Abstract

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Clinical Pharmacology and Toxicology Journal

2022
Vol6.No.1

Computational Analysis of Beta Carbolines Targeting Acetylcholinesterase Enzyme for Therapeutic Use in Alzheimer's

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Abstract

This study revolves around therapeutic importance of natural alkaloids known as beta carbolines. Beta carboline belongs to a group of indole alkaloids and consist of pyridine ring that is fused to an indole skeleton. These alkaloids serve as the most promising candidates for the inhibition of acetylcholinesterase and can be used in the treatment of Alzheimer's disease. A detailed computational analysis of beta carboline alkaloids with acetylcholinesterase has been carried out using Molecular Docking method.

To accomplish the task, a ligand dataset of simple derivatives of beta carboline is constructed that includes Huperzine A, Galantamine, norharmane, Tryptoline, Pinoline, Harmane, Harmine and Harmaline. The 3D structure of acetylcholinesterase has been used as a receptor. The identification of binding site is a crucial step in validation of computational docking results. So, the crystal structure of acetylcholinesterase complexed with huperzine A (PDB ID: 4EY5) was retrieved from Protein Data Bank (PDB) as a reference to identify the binding residues. As huperzine A is an alkaloid possessing acetylcholine inhibition properties, its interaction with selected acetylcholinesterase residues could serve as binding pocket of the receptor. So, the binding site residues of this complex were analyzed using 2D interaction diagram via Ligplot. The residues involved in the interaction of crystallized structure of acetylcholinesterase with huperzine are Tyr133, Tyr119, Gly120, Gly126, Gly122, Ser125, Tyr337, Gly121, Tyr124, His447, Trp86, Ser203, Glu202. To verify the interacting residues, acetylcholinesterase was detached from huperzine A and again redocked.

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Received: April 05, 2022 Accepted: April 16, 2022 Published: April 28, 2022

Biography

Muhammad Sibte Hasan Mahmood received his MBBS degree from Rawalpindi Medical College in Pakistan. He has worked as a physician in Pakistan for various health care providers. Since moving to Canada in 2015, he has focused more attention to research and study trials. Working with renowned researchers in various medical fields either under direct or indirect supervisions has offered invaluable experience and learning. His main areas of focus has been drug mechanics and therapeutic modelling. He strives to achieve a long lasting impact in the field of clinical and pharmacologic research and development.