Texila International Journal of Public Health
Special Issue-2024
DOI: 10.21522/TIJPH.2013.SE.24.03.Art009

Anti-diabetic Potential Mechanisms of Phytomedicines – A Review

A. Arockya Stafi[1], Sridevi Gopathy[1, *, †], S. Srividya[2], Selvaraj Jayaraman[3, *, †]
[1]*Department of Physiology, SRM Dental College, Bharathi Salai, Chennai, Tamil Nadu, India*
[2]*Department of Biochemistry, Sathyabama Dental College and Hospital, Chennai, Tamil Nadu, India*
[3]*Centre of Molecular Medicine and Diagnostics (COMManD), Department of Biochemistry, Saveetha Dental College & Hospital, Saveetha Institute of Medical & Technical Sciences, Saveetha University, Chennai, 600077, India*

**,†-Equally contributed to this work.*

Abstract

Diabetic mellitus is an endocrine disorder characterized by hyperglycemia, polyphagia, polyuria, and polydipsia. In this condition, the cells and tissues are unable to utilize glucose for energy due to inadequate insulin secretion. The complications of the disease include diabetic retinopathy, diabetic neuropathy, and diabetic nephropathy that affect the eyes, nerves, kidneys and stroke, renal failure, and heart attacks are other serious consequences of diabetes. The conventional modern medicines for treatment are oral hypoglycemic drugs, sulfonylureas and glinides, metformin and thiazolidinedione, dipeptidyl peptidase-4 (DPP4) inhibitors, and injections such as GLP-1 agonists. Due to the presence of a lot of side effects, the modern world is now turning to bioactive chemical components synthesized from plants. Today, drugs derived from herbs or plants are widely used because of the exploitation of specific compounds and their therapeutic actions. Various phytochemicals have notable and significant mechanisms for reducing the blood glucose level. These natural agents can have a protective and therapeutic effect on diabetes mellitus through cellular mechanisms such as the regeneration of pancreatic β cells, antioxidative stress, and intracellular signalling transduction pathways. The present study aims to review the mechanisms of various phytochemicals that play a role in antidiabetic activity. The possible mechanisms by which the antidiabetic herbs act are α-glucosidase inhibitors, PPAR activators, free radical scavengers, HMG Co suppressors, regenerators of beta cells, and cause an increase in insulin secretion and glycogen synthesis in glycemic control.

Keywords: *Cellular Mechanism, Diabetes Mellitus, Public Health, Health and Well-being, Glycemic Control, Phytomedicines, Signaling Pathways.*

Introduction

One of the biggest health issues facing people in the modern world is diabetes mellitus. Worldwide, hyperglycemia is a chronic condition that occurs when an insufficient amount of insulin is secreted from the pancreas or the insulin cannot be utilized by the body. Diabetic is distinguished due to the elevated glucose levels in the bloodstream. Diabetes is a metabolic disorder marked by an increased level of blood glucose which occurs by deficiencies in insulin secretion, the sensitivity of insulin or both [1]. The International Diabetes Federation reports stated that the "subcontinent is the epicenter of diabetes mellitus that had the second-greatest

Received: 12.06.2024 ***Accepted: 27.07.2024*** ***Published on: 30.08.2024***
****Corresponding Author: sridevig1@srmist.edu.in, selvarajj.sdc@saveetha.com***

number of diabetic patients in 2017 after China," with 73 million people living with the disease. Moreover, just 134 million more are expected to be added by 2045 [2]. In 2030, diabetes is predicted by the WHO to rank seventh among the main causes of mortality [3]. Persistent impairment, malfunction, and collapse of numerous organ systems (circulatory system, eyes, the heart, kidneys, bladder, and nervous system) are brought on by hyperglycemia, which can lead to early disability and death [4]. Heart, eye, nerve arteries and veins can be harmed by diabetes mellitus. The World Health Organization states that diabetes can increase the threat of cardiovascular problems, kidney failure, and stroke. Diabetic neuropathy, diabetic retinopathy, and diabetic nephropathy are among the consequences that diabetes mellitus can lead to. These conditions harm the kidneys, nerves, and eyes. [5].

