo; may be effective against restricted/repetitive behavior among patients with ASD. Acupuncture making some therapeutic effects on ASD using activate the hypothalamic oxytocin system releasing of neurotransmitters. In one study has been proved that use of Mesenchymal stem cells combining with cord blood CD34+ cells are effective in the treatment of autism. Moreover, Artificial Intelligence is one of the promising approaches helping diagnose and therapy of ASD in recent decay, in one study an Artificial Intelligence system for Robot-Child interaction has suggested to the aim of behavioral. Several studies have been proved that animal models (e.g. rodent models) can be effective tools specially to find appropriate treatment methods such as gene therapy approaches in neurodevelopmental disease. Knockout and humanized Knock-In mice for various mutations in ASD and comorbid neurodevelopmental disorders have been generated. CRISPR-Cas is one of the cost-effective gene therapy methods using in the recent decades as a promising cure approaches. It has been developed an in vivo newly designed CBE strategy targeting neurons in the brain via a BBB-crossing AAV system; to correcting a single nucleotide mutation in the whole-brain scale; in CRISPR-Cas system.

Results: This review focused on six potential treatment methods for autism patients such as behavioral therapy, pharmacological treatment, traditional medicine, artificial intelligence and gene therapy. However most of these therapeutic approaches are effective to improve the autism symptoms, most of these have focused on the environmental factors causing autism and have not been a final cure for autism. Specifically, there is another remarkable factor, which has played a critical role in etiology of autism. Genetic factors can play a key role to cure some subtypes of ASD such as fragile X syndrome, some polymorphisms like MTRR (rs1801394) and so on. Therefore, CRISPR-Cas system can be a targeted gene therapy to cure these subtypes of ASD.

Conclusion: To conclude, it has introduced several possible therapeutic approaches to improve autism. Among them, gene therapy is the only treatment that has focused on genetic factors of ASD and the most targeted therapy, although others have been helping to improve autism symptoms. Generally, more attention is needed for gene therapy methods in order to create a final and permanent treatment for some subgroups of autism.

Keywords: Autism, ASD, Behavior, Therapy, CRISPR

Therapeutic effect of aerosol inhalation of exosomes from allogeneic fat mesenchymal stem cell culture in a pulmonary fibrosis model in rats (Research Paper)

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Introduction: Pulmonary fibrosis is a chronic interstitial lung disease, which is caused by damage to the lung parenchyma by inflammatory factors and fibrosis. Today, research on extracellular vesicles derived from mesenchymal stem cells is one of the areas of interest in regenerative medicine. Studies show that therapeutic use of exosomes as a non-cellular treatment method has a number of advantages that can be a good justification for its replacement in conventional cell therapy methods.

Methods: In this study, we evaluate the effects of adipose-derived mesenchymal stem cells (adMSCs) originating exosomes to repair pulmonary fibrosis. Here we present a series of studies utilizing exosome by inhalation to treat models of lung injury and fibrosis. Male adult Sprague-Dawley (SD) rats were randomly divided into three groups: the control group, the exosome receiving group with a concentration of 500µg/ml, and 250 µg/ml. Tissue samples and the levels of oxidative stress and inflammatory factors in each group were compared.

Results: exosomes isolated ranged in size from 30 to 150 nm and demonstrated the characteristic cup-shaped morphology with TEM. We showed that an inhalation treatment of exosome exhibited therapeutic potential for lung regeneration in experimental models of pulmonary fibrosis. Pathologic alteration of lung tissue, levels of pro-inflammatory cytokines, were measured to evaluate the therapeutic effect of treatment with MSCs exosomes.

Conclusion: Our results demonstrate that exosomes, constitutively produced by adMSCs, have the potential to be utilised as a therapeutic tool for effective tissue-engineered lung.

Keywords: exosome,mesenchymal stem cells, fibrosis

Therapeutic effects of adipose-derived mesenchymal stem cells on gentamicin-induced renal failure (Research Paper)

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Introduction: Considering the limitations of conventional therapeutic methods in renal failure, researchers are paying attention to the application of adipose-derived mesenchymal stem cells (AD-MSCs) and their protective effects against acute renal failure. This study aims to assess the therapeutic effects of AD-MSCs in gentamicin-induced renal failure in rats

Methods: In this study, fourty male Wistar rats were studied in control, sham, gentamicin treated with and without receiving AD-MSCs. After ten days, blood samples were collected and hemodynamic parameters, malondialdehyde and ferric reducing antioxidant power (FRAP) measured in the right and left kidneys underwent histologic examination

Results: Gentamicin administration significantly increased plasma creatinine, blood urea nitrogen, oxidative stress parameters and histologic damages; while significantly reduced FRAP in the gentamicin-receiving group in comparison with the sham group. AD-MSCs treatment significantly improved renal function parameters, oxidative stress and histologic damages in comparison with the gentamicin receiving group.

Conclusion: Intravenous injection of AD-MSCs in gentamicin-induced renal failure improved renal function, oxidative stress parameters and histologic damages.

Keywords: Acute renal failure; Gentamicin; Mesenchymal stem cells; Oxidative stress

Therapeutic properties of phenolic compounds of natural products in cancer (Review)

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Introduction: Over the past 50 years, cancer has been considered as the second leading cause of death worldwide. Phenolic compounds are secondary metabolites found in most plant tissues. Various bioactivities of phenolic compounds are responsible for their chemopreventive properties such as antioxidant, anticarcinogenic, or anti-inflammatory effects. Natural phenolic compounds play an important role in cancer prevention and treatment. Due to the adverse side effects of chemical drugs, natural drug and products used in traditional medicine have been studied as possible alternatives to these therapeutic because they have minimal gastrointestinal toxicity.

Methods: Many studies have examined the effects of natural products and their compounds such as phenolics and flavonoids, tocopherols, peptides, sugars, etc. with diverse sources at in vivo levels with research on humans and mouse models, and in vitro using different cell lines such as HCT 116, LoVo, MDA-MB-231, MCF-7. At both levels, the effects of these compounds on cancer-related pathways such as oxidative stress, apoptosis, proliferation, autophagy, invasion, metastasis, and markers involved in these pathways have been investigated. This review focuses on many natural products that play a role in cancer prevention and that promote human health without recognizable side effects.

Results: Natural compounds can be administered to patients, usually without the side effects and toxicity of synthetic preparations and some natural compounds have been administered with success. While chemical drugs cause nonspecific killing of cells, the results of various studies around the world show that natural products offer protective and therapeutic actions to all cells with low cytotoxicity and are beneficial in producing nutrient repletion to high-risk people.

Conclusion: The potential of natural products as pharmaceutical resources to cover a wide range of therapeutic effects is currently being realized and they have been of increasing interest to science and food industry for their beneficial health effects and are case studies for further applications.

Keywords: Cancer, natural products, apoptosis, bioactive compounds, phenolic compounds

Three-Dimensional Epidermal Model from Human Hair Follicle-Derived Keratinocytes (Review)

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Introduction: Hair follicle (HF) has a heterogeneous cell source, including stem cells with high differentiation capacity. Therefore, it is an important source of cells for regenerative medicine purposes. HF is available with completely non-invasive plucking. The hair follicle consists of the primary coordinated function of ectoderm and mesoderm and is a small organ with a unique structure and function. Hair follicle-derived keratinocytes can be obtained in culture, either by direct growth of hair follicle-derived keratinocytes or by seeding cell suspensions from enzymatic digestion of hair follicles. The advantage of keratinocyte extraction from hair follicles compared to other methods (skin removal or biopsy) is its non-invasiveness. For example, wounds that penetrate deep into the dermis heal poorly due to a lack of keratinocytes (especially the epithelium), a 3D epidermal model of human hair follicle-derived keratinocytes as a less invasive treatment for wounds and skin disorders. Today, most in vitro human three-dimensional (3D) skin models, known as skin surrogates, are regenerated human epidermis (RHE) models. In one of these RHE models, keratinocytes derived from hair follicles are cultured with fetal calf serum or autologous serum. Preferably, simpler (no feeder cells) and safer (serum-free) techniques are used when preparing epidermal equivalents. A 3D epidermal model of human hair follicle-derived keratinocytes provides a useful tool for researching skin biology and studying epidermal barrier functions in patients with various skin disorders (such as atopic dermatitis or psoriasis). Our goal in this research is to investigate the 3D epidermal model of human hair follicle keratinocytes.

Methods: In the following article, we collected the required data by using key words using reliable databases such as Google Scholar, ProQuest, Scopus

and PubMed. Our statistical population consists of all the studies that have been conducted until 2022. After reviewing the findings, we reviewed 14 articles.

Results: 1- Due to the prohibition and limitation of other methods (testing on animals, treatment of chronic wounds and large burns), the use of 3D skin models is a more appropriate alternative (for example, atopic dermatitis or psoriasis). 2- Multipotent stem cells, which are a unique source for a wide range of therapeutic applications, have been identified in the hair follicle. These hair follicle stem cells (HFSCs) are used for skin, bone, cardiovascular and nerve tissue engineering.

Conclusion: With the positive results of various cell therapies currently under various studies, there is considerable interest in new stem cell sources with unique therapeutic properties. Studies over the past two decades have shown the possibility of isolating high-powered stem cells from hair follicles. Easy access, high proliferation and differentiation ability, as well as the lack of ethical concerns associated with these solutions, make hair follicle stem cells (HFSCs) attractive candidates for cell therapy and tissue engineering.

Keywords: Three-Dimensional, keratinocytes, epidermis

Three-Dimensional Scaffold for Renal Tissue Engineering (Review)

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Introduction: Global reports show that the shortage of kidney transplants in the world has become a social crisis, and a large number of dialysis patients with severe renal failure are unable to use kidney transplantation and die due to the lack of donor organs as well as the high-cost and side effects of allografts transplants. These limitations have increased efforts to regenerate tissue using scaffolds and research in the field of 3D matrices in this field.

Methods: This study reviews advances in the area of three-dimensional scaffold for renal engineering approaches. In the present study, PubMed, Google Scholar, and Scopus databases were searched to find relevant articles.

