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Original Research Article

Computational assessment of antidiabetic potential of bioactive constituents of Euphorbia.

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Abstract: About 2.8% of individuals worldwide struggle with diabetes mellitus (DM), a serious metabolic syndrome that is projected to rise to 4.4% by 2030. Biguanides, thiazolidinediones, α-glucosidase inhibitors, sulfonylureas, and non-sulfonylureas secretagogues belong to the class of medicines on the market that improve insulin sensitivity, secretion, complementing insulin, and boosting glucose uptake.The drugs that are now in use have been reported to have a number of unwanted effects, included hypothyroidism, weight gain, tachycardia, and hepatic failure. Medicinal plants have been used to treat a number of disorders, including diabetes mellitus. In comparison to synthetic medicines, herbal medications are safer, easier to obtain, have less adverse effects, and are more affordable. Euphorbia is a significant dicotyledon medicinal plant. Its phytoconstituents, which include flavanoids, terpenoids, and tannins, are used to treat a variety of conditions, including skin disorders, asthma, rhinitis, viral infections, and spasms. Although this plant has been shown to have in vivo hypoglycemic effects, the exact mechanism of action of its phytoconstituents is yet unknown and needs further research. For this reason, 25 known phytoconstituents of this plant were used in docking studies on the 3D structures of two proteins involved in type-2 diabetes, namely α-amylase and Peroxisome Proliferator-Activated Receptor gamma.The finding of the research is based on docking energies and the availability of significant amino acid interactions that offer insight into potential phytoconstituent mechanisms.

Keywords: Diabetes mellitus, Euphorbiacea, flavanoids, tannins, docking.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a common metabolic disease triggered by tissue resistance to insulin and improper insulin secretion. Currently recognized as the eighth most common cause of disability and death, diabetes is a serious globally health concern. Diabetes afflicted 830 million people in 2022, a substantial increase from the 200 million cases recorded in 1990. The prevalence of diabetes was 6.1% internationally in 2021, rising 90.5% from 3.2% in 1990. It is predicted to reach 9.8% by 2050, affecting 13.1 billion people[4-6]. With a male-to-female ratio of 1.14 in 2021, the incidence of diabetes was higher in men than in women worldwide, while regional variation was reported.[7] Researchers have looked into both pharmaceutical and non-pharmacological strategies to treat diabetes, but no drug has been proven to be absolutely safe.[8-10] Among non-pharmacological methods, regular exercise is often recommended to boost insulin sensitivity.[11-12] The main groups of medicines utilized in pharmacological approaches to treat diabetes include sulfonylureas, which increase the release of insulin from pancreatic islets; biguanides, which slow the production of glucose in the liver; peroxisome proliferator-activated receptor-γ (PPARγ) agonists, which enhance the action of insulin; and α-glucosidase inhibitors, which delay the intestinal absorption of glucose. [13-15].These categories of drugs possess problems such weight gain, severe hypoglycemia, metabolic side effects, and other complications with target selectivity, permeability, and solubility.[16-17]. However, they can be taken alone or in combination with other hypoglycemic medications. Conventional therapies

may result in long-term toxicity, adverse effects, and reliance [18–20]. Investigating alternative remedies, such as natural therapies, may assist in minimizing these dangers. Antioxidants are essential for lowering oxidative stress and scavenging dangerous free radicals [21]. Numerous studies have linked oxidative stress to problems associated with diabetes [22–23]. High blood sugar levels decrease the activity of antioxidant enzymes while increasing the generation of reactive oxygen and nitrogen species. Critical biomolecules like proteins, lipids, and DNA are harmed by this imbalance, which upsets cellular homeostasis and eventually produces toxic byproducts that accelerate the course of disease [24, 25]. Stress pathways are triggered when the body's antioxidant system is unable to combat this, which results in cellular damage and the advancement of diabetes. Antioxidant therapy protects β cells, maintains their function, and lessens problems, according to research. Because of their therapeutic advantages, safety, accessibility, and affordability, natural antioxidants are being employed more frequently [26]. By lowering oxidative stress, preventing lipid peroxidation, and promoting the activity of antioxidant enzymes, natural antioxidants can help prevent or reduce type 2 diabetes.

