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In Silico Screening of Phytoconstituents and Medicinal Plants as Antidiabetic Drug Discovery

Poonam Kumari[1], Rimmy Nandal[2$], Pooja Rani[3], Priyanka Rathi[4], Sarita Khatkar[4$], Anurag Khatkar[5]

1. Faculty of Pharmaceutical Sciences, Baba Mast Nath University, Asthal Bohar, Rohtak-124021, Haryana, India

2. Shri Baba Mast Nath Institute of Pharmaceutical Sciences and Research, Baba Mast Nath University, Asthal Bohar, Rohtak-124021, Haryana, India
3. Chandigarh Pharmacy College Jhanjeri, Mohali Punjab-140307

4 .Geeta Institute of Pharmacy, Geeta University, Panipat-132145, Haryana, India

5. Department of Pharmaceutical Sciences, M.D. University, Rohtak, Haryana, India

***Corresponding Author:**
Rimmy Nandal
Shri Baba Mast Nath Institute of Pharmaceutical Sciences and Research, Baba Mast Nath University, Asthal Bohar, Rohtak-124021, Haryana, India
Email: nandalrimmy17@gmail.com
Sarita Khatkar
Geeta Institute of Pharmacy, Geeta University, Panipat-132145, Haryana, India
Email Id:-drsaritamdu@gmail.com

Abstract:

Diabetes mellitus is a long-term metabolic disease marked by high blood sugar levels brought on by ineffective insulin synthesis or function. Two important enzymes in the metabolism of carbohydrates are alpha-amylase and alpha-glucosidase, which catalyze the conversion of complex carbs into glucose. One efficient way to control postprandial hyperglycemia is to inhibit these enzymes. Although significant research attention has been devoted to the development of diabetes regimens, which demonstrates success in lowering blood glucose levels, their efficacies are unsustainable due to undesirable side effects such as weight gain and hypoglycemia. To overcome side effects new entities were studied by using chemical constituents obtained from various plants by in silico approach to evaluate their antidiabetic activity against alpha amylase and alpha glucosidase. Molecular docking studies were used to find out affinity and interaction of chemical constituents from different plant with enzymes. In this research paper, chemical constituents from different antidiabetic plants were selected as ligands for the receptor alpha amylase and alpha glycosidase in molecular docking studies by using Schrodinger software for the inhibition of alpha amylase and alpha glucosidase activity. The molecular docking analyses presented in this study could lead to the development of potent α-amylase and alpha glycosidase inhibitors helpful in the treatment of diabetes. Molecular docking study confirmed the alpha-glycosidase and alpha amylase inhibitory activity further supported the observed % inhibitory activities.

Objectives: This study aims to explore the inhibitory potential of various plant-derived compounds against alpha-amylase and alpha-glucosidase using molecular docking techniques. By the identification and analysis of ligand binding interactions with the active sites of the enzyme, we aim to clarify their mode of action and possible effectiveness as antidiabetic drugs.

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Methods: Using in silico docking experiments, a large library of plant compounds, such as flavonoids, alkaloids, and polyphenols, were tested for their binding affinities to alpha-amylase and alpha-glucosidase. The Autodock Vina software was employed to perform the docking simulations, and the results were analyzed to identify key interactions between the plant compounds and the enzyme active sites. The binding energies, hydrogen bonding, hydrophobic interactions, and other relevant molecular interactions were evaluated to determine the inhibitory potential of each compound.
Results: The docking studies revealed several plant constituents with significant binding affinities to both alpha-amylase and alpha-glucosidase. Notably, compounds such as catechin, shikimic acid etc. Exhibited strong interactions with critical active site residues, suggesting their potential as effective inhibitors. These compounds formed stable hydrogen bonds, hydrophobic contacts, and pi-pi interactions with the enzymes, highlighting their capability to hinder enzymatic activity.

Keywords: Diabetes mellitus, hyperglycemia, α-glucosidase, α-amylase, docking

1. INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder causing hyperglycemia and other metabolic disturbances, primarily due to an absolute deficiency in insulin secretion or action. Diabetes Type 1 affects 10% of patients with insufficient insulin production, while Type 2 accounts for 90% of cases. Both types cause severe health issues like cardiovascular diseases, nephropathy, neuritis, and retinopathy [1]. Oxidative stress occurs when free radicals overpower the cellular antioxidant system, leading to complications like microvascular and cardiovascular damage. Diabetes, despite no cure, can be managed through a healthy diet, exercise and medication, reducing long-term complications [2]. Therapeutic targets for diabetes include carbohydrate hydrolyzing enzymes, glucose transporters and insulin receptor substrates. Inhibitors of α-amylase, responsible for converting carbohydrates into monosaccharides, are used as drug targets to prevent enzymes that reduce starch hydrolysis [3]. Alpha-amylase and α-glucosidase enzymes break down long-chain carbohydrates into glucose and starch, leading to hyperglycemia. Medicinal plants and natural products are a major source of therapy in developing countries. Modern analytical techniques have simplified drug discovery. Over 400 plants have antidiabetic potential, but few have received medical evaluation. A variety of α-amylase and α-glucosidase inhibitors are produced by microorganisms and plants to regulate these enzymes. Natural α-glucosidase inhibitors include alkaloids, flavonoids, anthocyanins, terpenoids, curcuminoids, and phenolic compounds [4]. Diabetes increases the risk of associated diseases like cardiovascular and hypertension, necessitating the use of a multi-drug therapeutic regimen. However, concomitant therapy can lead to complications and adverse effects. Research aims to identify new α-amylase and α-glucosidase inhibitors that can control diabetes and be therapeutically significant in prediabetes stage of insulin resistance. Antidiabetics are often prescribed in combination with other therapeutic agents to control associated conditions. Broad-spectrum carbohydrate digesting enzyme inhibitors are ideal for futuristic therapy for concurrent diseases, considering the complications involved in achieving an effective combination [5]. Type 2 diabetes drugs like acarbose and miglitol block alpha-amylase, but may cause side effects like flatulence, diarrhea, bloating, and abdominal discomfort. Diabetes is a global health concern, with 463 million type 2 diabetics (T2D) currently living in developing countries. By 2030, this number is expected to rise to 578 million (10.2%) and 700 million (10.9%) by 2045. Traditional treatments for T2D involve

dietary and activity changes, insulin, or oral hypoglycemic medications. However, due to the complexity, side effects, and expensive maintenance of allopathic drugs, there has been an increase in interest in herbal formulations and nutraceuticals made from medicinal plants. This has motivated medical professionals and the global population to seek alternative therapies and focused on plant-based remedies due to their affordability [6]. Natural substances could be useful supplements to existing diabetes treatments or viable substitutes for them and they might even lessen the likelihood of contracting the illness. One advantage is that large amounts can be included in a regular diet. Numerous plants and natural macromolecules have been the subject of literary discussions over their potential antidiabetic properties. For instance, people have utilized plants as a preventative measure against diabetes since ancient times. Usually, the mechanism of action remains unclear, although an increasing number of research are being carried out to clarify the mechanisms of action of various plants and natural chemicals [9]. In underdeveloped nations, traditional medicines are typically the first option for primary healthcare due to their greater cultural acceptability, more compatibility with the human body, and lower side effects when compared to modern remedies. Many medicinal plants have been used empirically as antidiabetic and antihyperlipidemic treatments and have recently been reported to be helpful in the treatment of diabetes worldwide. There have been over 400 plant species with hypoglycemic action reported in the literature [9-11].

