Sonali Mahadev Patil, 2026, 14:2
ISSN (Online): 2348-4098
ISSN (Print): 2395-4752

International Journal of Science, Engineering and Technology
An Open Access Journal

In Silicon Study Of Plant Based Phenolic Compounds

Sonali Mahadev Patil[1], Dhanashri Shivanand Chavan[2], Sanika vasant salgare[3], Laxmi Dhundappa Narute[4]

[1,2,3,4]Student, Dr. shivajirao Kadam College of pharmacy Kasbe Digraj

Abstract- Phenolic compounds (PCs) are plant-derived secondary metabolites recognized for their diverse biological activities, including antioxidant, anti-inflammatory, and anti-diabetic properties. While conventional oral hypoglycemic agents like metformin and glimepiride are widely used to manage blood glucose, they are often associated with adverse effects such as gastrointestinal distress, allergic reactions, and liver inflammation. This study utilized molecular docking to evaluate the anti-diabetic potential of 29 plant-based phenolic compounds compared to standard marketed drugs. The results demonstrate that all 29 natural compounds exhibited superior docking scores and glide energy relative to the reference standards, suggesting their potential as safer and more effective alternatives for blood glucose regulation.

Keywords: Phenolic compounds, Molecular docking study,Ligand Preparation,Silico study of Phenolic compounds.

I. INTRODUCTION

Phenolic compounds

Phenolic compounds (PCs) are widespread secondary metabolites with potent biological activity. Their sources are mainly plants from cultivated and natural states, providing valuable protective and health-promoting extracts. The wide biological activity of PCs (antioxidant, anti-inflammatory, antimicrobial, anti-atherosclerotic, anti-diabetic, anti-allergic, prebiotic, anti-mutagenic) means that new sources of PCs are constantly being sought, as exemplified by extracting these compounds from tissue culture or agricultural by-products.

Plant phenols show marked qualitative and quantitative variation not only at different genetic levels (between and within species and clones) but also between different physiological and developmental stages.

Plant phenolics are considered to have a key role as defense compounds when environmental stresses, such as high light, low temperatures, pathogen infection, herbivores, and nutrient deficiency, can lead to an increased production of free radicals and other oxidative species in plants.

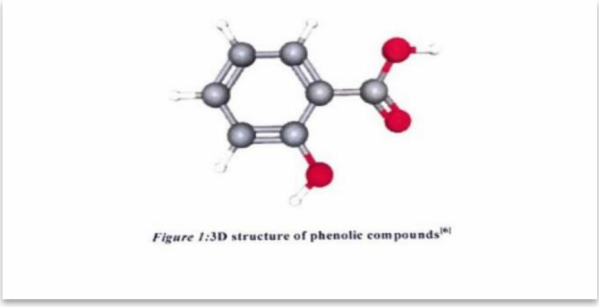


*Figure 1:*3D structure of phenolic compounds[8]

Classification

Phenolic compounds are classified into several groups according to their diverse chemical structures. Flavonoids, lignans, stilbenes, and phenolic acids are the four main families of phenolic compounds.

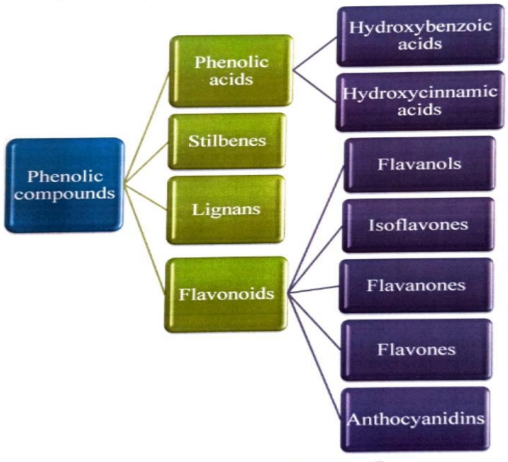


Fig.3: Classification of phenolic compounds [8]