Results: Tissue engineering and advances in biomanufacturing methods suggest likely solutions for organ shortages; though, because of the complex structure of kidney, previous efforts have fallen short. Recently, strategies such as 3D bioprinting, photolithography, 3D self-assembly, molding or manipulation of bulk acoustic cells have been developed to mimic the layered tissue structure. These methods are widely used in tissue engineering for the bioengineering of multilobed structures and for the basic understanding of many microphysiological and pathological processes such as cell differentiation. In the field of constructing a 3D renal scaffold, where it is difficult to prepare in vitro samples, various strategies have been developed

and many studies have been performed. For example, a decellularized kidney scaffold has been produced with structural, mechanical, and physiological properties necessary for engineering basic renal structures in vitro.

Conclusion: in vitro studies showed that the 3D printing method as a new method gives physicians the freedom to prepare a scaffold with the exact shape and size of damaged renal tissues using 3D design. However, this treatment method still needs more in vivo studies and clinical trials, but if successful, it can save many lives and is one of the low-cost and simple methods.

Keywords: Tissue Engineering, Renal, Kidney, Bioprinting

Thymoquinone-loaded exosomes for eliminating breast cancer cells
(Research Paper)

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Introduction: One of the important aspects of exosomes is using as a carrier in drug delivery. Thymoquinone (Tq), the main active component of black seed oil, has great anti-proliferative effect on cancer cells. However, its therapeutic applications are restricted because of poor solubility and weak bioavailability. In this study, exosomes secreted from human adipocyte-derived mesenchymal stem cells (AdMSCs) were isolated, loaded with Tq and their cytotoxic effect against cancer cells was investigated.

Methods: Exosomes were isolated via ultracentrifugation and characterized by electron microscopy and western blotting. Afterwards, Tq was incorporated into exosomes by the combination of incubation, freeze-thawing, and surfactant treatment. Next, the cytotoxicity of this complex (Tq@EXOs) in MCF7 and L929 cells were assessed.

Results: With our novel method, encapsulation efficiency of Tq in exosomes was improved about 60%. Efficient uptake of Tq@EXOs-FITC into cancer cells was shown using the fluorescent microscopy and flow cytometry. In addition, Tq@EXOs could effectively show the toxic effect on cancer cells without any evident cytotoxicity on normal cells, according to MTT results.

Conclusion: The results indicated that Tq@EXOs propose a valuable and safe design for drug delivery to cancer cells thus having a great potential for clinical studies.

Keywords: Exosome, Mesenchymal Stem Cells, Thymoquinone, Drug delivery, Cancer.

Tissue Distribution and Cell Renewal Dynamics of Polyploid Human Hepatocytes (Research Paper)

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Introduction: In many human organs, the rate of cell turnover in healthy and pathological conditions remains mostly unknown. This is mainly because it is challenging to research this process in humans. Although the liver has a remarkable ability to regenerate following partial hepatectomy, little is known about how hepatocytes are replaced to maintain homeostasis. Hepatocytes can develop multiple nuclei and polyploidy. It is unknown what causes polyploidy and whether it has any biological advantages for health and sickness. Due to the liver's amazing propensity for cell proliferation, it may repair itself after harm by producing new, functional tissue. Due to methodological limitations, there hasn't been a thorough investigation defining the dynamics of human hepatocyte turnover, including their age distribution and the effects on hepatocyte functionality in the aging liver. Establishing these aspects of adult liver cell regeneration is crucial, particularly to better understand age-related illnesses and the emergence of liver cancer. Consequently, we want to describe human hepatocyte turnover using retroactive birth dates.

Methods: In this study, we will use computational image analysis to quantify the distribution of nuclear ploidy and multinucleation in human hepatocytes and to ascertain the turnover dynamics of various ploidy levels in hepatocytes. By detecting the quantities of 14C, a byproduct of Cold War nuclear bomb tests, in the genomic DNA of flow cytometry-isolated hepatocyte nuclei with various ploidy levels, one may determine the dynamics of turnover. These investigations might serve as the foundation for therapeutic plans that target pharmacologically controlling hepatocyte renewal to enhance liver function in severe liver disease.

Results: In the current experiment, we were able to corroborate earlier findings that indicated polyploid hepatocytes renew at a slower rate than diploid hepatocytes due to differences in their 14C contents. Although some rodent research appears to confirm this theory, other rodent studies reveal a proliferative potential that is unaffected by the ploidy level of hepatocytes. It is difficult to compare hepatocyte regeneration across mice and humans because of their differing ploidy profiles.

Conclusion: Retrospective birth date using 14C shows that the human liver is still a young organ even in the elderly. We saw a continuous and significant

turnover of hepatocytes over the course of the lifetime, which is closely related to the ploidy level. In comparison to polyploid hepatocytes, diploid hepatocytes have an eight-fold higher yearly renewal rate. In humans, exchange between ploidy classes barely affects liver homeostasis. An essential topic that needs to be answered is whether long-lived polyploid cells render the liver more vulnerable to age-related disorders or whether they work as a resilience element to deal with cellular stress, preventing organ function loss and cancer. In conclusion, rodents are largely used to study the liver, a complicated organ with a population of hepatocytes that is highly heterogeneous. The current thesis identified variations in the turnover rates of the various ploidy classes of human hepatocytes. Additionally, we discovered early evidence that metabolic liver zonation affects polyploidy, which in turn affects cell cycle activity and may affect hepatocyte regeneration. To provide a complete picture of liver cell renewal, future studies must look into these consequences.

Keywords: Liver repopulation, Progenitor cells, Cell turnover, Hepatocyte transplantation, Streaming liver

Tissue engineering and stem cells: Introduction of stem cells and their applications (Review)

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2. High School Of Brilliant Talents

Introduction: The first question that comes to your mind after opening this article is, What a Stem Cell is? The stem cell is the mother of all cells and has the ability to transform into all cells in the body. These cells have the ability to self-renew and differentiate into all types of cells, including blood, heart, nerve and cartilage cells. Also, they are effective in the reconstruction and repair of different tissues of the body after damage and injury, and they can be transplanted into the damaged tissues where most of their cells have been lost, and replace the damaged cells and repair and fix the defects in that tissue. Due to the unique ability of stem cells, these cells are an attractive topic in biology and medical sciences today. Also, research in this field has increased our knowledge about how an organ grows and develops from a single cell, and more importantly, it has helped to understand the mechanism of replacement of healthy cells with damaged cells. In the following, you will get to know the different topics of stem cells.

Methods: According to the previous researches and the experiments that we have done, in addition to using these cells to treat diseases and draw and renew tissues, stem cell technology has also been focused on the production of these cells in the past years. The main sources of stem cells in humans include bone marrow, umbilical cord, dental pulp, some fatty tissues and placenta. The mechanism that determines which cell differentiates can be extrinsic or completely intrinsic, for example, in hematopoietic stem cells, this mechanism is extrinsic in the sense the result of division that two daughter cells, the cell that is related to the bone cell (seoplast), remains undifferentiated.As we have said, some mechanistic cells are introgressive. In these types of stem cells, when the two daughter cells are not yet completely separated, proteins are transferred to one of them and the fate of the cell leads to differentiation The research that have been carried out on the basic characteristics of stem cells have led to the creation of theories about how stem cells are made from differentiated cells. Recent research in molecular biology has shown that pluripotent stem cells have two main characteristics; first, the chromatin structure in their nucleus is not compact. Second, a specific balance between transcription factors and their chromatin structure affectsthe gene expression of transcription factors. In diseases in which cells undergo abnormal apoptosis or malfunction over time or are lost due to an attack by the immune system, the use of stem cells will realize new therapeutic horizons. The research we have done so far shows that stem cells

have effectively treated many diseases. Such as Parkinson's disease, type 1 diabetes, Alzheimer's, stroke and heart disease, liver disease, cornea treatment, diseases such as paralysis, and treatment of oral and dental diseases are effective, and some are in the laboratory stage.

Results: Omnipotent stem cells are cells that, in addition to the ability of self-regeneration, can not only create all the differentiated cells in the body but are also able to form the cells that form the extra-embryonic membranes, including amnion, yolk sac, and produce pairs. Only the egg cell itself and the cells of the three- to four-day-old embryo are omnipotent; that is, they can create not only the embryo but also extra-embryonic tissues such as the placenta. But after this stage, only pluripotent cells are seen in the embryo. So far, there is no successful report that it is possible to multiply and increase the number of pluripotent stem cells in the laboratory environment. Still, they can be maintained for a short period of time in the laboratory environment. In contrast, other types of stem cells (including omnipotent and multipotent) can be grown and propagated in a laboratory environment. Cells that have the ability to differentiate into several cells that are close to each other from family cells are called multipotent. Like cells in differentiated tissues, cells in different tissues (nerve, skin, etc.) of adults are included in this category. Unipotent cells only have the ability to make one differentiated cell, such as B lymphocytes, which only can become plasma cells.

Conclusion: Stem cells are divided into embryonic stem cells, adult stem cells, and umbilical cord blood stem cells based on their characteristics. Embryonic stem cells: From the internal cell mass of a 14-16-day-old fetus, it is able to make all the cells and tissues of a complete person, Cells that are separated from different tissues of an adult after birth. Somatic stem cells are present in different body tissues after the stages of fetal development and throughout life. By dividing and differentiating, they replace dead cells and repair damaged tissues. Most adult stem cells are pluripotent or unipotent. Today, it has been proven that stem cells are able to treat a wide range of chronic and acute diseases. Many types of research have been conducted in the field of using stem cells to treat diseases such as Parkinson's, heart diseases, liver diseases, diabetes, Muscular dystrophy, spinal cord injuries, and stroke. This is a brief summary of the vast topic of tissue engineering and stem cells, although the material collected in this article was a very small part of this field.(Introduction to Stem Cells; Do You Know the 5 Types of Stem Cells? | BioInformant; Moradi and Baharvand; LAFZI et al.; All Things Stem Cell » Embryonic Stem Cells)

Keywords: Stem cells; Omnipotent; Pluripotent; Monopotent; Self-renewal; Differentiation; Plasmocyte.

