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Research article

Computational Elucidation of the Antidiabetic Mechanism of Catechin and Apigenin via Network Pharmacology and Molecular Docking

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Abstract

Insulin resistance, poor glucose homeostasis, oxidative stress, inflammation, and pancreatic β-cell dysfunction are the hallmarks of Type 2 Diabetes Mellitus (T2DM), a chronic metabolic disease. The search for safer multitarget therapeutic agents made from natural products is necessary due to the rising incidence of type 2 diabetes and the drawbacks of traditional antidiabetic treatments. Apigenin and catechin have anti-inflammatory, antihyperglycemic, insulin-sensitizing, and antioxidant qualities. The current study examined the therapeutic mechanisms of apigenin and catechin against type 2 diabetes using integrated network pharmacology and molecular docking techniques. Protein-protein interaction (PPI), Gene Ontology (GO), and KEGG pathway enrichment studies were performed after T2DM-associated genes and potential phytochemical targets were found using publically accessible databases. Important hub genes linked to insulin signaling and glucose metabolism were found by network analysis, including PIK3R1, ESR1, AKT1, EGFR, and PTK2. PI3K-Akt and endocrine resistance pathways were significantly enriched, according to KEGG analysis. Catechin has a strong binding affinity for PIK3R1 (-6.1 kcal/mol) and AKT1 (-6.4 kcal/mol) according to molecular docking, whereas Apigenin had docking scores of -5.7 and -6.3 kcal/mol, respectively, when compared to Metformin. These results offer a scientific foundation for additional experimental confirmation and imply that catechin and apigenin may have antidiabetic effects through multitarget regulation.

1. Introduction

Type 2 diabetes mellitus (T2DM), also known as non-insulin dependent diabetes mellitus (NIDDM), is a metabolic disorder characterized by persistent hyperglycemia caused by insulin resistance and progressive pancreatic β-cell dysfunction. It accounts for approximately 90-95% of all diabetes cases worldwide. The pathophysiology of T2DM involves impaired insulin responsiveness, altered glucose metabolism, and disturbances in carbohydrate, lipid, and protein metabolism. Major risk factors include genetic predisposition, obesity, sedentary lifestyle, poor dietary habits, stress, and aging. The disease is associated with severe complications such as cardiovascular disease, nephropathy, neuropathy, retinopathy, diabetic foot ulcers, and increased susceptibility to infections [1-3].

According to the International Diabetes Federation, approximately 537 million people were affected by diabetes globally in 2021, and this number is expected to rise significantly by 2045. India is considered one of the countries with the highest diabetic populations due to urbanization, obesity, reduced physical activity, and dietary changes [4-6]. Current treatment strategies for T2DM include lifestyle modifications and pharmacological

interventions such as metformin, sulfonylureas, thiazolidinediones, DPP-4 inhibitors, SGLT-2 inhibitors, GLP-1 receptor agonists, and insulin therapy. Recent research has focused on phytoconstituents with antidiabetic potential due to their ability to regulate glucose metabolism, reduce oxidative stress, and improve insulin sensitivity [7-8]. Catechin, a flavan-3-ol flavonoid found in medicinal plants such as *Acacia catechu* and *Camellia sinensis*, possesses antioxidant, anti-inflammatory, antidiabetic, cardioprotective, neuroprotective, and anticancer activities. Studies have demonstrated that catechin improves insulin sensitivity, regulates glucose metabolism, and reduces oxidative stress and inflammatory responses [9-11].

Apigenin, a naturally occurring flavone present in parsley, chamomile, celery, onions, and *Matricaria chamomilla*, exhibits antioxidant, anti-inflammatory, antidiabetic, neuroprotective, and cardioprotective properties. Apigenin has been reported to improve insulin sensitivity, reduce hyperglycemia, and protect pancreatic β-cells from oxidative damage through modulation of signaling pathways such as MAPK, PI3K/Akt, and NF-κB [12-14]. In recent years, network pharmacology has emerged as a strong systems-level approach to studying the complex interactions between bioactive substances, target proteins, signaling pathways, and diseases. This computational method, when paired with molecular docking, enables the identification of new therapeutic targets as well as the assessment of ligand-protein binding affinities, therefore expediting drug development and mechanistic study. Although several studies have reported the antidiabetic potential of Catechin and Apigenin individually, limited research has explored their combined molecular mechanisms against T2DM using integrated computational approaches [15-20]. Therefore, the present study aimed to evaluate the therapeutic potential of Catechin and Apigenin against type 2 diabetes mellitus using network pharmacology and molecular docking.

2. Materials and Methods

2.1 Chemical Candidates and Compound Related Targets

The literature was used to aid the chemical selection process. The selected bioactive compounds were then searched in the PubChem database to obtain their chemical structures and SMILES notations. Potential target proteins linked with these chemicals, with potential scores higher than zero, were then predicted using the Swiss Target Prediction Database.

2.2 Identification of Type 2 Diabetes Mellitus-Related Targets

We searched the GeneCards database for possible targets related with breast cancer. This database combines data from several sources to provide complete information on human genes. The selected targets were collated for additional study and classified as type 2 diabetes mellitus-related targets [21].

2.3 Venn Diagram

We developed a Venn diagram to assess the overlap between type 2 diabetes mellitus-associated targets and possible targets for Catechin and Apigenin. (Figure 1)

2.4 Protein-Protein Interaction (PPI) Network

The STRING database (https://string-db.org/) collects known and projected protein-protein interactions, including functional and physical correlations. For this study, we utilized STRING [21] to look at the connections between the chemicals in our analysis and the targets associated with type 2 diabetes mellitus, finding potential therapy targets. To build a reliable protein-protein interaction (PPI) network for these targets, we employed the "Homo sapiens" organism with a confidence level of 0.4. This confidence score is commonly employed because it strikes a good balance between sensitivity and specificity, resulting in a credible criteria for interaction prediction. As a consequence, only proteins with interaction scores of 0.4 or higher were included to the PPI network, increasing the accuracy of our potential target identification.

2.5 Functional Enrichment and Pathway Analysis

To identify key pathways and related Gene Ontology (GO) concepts, all potential therapeutic targets were analyzed using pathway and GO enrichment analyses in the String database [21] (https://string-db.org/). This investigation shed light on the biological processes (BP), molecular functions (MF), and cellular components (CC) connected with the targets. Pathways and GO keywords having a significance level of $p < 0.05$ were chosen for further study.

2.6 Building A Compound-Target Network

The compound-target interaction network was created by linking the targets associated with each chemical. Cytoscape 3.10.2 (Cytoscape Consortium, San Diego, CA, USA) was used to visualize the network [21]. Nodes in the network represent drugs and their targets, while edges show their interactions.

