European Journal of Clinical Pharmacy

Print ISSN: 2385-409X **Online ISSN**: 3105-0409

Website: https://farmclin.com/

Original Research Article

In silico investigation of phytoconstituents from Euphorbia prostrata for antidiabetic activity

Article History:

Received: 07-10-2025
Revised: 20-10-2025
Accepted: 10-11-2025
Published: 25-11-2025

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Abstract: Globally, 2.8% of people suffer with diabetes mellitus (DM), a dangerous metabolic condition that is expected to increase to 4.4% by 2030. Biguanides, thiazolidinediones, α-glucosidase inhibitors, sulfonylureas, and non-sulfonylureas secretagogues are among the medications available that enhance insulin sensitivity, secretion, supplementing insulin, and increasing glucose absorption. Numerous adverse effects, including as hypothyroidism, weight gain, tachycardia, and hepatic failure, have been linked to the medications now in use. Diabetes mellitus is one of the many conditions that medicinal plants have been tried to cure. Herbal remedies are less harmful, more accessible, less expensive, and safer than synthetic ones. One important dicotyledon medicinal plant is Euphorbia. Numerous ailments, such as skin problems, asthma, rhinitis, viral infections, and spasms, are treated using its phytoconstituents, which include flavanoids, terpenoids, and tannins. Even though this plant has been demonstrated to have hypoglycemic effects in vivo, more research is necessary to determine the precise mechanism of action of its phytoconstituents. The 3D structures of two proteins involved in type-2 diabetes namely protein-tyrosine phosphatase 1B and α-Glucosidase were docked using 25 known phytoconstituents of this plant.The research's conclusion is based on docking energies and the presence of important amino acid interactions that provide information about possible phytoconstituent processes.

Keywords: Docking, Diabetes mellitus, Euphorbiacea, Flavanoids, Tannins.

INTRODUCTION

Tissue resistance to insulin and inappropriate insulin secretion are the main causes of type 2 diabetes mellitus (T2DM), a common metabolic illness. Diabetes is currently acknowledged as the eighth most common cause of death and disability, making it a major worldwide health concern. In 2022, 830 million individuals had diabetes, a significant rise from the 200 million cases reported in 1990. In 2021, the global prevalence of diabetes was 6.1%, up 90.5% from 3.2% in 1990. By 2050, it is expected to increase to 9.8%, impacting 13.1 billion people [4-6]. The incidence of diabetes was higher in males than in women globally in 2021, with a male-to-female ratio of 1.14, however regional variation was noted. [7] Although both pharmaceutical and non-pharmacological approaches to treating diabetes have been investigated, no medication has been shown to be completely safe.[8–10] Regular exercise is frequently advised as a non-pharmacological strategy to increase insulin sensitivity.[11–12] 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 intestinal absorption of glucose, are the main classes of medications used in pharmacological approaches to treat diabetes. [13–15] Weight gain, severe hypoglycemia, metabolic side effects, and other issues with target selectivity, permeability, and solubility are among the issues associated with these drug categories.[16–17] They can, however, be taken either by themselves or in conjunction with other hypoglycemic drugs. Conventional treatments may cause dependence, side effects, and long-term harm. [18–20] Examining alternate treatments, such natural medicines, could help reduce these risks. Antioxidants are crucial for scavenging harmful free radicals and reducing oxidative stress. [21] Many research have connected oxidative stress to diabetes-related issues. [22–23] Elevated blood sugar levels increase the production of reactive oxygen and

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nitrogen species while decreasing the activity of antioxidant enzymes. This imbalance damages vital biomolecules such as proteins, lipids, and DNA, disrupting cellular homeostasis and ultimately generating toxic byproducts that hasten the progression of illness. [24, 25] When the body's antioxidant system is unable to counteract this, stress pathways are set off, leading to cellular damage and the progression of diabetes. Research shows that antioxidant therapy protects β cells, keeps them functioning, and reduces issues. Natural antioxidants are being used increasingly often due to their therapeutic benefits, safety, affordability, and accessibility. [26] Natural antioxidants can help prevent or lessen type 2 diabetes by reducing oxidative stress, stopping lipid peroxidation, and increasing the activity of antioxidant enzymes. When assessing natural antioxidant products, it is important to take into account the intricate physiological processes that control Type 2 diabetes oxidative stress, such as glycemic control, postprandial oxidative stress [27], the polyol pathway, high-calorie, high-fat meals, exercise, and sleep. Increasing the use of natural antioxidant products and reducing the processes that lead to long-term detrimental oxidative stress may help prevent or slow the onset of Type 2 diabetes. [28, 29] Euphorbia prostrata, also known as "Hazar dani" [30–31], is a tiny annual herb that grows across India, particularly in the foothills of the Himalayas. It belongs to the Euphorbiaceae family. The plant has been widely used to treat a variety of conditions, including 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].It has also long been used to cure a variety of skin conditions and snake bites. [41] Euphorbia prostrata is crucial for research on diabetes in particular since its phytoconstituents have shown both antioxidant and antidiabetic properties. [42–43] Based on these results, this work employs docking methods to assess the antioxidant compounds' anti-hyperglycemic potential in the hydroalcoholic extracts of Euphorbia prostrata by measuring how well they bind to three specific proteins (α-glucosidase, and PTP-1B). Co-crystals of approved antidiabetic medications have been confirmed to be among these targets. Phytochemical screening of Euphorbia prostrata has revealed the presence of glycosides, phytosterols, flavonoids, polyphenols, tannins, alkaloids, terpenoids, saponins, anthraquinones, and other chemicals. [44] Through physicochemical and spectroscopic analysis, ten primary chemicals have been identified: gallic acid, corilagin, 1,2,3-Tri-O-Galloyl-D-Glucose, geraniin, tellimagrandin I and II, and rugosin A, D, E, and G. [45, 46] The dried leaf extracts of Euphorbia prostrata contain prostratins A, B, and C, euphorbin G and H, and additional hydrolyzable ellagitannins. oxidative stress associated with Type 2 diabetes. [48] Diets high in phytosterols have been shown in numerous trials to improve insulin sensitivity and increase fat and carbohydrate metabolism. [49]