Metabolism

Absorption and bioavailability of phenolic compounds mostly depend on their metabolic reactions conducted in small intestine. Biotransformation reactions involved during phase I of metabolism are oxidation, reduction, and hydrolysis. The biological activity of phenolic compounds can be increased, decreased or counteracted through these reactions. The first stage of the reaction aims to change the structure of exogenous bio molecules. This amendment is attained through introducing amino, carboxyl and

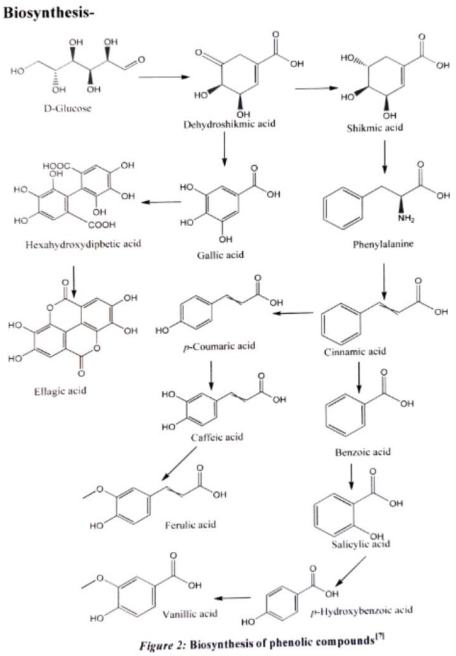


Figure 2: **Biosynthesis of phenolic compounds**[7]

hydroxyl groups, etc. The major purpose of this reaction is to enhance the polarity of heterogeneous phenolic compounds for facilitating their excretion.

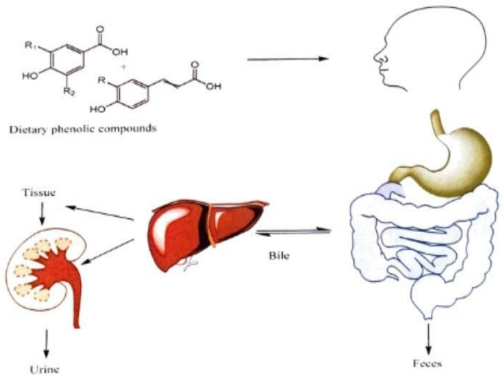


Fig.4: **Metabolism of phenolic compounds** [11]

The wide biological activity of PCs (antioxidant, anti-inflammatory, antimicrobial, anti-atherosclerotic, anti-diabetic, anti-allergic, pre-biotic, anti-mutagenic) means that new sources of PCs are constantly being sought, as exemplified by extracting these compounds from tissue culture or agricultural by-products, (12)

Fig.5 : **Pharmacological Properties**[13]

Oxidative stress and Diabetes mellitus (DM) have complex interactions whereby both intensify each other. A healthy and functional mass of pancreatic beta cells is necessary for normal glucose homeostasis, and DM is accompanied with varying levels of beta-cell dysfunction.14

Diabetes

The most proliferated disease recognized across the world is diabetes. [16]Diabetes mellitus (DM) is a chronic metabolic illness characterized by an increase in blood glucose, also known as hyper-glycemia, and is currently an epidemic affecting millions of individuals worldwide. According to a 2021 report from the International Diabetes Federation, 101 million people in India have diabetes, and that number is expected to climb to 693 million by 2045,

Types of diabetes

Type 1 Diabetes Mellitus

Type 1 Diabetes is characterized by insulin output deficiency, which involves routine insulin administration. The cause of type 1 diabetes is unclear, even despite current knowledge, it is not preventable.

Type 2 Diabetes Mellitus

It results from insulin being used ineffectively by the body. T2DMaffects most people with diabetes globally and is largely the result of excess body the most proliferated disease recognized across the world is diabetes

Symptoms of diabetes:-12

- Excessive urination and sweating
- Feeling vey thirsty and hungry
- Blurry vision
- Fatigue
- Weight loss
- Tiredness