Interestingly, natural chemicals derived from plants have been the focus of research for antidiabetic drugs in Africa, particularly from plants that are utilized in traditional medicine to treat diabetes mellitus. The creation of molecules with enhanced potency and safety profiles for the treatment of diabetes mellitus and its related problems is the ultimate aim of these studies. This is because medicinal plants play a crucial role in the delivery of healthcare in Africa[12-15]. Concoctions and studies based on crude extracts are becoming less important in today's modern research, as the emphasis has thankfully moved to the identification and exploitation of certain chemicals for their potential therapeutic benefits. Understanding certain components from different portions of herbal plants facilitates experimental investigations and helps to concentrate on improving the comprehension of the mechanism of action and potential future medicinal applications. Diabetes is a complex illness that affects nearly every organ in the body, thus more research and development is required to fully use plant resources in the search for more effective treatment compounds. Utilising plant-based resources saves time and money because there is no longer a requirement for drug development and testing [15-17]

2. METHODS

Using in silico docking experiments, a large library of plant compounds, such as flavonoids, alkaloids, and polyphenols, were tested for their binding affinities to alpha-amylase and alpha-glucosidase. The Autodock Vina software was employed to perform the docking simulations, and the results were analyzed to identify key interactions between the plant compounds and the enzyme active sites. The binding energies, hydrogen bonding, hydrophobic interactions, and other relevant molecular interactions were evaluated to determine the inhibitory potential of each compound.

2.1 Computational studies

To investigate the inhibitory activity of chemical constituents from various plants to the selected enzymes, namely α-glucosidase and α-amylase, molecular docking was carried out. Docking process showed that the chosen substances have several possibilities when compared to the intended enzymes. The crystal structure of protein molecules of α-glucosidase (PDB ID: 5NN5) and α-amylase (PDB ID: 4W93) were downloaded from the PDB to carry out molecular docking. The structures of the ligands were drawn using chem 3D 16.0. The docking simulation was conducted using Maestro Schrodinger Glide Software. ADME properties were calculated by the use of ADMET lab 2.0. Molecular docking is a helpful method of virtual screening which finds lead compounds in drug discovery. Using the Glide module in XP mode, the topmost compounds for alpha-amylase and for alpha-glucosidase were selected amongst several phytoconstituents based on their best docking scores[18-19].

2.2 Protein structure assessment

α-a mylase

The docking studies were based on the X-ray crystallographic structure (PDB code 4W93) of human pancreatic amylase, which was retrieved from the RCSB repository. The high crystallographic resolution of this three-dimensional protein structure (X-ray diffraction 1.352 Å) led to its selection. It is a hydrolase inhibitor protein with molecular weight around 57.24 KDa. Parameters like resolution 1.35 Å; R-value free 0.211; R-value work 0.198; R-value observed 0.198; unit cell crystal dimensions, a=52.37 Å, b= 74.1 Å, c= 135.88 Å; α angle= 90°, β angle= 90°, ϒ angle= 90° have been determined by X- ray diffraction studies data[20].

α-glucosidase

The docking studies were based on X-ray crystallographic structure (PDB ID 3W37) of sugar beet α-glucosidase with acarbose, which was retrieved from the RCSB repository. The high crystallographic resolution of this three-dimensional protein structure (X-ray diffraction 1.70 Å) led to its selection. It is a hydrolase protein and its molecular weight around 104.93 KDa. Parameters like resolution 1.70 Å; R-value free 0.182; R-value work 0.154; R-value observed 0.154; unit cell crystal dimensions, a=86.36 Å, b= 98.2 Å, c= 108.75 Å; α angle= 90°, β angle= 90°, ϒ angle= 90° have been determined by X- ray diffraction studies data. Ramchandran plot were also used to indicate the stability and dependability of protein structure as shown in fig 1. A key tool in structural biology, the Ramachandran plot shows the dihedral angles ψ (psi) and φ (phi) of amino acid residues in protein structures. Plotting these angles allows scientists to evaluate the sterically permissible regions for protein backbone conformations, which helps validate and improve protein models [21].

Protein Preparation

The X-ray protein structure was extracted from RCSB Protein Data Bank with PDB ID 3W37 and PDB ID 4W93 for antidiabetic activity. The selection of PDB ID was done on the basis of resolution and source species. Schrodinger's Prepwiz (protein preparation wizard) was used to prepare the proteins. The targeted protein structure was further refined to obtain an optimized, chemically accurate, and protein structure. The co-crystallized enzyme structure is directly

downloaded from Protein Data Bank on the Maestro workspace interface, followed by pre-process steps that include assigning bond order, using CCD database, replace hydrogen's, creating zero order bonds to metals, creating disulfide bonds, filling in missing side chains and missing loop chains using prime. All the water molecules were removed and the Epik tool was used to ionize heteroatom's at the biological pH (7.4) to maintain a biosimilar environment. After preprocess, an energy minimized structure was finally obtained [22].

Ligand Preparation

3-D structure libraries of phytoconstituents were built using Chemdraw Ultra software and saved in MDL molfile form. The LigPrep tool of the Maestro molecular modeling user interface was used to prepare ligands for energy minimization and to correct the coordinate's stereochemistry and generate tautomers to obtain appropriate conformation. A total of 32 stereoisomers per ligand were allowed; at the target pH, 7+/-2 was set as a default option, the force field was OPLS4 and Epik was used for ionization. Then these energy minimizing prepared ligands were used for molecular docking simulation.

Grid Generation

The receptor grid generation tool in Maestro was used to calculate the grids required for docking ligands to protein receptors. A receptor grid-generating file was used for docking to bind ligands to the binding site. There are several options in receptor grid generation tool like receptors, site, constraints, rotatable groups and excluded volumes. If the structure in the workspace is a receptor plus a ligand then you must identify the ligand molecule so it can be excluded from the grid generation. Especially when utilizing the Maestro program, which is a component of the Schrödinger suite for computational chemistry and molecular modeling, grid formation is an essential stage in this process.

