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THE ROLE OF HERBAL SUPPLEMENTS WITH METFORMIN IN MANAGING TYPE 2 DIABETES MELLITUS: REVIEW ARTICLE

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ABSTRACT

Diabetes mellitus represents a significant health challenge in India and worldwide, and its treatment traditionally involves combining synthetic and herbal drugs, which, along with diet and lifestyle modifications, can maximize therapy efficiency. Notably, while complementary medicines can potentially augment diabetes care, the first-line treatment for Type 2 Diabetes Mellitus (T2DM) remains metformin, a synthetic medication. This article aims to highlight the rationale for the clinical use of metformin and the circumstances under which it should not be prescribed. Herbal medicine has garnered considerable interest for its beneficial effects in T2DM management, primarily due to their traditional use, relative safety, and efficacy. This review provides preclinical and clinical evidence for the anti-diabetic potential of several commonly used medicinal plants, including Neem (Azadirachta indica), Turmeric (Curcuma longa), Cinnamon (Cinnamomum verum), Fenugreek (Trigonella foenum-graecum), Bitter Melon (Momordica charantia), Jamun (Syzygium cumini), and Aloe vera (Aloe barbadensis Miller). These plants are involved in reducing blood glucose levels via multiple mechanisms, namely, enhancing insulin secretion and sensitivity, inhibiting carbohydrate-digesting enzymes, and protecting pancreatic β-cells from damage. Moreover, this review describes the ethnobotanical applications of these plants, their phytochemistry, dosage, and recent clinical advances. The article also discusses the adjunctive use of these herbal medicines in combination with metformin to maximize therapeutic benefits for patients with DM.

KEYWORDS: Metformin, Herbal medicine, Antidiabetic plants, Plant-based therapy, Blood sugar control, combination therapy.

INTRODUCTION

The World Health Organization (WHO) describes diabetes mellitus as a long-term health problem marked by high blood sugar levels, which can lead to different symptoms. Importantly, more than 90% of diabetes cases are identified as type 2 diabetes mellitus (T2DM).

This condition is defined by the inadequate release of insulin from the islet of Langerhans (β-cells, which are responsible for producing insulin) that helps lower blood glucose by sending it to various organs like the kidneys, liver, and fat tissues.

According to the International Diabetes Federation (IDF), in 2019, diabetes led to 4.2 million deaths, and 463 million adults aged between 20 and 79 were living with diabetes—a number expected to increase to 700 million by 2045.

The risk factors for T2DM include genetic, metabolic, and environmental aspects that all contribute together. Although personal factors for T2DM may relate to ethnicity and family history/genetic risk, research from population studies shows that many T2DM cases could be avoided by improving major changeable risk factors like obesity, low physical activity, and unhealthy diets.

Throughout history, many cultures have used medicinal plants to treat various health problems, including diabetes. Numerous herbs have demonstrated potential in fighting diabetes through different ways, such as increasing insulin production, helping with glucose absorption, reducing oxidative stress, and protecting pancreatic β-cells. This review highlights important medicinal plants with anti-diabetic properties, explaining their active ingredients, how they work, and the clinical studies that confirm their effectiveness[5]

The goal of this review is to summarize the traditional uses, active compounds, methods of action, and clinical research supporting specific medicinal plants used to manage diabetes.

Pathophysiology

When the interaction between insulin release and its effects in beta cells fails, blood glucose levels rise abnormally. If beta cells don't work properly, insulin release decreases, which disrupts the body's ability to maintain normal glucose levels.

Insulin resistance (IR) causes an increase in glucose production in the liver, muscles, and fat tissues while also reducing glucose absorption in these areas, leading to higher blood sugar levels. Both of these processes can start early and significantly contribute to the development of the disease. However, when beta cell dysfunction and IR occur together, hyperglycemia worsens, promoting the progression of type 2 diabetes mellitus (T2DM).

Symptoms

People type 2 diabetes experience a range of symptoms, such as high blood sugar (shown by changes in appetite and frequent urination), signs of low blood sugar (which can happen as a side effect of treatment and includes dizziness, fatigue, pain, sleep issues, sensory problems, difficulties thinking, feelings of sadness, and anxiety), and changes in vision related to their condition or treatment.