Modern Medicine for Diabetic

There are a greater number of hypoglycemic medications accessible nowadays. Oral antidiabetic drugs differ in their modes of action, effectiveness in decreasing hemoglobin A1c, safety, and tolerance. Oral antidiabetic medicines comprise sulfonylureas, glinides, metformin, thiazolidinedione, α-glucosidase inhibitors, and DPP-4 inhibitors. Sulfonylureas (SUs) and glinides boost insulin secretion. Metformin and thiazolidinedione improve insulin sensitivity. α- glucosidase inhibitors reduce intestinal glucose absorption [6]. In 1996, alpha-glucosidase inhibitors such as miglitol and acarbose were introduced. It is a unique pharmacologic class that does not target a specific pathophysiological defect of type 2diabetes, and its mode of action is distinct. Enzyme α-glucosidase hydrolyzes complex carbohydrates and disaccharides; it was found on the bristles of the proximal small intestine epithelium [7].

Antidiabetic Effect of Phytoconstituents

Physiologically active substances originating from plants are known as plant-derived compounds. Organic substances known as phytochemicals are found naturally in microbes and plants. They are created by plant cells' secondary metabolic activities, which carry out a range of biological tasks. Among the various kinds of phytochemicals are compounds called flavonoids, phytoestrogens, phytosterols, carotenoids, alkaloid compounds, terpenoids, phenolic compounds, and glucosinolates [8]. Numerous mechanisms are employed by phytochemicals to reduce blood glucose levels by increasing the insulin sensitivity, activating beta cells in pancreas. Besides activating PPARγ and promoting glycogenesis and hepatic glycolysis, phytochemicals also possess anti-inflammatory and antioxidant qualities. Additionally, they block the action of enzymes including α-amylase, β-galactocidase, and α-glucosidase, as well as the absorption of glucose in the intestine can be used as substitute treatments for disorders related to glucose metabolism [9]. These discoveries have important ramifications for the creation of novel diabetes medications and therapeutic approaches.

Antidiabetic Plants

Gymnema sylvestre

Gymnema sylvestre belongs to the Asclepiadaceae family. The plant is indigenous to Australia, tropical Africa, and India's western and central regions. Other names for this woody climbing plant include "gurmar" or "the sugar destroyer" [10]. Gymnemic acids help delay the absorption of sugar in the bloodstream. They achieve this by enhancing insulin secretion and promoting islet cell regeneration. They enhance glucose metabolism by phosphorylase activity [11]. According to an in vitro study, the following mechanisms are used by an alcoholic G.

sylvestre extract to induce insulin release: The primary mode of action involves the permeability of the cell's plasma membranes, presumably due to the high concentration of saponin glycosides in the extract, leading to an uncontrolled release of insulin. The Ca2+-sensitive aspect of insulin release could be dependent on calcium entering β-cells without the need for a channel, possibly via holes in the plasma membrane [12].This illustrates the hypoglycemic activity that *Gymnema sylvestre* exhibits.

Nigella sativa

Nigella sativa comes from the family Ranunculaceae. It is originating to Western Asia and Eastern Europe. *Nigella sativa* referred to kalonji seeds [13]. In diabetic rodents, NSE (2 g equivalent plant/kg) enhances HDL cholesterol levels and glucose regulation. Insulin sensitivity in the peripheral tissues is enhanced, and circulation insulin levels are raised in Meriones Shawi. The latter effect is partially attributed to increased levels of Glut4 in skeletal muscle and activation of the Adenosine Monophosphate Pathway (AMPK) in the liver and skeletal muscle. The process entails increased insulin secretion and the proliferation of β cells. By stimulating the AMPK system in the muscle and enhancing GLUT4 translocation, which enhances glucose absorption, it exhibits sensitivity to insulin action [14]. These results suggest that the antidiabetic potential of *Nigella sativa* is very high.

