Abstract

Background and purpose: With the increase in the rate of gastric cancer in the world and investigation of its causative factors, special attention has been paid to Helicobacter pylori. Helicobacter pylori is the first known carcinogen bacterial and one of the most successful human pathogens, because it is involved the more than half of the world's population. If it is not treated, colonization of this bacterium usually continues .An important feature of this bacterium is the production of large amounts of urease enzyme, which can be an important feature in the colonization of bacteria in the gastric mucosa and mucosal damage.Therefore, designing and identifying new compounds with the ability to inhibit this urease enzyme using virtual screening, can be a step forward in the treatment of this illness.

Materials and methods: In the present project, the crystal structure of the urease enzyme of Helicobacter pylori was obtained from Protein Data Bank (PDB:1e9y).Then, a library of 2043 chemical compounds based on 70% structural similarity to the tetrahydropyrimidine structure were obtained from PubChem databases. Various stages and filters of the virtual screening process were applied to the filtered compounds using PyRx 0.8 software and Molinspiration, SwissADME and admetSAR servers, and finally, the energy and interactions of the compounds were studied using Autodock 4.2 software.

Results: Among the compounds in the library, 1152 compounds with a more negative free binding energies than the monastrol structure were screened; then, 1010 compounds with appropriate drug-like properties were isolated. Then, the pharmacokinetic properties of the compounds were investigated and finally the free binding energies and interactions of the twenty compounds obtained from previous filtrations were performed using the molecular docking simulation method at the active site of the enzyme. The compounds CID_670699, CID_2830421, CID_787121 and CID_2794050, respectively, with free binding energies of -11.45, -10.81, -10.73 and -10.72 kcal/mol showed the highest free binding energy among all selected compounds.

Conclusion: In the recent study with the aim of identifying new compounds as possible inhibitors of the urease enzyme; the results of evaluating the interactions and examining the results of molecular docking showed that a number of important amino acids were involved in establishing hydrogen and hydrophobic interactions with the compounds, which are: Asn168, His221, Asp362, Gly279, His322 , Met366, Cys321, Gly367, Arg338 , Ala169 and Ala365. Among the bonds formed between these compounds and the enzyme's active site, the most important interaction was the hydrophobic bond and then hydrogen bond.

Key words: Helicobacter pylori, urease enzyme, virtual screening