Molecular Docking

In silico docking studies were carried out on the Glide module of Maestro XP. The glide algorithm mode was utilized to check the interaction of ligands with proteins. In the ligand docking panel, the binding site is specified by browsing and selecting the grid file with a zip file extension. Docking site validation was done by splitting the co-crystallized ligand from minimized protein complex and then re-docking into active site. RMSD value found to be less than 2Å. It is considered as a good prediction by computational docking protocol[23]. The RMSD value was calculated between the co-crystallized ligand and docked pose by using the superposition tool of the structure alignment task of Maestro. The RMSD value was found to be 1.69 Å for α-amylase (PDB ID 4W93) and 1.26 Å for α-glucosidase (PDB ID 3W37). The docking score function was output for a specific ligand and the docking score result was presented as a Glide score (Grid Ligand Docking with Energetics).

ADME/Drug likeness study

It is a comprehensive scoring function for evaluation of chemical drug likeness. A drug likeness study of the drug is very important in the drug discovery process and for this purpose ADMET lab 2.0 is used. The purpose of this sophisticated computational tool is to forecast the features of chemical compounds related to Absorption, Distribution, Metabolism, Excretion, and

Toxicity (ADMET). ADMET Lab 2 offers researchers vital insights into the pharmacokinetic and toxicological profiles of drug candidates by utilizing cutting-edge machine learning algorithms and large datasets. This enables more informed decision-making during the early phases of drug discovery and development[24-26].

3. Result and Discussion

Several phytoconstituents that are widely distributed in plants have been shown to possess antidiabetic activity. According to study phytoconstituents have inhibitory effect on α-amylase and α-glucosidase enzymes. Therefore, molecular docking was performed to examine the inhibitory effects of several phytoconstituents on α-amylase and α-glucosidase enzymes. Molecular docking studies were carried out to identify the binding interactions and affinities of several phytoconstituents towards the targeted proteins. A library of phytoconstituents was docked against α-amylase and α-glucosidase enzymes. Results of α-amylase and α-glucosidase inhibition docking revealed that some phytoconstituents had good docking score. Ligands showed different types of interaction with amino acid residues in the binding pockets of α-amylase and α-glucosidase like hydrophobic interactions, hydrogen bond interactions, electrostatic interactions, pi-pi stacking. Docking score and glide energy of top-docked phytoconstituents for α-amylase (PDB ID 4W93) and α-glucosidase (3W37) based on bioactivity prediction scores shown in **table 2**.

Table 2: Gliding energy and docking score of top-docked for α-amylase (PDB ID 4W93)

S.No.	Phytoconstituents	Docking score (Kcal/mol)	Gliding energy (Kcal/mol)
***α-amylase* (PDB ID 4W93)**			
1.	Shikimic acid	−6.435	−25.469
2.	Luteolinidin	−6.379	−35.958
3.	Hibiscetin	−6.296	−42.136
4.	Myricetin	−6.263	−38.600
5.	Astragalin	−6.214	−43.426
6.	Quercetin	−6.170	−37.328
7.	Mearnsetin	−6.136	−39.488
8.	Rhamnetin	−6.029	−36.973
9.	Malvidin	−5.996	−38.951
10.	Diosmetin	−5.983	−34.955
***α-glucosidase* (PDB ID 3W37)**			
11.	Dulcisflavan	−6.389	−39.414
12.	Catechin	−6.07	−36.382

13.	Ent-epicatechin	−6.07	−36.382
14.	Epicatechin	−6.07	−36.382
15.	Epigallocatechin	−6.054	−38.324
16.	Benzyl isothiocynate	−5.974	−29.117
17	Hypolaetin	−5.862	−39.138
18	Hibiscetin	−5.753	−42.687
19.	Astragaline	−5.748	−47.107
20.	Luteolin	−5.677	−48.465

Binding/Docking poses of ligands with targeted protein

In this study phytoconstituents were docked against α-amylase and α-glucosidase proteins to gain insight into the binding affinities of these ligand with the targeted proteins. Comprehensive analyses of the interactions between visual ligands and proteins revealed that phytoconstituents strongly bind inside the binding region of the target protein through the creation of hydrogen bonds, salt bridges and hydrophobic interaction. Selected phytoconstituents interaction with α-amylase protein shown in **table 2**. The docking poses of most active ligands with PDB ID 4W93 as shown in fig 1-5. The docking pose of most active ligand (shikimic acid) with PDB ID 4W93, it interacts by hydrogen bond between hydroxyl group of ligand and residues ILE 312, GLN 302, ASP 317, ARG 346 and hydrophobic interaction with LEU 313, ALA 310, TRP 316, TRP 344, PHE 348 and ILE 312. Luteolinidin interacts with PDB ID 4W93 by hydrogen bond with ASN 352, ARG 303, ASP 317 and show hydrophobic interaction with ALA 310, ILE 312, LEU 313, TRP 316 and PHE 348. Hibiscetin show interaction with PDB ID 4W93 by forming hydrogen bond with ASN 352, ARG 303, GLY 351, ASP 317 and show hydrophobic interaction with ALA 310, ILE 312, LEU 313, TRP 316 and PHE 348. Myricetin interacts with PDB ID 4W93 by hydrogen bond with ASP 353, ASN 352, ARG 303, GLY 351, ASP 317and show hydrophobic interaction with PHE 348, TRP 316, LEU 313, ILE 312 and ALA 310. Astragalin with PDB ID 4W93 by hydrogen bond with ARG 267, ARG 346, ASP 317, GLN 302, GLY 304 and show hydrophobic interaction with TRP 269, PHE 348, TRP 316, ILE 312, ALA 310 and show pi-pi stacking with PHE 348. From fig 6-10 the docking poses of most active ligands with PDB ID 3W37. The docking pose of most active ligand (dulcisflavan) with PDB ID 3W37, it interacts by hydrogen bond between hydroxyl group of ligand and residues NAG C1, and hydrophobic integration with PRO A433, Pro A435, ALA A363, TYR A407. Catechin shows interaction with PDB ID 3W37 by forming hydrogen bond with FLU 105, GLU 109 and hydrophobic interaction with TRP 104, ILE 106, PRO 107, VAL 110, LEU 442, VAL 518 and TYR 515 . Entepicatechin shows hydrophobic interaction with TRP 104, ILE 106, PRO 107, VAL 110, LEU 442, VAL 518 and TYR 515 and H-Bond interaction with FLU 105, GLU 109. Epicatechin shows interaction with PDB ID 3W37 by forming hydrogen bond with FLU 105, GLU 109 and hydrophobic integration with TRP 104, ILE 106, PRO 107, VAL 110, LEU 442, VAL 518 and TYR 515. Epigallocatechin shows interaction with PDB ID 3W37 by forming hydrogen bond with FLU 105, GLU 109 and hydrophobic integration with TRP 104, ILE 106, PRO 107, VAL 110, LEU 442, VAL 518 and TYR 515

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Representation of superimposed orientation of the best conformational pose and energy valued docked complex of different compounds with α-amylase. The 3D model illustrate the interaction with amino acid residues of the catalytic pocket of the enzyme. In the 2D model, hydrophobic interaction (light green), hydrogen bond (purple arrow line) interactions. The amino acids are depicted with different colours.