The two targeted proteins in this work, α-Glucosidase (6C9X) [50] and PTP1B (4I8N) [51], were previously investigated as possible therapeutic targets for Type 2 diabetes mellitus.
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. [52]. Leukocyte antigen-related tyrosine phosphatase and protein tyrosine phosphatase 1B (PTP1B) both play important roles in controlling the transmission of insulin signals.

Tyrosine phosphorylation is necessary for insulin signaling in the insulin receptor activation loop, and PTP1B inhibits this process by dephosphorylating phosphotyrosine residues, which causes insulin signaling to be negatively regulated. [53–56]. PTP1B has also been linked in recent research to obesity, insulin sensitivity, and Type 2 diabetes mellitus (T2DM) [57–69]. Furthermore, PTP1B functions as a negative regulator of leptin signaling, which is crucial for maintaining metabolic homeostasis. Despite having plenty of energy reserves, obesity causes decreased leptin sensitivity, which impairs satiety. There is evidence that PTP1B affects the proliferation of pancreatic β-cells, as seen by the increased development of β-cells and higher glucose-induced insulin production in PTP1B knockout animals. These findings demonstrate how crucial PTP1B is to diabetes, which has sparked interest in PTP1B inhibitor research. The literature contains comprehensive reviews of reported PTP1B inhibitors [60,61].

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) [62–66]. 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 some of the new approaches that take into account the quantity of interactions between the

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ligands and amino acids in the binding pocket are used to evaluate the docking data [67,68]. 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

For the docking investigations, 25 bioactive phytoconstituents were selected from the literature (Table 1). Flavonoids (Apigenin, Apigenin 7-Glucoside, Kaempferol, Luteolin, 6-Methoxy Quercetin Glycoside, Quercetin, Quercetin 3-Rhamnoside, Rhamnetin 3-Galactoside), phenolic acids (Ellagic Acid, Gallic Acid), tannins (Corilagin, Euphorbin G, Euphorbin H, Rugosin A, Rugosin D, Rugosin E, Tellimagradin I, Tellimagradin II), and terpene alcohols (1,2,3-Tri-O-Glucose).

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

Two target proteins with pdb ids of 6C9X and 4I8N were obtained from the protein data bank for the docking investigations. With a resolution of 1.46 Å, the 6C9X protein, a member of the hydrolase class, represents the crystal structure of alpha-glucosidase in contact with voglibose. The crystal structure of Protein Tyrosine Phosphatase 1B in association with an inhibitor [4-{(2S)] is the 4I8N protein, which is a member of the hydrolase class.-2-(1,3-Benzoxazol-2-yl)-2-[(4-fluorophenyl)sulfamoyl]ethyl}phenyl)amino](oxo)acetic acid with a 2.50 Å resolution.

The downloaded target proteins were put into Autodock 4.2 for minimization. The polar hydrogens were provided after the unnecessary water molecules were removed, as seen by the co-crystallized ligands in each protein. The missing residues were introduced at the same time as the Kollmann charges. The generated proteins were saved in the pdbqt format for further docking studies.

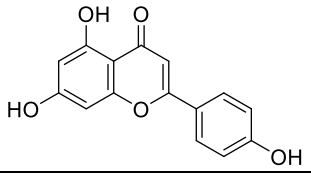
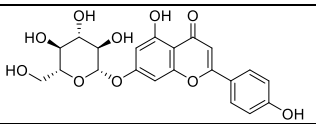
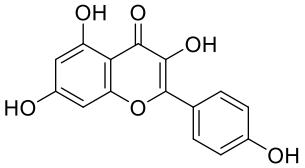
2.4 Preparation of the grid box

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 6C9X and 4I8N had coordinates of (8.190, -6.470, -10.450) and (-11.539, 39.85, 35.54), respectively.

