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Molecular Docking and Insilico Study of Selected Phytoconstituents of GuilandinaBonduc

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ABSTRACT : The hallmark of diabetes mellitus, a long-term metabolic disease, is hyperglycemia brought on by deficiencies in either insulin action or secretion, or both. The investigation of phytoconstituents obtained from medicinal plants has resulted from the search for new and potent antidiabetic medicines. Significant pharmacological actions, including possible antidiabetic effects, have been found for the traditional medicinal herb Guilandinabonduc.

In order to assess the binding associations of specific phytoconstituents from Guilandinabonduc with important target enzymes implicated in diabetes control, including α-amylase, α-glucosidase, and dipeptidyl peptidase-4 (DPP-4), this work used molecular docking and in silico molecular docking studies to evaluate the stability, interaction patterns, and binding affinity of the ligand-protein complexes. The pharmacokinetic characteristics and drug-likeness of the chosen compounds were further assessed using ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) predictions. We have also studied the standard compound and carry the comparative study of reference compound or phytoconstituent with standard compound and final resultwas the reference molecule shows better activity than standard molecule.

KEYWORDS: Guilandinabonduc, Molecular docking, Anti diabetic, Comparative study standard molecule

I. INTRODUCTION

The metabolic disease known as diabetes mellitus (DM) is typified by persistently high blood sugar levels brought on by either inadequate insulin synthesis, impaired insulin action, or both. A serious public health concern is the alarming rate at which the prevalence of diabetes has been increasing worldwide. The drawbacks of traditional antidiabetic medications, such as insulin secretagogues, insulin sensitizers, and enzyme inhibitors, include side effects, exorbitant prices, and decreased patient adherence.

Therefore, research into natural substances that may have antidiabetic effects is becoming more and more popular.Bioactive chemicals for therapeutic uses have been abundant in medicinal plants. Many pharmacological characteristics, such as anti-inflammatory, antimalarial, antioxidant, and antidiabetic actions, have been identified for Guilandinabonduc (L.), a well-known medicinal plant in traditional medicine. Guilandinabonduc's bioactive phytoconstituents may be essential for regulating important glucose metabolism-related enzymes such α-amylase, α-glucosidase, and dipeptidyl peptidase-4 (DPP-4), which are targeted in the treatment of diabetes.

Potential bioactive chemicals can be effectively and economically screened against certain protein targets using molecular docking and in silico research. Prior to in vitro and in vivo validation, these computational methods enable the prediction of binding affinities, interaction processes, and pharmacokinetic characteristics of bioactive substances.

Chemical Constituent :

The antidiabetic activity of Guilandinabonduc is due to its rich composition of bioactive phytoconstituents found in significant percentages. By altering important enzymes involved in the metabolism of carbohydrates, flavonoids (about 2–5%), alkaloids (1–3%), and tannins (3–6%) found in the seeds are known to have glucose-lowering properties. Gallic acid and quercetin (2–4%), two phenolic substances, are strong antioxidants that lower oxidative stress, a key

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contributor to the development of diabetes. Additionally, the plant includes glycosides (2–3%) and saponins (1–2%), which improve glucose absorption and support insulin-mimetic activity.

These findings demonstrate the potential of Guilandinabonduc phytochemicals in the development of natural antidiabetic therapeutics. Fatty acids like oleic acid and linoleic acid (10–15%) and phytosterols like β-sitosterol (0.5–1%) support lipid metabolism and insulin sensitivity. Together, these constituents help to inhibit α-amylase and α-glucosidase enzymes, lower postprandial glucose levels, and improve pancreatic β-cell function.

Drug Design :

Drug design is the process of finding and creating new pharmaceutical compounds with therapeutic potential. It uses computational and experimental methods to create molecules that can interact with particular biomolecules, like enzymes or receptors, to modify their activity in order to treat diseases.

Introduction of Docking:

In drug discovery, docking is a computer-based technique that forecasts how a tiny chemical (ligand) will attach to a target protein. It aids researchers in comprehending how medications interact with biological molecules, which is crucial for creating novel medications. Like a key fitting into a protein, docking involves fitting a ligand into the protein's active site and determining how effectively they attach.

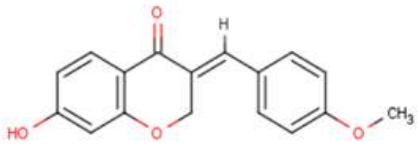
For molecular docking, a number of software applications are utilized, including Discovery Studio, AutoDock, AutoDock Vina, and Molecular Operating Environment Schrödinger Glide. Prior to laboratory testing, these techniques assist researchers in identifying possible drug candidates by analyzing the intensity and stability of drug-target interactions. Because it saves time and money while searching for new medications, docking is essential to modern drug design.