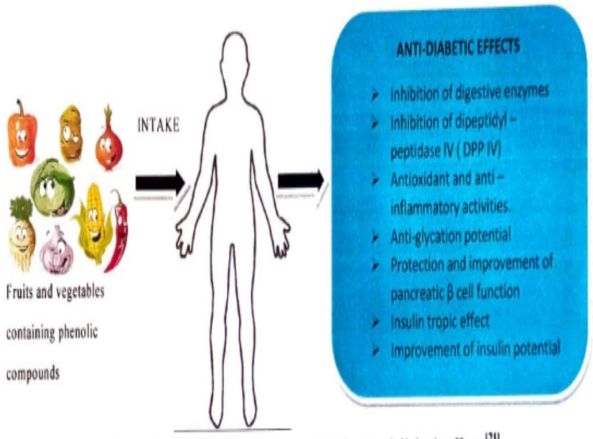


Fig.6 : **Mechanism of phenolic compounds show anti-diabetic effects[21]**

Anti-diabetic drugs are used to lower the concentration of glucose in the blood of people with diabetes mellitus. By keeping the blood sugar at or close to the normal range, these medicines reduce some of the risks associated with diabetes, (22)

Anti-diabetic drugs exert their useful effects through23)

- increasing insulin levels in the body
- increasing the body's sensitivity (or decreasing its resistance) to insulin
- decreasing glucose absorption in the intestine.

The table given below shows the demographic details of the patients.

Table 1: Demographic details of the patients[24]

VARIABLES	PERCENTAGE
GENDER	
MALE	53.1%
FEMALE	46.9%
AGE	
23 -30	1.8 %
31 -40	10.6%
41 -50	22.1%
51 -60	39.5%
61 – 70	16.4%
71- 80	10.1%
FAMILYHISTORY	
PRESENT	71.9%
ABSENT	28.1%

Molecular docking study is a computational method that described the best-fit orientation between ligand and protein. Docking generally involves the association of molecules mainly through hydrogen bonds, - stacking, hydrophobic interactions, side chain hydrogen bonds, polar interactions etc. 1251

- First step of docking is to take PDB (protein database) file format of required ligand and target.
- Second step involves the preparation of PDBQT files, grid and docking parameter files by using Schrodinger (Maestro 12.8).
- Final step is to perform docking and observed the results. 1261

Used to model the interaction between a small molecule and a protein at the atomic level, which allow us to characterize the behaviour of small molecules in the binding site of target proteins as well as to elucidate fundamental biochemical processes.

The docking process involves two basic steps

- Prediction of the ligand conformation as well as its position and orientation within these sites (usually referred to as pose).
- Assessment of the binding affinity, (27)

II.LITERATURE SURVEY

1. Nurzyńska-Wierdak R. (2023) reported that phenolic compounds (PCs) are widespread secondary metabolites with potent biological activity. The wide biological activity of PCs (antioxidant, anti-inflammatory, anti-microbial, anti-atherosclerotic, anti-diabetic, anti-allergic, pre biotic, anti-mutagenic) means that new sources of PCs are constantly being sought, as exemplified by extracting these compounds from tissue culture or agricultural by-products. 128)

2. Rana A, Samtiya M, Dhewa T et al, (2022) reported that plants produce poly-phenols, which are considered highly essential functional foods in our diet. They are classified into several groups according to their diverse chemical structures. Flavanoids, lignans, stilbenes, and phenolic acids are the four main families of polyphenols. Polyphenols in the diet also help to improve lipid profiles, blood pressure, insulin resistance, and systemic inflammation. For instance, cocoa flavan-3-ols have been associated with a decreased risk of myocardial infarction, stroke, and diabetes, 12

3. Deka, Himangshu Choudhury et al., (2022) reported that plant-derived phenolic compounds produce anti-diabetic effects through various mechanisms, such as AMPK pathway activation, a glucosidase/a amylase inhibition, glucose uptake and insulin sensitivity improvement. Furthermore, these compounds can be utilized as alternative medicines in the treatment and management of other associated diseases, D01

4. Nazurah Hamizah Salleh et al., (2021) reported that turmeric (Curcuma longa), garlic (Allium sativum L.), bitter melon (Momordica charantia), and Rosella flower (Hibiscus sabdariffa L.). Of these, only the bitter melon study did not show any significant change in the blood glucose of participants after intervention. 1311

5. Samec D, Karalija E et al., (2021) reported that Polyphenols, which are the largest group of plant-specialized metabolites, are generally recognized as molecules involved in stress protection in plants. This diverse group of metabolites contains various structures, from simple forms consisting of one aromatic ring to more complex ones consisting of large number of polymerized molecules.