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		[69,70]
2.	Apigenin 7-Glucoside		[47]
3.	Kaempferol		[47]

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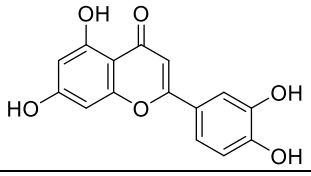
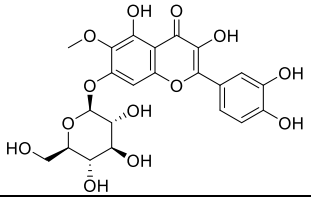
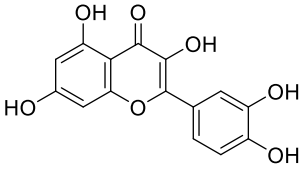
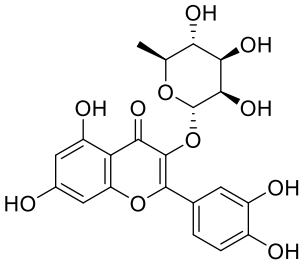
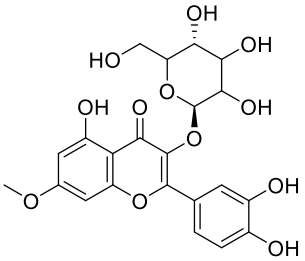
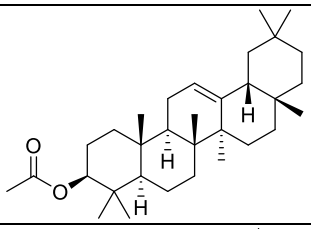
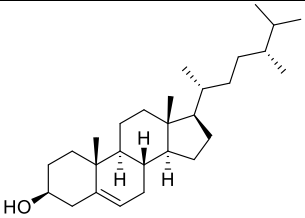
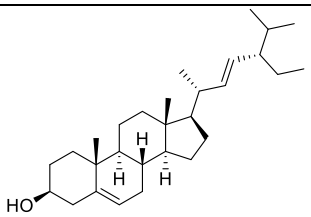
4.	Luteolin		[69,70]
5.	6-Methoxy Quercetin Glycoside		[47]
6.	Quercetin		[69,70]
7.	Quercetin 3-Rhamnoside		[47]
8.	Rhamnetin 3-Galactoside		[47]
9.	Beta-AmyrinAcetate		[47]
10.	Campesterol		[69]
11.	Stigmasterol		[69]

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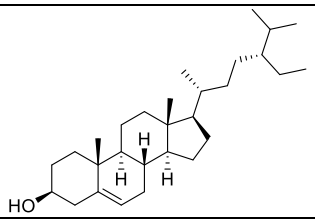
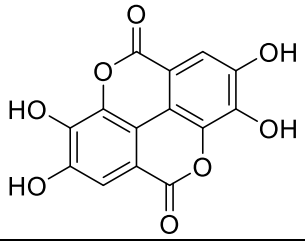
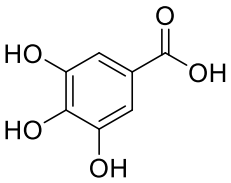
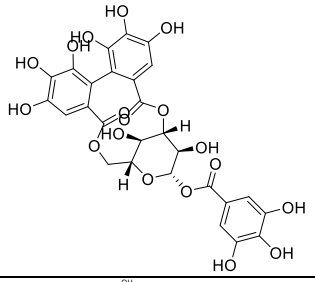
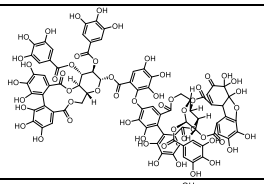
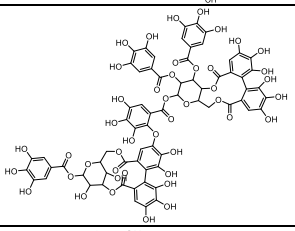
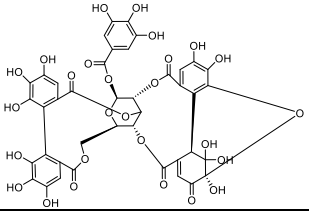
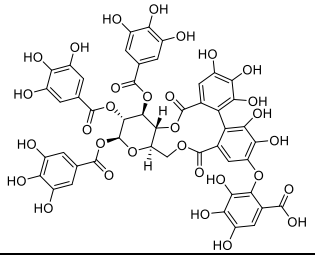
12.	Beta-Sitosterol		[69]
13.	Ellagic Acid		[69]
14.	Gallic Acid		[69-71]
15.	Corilagin		[69]
16.	Euphorbin G		[47]
17.	Euphorbin H		[47]
18.	Geraniin		[69]
19.	Rugosin A		[69]

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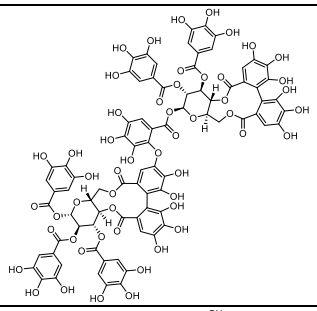
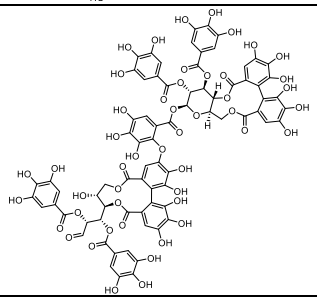
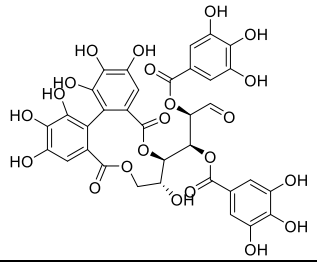
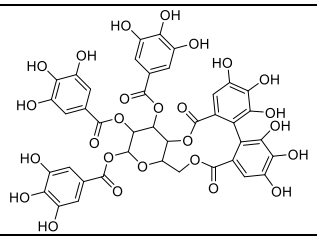
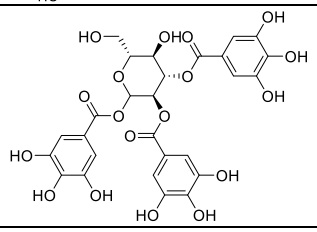
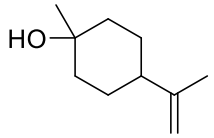
20.	Rugosin D		[69]
21.	Rugosin E		[69]
22.	Tellimagradin I		[69]
23.	Tellimagradin II		[69]
24.	1,2,3-Tri-O-Galloyl--D-Glucose		[69]
25.	Beta -Terpineol		[47]

