Abstract

Introduction: The development of new drugs for MS is an urgent and unavoidable need, since the controling treatments impose a very high economic burden on society. On the other hand, the vast time and high cost of developing new drugs has led scientists to think about repurposing or reusing new drugs. since MS affects the central nervous system, In this study, a set consisting of approved drugs that affect CNS disorders were analysed using in silico docking and molecular dynamic techniques under qualitative and quantitative analysis of ligands binding into important and influential biological receptors in the course of MS disease (sphingosine-1 phosphate lyase, cyclophyline D, phosphoinositide-3-kinase gamma).

Methods: In this project, after drawing two-dimensional and three-dimensional structures of drug molecules by ChemDraw software and structural preparation of receptor macromolecules using AutoDock tools 1.5.6, molecular docking was done using AutoDock 4.2 software. Then, based on the application of Gibbs binding free energy threshold in each target receptor, a number of drug molecules were selected as stronger interacting agents to finally stabilize the superior complexes by simulating molecular dynamics in water by soft GROMACS 5.1.1 software and its algorithms should be examined.

Results and Discussion: Based on molecular docking calculations, the best binding free energy for Luracidone binded into PI3Kγ (ΔG_b = -11.91kcal / mol) and CypD (ΔG_b = -8.84 kcal / mol) receptors was calculated. Zuclopenthixol was also determined to be the best ligand for S1PL receptor with ΔG_b = -7.96 kcal / mol. The parameters RMSD, RMSF, Rg, intermolecular and intramolecular hydrogen bonds were also calculated by molecular dynamic studies, which showed the trend of minor changes in the stability of superior drug complexes in the simulated physiological environment of the body.

Conclusion: The results of molecular docking showed that the best drugs in terms of their ability to bind into the receptors studied for neuron inflammation are antipsychotic drugs. Luracidone and Zuclopenthixol were suggested in this study as new anti-inflammatory agents for new repurposed drugs OF MS. Molecular dynamic studies have shown that drug-receptor complexes, especially Luracidone, have good stability with their targets. Therefore, it can be concluded that in this category, there are drugs with high potential for binding to new inflammatory pathways that have higher capabilities in terms of virtual analysis than approved and available drugs on the market.

Keywords: MS, Drug Reporposing, Molecular docking, Molecular dynamics