2.7 Molecular Docking

Molecular docking investigations were carried out in accordance with the previously published approach described by Ahmad *et al.* (2024). The three-dimensional structures of target proteins were obtained from the Protein Data Bank, while ligand structures were obtained from PubChem. AutoDock Vina was used to investigate binding affinity and protein-ligand interactions. The docked complexes with the lowest binding energy were chosen and visualized using PyMOL and Discovery Studio, following the previously defined computational process [21].

3. Result and Discussion

3.1 Potential therapeutic targets of compounds used to treat Type 2 Diabetes Mellitus

Applying type 2 diabetes mellitus as a keyword, data were extracted from the GeneCards database, providing 18223 target genes. Among these, 123 targets were identified as shared by the chemicals and type 2 diabetes mellitus-related genes, indicating prospective therapeutic targets for compounds used to treat type 2 diabetes. A Venn diagram (Figure 1) depicts these overlapping targets.

3.2 Construction of the Compound-Target network

To investigate the signaling pathways and functional functions of the identified target genes, we used Cytoscape data analysis. This strategy helped create a thorough compound-target network, as shown in Figure 2. The network highlights the pharmacological pathways by which the drugs may impact type 2 diabetes therapy, with a focus on interactions with 163 target proteins. Network analysis shows that different components are converging across numerous targets, implying that these bioactive chemicals may have synergistic effects. These interactions may improve the therapeutic efficacy of these medications not only in the management of type 2 diabetes mellitus, but also in the treatment of other disorders.

3.3 PPI network visualization and analysis

The STRING database was used to investigate interactions between 123 putative medicinal targets. The final protein-protein interaction (PPI) network included 123 nodes and 119 edges, with an average node degree of 1.93 and a local clustering coefficient of 0.411 (Figure 3). In this network, nodes represent individual proteins, while edges represent the relationships between them. A higher degree value indicates a more important involvement for the protein in the network. Following a filtering procedure based on the defined criteria, numerous hub genes were found, including PIK3R1, ESR1, AKT1, EGFR, PTK2, ERBB2, IGF1R, KDR, and MMP2. These proteins, which include biological enzymes and cytokines, play critical roles in a variety of regulatory processes such as signal transduction and protein phosphorylation. Among these genes, the top five nodal targets were PIK3R1, ESR1, AKT1, EGFR, and PTK2. The substantial connections between these genes and other possible therapeutic targets highlight their significance in type 2 diabetes mellitus therapy.

3.4 GO enrichment analyses

To further understand the molecular processes by which drugs affect type 2 diabetes mellitus, we performed Gene Ontology (GO) enrichment analysis on 123 possible therapeutic targets linked with these medications using the string database. This study divided into three categories: biological process (BP), molecular function (MF), and cellular component. The top ten GO keywords found in each category are displayed in a bar plot, with data described in Tables 1 (BP), 2 (MF), and 3 (CC), as well as Figure 4A, 4B, and 4C. In the visualizations, the size of each bar correlates to the number of enriched genes linked with that GO word, while the color gradient indicates the importance of the p value, with deeper colors representing lower p values. A higher bar indicates a greater number of enriched therapeutic genes inside the associated GO word, implying a stronger link between that phrase and type 2 diabetes mellitus therapy than the other terms.

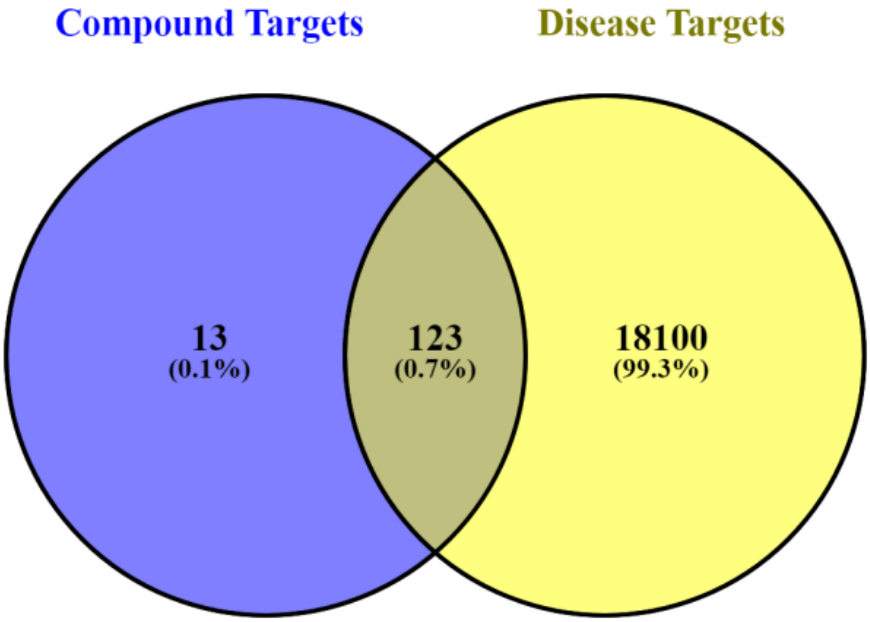


Figure 1. Venn Diagram.