Treatment

A thorough approach that aims to protect the heart and kidneys while controlling blood sugar levels. The main treatment involves medication (oral hypoglycemic agents) and lifestyle changes.[1-5]

Classification of Oral Hypoglycemic Agents (OHA):

Oral diabetes medicines and their types: Biguanides are older drugs that lower the amount of sugar the liver produces and, to a smaller extent, help the liver and other tissues use insulin better. Phenformin was taken off the market in the United States in the 1970s because it could cause lactic acidosis and had a death rate close to 50%. On the other hand, metformin has proven to be effective and safe, used in Europe for more than thirty years and available in the United States since 1995. Metformin is suggested for all people with type 2 diabetes unless certain situations make it unsafe to use. Currently, the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) support using metformin, along with diet changes and exercise, as the first-choice treatment for individuals with type 2 diabetes, regardless of whether they are considered overweight.[47]

Table No 1: Classification of Oral Hypoglycemic Agents.

Sr. No.	Type	Examples	Glucose lowering efficacy	Hypoglycemia	Weight effects	Major advantages	Limitations	References
1	Biguanides	Metformin	High	Low	Neutral	Effective, inexpensive, widely available; extensive clinical experience	GI adverse effects; B12 deficiency; avoid if eGFR <30	[49]
2	Sulfonylureas	Glimepiride, gliclazide	High	High	Gain	Effective and relatively inexpensive	Hypoglycemia and weight gain	[50]
3	DPP-4 inhibitors	Sitagliptin, linagliptin	Intermediate	Low	Neutral	Generally well tolerated; low hypoglycemia risk	Less glucose-lowering efficacy	[51]
4	SGLT2 inhibitors	Dapagliflozin, empagliflozin	Intermediate	Low	Loss	Cardiovascular and renal benefits in appropriate patients	Genital infections, volume depletion; efficacy affected by renal function	[52]
5	Thiazolidinedione	Pioglitazone	High	Low	Gain	Durable glucose-lowering effect	Weight gain, edema and other adverse effects	[53]
6	A-Glucosidase inhibitors	Acarbose, voglibose	Low to intermediate	Low	Neutral	Useful for postprandial glucose control	GI adverse effects	[54]

Among the oral medications for lowering blood sugar levels, metformin has a generally positive treatment profile. It effectively lowers glucose while having a low risk of causing low blood sugar and often helps with moderate weight loss or has no impact on weight. Moreover, it is affordable, easy to get, and has a lot of clinical experience supporting its use. Compared to sulfonylureas, metformin avoids the risks of low blood sugar and weight gain, and it provides better blood sugar control than DPP-4 inhibitors when used alone. While SGLT2 inhibitors offer important heart and kidney benefits for patients with certain additional health issues, the choice of these medications depends on a person's heart health and kidney function. Therefore, metformin is a wise drug to consider for further study, especially when used with plant-based treatments.

Metformin is often prescribed for managing Type 2 diabetes because of its features, including wide availability, low cost, better patient access, and fewer side effects.

Metformin: How It Works, Side Effects, and Precautions

Metformin, which belongs to a class called biguanides, mainly lowers blood sugar by reducing glucose production in the liver. It also improves insulin sensitivity in body tissues

and decreases glucose absorption in the intestines. One suggested way it works is by activating AMP-activated protein kinase (AMPK). It does not stimulate insulin release, which helps keep the risk of low blood sugar low when taken alone.

The most common side effects are stomach problems like nausea, diarrhea, and stomach pain, and long-term use can cause a vitamin B12 deficiency. Although lactic acidosis is rare, it can be serious. Care should be taken when giving metformin to patients with severe kidney issues (eGFR <30 mL/min/1.73 m^2), serious liver disease, acute or unstable heart failure, and other conditions related to low oxygen, high alcohol use, and situations that can cause dehydration or infection. It is also suggested to stop metformin temporarily before procedures involving iodinated contrast for at-risk patients.

However, this medication by itself is not enough for effective diabetes management; some herbal remedies are often used alongside these drugs to improve patient outcomes along with certain lifestyle changes. These medicinal herbs are easy to find, affordable, have few side effects, and can effectively help in lowering blood sugar levels.

