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Exploring Glucagon-like peptide-1 as a Target Protein for Diabetes Mellitus Treatment: Molecular Docking and Pharmacokinetic Analysis of Phytocompounds from *Momordica charantia*

Dishant Chandgude*

Abstract

Objective: *This study aimed to use molecular docking techniques to explore the potential of GLP-1 (glucagon-like peptide-1) as a target protein for the treatment of diabetes mellitus, a chronic metabolic disease marked by elevated blood glucose levels. Given its crucial role in maintaining insulin secretion and glucose homeostasis, GLP-1 may serve as a future target for diabetes therapy.* ***Method:*** *The study employed a multi-phase method. Initially, protein extraction was carried out using the Protein Data Bank ID 3C59 for GLP-1. The extracted structure was then verified through secondary structure prediction and Ramachandran Plot analysis to ensure its reliability. Phytocompounds from "Momordica charantia" were obtained using the IMPPAT Database. An ADME study was conducted to evaluate the pharmacokinetic characteristics of these compounds, including their absorption, distribution, metabolism, and excretion profiles. Molecular docking was then performed using PyRx to assess the binding affinity and interaction patterns between GLP-1 and the identified phytocompounds. The 3D and 2D interaction structures were subsequently examined using BIOVIA Discovery Studio to visualize the binding interactions and to identify key amino acid residues involved.* ***Result:*** *The molecular docking study identified diosgenin, alpha-spinasterol, and momordicoside I as potential drug candidates capable of modulating the activity of GLP-1. These compounds exhibited strong binding affinities and favorable interaction patterns with the GLP-1 protein.* ***Conclusion:*** *The study suggests that GLP-1 is a promising target for diabetes treatment, demonstrating favorable molecular interactions with phytocompounds derived from Momordica charantia. Structural validation and ADME analysis further support the potential efficacy of these compounds. These findings could lead to the development of new therapeutic approaches for managing diabetes, highlighting the significance of GLP-1 in diabetes therapy.*

Keywords: GLP-1, diabetes treatment, molecular docking, *Momordica charantia*, phytocompounds, ADME analysis, structural validation

***Author for Correspondence**
Dishant Chandgude
E-mail: dishant.chandgude15@gmail.com

Student, BioNome for Genomics and Bioinformatics Solution, Bengaluru, Karnataka, India

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INTRODUCTION

Elevated blood glucose levels caused by deficiencies in insulin action, secretion, or both characterize diabetes mellitus (DM), a chronic metabolic disease. As a hormone secreted by the pancreas, insulin helps cells to absorb glucose, which is essential for controlling blood sugar levels. Hyperglycemia is the result of glucose build-up in circulation due to insufficient insulin production or biological resistance to its effects [1]. It is influenced by a mix of lifestyle, environmental, and genetic

factors. A significant factor is genetic predisposition, which includes certain variations in genes that make a person more susceptible to diabetes [2]. Furthermore, the increasing prevalence of diabetes is primarily driven by environmental factors such as obesity, poor nutrition, and sedentary lifestyles [3]. Type 2 diabetes can arise from a combination of these variables, and can cause insulin resistance, reduced insulin production, or both. According to estimates, 451 million people globally, aged 18 to 99 years, suffered from diabetes in 2017. It is estimated that by 2045, there will be 693 million of them. It has been estimated that 49.7% of individuals with diabetes go undiagnosed [4].

Bitter melon, or *Momordica charantia*, has been traditionally used for its therapeutic properties, including anti-diabetic benefits, in various cultures [5]. *Momordica charantia* contains some bioactive chemicals that have been shown in recent studies to have anti-diabetic properties [6]. Moreover, bitter gourd has anti-inflammatory and antioxidant properties that are important in reducing diabetes-related inflammation and oxidative stress [7]. The presence of flavonoids, phenolic compounds, and various vitamins in bitter gourd contributes to its overall therapeutic effects in diabetes [6]. These findings underscore the potential of Momordica charantia as a rich source of pharmacologically relevant compounds for developing targeted therapies against diabetes [5–8].

Role of Glucagon-Like Peptide-1 In Diabetes

The peptide hormone GLP-1 is essential for regulating insulin secretion and glucose homeostasis [9, 10]. It is synthesized by L cells of the small intestine and is secreted in response to food intake [9]. GLP-1 primarily affects the pancreas, increasing the release of insulin in response to elevated blood glucose levels by promoting insulin secretion through a glucose-dependent mechanism [9]. It plays a critical role in maintaining glucose homeostasis by promoting glucose-dependent insulin secretion, inhibiting glucagon release, and slowing emptying of the stomach [9, 13]. Collectively, these effects contribute to improved glycemic control [9]. Additionally, GLP-1 has been associated with promoting beta-cell proliferation and survival, potentially preserving pancreatic function in individuals with diabetes [9]. Furthermore, GLP-1-based therapies such as agonists of the GLP-1 receptor have shown promise as potent pharmaceuticals for the treatment of diabetes [10, 11]. These drugs not only improve glycemic control but also offer cardiovascular benefits [10]. Understanding the many functions of GLP-1 in diabetes is vital for facilitating the development of novel treatment strategies to address the complex pathophysiology of this common metabolic illness [12].

METHODS

Protein Extraction and Purification of the Target Protein

GLP-1 with Protein Data Bank ID-3C59 was selected as the target protein after a review of the relevant literature, and its structure was obtained from the Protein Data Bank [14]. The protein was retrieved using ID- 3C59 and downloaded in PDB format. The overall resolution was 2.2 (High), and the Deposited Residue Count was 153. Following structural validation, the protein was purified using the BIOVIA Discovery Studio Visualizer, which is a powerful software suite widely used for 3D molecular modeling, simulation, and visualization [15]. It was purified by eliminating prebound heteroatoms and water molecules, which could potentially affect the docking outcomes. Chain A was retained and employed in the simulation with the ligand, while the other chains were removed.