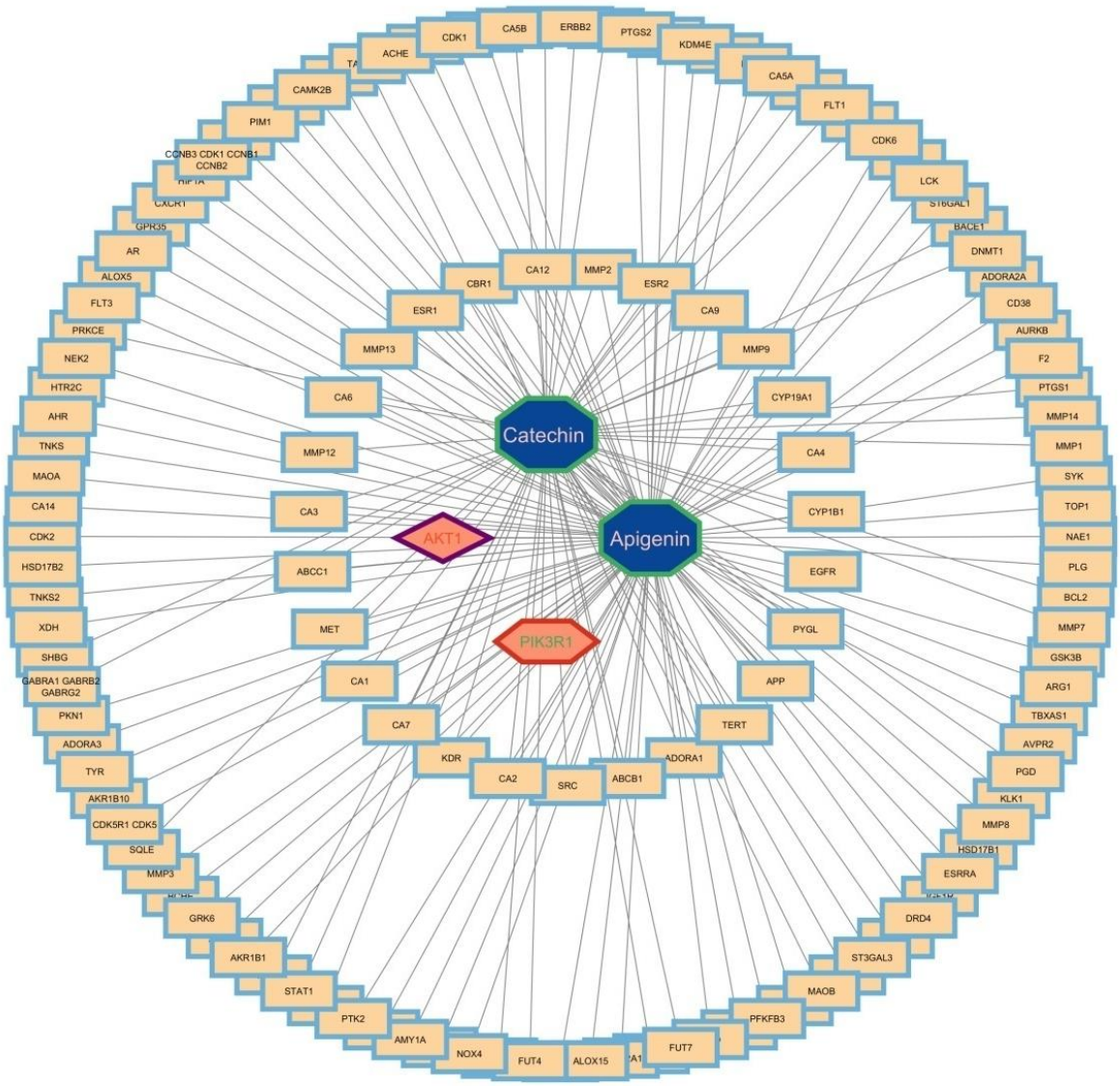


Figure 2. Compound Target Network.

Table 1. Biological Process.

Description	Observed gene count	False discovery rate
Response to chemical	86	8.94E-28
Response to organic substance	71	6.06E-26
Response to oxygen-containing compound	56	3.21E-25
Metabolic process	105	6.37E-21
Cellular response to chemical stimulus	64	6.37E-21
Regulation of cell population proliferation	52	3.15E-20

Table 2. Molecular Function.

Description	Observed gene count	False discovery rate
Catalytic activity	92	5.82E-23
Ion binding	89	7.38E-18
Protein kinase activity	32	9.83E-18
Phosphotransferase activity, alcohol group as acceptor	33	9.77E-17
Kinase activity	33	3.33E-15
Transferase activity, transferring phosphorus-containing groups	34	4.14E-14

Table 3. Cellular Components.

Description	Observed gene count	False discovery rate
Extracellular region	57	9.42E-07
Cell periphery	71	9.42E-07
Vesicle	54	1.52E-06
Extracellular space	47	3.81E-06
Plasma membrane	63	2.62E-05
Receptor complex	15	2.69E-05

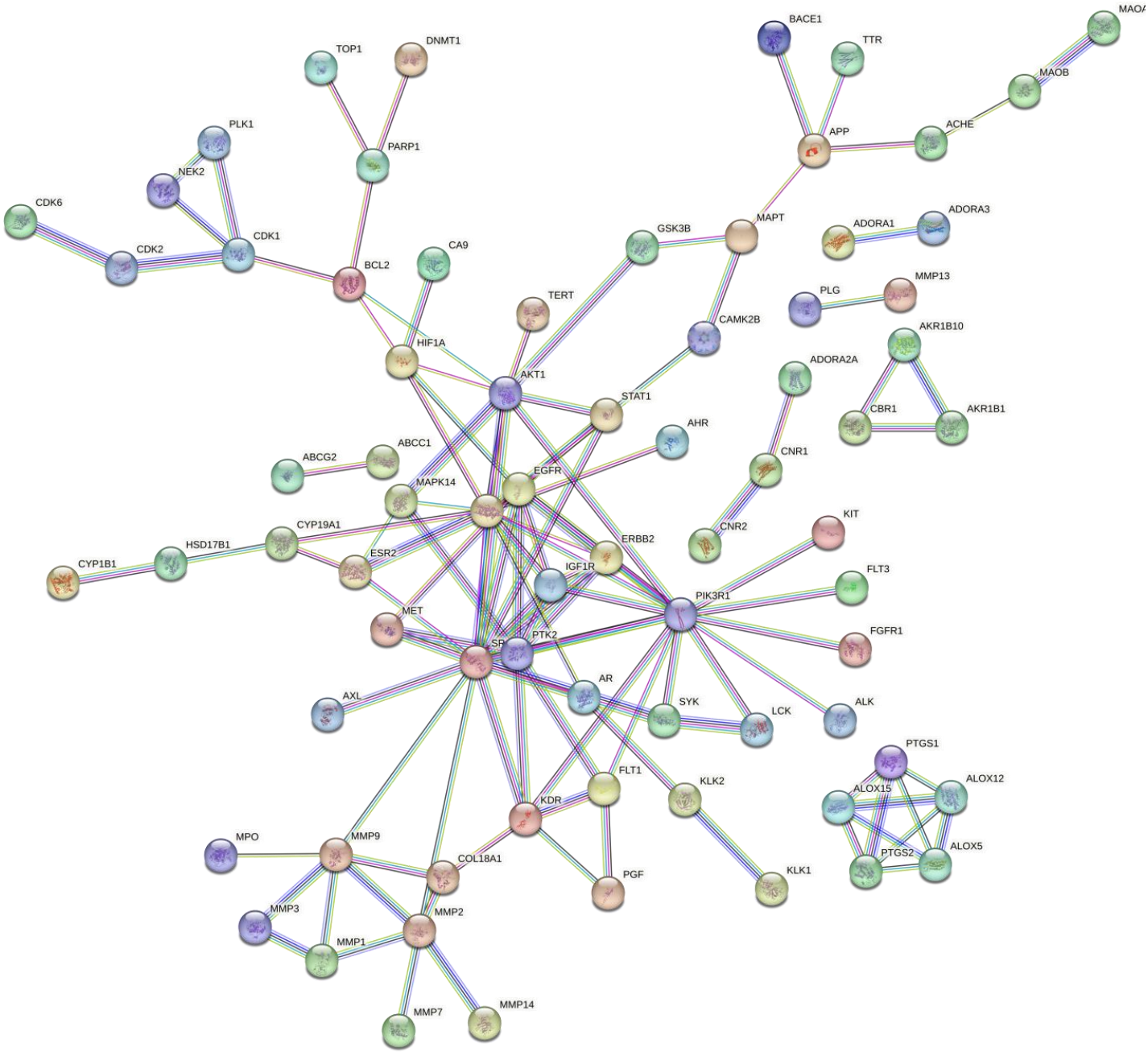


Figure 3. PPI Network.