RESULT AND DISCUSSION

Table 2 provides a description of each of the 25 phytoconstituents' docking scores. The binding energies for the pdb id 6C9X (α-Glucosidase) and 4I8N (PTP1B) vary from -4.3 to -9.5 and -4.8 to -9.9 kcal/mol, respectively, according to the docking score analysis of the phytoconstituents for each target protein. It's interesting to note that the beta-terpineol binding energies for each of the target proteins under study were the lowest of all the phytoconstituents: -4.3 for α-glucosidase and -4.8 for PTP1B. This finding suggests that Ψeta-terpineol plays a very small part in inhibiting any of the two targets. Quercetin had the highest binding energy (-9.5 kcal/mol) for α-glucosidase among the phytoconstituents, while gallic acid had the highest binding energy (-9.9 kcal/mol) for PTP1B. It was noteworthy that every phytoconstituent with the highest binding energies belonged to the family of flavanoids and tannins.

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Table 2: Binding energy (kcal/mol) of bio-molecules in *Euphorbia prostrata* to 6C9X, and 4I8N.

Category	Phytoconstituents	Binding Energy (kcal/mol)	
		Alpha Glucosidase Inhibitors (6C9X)	**Protein Tyrosine Phosphatase (4I8N)**
Flavanoids	Apigenin	-7.8	-8.0
	Apigenin 7-Glucoside	-9.3	-8.5
	Kaempferol	-7.2	-7.7
	Luteolin	-8.1	-8.0
	6-Methoxy Quercetin Glycoside	-7.8	-7.8
	Quercetin	-9.5	-9.8
	Quercetin 3-Rhamnoside	-6.9	-7.7
	Rhamnetin 3-Galactoside	-7.3	-6.6
Sterols	Beta-Amyrin Acetate	-8.7	-7.6
	Campesterol	-7.8	-6.3
	Stigmasterol	-7.7	-8.6
	Beta-Sitosterol	-8.7	-6.3
Tannins	Ellagic Acid	-7.0	-7.2
	Gallic Acid	-9.4	-9.9
	Corilagin	-9.4	-8.6
	Euphorbin G	-6.9	-7.8
	Euphorbin H	-9.0	-9.8
	Geraniin	-8.3	-8.2
	Rugosin A	-8.4	-8.2
	Rugosin D	-7.7	-7.5
	Rugosin E	-8.1	-8.2
	Tellimagradin I	-8.8	-9.4
	Tellimagradin II	-9.5	-8.3
Terpene Alcohol	Beta -Terpineol	-4.3	-4.8
	1,2,3-Tri-O-Galloyl--D-Glucose	-8.5	-8.1

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 necessary for interacting with the various ligand atoms are revealed 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-glucosidase

In addition to some water molecules, the co-crystallized ligand of the α-glucosidase protein 6C9X exhibits binding with ASP420, ARG404, ASP73, TRP169, ASP197, HIS78, and TYR62 residues. Apigenin, Luteolin, Quercetin 3-Rhamnoside, Ellagic Acid, Corilagin, Geraniin, Gallic acid, and Rugosin A were among the significant residues that included ASP420. Apigenin 7-Glucoside, Quercetin 3-Rhamnoside, Beta-Sitosterol, Gallic Acid, Geraniin, Rugosin A, and Tellimagradin II were all confirmed to have TRP169. Corilagin, Euphorbin H, Euphorbin G, Rugosin D, Rugosin E, Quercetin, and Gallic Acid were shown to contain ARG404. Along

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with these crucial amino acid residues, According to our research, LYS422, PRO75, and VAL351 were present in 10, 9, and 9 phytoconstituents, respectively, and were likewise crucial for demonstrating binding affinity. The two phytoconstituents with all three residues—LYS422, PRO75, and VAL351—were beta-amrin acetate and campesterol. Common Beta-Amyrin Acetate, Campesterol, Ellagic Acid, and Beta-Terpineol were the residues LYS422 and PRO75. Rhamnetin3-Galctoside, beta-amyrin acetate, and beta-sitosterol were frequently reported to include the residues PRO75 and VAL351. Similarly, LYS422 and VAL351 were detected in Rugosin E, Kaempferol, Beta-Amyrin Acetate, and Campesterol. Furthermore, HIS478, TRP271, ALA480, and ASP307, which are present in 6, 7, 8, and 8 phytoconstituents, respectively, were the other notable interacting residues discovered in docking experiments.