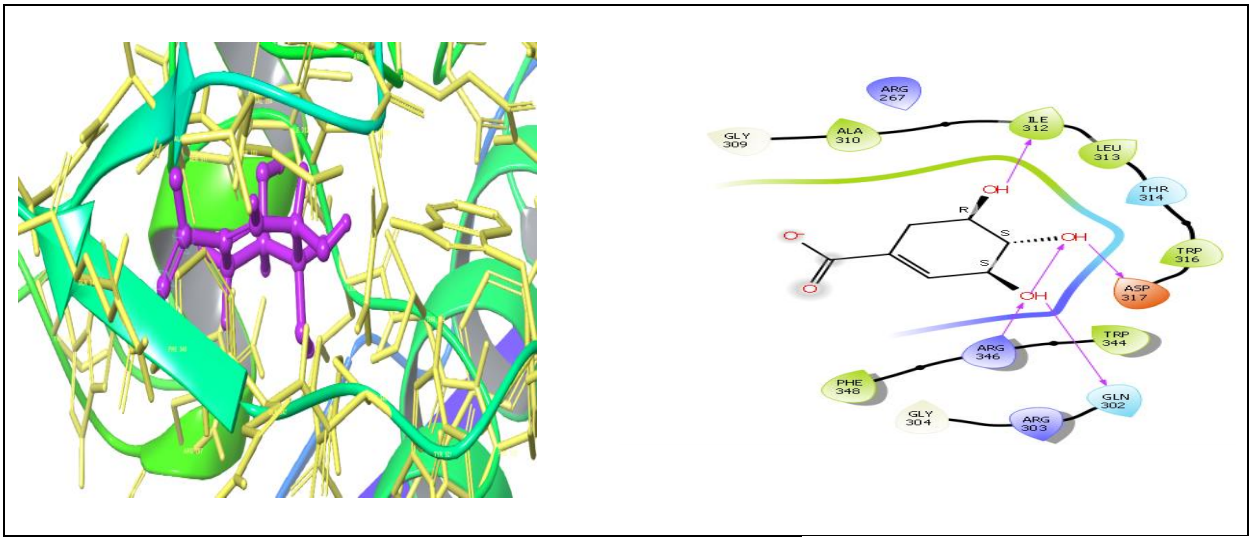

Fig 1. Protein ligand interaction (PLI) of shikimic acid against α-amylase enzyme and its 3D (left) and 2D (right) diagrams.

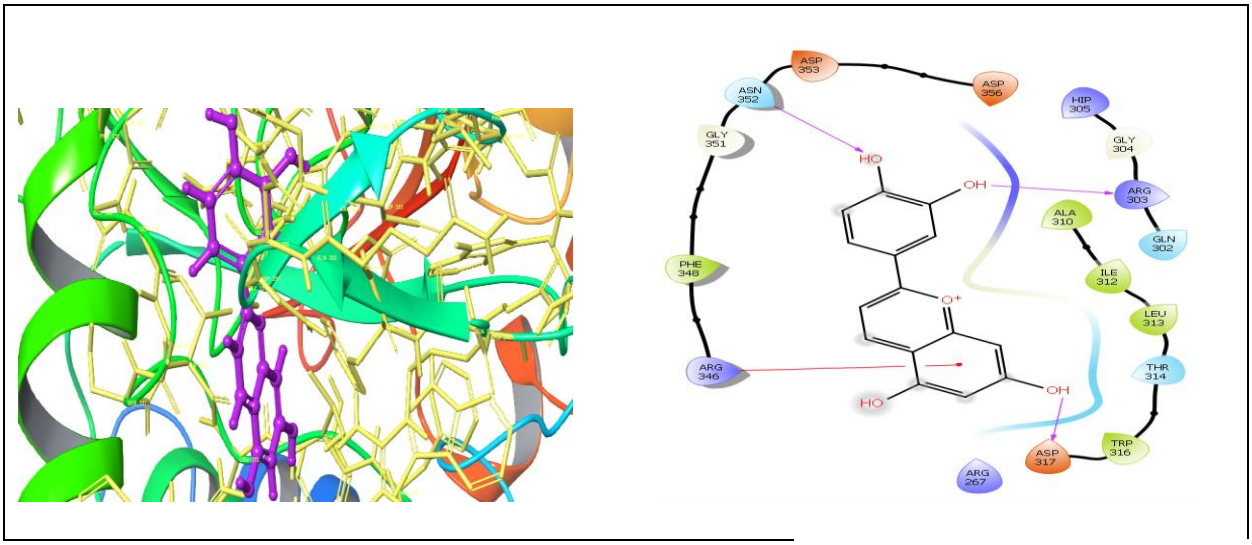

Fig 2. Protein ligand interaction (PLI) of luteolinidin against α-amylase enzyme and its 3D (left) and 2D (right) diagrams.

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HIBISCETIN

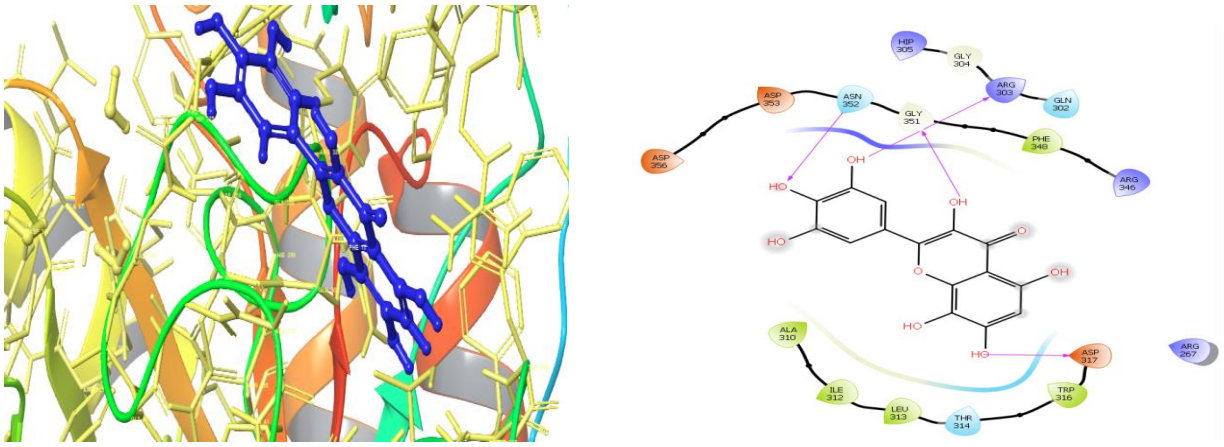

Fig 3. Protein ligand interaction (PLI) of hibiscetin against α-amylase enzyme and its 3D (left) and 2D (right) diagrams.