Structure Validation

A Ramachandran Plot generated on the PROCHECK server was used to validate the retrieved protein structure [16]. The secondary structure of the protein was determined using PDBsum [17].

Phytocompound Retrieval

Using the IMPPAT Database, a digital database of phytochemicals of Indian medicinal plants, 25 phytocompounds were retrieved from *Momordica charantia* plants [18]. The list of all retrieved 25 phytocompounds is given in Table 1. To obtain the standard SMILES and 3D SDS structures, the PubChem database was used, which contains chemical compounds and their actions against biological tests [19].

ADME Analysis

To evaluate phytocompounds as potential medication candidates, their ADME properties were examined. SwissADME, a software for analyzing chemical absorption, distribution, metabolism, excretion, and toxicity that is important in drug development and discovery, was used to analyze ADME properties [20]. SwissADME was provided with the canonical SMILE of the phytocompounds, sourced from PubChem.

Drug-likeness Analysis

One important step in the drug design process is drug-likeness analysis, which confirms that the selected compounds have the necessary pharmacological characteristics. This indicates that the molecular weight cannot exceed 500 Da, the lipophilicity (log p) value cannot exceed 5, the hydrogen bond donor cannot exceed 5, and the hydrogen bond acceptor cannot exceed 10.

Molecular Docking and Visualization

Molecular docking is a computational technique that predicts the interaction between a ligand and a receptor at the atomic level. This helps in understanding the optimal binding posture and binding affinity of the ligand-receptor complex. Using PyRx virtual screening software that integrates various tools for molecular dynamics simulations and docking studies, this technique uses a number of embedded applications, including Vina Wizard, AutoDock Wizard, and Open Babel [21]. If the ligand molecule complies with Lipinski's rule, it possesses favorable oral bioavailability characteristics and is a promising therapeutic candidate. To begin the docking process, the ligand molecule that met Lipinski's rule and the purified structure from BIOVIA Discovery Studio were uploaded to PyRx. A comma-separated value (CSV) file containing binding energy information was downloaded, which included the docking simulation results. The binding energy (kcal/mol) was used to identify potential drug candidates. Stronger ligand-receptor interactions are usually indicated by lower binding energies.

RESULTS

Protein Extraction and Purification of the Target Protein

The protein GLP-1 was uploaded to BIOVIA Discovery Studio, and all the heteroatoms and water molecules were removed, as cleaning protein structures is an essential step to ensure the accuracy and reliability of computational simulations to prevent unwanted interactions that could impair the docking results and lead to inaccurate predictions of ligand binding. Figure 1(a) shows the unpurified protein and Figure 1(b) shows the purified protein.

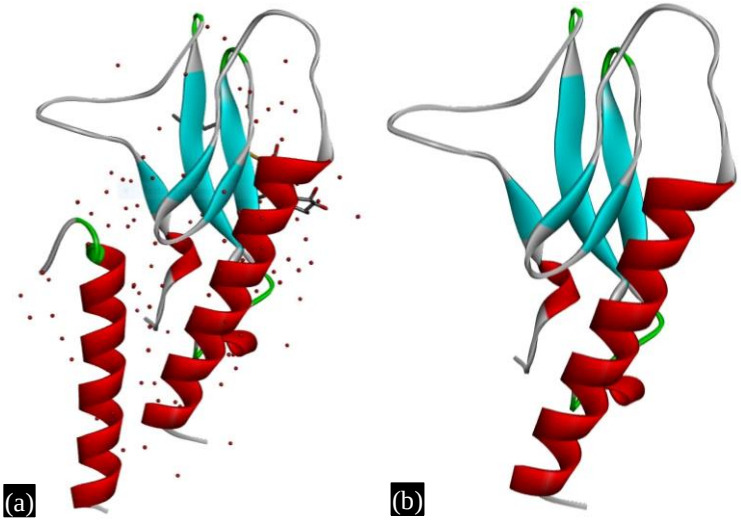


Figure 1. '(a)' represents unpurified protein, '(b)' is purified protein.

Structure Validation

The alpha helices, beta sheets, left-handed helices, and loops together make up the protein's secondary structure, which is represented by the four quadrants of the Ramachandran Plot. This method was used to visualize the range of allowed energies for the backbone dihedral angles as a function of protein residues. The plot displays the overall quality of the protein structure as follows: 82.6% of the residues fell under the most favored areas, 12.8% fell under additional allowed regions, 2.8% fell under generously allowed regions, and 1.8% fell under disallowed regions (Figures 2 and 3). A wide variety of structural features, including two sheets, two beta hairpins, one beta bulge, four strands, three helices, one helix-helix interact, eight beta turns, and three disulfides, are found in the 103 amino acid secondary structure of the protein.

Phytocompound Retrieval

The list of all retrieved 25 phytocompounds is given in Table 1. The compounds were evaluated using the SwissADME tool. Docking ligands for the target protein were narrowed down to molecules that passed the Lipinski Rule of 5. Phytochemical compounds were screened, and those that met the Lipinski Rule of 5 were chosen for future investigation.