3.1.2 Interaction analysis of PTP-1B

Protein Tyrosine Phosphatase (PTP-1B) and pdbid:4I8N co-crystalsshown contact with several significant water molecules as well as ARG221, SER216, ALA217, PHE182, TYR46, GLY220, MET258, and GLN262. Luteolin, Quercetin 3-Rhamnoside, Quercetin, Stigmasterol, Beta-Sitosterol, Tellimagradin I, Gallic acid, and Beta-Terpineol all frequently contained the residues ALA217 and TYR46. Interestingly, ALA217 and TYR46 amino acid interactions were detected in 19 and 12 phytoconstituents, respectively. Furthermore, our docking studies revealed that the amino acids found in the co-crystallized ligand, such as SER216 and PHE182, were also present in the phytoconstituents. Specifically, 6-Methoxy Quercetin Glycoside, Campesterol, Stigmasterol, Beta-Sitosterol, Ellagic Acid, and Euphorbin G interacted with PHE182, while Apigenin, Apigenin 7-Glucoside, 1,2,3-Tri—O-Galloyl-D-Glucose, and Beta-Amyrin Acetate interacted with SER216 residue. Furthermore, our docking investigations revealed 11 interactions for ASP181 and 8 interactions for ASP48.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. Good binding energies ranging from -8.7 to -10.3 were also displayed by the phytoconstituents of the flavonoid family. 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). There was no discernible interaction between the phytoconstituents of the flavonoid family and significant amino acid residues. All of the phytoconstituents of the tannin family had the interaction residue ALA217, according to docking experiments on PTP1B. All of the phytoconstituents in the flavonoid family, with the exception of rhamnetin 3-galactoside, included the same residue. According to the aforementioned research, the most significant bonding interactions were hydrogen and hydrophobic bonds, and the most significant phytoconstituents were found to be Apigenin 7-glucoside, Luteolin, and Quercetin among the flavonoids, and Rugosin E, Tellimagradin I, and Gallic acid among the tannins.

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, 6C9X and 4I8N, 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 (-6.6 to -9.8 kcal/mol) and tannins (-6.9 to -9.8 kcal/mol). The phytoconstituents of these two families exhibited the greatest number of interactions with significant amino acid residues of each protein target, namely ARG404 for 6C9X and ALA217 for 4I8N, according to the docking interaction studies. According to these findings, tannins and flavonoids may have the strongest antidiabetic efficacy, as shown by their binding energies and modalities of interaction with ARG404 and ALA217. 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 quercetin, apigenin 7-glucoside, and luteolin among the flavonoids, and gallic acid, rugosin E, and tellimagradin I 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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REFERENCES