TRAF3IP2-AS1/hsa-let-7d-3p/RGS2 ceRNA axis might regulate the development of STAD by regulation of cGMP-PKG signaling pathway: integrated systems biology approach. (Research Paper)

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Introduction: Gastric cancer(STAD) is one of the leading causes of cancer-related death worldwide [1]. This investigation aimed to find a novel differentially expressed gene in (STAD) patients compared to control samples.

Methods: Expression analysis of GSE112369 achieved from GEO2R[2] online software and validation of expression analyses also constructing survival chart and box pot performed by ENCORI[3] and GEPIA2 [4] databases. Through ENRICHR [5] ,KEGG [6] and GeneCards[7] , gene ontology information and biological pathway involvement were understood. Furthermore, miRWalk [8], PUBMED [8] and ENCORI were utilized to find significant miRNA-mRNA interactions. Additionally, the selected miRNA was searched in LncBase v.3[9] to find strong interactions with lncRNAs.

Results: Through analysis of the GEO dataset, a gene named (RGS2) was found with (FC=0.33), adj. P value =1.9e-12 moreover in survival analysis with (Logrank p=0.0085) and understood the death rapidity of Low RGS2 Group is more than High RGS2 Group in STAD samples besides RGS2 is involved in cGMP-PKG signaling pathway. Analysis of possible miRNA-mRNA interactions revealed this novel (hsa-let-7d-3p) miRNA with (0.92) score This miRNA was then searched in LncBase v.3 then find TRAF3IP2-AS1 and searched GENCARDS to be sure it’s a LncRNA.

Conclusion: In conclusion, the high expression of miRNA(hsa-let-7d-3p) lead to reduced expression of the gene (RGS2) in STAD patients, also TRAF3IP2-AS1 by regulating the expression of RGS2 indirectly can work as a ceRNA and adjusted cGMP-PKG signaling pathway.

Keywords: Microarray; Data analysis; STAD; cancer ; RGS2 ; lncRNA

Transfection of CRISPR vector for MTRR (rs1801394) polymorphism in HEK293T cell line (Research Paper)

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Introduction: The human methionine synthase reductase gene (MSR; gene symbol: MTRR) is a housekeeping gene located on chromosome 5 and consists of 21 exons. MTRR is a family of electron transferases. It has been reported in several studies that the MTRR (rs1801394) polymorphism is one of the single nucleotide polymorphisms associated with many diseases such as autism, schizophrenia, cervical cancer, and meningioma and so on. Therapeutic benefits have been provided to gene therapy, including the modification of genes through disruption, editing, or replacement. Gene therapies are increasingly being used in human patients and non-human models to treat human diseases. One of the recently used gene therapy techniques is the CRISPR-Cas system. Many approaches have been developed and applied in a variety of fundamental research using CRISPR-Cas9 systems. Among the various methods of this technique, knock-in/out, base editing, and prime editing are most promising. The purpose of this study is to transfect the CRISPR vector for the MTRR (rs1801394) polymorphism into HEK293T cell line.

Methods: The sgRNA was designed for the polymorphism MTRR (rs1801394). Our vector was a 3rd generation lentiviral expressing plasmid specialized for base editing-4 and having mCherry as a marker. The NEB strain of transformed bacteria harboring the plasmid was cultured on an LB agar plate. The ampicillin 100 g/ml was our bacterial resistance. The transformed bacteria were cultured in two LB agar plates named plasmid A and plasmid B with different amounts of bacteria from the semi-liquid primary culture medium. We performed the plasmid extraction using the Roche kit. Electrophoresis and also NanoDrop, which examines the purity of our plasmid, have been performed. The HEK293T cell line cultured and counted in Neobar lam. We separately transfected our mCherry and control plasmids, which had GFP as a marker, into HEC293T cells with Lipofectamine 2000. Finally, we observed the transfection results under a fluorescence microscope.

Results: The plasmid plates A and B both grew well. The results of electrophoresis and NanoDrop showed that at a concentration of almost 120 ng of the extracted plasmid, a bright band was generated on the electrophoresis gel, indicating the correct extraction of our plasmid. About 10,000 to 15,000 HEK293T cells were observed in the 96-well plate. In this research, we observed the transfected cells under a fluorescence microscope to ensure that the desired plasmid entered the HEK293T cells. The presence of red fluorescent color under the fluorescence microscope indicated that our plasmids were correctly introduced into the cells. Also those cells transfected separately for the control plasmid containing the GFP marker were also examined. The presence of green fluorescent color under the fluorescence microscope indicated that our control plasmids were also correctly introduced into the cells.

Conclusion: It can be concluded that the base editing method, especially the fourth generation of base editing called BE4max, in the CRISPR-Cas9 technique can be a targeted and potential treatment method for those suffering from MTRR (rs1801394) polymorphism and similar polymorphisms. Furthermore, it was shown that the 3rd generation lentiviral CRISPR plasmids can be a suitable and effective vector in the field of base editing.

Keywords: CRISPR, MTRR, Polymorphism, HEK293T, Base-Editing

Treatment of Breast cancer (Review)

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Introduction: Breast cancer (BC) is the second most common cancer worldwide and one of the well-known malignant tumors among women. Breast cancer is classified into 3 major groups based on the presence or absence of molecular markers for estrogen or progesterone receptors and human epidermal growth factor 2 (ERBB2; formerly HER2): ERBB2 positive (15%-20%), hormone receptor positive/ERBB2 negative (70% of patients), and triple-negative (tumors lacking all 3 standard molecular markers; 15%). Each of these subtypes has different risk factors for incidence, therapeutic response, disease progression, and preferential organ sites of metastases. With the advancements in the chemotherapy for BC, the mortality rate from BC is decreasing in the last decade. Targeting ER has proved one of the most powerful treatment modalities against HR+ BC. Moreover, the success of the biological drugs such as anti-HER2 monoclonal antibody, also highlighted the feasibility and significance of the molecular targeting approach in BC therapy. However, among all BC subtypes, TNBC has the fewest therapeutic options due to the lack of well-defined molecular target(s). Identification of new therapeutic targets and development of effective targeted agents is urgently needed. So, Metastasizing TNBC remains a deadly disease with limited treatment options.

Methods: review article

Results: In recent years, the molecular mechanisms driving the heterogeneous treatment response in BC are better elucidated. This has fueled the development of novel targeted agents, including inhibitors of PARP, CDK4/6, PI3K/AKT/mTOR, multiple kinases, or immune checkpoint, for the treatment of specific molecular subtypes of BC. Treatment options should be tailored to individual patient accordingly.

Conclusion: Breast cancer consists of 3 major tumor subtypes categorized according to estrogen or progesterone receptor expression and ERBB2 gene amplification. The 3 subtypes have distinct risk profiles and treatment strategies. Optimal therapy for each patient depends on tumor subtype, anatomic cancer stage, and patient preferences.

Keywords: Breast cancer, TNBC, treatment, subtypes

Treatment of oral cancer using mechanical and biochemical methods (Review)

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Introduction: Oral cancer is one of the most important types of cancer, and under the name of oral cancer, tumors of the tongue, lips, mouth, and oropharynx are classified. Oral squamous cell carcinoma (OSCC) accounts for 90% of oral cancer. Recurrent periods and emergence of drug resistance are the main challenges in the treatment of oral cancer. For this reason, the existence of improved therapeutic candidates that go beyond these issues is essential. The key elements in the pathological and physiological processes of various cancers are coding RNAs (ncRNAs). These key elements are also reflected in the progression and development of oral cancer.

Methods: In the forthcoming systematic review, the required data were collected using keywords and citing valid databases such as Scopus, PubMed, Google Scholar and ProQuest. The statistical population includes all studies conducted until 2022 in the field of Treatment of oral cancer using mechanical and biochemical methods. After reviewing the relevant findings and evaluating the quality of the data, 17 articles were analyzed.

Results: Based on the size, nRNAs are divided into two main categories, small ncRNA and IncRNA. The role of ncRNAs in oral cancer has been proven. The main classes of small ncRNAs: microRNAs (miRNAs), short interfering RNAs (siRNAs), and PIWI-interacting RNAs (piRNAs), as well as small nuclear RNAs (snoRNA), small nuclear RNA (snRNA) and repeat-associated RNAs (rasiRNAs). MiRNAs may take part in tumorigenesis by functioning either as oncogenes or as tumor suppressors. Since they are involved in basically all biological processes, aberrant miRNA expression can trigger the initiation of many diseases, including cancer. In oral cancer, as well as in other cancer types, miRNAs take part in cancer hallmarks. A large number of miRNAs have been introduced as key participants in

tumorigenesis, acting either as oncogenes (oncomiRs) or tumor suppressors. Among them, miR-21 plays a pivotal role as an oncomiR by participating in apoptosis and cell proliferation. miR-21 has been found to be deregulated in various tumor types. There is another miRNA with an oncogenic role, miR-184, which is overexpressed in TSCC. miR-184 can act as a cell proliferation and anti-apoptotic agent by changing the expression of c-Myc. According to another research, this transcript shows lower levels in tumor cells compared to normal mucosa for the same type of tumor. In normal cells, compared to poorly differentiated cancer cells, the expression of these miRNAs is higher. This shows the close relationship between cell differentiation and miRNA expression.

Conclusion: The altered expression of ncRNAs was related to regulating key cellular processes. In order to develop more effective treatments, a better understanding of these molecular mechanisms regulated by ncRNAs, as well as how to control the phenotype of oral cancer and its relationship with environmental factors, can be based. Each of the different miRNAs, with their palette of target genes, act in various signaling pathways that maintain oral cancer symptoms such as sustained proliferation, apoptosis escape, autonomous growth, invasion, metastasis and angiogenesis. This is why microRNAs are usually introduced as the best candidates for the development of new cancer treatments. MicroRNAs are pivotal regulators of diverse cellular processes including proliferation, differentiation, apoptosis, survival, motility, and morphogenesis. Recent advances in microRNA expression profiling have led to a better understanding of OSCC pathogenesis. This information is used to identify microRNA expression patterns that are likely to become powerful biomarkers called OCC.