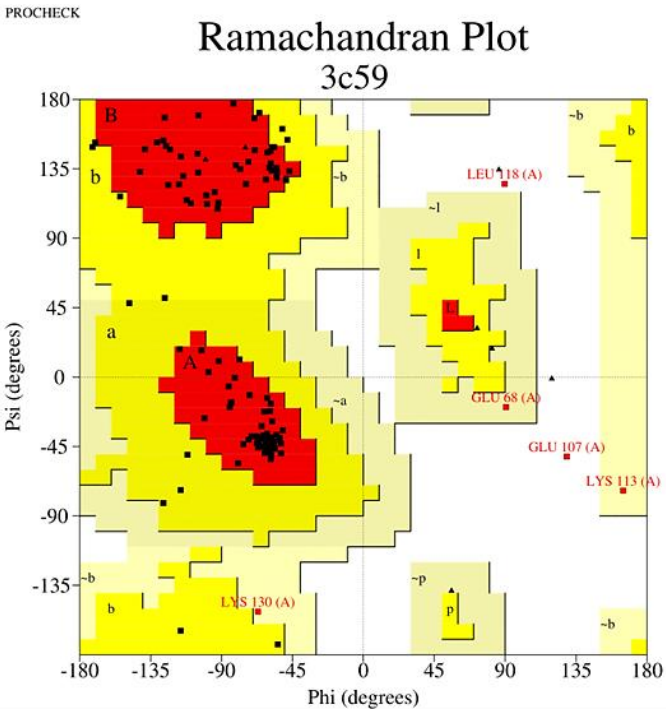


Figure 2. Ramachandran Plot for protein 3C59 using PROCHECK.

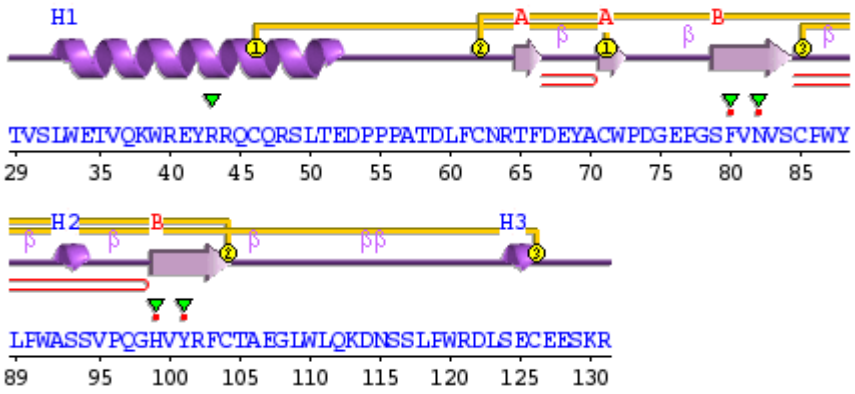


Figure 3. Secondary structure of 3C59 protein.

Table 1. Phytocompounds of *Momordica charantia* extracted from IMPPAT.

S.N.	Phytocompounds
1	Charantin
2	Vicine
3	Quercetin
4	beta-Carotene
5	Zeaxanthin
6	alpha-Spinasterol
7	alpha-Carotene
8	4-Hydroxybenzoic acid
9	Momordicoside I
10	Momordicine I
11	Momordicine II
12	beta-Sitosterol
13	Diosgenin
14	Nicotinic acid
15	beta-Cryptoxanthin
16	Linoleic acid
17	Kaempferol
18	Momordicoside G
19	Oleanolic acid
20	Momordicoside F2
21	Cycloeucalenol
22	Luteolin
23	alpha-Carotene
24	Oleic acid
25	Stearic acid

ADMET Analysis

The ADME characteristics of pharmaceuticals play a major role in determining their pharmacokinetics and bioavailability. Human pharmacokinetic studies of compounds with potential therapeutic uses are essential to accelerate the drug development process because they lower the risk of clinical trial failure. The pharmacokinetic characteristics of drug candidates are predicted using computational techniques such as SwissADME, enabling a more accurate evaluation of their potential. Examination of the blood-brain barrier and gastrointestinal absorption was performed. The results are compiled in Table 2, and Figure 4 illustrates how efficiently each ligand penetrates the BBB and is taken up by GI using a boiled-egg design. The ligand molecules in the yellow-yolk portion, which show the ability to pass through the blood-brain barrier, and the white area, which shows enhanced gastrointestinal absorption, are particularly noteworthy.

Drug-likeness Analysis

The ligands (molecules 2, 4, 5, 7, 11, and 23) listed in Table 3 failed to adhere to the Lipinski Rule of 5. In contrast, molecules 1, 3, 6, 8, 9, 10, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 24, and 25 were appropriate for future drug design considerations because they matched the Lipinski criteria.

H bond donors < 5, H bond acceptors ≤ 10, and molecular weights in the 150–500 g/mol range are the requirements for the Lipinski filter. All phytochemicals in the table passed the Lipinski filter analysis and exhibited possible medicinal qualities, with the exception of Vicine, alpha-, beta-, and beta-carotene, zeaxanthin, and momodicine II, whose values were not found to be within the acceptable range for human use.