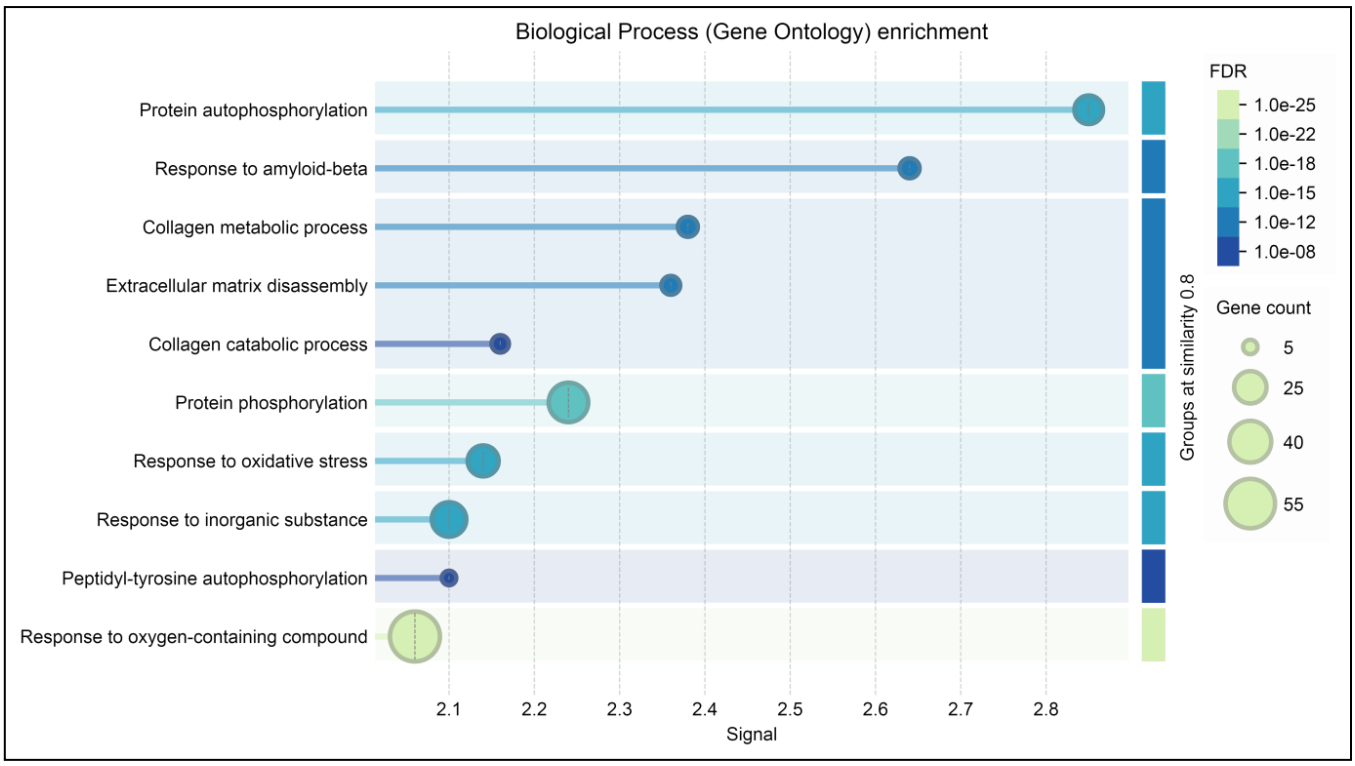


Figure 4A. Biological Process.

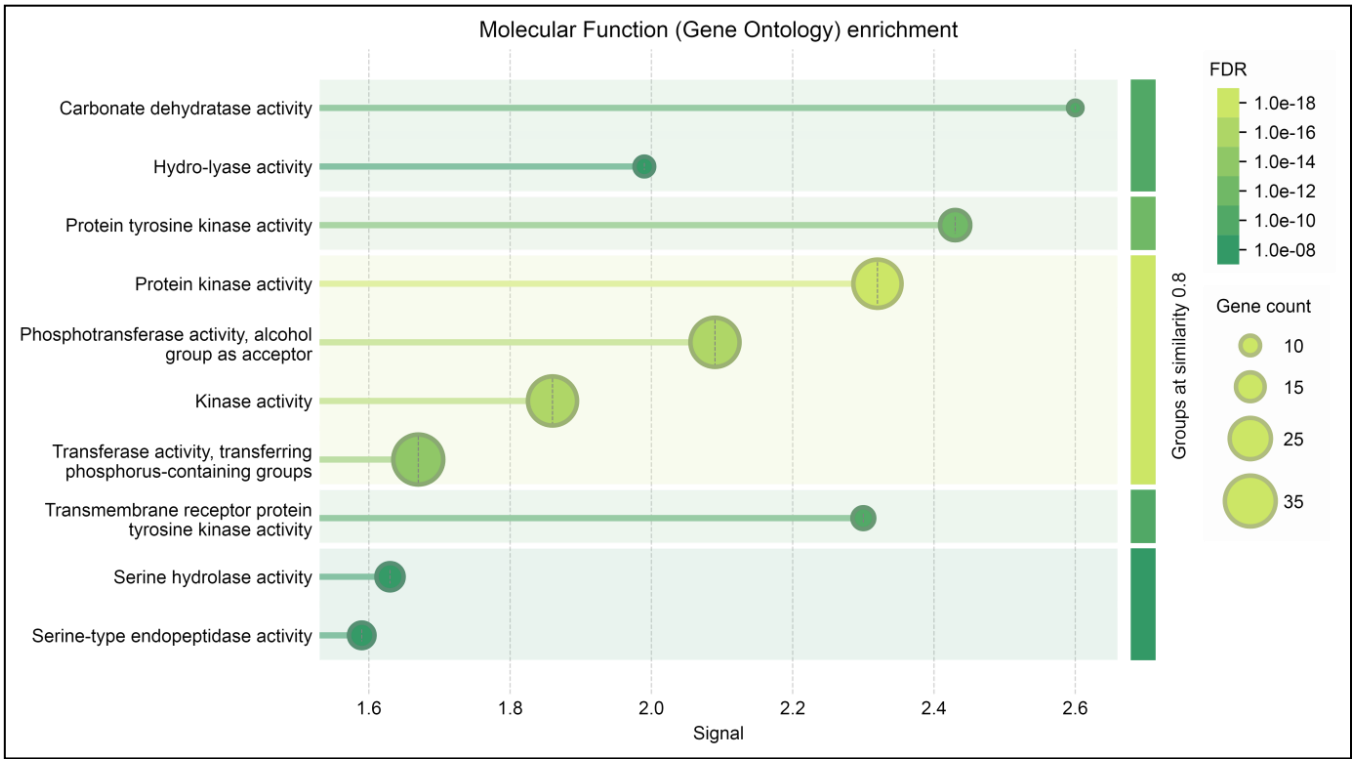


Figure 4B. Molecular Function.