1. Batori, Z., Erdos, L., Somlyay, L.:Euphorbia prostrata (Euphorbiaceae), a new alien in the Carpathian Basin. Acta Bot Hung.54, 235–243 (2012)
2. Varsha, A.,Tarate, S., Kshirsagar, M., Jagtap, M.:Pharmacognostical and phytochemical investigation of Euphorbia prostrata. 8,980 – 983 (2023)
3. Sharma, G. D., Tripathi, S. N.: Experimental evaluation of dugdhika (Euphorbia prostrata w. ait) for the treatment of 'tamakasvasa' (bronchial asthma). Anc Sci Life.3, 143 (1984)
4. Gupta, P.: The efficacy of Euphorbia prostrata in early grades of symptomatic hemorrhoids--a pilot study. Eur Rev Med Pharmacol Sci.15, 199-203 (2011)
5. Alarcon, A.F.J., Roman, R.R., Perez, G.S., Aguilar, C.A., Contreras, W.C.C., Flores, S.J.L.:Study of the anti-hyperglycemic effect of plants used as antidiabetics. J Ethnopharmacol.61, 101–110 (1998)
6. Larbie, C., Torkornoo, D., Dadson, J.:Anti-diabetic and hypolipidaemic effect of botanicals: a review of medicinal weeds on KNUST campus, Kumasi. J Appl Pharm Sci. 4, 097–104 (2014)
7. Patil, T.R., Limaye, R.P.:Effect of Euphorbia Prostrata on the Wound Healing in Excisional Wound Model in Rats. International Journal of Pharmacognosy and Phytochemical Research 9, 1223–1236 (2017)
8. Hariyadi, D.M., Sahu, V.K.: Euphorbia prostata exerts potent anti-inflammatory and anti-arthritic activity in downregulating the increased expression of pro-inflammatory cytokines. Pharmaceutical Sciences. 26, 370–378 (2020)
9. Biwott T., Kiprop A., Cherutoi J., Munyendo W., Biwott G.: Analgesic Properties of Euphorbia prostrata Crude Extracts. Sci. J. Chem. 3, 100 (2015)
10. Sharma, S. K., Singh, S., Singh, J.: Anthelmintic effect of Euphorbia prostrata Ait. extracts. Indian J Pharmacol. 43, 743 (2011)
11. Garg, N., Mannan, A., Mohan, M., Singh, T. G.:Therapeutic efficacy of hydroalcoholic extract of Euphorbia prostrata Aiton in NAD-STZ-induced diabetic nephropathy: A multifaceted intervention targeting oxidative stress and inflammation. Obes Med. 54, 100579 (2025)
12. Sharma, S.K., Singh, J., Singh,S.:Pharmacognostical and phytochemical investigation of Euphorbia prostrata ait. IJPSR 3(4) 1043-1048 (2012)
13. Stumvoll, M., Goldstein, B.J., Van Haeften, T.W.:Type 2 diabetes: Principles of pathogenesis and therapy. Lancet.365, 1333–1346 (2005)
14. Samar, A. A., Nada, A. A., Marwa, Sh., Muhammad, K., Naira, A.A., Roaa, T. Z., EunJoo, R., Ahmed, E., Ahmed, A. A.K.:Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments. Biomedicine & Pharmacotherapy.168, 115734 (2023)
15. Tomic, D., Shaw, J.E., Magliano, D.J.:The burden and risks of emerging complications of diabetes mellitus. Nature Reviews Endocrinology. 18, 525–539 (2022)
16. Unai, G.G., Asier, B.V., Shifa, J., Asier, L.S., Haziq, S., Kepa, B.U., Helena, O., Cesar, M.:Pathophysiology of Type 2 Diabetes Mellitus. Int J Mol Sci. 21, 6275 (2020)
17. Ong, K. L.:Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. The Lancet. 402, 203–234 (2023)
18. Varghese,J.A., Anjana,R.R., Geldsetzer, P., Sudharsanan, N., Manne-Goehler, J., Thirumurthy, H., Bhattacharyya, S., Narayan,K.M.V., Mohan, V., Tandon, N., Ali, M.K.:National Estimates of the Adult Diabetes Care Continuum in India, 2019-2021. JAMA Intern Med183, 963–972 (2023)
19. Wei, J., Fan, L., He, Z., Zhang, S., Zhang, Y., Zhu, X., Xia, F., Song, X., Chen, L., Zou Z., Wang, T.:The global, regional, and national burden of type 2 diabetes mellitus attributable to low physical activity from 1990 to 2021: a systematic analysis of the global burden of disease study 2021. Int J Behav Nutr Phys Act. 22, 8 (2025)
20. American Diabetes Association. Standards of care in diabetes-2023 abridged for primary care providers. Clin. Diabetes 41, 4–31 (2022)
21. Yu, J., Lee, S.-H., Kim, M.K.:Recent updates to clinical practice guidelines for diabetes mellitus. Endocrinol. Metab. (Seoul) 37, 26–37 (2022)
22. Singh, H., Singh R., Singh, A., Singh, H., Singh, G., Kaur, S., Singh, B.:Role of oxidative stress in diabetes-induced complications and their management with antioxidants. Arch. Physiol. Biochem. 130, 616–641 (2024)
23. Bhatti, J.S., Sehrawat, A., Mishra, J., Sidhu, I.S., Navik, U., Khullar, N., Kumar S., Bhatti, G.K., Reddy, P.H.:Oxidative stress in the pathophysiology of type 2 diabetes and related complications: Current therapeutics strategies and future perspectives. Free Radic. Biol. Med. 184, 114–134 (2022)
24. Reynolds, L., Luo, Z., Singh, K.:Diabetic complications and prospective immunotherapy. Front. Immunol. 14, 1219598 (2023)
25. Nguyen Vo, T. H., Tran, N., Nguyen, D., Le, L.:An in silico study on antidiabetic activity of bioactive compounds in Euphorbia thymifolia Linn. Springerplus.5, 1–13 (2016)

