World Journal of
Pharmacognosy & Phytochemistry

IDAAM Publications

World J Pharmacog Phytochem 2023; 1(1): 9-13

RESERCH ARTICLE

Molecular docking studies on phytoconstituents of *Barleria prionitis* L. against α-amylase enzyme

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ARTICLE DETAILS

Article history:
Received on 18 February 2021
Modified on 22 March 2021
Accepted on 29 March 2021

Keywords:
Barleria prionitis L.,
Molecular Docking,
α-Amylase,
Anti-diabetic.

ABSTRACT

The objective of the analysis is to determine the inhibitory function of α-amylase active compounds in *Barleria prionitis* L. Usage in studies of silico docking. In this respect the docking evaluation was for active plant constituent ligands. The standard inhibitor was acarbose, a known α-amylase inhibitor. The latest version of GLIDE Software v5.5 developed by Schrödinger has taken the place of silico docking studies. These results demonstrate that binding energy ranged from - 3.1 to -8.9 kcal/mol in all active components. If compared (-6.3 kcal/mol) to the norm. The inhibitors of α-amylase are excellent because of their structural parameters, as well as 1,8-dihydroxy-2,7-dimethyl 3,6-dimethoxy anthraquinone and Melilotic acid and Barlerin. Through these molecular docking studies, the effective α-amylase inhibitors for the treatment of diabetes are further developed.

INTRODUCTION

Diabetes mellitus described as a hyperglycemia metabolic condition caused by fault of insulin or both. The regulation of postprandial hyperglycemia after a meal is the most effective treatment for type II diabetes [1]. Blood glucose stabilization is required in diabetic patients because it prevents diabetes-related hyperglycemia and complexity. The diabetes mellitus characteristics consist of long lasting wounds, inflammation and organ failure. At present, 150 million people are expected to have diabetes uniformly and this will grow to 300 million by 2050. Modern drugs for the treatment of diabetes are sulfonylureas, biguanides and thiozolidinedions. They have unwanted effects on their uses, however. Natural or herbal products reduce glucose absorption by -hydrolysis enzymes such as pancreatic amylase from carbohydrates [2]. The enzyme's inhibition delays the carbohydrate digestion and extends the total time it takes to digest carbohydrates and thereby reducing the rate of glucose absorption. Several indigenous plants have a wide potential for the inhibition of α-amylase. In contrast to modern pharmaceutical medicines, herbal medicines play an important role in treating various chronic diseases. Because of its limited side effects they are very healthy. Proper understanding of the crude medicinal product is very important for developing the herbal formulation, protection and effectiveness of the herbal product. Pharmacognosy, a discipline devoted to the full knowledge gathered on the crude drug [3].

B. prionitis is also known as the flower of porcupine that is part of the Acanthaceae Family, the Barleria genus. It is native to India and is widely spread throughout Asia, including Malaysia, Pakistan, the Philippines, Sri Lanka, Bangladesh, Yemen and tropical Africa. The tubes, typically single-groove, grow to about 1.5 meters above a single taproot in height, are erect,

permanent, snug, and perennial. The branching lateral roots all over the place. Because of its normal usage for various forms of pharmacological activities *B. prionitis* has been studied. Several studies have been recorded *in vitro* and *in vivo* in various cell lines and animals. Now for a few days herb means any part of the plant such as fruit, seed, stem, bark, flower, leaf, stigma or root and a non-woody plant. In the past, only non-woody plants, including those derived from trees and shrub, used to use the word "herb." These herbs are also being used in many spiritual practices as food, flavonoids, medicines or perfume. Plants were used even before ancient times for medicinal purposes.

Old Unani manuscripts the use of herbs was described by Egyptian papyrus and Chinese texts. There is evidence that for over 4000 years, herbs have been used as medicines in Unani Hakims, Indian Vaids and in European and mediterranean cultures. In their healing rituals indigenous cultures like Rome, Egypt, Iran, Africa and America have used herbal herbs while other traditional medical system systems have been developed, such as Unani, Ayurvedic and Chinese medicines. On various sources, traditional medical methods are still commonly practised. Increased population, insufficient supply of medicines, prohibitive treatment costs, side-effects of various synthetic medicine and the growth of resistance against currently-used drugs for contagious diseases have resulted in greater emphasis on the use as a source of medicines for a wide range of human ailments of plant material. India is recognized as a rich repository of medicinal plants among ancient civilizations.