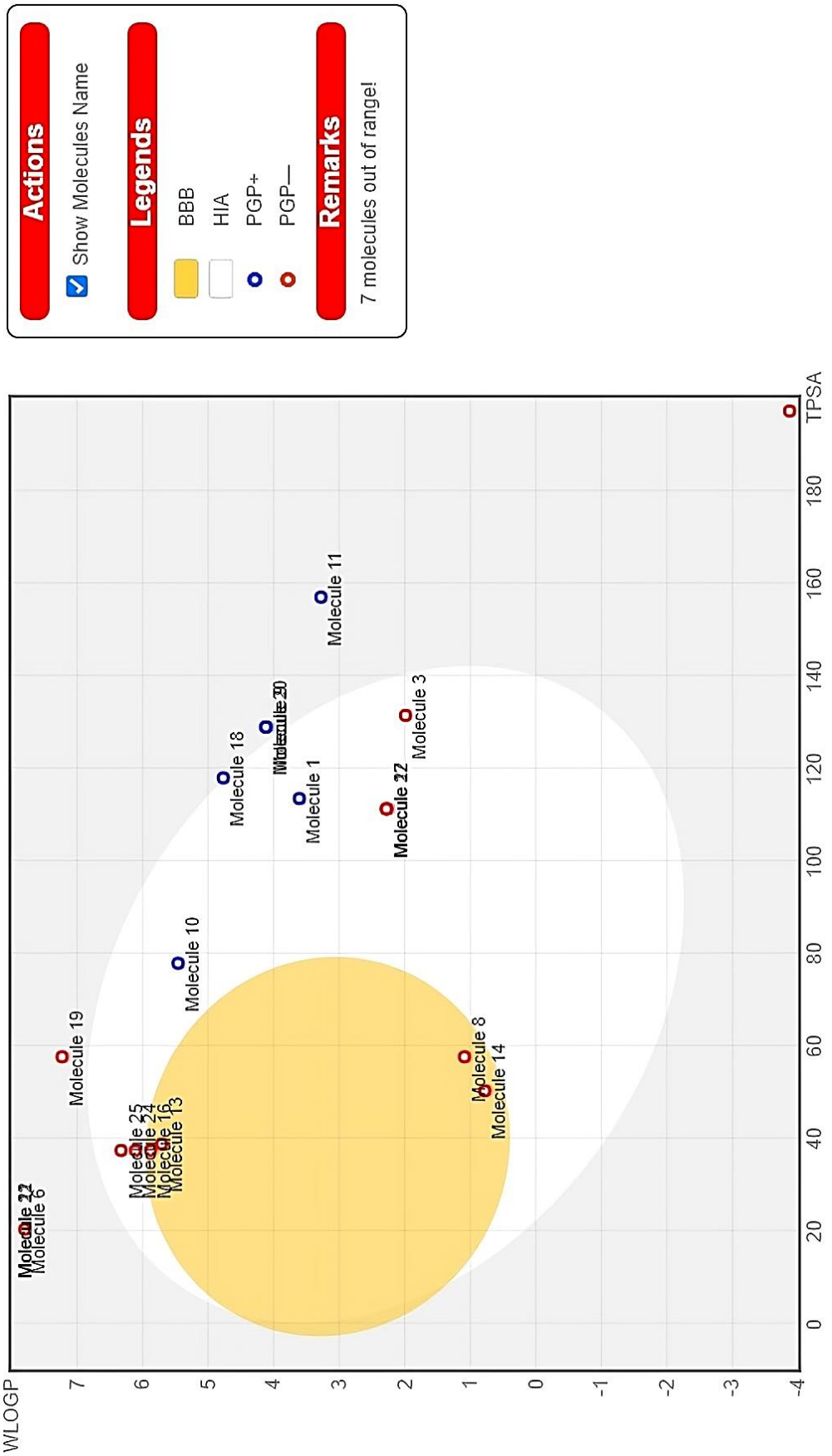


Figure 4. Boiled-egg generated on SwissADME.

Table 2. ADME prediction for the blood-brain barrier, GI absorption, and p-GP substrate.

Ligands	Blood-brain barrier	GI absorption	p-GP substrate
Charantin	-	High	+
Vicine	-	Low	-
Quercetin	-	High	-
beta-Carotene	-	Low	+
Zeaxanthin	-	Low	+
alpha-Spinasterol	-	Low	-
alpha-Carotene	-	Low	+
4-Hydroxybenzoic acid	+	High	-
Momordicoside I	-	Low	+
Momordicine I	-	High	+
Momordicine II	-	Low	+
beta-Sitosterol	-	Low	-
Diosgenin	+	High	-
Nicotinic acid	+	High	-
beta-Cryptoxanthin	+	High	-
Lileic acid	+	High	-
Kaempferol	-	High	-
Momordicoside G	-	Low	+
Olealic acid	-	Low	-
Momordicoside F2	-	Low	+
Cycloeucale-l	-	Low	-
Luteolin	-	High	-
alpha-Carotene	-	Low	+
Oleic acid	-	High	-
Stearic acid	-	High	-

** In a table '-' indicates No, '+' is for Yes.*

Molecular Docking and Visualization

PyRx software was used to produce a CSV file containing docking results for the protein receptor 3C59. This file details the diverse binding energies associated with the different poses of ligands interacting with the protein. The ligands diosgenin, alpha-spinasterol, and momodicoside I, which exhibited the lowest binding affinities, were chosen for visualization in BIOVIA in both 3D and 2D. Table 4 shows the binding affinities of these ligands for the protein 3C59 (kcal/mol). Three-dimensional structures of the ligands were generated using the BIOVIA Discovery tool (Figure 5).

The binding energies of ligands and receptors decreased with the stability of their binding, as demonstrated by docking experiments, which indicated that the binding energies of all ligands with target proteins were ≤-7 kcal/mol. The molecular models of the binding of ligands with 3C59 (-8.1 kcal/mol) are displayed in Figures 6–8, with the results displayed as 2D (interactions) and 3D (hydrophobicity) diagrams.

Diosgenin had the lowest binding free energy with the target (-8.1 kcal/mol), and van der Waals forces were the primary forces at play with LEU A:32, THR A:35, LEU A:89, TYR A:69, TRP A:91, PRO A:90, Conventional hydrogen bond with GLU A:68 and Pi-donor hydrogen bond with TRP A:39 (Figure 6). This was followed by alpha-Spinasterol (-8.0 kcal/mol), and there were van der Waals forces with LEU A:32, THR A:35, LEU A:89, and the conventional hydrogen bond with ARG A:121 (Figure 7). Momordicoside I (-7.8 kcal/mol). The main forces involved were van der Waals forces and conventional hydrogen bonds with SER A:49 (Figure 8). Table 4 shows the binding affinities of the ligands with protein 3C59.