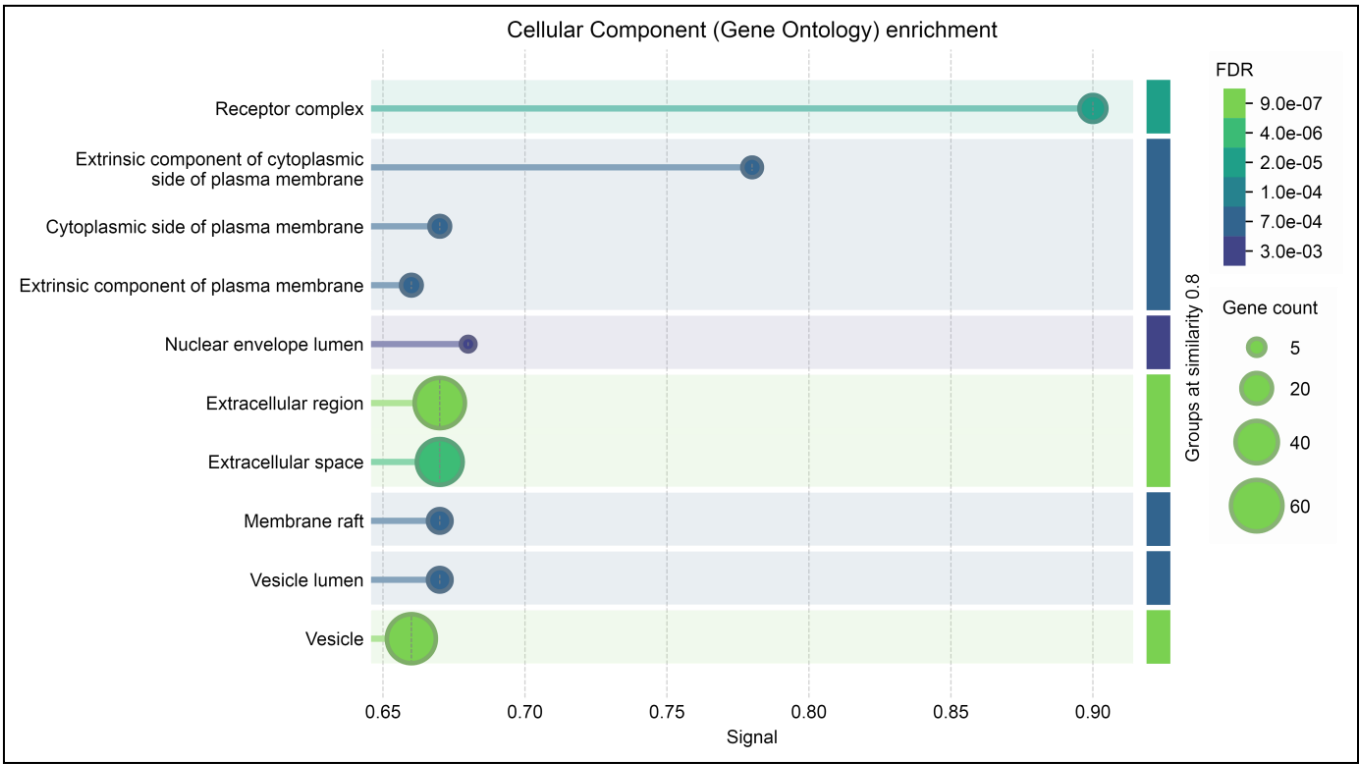


Figure 4C. Cellular Components.

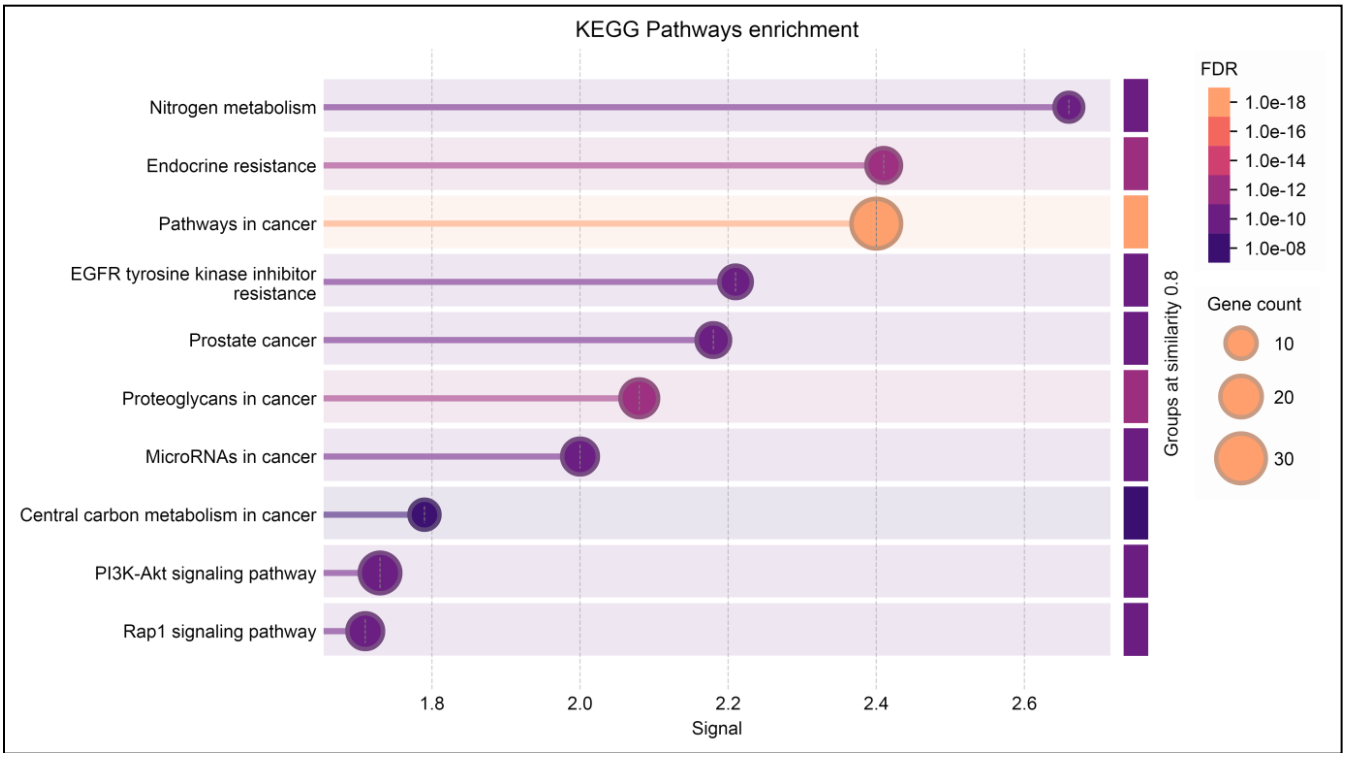


Figure 5. KEGG Pathway.