A type of computer modeling of complexes that are created when two or more molecules interact is called molecular docking. Based on the binding characteristics of the participating ligand and target molecules, it forecasts the three-dimensional structure of adducts. The software of the molecular docking tool uses a scoring mechanism to rank and group the various potential candidate structures that are produced by molecular docking. Docking models forecast the ideal docked conformer based on the system's overall energy. This article presents several computational features of molecular docking in relation to its types and techniques

.

Preparation of Ligand:

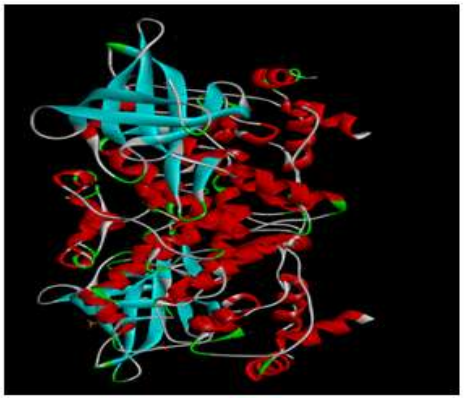
A ligand structure was drawn on Marvin sketch application and saved in Mol2 format



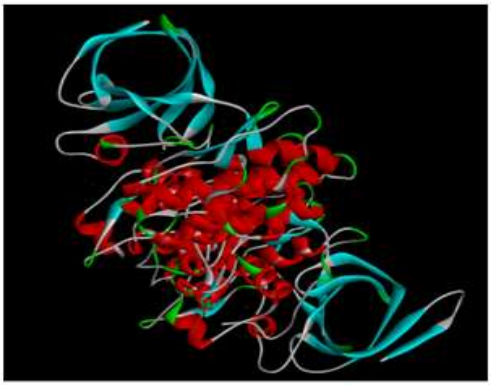
Structure of ligand molecule

Preparation of Protein:

Open the PDB file of the protein i.e.1gng, 1i09 in Discovery Studio. When the file is open, press CTRL+ H. This shows the side panel containing the components of the PDB structure.



Protein 1gng



Protein 1i09

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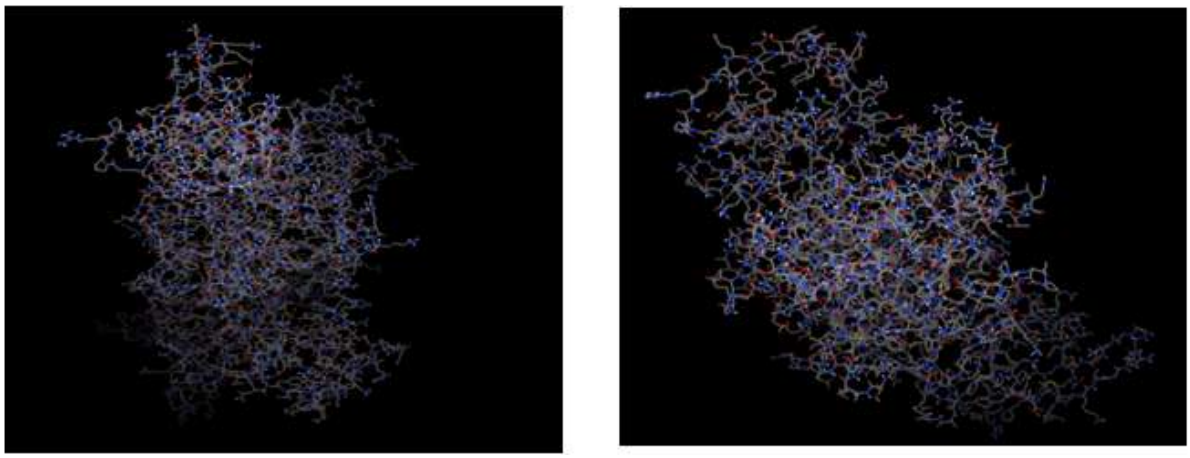
Preparation of Grid:

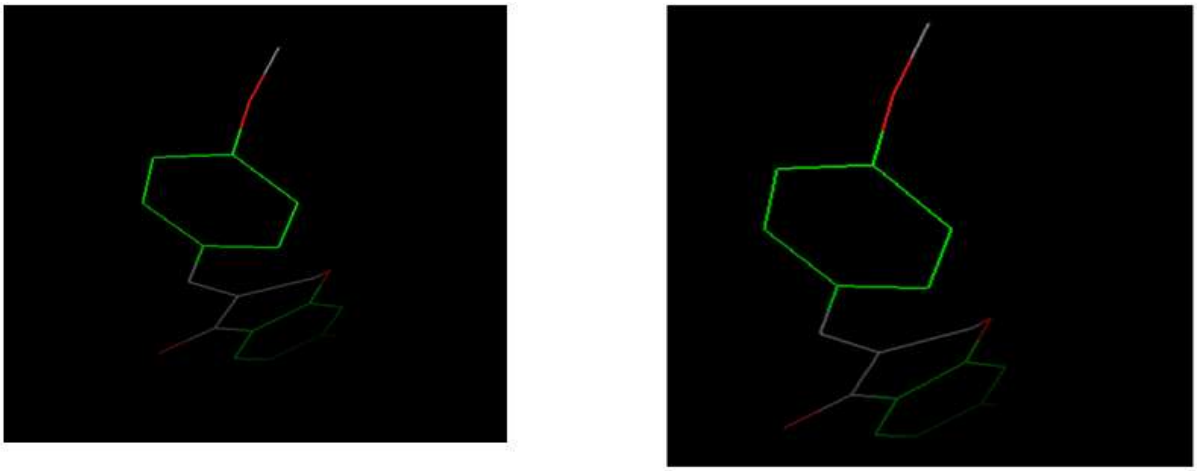
The protein file1gng_H.pdb was opened in AutoDock. The atoms ACH Cl Br I F SP HD N NAOA were added. In the "number of points in x, y and z dimensions", slide to 60, 60 and 60 respectively. The grid file saves as output 1gng.gpf, 1i09.gpf.



Preparation of grid

Preparation of Docking:

For the preparation of the docking parameter file (DPF), click on Docking > Macromolecule> Set rigid filament> Open in the ADT window to open the target PDBQT



Preparation of docking

Executing the commands for Docking:

Type the following command for running autogrid (Note: Change the protein name accordingly) 'autogrid4.exe–p1gng.gpf– l 1gng.glg'Wait until it shows 'complete' and then enter the following command for running Auto Dock. (Note: Change the ligand name accordingly) 'autodock4.exe–p bonducellin. DPF –l bonducellin. DLG' Wait until it shows complete

Docking Analysis (RMSD Table)

Enter the Run which had minimum binding energy and maximum rank from the 'RMSDTABLE' i.e. Change RUN from'1' to a desired RUN value and press Enter. Check the Conformation Info window to see if ligand is interacting with the receptor.

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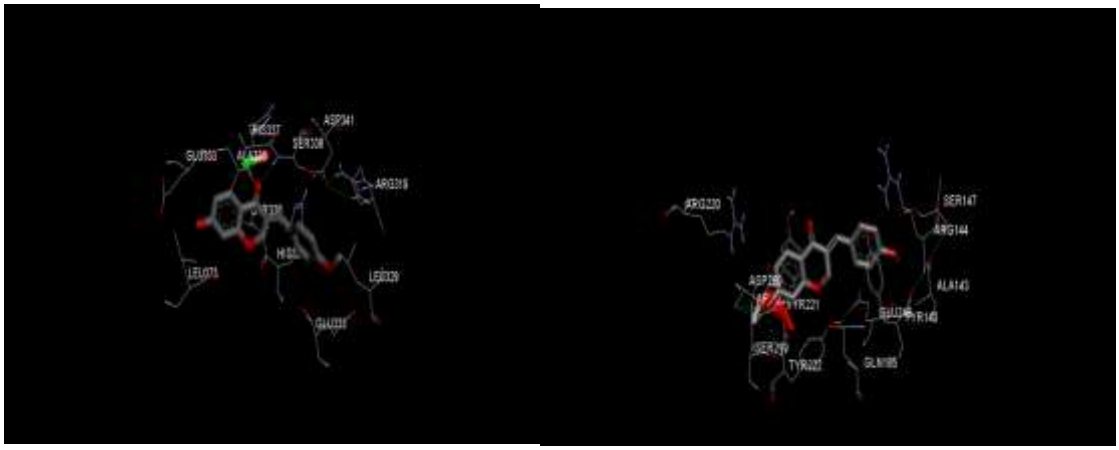
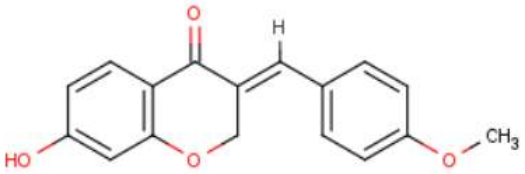
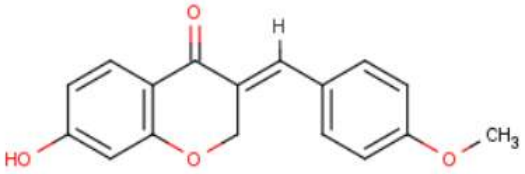
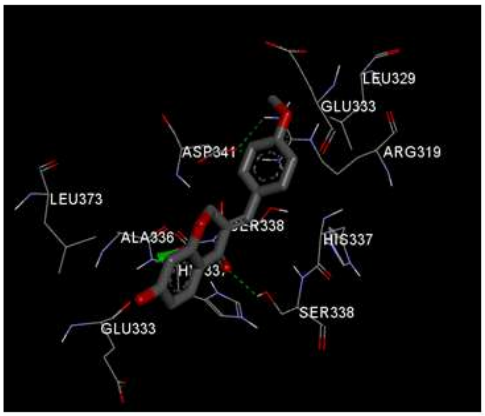
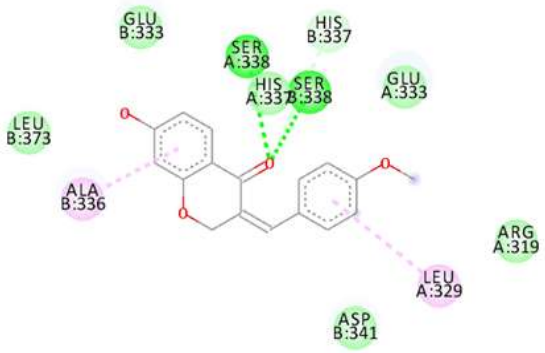