Table 3. Lipinski analysis.

Molecule	Ligand	Molecular weight	Hydrogen bond acceptor	Hydrogen bond donor	MLogP
1	Charantin	473.56	8	2	2.03
2	Vicine	304.26	8	7	-3.36
3	Quercetin	302.24	7	5	-0.56
4	beta-Carotene	536.87	0	0	8.96
5	Zeaxanthin	568.87	2	2	8.96
6	alpha-Spinasterol	412.69	1	1	6.62
7	alpha-Carotene	536.87	0	0	8.96
8	4-Hydroxybenzoic acid	138.12	3	2	0.99
9	Momordicoside I	618.84	8	5	2.44
10	Momordicine I	472.7	4	3	4.06
11	Momordicine II	634.84	9	6	1.57
12	beta-Sitosterol	414.71	1	1	6.73
13	Diosgenin	414.62	3	1	4.94
14	Nicotinic acid	123.11	3	1	-1.13
15	beta-Cryptoxanthin	552.87	1	1	-1.13
16	Linoleic acid	280.45	2	1	4.47
17	Kaempferol	286.24	6	4	-0.03
18	Momordicoside G	632.87	8	4	2.62
19	Oleanolic acid	456.7	3	2	5.82
20	Momordicoside F2	618.84	8	5	2.44
21	Cycloeucalenol	426.72	1	1	6.92
22	Luteolin	286.24	6	4	-0.03
23	alpha-Carotene	536.87	0	0	8.96
24	Oleic acid	282.46	2	1	4.57
25	Stearic acid	284.48	2	1	4.67

Table 4. The binding affinity of ligands with protein 3C59.

S.N.	Phytocompounds	Binding affinity in kcal/mol
1	Charantin	-6.7
2	Quercetin	-6.4
3	alpha-Spinasterol	-8.0
4	4-Hydroxybenzoic acid	-4.5
5	Momordicoside I	-7.8
6	Momordicine I	-6.7
7	beta-Sitosterol	-6.9
8	Diosgenin	-8.1
9	Nicotinic acid	-4.1
10	beta-Cryptoxanthin	-7.9
11	Linoleic acid	-5.1
12	Kaempferol	-6.3
13	Momordicoside G	-7.3
14	Oleanolic acid	-7.5
15	Momordicoside F2	-7.3
16	Cycloeucalenol	-7.6
17	Luteolin	-6.8
18	Oleic acid	-4.5
19	Stearic acid	-4.1