The complex physiological processes that regulate Type 2 diabetes oxidative stress, including glycemic management, postprandial oxidative stress [27], the polyol pathway, high-calorie, high-fat meals, exercise, and sleep, should also be taken into consideration when evaluating natural antioxidant products. It may be possible to prevent or decrease the onset of Type 2 diabetes by minimizing processes that cause long-term harmful oxidative stress and increasing the consumption of natural antioxidant products [28,29]. Euphorbia prostrata, a small annual herb found throughout India, especially in the Himalayan foothills, is a member of the Euphorbiaceae family and is commonly referred to as "Hazar dani" [30–31]. Asthma [32], hemorrhoids [33], diabetes mellitus [34], dysentery [32], hyperlipidemia [35], wound healing [36], anti-inflammatory [37], analgesic [38], anthelmintic [39], and diabetic nephropathy [40] are only a few of the illnesses for which the plant has been used extensively.

Additionally, it has long been used to treat snake bites and various skin illnesses [41]. Euphorbia prostrata phytoconstituents have demonstrated both antioxidant and antidiabetic qualities, making the plant essential for research on diabetes in particular [42–43].Based on these findings, this study uses docking methodology to evaluate the anti-hyperglycemic activity of antioxidant compounds in the hydroalcoholic extracts of Euphorbia prostrata by evaluating their binding efficacy as ligands for two targeted proteins (α-amylase and PPAR gamma). These targets have been verified to include co-crystals of recognized antidiabetic drugs. Glycosides, phytosterols, flavonoids, polyphenols, tannins, alkaloids, terpenoids, saponins, anthraquinones, and other compounds have been found in Euphorbia prostrata through phytochemical screening. [44]. Ten main compounds—Gallic Acid, Corilagin, 1,2,3-Tri-O-Galloyl-D-Glucose, Geraniin, Tellimagrandin I and II, and Rugosin A, D, E, and G—have been identified by physicochemical and spectroscopic study [45, 46].Prostratins A, B, and C, Euphorbin G and H, and other hydrolyzable ellagitannins are present in the dried leaf extracts of Euphorbia prostrata. Kaempferol, Cosmosiin, Rhamnetin 3-Galactoside, Quercetin, Luteolin, and many Quercetin Glycosides are among the flavonoids present in the aerial portions. Amino acids, the terpene alcohol Beta-Terpineol, and sterols (Beta-Amyrine Acetate, Beta-Sitosterol, Campesterol, Stigmasterol, and Cholesterol) are also present in the aerial sections. Myricylic alcohol and the triterpenes Tirucallol and Taraxerol have been discovered from the roots [47]. Because tannins and flavonoids have polyphenol structures with many hydroxyl groups, they are powerful antioxidants. They can create hydrogen bonds with reactive oxygen species that injure cells, such as hydrogen peroxide, singlet oxygen, and peroxy nitrite. This mechanism implies that they may play a part in lowering the oxidative stress linked to Type 2 diabetes [48]. Numerous studies show that diets rich in phytosterols can enhance insulin sensitivity and boost the metabolism of fats and carbohydrates [49]. The two targeted proteins in this work, α-Amylase (2QV4) and (2ZNP) Peroxisome Proliferator-Activated Receptor gamma, were previously investigated as possible therapeutic targets for Type 2 diabetes mellitus [50]. The calcium-dependent enzyme alpha (α)-amylase breaks down polysaccharides to aid in digestion, but it also results in postprandial hyperglycemia. Acarbose, miglitol, and voglibose are examples of α-amylase inhibitors that have proven to be an important target for efficiently controlling blood sugar levels. By favorably controlling blood pressure, lipids, platelet aggregation, and vascular health, acarbose in particular aids in weight control, lowers cardiovascular risks, and delays the onset of diabetes [53]. By momentarily inhibiting the several alpha-glucosidase enzymes, including maltase, alpha-glucosidase inhibitors (AGIs) decrease the intestinal absorption of carbohydrates. AGIs may be a suitable first-line treatment for Type 2 diabetes since they directly addressed postprandial hyperglycemia, which is thought to be a potential independent risk factor for cardiovascular problems. Alpha-glucosidase inhibitors (AGIs) are regarded as safe because they do not result in hypoglycemia, weight gain, or other serious side effects. [54]. The PPAR family includes the nuclear hormone receptor