6. Vinay Bharadwaj Tatipamula, Biljana Kukavica (2021) reported that phenolic compounds, widespread in plants, are a necessary part of the human regimen due to their antioxidant and pro-oxidative properties. Naturally, phenolics compounds structurally range from a very simple phenolic molecule moiety to a polymer. Phenolic compounds have gained much attention because of their protective effects against degenerative disorders such as inflammation, diabetes and cancer.

7. Cao H, Ou J, Chen L, Zhang Y et al, (2019) reported that significant evidence from epidemiological investigations showed that dietary poly phenols might manage and prevent type 2 diabetes (T2D). Poly phenols from coffee, guava tea. olive oil, chocolate, red wine, grape seed, and cocoa have been reported to show anti-diabetic effects in T2D patients through increasing glucose metabolism. improving vascular function as well as reducing insulin resistance. (4)

8. Selvankumar Thangaswamyet al., (2017) reported that Intermolecular interactions between target proteins and different anti-diabetic compounds were observed. Five phyto compounds were selected from Plumbago zeylanica, Neolitsea cassia and Wrightia tinctoria and taken for molecular docking against human pancreatic alpha-amylase and human dipeptidyl peptidase.6 urs-12-en-24-oic acid Plumbago zeylanica is the best compound for both the human pancreatic alpha-amylase and human dipeptidyl peptidase IV inhibition, (5)

III. RESEARCH AND METHODOLOGY

Molecular docking study

ChemDraw 19.0 was used to sketch the structures of phenolic acid derivatives for virtual derivative screening. Schrodinger suite v 12.8 was used for molecular docking, (36.37)

Protein preparation

Transcriptional regulation (PDB Id: 5NN6) was picked from the Protein Data Bank for the molecular docking research of a selected data set of phenolic compounds. The average structure file retrieved from the PDB isn't ready for instant use in molecular modelling calculations.

A typical PDB structure file contains heavy atoms, a co-crystallized ligand, water molecules, metal ions, and cofactors, among other things. Protein was created using the protein preparation wizard, which preprocessed, optimised, and reduced protein. The end result is a refined, hydogenated ligand and ligand-receptor complex structure that can be used with other Schrodinger modules. (36,37]

Ligand Preparation

To achieve the best docking results, ligand preparation is done using the maestro v 12.8 LigPrep module. The docked structures must be good approximations of the actual ligand structures as they would look in a complex of protein-ligand. This means that the structures must meet the following Glide docking software requirements.

They must be three-dimensional. Glid only changes the internal torsional coordinates of the ligand during the process, therefore the remaining geometric parameters must be tuned beforehand. They must each be made up of a single molecule with no covalent receptor linkages and no other fragments like counter ions or solvent molecules. They must be completely filled with hydrogen (valences). They must have a proper protonation condition for physiological pH values (about 7)

Grid generation

The receptor grid generating module of maestro version 12.8 is used to create the grid. A grid is created around the binding site already occupied by the co-crystallized ligand, allowing additional molecules to be attached to the same binding site while the co-crystallized ligand is excluded, (36,37)

Molecular docking

Docking was done with the maestro v 12.8 ligand docking module after producing the glide grid zip file and prepping the ligands. The XP module performs more precise molecular docking of chosen phenolic compounds. At each level, the size of the data collection shrinks as the precision of the data grows. The XP parameters docking score, glide energy value were estimated in maestro v 12.8.36.37)

Selection parameters of PDB ID

Table 2: Selection parameters of PDB ID

Pdb id	5NN6
Classification	Hydrolase
Organism	Homo-sapiens
Mutation	No
Method	X – diffraction
Resolution	2.00 A

IV. RESULT AND DISCUSSION

There are many drugs available in the market playing a major role in reduction of blood glucose level in the body.

Some of the available marketed drugs are glimepiride, glizipride, metformin, biguanides, chlorpropamide, tolbutamide, repaglinide, nateglinide etc.