The Indian forest is the main depot of many medicinal and aromatic plants that are collected primarily as raw ingredients in the production of drugs and perfumery products. In India system of AYUSH approximately 8,000 herbal remedies were codified. The key systems of indigenous medicines are Ayurveda, Unani, Siddha and folk (tribal) medicines. Among these systems are most developed and widely practiced Ayurveda and Unani Medicine in India. Recently, the WHO reports that 80% of the worldwide population relies on herbal medicines for some part of their primary health needs. According to the World Health Organization (WHO), about 21,000 plants have potential for medicinal use. More than three quarters of the world's population, according to available data, relies primarily on plants and plant extracts for their medical needs.

More than 30% of the whole plant species is used for medicinal purposes at one time or for another. The estimate is that plant medicinal products make up as much as 25% of the total drugs in developed countries like the United States, whereas the contribution is as high as 80% in the rapidly developing countries like India and China. Thus for countries such as India than the world, the economic value of medicinal plants is much greater. Two thirds of the plants used in the modern medicine system are developed in these countries and the rural health care system relies upon indigenous medicine systems. Many herbs in different parts of the world honor their Kings as a sign of happiness. Now, when many consumers had found the role of herbs in medicine, tulsi and other medicinal plants started plantation in their home gardens. The rich ingredients of medicinal plants that can either be used as pharmacopeia, non-pharmacopoeial or synthetic drugs in drug production are regarded. These plants play a crucial role in the growth of human societies all over the world. In addition, certain plants are recognized as essential nutrient sources and are recommended for their therapeutic values, includes ginger, green tea, aloe, pepper and turmeric. Certain plants and their derivatives are seen as an essential source of actives used in aspirin, toothpaste etc. In addition, in natural dye, pest prevention, food, perfume and tea weeds are also used in the treatment of medicinal goods. Various medicinal plants/herbs are used in many countries to keep the ounces, the flies, the mouse and escape from home and office. Medicinal herbs have been essential sources for pharmaceutical development for many days now. Molecular docking is an appealing scaffold for understanding medicinal biomolecular interactions in rational drug design as well as in the mechanical analysis in order, primarily noncovalently, to insert the molecule (ligand) into the favorite binders of the particular target area of the DNA/protein (receptor). The information gathered from the docking method can be used to demonstrate the binding energy, free energy and complex stability. The docking are currently used to forecast the preliminary ligand-receptor complex binding parameters [4-10].

MATERIAL AND METHODS

Molecular Modeling Studies

The GLIDE software v5.5 built by Schrödinger on the Red Hat Enterprise Linux5 workstation has also been used for molecular modeling studies. For all steps involved in ligand preparation, protein preparation, HTVS, Maestro v9.5 Graphical User Interface (GUI) workspace was used (High Throughput Virtual Screening) [11].

Ligand Preparation

The ligands used in this study have been developed with the Schrödinger Suite 2013 LigPrep module v2.3. LigPrep follows the energy minimization force fields in OPLS-AA (Optimized Potential Liquid Simulations for All Atoms) [12].

Protein Preparation

The α-amylase X-ray crystal structure (PDB: 1HNY) was found from the PDB database as the raw material could not be suitable for research molecular docks. Only high atoms, water, cofactors and metal ions can be used in a standard PDB structure, and multimeric structures can be used. These entities are not familiar with bond instructions, topologies or formal atomic costs. The raw PDB structure should therefore be prepared for docking in a suitable way. GLIDE software protein preparation Wizard for the processing and preparation of protein was used. This is also in line with the optimized power potentials in the energy reduction fields for liquid simulations-all atoms (OPLS-AA) [13].

Docking Protocol

The GLIDE Extra Precision (XP) mode was used for all docking calculations. The position of the bond for the different energy networks is defined in two concentration-cubed terms: the bounding box with the center of every appropriate ligand pose and the enclosing box with a Root Mean Square Diversion (RMSD) of less than 0.5 Å and a maximum atomic displacement of less than 1,3 Å The binding site for which various energy grids have been determined and stored. For those atoms with absolute partial loads below 0,15 (scale factor of 0.8) and 1,0 electrons of the ligand and proteins, respectively, the scale factor for van der Waals radii was added. In the initial calculation process, the maximum number of poses produced by the max keep variable was set at five thousand and the best hold variable was set at one thousand, which determines the number of poses per ligand in the energy minimum. Energy minimization protocol includes dielectric constant of 4.0 and 1000 cycle of conjugate gradient. At most 100 poses per ligand were produced when each docking calculation was completed. A GLIDE (Gscore) function was used to choose the best docked structure. The E-model, which comes from a combination of gscore, coulombic, van der Waals and the ligand strain energy, is another scoring feature used by GLIDE [14].