peroxisome proliferator-activated receptor gamma (PPARγ). All of the PPAR family's endogenous activators are different fatty acids, indicating that the PPARs play a significant role in lipid metabolism. It plays a significant role in controlling adipocyte differentiation. Since 1997, a class of PPARγ-agonists known as thiazoledinediones (TZDs) has been used to treat type 2 diabetes (T2D). [54-57]. They have been proposed to slow the advancement of insulin resistance and are distinguished by their capacity to reduce insulin resistance. TZD therapy significantly lowers plasma triglycerides and free fatty acids, although it takes several weeks to lower plasma glucose levels. Body fat increase is one of the main side effects of TZD treatment; nevertheless, there is evidence that the fat is reallocated favorably, from visceral to subcutaneous depots. However, the impact of long-term treatment on weight gain after TZD medication is unknown, and given that excess body fat is practically a requirement for the development of type 2 diabetes, it may be questioned if the use of these "adipogenic compounds" is suitable [58–63]. In the realm of drug development, computer-aided drug design, or CADD, is a useful tool. One method that aids in identifying interactions crucial for ligand binding with amino acid residues is structure-based drug design (SBDD) [64-68]. These interactions could be useful in figuring out the underlying molecular processes that cause binding. SBDD mostly uses docking experiments in which the ligand and protein structures are known. Docking scores, the positions of the ligands in the binding pocket, and other innovative approaches that take into account the quantity of interactions between the ligands and the amino acids in the binding pocket are used to evaluate the docking data [69,70]. The objective of this study was to investigate a wide variety of bioactive substances (phytoconstituents) from all four families of Euphorbia prostrata, including flavonoids, tannins, phenolic acids, and sterols, and to examine how these substances interacted with target proteins in order to potentially clarify the underlying molecular mechanisms necessary for enzyme inhibition.

Materials and methods

2.1 Dataset

25 bioactive phytoconstituents used for the docking studies were taken from the literature (Table 1). The molecules belonged to the category of flavonoids (Apigenin, Apigenin 7-Glucoside, Kaempferol, Luteolin, 6-Methoxy Quercetin Glycoside, Quercetin, Quercetin 3-Rhamnoside, Rhamnetin 3-Galactoside), sterols (Beta -Amyrin Acetate, Campesterol, Stigmasterol, Beta -Sitosterol), Phenolic Acids (Ellagic Acid, Gallic Acid), Tannins (Corilagin, Euphorbin G, Euphorbin H, Geraniin, Rugosin A, Rugosin D, Rugosin E, Tellimagradin I, Tellimagradin II), and Terpene Alcohols (1,2,3-Tri-O-Galloyl-D-Glucose, β -Terpineol).

2.2 Preparation of ligands

ChemDraw was used to draw the ligands or compounds from the dataset. The identical two-dimensional structures were imported into Chem3D, which transforms them into three dimensions. The structures were minimized using the default parameters as part of additional preparation. After being stored in the mol format, the structures were imported into the Autodock 4.2 program to identify torsions. Finally, the structures were saved in the pdbqt format for more docking research.

2.3 Preparation of protein

For the docking studies, three target proteins with pdb ids of 2QV4 and 2ZNP were retrieved from the protein data bank. The 2QV4 protein is a member of the hydrolase class and is a human pancreatic alpha-amylase complexed with nitrite and acarbose with a resolution of 1.97 Å. For minimization, the downloaded target proteins were imported into the Autodock 4.2 program. As indicated by the co-crystallized ligands in each protein, the polar hydrogens were supplied after the non-essential water molecules were eliminated. The Kollmann charges were added concurrently with the addition of the missing residues. For additional docking research, the produced proteins were stored in the pdbqt format.

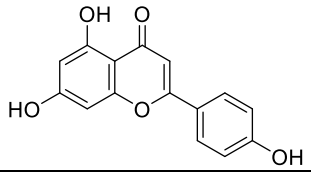
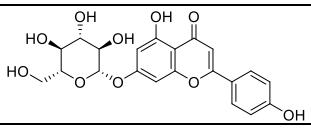
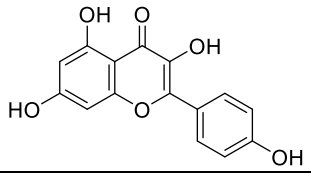
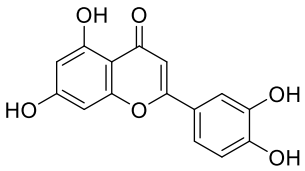
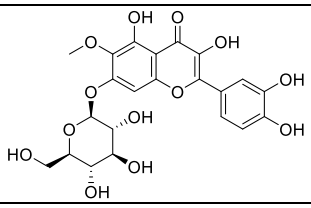
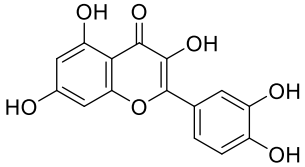
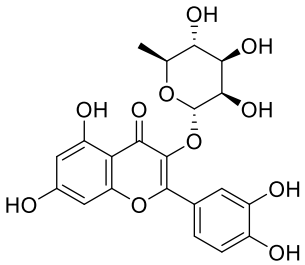
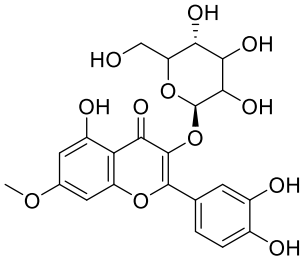
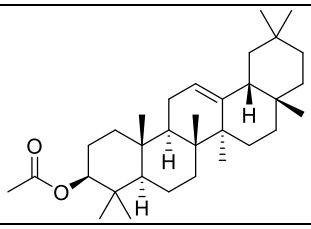
2.4 Preparation of the grid box

