Synthesis and Molecular Docking of 2-Methyl-5-nitro-1-(2-(halophenoxy)ethyl)-1*H*-imidazole Derivatives as Potential Biologically Active Agents

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Abstract

Introduction: Nowadays, due to many years of taking antibacterial, antifungal and antiprotozoal drugs, human has faced drug resistance. It is predicted that death caused by drug resistance will surpass the death from cancer in future. Therefore, studies done by world's pharmacy researchers have been extended to synthesis of new compounds which potentially influence micro-organisms and protozoa. One of the acceptable methods of medicinal chemistry researches is propagation of new molecules according to known previous structures. One of these structures is 5-nitro-2-methyl imidazole that is a component of some drugs such as Metronidazole, Tinidazole and Secnidazole. In the present study we propagated this molecule further and synthesized some of the new derivatives of this family. Subsequently, according to the previous reports for similar compounds and their ability to link to FabH enzyme, new structures were surveyed using molecular docking approaches.

Methods and Results: First, the compounds 5a-e were synthesized. The structures of synthesized compounds were determined by IR, ^{1}HNMR and ^{13}CNMR spectra. Then, the components were drawn in ChemDraw software. The structures were energetically optimized by Open Babel software and they were saved in AutoDock software as ligand with PDB format. Then the receptor structure (FabH) was obtained from Protein Data Bank (www.rcsb.org) and refined for docking simulation. AutoDock 4.2 software was applied for molecular docking approach.

Results: IR, ^{1}HNMR and ^{13}CNMR spectra indicated that all the derivatives were successfully synthesized in laboratory and they had an appropriate intermolecular binding energy upon docking modeling.

Conclusion: According to the docking results, all the synthesized derivatives were accommodated properly in the active site of FabH enzyme and they made hydrogen and hydrophobic bondings with the amino acids. Amongst the synthesized compounds, compound 5b showed the best inhibition activity against enzyme FabH due to its lowest ΔG and highest lipophilicity.

Keywords: Nitroimidazole derivatives, Synthesis, Molecular docking