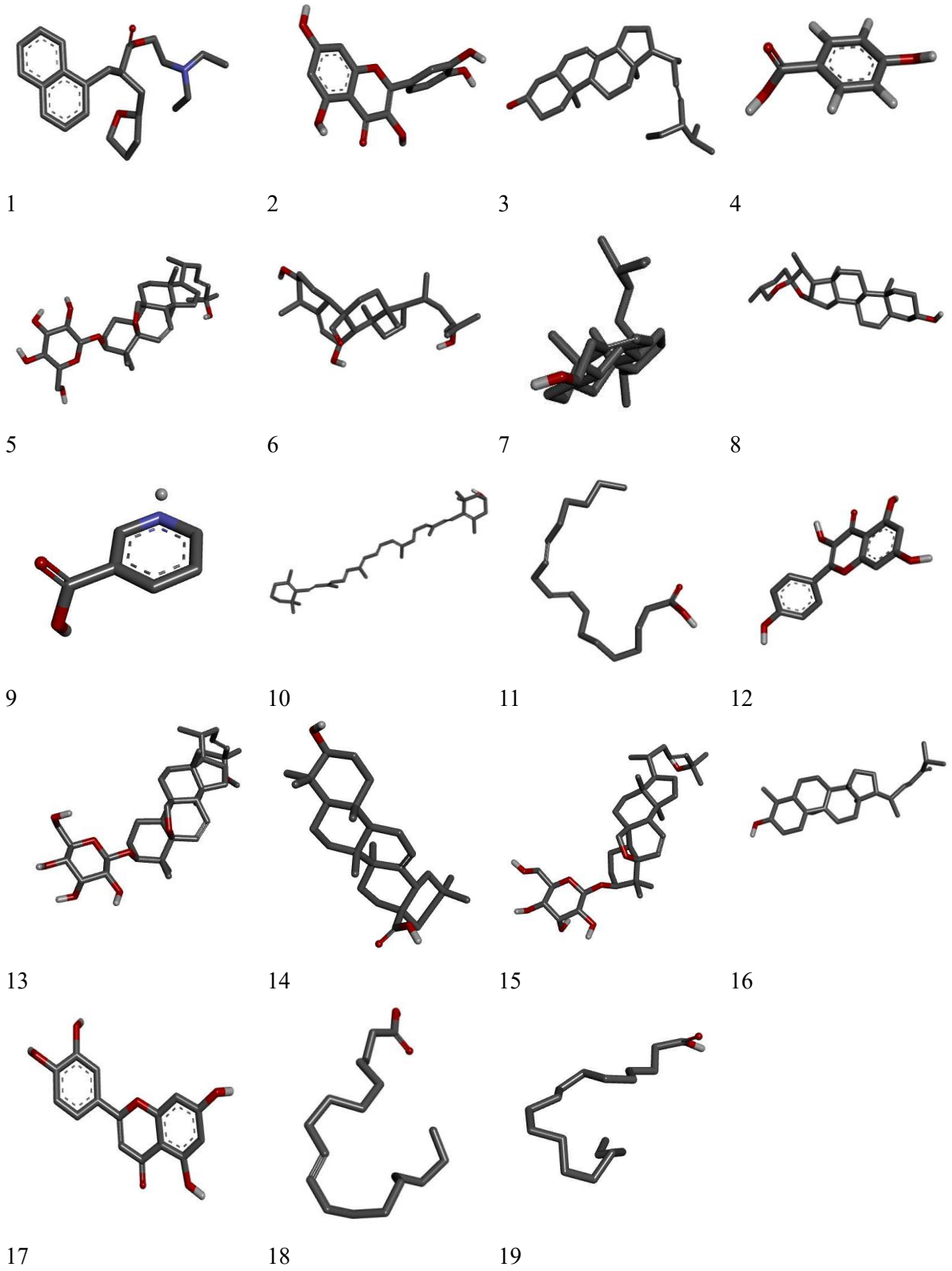


Figure 5. 3-Dimensional structures of ligands generated on BIOVIA tool. 1-19 represents charantin, quercetin alpha-spinasterol, 4-hydroxybenzoic acid, momordicoside I, momordicine I, beta-sitosterol, diosgenin, nicotinic acid, beta-cryptoxanthin, linoleic acid, kaempferol, momordicoside G, oleanolic acid, momordicoside F2, cycloeucalenol, luteolin, oleic acid and stearic acid, respectively.

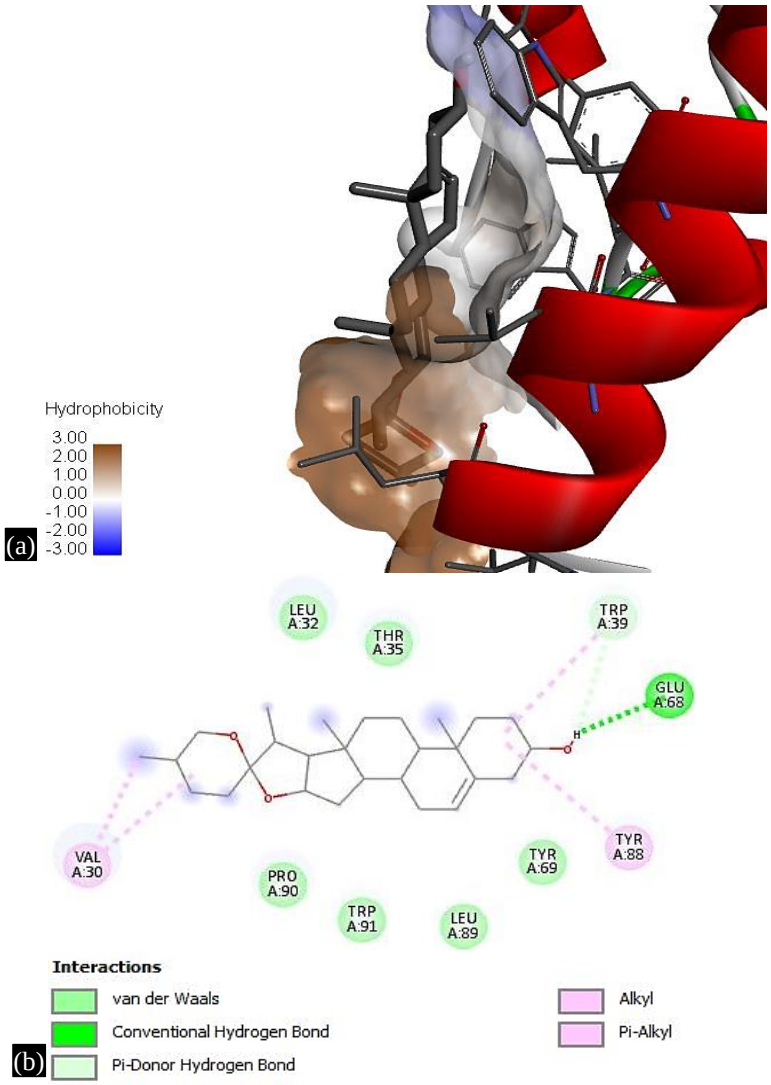
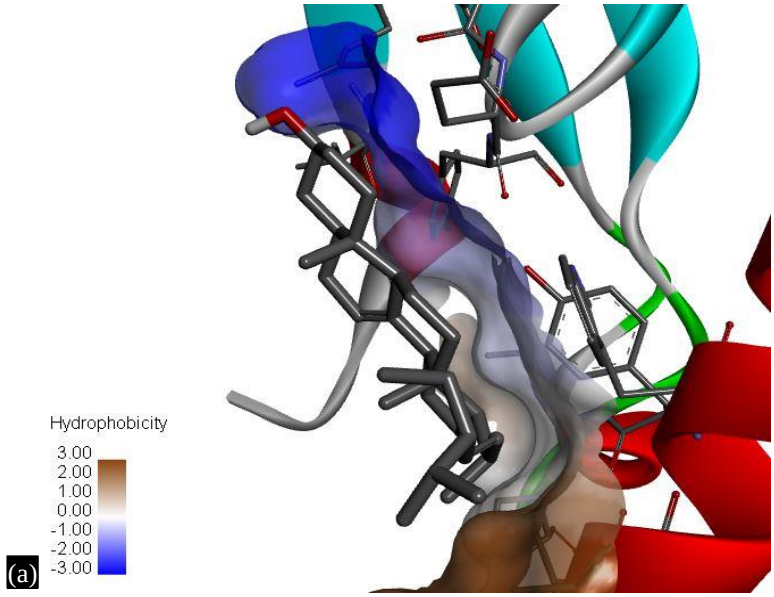


Figure 6. Molecular models of the binding of diosgenin with 3C59 (-8.1kcal/mol), the results are displayed as 2D and 3D images.



