World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Review Article
ISSN: 2583-6579
SJIF Impact Factor: 5.111
Year - 2025
Volume: 4; Issue: 2
Page: 35-41

A REVIEW ARTICLE OF DOCKING STUDIES ON ANTIDIABETIC AGENT BY USING AUTODOCK

Subramaniam P.*, Velmurugan S., Vignesh Raj S., Vikram Prasath K., Sangameswaran B., Vaijayanthimala P.

SSM College of Pharmacy, Jambai, Erode.
The Tamilnadu Dr. MGR Medical University, Chennai.

Article Received: 03 February 2025 | | ***Article Revised: 25 February 2025*** | | ***Article Accepted: 18 March 2025***

Corresponding Author: Subramaniam P.
SSM College of Pharmacy, Jambai, Erode, The Tamilnadu Dr. MGR Medical University, Chennai.
DOI: https://doi.org/10.5281/zenodo.15109035

How to cite this Article: Subramaniam P., Velmurugan S., Vignesh Raj S., Vikram Prasath K., Sangameswaran B., Vaijayanthimala P. (2025). A REVIEW ARTICLE OF DOCKING STUDIES ON ANTIDIABETIC AGENT BY USING AUTODOCK. World Journal of Pharmaceutical Science and Research, 4(2), 35-41. https://doi.org/10.5281/zenodo.15109035

ABSTRACT

Docking studies of molecules is a computational system widely used for unexpectedly predicting the binding modes and affinity of small molecules against the target molecules [normally protein &carbohydrate]. This in silico system has accomplished a function of great significance inside the drug discovery field. Autodock is a java script/web assembly library that runs popular software for molecular docking completely in a internet browser. Molecular docking has been dramatic growth in computer power has been into consideration as necessary device for CADD &biological studies of proven in the drug discovery methods. A running modes of the app may be accepted free of fees. We have proposed & designed the antidiabetic alpha glucosidace (enzyme) inhibitor of acarbose with complex of the receptor of alpha amylase B, for oral administration .the complex has been showed good activity during the molecular docking studies.

KEYWORD: Docking studies, Autodock, molecules.

INTRODUCTION

Diabetes mellitus is one of the most prevalent chronic diseases in global health care settings and the prevalence of diabetes is projected to increase. WHO believes that approximately 200 million people worldwide are struggling with diabetes today, and this number is expected to increase to 400 million by 2030.The majority of deaths that happen annually due to complications of diabetes are in middle-income nations, according to WHO.

Diabetes has two well-known categories under type being type one and type two. In one type, the body no longer produces insulin while in the other type insulin production is impaired and the hormone no longer functions as it should. Diabetes is otherwise managed by dieting, exercise, and the use of synthetic or natural drugs and leading a healthy lifestyle.

The cross-sectional, recently published cohort based ICMR-INDIAB national study estimates the burden of T2DM at 62.4 million, and prediabetes at 77 million in India. This will be raised to one hundred million by the year 2030. T2DM mainly impacts post menopausal women in developed country; conversely in developing countries particularly in India even young working adults are getting affected by T2DM, which is more disastrous for health care of such individuals.[1]

Type–2Diabetes mellitus

A complex metabolic disease of maintenance of normal blood glucose levels due to insulin resistance. Patients usually present an obese body constitution and clinical signs of a metabolic syndrome comprising diabetes, insulin resistance, hypertension, hypertriglyceridemia. Diabetes mellitus are complex as it can be brought about by lesions in any body organ, protein or enzyme. Because of the polyetiology of this disease, it is impossible to rely only on one experimental model and, at the same time, one treatment cannot avoid this multifactorial disease.[2]

Molecular Docking

Molecular docking is a kind of computational modeling, which facilitates the prediction of preferred binding orientation of one molecule (eg. ligand) to another (eg. Receptor), when both interact each other in order to form a stable complex.

Information gained from the preferred orientation of bound molecules may be employed to predict the energy profiling (such as binding free energy), strength and stability (like binding affinity and binding constant) of complexes. This can be done using scoring function of molecular docking.