Vernoria amygdalina

Vernoria amygdalina is a small shrub or tree. The Asteraceae family contains it. It is native to tropical Africa. It is known as Bitter leaf. The leaves of *Vernoria amygdalina* contain phytoconstituents that have been demonstrated to have antidiabetic effects, including tannins, saponins, flavonoids, phenolic substances, and alkaloids [15]. Luteolin inhibits ά-glucosidase activity in the intestinal tract, reducing the amount of glucose available for systemic uptake [16]. However, vernandol did not demonstrate a substantial benefit in reducing glucose levels.

Trigonella foenum graecum

Trigonella foenum graecum is part of the Fabaceae family. It has evolved in South-East Europe and Western Asia. Saponins, flavonoids, and alkaloids are the main components that provide antiglycemic activity. These drugs have been shown to produce hypoglycemic effects by enhancing insulin sensitivity, boosting pancreatic beta cell production of insulin, and reducing intestinal glucose absorption [17]. The process includes raising the calcium concentrations within beta cells. Fenugreek seeds contain compounds that activate beta cells, causing them to depolarize and open calcium channels that are in a depolarized state. This allows the entry of calcium ions and raises the intracellular calcium concentration. The insulin-containing vesicles, sometimes referred to as insulin granules, are released from beta cells when intracellular calcium levels are raised. Through the process of exocytosis, these granules fuse with the cell membrane to release insulin into the bloodstream [18]. This shows the antidiabetic effect of *Trigonella foenum graecum.*

Aloe vera

Aloe vera also has another name, Aloe barbadensis Miller. It belongs to the family Liliaceae. It evolved in the Arabian Peninsula. About 32 different types of anthraquinones and related glycosidic derivatives are found in *Aloe vera*. Barbaloin is the most common kind, followed by aloe-emodin and chrysophanol [19]. By effectively reducing the processes of gluconeogenesis lophenol and cycloartanol have an effect on lowering blood glucose levels. Reduced hepatic glucose synthesis is the outcome of this action, which is thought to be primarily mediated by AMPK

and PPAR receptors. It is also accompanied by a reduction of PEPCK and G6P expressions or suppression of ACC and FAS enzymatic activity [20]. This shows the antidiabetic effect of *Aloe vera*.

Azadirachta indica

Azadirachta indica is often known as a neem tree. It belonged to the Meliaceae family. It originated in Bangladesh and the Indian subcontinent. It has been demonstrated that azadirachtin inhibits alpha-glucosidase and alpha-amylase, two crucial targets for the management of diabetes [21]. Azadirachtin has the ability to lower postprandial hyperglycemia because it suppresses human pancreatic α-amylase, an enzyme that's involved in the digestion of starch [22]. According to these results, azadirachtin could serve as a viable therapy for diabetes as it lowers blood sugar levels and inhibits important enzymes that are involved in the metabolism of glucose. The (Table-1) shows the antidiabetic role of different bioactive compounds.

Table 1. Antidiabetic Role of Bioactive Compounds

S.No	Plant Name	Common Name	Bioactive Compounds	Action
1.	***Aloe vera***	Aloe	Barbaloin, Aloe-Emodin	Increases insulin production, Reducing the processes of gluconeogenesis [20]
2.	***Azadirachta indica***	Neem Tree	Azadirachtin	Inhibits alpha-glucosidase and alpha-amylase enzymes [21]
3.	***Cassia fistula***	Golden Shower Tree	Triterpenoid Compounds	Decreases plasma glucose concentration, Increases plasma insulin levels [23]
4.	***Cinnamomum tamala***	Indian Bay Leaf	Cinnamic Acid	Uptake of glucose in skeletal muscle [24]
5.	***Carica papaya***	Papaya	Transferulic Acid	Improves insulin sensitivity [25]
6.	***Acacia arabica***	Babool	Quercetin and Kaempferol	Synthesis of insulin [26]
7.	***Gymnema sylvestre***	Gurmar	Gymnemic Acids	Enhances insulin secretion, Promotes islet cell regeneration [11]
8.	***Vernonia amygdalina***	Bitter Leaf	Luteolin	Inhibits alpha-glucosidase activity [16]
9.	***Trigonella foenum graecum***	Fenugreek	4-Hydroxyisoleucine and Trigonelline	Enhancing insulin sensitivity, Boosting pancreatic beta cell production of insulin