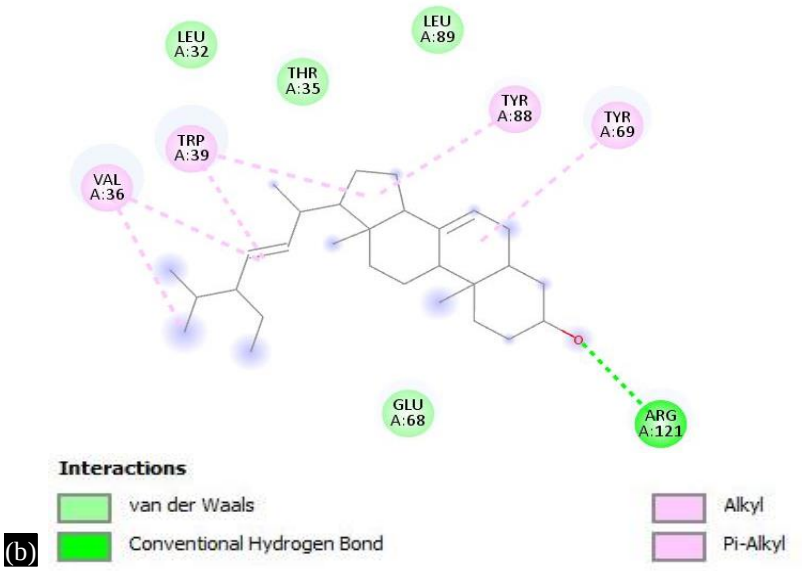


Figure 7. Molecular models of the binding of alpha-spinasterol with 3C59(-8.0kcal/mol), the results are displayed as 2D and 3D images.

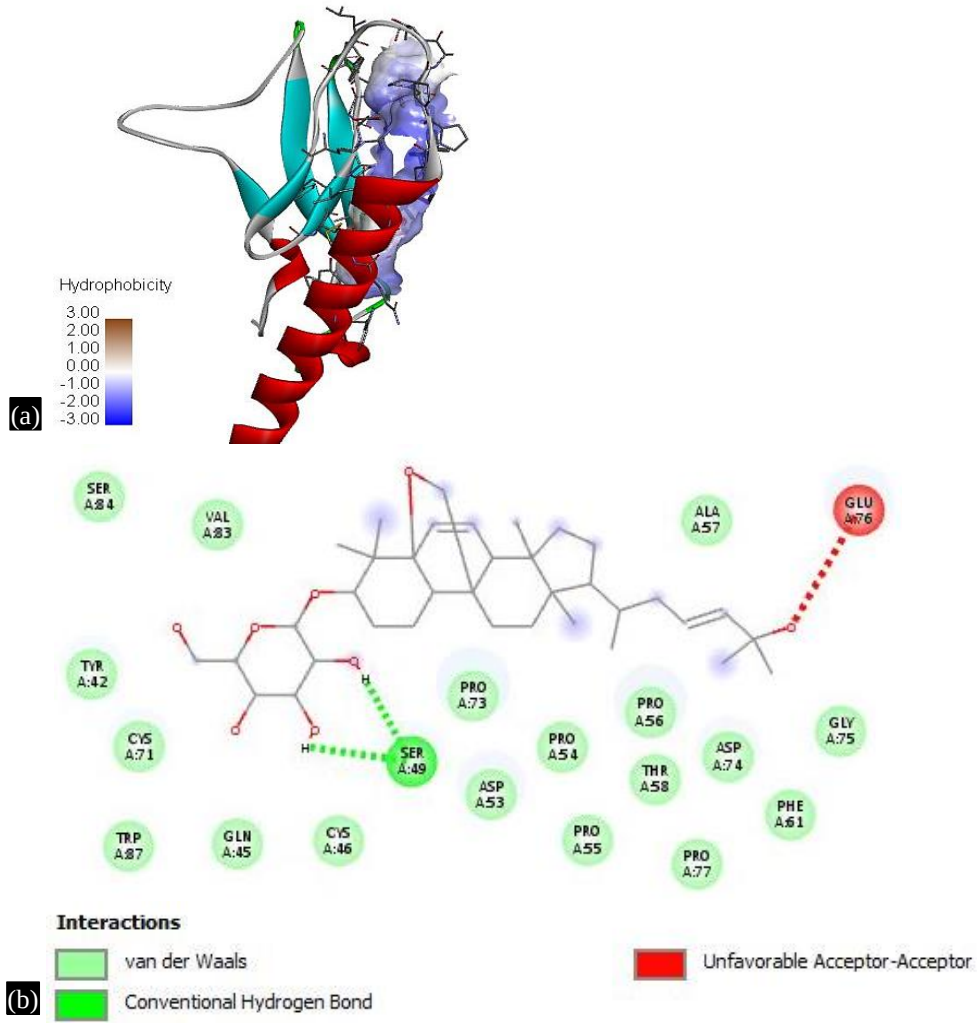


Figure 8. Molecular models of the binding of Momordicoside I with 3C59(-7.8kcal/mol), the results are displayed as 2D and 3D images.

DISCUSSION

The results of this study support the theory that GLP-1 is a promising target for diabetic therapy. It is well-recognized that GLP-1 is essential for maintaining insulin secretion and glucose homeostasis [9, 10]. According to the molecular docking data, GLP-1 and phytocompounds from *Momordica charantia*, namely diosgenin, alpha-spinasterol, and momordicoside I, interact favorably. These interactions imply that these substances may modify GLP-1 activity, which is necessary for glucose homeostasis and insulin production. The work used rigorous techniques, such as secondary structure prediction and Ramachandran Plot analysis, for the structural validation of GLP-1.