But these drugs show side effects in the body such as-

- Nausea
- Gastrointestinal disturbance including diarrhoea and constipation
- Abdominal pain
- Allergic skin reactions
- Liver inflammation

Here we performed docking of 29 plant based phenolic compounds and compare with standard Metformin, Glizipride, Biguanides, Glimepiride tablets out of which all the compounds show better 1docking results as compared to marketed compounds.The table shows phenolic compounds having higher docking score and glide energy as below:

Table 3: In-Silico study of Phenolic compounds(39.40)

COMPOUNDS	DOCKING SCORE	GLIDE ENERGY
Quercetin	-7.311	-42.046
L dopa	-7.019	-34.75
Rosmarinic acid	-6.868	-47.314
Protocatechuic acid	-6.817	-36.192
Gallic acid	-6.668	-40.301
Matairesinol	-6.598	-40.036
Pinoresinol	-6.478	-38.946
Caffeic acid	-6.246	-31.674
Chalcones	-6.075	-39.708
Flavanol	-6.03	-32.65
Coumaric acid	-5.569	-30.378
Cinnamic acid	-5.563	-30.372
Vanillic acid	-5.14	-23.412

COMPOUNDS	DOCKING SCORE	GLIDE ENERGY
Quercetin	-7.311	-42.046
L dopa	-7.019	-34.75
Rosmarinic acid	-6.868	-47.314
Protocatechuic acid	-6.817	-36.192
Gallic acid	-6.668	-40.301
Matairesinol	-6.598	-40.036
Pinoresinol	-6.478	-38.946
Caffeic acid	-6.246	-31.674
Chalcones	-6.075	-39.708
Flavanol	-6.03	-32.65
Coumaric acid	-5.569	-30.378
Cinnamic acid	-5.563	-30.372
Vanillic acid	-5.14	-23.412

Syringic acid	-4.996	-25.379
Sinapic acid	-4.971	-31.337
p- coumaric acid	-4.811	-25.067
Ferulic acid	-4.805	-27.837
Flavononols	-4.681	-27.521
Resveratrol	-4.673	-29.459
Isoflavones	-4.582	-26.929
p- hydroxybenzoic acid	-4.497	-22.907
Flavonols	-4.451	-26.349
Phenol	-4.3	-21.157
Gliclazide	-3.929	-37.355
Flavones	-3.854	-26.251
Flavonones	-3.854	-26.251
Ellagic acid	-3.706	-25.148
***Metformin**	-2.781	-28.086
***Glimepiride**	-1.428	-46.952