3.5 KEGG Pathway Enrichment Analyses

The pathways related with potential therapeutic targets for type 2 diabetic mellitus therapy were discovered using KEGG pathway enrichment analysis. Signalling pathways were obtained using the string database. The top ten signalling pathways were then shown in a bar graph (Table 4 and Figure 5), sorted by P value in ascending order. The results revealed that the major targets were significantly overrepresented in the Endocrine resistance pathway (Figure 5A).

3.6 Molecular docking

Molecular docking (MD) studies of Catechin and Apigenin with key type-2-Diabetes mellitus-associated targets, including PIK3R1 (node degree = 15) and AKT1 (node degree = 9), were performed using AutoDock Vina to evaluate binding affinities and interaction profiles. The docking analysis assessed parameters include binding affinity (kcal/mol), interacting amino acid residues. The obtained docking results demonstrated favorable ligand-protein interactions and are summarized in Table 5 and illustrated in Figure 6.

Metformin was used as the reference standard in the molecular docking investigation to assess the binding affinities of Catechin and Apigenin against the type 2 diabetes mellitus-associated target proteins PIK3R1 (PDB ID: 1UNQ) and AKT1 (PDB ID: 1PBW). Docking scores were represented in kcal/mol, where higher binding stability and a stronger ligand-protein interaction are indicated by lower binding energy. With a docking score of -6.1 kcal/mol, catechin showed the highest binding affinity among the phytochemicals examined, followed by apigenin with -5.7 kcal/mol, according to docking analysis against PIK3R1. Metformin, a common medication, had a docking score of -4.4 kcal/mol, indicating a reduced binding affinity. These findings suggest that Catechin and Apigenin may interact more effectively with the active binding pocket of PIK3R1, which is an important regulatory component of the PI3K signaling pathway involved in insulin signaling and glucose metabolism.

In a similar molecular docking against AKT1 revealed that Apigenin had a similar docking score of -6.3 kcal/mol while Catechin had the greatest interaction with a docking value of -6.4 kcal/mol. Metformin, on the other hand, showed a docking score of -4.3 kcal/mol, indicating a relatively lower binding affinity toward AKT1. The potential relevance of catechin and apigenin in regulating insulin signaling, glucose absorption, and cellular metabolic regulation linked to type 2 diabetes mellitus is suggested by their significant interaction with AKT1. Favorable hydrogen bonding, hydrophobic interactions, and stable molecule orientation within the target proteins' active sites may be responsible for the increased binding affinity of apigenin and catechin. Modulation of PIK3R1 and AKT1 may lead to better glycemic control and a decrease in diabetic complications since these proteins are essential for the PI3K/Akt signaling pathway, which controls glucose homeostasis, insulin sensitivity, and cellular survival. Compared to the common medication Metformin, the molecular docking results show that Catechin and Apigenin have greater binding affinities toward diabetes-associated targets, suggesting that they have promising antidiabetic potential. These results support the therapeutic significance of these phytochemicals as multitarget candidates for the management of type 2 diabetes mellitus.

Table 4. KEGG Pathway.

Description	Observed gene count	False discovery rate
Endocrine resistance	13	1.97E-11
PI3K-Akt signaling pathway	19	1.13E-10
Nitrogen metabolism	8	1.16E-10
Pathways in cancer	30	8.45E-18
Proteoglycans in cancer	16	2.77E-11
MicroRNAs in cancer	14	1.99E-10

Table 5. Molecular Docking Analysis.

Sr. No.	Compound	Target Protein	PDB ID	Binding Energy (kcal/mol)
1	Metformin	PIK3R1	1UNQ	-4.4
2	Catechin	PIK3R1	1UNQ	-6.1
3	Apigenin	PIK3R1	1UNQ	-5.7
4	Metformin	AKT1	1PBW	-4.3
5	Catechin	AKT1	1PBW	-6.4
6	Apigenin	AKT1	1PBW	-6.3