Keywords: Mouth Neoplasms, miRNA, ncRNA

Treatment With Hydroxyurea Leads To Fetal Hemoglobin Reactivation Through CA1 And LIN28B Genes; An In Vitro Study (Research Paper)

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Introduction: Thalassemias are among the most common autosomal recessive monogenic diseases, which occur due to mutations in the beta-globin gene and lead to a decrease or non-synthesis of the globin chain and thus a reduction in hemoglobin levels. Induced production of the γ -globin chains reduces α/β-chain imbalance in β-thalassemia through the creation of fetal Hb (HbF), thereby increasing effective erythropoiesis and reducing hemolysis and the level of anemia. A score of studies has identified that HU is well accepted in clinical practice and can be associated as another option for β-thalassemia treatment. the exact mechanisms by which HU induces HbF production are not fully understood and are still controversial. we applied Weighted Gene Co-expression Network Analysis (WGCNA) approach to identify and quantify changes in gene expression that were reflected in the HU-treated human erythroblastic leukemia cells.

Methods: LIN28B and CA1 were selected as two related genes in the switching and expression of fetal hemoglobin and their expression behavior was evaluated under HU treatment. K562 cell line was cultured and cells for examination in two groups of control and treatment with hydroxyurea in 3 concentrations of 50,100 and 150 µM and 24, 48, and 72 hours with 3 replications were cultured. The RNA was extracted by RNA Extraction Kit Then, cDNA synthesis was conducted and quantitative PCR (qRT-PCR) was accomplished.

Results: LIN28B showed an increased expression level in all treated groups compared to the controls. But CA1 expression showed a decrease in all-time series and dosage of treatment. Along with this γ-globin gene expression was significantly elevated.

Conclusion: The LIN28 gene is known to regulate the let-7 family of miRNAs, and the expression of LIN28 transcripts is associated with the inhibition of let-7. It has been shown that the expression of LIN28 protein in adult erythrocytes not only leads to a decrease of let-7 miRNAs expression but also can upregulate HbF expression. Since the CA1 gene is involved in the c-MYB

factor pathway, its downregulation under HU treatment conditions suggests the key role of the c-MYB pathway in HbF expression. C-MYB is a key factor in regulating HbF production and may be involved in the modification of the globin gene by controlling cell cycles.

Keywords: Thalassemia, Fetal hemoglobin, hydroxyurea, CA1, LIN28B

Tuberculosis (Review)

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Introduction: Tuberculosis is one of the most important single-agent infectious diseases in the world, which is one of the deadliest diseases in the world every year. The target tissues of tuberculosis are the respiratory system and lungs, and with the progress of the disease, it has a special effect on other organs of the body, especially the bone marrow, reproductive system, and glands. The agent that transmits tuberculosis is actually cough, sneeze, and mouth saliva, and it infects other people .through droplets In most cases, there is latent or inactive and active tuberculosis, and in latent tuberculosis, its diagnosis takes between 6 months and one year, when the patient is a carrier of the disease, but does not have any specific symptoms. The symptoms of active tuberculosis actually include chronic cough along with Bloody sputum, fever, night sweats and severe weight loss. Active tuberculosis is diagnosed through chest X-ray + microscopic tests and microbiological culture of body fluids.

Methods: Unfortunately, the most people who are at risk of tuberculosis are people are related to immunodeficiency infections such as AIDS and HIV, and recently the percentage of people infected with the corona virus is higher than others. Considering the age of tuberculosis and the fact that it has been several years since such a disease was diagnosed, there are still many Different vaccines have not been made for this disease, which requires global attention and consideration. Tuberculosis, with its high infectivity, has only one vaccine called the BCG vaccine, which is practically useless in adults and the elderly, and its use is This .determined when To be injected to children under 5 years old at birth and up to 5 years old statistical data has been analyzed among 14,927 people measured in 26 different countries of the world, and the percentage of vaccination was actually 18%, and the final result is the effectiveness of vaccination for children less than 5 years old. And attention should be paid to remaking the vaccine to be effective for all. The other cases that are investigated are about the emergence of treatmentresistant tuberculosis in Asian and African countries.

Results: The largest number of tuberculosis patients are The main reason for. Microbacteria are actually Gram-positive, but they do not stain because their cell walls It consists of three molecules Tuberculosis bacilli survive well in cool, dark and humid environments symptoms of tuberculosis disease in cattle are cough resulting from lung infection, body temperature change, lack

of appetite, weight loss, mastitis, decrease in the amount of milk, abortion and infertility in cows. In fact, humans get infected through livestock, through the feces of infected animals, through milk, through uterine vaginal secretions, and through the mucous membranes of the nose and trachea, and through the skin. And in fact, in the end, the infected animal must be Drug-resistant

Conclusion: It has been about this. In fact, based on gender, men have higher infection rates than women, and in fact, because they are more likely to consume alcohol, smoke and smoke, they are actually at a more serious risk. And so are people who have diabetes.

Keywords: HIV, infectious diseases, Low economic situation, Smoking, Tuberculosis

Tumor-associated Antigens of Breast Cancer (Review)

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2.

Introduction: Antigens are the targets for the immune system which are present in cancer cells. However, many are not cancer-specific and may also be found on normal tissues. These antigens are often products of mutated cellular genes, aberrantly expressed normal genes, and genes encoding viral proteins. Furthermore, tumor antigens are responsible for initiating an immune respond in cancer patients and their recognition may provide new biomarkers for cancer diagnosis and targets for immunotherapy. In addition, Antigens that are found and studied in breast cancer include CEA, HER2, MUC-1 which is hyperglycosylated in adenocarcinomas, carbohydrate antigens (Tn, TF, STn), p53 – a tumor suppressor gene mutated in cancers, TERT, WT1 and so more

Methods: Further, the human epidermal growth factor receptor 2 (HER2) is a 185-kDa protein receptor with tyrosine kinase activity and extensive homology to the epidermal growth factor receptor. HER2 is expressed in many epithelial tumors and overexpressed in approximately twenty five percent of all primary breast carcinomas.

Results: Overexpression of HER2 is associated with poor prognosis. HER2 is a suitable target because it involves an extracellular domain (ECD) that can be targeted by antibodies produced by B cells. Moreover, Mucin 1 (MUC-1) is a membrane-associated glycoprotein expressed by many types of ductal epithelia, including the pancreas, breast, lung, and gastrointestinal tract. It is overexpressed and aberrantly glycosylated in malignant cells. It is a multifunctional protein involved in the protection of mucous membranes, signal transduction, and modulation of the immune system. More than seventy percent of cancers overexpress MUC-1, making this antigen a potential target for immunotherapy.

Conclusion: Also, carcinoembryonic antigen (CEA) is a 180-kDa glycoprotein that is overexpressed in a wide range of carcinomas, including colorectal, gastric, pancreatic, non-small cell lung, and breast carcinomas. The Tn, TF, and sialyl-Tn (STn) antigens represent the immature glycosylation products of serine and threonine of the protein core and are naturally masked by the complete glycosylate chain. All 3 epitopes are strongly expressed on cancer cells and may be associated with disease progression and metastasis. Additionally, the Wilms' tumor gene (WT1) was initially identified in sporadic

and hereditary cases of Wilms' tumor as being either mutated or overexpressed, and WT1 is involved in cell growth regulation or differentiation.

Keywords: Antigen- Breast Cancer

Twin-to-twin blood transfusion syndrome (Review)

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Introduction: Twin-to-twin blood transfusion syndrome Embryos are monochorionic, which are unequally nourished and oxygenated by common blood vessels. Vascular grafts and superficial and deep anastomosis are formed, which cause arterial-venous flow imbalance. The donor is wrinkled with an empty and small bladder And the recipient is edematous and the bladder is dilated, causing the amnion to increase. types of anastomosis There are 3 types 1-Artery to artery (AA): There are 37% pairs of ttts, it has less resistance, and they correct the balance (AA and VV are bilateral and by creating an intertwined pressure gradient, they transfer blood in two directions) 2-Venous to venous (VV): It is seen in 32% of TTTS pairs.And it may have a special role in creating this syndrome. They are flexible and located deep in the tissue. AA anastomoses can compensate for unbalanced flow through AV.

Methods: TTTS staging In general, TTTS is divided into 5 stages based on the findings of two-dimensional ultrasound and Doppler velocimetry in the umbilical artery, as well as QUINTERO criteria: • First stage: Evidence of oligohydramnios/polyhydramnios sequence in sonography • Second stage: lack of visualization of the bladder of the donor embryo • Third stage: Abnormal Doppler of umbilical artery or venosus in one or both twins • The fourth stage: presence of hydrops In the first stage, pathological symptoms are not shown. The first and second stages are related to the evaluation of the donor (not the evaluation of the recipient). Because if the recipient with hydrops (stage 4) and the donor with visible edema (stage 1) are presented according to this classification, we will have a confusion syndrome (treatment of the recipient with the most invasive method, treatment of the donor with the least invasive method)

Results: Solomon's method In this method, to eliminate the remaining anastomosis, the entire equator of the vessels is destroyed. In addition to coagulating all the vessels and creating a cannula, a thin line of tissue is coagulated on the surface of the placenta, to connect the selected erosion sites from edge to edge. Complications)Grade 2 necrotizing enterocolitis, stage 3 retinopathy of prematurity, amniotic band syndrome (are reduced by 8% with Solomon's method. However, a small percentage of remaining anastomosIs may reappear as recurrent TTTS and TAPS. In Solomon's method, the rate of separation of the placenta is higher, but survival is better,And the probability of premature rupture of the membrane is higher.

Solomon's method needs more studies. Solomon's neonatal outcomes: intraventricular hemorrhage, dysplasia, bronchopulmonary (BPD), transient tachypnea of the newborn (TTN) BMI was measured at the start of treatment. It probably increases due to polyhydramnios and deserves to be considered as a risk factor. Septostomy This method creates a hole with a balloon so that the amniotic fluid is evenly distributed between the twins.