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26. Huang, D. D., Shi, G., Jiang, Y., Yao, C. & Zhu, C.:A review on the potential of Resveratrol in prevention and therapy of diabetes and diabetic complications. Biomedicine & Pharmacotherapy. 125, 109767 (2020)
27. Padhi, S., Nayak, A.K., Behera, A.:Type II diabetes mellitus: a review on recent drug based therapeutics. Biomedicine & Pharmacotherapy.131, 110708 (2020)
28. Corathers, S.D., Peavie, S., Salehi, M.:Complications of Diabetes Therapy. Endocrinol Metab Clin North Am.42, 947 (2013)
29. Barrientos-Avalos, J.R., Morel-Cerda, E.C., Felix-Tellez, F.A., Vidrio-Huerta, B.E., Aceves-Ayala A.R., Flores-Rendon, A.R., Velarde-Ruiz J.A.V.: Gastrointestinal adverse effects of old and new antidiabetics: How do we deal with them in real life? Rev. Gastroenterol. Méx. (Engl. Ed.) 89, 521–532 (2024)
30. Feingold, K. R.:Oral and Injectable (Non-Insulin) Pharmacological Agents for the Treatment of Type 2 Diabetes. Endotext. (2024)
31. Chong, K., Chang, J. K. J., Chuang, L. M.:Recent advances in the treatment of type 2 diabetes mellitus using new drug therapies. Kaohsiung J Med Sci. 40, 212–220 (2024)
32. Elsayed, N., Aleppo, G., Bannuru, R., Bruemmer, D.:Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2024. Diabetes Care47, S158–S178 (2024)
33. Jain, A.B., Lai, V., Jain, A.B., Lai, V.:Medication-Induced Hyperglycemia and Diabetes Mellitus: A Review of Current Literature and Practical Management Strategies. Diabetes Therapy. 2024. 15, 2001–2025 (2024)
34. Weinberg Sibony, R., Segev, O., Dor, S., Raz, I.:Drug Therapies for Diabetes. International Journal of Molecular Sciences. 24, 17147 (2023)
35. Fatima, M.T., Bhat, A.A., Nisar, S., Fakhro, K.A., Al-Shabeeb Akil, A.S.: The role of dietary antioxidants in type 2 diabetes and neurodegenerative disorders: An assessment of the benefit profile. Heliyon. 9, e12698 (2022)
36. Ghasemi-Dehnoo, M., Amini-Khoei, H., Lorigooini, Z., Rafieian-Kopaei, M.:Oxidative stress and antioxidants in diabetes mellitus. Asian Pac J Trop Med. 13, 431–438 (2020)
37. Rahimi, R., Nikfar, S., Larijani, B., Abdollahi, M.:A review on the role of antioxidants in the management of diabetes and its complications. Biomedicine & Pharmacotherapy.59, 365–373 (2005)
38. Shafras, M., Sabaragamuwa, R., Suwair, M.:Role of dietary antioxidants in diabetes: An overview. Food Chemistry Advances. 4, 100666 (2024)
39. Tuell, D.S., Los, E.A., Ford, G.A., Stone, W.L.:The Role of Natural Antioxidant Products That Optimize Redox Status in the Prevention and Management of Type 2 Diabetes. Antioxidant. 12, 1139 (2023)
40. Montonen, J., Knekt, P., Jarvinen, R., Reunanen, A.:Dietary Antioxidant Intake and Risk of Type 2 Diabetes. Diabetes Care.27, 362–366 (2004)
41. Suresh, V., Reddy, A., Muthukumar, P. & Selvam, T. Antioxidants: Pharmacothearapeutic boon for diabetes. in Antioxidants - Benefits, Sources, Mechanisms of Action (IntechOpen, 2021) doi:10.5772/INTECHOPEN.98587
42. Nawaz, H., Aslam, M., Shahzad, H., Mehboob, F., Waheed, R., Jabeen, R., Nawaz, M., Ahmed, M. Z.: Comparative evaluation of phytochemical composition and antioxidant potential of some medicinally-important euphorbiaceous plants. J. Anim. Plant Sci. 32,1703–1712 (2022)
43. Estrada, J.M., Reyes, H.M., Hernández, T.R., Sansininea, A.J.J., Alvarez, A.B.: Contributions from Mexican flora for the treatment of diabetes mellitus: Molecules of Psacalium decompositum (A. gray) H. rob & brettell. Molecules. 26, 2892 (2021)
44. Yadav, N.K., Yadav, R.:Medicinal Effects, Phytochemistry, Pharmacology of Euphorbia prostrata and Promising Molecular Mechanisms. Chin J Integr Med.30, 181–192 (2024)
45. Chen, L., Chen, R., Wei, K.:Constituents of tannins from Euphorbia prostrata Ait. hongguo Zhong Yao Za Zhi. 17, 225-255 (1992)
46. Aslam, M.A., Asif, H.M., Alamri, A., Bhutto, A.A., Mukhtiar, M., Ahmad, K., Ashfaq, M.M., Sattar, H.A., Hayee, A., Jabbar, S., Zahid, R., Nawaz, A.:Phytochemical screening, antioxidant, immunomodulatory and analgesic potential of aqueous-ethanolic extracts of Euphorbia prostrata ait. and Crotalaria burhia Buch–Ham. Heliyon.10, e27279 (2024)
47. Meghana, B.P., Balasubramanian, T., Suresha, B.S., Rakshitha, S., Soujanya, N.:Euphorbia prostrata : A Plant Review. Asian J. Pharm. Health Sci. 12, 2713–2717 (2022)
48. Das, K., Lyer, K.R., Orfali, R., Asdaq, S.M.B., Alotaibi, N.S., Alotaibi, F.S., Alshehri, S., Quadri, M.S.A., Almarek, A., Makhashin, N.B., Alrashed, A.A., Mohzari, Y., Ghoneim, Y.:In silico studies and evaluation of in vitro antidiabetic activity of berberine from ethanol seed extract of Coscinium fenestratum (Gaertn.) Colebr. J. King Saud Univ. Sci. 35, 102666 (2023)
49. Ahmad, M., Shah, A.S., Khan, R.A., Khan, F. U., Khan, N.A., Shah, M.S., Khan, M. R.:Antioxidant and antibacterial activity of crude methanolic extract of Euphorbia prostrata collected from District Bannu (Pakistan).African Journal of Pharmacy and Pharmacology. 5, 1175-1178 (2011)