Furthermore, the utilization of computational techniques for drug development, including ADME analysis and molecular docking, is in line with modern methodologies for identifying potential therapeutic agents [20, 21]. This study adds to the expanding literature on the use of natural substances in the management of diabetes. Even though this study offers insightful information, it is important to recognize its limitations. Despite their strengths, computational predictions might not be able to fully capture the complexity of *in vivo* environments. Further i*n vitro* and *in vivo* studies are necessary to confirm the safety and effectiveness of the discovered phytocompounds.

CONCLUSION

The findings of this study suggest that GLP-1 might be a useful target for the management of diabetes owing to the favorable interactions observed during molecular docking with the ligands momordicoside I, alpha-spinasterol, and diosgenin. Overall confidence in the study findings was strengthened by structural validation and ADME analysis. To confirm the potential therapeutic benefits of phytocompounds, further *in vitro/vivo* research is necessary. These findings provide the basis for further research into the molecular processes underlying the interaction between Momordica charantia ligands and GLP-1, which is necessary to investigate possible treatments for diabetes mellitus. Future studies should examine the pharmacological activity of these compounds in vivo to better understand their potential as lead compounds for the development of novel drugs for the treatment of diabetes.

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Authors Contribution

The contribution of all the authors to the manuscript has to be clearly stated.

Conflict of Interest

The authors declare no conflict of interest.

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REFERENCES

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care [online]. 2009;32(Suppl_1):S62–7. DOI: 10.2337/dc09-s062.
2. Cole JB, Florez JC. Genetics of diabetes mellitus and diabetes complications. Nat Rev Nephrol [online]. 2020;16(7):377–90. DOI: 10.1038/s41581-020-0278-5.
3. Schellenberg ES, Dryden DM, Vandermeer B, Ha C, Korownyk C. Lifestyle interventions for patients with and at risk for type 2 diabetes: A systematic review and meta-analysis. Ann Intern Med [online]. 2013;159(8):543. DOI: 10.7326/0003-4819-159-8-201310150-00007.
4. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract [online]. 2018;138:271–81. DOI: 10.1016/j.diabres.2018.02.023.

5. Grover JK, Yadav S, Vats V. Medicinal plants of India with anti-diabetic potential. J Ethnopharmacol [online]. 2002;81(1):81–100. DOI: 10.1016/s0378-8741(02)00059-4.
6. Richter E, Geetha T, Burnett D, Broderick TL, Babu JR. The effects of Momordica charantia on type 2 diabetes mellitus and Alzheimer's disease. Int J Mol Sci [online]. 2023;24(5):4643. DOI: 10.3390/ijms24054643.
7. Cortez-Navarrete M, Pérez-Rubio KG, Escobedo-Gutiérrez M de J. Role of Fenugreek, Cinnamon, Curcuma longa, Berberine, and Momordica charantia in type 2 diabetes mellitus treatment: A review. Pharmaceuticals (Basel) [online]. 2023;16(4):515. DOI: 10.3390/ph16040515.
8. Dans AML, Villarruz MVC, Jimeno CA, Javelosa MAU, Chua J, Bautista R, et al. The effect of Momordica charantia capsule preparation on glycemic control in type 2 diabetes mellitus needs further studies. J Clin Epidemiol [online]. 2007;60(6):554–9. DOI: 10.1016/j.jclinepi.2006.07.009.
9. Drucker DJ. Mechanisms of action and therapeutic application of glucagon-like peptide-1. Cell Metab [online]. 2018;27(4):740–56. DOI: 10.1016/j.cmet.2018.03.001
10. Nauck MA, Quast DR, Wefers J, Meier JJ. GLP-1 receptor agonists in the treatment of type 2 diabetes – state-of-the-art. Mol Metab [online]. 2021;46(101102):101102. DOI: 10.1016/j.molmet.2020.101102.
11. Bailey CJ, Flatt PR, Conlon JM. An update on peptide-based therapies for type 2 diabetes and obesity. Peptides [online]. 2023;161(170939):170939. DOI: 10.1016/j.peptides.2023.170939.
12. Muzurović EM, Volčanšek Š, Tomšić KZ, Janež A, Mikhailidis DP, Rizzo M, et al. Glucagon-like peptide-1 receptor agonists and dual glucose-dependent insulinotropic polypeptide/glucagon-like peptide-1 receptor agonists in the treatment of obesity/metabolic syndrome, prediabetes/diabetes and non-alcoholic fatty liver disease—current evidence. J Cardiovasc Pharmacol Ther [online]. 2022;27:107424842211463. DOI: 10.1177/10742484221146371.
13. Klen J, Dolžan V. Glucagon-like peptide-1 receptor agonists in the management of type 2 diabetes mellitus and obesity: The impact of pharmacological properties and genetic factors. Int J Mol Sci [online]. 2022;23(7):3451. DOI: 10.3390/ijms23073451
14. RCSB Protein Data Bank. RCSB PDB: Homepage [online]. Rcsb.org. Available from: https://www.rcsb.org/
15. Systèmes D. Free download: BIOVIA Discovery Studio Visualizer [online]. Dassault Systèmes. 2020. Available from: https://discover.3ds.com/discovery-studio-visualizer-download
16. PROCHECK home page [online]. Ebi.ac.uk. Available from: https://www.ebi.ac.uk/thornton-srv/software/PROCHECK/
17. PDBsum home page [online]. Ebi.ac.uk. Available from: https://www.ebi.ac.uk/thornton-srv/databases/pdbsum/
18. AS. IMPPAT [online]. Res.in. Available from: https://cb.imsc.res.in/imppat/
19. PubChem. PubChem [online]. Nih.gov. Available from: https://pubchem.ncbi.nlm.nih.gov/
20. SwissADME [online]. Swissadme.ch. Available from: http://www.swissadme.ch/
21. Welcome to the PyRx website [online]. Sourceforge.io. Available from: https://pyrx.sourceforge.io/