Conclusion: Twin anemia polycythemia sequence (TAPS) In two fetuses with a common placenta on the surface, their blood circulation is connected. The imbalance of blood exchange is due to TTTS and TAPS. TAPS: It happens after the 26th week. Occurs in 50% of monochorionic pregnancies. Appears 1 to 5 weeks after laser treatment It is associated with the development of chronic anemia in the donor and chronic polycythemia involved. in 2-13% of TTTS pregnancies occur after laser treatment. Neutropenia and decreased levels of hemoglobin, albumin and total protein have been reported in the donor. The absolute leukocyte level does not differ between the recipient and the donor, but there are fewer neutrophils in the donor. Reticulocytosis and increased erythropoiesis in TAPS donors are more than TTTS, therefore TAPS is associated with intrauterine growth restriction. TTTS and TAPS both have blood imbalances But in TTTS, a volume change is seen, which is to correct the incompatibility of hemoglobin. TTTS and TAPS are two distinct pathologies We expect TTTS to start with TAPS first. IATROGENIC MONOAMNIOTIC TWINS (IMAT) Iatrogenic perforation of the membrane occurs after laser treatment with a probability of 20%.

Keywords: TTTS Anastomosis Solomon Amnio Redaction Photoscopic laser occlusion Premature labor Monochorionic

Umbilical Cord Blood (Review)

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Introduction: Umbilical cord blood (UCB) is an accessible source of hematopoietic stem cells (HSCs) with the ability of self-renewing and differentiation into all blood cells. Along with the advantages, UCB also has limitations: the low volume and the absolute number of HSCs available in UCB leading to the delayed engraftment. Given the limitations, many investigators have sought to accelerate engraftment and increase the absolute number of stem cells in UCB units.

Methods: n the present study more than 200 published articles about UCB were reviewed untill 2020.This review article is aimed to focus on the importance of using cord blood, and ex vivo expansion techniques of UCB HSB. Also in this review article has been used some related keywords, includingUmbilical Cord Blood, Stem Cells, and Cord Blood Stem Cell Transplantation that were collected from reliable databases, including Google Scholar, PubMed, Scopus, and Elsevier. Among potential candidates, those which were the most relevant to the purposes of the study were selected and evaluated.

Results: UCB HSCs possess higher proliferative potentials and contain a higher proportion of primitive compartment as compared to bone marrow and peripheral blood. Several studies have reported the presence of different cell populations besides HSCs in cord blood that enable the use of these sources in immunotherapy, tissue engineering, and regenerative medicine. Thus, the strategies to isolate and expand selected subpopulations from UCB and the use of these cells in treatment of various diseases are the areas of active research.

Conclusion: Umbilical cord blood is an attractive source in both research and modern clinical applications providinh a potentially useful alternative for patients who do not have an HLA-matched bone marrow donor. Besides the safety and feasibility of UCB, the other areas including the acceleration of the engraftment, the extension of access, the quality assurance, and the outcomes in the specific subgroups of patients are also required to be investigated.

Keywords: Umbilical Cord Blood, Stem Cells, Cord Blood Stem Cell Transplantation.

Understanding Charcot-Marie-Tooth Through CRISPR/Cas9-Mediated Gene Editing (Review)

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Introduction: A diverse collection of hereditary illnesses known as Charcot-Marie-Tooth (CMT) disease manifests as a chronic, progressive neuropathy that impairs both the motor and sensory neurons. Autosomal dominant is the most prevalent inheritance pattern, while there are X-linked and autosomal recessive variants. A multitude of genes are linked to CMT, demonstrating the variability of this condition, in addition to a range of inheritance patterns.

Methods: This review focuses on the usage of CRISPR/Cas9 as a genome editing tool in in vivo and in vitro CMT models in order to have a better comprehension of current developments in CRISPR/Cas9-mediated genome editing and how they might be used to treat CMT.

Results: CRISPR/Cas9 can shed light on the pathophysiology and underlying genetics of CMT since it has been used to compare the phenotypes of patient-derived and gene-corrected induced pluripotent stem cells (iPSCs) and to confirm the impact of CMT-related mutations in animal models and patient-derived iPSCs.

Conclusion: The pathophysiology of CMT has also been studied using this technique to produce mutations. Here, we bring current research that makes use of CRISPR/Cas9 to comprehend the genetic foundations of CMT.

Keywords: Charcot-Marie-Tooth(CMT); CRISPR/Cas9; induced pluripotent stem cells (iPSCs); gene correction

Update of the cancer-associated molecular mechanisms in oral lichen planu (Review)

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Introduction: Lichen planus (LP) is a common chronic inflammatory disease that can affect the skin and mucous membranes, including the oral mucosa.The World Health Organization (WHO) has defined OLP as a potentially malignant disorder that represents a general condition with a significant increase. This disease affects 0.5 to 2.2% of the population and is more common in women than men. Although the usual age of presentation is 30 to 60 years, it is more common in middle-aged women and young men. In children, OLP is uncommon and usually presents with skin disease, and only 17% of patients with OLP recover completely, but recovery has been reported in 39%. Various risk factors have been implicated, such as smoking, immunosuppressive agents, chronic inflammation, certain viruses, accumulation of genetic mutations, and a diet low in vegetables and fresh fruits.This disorder is further considered as a multifactorial process with various stimuli including mechanical, electrochemical and since OLP is an immune-related disorder, stress and anxiety and other related factors. The immune system can be one of the causes of this disease.But the exact cause of OLP has not yet been discovered, and unfortunately, reliable results cannot be obtained from clinical studies of OLP, and this is not due to the lack of other studies, but due to the lack of an accepted standard in diagnosis.The aim of this study is to investigate the molecular mechanism related to cancer in oral lichen planus.

Methods: In this review article, the required data was collected by using keywords, referring to reliable databases such as ProQuest, Scopus, PubMed and Google Scholar. Our statistical population consists of all studies conducted until 2022.

Results: Considers have appeared that OLP happens through specific and non-specific antigenic mechanisms. In antigen-specific mechanisms, antigen-based keratinocytes and antigen-specific keratinocytes are destroyed by CD8 cytotoxic T lymphocytes. In non-specific mechanisms,mast cells are

granulated and matrix metalloproteinases are activated in OLP lesions. Epidemiological distribution of lesions is different in each geographical region . Identification of new non-invasive biomarkers is a rapid way to detect disease in early stages. Antioxidant supplements such as vitamin C and E have a good effect in preventing this type of cancer. Using string software, a method was designed to identify genes related to diseases and disease interactions, which showed that CDKN1A and p53 interact with OLP. According to immunohistochemical studies, higher bcl2 expression in OLP-associated lymphocytes serves as a suspicious marker.Disruption in the G1 phase of the cell cycle creates a high potential in the development of OLP malignancy. The increased expression of NF kappaB in OLP is related to the level of inflammation and cytotoxicity.Also, MMPS in OLP is associated with the basal zone disorder process and keratinocyte death and T cell migration.

Conclusion: Many researches have been done in the field of pathology and treatment of OLP. Within the show consider, we attempted to outline both pathologic and restorative accomplishments in this issue with respect to the noteworthiness of biomarkers for OLP determination, OLP connection with other illnesses,and more successful medications on OLP. It has moreover been suggested to screen, within the spit of OLP patients,the NF kappaB-related cytokines TNF-a, IL-1,IL-6 and IL-8, as markers of illness seriousness and possible harmful change.

Keywords: Lichen Planus, Neoplasms, Molecular mechanisms

Use of microRNA strategy for targeting oncolytic viruses to cancer cells (Review)

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Introduction: Cancer, as one of the most serious public health problems, is the second-leading cause of death in the world after cardiovascular disease. The number of patients and mortality are increasing worldwide; therefore, early diagnosis, prevention, and effective treatment of cancer are very important. Current treatments such as chemotherapy and radiation therapy are often non-selective and have side effects. The use of oncolytic viruses (viral therapy) is a new approach to treating cancer. One problem with viral therapy is the lack of selective replication for the virus in cancer cells, meaning that the virus replicates in normal cells. In recent years, various methods have been used to inhibit virus replication in healthy cells and to make selective replication in tumors. Correspondingly, miRNA targeting is the newest method. The present study describes the different aspects of making selectivity for replication of oncolytic viruses by the miRNA targeting mechanism.

Methods: We searched PubMed, web of science, Scopus, google scholar and ProQuest databases to find articles which were used from microRNA strategy for targeting oncolytic viruses to cancer cells. All articles were collected, studied and analyzed by two researchers.

Results: Adenovirus type 5 is targeted to pancreatic cancer cells by insertion of 8 copies of miR-148a and miR-216a target sequences to the viral genome. Oncolytic adenovirus type 5 is targeted to breast cancer cells by microRNA-145 and to hepatocarcinoma by microRNA-199, microRNA-143, microRNA-148a and microRNA- let-7. Four copies of miR-122 complementary sequences were inserted at E1A gene of adenovirus 6 to target it toward liver cancer cells. Six miR-124 target sequences were introduced to genome of oncolytic Semilki Forest Virus for increasing its selectivity. microRNA target sequences complementary to miR-124, miR-125, miR-133 and miR-208 were inserted into the Mengovirus genome to make a more selective virus. A let-7 MicroRNA-sensitive vesicular stomatitis virus showed tumor-specific replication. Inserting target sequences of miR-122, miR-7 and miR-148a to measles virus genome could target it to pancreatic cancer cells. miRNA-145

regulated oncolytic herpes simplex virus-1 (HSV-1) selectivly was killed human non-small cell lung cancer cells. MicroRNA modification of Coxsackievirus B3 (miR-145/miR-143) was decreased its toxicity, while retaining oncolytic potency against lung cancer.

Conclusion: microRNA targeting strategy is an acceptable method for attenuation of oncolytic viruses in normal cells and for increasing selective replication in tumor cells. This strategy can be used to make a more specific oncolytic virus that only targets cancer cells.

Keywords: microRNA, oncolytic viruses, cancer

Use of phage display technique for vaccine production (Review)

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Introduction: Conventional vaccines mainly originate from bacteria or viruses and have been commonly used in the disease prevention. Phage display technology is a unique gene recombination expression technology, and it is also a simple and effective screening tool. Phage display technology is a unique gene recombination expression technology, and it is also a simple and effective screening tool.

Methods: According to the articles read, Bacteriophages or phages are viruses that specifically infect bacteria and use the cellular machinery to create more phage proteins and eventually release new phage particles. The genome of these viral particles can be harnessed for DNA vaccination, or the surface proteins can be exploited for antigen display. More specifically, genes that encode an antigen of interest can be spliced into the phage genome, allowing antigenic proteins or peptides to be displayed by fusion to phage capsid proteins. Therefore, phages present antigens to immune cells in a regular and repetitive manner.