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50. Tan, K., Tesar, C., Jedrzejczak, R., Joachimiak, A.: The crystal structure of the alpha-glucosidase (gh 31) from ruminococcus obeum ATCC 29174 in complex with voglibose. Midwest Center for Structural Genomics (MCSG). (2018) Preprint at https://doi.org/10.2210/pdb6c9x/pdb
51. Reddy, S.M.V.V.V., Rao, K.N., Subramanya, H.:Crystal structure of protein tyrosine phosphatase 1b in complex with an inhibitor [(4-{(2s)-2-(1,3- fluorophenyl) sulfamoyl] ethyl} phenyl) amino] (oxo) acetic acid. (2012) doi:10.2210/PDB4I8N/PDB.
52. McCarty, M. F., Di Nicolantonio, J. J.:Acarbose, lente carbohydrate, and prebiotics promote metabolic health and longevity by stimulating intestinal production of GLP-1. Open Heart 2, e000205 (2015)
53. Eleftheriou, P., Geronikaki, A., Petrou, A.:PTP1b Inhibition, A Promising Approach for the Treatment of Diabetes Type II. Curr Top Med Chem.19, 246–263 (2019)
54. Behl, T., Gupta, A., Sehgal, A., Albarrati, A., Albratty, M., Meraya, A.M., Najmi M., Bhatia S., Bungau, S.:Exploring protein tyrosine phosphatases (PTP) and PTP-1B inhibitors in management of diabetes mellitus. Biomedicine & Pharmacotherapy.153, 113405 (2022).
55. Teimouri, M., Hosseini, H., Arab Sadeghabadi, Z., Babaei-Khorzoughi, R., Gorgani-Firuzjaee, S., Meshkani, R.:The role of protein tyrosine phosphatase 1B (PTP1B) in the pathogenesis of type 2 diabetes mellitus and its complications. J. Physiol. Biochem. 78, 307–322 (2022)
56. Liu, Z., Gao, H., Zhao, Z., Huang, M.,Wang, S., Zhan, J.:Status of research on natural protein tyrosine phosphatase 1B inhibitors as potential antidiabetic agents: Update. Biomedicine & Pharmacotherapy.157, 113990 (2023)
57. Sun, J., Qu, C., Wang, Y., Huang, H., Zhang, M., Zou1, W.:Type 2 diabetes mellitus and protein-tyrosine phosphatase 1b. J Diabetes Metab Disord Control. 3, (2016)
58. Hsing, H. Y., Rathnasamy, S., Dianita, R., Wahab, H. A.:Docking-based virtual screening in search for natural PTP1B inhibitors in treating type-2 diabetes mellitus and obesity. Biomedical Research and Therapy.7, 3579–3592 (2020)
59. Rocha, S., Corvo, M. L., Fernandes, E., Freitas, M.:The Emerging Target Protein Tyrosine Phosphatase 1B (PTP1B) for Type 2 Diabetes Mellitus Management. Journal of Diabetes and Clinical Research. 3, 99-105 (2021)
60. Kanwal, A., Kanwar, N., Bharati, S., Srivastava, P., Singh, S.P., Amar, S.:Exploring new drug targets for type 2 diabetes: Success, challenges and opportunities. Biomedicines 10, 331 (2022)
61. Maurus, R., Begum, A., Williams, L.K., Fredriksen, J.R., Zhang, R., Withers, S.G., Brayer, G.D.:Alternative catalytic anions differentially modulate human α-amylase activity and specificity. Biochemistry.47, 3332–3344 (2008)
62. Ahmed, S., Prabahar, A.E., Saxena, A.K.:Molecular docking-based interactions in QSAR studies on Mycobacterium tuberculosis ATP synthase inhibitors. SAR QSAR Environ Res.33, 289–305 (2022)
63. Ahmed, S., Prabahar, A. E., Saxena, A. K.:Molecular docking-based interaction studies on imidazo[1,2-a] pyridine ethers and squaramides as anti-tubercular agents. SAR QSAR Environ Res. 34, 435–457 (2023).
64. Kumar, M., Dewangan, H. K., Arya, G. C. & Sharmar.:R. Design, development and evaluation of QSAR and molecular modelling of benzothiazole analogues for antibacterial drug discovery. Results Chem 4, 100482 (2022).
65. Wang, K., Huang, Y., Wang, Y., You, Q. & Wang, L.:Recent advances from computer-aided drug design to artificial intelligence drug design. RSC Med Chem 15, 3978–4000 (2024).
66. Nandi, S., Kumar, M., Saxena, M. & Saxena, A. K.:The Antiviral and Antimalarial Drug Repurposing in Quest of Chemotherapeutics to Combat COVID-19 Utilizing Structure-Based Molecular Docking. Comb Chem High Throughput Screen 24, 1055–1068 (2020).
67. Nandi, S., Kumar, M. & Saxena, A. K.:Repurposing of Drugs and HTS to Combat SARS-CoV-2 Main Protease Utilizing Structure-Based Molecular Docking. Lett Drug Des Discov 19, 413–427 (2021).
68. Nandi, S., Kumar, M., Kumari, R. & Saxena, A. Exploring the inhibitory mechanisms of indazole compounds against SAH/MTAN-mediated quorum sensing utilizing QSAR and docking. Drug Target Insights 16, 54–68 (2022).
69. Singla, A. K., Pathak, K.:Topical antiinflammatory effects of Euphorbia prostrata on carrageenan-induced footpad oedema in mice. J Ethno pharmacol .29, 291–294 (1990)
70. Shahwan, M.J., Al-Qirim, T.M., Daradka, H.:Hypolipidaemic Effects of Euphorbia prostrata in Rabbits. J. Biol. Sci. 9, 88–91 (2008)
71. Rauf, A., Qaisar, M., Uddin, G., Akhtar, S., Muhammad, N.: Preliminary Phytochemical Screening and Antioxidant Profile of Euphorbia prostrate. Middle-East Journal of Medicinal Plants Research. 1, 09-13 (2012)

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