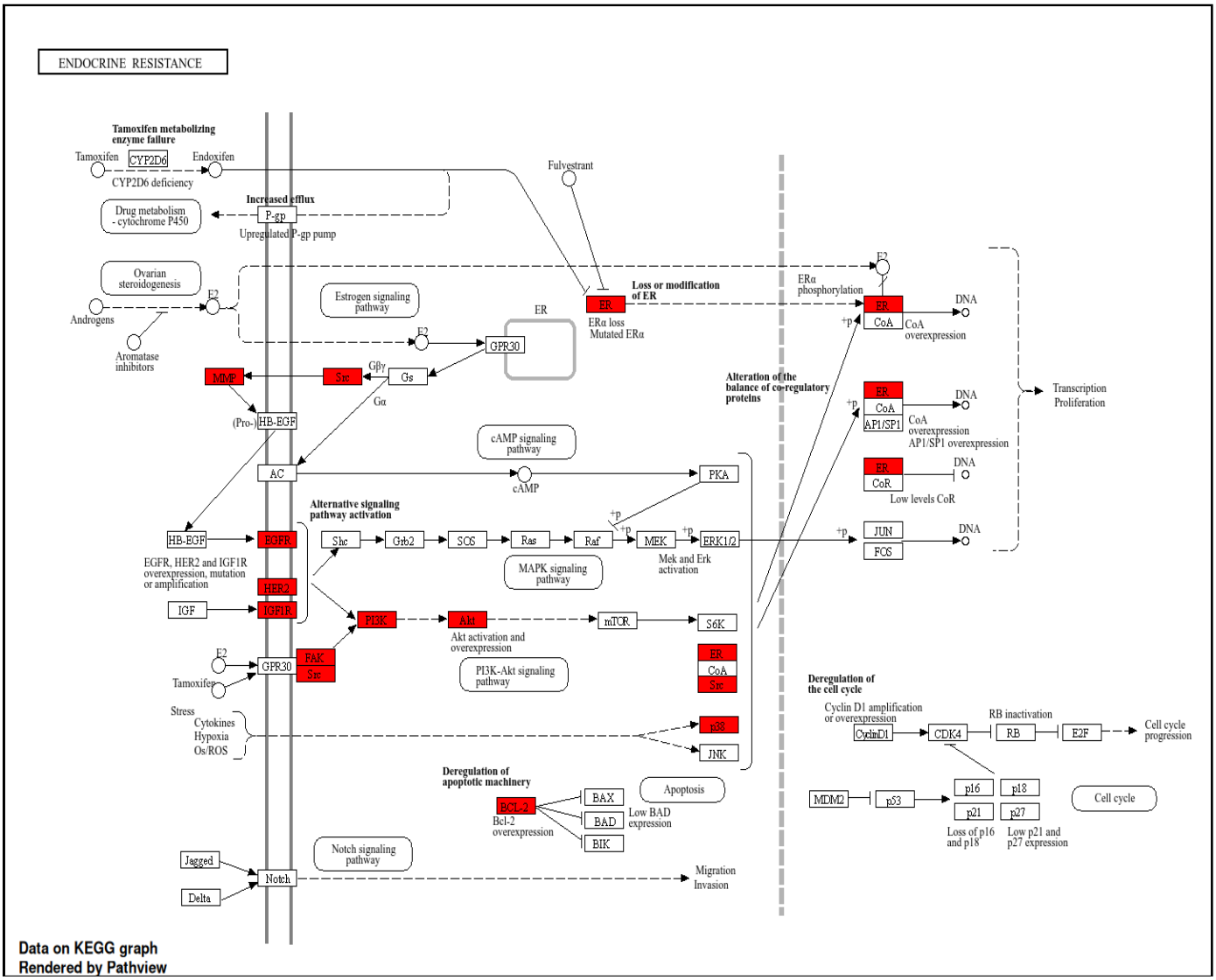
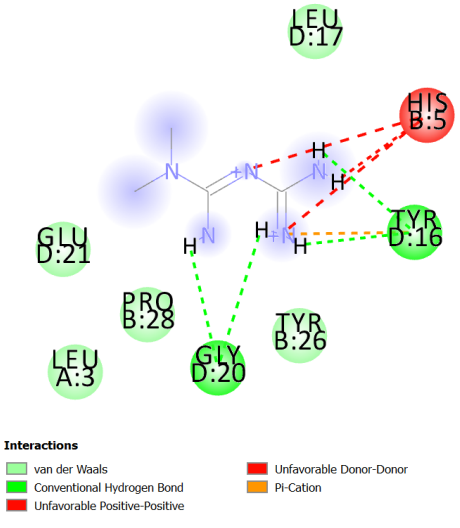
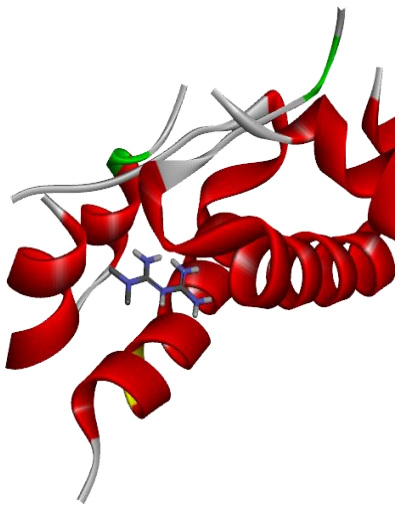


Figure 5A. Endocrine Resistance Pathway.

Compound/Targets	2D	3D
Metformin-(1PBW)		

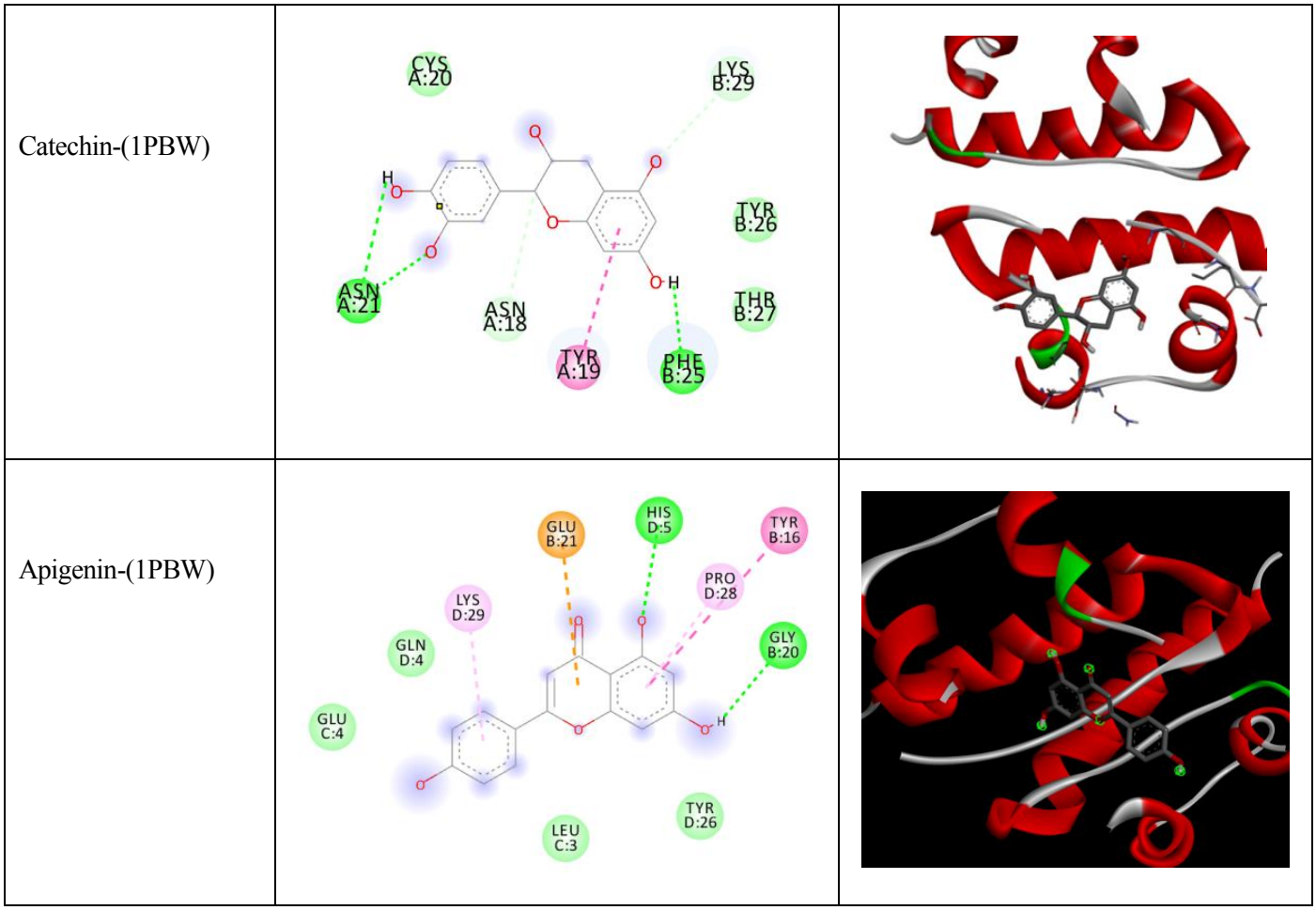


Figure 6. Illustrates 2D and 3D docking poses of Metformin, Catechin and Apigenin with protein AKT1 (1PBW).