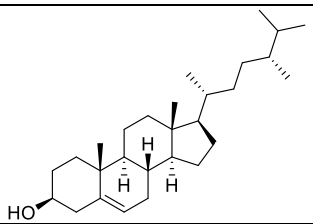
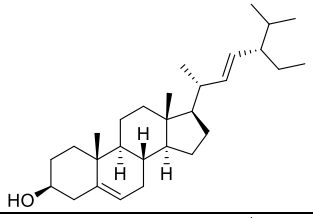
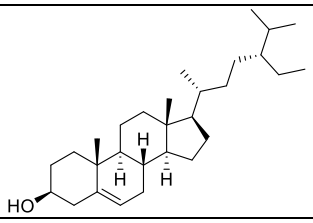
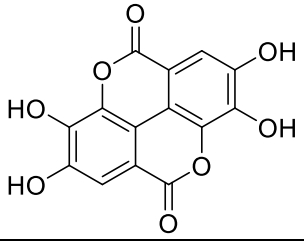
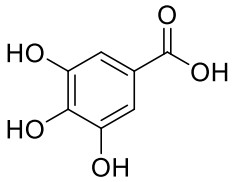
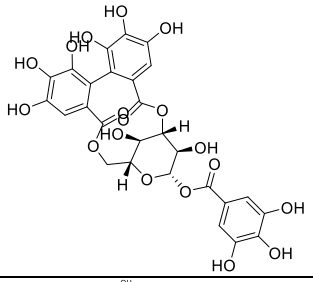
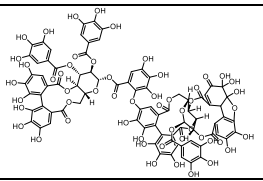
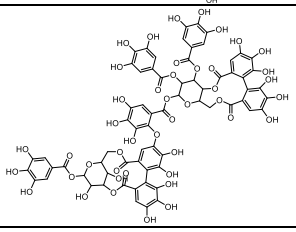
The precise region of the protein structure where the ligands bind is known as the docking grid box. The co-crystallized ligand is mostly responsible for identifying this. The grid box was defined using the XYZ coordinates of the co-crystallized ligands of the downloaded targets. The proteins 2QV4 and 2ZNP had the following coordinates: (12.384, 48.136, 26.209) and (15.38, 2.56, 38.04)

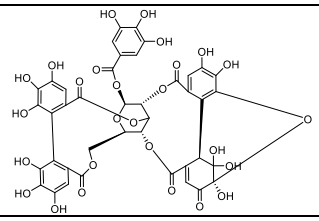
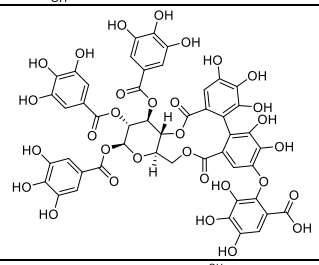
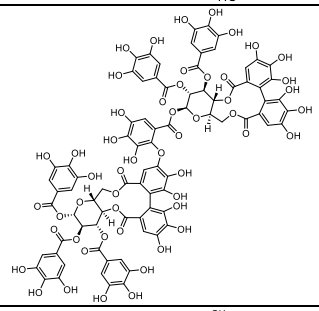
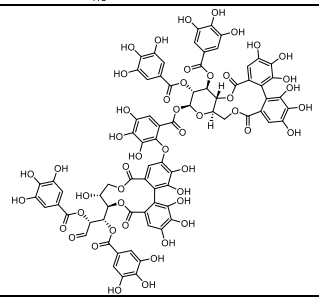
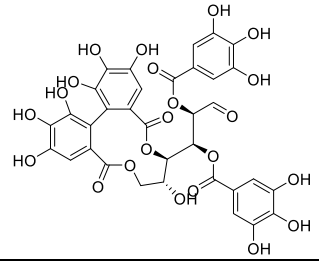
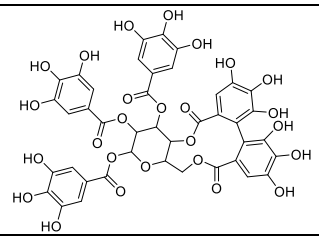
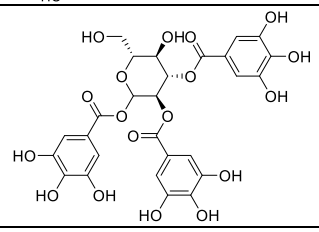
2.4 Docking studies