MYRICETIN

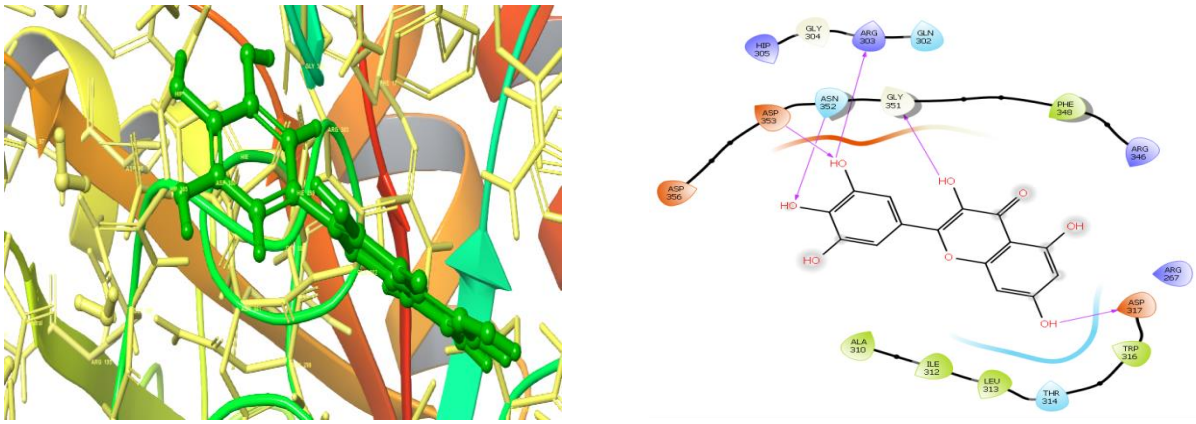

Fig 4. Protein ligand interaction (PLI) of myricetin against α-amylase enzyme and its 3D (left) and 2D (right) diagrams.

ASTRAGALINE

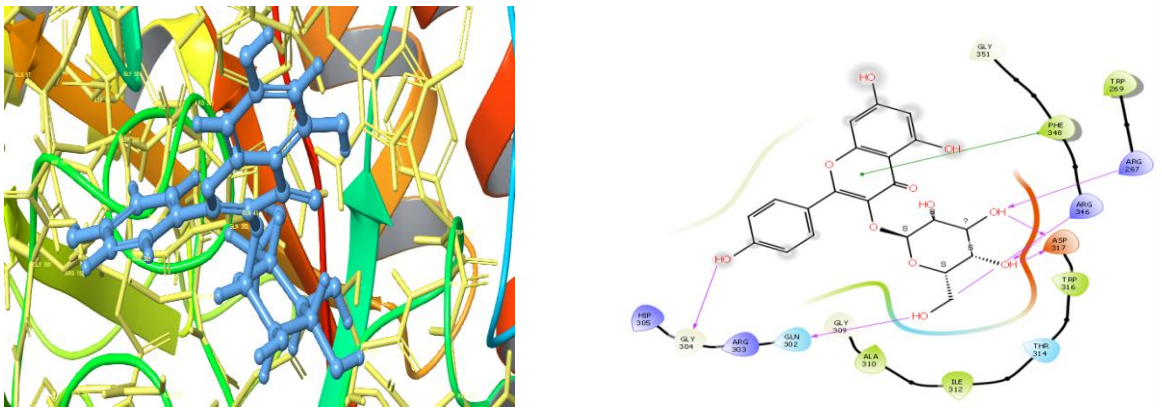

Fig 5. Protein ligand interaction (PLI) of astragaline against α-amylase enzyme and its 3D (left) and 2D (right) diagrams.

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RAMCHANDRAN PLOT

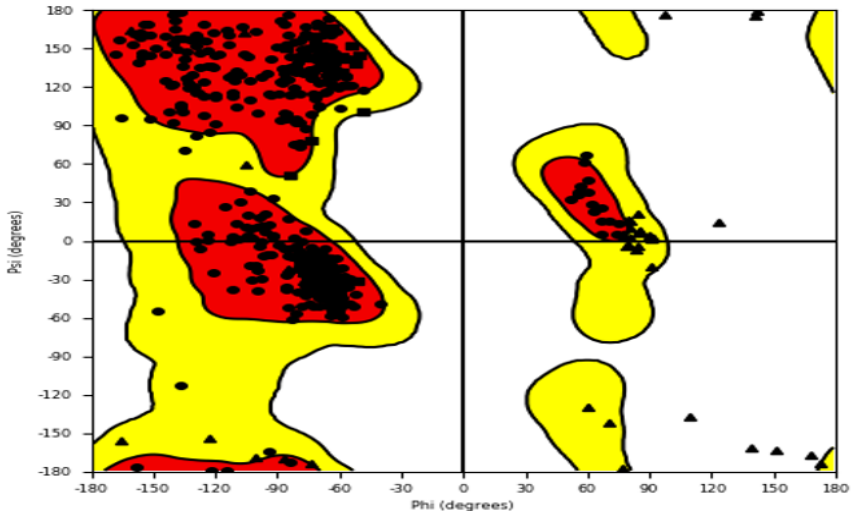

Fig 6. Ramchandran plot of targeted protein α-amylase (PDB ID 4W93) showing 90% of amino acid residues in the core region into binding site of protein.

ALPHA GLUCOSIDASE

DULCISFLAVAN

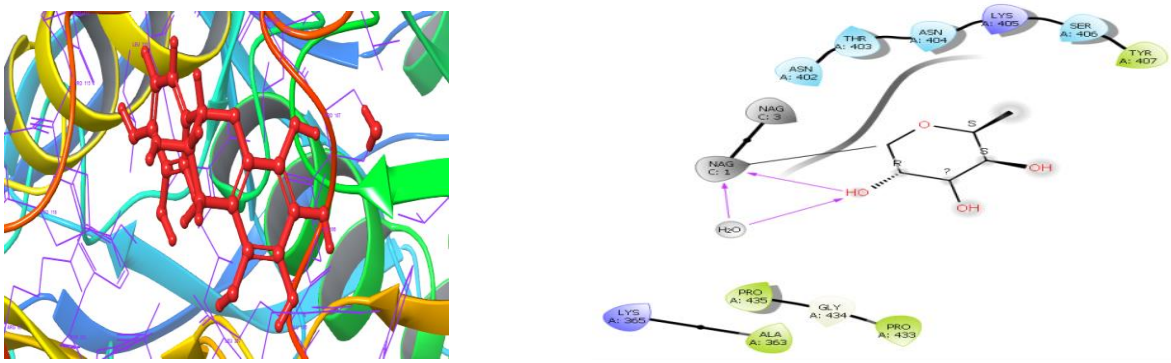

Fig 7. Protein ligand interaction (PLI) of dulcisflavan against α-glucosidase enzyme and its 3D (left) and 2D (right) diagrams**.**

