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In Silico Evaluation of the Anti-Diabetic Potential of Quercetin from *Macaranga peltata*

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Abstract

Molecular docking studies have become an essential tool in drug discovery, facilitating the identification of potential drug candidates through computational methods. This study focuses on *in silico* molecular docking of phytoconstituents from *Macaranga peltata*, particularly - Quercetin, for their potential anti-diabetic activity. Using AutoDock Vina within PyRx software, the binding interactions of these compounds with diabetes-related receptors 1HIT and 1HIQ were analyzed. The docking results suggest a strong binding affinity, indicating their potential as therapeutic agents. These findings highlight the significance of computational approaches in natural product-based drug discovery, reducing the reliance on animal models and enhancing the rational design of novel drugs.

Keywords: Docking, Quercetin, Anti-diabetic, Ligand, sdf mol format.

INTRODUCTION

In silico studies are playing an ever-increasing role in drug discovery that are critical in the cost-effective identification of promising drug candidates. These computational methods are relevant in limiting the use of animal models in pharmacological research, for aiding the rational design of novel and safe drug candidates. Molecular docking is the most common method which has been widely used for the structure-based drug design. Molecular docking tries to predict the molecular interaction between ligand and target macromolecules. Molecular docking is used to positioning the computer-generated 3D structure of small ligands into a receptor structure in a variety of orientations, conformations, and positions. Docking studies are proved to be the best tool to investigate the level of interaction at the molecular level between the compounds of natural and synthetic origin and potential target. This method is useful in drug discovery and medicinal chemistry providing insights into molecular recognition. The docking based virtual screening approach was performed by using Auto dock VINA implicated in the PyRx 0.8 tools and visualized using PyMOL. PyRx is software used to screen libraries of compounds against potential drug targets. PyMOL has been widely used for 3D visualization of macromolecules and it becomes one of the most popular tools for preparing high- resolution images of macromolecules [1-6].

AIMS OF MOLECULAR DOCKING

- To give a prediction of the ligand-receptor complex structure using computation methods.
- To predict the predominant binding mode of a ligand with a protein of known three- dimensional structure.
- To limit the use of animal models in pharmacological research, for aiding the rational design of novel and safe drug candidates

STEPS INVOLVED IN THE DOCKING STUDY OF LEAD COMPOUNDS

Step 1: Ligand preparation

The chemical structure of the compound was obtained from open chemistry database PubChem. The chemical structures of the compound were downloaded in the 3D conformer format and then converted to sdf mol format. Finally, the input format prepared as pdb ligand format and can be visualized in Open babel.

Step 2: Protein preparation

The target macromolecules or proteins can be determined and their respective 3D structure was downloaded from Protein Data Bank. The protein is downloaded in their crystal structure and after protein processing it was converted to the input format.

Step 3: Protein processing

Protein structure processing / refinement of protein include removal of hydrogens, water molecules, heteroatoms and bound ligands if any.

Step 4: Docking analysis

Docking analysis was done by Auto dock Vina Program in PyRx software. For this installed Auto dock tools (Python 2.7.1, MGL tools l.5.4 and Open babel) and PyRx. Installed Auto dock tools (Python 2.7.1, MGL tools 1.5.4 and Open babel) and PyRx.

Procedure:

- Opened PyRx→ File Load molecule → Open protein and ligand in PyRx window.
- Right click on ligand→ Autodock → Make ligand.
- Right click on protein → Auto dock → Make macromolecule.
- Vina wizard→ Start button→ Forward [In this step a grid box (white box with spherical handles) appears in the 3D scene. The grid box allows to select search space (Part of the protein, where are going to perform docking, typically the binding site) in the protein] →Maximize→ Forward [7,8].

Step 5: Molecular visualization

PyMOL is software used for the protein preparation and molecular visualization. It produces high quality 3D images of protein.

RESULTS

In silico* docking study of *Macaranga peltata

In silico docking studies facilitates interactions among the components in a system and mathematical and computed models are established and predict the interaction between ligand and target molecules.

From various literature reviews founded that *Macaranga peltata* whole plant possess flavonoid i.e. Quercetin which has the ability to produce anti-diabetic activities [9]. Quercetin shows binding affinity with 1HIT, 1HIQ receptors.

Figure No 1 and 2 shows the docking images of Quercetin with receptors 1HIT, 1HIQ respectively.