RESULTS AND DISCUSSION

To assess the size of the active site, the GLIDE receptor grid has been created. The ligands are most likely to orientate in the binding pocket and a score function is employed to calculate the frequency of the interaction that a molecule may conduct with a specific orientation. The GLIDE XP precision was preferred over the standard mode to provide a stronger connection between good poses and good score. The study of the docking was performed using GLIDE docking software for ligands such as the α-amylases target protein and the pictures are shown. GLIDE docking structures are usually graded as per GLIDE scoring feature (more negative). The GLIDE docking software scoring feature is viewed as a G-score. The easiest way to test the accuracy of the docking method is to decide how near, with the object score feature, the lowest energy (binding conformation) is expected. Extra Precision GLIDE docking procedure was assessed by removing the α-amylase protein compound from G-score (GLIDE), GLIDE energy (GLIDE) and H-bonds. In this study both ligands are docked into the active site of α–amylase to explore the molecular basis for the interaction and affinity between ligand analogs and α-amylase protein. Table 1 shows the docking result of the ligands. For each of the minimized complexes, the interaction energy involves the energy of van der Waal, electrostatic energy, and intermolecular hydrogen bonding. GLIDE attraction ranged from α-amylase to -3.6 to -7.7. The standard α-amylase Acarbose score for GLIDE was found to be -6.3. This shows that the plant's chemical component may be potential drugs for the development of anti-diabetic activity drug. The GLIDE score may be used to describe ligands to bind to a certain conformation of a protein receptor as a semi-quantitative descriptor. In general, a strong ligand affinity to the receptor can be expected for a low GLIDE score. Especially, compounds Barlerin and 1,8,dihydroxy-2,7-dimethyl 3, 6-dimethoxy anthraquinone were found to be potent with a docking score of -8.9 and -8.6 respectively. The position of the inhibitor at the

docking and the cry structures of the protein were very well agreed. We have found compliance study of different docking complexes also show that residues of α-amylase protein (ASP 197, ALA 198, LYS 200, HIS 201, GLU233, ILE 235, HIS 305 and ALA 307) play an important role. GLIDE-led docking studies have verified that the above-mentioned inhibators fit into the α-amylase protein binding pocket. The findings show that intermolecular hydrogen and liphophilic interactions between the ligand and the receptor are very necessary for effective docking. The key explanation why the GLIDE score has improved is because of intra-ligand penalties.

Table 1: Glide score of Phytoconstituents of *Barleria prionitis L.* against α–amylase protein

S. No	Compounds	Glide score
1	Balarenone	-4.2
2	Pipataline	-3.8
3	Lupeol	-3.1
4	prioniside A	-4.8
5	prioniside B	-3.3
6	prioniside C	-5.2
7	Verbascoside	-3.9
8	shanzhiside methyl ester	-5.1
9	6-O-trans-p-coumaroyl-8-O-acetylshanzhiside methyl ester	-6.9
10	Barlerin	-8.6
11	Acetylbarlerin	-4.2
12	7-methoxydiderroside	-4.4
13	Lupulinoside	-3.4
14	1,8, dihydroxy-2,7-dimethyl 3, 6-dimethoxy anthraquinone	-8.9
15	1,3,6,8-tetramethoxy-2,7-dimethyl anthraquinone	-5.1
16	Scutellarein	-6.7
17	melilotic acid	-7.4
18	syringic acid	-3.9
19	Glucoside	-4.3
20	β-sitosterol	-5.2
21	scutellarein 7-neohesperidoside	-3.3
22	apigenin 7-O-glucoside	-4.1
23	13, 14-seco-stigmasta-5, 14-diene-3-a-ol	-2.5
24	Standard (Acarbose)	-6.3

CONCLUSION

In conclusion, the results of the present study clearly demonstrated that, Barlerin and 1,8, dihydroxy-2,7-dimethyl 3,6-dimethoxy anthraquinone and melilotic acid excellent binding sites and interactions with α-amylase compared to the standard. In order to establish possible chemical entities for the prevention and treatment of diabetes, further investigations of this compound and in vivo studies are required.

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