Now days, molecular docking is often utilized to forecast the binding orientation of small molecules (drug candidates) to their biomolecular target (such as protein, carbohydrate and nucleic acid) with the aim to determine their tentative binding parameters. This establishes raw data for the rational drug designing (structure-based-drug development) of new agents with better efficacy and more specificity. The main objective of molecular docking is to attain an optimized docked conformer of both the interacting molecules in furtherance of achieving lessen free energy of the whole system.[3]

THEORY OF DOCKING

Essentially, the aim of molecular docking is to give a prediction of the ligand-receptor complex structure using computation methods. Molecular docking is to simulate the optimal conformation according to the complementarity and pre-organization, which could predict and obtain the binding affinity and interactive mode between ligand and receptor.

The firs proposed “lock-and-key model”, which refers to the rigid docking of receptors and ligands to find the correct orientation for the “key” to open up the “lock”. This model emphasizes the importance of geometric complementarity.[4]

AUTODOCK

The first version of AutoDock was distributed to over 35 sites around the world, and that number has since grown to over 600 sites with the latest versions of AutoDock. This user guide is the first version to accompany a significantly enhanced version of AutoDock, version 3.0, which includes powerful new search methods and a new empirical free energy function.

These structures could be targets for bioactive agents in the control of animal and plant diseases, or simply key to understanding of a fundamental aspect of biology.

The precise interaction of such agents or candidate molecules is important in the development process. Indeed, AutoDock can be a valuable tool in the x- ray structure determination process itself: given the electron density for a ligand, AutoDock can help to narrow the conformational possibilities and help identify a good structure. Our goal has been to provide a computational tool to assist researchers in the determination of biomolecular complexes.

The method invented at the start of the AutoDock employed a Monte Carlo simulated annealing SA method for configuration searches with a fast energy estimation by means of 3D grid-based molecular affinity potentials, which created a hybrid mechanism of a vast search area and precise energy estimations.[5]

ANTIDIABETIC AGENT

Acarbose

Acarbose is an alpha-glucosidase inhibitor used inadjunctly with diet and exercise for the management of glycemic control in patients with type 2diabetes mellitus.

Chemical Formula: $C_{25}H_{43}NO_{18}$

Weight: Average: 645.608

Monoisotopic: 645.248013549[6]

PROCESS INVOLVED IN MOLECULAR DOCKING

1. Get the complex (CPLX) coordinates (i.e.from the PDB).
2. Clean the complex (delete all the water and the solvent molecules and all non interacting ions).
3. Add the missing hydrogens/side chain atoms and minimized the complex (AMBER Program).
4. Clean the minimize complex (delete all the water and the solvent molecules and all non-interacting ions).
5. Separate the minimized CPLX in macromolecule (LOCK) and ligand (KEY).
6. Prepare the docking suitable files for LOCK and KEY (pdbqtfiles).
7. Prepare all the needing files for docking (grid parameter file, map files, docking parameter files).
8. Run the docking.
9. Analyze the docking results.

Step 1: Preparation of protein

The three-dimensional (3D) structures of Acarbose (PDB ID:3bc9) and Alpha-amylase B in complex with acarbose as receptor proteins were retrieved from the RCSB Protein Data Bank (https://www.rcsb.org/) in .pdb format.

Crystal Structure of the Polyextremophilic alpha-Amylase AmyB from Halothermothrixorenii: Details of a Productive Enzyme-Substrate Complex and an N Domain with a Role in Binding Raw Starch. **PubMed**: **18387632**

DOI: https://doi.org/10.1016/j.jmb.2008.02.041

3d structure of acarbose

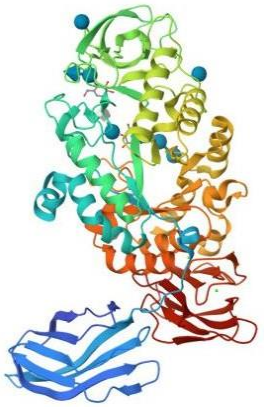


Figure 1: Alpha amylase B in complex with acarbose.