***Standarddrugs**

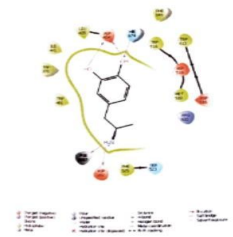


Fig.7 :2D Structure of L-Dopa

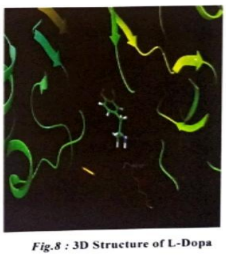


Fig.8 : 3D Structure of L-Dopa

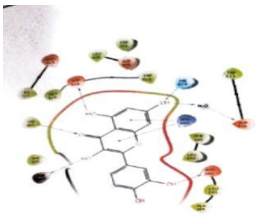


Fig.9 :2D Structure of Quercetin

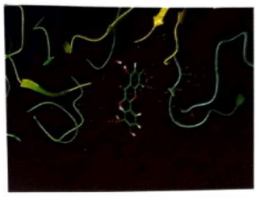


Fig.10 : 3D Structure of Quercetin

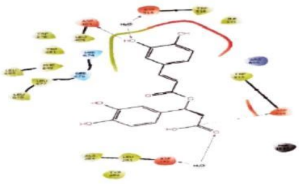


Fig.11:2D Structure of Rosmarinic acid

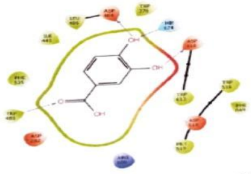


Fig.12:2D Structure of Procatechuic acid

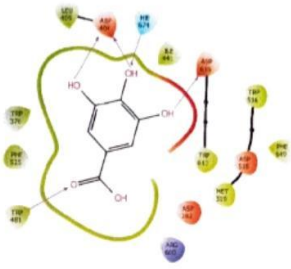


Fig.13:2D Structure of Gallic acid

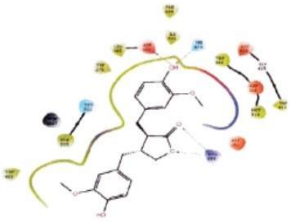


Fig.14:2D Structure of Matairesinol

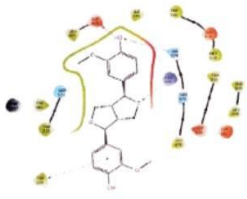
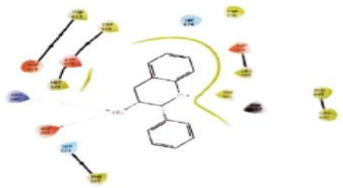


Fig. 15: 2D Sturcture of Pinoresinol

Fig.16: 2D Structure of Caffeic acid

Fig. 17: 2D Structure of Chalcone



V. CONCLUSION

According to a 2021 report from the International Diabetes Federation, 101 million people in India have diabetes, 136 million with pre diabetes and 315 had high blood pressure and that number is expected to climb to 693 million by 2045. We have studied the 29-plant based phenolic compounds. First, we draw the structure with the help of CHEMDRAW19.1then minimise the ligand and save the compound in PDB format to perform the docking. The molecular docking was performed using MAESTRO v. 12.8 and results came out and we studied them.

All the phenolic compounds showed better results as compared to the marketed formulations. Among them top three compounds showed the best docking score: Quercetin[-7.311] L-Dopa[-7.019] Rosmarinic acid[-6.868] while the market formulation having these results Metformin [-2.781] >Glimepiride(-1.428].Higher the negative value of docking score of a compound showsthat the compound having the better binding affinity.

As we know that marketed synthetic drugs like glimepiride. glizipride, metformin, biguanides, chlorpropamide, tolbutamide, repaglinide, nateglinide which shows many side effects including nausea, gastrointestinal disorders, liver damage but the natural compounds show less or null side effects. Hence, we can conclude that these phenolic compounds may show the better efficiency and results for the treatment of diabetes mellitus worldwide. Therefore, further research can be done on the plant based phenolic compounds and can be an alternative method to control diabetes.

REFERENCES

1. Farhat N., Hussain S., Syed S.K., Amjad M., Javed M., Iqbal M., Hussain M., Haroon S.M., Raza H., Butt S.Z., et al. Dietary phenolic compounds in plants: Their antioxidant and pharmacological potential. Post. Biol. Kom. 2020:47:307-320.
2. Šamec D., Karalija E., Šola I., Vujčić Bok V., Salopek-Sondi B. The Role of Polyphenols in Abiotic Stress Response: The Influence of Molecular Structure. Plants. 2021:10:118. doi: 10.3390/plants10010118.
3. Eseberri 1., Trepiana J., Léniz A., Gómez-García 1., Carr-Ugarte H., González M., Portillo M.P. Variability in the Beneficial Effects of Phenolic Compounds: A Review. Nutrients. 2022:14:1925. doi: 10.3390/nu14091925.
4. O'Neil, M.J. (ed.). The Merck Index An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 20016., p. 1438
5. 5. Zhang Y., Cai P., Cheng G., Zhang Y. A Brief Review of Phenolic Compounds Identified from Plants: Their Extraction, Analysis, and Biological Activity. Nat. Prod. Commun. 2022;17:1-14. doi: 10.1177/1934578X211069721.
6. National Center for Biotechnology Information (2023). PubChem Compound Summary for CID 338, phenolic Acid. Retrieved July 14, 2023.
7. Marchiosi, R., dos Santos, W.D., Constantin, R.P. et al. Biosynthesis and metabolic actions of simple phenolic acids in plants. Phytochem Rev