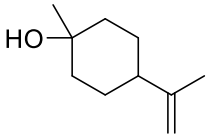
Autodock Vina was used to dock the ligands. With the help of this software, configuration files are created that mainly contain the protein and ligands in pdbqt formats as well as the XYZ coordinates of the grid box.

Table-1: Structure of phytoconstituents of *Euphorbia prostrata*

S.No.	Componds	Structure	Reference
1.	Apigenin		[71,72]
2.	Apigenin 7-Glucoside		[47]
3.	Kaempferol		[47]
4.	Luteolin		[71,72]
5.	6-Methoxy Quercetin Glycoside		[47]
6.	Quercetin		[71,72]
7.	Quercetin 3-Rhamnoside		[47]
8.	Rhamnetin 3-Galactoside		[47]
9.	Beta-AmyrinAcetate		[47]

10.	Campesterol		[71]
11.	Stigmasterol		[71]
12.	Beta-Sitosterol		[71]
13.	Ellagic Acid		[71]
14.	Gallic Acid		[71-73]
15.	Corilagin		[71]
16.	Euphorbin G		[47]
17.	Euphorbin H		[47]

18.	Geraniin		[71]
19.	Rugosin A		[71]
20.	Rugosin D		[71]
21.	Rugosin E		[71]
22.	Tellimagradin I		[71]
23.	Tellimagradin II		[71]
24.	1,2,3-Tri-O-Galloyl--D-Glucose		[71]

25.	Beta -Terpineol		[47]

RESULT AND DISCUSSION

Table 2 provides a description of each of the 25 phytoconstituents' docking scores. The binding energies for the pdb id 2QV4 (α-Amylase) range from -5.7 to -10.8 kcal/mol, according to the docking score analysis of the phytoconstituents for each target protein. Comparably, 2ZNP (Peroxisome Proliferator-Activated Receptor gamma) has binding energies between -5.2 and -10.6 kcal/mol. It's interesting to note that, of all the phytoconstituents, beta-terpineol had the lowest binding energies for each of the target proteins under study: -5.7 for α-Amylase and -5.2 for Peroxisome Proliferator-Activated Receptor gamma.This finding suggests that beta-terpineol plays a very small part in inhibiting any of the two targets. Quercetin had the highest binding energy (-10.6 kcal/mol) for α-Amylase among the phytoconstituents, while gallic acid had the highest binding energy (-10.8 kcal/mol). It was noteworthy that every phytoconstituent with the highest binding energies belonged to the family of flavanoids and tannins.

Table 2: Binding energy (kcal/mol) of bio-molecules in *Euphorbia prostrata* to 2QV4 and 2ZNP.

Category	**Phytoconstituents**	**Binding Energy (kcal/mol)**	
		Alpha Amylase Inhibitors (2QV4)	**Peroxisome Proliferator-Activated Receptor gamma agonists (2ZNP)**
Flavanoids	Apigenin	-9.5	-7.7
	Apigenin 7-Glucoside	-10.3	-8.9
	Kaempferol	-9.0	-7.6
	Luteolin	-9.6	-7.8
	6-Methoxy Quercetin Glycoside	-8.8	-8.7
	Quercetin	-9.0	-10.6
	Quercetin 3-Rhamnoside	-8.9	-9.0
	Rhamnetin 3-Galactoside	-8.7	-9.1
Sterols	Beta-Amyrin Acetate	-8.0	-9.3
	Campesterol	-9.4	-9.2
	Stigmasterol	-9.6	-7.6
	Beta-Sitosterol	-8.9	-7.5
Tannins	Ellagic Acid	-9.1	-8.3
	Gallic Acid	-10.8	-8.3
	Corilagin	-8.9	-8.3
	Euphorbin G	-10.7	-5.3
	Euphorbin H	-10.0	-8.4
	Geraniin	-8.3	-8.5
	Rugosin A	-9.8	-9.4
	Rugosin D	-9.7	-5.5
	Rugosin E	-9.2	-9.4
	Tellimagradin I	-9.6	-8.4
	Tellimagradin II	-8.9	-10.5