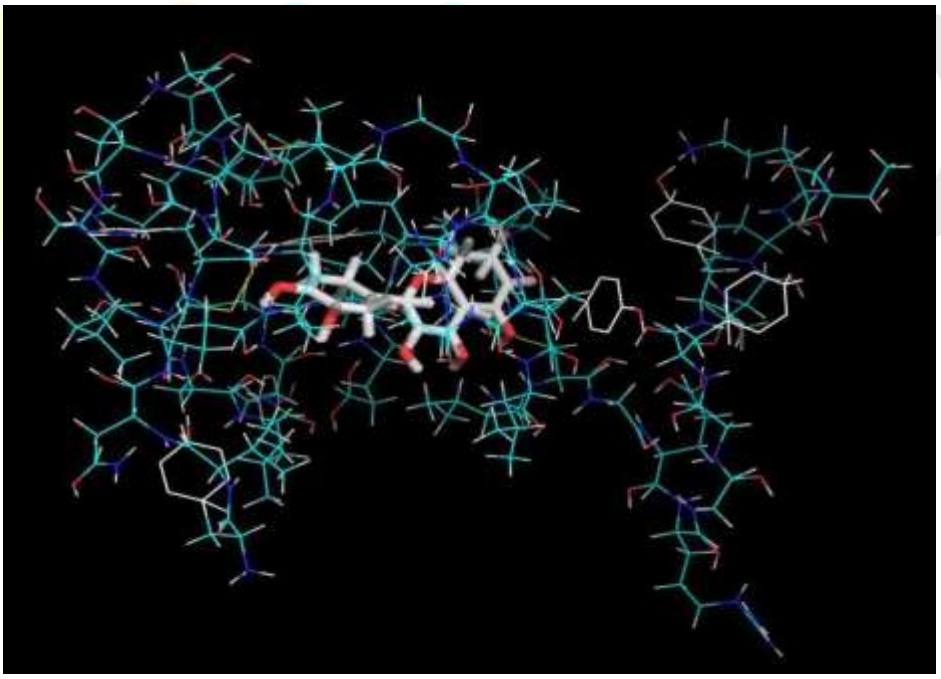

Figure No 1: Docking image of quercetin with receptor 1HIT

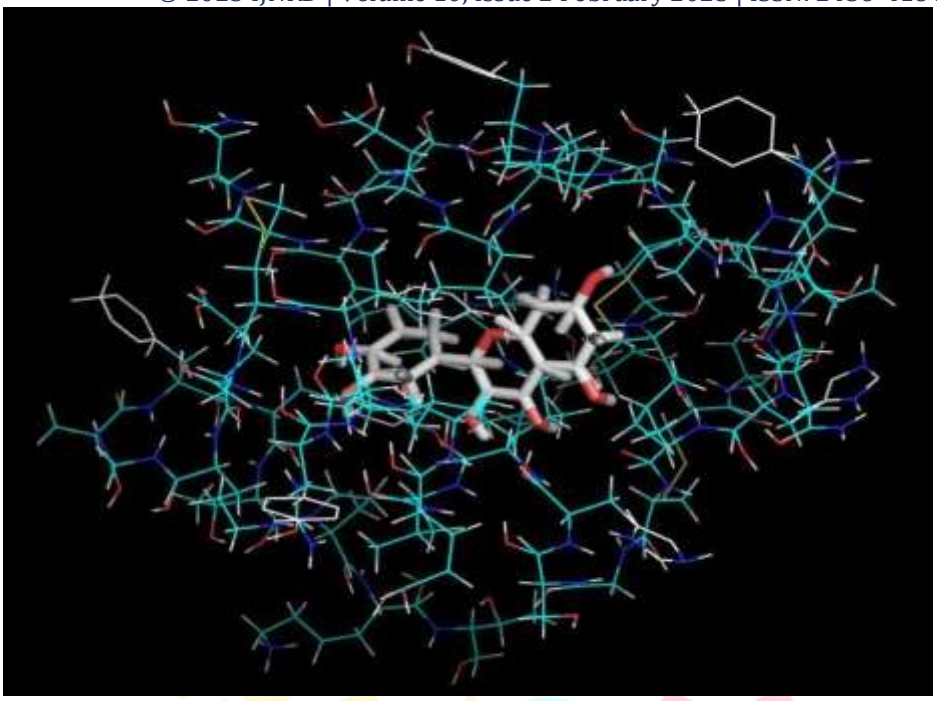

Figure No 2: Docking image of quercetin with receptor 1HIQ

LIGAND	RECEPTOR	NUMBER OF HYDROGEN BOND INTERACTIONS	BINDING AFFINITY (KCAL/MOL)
Quercetin	1HIT	3	-6.2
	1HIQ	5	-6.4

Table No 1: Hydrogen bond interaction and binding affinity of Quercetin.

CONCLUSION

The *in silico* molecular docking study of *Macaranga peltata* phytoconstituents, particularly Quercetin, demonstrated strong binding affinity with diabetes-related receptors 1HIT and 1HIQ, suggesting potential anti-diabetic activity. The docking results indicated multiple hydrogen bond interactions and favorable binding energy (-6.2 kcal/mol for 1HIT and -6.4 kcal/mol for 1HIQ), supporting its role as a promising lead compound for diabetes treatment.

These findings reinforce the importance of computational drug discovery in identifying natural compounds with therapeutic potential, reducing reliance on animal models, and guiding further *in vitro* and *in vivo* studies for drug development. Further investigations, including pharmacokinetic and toxicity assessments, are needed to validate Quercetin's efficacy and safety as an anti-diabetic agent.

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