Step 2: Preparation of ligand (or) Ligand Selection

The 2D structure was prepared using the pubchem software in SD format. Acarbose is a tetrasaccharide derivative consisting of a dideoxy-4-{[4,5,6- trihydroxy-3-(hydroxymethyl)cyclohex-2-en-1-yl C7 cyclitol moiety [called valienol (or valienamine)] linked via nitrogento isomaltotriose. It has a role as an EC 3.2.1.20 (alpha-glucosidase) inhibitor, an EC 3.2.1.1 (alpha-amylase) inhibitor, a hypoglycemic agent and a geroprotector.

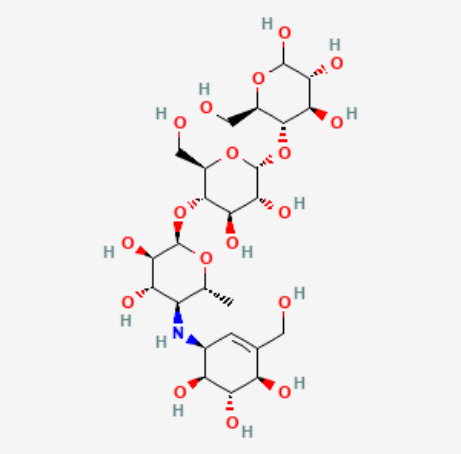


Figure 2: Acarbose.

Molecular formula: $C_{25}H_{43}NO_{18}$ **Molecular Weight:** 645.6 g/mol

Step 3: Convert to target(protein)into pdbqt format

i. Go to auto dock…….
ii. File/open…target.pdb
iii. Remove unwanted residue
iv. Delete water molecules
v. Add hydrogen/add polar only
vi. Add charges-
a. Kollman charge
b. Compute gasteiger charges
vii. Save as…target .Pdbqt

Step 4: Convert to ligand into pdbqt format

i. Goto autodock….
ii. Ligand/input/open
iii. Ligand output
iv. Save as ligand.Pdbqt

Step 5: Grid map optimization

i. Select grid/macromolecule/choose…target….save target.pdbqt
ii. Select grid/grid box…grid parameters…….file/choose saving current.
iii. Grid/output/savetarget.gpf

Step 6: Docking

1. Docking/macromolecule/set rigid filename
2. Docking/ligand/choose…ligand
3. Docking/search parameters/genetic algorithm.accept
4. Docking/docking parameters…accept
5. Docking/output/Lamarckian…savetarget.dpf

Step 7: Run autodock

Autogrid

Select tab **RUN>>RUN AUTOGRID**>>Click **BROWSE**>>Select **AUTOGRID APPLICATION FILE** in **PROGRAM PATH NAME**>Click **BROWSE** Select **TARGET.GPF** in **PARAMET FILENAME**>>Click **LAUNCH**

Autodock

Select tab **RUN**>>**RUN AUTODOCK**>>Click **BROWSE**>>Select **AUTODOCK APPLICATION FILE** in **PROGRAMPATH NAME**>>Click **BROWSE**>>Select **TARGET.DPF** in **PARAMETFILENAME**>> Click **LAUNCH**

Step 8

Analyse

i. Analyse/Docking/Open/target.dlg
ii. Analyse/Macromolecule/Choose/target
iii. Analyse Conformations/Play,rankedbyenergy...show conformations
iv. Build current+write complex save as…..result.pdb.

Energy map

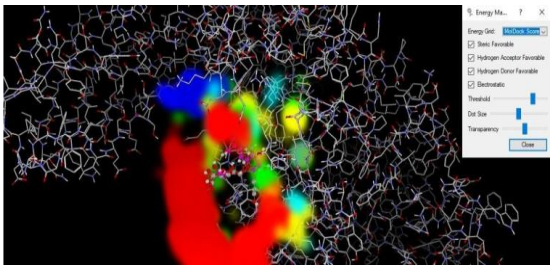


Figure 3: Energy map.