Figure 6 : Docked molecule from drug discovery

II. RESULTS AND DISCUSSION :

Sr. no	Binding energy	Structure
Str. Bonducellin Protein name : 1gng	-8.00	
Str. Bonducellin Protein name : 1i09	-7.50	





3D Image and 2D image of Docked molecule (protein 1gng)

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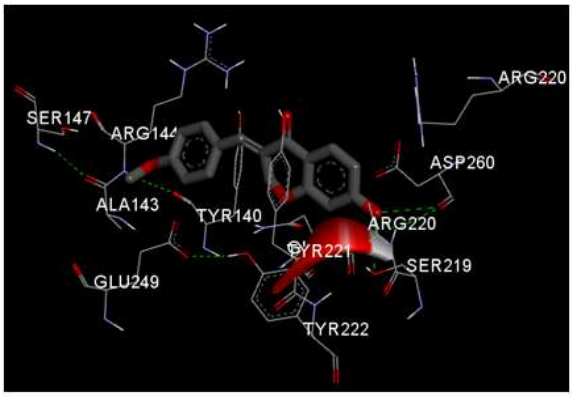
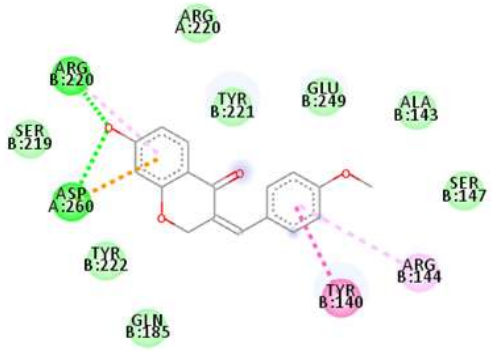
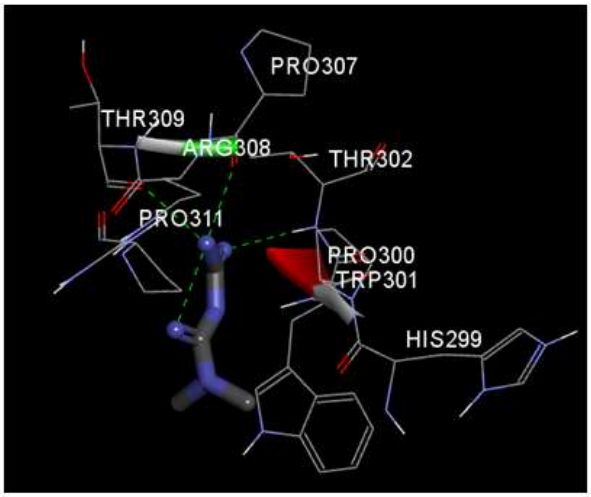
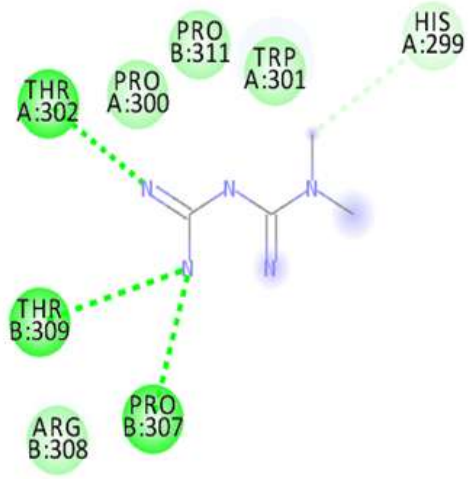