Results: It is now confirmed that phage display system can play a pivotal role in a wide areas of researches including development of antibody fragments, affinity maturation of antibodies, vaccines development, peptide drugs, and catalytic antibodies production. With this inspiring technology, mechanisms of many diseases can be investigated, which may lead to development and improvement of diagnostic methods and therapies.

Conclusion: This review discusses the use of phage with adjuvant activity as an antigen delivery vehicle for vaccination against infectious diseases, antibody production, cancer, and autoimmune diseases. Phages are heavily used in bioengineering for various applications ranging from tissue engineering scaffolds to immune signal transduction.

Keywords: Bacteriophages, Phage, Vaccination, Phage display, Antibody production

use of targeting peptides for cancer detection and drug delivery (Review)

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Introduction: The use of peptide and protein sequences in the treatment of cancer, as well as the transfer of drugs related to it, is a new method that has led researchers to focus their research from old treatment methods to the mentioned method. Surgery, as the first step in cancer treatment in the 19th century, cannot always be an effective way to completely remove cancer. Invasive tumors. Radiation therapy is another treatment that can extensively remove localized tumors and has been used since the 1960s. But it causes damage to normal tissues and even in combination with surgery, it cannot control metastatic disease. Intravenous cytotoxic chemotherapy has been the hallmark of medical cancer treatment for decades, targeting rapidly dividing cells. The main challenge of the pharmaceutical industry is its non-specific distribution. The use of chemotherapy drugs in the human body leads to acute toxicity against normal tissues with a higher proliferation rate, such as hair follicles, bone marrow, and digestive tissues, and thus limits treatment. Peptides have emerged as an attractive therapeutic tool due to their broad biological activity, high membrane permeability, and low manufacturing costs. new research has provided various therapeutic peptides, many of which are undergoing clinical trials.The current treatments against cancer are relatively good treatment methods, but the efficiency and the amount of risk that the patient faces in using these methods , It forces researchers to look for cheaper and more efficient methods and reduce the risk of treatment methods for the patient. This method is the strategy of using transporters such as nanoparticles, a method that due to their size and other physical and chemical properties are able to accumulate in tumors by passing through the gap in the endothelial cells covering the vascular wall. "Leaky" vessels around tumors for drug delivery is known as a permeability effect and represents a therapeutic modality.

Methods: This systematic study was mentioned using key words and referring to reliable scientific databases such as Scopus, PubMed, Google Scholar and ProQuest from the studies that were conducted until 2022 and a total of 16 articles were reviewed.

Results: Since 1988, two types of peptides have been discovered that have the ability to stimulate cells in the treatment process : peptide conjugation with nanoparticles and cell-penetrating peptides alone, those are the two cases. Short peptides increase the permeability of cells to the tumor . Cell-penetrating peptides can be converted into conjugated nanoparticles through short sequences of peptide linkers to create more functionality on polymeric nanoparticles, lipid nanoparticles or drug treatments.

Conclusion: Compared to proteins and antibodies, they are significantly less immunogenic and more stable at room temperature. Conjugation of cell-penetrating peptides with other nanoparticulate systems can enhance chemotherapy delivery. Additional advantages of using peptides as targeting agents include lower production costs, increased efficiency For the penetration of tumor masses, high stability and high adjustability. Target peptides, specificity Drug delivery systems to target tumors and cancer cells enhance absorption It increases drugs in cancer cells . Target peptides increase the specificity of drug delivery systems for targeting tumors and cancer cells, increase the absorption of drugs in cancer cells, and minimize the effects of the target.

Keywords: Peptides, neoplasms, drug delivery

Using in silico methods for designing novel aptameric ligands against therapeutic proteins (Review)

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Introduction: Aptamers are single-stranded DNA or RNA structures that interact with specified targets with a high affinity. A wide range of targets, including whole cells of different organisms, inorganic materials, large biomolecules (proteins, peptides, lipids, even other nucleic acids) have been considered for aptamer development. Among them, protein targets are of great importance in medicine due to the value of proteins activities in health and pathogenesis of disease. Selection of aptamers through experimental effort using Systematic Evolution of Ligands by EXponential enrichment (SELEX) or non-SELEX process are time and cost consuming. Therefore, using computational methods for in silico design of aptameric ligands has become an interesting field of research in this regard.

Methods: The publication of Science Direct and PubMed as well as Google Scholar was searched using keywords of “aptamer” AND “protein” AND “in silico design” OR “computational design”.

Results: There an increasing numbers of reports using molecular docking and molecular modelling (MD) simulations methods or using methods based on machine learning and artificial intelligence in the design and prediction of specific aptamers against protein targets, in recent years. Although using these strategies is time- and cost-saving, however, the results of in silico design do not have essentially shown similar potent in vitro or in vivo affinity and activity.

Conclusion: In this review, we discussed different methods have been reported for in silico aptamer design against protein targets, so far; and discussed about their cons and pros.

Keywords: Aptamer, Nucleic acids, Protein, In silico, Design

Using Lyapunov stability theory and artificial neural networks to create a facial beauty evaluation model (Research Paper)

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Introduction: In this research, using the images available in social networks, we classified only the faces in terms of similarity using image processing and classified them into 30 classes. Then we invited 230 people to rate these faces on the web application. In this software, we established each person's 30 images; it related each image to a class of the relevant classification, and people gave each image a score from 1 to 10. Images were re-classified using the received scores and Lyapunov stability theory, and users were asked to participate in the survey again. The results of the first and second surveys were entered into the artificial neural network and the neural network was able to classify the faces in terms of beauty with 95.8% accuracy. The created model can be evaluated before cosmetic surgery.

Methods: To analyze the images of faces, we used the OpenCV image processing library, and we also used parameters such as facial redness, the width of lips and mouth, and the length ratios of the facial parts as biasing of the artificial neural network. Then our neural network analyzed the statistical data collected from the surveys with the Reinforcement Learning method and Lyapunov's stability function was used to adjust the neural network.

Results: Using the neural network trained using the results of the first survey, we evaluated the dataset related to the images of faces and compared the results with the second survey, the success of the neural network was 66.4%, again the neural network using the theory Lyapunov's stability has been toned down and beauty criteria such as facial symmetry, dividing the width of the face into five parts and comparing the width of each part with the width of the eyes, comparing the ratio of the eyebrow distance to the hairline and the distance between the eyebrow and the end of the snout as well as the distance between the bottom of the nose and Chin is added as a bias parameter to the artificial neural network. This time, the artificial neural network was able to classify faces in terms of beauty with 95.8% accuracy compared to the survey.

Conclusion: By using Lyapunov stability theory and simple parameters, we can build an artificial neural network that can rate the beauty of people's faces and use it to help cosmetic surgeons in planning and designing facial cosmetic surgeries.

Keywords: Artificial neural network, facial beauty, Lyapunov stability theory, cosmetic surgery, facial beauty

Using the anticancer potential of pediococcus probiotic in the diagnosis and treatment of colorectal cancer (Research Paper)

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Introduction: Colorectal cancer is one of the most common and most diagnosed cancers in the world. There are many predisposing factors, for example, genetic predisposition, smoking, or a diet rich in red, processed meat and poor in vegetables and fruits. Probiotics may be helpful in the prevention of cancer and may provide support during treatment. The main aim of this study is to characterize the potential mechanisms of action of probiotics, in particular the prevention and treatment of colorectal cancer. Probiotics' potential mechanisms of action are, for example, modification of intestinal microbiota, improvement of colonic physicochemical conditions, production of anticancerogenic and antioxidant metabolites against carcinogenesis, a decrease in intestinal inflammation, and the production of harmful enzymes. The prevention of colorectal cancer is associated with favorable quantitative and qualitative changes in the intestinal microbiota, as well as changes in metabolic activity and in the physicochemical conditions of the intestine. In addition, it is worth noting that the effect depends on the bacterial strain, as well as on the dose administered. Age, genetic and environmental factors play an important role in the development of colorectal cancer. Hereditary colorectal cancer syndromes include Lynch syndrome (hereditary non-polyposis colon cancer), familial adenomatous polyposis (FAP), MUTYH-associated polyposis (MAP).

Methods: Gram Staining The Gram staining of the isolate was determined by light microscopy using Gram staining reagents. It is known that LABs are gram-positive. This means that these cultures will produce blue-violet color for Grampositive bacteria and vice-versa. The cultures were grown in MRS media at 37 °C for 24 h under micro-aerophilic conditions. Fresh cultures were used for gram staining. After incubation, the cultures were aseptically transferred into 1.5 ml of eppendorf tubes and centrifuged for 3 min at 9000 rpm. The cells were resuspended in sterile water by removing the supernatant. Catalase test The catalase test was carried out on the isolates to see their reactions to catalase. To do this, two methods can be performed. 18 h