Terpene Alcohol	Beta -Terpineol	-5.7	-5.2
	1,2,3-Tri-O-Galloyl--D-Glucose	-9.5	-9.4

The docking studies include interactions between the ligands (phytoconstituents in this case) and the target protein in addition to the docking energy or binding energy. Important amino acid residues that are essential to interacting with the various ligand atoms can be seen by these interactions. Furthermore, it discloses the kinds of interactions necessary for the target and ligand to bind.

3.1 The binding interactions of each protein target has been classified in two categories.

3.1.1 Interaction analysis of α-Amylase

TRP59, THR163, GLY164, ASN105, ALA106, VAL107, GLN63, HIS101, GLU233, ARG195, ASP300, HIS299, and some water molecules are bound by the co-crystallized ligand of the α-Amylase protein 2QV4. In general, the researched phytoconstituents must exhibit interaction with some of the key amino acid residues in order to comprehend the activity of more recent phytoconstituents. The phytoconstituents Apigenin, Kaempferol, Luteolin, 6-Methoxy Quercetin Glycoside, Quercetin, and Tellimagradin I contained the amino acids TRP59, GLN63, and TYR62. The TRP59 interaction was found in 23 of the 25 phytoconstituents examined, including Apigenin 7-Glucoside, Quercetin 3-Rhamnoside, Rhamnetin 3-Galactoside, Beta-Amyrin Acetate, Campesterol, Stigmasterol, Beta-Sitosterol, Ellagic Acid, Corilagin, Euphorbin G, Euphorbin H, Geraniin A, Rugosin D, Rugosin E, Tellimagradin II, 1,2,3-Tri-O-Glucose, and beta-Terpineolin. Quercetin 3-Rhamnoside, Rhamnetin 3-Galactoside, Beta-Amyrin Acetate, Campesterol, Stigmasterol, Beta-Sitosterol, Corilagin, Tellimagradin II, and Beta-Terpineol all interacted with the TYR62 residue. Apart from the aforementioned significant amino acid residues found in the majority of phytoconstituents, there are other significant residues found in fewer phytoconstituents, such as GLU233, ASP300, and THR163, which were found in the Apigenin 7-Glucoside. Together with GLU233 and ASP300, which were discovered in Tellimagradin I, GLU233 and THR163 were also discovered in Euphorbin G and Rugosin D. Euphorbin H, 1,2,3-Tri-O-Galloyl--D-Glucose, and beta-terpineol were also found to interact with GLU233; Luteolin, Quercetin, Ellagic Acid, and Gallic Acid were found to interact with ASP300; Rugosin E and Tellimagradin II were also found to interact with THR300.

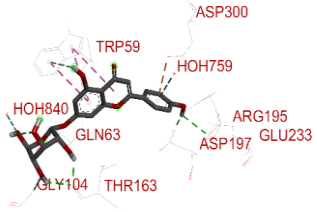
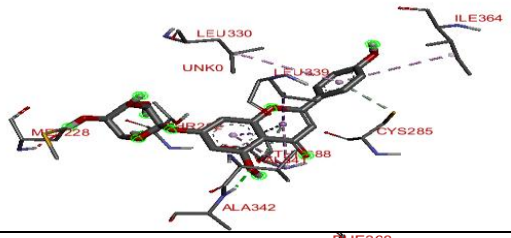
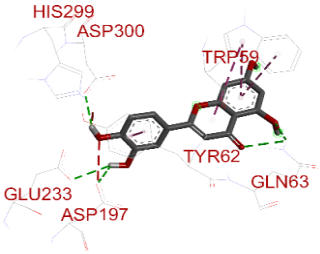
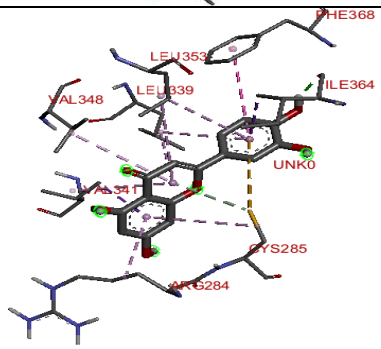
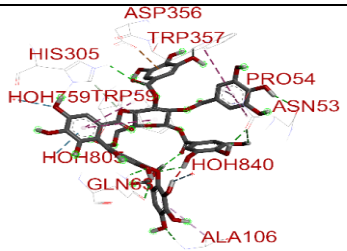
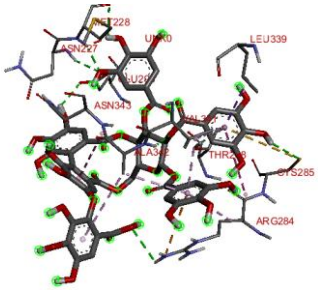
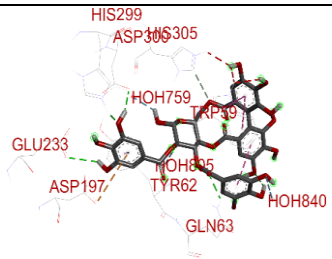
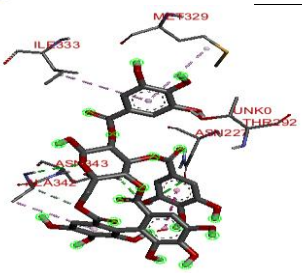
3.1.2 Interaction analysis of Peroxisome Proliferator-Activated Receptor gamma