19, 865-906 (2020). https:/ /doi.org/10.1007/s11101-020-09689-2

8. Gonçalves A.C., Nunes A.R., Falcão A., Alves G., Silva L.R. Dietary effects of anthocyanins in human health: A comprehensive review. Pharmaceuticals. 2021:14:690. doi: 10.3390/ph14070690.
9. Di Lorenzo C., Colombo F., Biella S., Stockley C., Restani P. Polyphenols and Human Health: The Role of Bioavailability. Nutrients. 2021;13:273. doi: 10.3390/nu13010273.
10. Santos S C, Fortes G A C, Camargo LTFM, Camargo A J, Ferri P H: Antioxidant effects of polyphenolic compounds and structure-activity relationship predicted bymultivariate regression tree. LWT Food Science and Technology. 2021;137:110366-110381.
11. Durrazo A, Caiazzo E, Lucarini M, Cicala C, Izzo A: Polyphenols: a concise overview on the chemistry, occurrence, and human health. Phytother Res. 2019:33:2221-2243.
12. Tsimogiannis D, Oreopoulou V. Classification of Phenolic Compounds in Plants in Polyphenols in Plants. 2nd ed; 2019; p 263-284.
13. Santos-Sánchez NF, Salas-Coronado R, Hernández-Carlos B. Villanueva-Cañongo C. Shikimic acid pathway in biosynthesis of phenolic compounds. Plant physiological aspects of phenolic compounds. 2019 Jan 31:1:1-5.
14. Treutter D. Biosynthesis of phenolic compounds and its regulation in apple. Plant Growth Regulation, 2019 May:34:71-89.
15. De la Rosa L.A. Moreno-Escamilla JO, Rodrigo-Garcia J, Alvarez-Parrilla E. Phenolic compounds. InPostharvest physiology and biochemistry of fruits and vegetables 2019 Jan 1 (pp. 253-271). Woodhead publishing.
16. He H. Wang H. Fang C, Wu H, Guo X, Liu C, Lin Z, Lin W. Barnyard grass stress up regulates the biosynthesis of phenolic compounds in allelopathic rice. Journal of Plant Physiology. 2021 Nov 15:169(17):1747-53.
17. Bai L, Li X, He L., Zheng Y, Lu H. Li J, Zhong L, Tong R, Jiang Z, Shi J. Li J. Antidiabetic Potential of Flavonoids from Traditional Chinese Medicine: A Review. Am J Chin Med. 2019;47(5):933-957. doi: 10.1142/50192415X19500496. Epub 2019 Jun 27. PMID: 31248265.
18. WHO Expert Committee on Diabetes Mellitus. Second Report. Geneva: WHO. 2020. Technical Report Series 646.
19. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2020;20:0183-97.
20. Lin X. Xu Y, Pan X, Xu J, Ding Y, Sun X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Sci Rep. 2020;10(1):14790. doi: 10.1038/s41598-020-71908-9.
21. Salehi B, Ata A, Sharopov F, Ramirez-Alarcón K, Ruiz-Ortega A, et al. V Anil Kumar N, author. Antidiabetic potential of medicinal plants and their active components. Biomolecules. 2019;9(10):551. doi: 10.3390/biom9100551.
22. Santos-Sánchez NF, Salas-Coronado R, Hernández-Carlos B, Villanueva-Cañongo C. Shikimic acid pathway in biosynthesis of phenolic compounds. In: Soto-Hernández M. Garcia-Mateos R. Palma-Tenango M, editors. Plant physiological aspects of phenolic compounds. IntechOpen; London: 2019. pp. 1-5.
23. Oršolić N. Sirovina D, Odeh D, Gajski G, Balta V, Šver L., et al. Efficacy of caffeic acid on diabetes and its complications in the mouse. Molecules. 2021;26(11):3262, doi: 10.3390/molecules26113262.
24. Kahkeshani N, Farzaei F, Fotouhi M, Alavi SS, Bahramsoltani R. Naseri R, et al. Pharmacological effects of gallic acid in health and diseases: a mechanistic review. Iran J Basic Med Sci. 2019;22(3):225-37.
25. 25. Madhavi Sastry G, Adzhigirey M. Day T, Annabhimoju R, Sherman W. Protein and ligand preparation: parameters, protocols, and influence on virtual screening enrichments. Journal of computer-aided molecular design. 2013 Mar;27(3):221-34.
26. Sethi, Aaftaab et al. "Molecular Docking in Modern Drug Discovery: Principles and Recent Applications" In Drug Discovery and

Development: New Advances, edited by Vishwanath Gaitonde, Partha Karmakar, Ashit Trivedi. London: IntechOpen, 2019. 10.5772/intechopen.85991.