				[17]
10.	***Ocimum sanctum***	Tulsi	Eugenol	Inhibits alpha-glucosidase enzyme [27]
11.	***Phyllanthus amarus***	Carry Me Seed	Triterpenes, Quercetin	Inhibits alpha-glucosidase enzyme, Increases insulin production [28]
12.	***Momordica charantia***	Bitter Gourd	Vicine, Charantin	Synthesizes glycogen in muscles, liver, and fat cells [29]
13.	***Murraya koenigii***	Curry Leaves	Quercetin	Increases insulin sensitivity [30]
14.	***Nigella sativa***	Black Cumin	Thymoquinone	Increases insulin secretion, Proliferation of beta cells [14]
15.	***Psidium guajava***	Guava	Triterpenes and Phenolic Compounds	Enhances glycogen synthase activity, Reduces glycogen phosphorylase activity [31]
16.	***Curcuma longa***	Turmeric	Curcumin	Improves insulin sensitivity, Inhibits diabetes-related enzymes [32]
17.	***Emblica officinalis***	Indian Gooseberry	Beta-Glucogallin	Inhibits pancreatic alpha-amylase, alpha-glucosidase, and DPP-4 enzyme [33]
18.	***Zingiber officinale***	Ginger	Gingerol, Meso–3,5–Diacetoxy–1,7–bis Heptane	Improves insulin resistance, Increases insulin levels, Normalizes pancreatic beta cell damage [34]
19.	***Syzygium cumini***	Jamun	Gallic Acid, Ellagic Acid, Catechin, Kaempferol	Inhibits alpha-glucosidase enzyme, Enhances insulin release by binding to the sulfonylurea receptor 1 [35]
20.	***Berberis aristata***	Indian Barberry	Berberine	Increases insulin sensitivity, Improves glucose metabolism

				[36]
21.	***Plectranthus amboinicus***	Indian Borage	Parvifloron D, F, and G	Inhibits alpha-glucosidase enzyme [37]
22.	***Withania somnifera***	Ashwagandha	Withanolides	Inhibits alpha-glucosidase enzyme[38]
23.	***Morus alba***	White Mulberry	Quercetin, Rutin	Improves insulin sensitivity [39]
24.	***Allium sativum***	Garlic	Allicin, Allin	Increases insulin level, Enhances the insulin sensitivity [40]

Conclusion

In conclusion, the assessment of phytomedicines with anti-diabetic properties showed great potential for plant-based treatments in the treatment of diabetes, highlighting the importance of natural ingredients and traditional medicine in contemporary pharmacotherapy. These phytomedicines work by stimulating glucose absorption, inhibiting the activity of enzymes that break down carbohydrates, and increasing insulin production. These substances, originating from plants, are more beneficial medicinally since they have fewer side effects and are less expensive than manufactured drugs. The study advocates for a multidisciplinary approach involving phytochemistry, pharmacology, and clinical research in order to mainstream these natural medicines for a more all-encompassing approach to diabetes treatment. Future studies should examine and assess these bioactive compounds, determine suitable dosages, and comprehend how they interact with common anti-diabetic medications in order to fully appreciate their potential as a component of an all-encompassing diabetes treatment plan.

Conflict of Interest

The authors hereby declare that there is no conflict of interest.

Acknowledgement

Authors would like to thank SRM Dental College, Ramapuram for providing facilities to carry out this work.

References

[1] American Diabetes Association, 2012, Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*, *36*(Supplement_1), S67–S74. https://doi.org/10.2337/dc13-S067

[2] International Diabetes Federation, 2021, IDF Diabetes Atlas, 10th edition. Brussels, Belgium: https://www.diabetesatlas.org/.

[3] Kakkar, R., 2016, Rising burden of Diabetes-Public Health Challenges & way out. *Nepal Journal of Epidemiology*, *6*(2), 557–559. https://doi.org/10.3126/nje.v6i2.15160

[4] Ali, M. K., Narayan, K. M., & Tandon, N. 2010, Diabetes & coronary heart disease: current perspectives. *The Indian journal of medical research*, 132(5), 584–597.