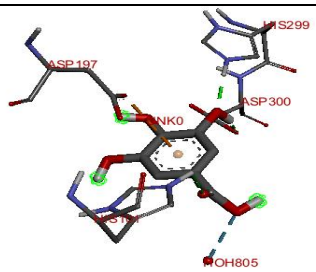
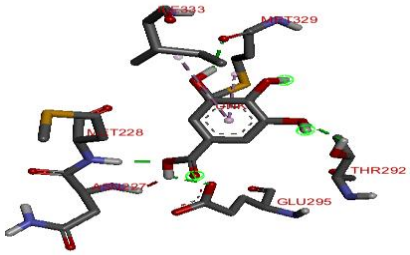
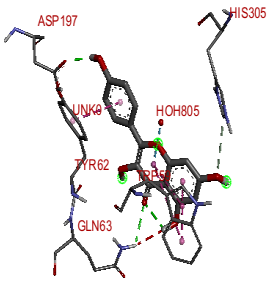
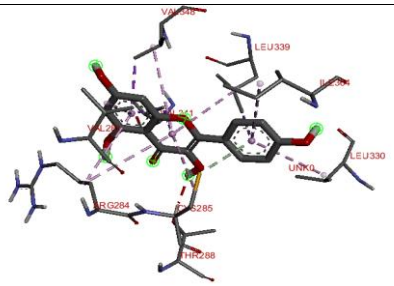
The co-crystallized ligand of the Peroxisome Proliferator-Activated Receptor gamma protein 2ZNP binds to residues ARG284, VAL341, LEU339, CYS285, VAL348, VAL281, LEU330, PHE368, LEU255, LYS367, and VAL334. Apigenin, 1,2,3-Tri-O-Galloyl-D-Glucose, Compesterol, Euphorbin G, Kaempferol, Prostratin A, Quercetin, Rhamnetin-3-Galactase, Quercetin 3-Rhamnoside, Tellimagradin II, Corilagin, Geraniin, and Rugosin A, Rugosin D, and Rugosin E were among the significant residues that contained ARG284. Apigenin, 1,2,3-Tri-O-Galloyl-D-Glucose, Compesterol, Apigenin-7-Glucoside, Kaempferol, Prostratin A, Quercetin, Rhamnetin-3-Galactase, Quercetin 3-Rhamnoside, Tellimagradin II, Corilagin, Geraniin, and Rugosin A all contained VAL341. 1,2,3-Tri-O-Galloyl-D-Glucose, 6-Methoxy-Quercetin, Apigenin, Apigenin-6-Glucoside, Beta-Terpineol, Compesterol, Kaempferol, Luteolin, Quercetin, Quercetin-3-Rhamnoside, Rhamnetine-3-Galactoside, and Rugosin A were found to contain CYS285. Our research also showed that ARG284, VAL341, LEU339, and CYS285, which were present in phytoconstituents 13, 13, 11, and 12, respectively, were crucial for demonstrating binding affinity. Additionally, VAL348, LEU330, VAL281, and PHE368, which are present in 5,5, 2, and 2 phytoconstituents, respectively, were the additional significant interacting residues discovered in docking experiments.