27. Sharma V. Sharma PC, Kumar V. In silico molecular docking analysis of natural phenolic compounds as anti-diabetic agents. Adv Chem. 2016 Nov:2016:1-9.
28. De Paulo Farias D. de Araújo FF, Neri-Numa IA, Pastore GM. Antidiabetic potential of dietary polyphenols: A mechanistic review. Food Res Int. 2021 Jul:145:110383. doi: 10.1016/j.foodres.2021.110383. Epub 2023 May 5. PMID: 34112386.
29. Rana A. Samtiya M, Dhewa T, Mishra V. Aluko RE. Health benefits of polyphenols: A concise review. J Food Biochem. 2022 Oct;46(10):e14264. doi: 10.1111/jfbc. 14264. Epub 2022 Jun 13. PMID: 35694805.
30. Oboh G. Ogunbadejo MD, Ogunsuyi OB, Oyeleye SI. Can gallic acid potentiate the antihyperglycemic effect of acarbose and metformin? Evidence from streptozotocin-induced diabetic rat model. Arch Physiol Biochem. 2022;128(3):619-27. doi: 10.1080/13813455.2020.1716014.
31. Nazurah Hamizah Salleh et al.,. The inhibitory mechanism of chlorogenic acid and its acylated Bderivatives on a-amylase and a-glucosidase. Food Chem. 2021;372:131334.
32. Draganescu D, Andritoiu C, Hritcu D, Dodi G, Popa MI. Flaxseed lignans and polyphenols enhanced activity in diabetic rats. Biology (Basel) 2021;10(1):43.
33. Tatipamula VB. Kukavica B. Phenolic compounds as antidiabetic, anti-inflammatory. and anticancer agents and improvement of their bioavailability by liposomes. Cell Biochem Funct. 2021 Dec;39(8):926-944. doi: 10.1002/cbf.3667. Epub 2021 Sep 9. PMID: 34498277.
34. Cao H, Ou J, Chen L, Zhang Y, Szkudelski T, Delmas D, Daglia M, Xiao J. Dietary polyphenols and type 2 diabetes: Human Study and Clinical Trial. Crit Rev Food Sci Nutr. 2019;59(20):3371-3379. doi: 10.1080/10408398.2018.1492900. Epub 2018 Nov 19. PMID: 29993262.
35. S. Bolen, L. Feldman, J. Vassy et al., "Systematic review: comparative effectiveness and safety of oral medications for type 2 diabetes mellitus," Annals of Internal Medicine, vol. 147, по. 6, pp. 386-399, 2017.
36. Al-Ishaq RK, Abotaleb M, Kubatka P. Kajo K. Büsselberg D. Flavonoids and their anti-diabetic effects: cellular mechanisms and effects to improve blood sugar levels. Biomolecules. 2019;9(9):430. doi: 10.3390/biom9090430.
37. Wang S, Li Y, Huang D, Chen S, Xía Y, Zhu S. The inhibitory mechanism of phenolic acid and its derivatives on a-amylase and a-glucosidase. Food Chem. 2022;372:131334.
38. Roig-Zamboni, V.Cobucci-Ponzano, B.,Iacono, R., Ferrara, M.C., Germany. S.. Parenti, G., Bourne, 01https: //www.rcsb.org/structure/5NN6 Y, Version. 1.1 2017-11-
39. Chen G, Seukep AJ, Guo M. Recent Advances in Molecular Docking for the Research and Discovery of phenolic compounds 2020 Oct 30;18(11):545. doi: 10.3390/md18110545.
40. Chowdhury Md.R., Chowdhury H.K., Hanif B.N., In silico evaluation of therapeutic potentials of phenolic acid against diabetic diseases, https //www.researchgate.net, published by research te.