[5] Singh, N., Armstrong, D. G., & Lipsky, B. A., 2005, Preventing foot ulcers in patients with diabetes. *JAMA*, *293*(2), 217. https://doi.org/10.1001/jama.293.2.217

[6] Levetan, C., 2007, Oral antidiabetic agents in type 2 diabetes. *Current Medical Research and Opinion*, *23*(4), 945–952. https://doi.org/10.1185/030079907x178766

[7] Inzucchi, S. E., 2002, Oral antihyperglycemic therapy for type 2 diabetes. *JAMA*, *287*(3), 360. https://doi.org/10.1001/jama.287.3.360

[8] Mendoza, N., & Silva, E. M. E., 2018, Introduction to phytochemicals: Secondary metabolites from plants with active principles for pharmacological importance. In *Phytochemicals - Source of Antioxidants and Role in Disease Prevention*. InTech.http://dx.doi.org/10.5772/intechopen.78226

[9] Vinayagam, R., Xiao, J., & Xu, B., 2017, An insight into anti-diabetic properties of dietary phytochemicals. *Phytochemistry Reviews*, *16*(3), 535–553. https://doi.org/10.1007/s11101-017-9496-2

[10] Singh, V. K., Umar, S., Ansari, S. A., & Iqbal, M., 2008, Gymnema sylvestre for Diabetics. *Journal of Herbs, Spices & Medicinal Plants*, *14*(1–2), 88–106. https://doi.org/10.1080/10496470802341508

[11] Gulab S. Thakur., 2012, Gymnema sylvestre: An Alternative Therapeutic Agent for Management of Diabetes. *Journal of Applied Pharmaceutical Science*, 2(12), 001-006. https://doi.org/10.7324/japs.2012.21201

[12] Persaud, S., Al-Majed, H., Raman, A., & Jones, P., 1999, Gymnema sylvestre stimulates insulin release in vitro by increased membrane permeability. *Journal of Endocrinology*, *163*(2), 207-212. https://doi.org/10.1677/joe.0.1630207

[13] AlAttas, S. A., Zahran, F. M., & Turkistany, S. A., 2016, Nigella sativa and its active constituent thymoquinone in oral health. *Saudi Medical Journal*, *37*(3), 235–244. https://doi.org/10.15537/smj.2016.3.13006

[14] Varghese, R. M., Kumar, S. A., & Selvaraj, Y., 2023, Assessment of Soft Tissue, Airway Dimension and Hyoid Bone Position in Class II Patients Treated by PowerScope Class 2 Corrector. The Journal of Contemporary Dental Practice, 24(5), 308–313. https://doi.org/10.5005/jp-journals-10024-3485

[15] Atangwho, I. J., Ebong, P. E., Eyong, E. U., Williams, I. O., Eteng, M. U., & Egbung, G. E., 2009, Comparative chemical composition of leaves of some antidiabetic medicinal plants: Azadirachta indica, Vernonia amygdalina and Gongronema latifolium. *African Journal of Biotechnology*, 8(18), 4685-4689.

[16] Djeujo, F. M., Stablum, V., Pangrazzi, E., Ragazzi, E., & Froldi, G., 2023, Luteolin and Vernodalol as Bioactive Compounds of Leaf and Root Vernonia amygdalina Extracts: Effects on α-Glucosidase, Glycation, ROS, Cell Viability, and In Silico ADMET Parameters. *Pharmaceutics*, *15*(5), 1541. https://doi.org/10.3390/pharmaceutics15051541

[17] Baquer, N. Z., Kumar, P., Taha, A., Kale, R., Cowsik, S., & McLean, P., 2011, Metabolic and molecular action of Trigonella foenum-graecum (fenugreek) and trace metals in experimental diabetic tissues. *Journal of Biosciences*, *36*(2), 383–396. https://doi.org/10.1007/s12038-011-9042-0

