In silico STUDY OF THE BINDING AFFINITIES OF ACETYLCHOLINESTERASE AND SYNTHETICALLY VIABLE COUMARIN ANALOGS

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Acetylcholinesterase (AChE) is a serine hydrolase that is responsible for the hydrolysis of acetylcholine-a neurotransmitter associated with the transmission of nerve impulses. The reversible inhibition of AChE can be useful in combatting Alzheimer's disease (AD). A computational study of the inhibition of AChE was conducted by Molecular Docking using a series of synthetically viable coumarin analogs generated by a program called Autogrow 3.0 using the parent structure as 7-hydroxy-5-methyl-4-(phenoxymethyl)-2H-chromen-2-one. Each of the generated structures were subjected to an energy minimization via Spartan version 14 programme, the level of theory being B3LYP/6-31G**. The drugs rivastigmine and tacrine were used as reference molecules.The docking software used was AutodockVina, with the crystal structure bearing the PDB ID- 1GQR as the receptor. Out of the 20 ligands investigated 6 of the ligands, namely, C18, C3, C1, C17, C8 and C2 were calculated to have binding affinities of -10.0, -9.5, -9.2, -9.2,-9.2 and -9.0 kJ/mol respectively, all of which are higher in value than the values for those of the two standard drugs, rivastigmine and tacrine, which have values of -7.9 and -8.9 kJ/mol respectively. In addition to this, 9 more ligands showed binding affinities that lay between the range of the two commercial drug molecules used as references. These were- C16, C6, C12, C10, C20, C15, C5, C7 and C14, which showed the values -8.8, -8.8, -8.7, -8.5, -8.4, -8.3, -8.3,-8.2 and -8.0 kJ/mol. Given these evidences, these two groups appear to have the most likely chance of being effective drug candidates for treating Alzheimer's disease.

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