The phytoconstituents from the tannin and flavonoid families demonstrated the highest binding energies, according to a summary of the docking results in both protein targets. For every protein target, a thorough examination of the interactions present in the phytoconstituents has already been covered. TRP59, which was present in 23 of the 25 phytoconstituents examined, is the most significant amino acid residue that binds to the α-Amylase enzyme. All of these phytoconstituents, including Rugosin D, Rugosin E, Rugosin A, Tellimagradin I, Tellimagradin II, Corilagin, Geraniin, Euphorbin H, and Euphorbin G, exhibited interactions with TRP159. All of the phytoconstituents of the tannins, with the exception of Corilagin and Rugosin D, had another significant residue, GLN63. Other significant interacting residues were frequently found in phytoconstituents of the tannin family, including GLU233 (found in Euphorbin G, Euphorbin H, Rugosin D, and Tellimagradin I), ASP300 (found in Tellimagradin I), and THR163 (found in Euphorbin G, Rugosin D, Rugosin E, and

Tellimagradin II). Good binding energies ranging from -8.7 to -10.3 were also displayed by the phytoconstituents of the flavonoid family. Furthermore, every phytoconstituent in the flavonoid family, including Apigenin, Apigenin 7-Glucoside, Kaempferol, Luteolin, 6-Methoxy Quercetin Glycoside, Quercetin, Quercetin 3-Rhamnoside, and Rhamnetin 3-Galactoside, interacted with the most significant residue TRP59. Similar interactions were seen between the phytoconstituents of the tannins family and significant residues such ARG404 (Corilagin, Euphorbin G, Euphorbin H, Rugosin D, Rugosin E), TRP169 (Gernaiin, Rugosin E, and Tellimagradin II), and ASP420 (Corilagin, Gernaiin, and Rugosin A). According to the aforementioned research, the most significant bonding interactions were hydrogen and hydrophobic bonds, and the most significant phytoconstituents were Apigenin 7-glucoside, Luteolin, and Rugosin E and Tellimagradin I among the flavonoids.

Table 3 lists the most significant amino acids in their optimal positions.

S.NO.	Phytoconstituents	3D poses of the docking interactions	
		Alpha Amylase Inhibitors(2QV4)	**Peroxisome Proliferator-Activated Receptor gamma agonists (2ZNP)**
1.	Apigenin 7-Glucoside		
2.	Luteolin		
3.	Rugosin A		
4.	Tellimagradin I		

5.	Gallic acid		
	Quercetin		

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CONCLUSION

Diabetes mellitus is a serious condition brought on by insufficient insulin synthesis, inefficient insulin utilization by the body, and insulin resistance due to lifestyle choices. Although the medications on the market operate in various ways, they are known to have detrimental side effects. Moving toward safer substitutes like herbal medications is crucial in light of this. Although Euphorbia prostrata has demonstrated effectiveness against hyperglycemia, its precise mode of action is still unknown. In order to clarify the molecular mechanisms behind its activity, we conducted docking investigations in this investigation. Two significant protein targets, 2QV4 and 2ZNP, were docked against the structure of the plant's phytoconstituents. According to the research, some of the highest binding energies were found in phytoconstituents from the families of flavonoids (-7.7 to -10.7 kcal/mol) and tannins (-5.5 to -10.8 kcal/mol). The phytoconstituents of these two families exhibited the greatest number of interactions with significant amino acid residues of each protein target, namely TRP59 for 2QV4 and ARG284, VAL341, LEU339, and CYS285 for 2ZNP, according to the docking interaction studies. Based on their binding mechanisms (interaction with TRP59, ARG284, VAL341, LEU339, and CYS285) and binding energies, these investigations indicate that tannins and flavonoids may exhibit the greatest effectiveness as antidiabetic drugs. The most significant bond type for binding, according to the study, was hydrogen bonding, which was followed by hydrophobic bonding. The most significant phytoconstituents were determined to be Apigenin 7-glucoside, luteolin, and quercetin among the flavonoids, and Rugosin E, Tellimagradin I, and gallic acid among the tannins, based on the quantity of interactions, interactions with significant amino acid residues, and binding energies. These investigations have aided in the identification of the molecular mechanisms underlying the action of the phytoconstituents of the plant Euphorbia Prostrata, listing significant amino acids, interactions, and particular families of the chemical constituents that may be further tested using in-vitro and in-vivo techniques to create novel antidiabetic agents with the fewest possible side effects.

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