4. Conclusion

Through multitarget and multipathway regulation, the current study showed that apigenin and catechin had remarkable therapeutic potential against Type 2 Diabetes Mellitus. Important hub genes and signaling pathways linked to insulin resistance, glucose metabolism, oxidative stress, and inflammation were found by network pharmacology analysis. When compared to metformin, molecular docking further demonstrated the great binding affinity of apigenin and catechin toward important target proteins PIK3R1 and AKT1. All things considered, the results point to these phytochemicals as possible multitarget antidiabetic drugs and offer a solid basis for further experimental and clinical research.

Author Contribution

Shaikh Faizan contributed to data collection, network pharmacology analysis, and manuscript drafting. Shaikh Asif Ayyub performed molecular docking studies and interpretation of the results. Dr. Shaikh Mehmood Dawood conceptualized and supervised the study, reviewed the manuscript and approved the final version for publication.

Funding Statement

The authors declare that no financial support or funding was received for this study.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

Ethics Approval and Consent to Participate

This study was entirely based on computational and *in silico* methodologies including network pharmacology and molecular docking approaches. Therefore, ethical approval and informed consent were not required as no human participants or experimental animals were involved in the study.

Consent for Publication

All authors have read and approved the final version of the manuscript for publication.

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Declaration of Generative AI

During the preparation of this manuscript, generative artificial intelligence (AI)-assisted tools were utilized only for language refinement, grammatical correction, and improvement of scientific readability.

References

1. DeFronzo RA, Ferrannini E, Groop L, Henry RR, Herman WH, Holst JJ, Hu FB, Kahn CR, Raz I, Shulman GI, Simonson DC. Type 2 diabetes mellitus. Nature reviews Disease primers. 2015 Jul 23;1(1):15019.
2. Care D. 2. Diagnosis and classification of diabetes: Standards of care in diabetes—2024. Diabetes Care. 2024 Jan;47(Suppl 1):S20-s42.
3. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nature reviews endocrinology. 2018 Feb;14(2):88-98.
4. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, Stein C, Basit A, Chan JC, Mbanya JC, Pavkov ME. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes research and clinical practice. 2022 Jan 1;183:109119.
5. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, Adhikari P, Rao PV, Saboo B, Kumar A, Bhansali A. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR–INDIAB population-based cross-sectional study. The lancet Diabetes & endocrinology. 2017 Aug 1;5(8):585-96.
6. Magliano DJ, Boyko EJ; IDF Diabetes Atlas 10th edition scientific committee . IDF DIABETES ATLAS [Internet]. 10th edition. Brussels: International Diabetes Federation; 2021. Available from: https://www.ncbi.nlm.nih.gov/books/NBK581934/
7. Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P. Management of hyperglycaemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 2022 Dec;65(12):1925-66.
8. Xiao JB, Hogger P. Dietary polyphenols and type 2 diabetes: current insights and future perspectives. Current medicinal chemistry. 2015 Jan 1;22(1):23-38.
9. Subhan S, Zeeshan M, Rahman AU, Yaseen M. Fundamentals of polyphenols: nomenclature, classification and properties. Science and Engineering of Polyphenols: Fundamentals and Industrial Scale Applications. 2024 Apr 2:1-36.
10. Cory H, Passarelli S, Szeto J, Tamez M, Mattei J. The role of polyphenols in human health and food systems: A mini-review. Frontiers in nutrition. 2018 Sep 21;5:370438.
11. Bernatoniene J, Kopustinskiene DM. The role of catechins in cellular responses to oxidative stress. Molecules. 2018 Apr 20;23(4):965.
12. Wang MC. Natural plant resource flavonoids as potential therapeutic drugs for pulmonary fibrosis. Heliyon. 2023 Aug 1;9(8).
13. Shevchenko A, Akhelova A, Nokerbek S, Kaldybayeva A, Sagyndykova L, Raganina K, Dossymbekova R, Meldebekova A, Amirkhanova A, Ikhsanov Y, Sauranbayeva G. Phytochemistry, Pharmacological Potential, and Ethnomedicinal Relevance of Achillea nobilis and Its Subspecies: A Comprehensive Review. Molecules. 2025 Jun 4;30(11):2460.
14. Sen P, Sahu PK, Haldar R, Sahu K, Prasad P, Roy A. Apigenin naturally occurring flavonoids: Occurrence and bioactivity. Pharmaceutical and Biosciences Journal. 2016 Dec 22:56-68.
15. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of type 2 diabetes mellitus. International journal of molecular sciences. 2020 Aug 30;21(17):6275.
16. Riyaphan J, Pham DC, Leong MK, Weng CF. In silico approaches to identify polyphenol compounds as α-glucosidase and α-amylase inhibitors against type-II diabetes. Biomolecules. 2021 Dec 14;11(12):1877.
17. Wen X, Lv C, Zhou R, Wang Y, Zhou X, Qin S. The molecular mechanism underlying the therapeutic effect of dihydromyricetin on type 2 diabetes mellitus based on network pharmacology, molecular docking, and transcriptomics. Foods. 2024 Jan 22;13(2):344.
18. Wu W, Zheng Z, Wang Z, Gao C, Liang Y, Zeng W, Sun W. Profiling of Potential Anti-Diabetic Active Compounds in White Tea: An Integrated Study of Polyphenol-Targeted Metabolomics, Network Pharmacology, and Computer Simulation. Foods. 2024 Oct 22;13(21):3354.
19. El-Banna AA. An integrated approach of network pharmacology and molecular docking analyses for identification of Lepidium sativum L. antidiabetic molecular targets. Records of pharmaceutical and biomedical sciences. 2023 Jan 1;7(2):111-27.
20. Basaldúa-Maciel V, Guzmán-Flores JM, Reyes-Chaparro A, Martínez-Esquivias F. Therapeutic potential of quercetin in type 2 diabetes based on a network pharmacology study. Current Topics in Medicinal Chemistry. 2025 Aug;25(20):2461-73.
21. Vikhar Danish Ahmad A, Khan SW, Ali SA, Yasar Q. Network pharmacology combined with molecular docking and experimental verification to elucidate the effect of flavan-3-ols and aromatic resin on anxiety. Scientific Reports. 2024 Apr 29;14(1):9799.