

Molecular Docking of Amino Acid Analogues of Rimantidine

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M2 channel is a 97-residue single-pass membrane protein with its N- and C-termini directed toward the outside and inside of the virion, respectively; it is a homotetramer in its native state. The four TM helices form a channel in which His37 is the pH sensor and Trp41, the gate. The adamantane-based drugs, amantadine and rimantadine, which target the M2 channel, have been used as first-choice antiviral drugs against community outbreaks of influenza A viruses for many years, but resistance to the adamantanes has recently become widespread. To overcome this different analogues of rimantidine have been synthesized. The aim of this study is to predict the biological activity of amino acid analogues of rimantidine with a help of docking studies in order to synthesize only promising candidates. Twenty analogues of rimantidine with natural amino acids were used. Docking was performed with the M2 channel as it is very important in the replicative cycle of influenza A virus. Crystal structure of the channel was obtained from RCSB (PDB id: 2rlf). Docking was performed with GOLD 5.2 using GoldScore fitness function. The complexes of rimantidine analogues with M2 channel were analyzed and their total energies were calculated in Molegro Molecular Viewer. Total energy of the complex rimantidine/M2 channel is -29.437 kJ/mole. All complexes of amino acid analogues of rimantidine with the channel have lower energies, but the lowest are the energies of the complexes of Asn-Rim/M2 channel and His-Rim/M2 channel with -72.475 and -76.440 kJ/mole, respectively. From the energetically point of view complexes will be more stables. This means that all rimantidine analogues will block the M2 channel thus will affect the viral replication cycle. Docking studies are an useful tool for prediction of biological effect of different type of compounds and could be applied in shortening the drug design process.