[18] Sowmithra Devi, S., Sundari, S.,2023, Occlusal Contact Changes With Traumatic Occlusion After Orthodontic Treatment: A Prospective Study. Journal of Advanced Oral Research. 14(2):134-142. doi:10.1177/23202068231190202

[19] Kahramanoğlu, İ., Chen, C., Chen, J., & Wan, C., 2019, Chemical Constituents, Antimicrobial Activity, and Food Preservative Characteristics of Aloe vera Gel. *Agronomy*, *9*(12), 831. https://doi.org/10.3390/agronomy9120831

[20] Tanaka, M., Misawa, E., Ito, Y., Habara, N., Nomaguchi, K., Yamada, M., … Higuchi, R., 2006, Identification of five phytosterols from aloe vera gel as anti-diabetic compounds. *Biological and Pharmaceutical Bulletin*, *29*(7), 1418–1422. https://doi.org/10.1248/bpb.29.1418

[21] Kumar, D., Mitra, A., & M, M., 2011, Azadirachtolide: An anti-diabetic and hypolipidemic effects from Azadirachta indica leaves. *Pharmacognosy Communications*, *1*(1), 78–84. https://doi.org/10.5530/pc.2011.1.5

[22] Ponnusamy, S., Haldar, S., Mulani, F., Zinjarde, S., Thulasiram, H., & RaviKumar, A., 2015. Gedunin and Azadiradione: Human Pancreatic Alpha-Amylase Inhibiting Limonoids from Neem (Azadirachta indica) as Anti-Diabetic

Agents. *PLOS ONE*, *10*(10), e0140113. https://doi.org/10.1371/journal.pone.0140113

[23] Aabideen, Z. U., Mumtaz, M. W., Akhtar, M. T., Raza, M. A., Mukhtar, H., Irfan, A., Saari, N., 2021, Cassia fistula Leaves; UHPLC-QTOF-MS/MS Based Metabolite Profiling and Molecular Docking Insights to Explore Bioactives Role towards Inhibition of Pancreatic Lipase. *Plants*, *10*(7), 1334. https://doi.org/10.3390/plants10071334

[24] Adisakwattana, S., 2017, Cinnamic acid and its derivatives: Mechanisms for prevention and management of diabetes and its complications. *Nutrients*, *9*(2), 163. https://doi.org/10.3390/nu9020163

[25] Roy, J. R., Janaki, C. S., Jayaraman, S., Periyasamy, V., Balaji, T., Vijayamalathi, M., & Veeraraghavan, V. P., 2022, Carica papaya Reduces Muscle Insulin Resistance via IR/GLUT4 Mediated Signaling Mechanisms in High Fat Diet and Streptozotocin-Induced Type-2 Diabetic Rats. *Antioxidants*, *11*(10), 2081. https://doi.org/10.3390/antiox11102081

[26] Ansari, P., Flatt, P. R., Harriott, P., Hannan, J. M. A., & Abdel-Wahab, Y. H. A., 2021, Identification of Multiple Pancreatic and Extra-Pancreatic Pathways Underlying the Glucose-Lowering Actions of Acacia arabica Bark in Type-2 Diabetes and Isolation of Active Phytoconstituents. *Plants*, *10*(6), 1190. https://doi.org/10.3390/plants10061190

[27] Srinivasan, S., Sathish, G., Jayanthi, M., Muthukumaran, J., Muruganathan, U., & Ramachandran, V., 2013, Ameliorating effect of eugenol on hyperglycemia by attenuating the key enzymes of glucose metabolism in streptozotocin-induced diabetic rats. *Molecular and Cellular Biochemistry*, *385*(1–2), 159–168. https://doi.org/10.1007/s11010-013-1824-2

[28] Adebanke, O., Babatunde, A., Franklyn, I., Keleeko, A., Joseph, O., & Olubanke, O., 2023, Free radical scavenging activity, pancreatic lipase and a-amylase inhibitory assessment of ethanolic leaf extract of Phyllanthus amarus. *Plant ScienceToday*, 10(2), 20–26. https://doi.org/10.14719/pst.1809