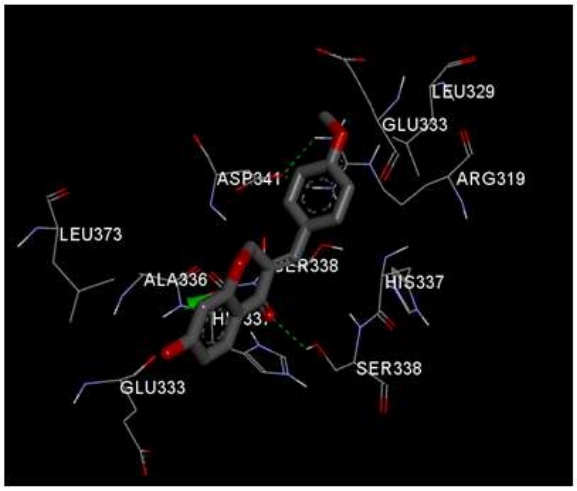


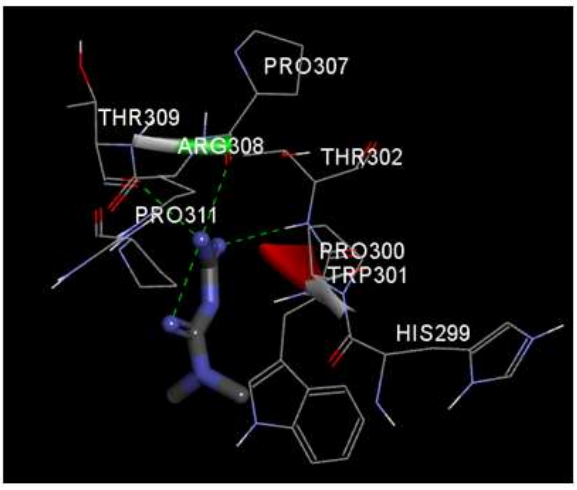
3D Image and 2D image of Docked molecule (protein 1i09)





Compare with standard compound Metformin





Compare with reference and standard compund

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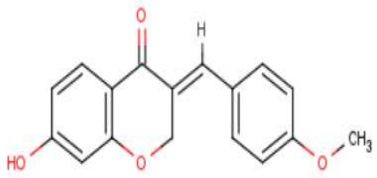
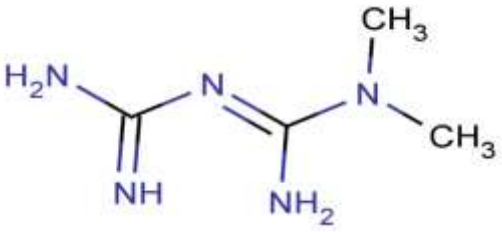
	Bonducellin	Metformin
structure		
Binding energy	-8.00	-5.42

ADMET Properties :

Sr. no	Ligand	Mol.weight	Log-p	carcinogenicity	Water solubilty
1	Str. bonducellin	282.29 g/mol	2.71	0.6628	-3.74

III. CONCLUSION:

From the Rscbprotein Data Bank, a protein PDB 1gng was chosen for binding. The molecules with the lowest binding have greater efficacy, according to the results of molecular docking. It also showed that the key amino acids interact well with the designed compounds through hydrogen bonds. In order to determine which chemical or ligands had a higher binding energy than the others, a docking analysis of the compounds was conducted. It was discovered that the compounds interacted with protein 1gng. Therefore, since bonducellin is the primary phytoconstituent that lowers blood sugar levels, we can conclude that the synthesized compounds have the potential for further development as antidiabetic agents.Additionally, we examined the standard chemical and conducted a comparative analysis between it and the reference compound or phytoconstituent. The end conclusion was that the reference molecule exhibited greater activity than the standard molecule.

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