incubated cultures of isolates were grown on MRS agar at room temperature. Furthermore, for the catalase test fresh liquid cultures of LAB were used in which 3% hydrogen peroxide solution was added to 1 ml of cultures. Arginine hydrolysis test The arginine MRS modified medium and the Nessler reagent was used to view ammonia release from arginine. The freshly prepared 1% culture of the isolates was added into the MRS of 5 ml tubes containing 0.3% of L-arginine hydrochloride. The tubes were further incubated for 18 hours at 37 °C. After incubation, 50 µl of cultures were observed against the white background. 50 µl of the Nessler reagent was pipetted into the cultures and the change in the color was observed. The positive reaction was indicated by a bright orange color, while the yellow color determines the negative reaction. For the negative control, arginine free MRS was used Hemolysin production test Hemolysin production was detected using Columbia agar plates supplemented with 5% of sheep blood. The presence of α or β-hemolysis was assessed by the formation of clear or greenish zones around the colonies, respectively. Low pH and high bile salt concentration tolerance test The isolate was incubated in 5 mL MRP broth. The 24-h incubated cells were centrifuged at 2000 g for 10 min. The cell plates were suspended in PBS (pH 2.5), followed by incubation for 2 h at 37 C. The cells resistant to low pH were calculated by using the pour plate technique on MRS agar and compared with the isolates in normal PBS for 0 and 3 h. Each examination was conducted twice with three repetitions for each time. MRS broth medium supplemented with 0.3% Oxgall (Sigma, UK) was inoculated with active cultures (1% v/v) and incubated at 37˚C. Control consisted of MRS broth with the respective bile salt concentrations. Growth was monitored at 0 and 8 hours by recording absorbance at 650 nm. Calculation of coefficient of inhibition (Cinh) was performed via this formula: Formula Cinh = ΔT8-T0 Control – ΔT8 - T0 Treatment / ΔT8 - T0 Control Where, ΔT8 - T0 represents the difference in absorbance at time zero (T0) and after 8 hours (T8). Cinh of less than 0.4 is desirable. Heat-killed cells (HK cell) Overnight cultures of the strain was centrifuged (9000 g, 10 min, 4º C) to harvest bacterial cells mass. Next, the cells were washed twice with PBS buffer and resuspended in the buffer and heated at 95º C for 1 h. After that, the mixtures were lyophilized, and the 50mg of lyophilized cells mass were suspended in 1 mL cell culture medium. The prepared stocks were stored at 20º C until they were used in further experiments Cell-free supernatant (CFS) The CFS samples were provided by centrifuging overnight bacterial cultures (9000 g, 10 min, 4º C), lyophilizing the supernatant, and solving 50mg of them in 1 mL RPMI media. The final suspension was sterilized using 0.22mm Millipore filters. In a parallel path, to minimize the probable effects of organic acids, the pH of the CFS was adjusted to 7.4 by adding NaOH (1 M), which resulted in neutralized cell-free supernatant (NCFS). Assessment of cell viability using MTT assay CLORECTALcancer cell lines HT29 were seeded in a 96-well plate (1.5 × 104 cells/well) and incubated for 24 hours in standard conditions. The cells were treated with different concentrations of supernatant (25, 50, and 100 µg/ml)

and heat killed cells (25, 50, and 100 µg/ml) of of isolated strain for 24, 48, 72, and 96 hours. The cancer cell viability was evaluated using the MTT assay (Gibco, United States America).

Results: Conventional lab techniques The isolated strain was subjected to Gram staining and examined under a light microscope (100X magnification). The strain showed blue-purple color staining. Hence the isolated strain was found Gram-positive bacterium. According to our result the strain was recorded as catalase negative. Absence of hemolytic activity was also observed. The result of Arginine hydrolysis test showed that the isolated stain did not produce ammonia from arginine. Identification of Lactobacillus stain The result showed that the isolated strain belonged to genus Lactobacillus. The 16S rDNA gene sequence result showed that isolate had 99% homology with L.Pediococus MTT assay results The MTT assay result showed that the CFS of isolated strain in concentration of 100 µg/ml after 72 hours decreased the viability of HT29 cell line. The heat killed cells in concentration of 25 µg/ml after 72 hours decreased the viability of HT29 cell lines.

Conclusion: In the present study, the probiotic characteristics and anti-tumor activity of a human breast milk isolated Lactobacillus was investigated. Our results demonstrated that Lactobacillus strain exhibited many typical probiotic characteristics such as Gram staining (Gram-Positive Bacilli), higher survival rate under gastric conditions (lower pH), catalase-negative, L-Arginine test, Lack of hemolytic activity, Lack of Arginase activity. Despite the fact that this strain had most of the properties of probiotic bacteria, it did not show resistance to bile salts, and among the 6 antibiotics that were examined in this study, this strain was only resistant to gentamicin and sensitive to 5 other antibiotics. In the investigation of the effect of cell-free supernatant and killed cells of the isolated strain on the viability of two breast cancer cell lines, it was found that the cell-free supernatant of this strain had no effect on the viability of HT29 cell line but decreased the viability of HT29 cell line in concentration of 100 µg/ml after 72 hours. The heat killed cells of this strain (in concentration of 25 100 µg/ml after 2 h and 100 µg/ml after 48 hours) significantly reduced the viability of HT29cell line. In investigating the effect of killed cells on HT29cell line in all three concentrations (25, 50, and 100 µg/ml) after 2h the viability) significantly decreased.

Keywords: cancer- colorectal cancer - probiotic - Lactobacillus pediococcus- anti cancer

Vaccines are a sure way to treat diseases. (Review)

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1.

Introduction: One of the most important ways to prevent diseases is making and using vaccines. Vaccines contain information that is necessary for the body to build protective cells. In general, a vaccine is a biological substance designed to protect humans against infection caused by bacteria and viruses. Vaccines train the body's defense army to deal with strong pathogens.

Methods: This information has been collected by searching the internet and biomedical sites and reviewing various articles in this field and is presented in the form of a review article.

Results: In 1796, Edward Jenner invented a way to treat cow pox, in which the liquid in another blister was extracted and inoculated into another skin, this method is called hand inoculation. Vaccines are also called immunogenic because they use the power of the body's immune system to prevent infectious diseases. Common ingredients in making vaccines are antigen: an active component. Preservatives: To prevent contamination of the vaccine. Stabilizers: To prevent chemical reactions in the vaccine. Surfactants: to mix the ingredients in the vaccine and prevent it from settling. Residues: are substances that are added during vaccine production and are not effective in the complete vaccine. Diluent: It is used immediately before the vaccine to dilute the vaccine. Adjuvants: These substances keep the vaccine at the injection site to improve the immune response. One of the methods of making vaccines is live, weakened viruses: in this method, which is the most effective, live but weakened viruses are used. Like the corona vaccine. Inactive: In this method, killed viruses are used to produce vaccines. such as inactivated polio vaccine. Subunit: In this method, a part of the virus, such as the outer layer, is used to make a vaccine. Like hepatitis B vaccine. Conjugate: The purpose of producing this vaccine is to deal with bacterial pathogens that cannot be detected by the immune system, including T lymphocytes. Example, HIB vaccine. Toxoid: This vaccine uses inactive poison for immune response and possible elimination of diseases and contains inactive or killed poisons. Such as pertussis and diphtheria vaccine for children DTAP and adults TDAP.

Conclusion: We found that vaccines are one of the most important prevention factors and prepare the body for strong pathogens. These materials contain important information about viruses. Vaccines save about 3 million lives every year. And we also learned about the way and method of making vaccines.

Keywords: vaccine. Safety system. virus Pathogen. cell

Vaccines made for colorectal cancer based on recombinant proteins (Review)

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Introduction: Colorectal cancer (CRC) is the third most common cause of cancer death worldwide. It begins with the uncontrolled growth of cells, known as a polyp. The common treatments for CRC are chemotherapy, surgery, and radiotherapy. The common treatments are considered hazardous and invasive and have failed in distant metastasis; therefore, the need to introduce novel treatment strategies is well perceived. The current focus of many types of research is designing vaccines with the hope of triggering the immune system to attack cancer cells in a more effective, reliable, and safe manner. In recent decades, developing new cancer vaccines based on highly purified recombinant proteins and designing several clinical trials with vaccine therapy have been considered in colon cancer patients. In CRC patients, the use of recombinant protein vaccine is based on the identification and synthesis of peptides generally found in protein structures, which can induce TAA (tumor-associated antigens) or TSA-specific antitumor immune responses. These vaccines can trigger specific T cell responses and commonly have been used with adjuvants to improve immune responses against the tumor. However, developing vaccines based on recombinant proteins in the battle against colorectal cancers offers several advantages but will also face continued challenges.

Methods: This study was written based on searching PubMed, Web of Science, Scopus, and Google Scholar databases and scientific articles extracted from these databases. In addition, authoritative scientific books and studies published in international congresses were used.

Results: Colorectal cancer (CRC) begins with the uncontrolled growth of polyps on the inner lining of the rectum or colon that can become cancerous and lead to the development of metastasis. A unique aspect of cancer is its ability to survive in the presence of an immune system. One such method is immunotherapy. Immunotherapy consists of Immune Checkpoint Inhibitors, Monoclonal Antibodies, Immune System Modulators, and Cancer

Vaccines.The use of cancer vaccines is designed to trigger the intense response of the immune system to one or more tumor-specific antigens, which leads to a cytotoxic attack against cancer cells expressing these antigens. In recent decades, the development of new cancer vaccines based on highly purified recombinant proteins which can induce TAA or TSA-specific antitumor immune responses, and designing several clinical trials with vaccine therapy, have been taken into consideration in colon cancer patients. CRC cells express TAAs such as carcinoembryonic antigen (CEA), epidermal growth factor receptor (EGFR), squamous cell carcinoma antigen recognized by T cells 3 (SART3), Survivin-2B, p53, or mutated KRAS, which are potential targets for immunotherapy. The most commonly used protein markers are carcinoembryonic antigen (CEA) and CA19-9. If a cancer vaccine is to be developed against colorectal cancer, these two antigens need to be used. The proper choice of domains of the antigens and the construction of a new cancer antigen that can stimulate the immune system against colorectal cancer cells have a vital impact on the quality of the vaccine. Generally, there is a clear role for tumor-specific T-cell immunity in the final clinical outcome of colorectal cancer. Despite evidence that some current vaccines are able to induce strong antigen-specific immune responses in the absence of serious adverse events, there is hardly any evidence generated to demonstrate the clinical impact of these vaccines in patients with colorectal cancer.

Conclusion: Studies suggested that recombinant protein vaccine could induce B-cell and T-cell mediated immune responses, which are important for a protective vaccine against colorectal cancer. However, the development of peptide/protein vaccines in the battle against various human cancers holds great promise but also will face continued challenges.

Keywords: colorectal cancer, recombinant protein vaccine, recombinant subunit vaccines, Immunotherapy, cancer

Wearable biosensors for human fatigue diagnosis (Review)

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Introduction: After long-term high-intensity work, problems such as lack of concentration, fatigue, and suppression of the immune system occur, which reduce immunity, damage the nervous system, and slow alertness and coordination. This situation is summarized as fatigue. In addition, in manufacturing, physical fatigue is a challenging ergonomic/safety “issue” since it lowers productivity and increases the incidence of accidents. Therefore, physical fatigue should be controlled. Different measurement devices and techniques can be used to identify physical fatigue. Specially the wearable ones. Wearable biosensors are biosensing devices that can detect biomarkers accurately, instantly, and portable. In this field, Smart bracelets are popular today. While these wearables primarily monitor simple biometric signatures, new devices that can report human fitness levels by measuring molecular biomarkers are critical to human factor optimization in the commercial and DoD sectors.