CATECHIN

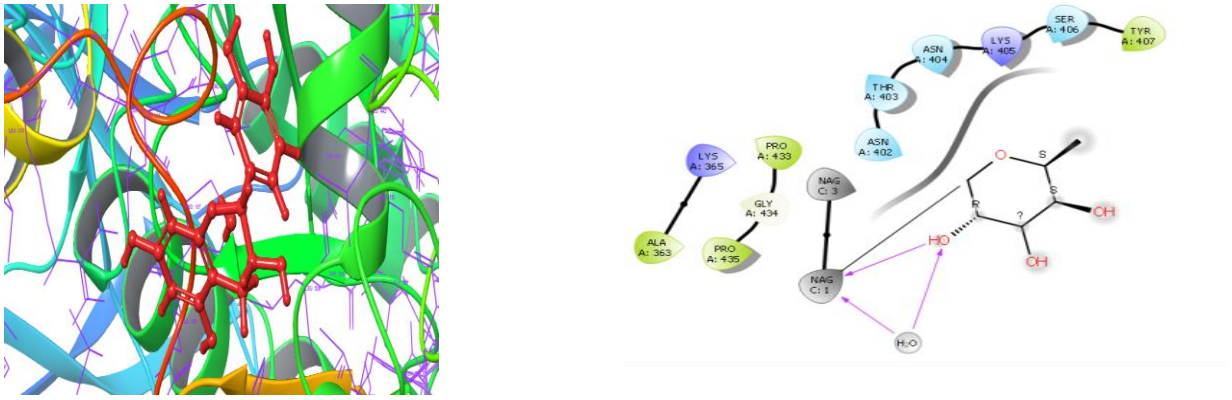

Fig 8. Protein ligand interaction (PLI) of catechin against α-glucosidase enzyme and its 3D (left) and 2D (right) diagrams.

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ENT-EPICATECHIN

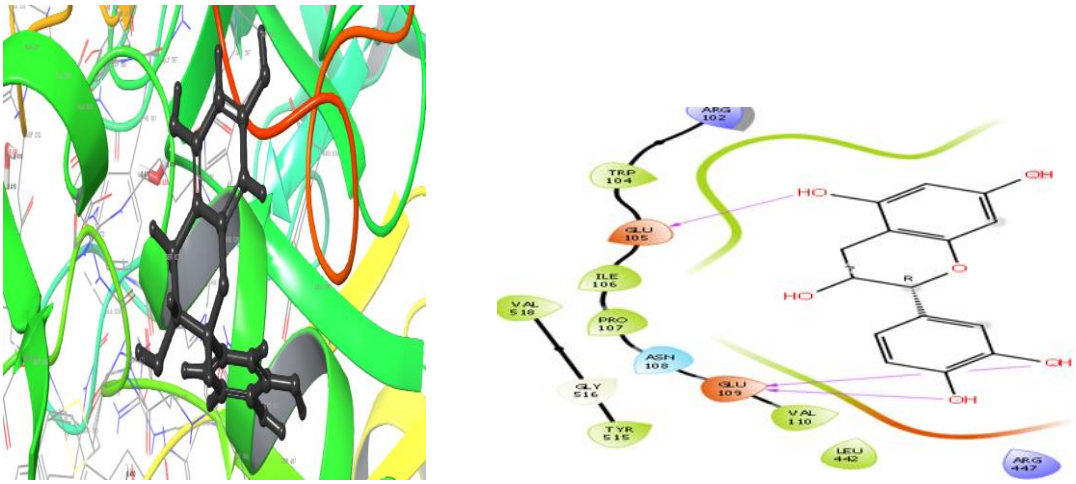

Fig 9. Protein ligand interaction (PLI) of ent-epicatechin against α-glucosidase enzyme and its 3D (left) and 2D (right) diagrams.

Epigallocatechin

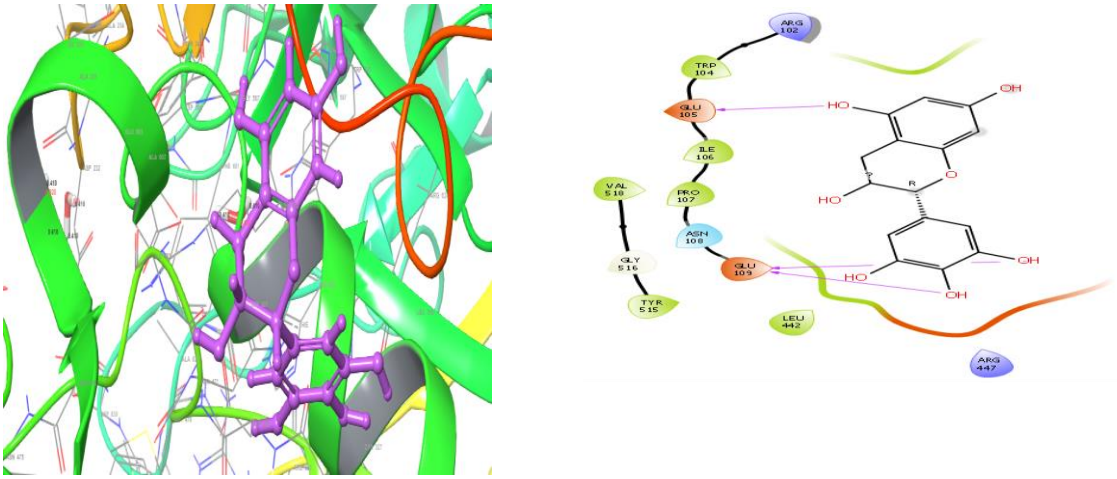

Fig 10. Protein ligand interaction (PLI) of epigallocatechin against α-glucosidase enzyme and its 3D (left) and 2D (right) diagrams.

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Epicatechin

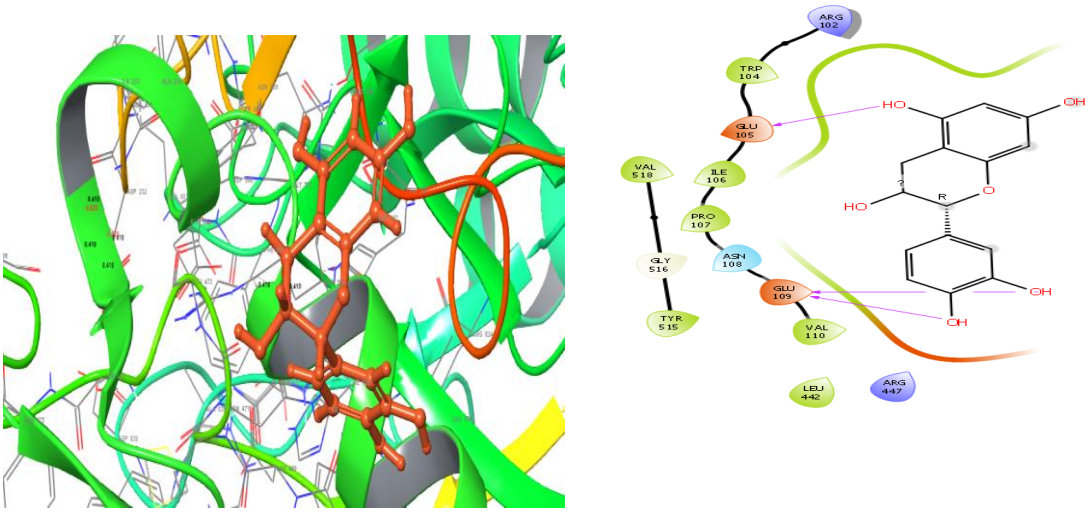

Fig 11. Protein ligand interaction (PLI) of epicatechin against α-glucosidase enzyme and its 3D (leftz) and 2D (right) diagrams.

