Identification of a Potential Beta-site Amyloid Precursor Protein Cleaving Enzyme-1 Inhibitor as a Disease Modifying Agent for Alzheimer's Disease

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BETA-site amyloid precursor protein cleaving enzyme 1 (BACE1) has medical significance for forming a drug target to treat Alzheimer's disease (AD). The activity of BACE1 toward amyloid precursor protein (APP) generates the first factor of AD pathogenesis. Consequently, the inhibition of BACE1 is needed to block one of the earliest neuropathological hallmarks in AD. The current study aims to identify novel, potent, safe and selective BACE1 inhibitors and to validate their pharmacokinetics features. In order to inhibit BACE1, virtual screening was performed into a library of drugs using Maestro software. The pharmacokinetics features of the best hit drug from virtual screening were assessed using the SwissADME tool. Then to assess the stability of inhibitor in the binding pocket of BACE1, molecular dynamic (MD) simulation was performed using the Desmond program. A total of 1615 Food and Drug Administration (FDA) approved drugs were screened on BACE1, of which Iohexol was the most effective among the examined drugs due to its best glide score (-11.534 kcal/mol). Furthermore, ADMET profiling tests showed that Iohexol is of low toxicity rate and is unlikely to cause adverse side effects. As stated in the MD simulation results, the interaction of Iohexol and BACE1 is considerably stable. Overall, BACE1 was successfully inhibited using Iohexol, which was non-toxic or did not cause adverse side-effects. The next step is to apply this novel inhibitor in vitro, in vivo, and run clinical trials to identify it as a drug treatment for AD.

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