Methods: In the upcoming systematic review, the required data were collected using keywords and also by using reliable databases such as PubMed, Scopus, ProQuest and Google Scholar. In this study, the statistical population includes all studies that have been conducted until 2022. After reviewing the relevant findings and also evaluating the quality of the data, 16 articles were analyzed.

Results: In the following we review 3 of new wearable biosensors: 1. wearable tear biosensors One of the biological fluid that can be exploited for monitoring physiological status is tears. Not only are the biomarker molecules in tears directly released from the blood and show close tear-blood concentration correlations, but tear analysis also offers opportunities for the diagnosis of ocular disease. Tears are also less complex than blood and are part of the eye's anti-fouling mechanism. These properties make human tears an attractive diagnostic biofluid for healthcare monitoring applications that can be sampled without contact with blood. Wearable tear biosensors have been widely developed; The first samples were flexible strip-like devices which have been developed by using other materials to be more flexible and comfortable for users. Despite solving the comfort issues of wearable tear

sensors, the possibility of eye diseases caused by the heating of the wireless transmission device should be considered. To prevent possible eye damage from wearable tear biosensors, the new ones ,that are frame-like, have been designed. This tear sensor are able to collect tears from the corners of eyes and could simultaneously detect glucose, vitamins, and extraocular tears via bioenzyme-substrate reaction without any direct contact with eyeball. 2. wearable saliva biosensors The direct passage of a large number of saliva biomarkers through intercellular or paracellular pathways allows us to use saliva to investigate the physiological state of the body, and this method is a non-invasive alternative to blood analysis. Therefore, saliva can be a "mirror of the human body". The prototype of wearable saliva biosensors was the traditional paperbased saliva test strips, which collected saliva from subjects. To achieve continuous monitoring, paper-based saliva test strips were replaced with wearable 3D-printed microfluidic paper-based silicone braces. However, the brace required repeated removal from mouth for colorimetric analysis, which limited the widespread applicability of the braces. To improve The creation of wearable electrochemical sensor "Brace" improved these bottlenecks. These biosensors could analyze amount of glucose, cortisol, lactic acid, uric acid and etc. 3. wearable epidermal biosensors Sweat is vigorously secreted to the skin surface during exercise and containing many biomarkers related to fatigue, and hence can be a satisfactory basis for fatigue diagnosis. For sweat analyzing, devices have been realized through direct transfer of sensors onto the (using E-skin or printed temporary tattoos), using sensors in wristbands and patches, or by embedding sensors directly into textiles to ensure firm contact with the skin while allowing the sensors to To withstand the mechanical pressures encountered during body movements. These sensors collect fatigue information by analyzing sweat’s biomarkers.

Conclusion: In conclusion, also these wearable biosensors are greatly high-tech, but they need to be more developed. For example, the fragility of wearable tear biosensors are hinder the widespread application by people who are prone to exercise fatigue, such as soldiers and athletes. And we have such these problems for the others. But these devises show considerable promise for noninvasive sensing of other physiologically important biomarkers.

Keywords: biosensors, fatigue, humans

White Blood Cell Membrane-Coated Nanoparticle (Review)

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Introduction: White blood cells (WBCs) are immune cells that play essential roles in critical diseases including cancers, infections, and inflammatory disorders. Their dynamic and diverse functions have inspired the development of WBC membrane-coated nanoparticles (denoted “WBC-NPs”), which are formed by fusing the plasma membranes of WBCs, such as macrophages, neutrophils, T cells, and natural killer cells, onto synthetic nanoparticle cores. Inheriting the entire source cell antigens, WBC-NPs act as source cell decoys and simulate their broad biointerfacing properties with intriguing therapeutic potentials. Herein, the recent development and medical applications of WBC-NPs focusing on four areas, including WBC-NPs as carriers for drug delivery, as countermeasures for biological neutralization, as nanovaccines for immune modulation, and as tools for the isolation of circulating tumor cells and fundamental research is reviewed. Overall, the recent development and studies of WBC-NPs have established the platform as versatile nanotherapeutics and tools with broad medical application potentials.

Methods: WBC-NPs As Carriers for Drug Delivery WBC-NPs As Countermeasures for Biological Neutralization WBC-NPs As Nanovaccines for Immune Modulation WBC-NPs As Tools for CTC Isolation and Fundamental Studies

Results: As the cell membrane-coating technology advances rapidly, additional engineering strategies can be applied to further de- velop WBC-NPs for even broader applications. For example, researchers have mixed membranes from different cell types and used them as coating materials to make cell membrane- coated nanoparticles with “hybrid” properties.

Conclusion: As the cell membrane-coating technology advances rapidly, additional engineering strategies can be applied to further de- velop WBC-NPs for even broader applications. For example, researchers have mixed membranes from different cell types and used them as coating materials to make cell membrane- coated nanoparticles with “hybrid” properties. It is anticipated that WBC-NPs will soon move toward clinical tests and play more significant roles in the field of biomedicine.

Keywords: WBCs Membrane/Nanoparticle/vaccine/Drug Delivery

Women with spina bifida and reproductive health (Review)

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Introduction: The term "spina bifida" (SB) means diseases caused by failure of the caudal neural tube in the fusion in the developing fetus, which is divided into three categories: open, occult (closed), and dysraphism. Lesions are usually in the lumbar and sacral regions, and higher lesions cause more severe disability and worse cognitive function. Myelomeningocele is the most severe and common form of SB. Myelomeningocele can lead to lifelong problems with mobility, sensation, urination, and bowel movements. The level of spinal deformity has a large impact on long-term survival rates. Advances in surgical techniques to repair defects associated with SB mean that more patients are now surviving to reproductive age and that there are no reports of decreased fertility. An increasing number are potentially pregnant.

Methods: The next systematic review of the studies conducted until 2022 was conducted using Scopus, PubMed, and Google Scholar databases, and among the collected articles corresponding to keywords, 21 articles were reviewed.

Results: Despite more women with SB seeking motherhood and more research on pregnancy in women with disabilities more broadly, little is known about the experiences of women with SB specifically in considering, planning, or experiencing pregnancy. However, the current literature on pregnancy in spina bifida is limited mainly to small case series that are specific to their obstetric outcomes. Even health care providers specializing in SB feel that they lack a basic understanding of the subject. Preconception counseling of women with SB is strongly recommended for those at or near childbearing age. Whether the risk of SB is related to the interaction between these genes, the presence of genes on the maternal or fetal genome, or the interaction of these genes with environmental factors is unclear. Daily intake of folic acid before pregnancy and during the first trimester of pregnancy significantly reduces the risk of fetal NTDs. During pregnancy, epilepsy management should optimize seizure control with the lowest and lowest dose of antiepileptic drugs (AEDs) and at the start of 5 mg of folic acid

supplementation. Diabetes mellitus is already an independent risk factor for the development of fetal malformations in the central nervous system. Urological abnormalities in patients with SB can be complex and are best managed by a urologist.

Conclusion: The results of this study show that women with SB do not have a good understanding of their potential and risks during pregnancy. Additionally, women's negative experiences with health care providers when discussing pregnancy goals and being pregnant highlight the urgent need to educate health care providers about fertility, pregnancy, and birth outcomes specific to women with spina bifida. The persistent stigma and discrimination that many women with disabilities face in discussing and pursuing their fertility goals must be addressed and its adverse impact on the quality of health care reduced. Women with SB who wish to become mothers through childbirth deserve what all women deserve.

Keywords: Spina Bifida, Women, Reproductive Health

Women's pregnancy with the method of ovulation biometry (Review)

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Introduction: Ovulation disorder is the main cause of female infertility. We investigated the use of continuous body temperature monitoring with a vaginal biosensor to improve standard diagnostic methods to indicate ovulation inefficiencies. Biphasic basal body temperature (BBT) rates during the menstrual cycle have been reported and studied since the early 1900s. As the body's core temperature during resting state, BBT is usually assessed by measuring oral, rectal, or vaginal temperature immediately after waking up and before any physical activity. BBT fluctuates in response to hormonal changes during the menstrual cycle for most women. A woman's BBT reaches its lowest point (nadir) in a certain process around her fertile window, just before ovulation and corresponding to the peak of estrogen. Therefore, we define the fertile case or the time frame in which conception can occur. Consequently, we describe the fertile window, or time frame in which vision may occur, as the five days closest to ovulation and the time of ovulation. The chance of getting pregnant again after ovulation is greatly reduced, which means that eggs can only survive for 12 to 24 hours without fertilization. Therefore, a decrease in BBT may indicate impending ovulation. After ovulation, a woman's BBT is usually boosted by increased progesterone levels.

Methods: In the forthcoming systematic review, the required data were collected using keywords and citing valid databases such as Scopus, PubMed, Google Scholar and ProQuest. The statistical population includes all studies conducted until 2022 in the field of Women's pregnancy with the method of ovulation biometry. After reviewing the relevant findings and evaluating the quality of the data, 15 articles were analyzed.

Results: the finding of ovulation Ovulation was detected in 47 women using cycle monitoring and promotion of progesterone levels to over five nmol/l, reconnoitering the luteal stage. Three women had anovulatory processes; no ovulation was found even after prolonged cycle monitoring with repeated controls. The luteal command was not repeated in one woman with delayed follicular maturation and, presumably, late ovulation. Due to the lack of data, it was impossible to distinguish luteinized unruptured follicle syndrome from luteal insufficiency in this woman. The short luteal phase was found in seven women, low progesterone levels in nine, and both values were unusual in three women. The temperature turns of women with signs of LPD demonstrate statistically considerable differences compared to the group of women with typical luteal phase processes.

Conclusion: Continuous body temperature monitoring with a vaginal biosensor can lessen the standard diagnostic procedures used to characterize ovulatory inefficient, especially if dysfunction is due to luteal phase deficiency and polycystic ovary syndrome.

Keywords: pregnancy, woman, ovulation, Biometry