Ramchandran plot

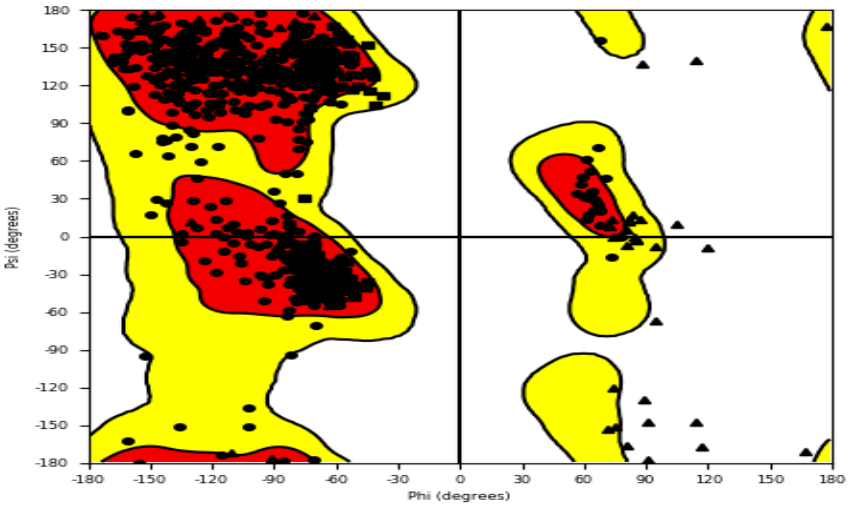

Fig 11. Ramchandran plot of targeted enzyme α-glucosidase (PDB ID 3W37) showing 90% of amino acid residues in the core region into binding site of protein.

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Table 2: Plant chemical constituents docked against alpha-amylase(PDB ID 4W93) indicating nature of interaction and amino acids involved in interaction in the active site.

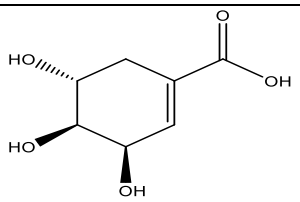
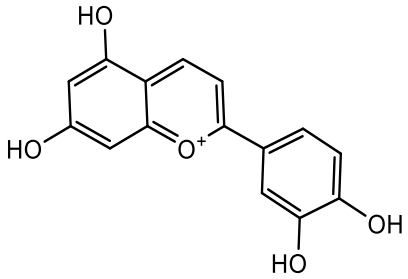
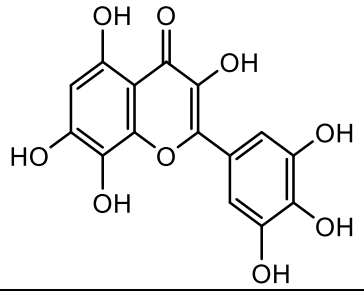
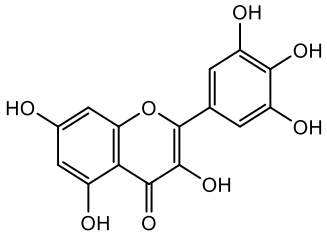
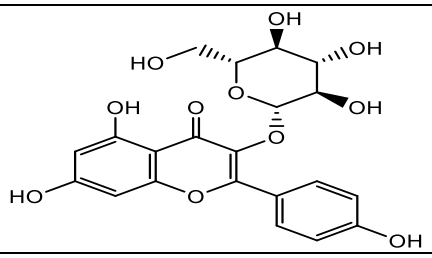
S.NO.	Chemical constituent	Chemical structure	Interactions involve Amino acid residue of binding site	
1.	Shikimic acid		Hydrophobic interaction	LEU 313, ALA 310, TRP 316, TRP 344, PHE 348, ILE 312
			H-Bond interaction	ILE 312, GLN 302, ASP 317, ARG 346
			Pi-pi stacking	
2.	Luteolinidin		Hydrophobic interaction	ALA 310, ILE 312, LEU 313, TRP 316, PHE 348
			H-Bond interaction	ASN 352, ARG 303, ASP 317
			Pi-pi stacking	
3.	Hibiscetin		Hydrophobic interaction	ALA 310, ILE 312, LEU 313, TRP 316, PHE 348
			H-Bond interaction	ASN 352, ARG 303, GLY 351, ASP 317
			Pi-pi stacking	
4.	Myricetin		Hydrophobic interaction	PHE 348, TRP 316, LEU 313, ILE 312, ALA 310
			H-Bond interaction	ASP 353, ASN 352, ARG 303, GLY 351, ASP 317
			Pi-pi stacking	
5.	Astragalin		Hydrophobic interaction	TRP 269, PHE 348, TRP 316, ILE 312, ALA 310
			H-Bond interaction	ARG 267, ARG 346, ASP 317, GLN 302, GLY 304
			Pi-pi stacking	PHE348

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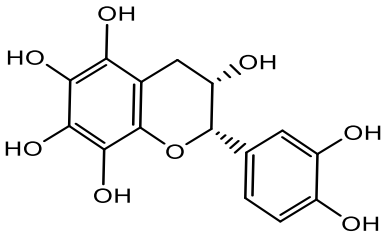
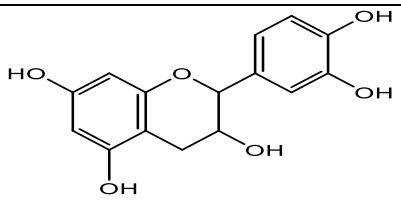
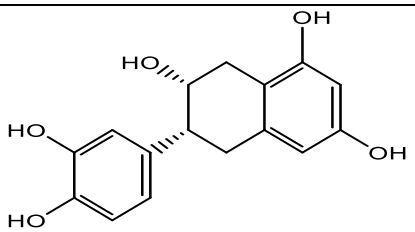
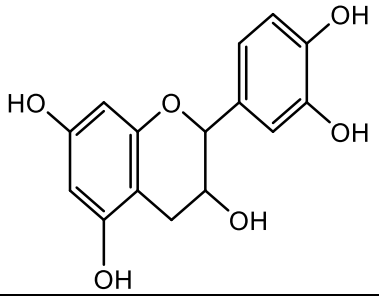
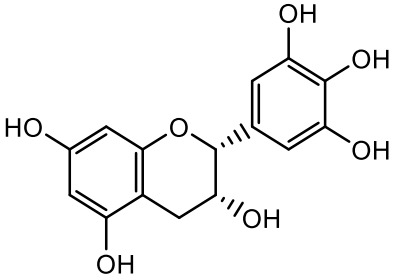
Table 3: Plant chemical constituents docked against alpha-glucosidase (PDB ID 3W37) indicating nature of interaction and amino acids involved in interaction in the active site.