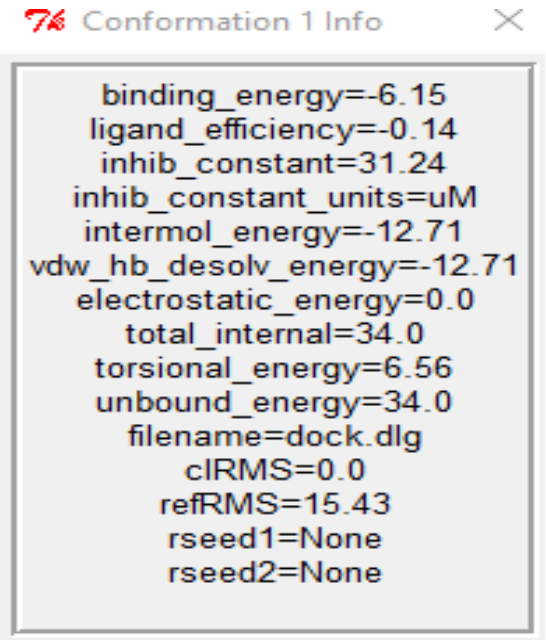
Steric favorable, Hydrogen acceptor favorable, Hydrogen donor favorable, Electrostatic

An energy map is defined as the graphical distribution of the energy that a protein-ligand interaction involves. It shows the strength at which the ligand sticks to the protein depending on ligand's position, orientation, or confirmation.

RESULT

1. Binding mode: Determine the oral antidiabetic agent of binding orientation and position.
2. Binding affinity: Forecast the binding energy or inhibition constant that points to the intensity of interaction of the interacting molecules. Psychologically, analyze the hydrogen bond, the hydrophobic contact, and other binding configuration between the ligand and the protein.
3. Binding affinity: Predict the binding energy or inhibition constant, indicating the strength of the interaction.
4. Key interactions: Analyze the hydrogen bonds, hydrophobic contacts, and other interactions between the ligand and protein.

Table 1: Result.



CONCLUSION

Diabetes mellitus is an inevitable disease, and in spite of all the available treatments, its consequences are rapidly increasing epidemiologically. The protein-ligand docking and simulation techniques have immensely enhanced the identification of new antidiabetic compounds. In the current study employing an in-silico strategy, we have identified, characterized, and described orally-given antidiabetic peptides.

This research gives an evidence that molecular docking studies using autodock programme will provide binding mode and binding affinities of the antidiabetic agent to the target protein.

We have therefore highlighted the different types or molecular docking and their approaches in brief. The primary goal of molecular docking simulations is therefore in the prediction of new leads. Therefore, in optimizing this aim's effectiveness, there appear to be one among the difficulties: development of a robust and reliable scoring function.

REFERENCES

1. Mohan V. and Alberti K. G., K. G. M. M. Alberti, P. Zimmet, R. A. Defronzo, and H. Keen, Diabetes in the tropics, International Text Book of Diabetes Mellitus, 2nd edition, John Wiley & Sons, Chichester, UK, 171–187.
2. Huang J., Xiao Y., Zheng P., etal. Distinct neutrophil counts and functions in newly diagnosed type 1 diabetes, latent autoimmune diabetes in adults, and type 2 diabetes. *Diabetes/Metabolism Research and Reviews*, 2019; 35(1, article e3064).
3. B Mukesh, K Rakesh. Molecular docking: a review. IJRAP, 2011; 2: 1746-1751.IA Guedes, CS de Magalhaes, LE Dardenne. Receptor–ligand molecular docking, Biophysical Reviews, 2014; 6: 75-87.
4. Morrison, J.L., Breitling, R., Higham, D.J. and Gilbert, D.R., A lock-and-key model for protein-protein interactions. Bioinformatics, 2006; 22: 2012– 2019.
5. Goodsell, D.S. & Olson, A.J. "Automated Docking of Substrates to Proteins by Simulated Annealing", Proteins: Str. Func. Genet, 1990.
6. Martin A E, Montgomery PA: Acarbose: analpha-glucosidaseinhibitor. Am J Health Syst Pharm, 1996 Oct 1; 53(19): 2277-90; quiz2336-7.