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MOLECULAR DOCKING COMPLEX PIRACETAM.

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Abstract

Piracetam improves the function of the neurotransmitter acetylcholine muscarinic cholinergic receptors, which are implicated in memory process. Among the possible therapeutic interventions, 2-pyrrolidine derivatives such as piracetam and related nootropics are currently used for their facilitatory effects in learning and memory in animal models.

Introduction

Piracetam (2-oxo-1-pyrrolidineacetamide) is a cyclic derivative of GABA and in the groups of racetams. Numerous positive individual studies supported the use of piracetam in people suffering from a wide range of cognitive disorders [1]. Piracetam has been studied in an extensive number of clinical experiments, and has shown positive results in the treatment of post-stroke aphasia, epilepsy, congnitive decline following heart and brain surgery, dementia and myoclones [2,3]. Piracetam improves the function of the neurotransmitter acetylcholine muscarinic cholinergic receptors, which are implicated in memory processes. Among the possible therapeutic interventions, 2-pyrrolidine derivatives such as piracetam and related nootropics are currently used for their facilitatory effects in learning and memory in animal models [4].

Molecular docking.Molecular docking is a computational technique used to predict the preferred orientation and binding affinity of one molecule (typically a small molecule, such as a drug) to a target molecule (usually a protein or nucleic acid). It is a vital tool in drug discovery, biochemistry, and structural biology as it helps in

understanding how ligands (small molecules, peptides, or drugs) interact with biological macromolecules.

Molecular docking is a computational technique used in the field of computational chemistry to predict the preferred orientation of one molecule to a second when they are bound to each other to form a stable complex. This technique is widely used in drug design and discovery, as it helps in understanding the interaction between a small molecule (ligand) and a protein target (receptor).

During molecular docking, the ligand is typically a potential drug molecule, and the receptor is a target protein involved in a disease process. The goal of molecular docking is to predict the most favorable binding mode of the ligand within the binding site of the receptor. This information can help in designing new drugs or optimizing existing ones to enhance their binding affinity and specificity.

Molecular docking algorithms evaluate the interactions between the ligand and receptor, such as hydrogen bonding, van der Waals forces, and electrostatic interactions. By calculating the binding energy between the ligand and receptor in different conformations, researchers can identify the most promising drug candidates for further experimental validation.

For determine possible antitumor, antibacterial and antifungal activities of 2HBA, pirocetam and its complex with Cu(II) molecular docking studies have been carried out. For these purpose interactions of 3N-4ABA and its Cu-complex with the KDM4 (PDB ID: 7JM5), E.Coli (PDB ID: 6F86), S.aureus (PDB ID: 1JIJ) and C.albicans (PDB ID: 2QZX) proteins studied by the CB-Dock2 server. The KDM4 histone lysine demethylase family has recently emerged as a target for tumor therapy . X-Ray determined structures of the KDM4 (PDB ID: 7JM5), E.Coli (PDB ID: 6F86), S.aureus (PDB ID: 1JIJ) and C.albicans (PDB ID: 2QZX) were obtained from protein data bank (PDB data bank) and prepared for docking investigations using BIOVIA DS Visualizer . The structure of the ligand 3N-4ABA and Cu-complex are converted to pdb file from cif files.

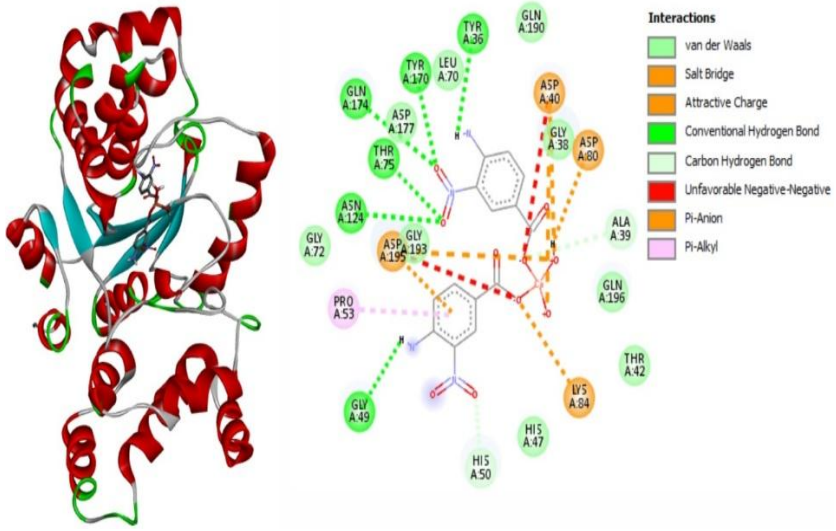

Figure 1. Cu-complex in the active center of the S.aureus protein (1JIJ) (left) and contacting amino acid residues

There are several reviews in the literature devoted to the biological activities of coordination compounds and it has been found that metal complexes exhibit higher biological activity than ligands. Therefore, preliminary analysis of the biological activity of coordination compounds is of great interest for submitting the compound for pharmacological studies. The molecular docking method is a convenient in silico approach for predicting possible biological activity by studying the interaction of a complex with specific proteins . Obtained results of interaction of ligand 2HBA and its copper complex with target proteins (1JIJ, 2QZX, 6F86 and 7JM5) are given.

The table data shows a higher activity of the complex compared to the ligand molecule in the case of all target proteins. Based on the binding energy, it can be assumed that the complex has good antitumor activity with binding energy of -9.2 kkal/mol because it fits well in the active site of the 1JIJ protein and has H-bond contacts with GLY49, TYR36, THR75, ASN124, TYR170 and GLN174 amino acid residues (Fig.7) and enhanced antibacterial activity against S.aureus with binding energy of -9.6 kkal/mol which makes very promising of the synthesized complex for further biological tests.

References

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