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

Gowri Krishna K S*[1], Bhagath K L[2], Gokul Raj R S[3], Savitha Mol G M[4], Divya S Nair[5], Kiran K J[6], Prasobh G R[6]

1,2,3 Students, Eight Semester B Pharm, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India-695502.

4 Associate Professor, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India-695502.

5 Assistant Professor, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India-695502.

6 Vice Principal, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India-695502.

7 Principal, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India-695502.

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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 insilico molecular docking of phyto constituents from Macarangapeltata, particularly Rhamnetin, for their potential anti-diabetic activity. Using Auto Dock Vina within PyRx software, the binding interactions of these compounds with diabetes-related receptors 1 HIT and 1 HIQ were analyzed. The docking results suggest a strong binding affinity, indicating their potential as the rapeutic agents. These findings high light 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, Macaranga peltata, Anti-diabetic, Lead molecule, sdf mol format.

I. 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 Autodock 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

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STEPS INVOLVED IN THE DOCKING STUDY OF LEAD COMPOUNDS

Step1: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 sdfmol format. Finally, the input format prepared as pdb ligand format and can be visualized in Open babel.

Step2: 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.

Step3: Protein processing

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

Step4: Docking analysis

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

II. RESULTS

In silico docking study of Macarangapeltata

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 flavonoids i.e. Rhamnetin which has the ability to produce anti-diabetic activities[9].Rhamnetin shows binding affinity with 1HIT, 1HIQ receptors.

Figure No1.1and1.2 shows the docking images of Rhamnetin with receptors1HIT,1HIQ respectively.

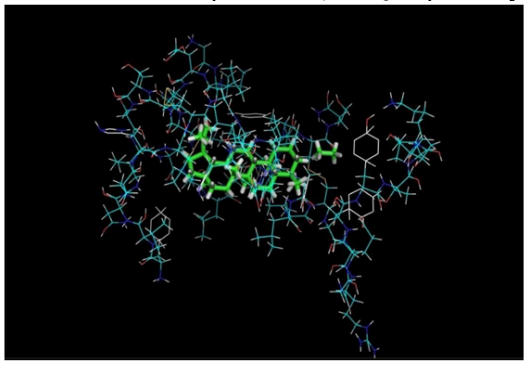

Figure No 5.1.3.3: Docking image of Rhamnetin with receptor1HIT

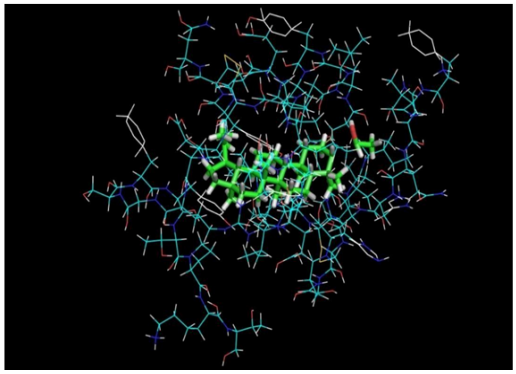

Figure No 5.1.3.4:Docking image of Rhamnetin with receptor 1HIQ

Ligand	Receptor	Number Of Hydrogenbond Interactions	Binding Affinity (Kcal/Mol)
Rhamnetin	1HIT	6	-7.9
	1HIQ	3	-6.8

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

CONCLUSION

The *in silico* molecular docking study of *Macaranga peltata* phytoconstituents, particularly Rhamnetin, 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 (-7.9 kcal/mol for 1HIT and -6.8 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 Rhamnetin's efficacy and safety as an anti-diabetic agent.

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