S.NO.	Chemical constituent	Chemical structure	Nature of interaction	Interactions involve Amino acid residue of binding site
1.	Dulcisflavan		Hydrophobic interaction	PRO A433, PRO A435, ALA A363,TYR A407
			H-Bond interaction	NAG C1
			Pi-pi stacking	
2.	Catechin		Hydrophobic interaction	TRP 104, ILE 106, PRO 107, VAL 110, LEU 442, VAL 518, TYR 515
			H-Bond interaction	GLU 105, GLU 109
			Pi-pi stacking	
3.	Entepicatechin		Hydrophobic interaction	TRP 104, ILE 106, PRO 107, VAL 110, LEU 442, VAL 518, TYR 515
			H-Bond interaction	GLU 105, GLU 109
			Pi-pi stacking	
4.	Epicatechin		Hydrophobic interaction	TRP 104, ILE 106, PRO 107, VAL 110, LEU 442, VAL 518, TYR 515
			H-Bond interaction	GLU 105, GLU 109
			Pi-pi stacking	
5.	Epigallocatechin		Hydrophobic interaction	TRP 104, ILE 106, PRO 107, VAL 110, LEU 442, VAL 518, TYR 515
			H-Bond interaction	GLU 105, GLU 109
			Metal coordination	

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ADME Studies

In silico ADMET profiles of selected phytoconstituents for α-amylase(PDB ID 4W93) predicted and selected properties are presented in Table 6 and for α-glucosidase(PDB ID 3W37) presented in Table 7. The prediction probability values are transformed into six symbols: 0-0.1(---), 0.1-0.3(--), 0.3-0.5(-), 0.5-0.7(+), 0.7-0.9(++), and 0.9-1.0(+++).

Table 6: ADMET studies of selected phytoconstituents for alpha-amylase(PDB ID 4W93)

Properties		Shikimic acid	Luteolinidin	Hibiscetin	Myricetin	Astragalin
Medicinal chemistry	Lipinski rule	Accepted	Accepted	Accepted	Accepted	Rejected
Absorption	Caco-2Pearmeability	-5.707	-4.989	-5.961	-5.653	-6.164
	MDCK Permeability	0.00036	9.6e-06	6e-06	6.4e-06	9.1e-06
	Pgp-inhibitor	---	---	---	---	---
	Pgp-substrate	---	----	---	---	--
	HIA	+ +	---	---	---	--
	F20%	---	+ + +	+ +	+ + +	---
	F30%	+ + +	+ + +	+ + +	+ + +	+ + +
Distribution	PPB 13.839%	13.839%	97.627%	91.800 %	92.766 %	90.798 %
	VD	0.292	0.610	0.656	0.633	0.916
	BBB Penetration	-	---	---	---	---
	Fu 67.353%	67.353%	3.290%	14.485 %	10.346 %	10.980 %
Metabolism	CYP1A2 inhibitor	---	+ + +	+	+ +	--
	CYP1A2 substrate	---	-	---	--	---
	CYP2C19 inhibitor	---	--	---	---	---
	CYP2C19 substrate	---	---	---	---	---
	CYP2C9 inhibitor	---	-	+	+	---
	CYP2C9 substrate	-	+ +	--	-	+
	CYP2D6 inhibitor	---	+	---	---	-

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	CYP2D6 substrate	--	+ +	--	--	--
	CYP3A4 inhibitor	---	-	---	--	--
	CYP3A4 substrate	---	--	---	---	---
Toxicity	hERG Blokers	---	---	--	--	--
	Rat Oral Acute Toxicity	---	--	---	-	---
	AMES Toxicity	---	+	+	---	+ +
	Carcinogencity	---	--	---	---	---
	Respiratory Toxicity	--	-	---	---	---
Excretion	CL	2.164	12.924	8.233	7.716	4.258
	T ½	0.854	0.912	0.947	0.945	0.888

Table 7: ADMET studies of selected phytoconstituents for alpha-glucosiadse(PDB ID 3W37)

Properties		**Dulcisflavan**	**Catechin**	**Benzyl-isothiocynate**	**Hypolaetin**	**Hibiscetin**
Medicinal chemistry	Lipinski rule	Accepted	Accepted	Accepted	Rejected	Accepted
Absorption	Caco-2Pearmeability	-6.161	-6.052	-4.336	-6.280	-5.961
	MDCK Permeability	4.5e-06	4.6e-06	4e-05	8.2e-06	6e-06
	Pgp-inhibitor	---	---	---	---	---
	Pgp-substrate	---	---	---	+ + +	---
	HIA	-	---	---	+	---
	$F_{20\%}$	+ + +	+ + +	---	---	+ +
	$F_{30\%}$	+ + +	+ + +	---	+ + +	+ + +
Distribution	PPB 13.839%	94.701%	89.230 %	25.729%	90.746%	91.800%
	VD	0.575	0.656	4.429	0.755	0.656
	BBB Penetration	---	---	--	---	---
	Fu 67.353%	12.305%	12.916 %	63.379%	12.561%	14.485%
Metabolism	CYP1A2 inhibitor	---	-	+	--	+
	CYP1A2 substrate	---	--	-	---	---

	CYP2C19 inhibitor	---	---	---	---	---
	CYP2C19 substrate	---	---	-	---	---
	CYP2C9 inhibitor	--	--	---	--	+
	CYP2C9 substrate	--	+ +	---	--	--
	CYP2D6 inhibitor	---	--	--	---	---
	CYP2D6 substrate	--	-	-	--	--
	CYP3A4 inhibitor	---	-	---	---	---
	CYP3A4 substrate	---	--	--	---	---
Toxicity	hERG Blokers	--	---	---	--	--
	Rat Oral Acute Toxicity	---	+	+ +	---	---
	AMES Toxicity	--	+	--	+ +	+
	Carcinogencity	---	--	--	---	---
	Respiratory Toxicity	---	--	+ + +	---	---
Excretion	CL	11.546	17.301	7.139	4.372	8.233
	T ½	0.898	0.896	0.585	0.841	0.947

CONCLUSION

Based on the *in silico* evaluations, selected phytoconstituents as targets for the inhibition of α-amylase and α-glucosidase enzymes. The docking score selected phytoconstituents against target enzymes using molecular docking further supported our claim regarding the antidiabetic activity of these selected phytoconstituents. The study suggests that finding natural antidiabetic medicines by the docking of plant components against alpha-amylase and alpha-glucosidase is a promising approach. Building on the knowledge gathered from investigations, we may be able to create safe, natural, and efficacious therapeutic solutions for the management of diabetes and enhancement of public health by concentrating on rigorous experimental validation and optimization.

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