[29] Ahmad, N., Hasan, N., Ahmad, Z., Zishan, M., & Zohrameena, S., 2016, MOMORDICA CHARANTIA: FOR TRADITIONAL USES AND PHARMACOLOGICAL ACTIONS. *Journal of Drug Delivery and Therapeutics*, *6(2),* 40-44. https://doi.org/10.22270/jddt.v6i2.1202

[30] Yan, L., Vaghari-Tabari, M., Malakoti, F., Moein, S., Qujeq, D., Yousefi, B., & Asemi, Z., 2022, Quercetin: An effective polyphenol in alleviating diabetes and diabetic complications. *Critical Reviews in Food Science and Nutrition*, *63*(28), 9163–9186. https://doi.org/10.1080/10408398.2022.2067825

[31] Varghese, R.M., Subramanian, A.K., Maliael, M.T., 2023, PowerScope™ for Class II Malocclusions: A Systematic Review and Meta-analysis. World Journal of Dentistry,14(7):639–647

[32] Bozkurt, O., Kocaadam-Bozkurt, B., & Yildiran, H., 2022, Effects of curcumin, a bioactive component of turmeric, on type 2 diabetes mellitus and its complications: An updated review. *Food & Function*, *13*(23), 11999–12010. https://doi.org/10.1039/d2fo02625b

[33] Majeed, M., Mundkur, L., Paulose, S., & Nagabhushanam, K., 2022, Novel Emblica officinalis extract containing β-glucogallin vs. metformin: A randomized, open-label, comparative efficacy study in newly diagnosed type 2 diabetes mellitus patients with dyslipidemia. *Food & Function*, *13*(18),9523–9531. https://doi.org/10.1039/d2fo01862d

[34] Mathiyazhagan, J., & Kodiveri Muthukaliannan, G., 2020, The role of mTOR and oral intervention of combined Zingiberofficinale Terminalia chebula extract in type 2 diabetes rat models. *Journal of Food Biochemistry*, *44*(7). https://doi.org/10.1111/jfbc.13250

[35] Mahindrakar, K. V., & Rathod, V. K., 2020, Antidiabetic potential evaluation of aqueous extract of wasteSyzygium cuminiseed kernel's byin vitroα-amylase and α-glucosidase inhibition. *Preparative Biochemistry & Biotechnology*, *51*(6), 589–598. https://doi.org/10.1080/10826068.2020.1839908

[36] Rasool, S., Al Meslmani, B., & Alajlani, M., 2023, Determination of hypoglycemic, hypolipidemic and nephroprotective effects of berberis calliobotrys in alloxan-induced diabetic rats. *Molecules*, *28*(8), 3533. https://doi.org/10.3390/molecules2808353

[37] Etsassala, N. G. E. R., Badmus, J. A., Marnewick, J. L., Egieyeh, S., Iwuoha, Emmanuel. I., Nchu, F., & Hussein, A. A., 2022, Alpha-Glucosidase and Alpha-Amylase Inhibitory Activities, Molecular Docking, and Antioxidant Capacities of Plectranthus ecklonii Constituents. *Antioxidants*, *11*(2), 378. https://doi.org/10.3390/antiox11020378

[38] Maher, S., Choudhary, M. I., Saleem, F., Rasheed, S., Waheed, I., Halim, S. A., … Ahmad, S., 2020, Isolation of Antidiabetic Withanolides from Withania coagulans Dunal and Their In Vitro and In Silico Validation. *Biology*, *9*(8), 197. https://doi.org/10.3390/biology9080197

[39] Hsu, J.-H., Yang, C.-S., & Chen, J.-J., 2022, Antioxidant, Anti-α-Glucosidase, Antityrosinase, and Anti-Inflammatory Activities of Bioactive Components from Morus alba. *Antioxidants*, *11*(11), 2222. https://doi.org/10.3390/antiox11112222

[40] Kumar, R., Sood, P., Rana, Dr. V., & Prajapati, A. K., 2023, Combine therapy of gallic acid and allicin in management of diabetes. *Journal for Research in Applied Sciences and Biotechnology*, *2*(3), 91–99. https://doi.org/10.55544/jrasb.2.3.12