Table No. 2: **Mechanism of Herbal Drugs.**

Sr. No.	Biological Source of herbal drugs	Mechanism of action	Description	References
1	Neem (Azadirachta indica) obtained from leaves and seeds of Azadirachta indica belonging to Family Meliaceae	Stimulates insulin secretion, improves insulin sensitivity, and reduces oxidative stress.	Herbs that act like insulin to promote glucose uptake	[6,9]
2	Turmeric (Curcuma longa) – obtained from dried rhizomes of Curcuma longa belonging to Family Zingiberaceae	Improves insulin sensitivity, reduces inflammation and oxidative stress, and protects pancreatic β-cells.	Stimulate pancreatic β-cells to release insulin	[11,13]
3	Cinnamon (Cinnamomum verum) obtained from Dried inner bark of Cinnamomum verum belonging to Family: Lauraceae	Exhibits insulin-mimetic activity, enhances glucose uptake, and inhibits α-glucosidase enzyme	Inhibit α-glucosidase and α-amylase to delay carbohydrate absorption	[16,18]
4	Fenugreek (Trigonella foenum-graecum) – obtained from ripe seeds of Trigonella foenum-graecum belonging to Family: Fabaceae	Stimulates insulin secretion, delays glucose absorption, and improves insulin receptor sensitivity.	Neutralize oxidative stress and protect β-cells	[21,23]
5	Bitter Melon (Momordica charantia) obtained from Fresh fruits and seeds of Momordica charantia belonging to Family Cucurbitaceae	Possesses insulin-like activity, enhances peripheral glucose uptake, and inhibits gluconeogenesis.	Enhance insulin receptor response in cells	[26,33]
6	Jamun (Syzygium cumini) obtained	Regulates insulin activity, delays	Providing decreased	[31,33]

	from Seeds and fruits of Syzygium cumini belonging to Family Myrtaceae	carbohydrate absorption, and provides antioxidant protection to pancreatic β-cells.	effects of insulin while decreasing absorption.	
7	Aloe vera (Aloe barbadensis Mill.) – obtained mainly from the gel/inner leaf of Aloe vera, belonging to family Asphodelaceae (formerly Liliaceae)	Improves insulin sensitivity and glucose uptake, inhibits carbohydrate-digesting enzymes such as α-amylase and α-glucosidase, and reduces oxidative stress and inflammation. Aloe polysaccharides such as acemannan may contribute to glucose-regulating and β-cell protective effects.	Helps reduce blood glucose by enhancing peripheral glucose utilization, delaying carbohydrate digestion/absorption, and improving insulin sensitivity.	[36,37]

These various targets make plant-based treatments hopeful for managing diabetes together with other approaches, especially in the early and moderate stages of diabetes, even for prediabetes, along with ongoing issues like kidney failure and heart diseases.

Table No. 3: Role of Herbal Supplements In Diabetes Mellitus.

Sr. No.	Name	Active Constituents	Role in Diabetes Management	Dosage forms	References
1	Neem (Azadirachta indica	Nimbin, Azadirachtin	Stimulates insulin secretion, reduces blood glucose levels, exhibits antioxidant activity, improves insulin sensitivity	Capsule	[9]
2	Turmeric (Curcuma longa)	Curcumin	Improves insulin sensitivity, reduces inflammation and oxidative stress, protects pancreatic β-cells	Capsules	[14]
3	Cinnamon (Cinnamomum verum)	Cinnamaldehyde	Mimics insulin action, enhances glucose uptake, inhibits α-glucosidase, lowers postprandial glucose Powder, capsules, tea, extracts	Powder	[19]
4	Fenugreek (Trigonella foenum-graecum)	4-Hydroxyisoleucine	Stimulates insulin release, delays carbohydrate absorption, and improves glucose tolerance Seeds, powder, capsule.	Powder	[24]
5	Bitter Melon (Momordica charantia)	Charantin, Polypeptide	Exhibits insulin-like activity, enhances glucose uptake, reduces blood glucose levels	Liquid	[30]
6	Jamun (Syzygium cumini)	Jamboline, Ellagic acid, Anthocyaninss	Delays glucose absorption, improves insulin activity, protects against diabetic complications.	Powder	[34]
7	Aloe vera	Acemannan, glucomannan, aloin, aloe-emodin	Increases peripheral glucose uptake (moves glucose from blood into muscle or adipose tissue), improves insulin signalling, and reduces hepatic glucose production	Gel, capsules, juice	[37]

Clinical Evidence of Herbal Plants Helping in Diabetes Treatment:

Clinical Evidence of Herbal Effectiveness in Diabetes Clinical Studies Supporting Herbal Antidiabetic Treatments Several herbs used in traditional medicine have moved from laboratory studies to human clinical trials. Below are examples of clinical studies and animal studies that demonstrate the effectiveness of the herbs mentioned

Table No 4: Clinical Evidence of Herbal Drugs.

Sr. No	Herb (Scientific name)	Study design	Dose and duration	Key findings	Author and year	References
1	Neem (Azadirachta indica)	Randomized clinical trial in Type 2 diabetic patients	500 mg neem leaf extract twice daily for 12 weeks	Significant reduction in fasting blood glucose (FBG) and HbA1c levels; improved lipid profile; no major adverse effects reported.	Usharani pingali,Mohammed abid ali,et.al 2020	[8]
2	Turmeric (Curcuma longa)	Double-blind placebo-controlled study	1500 mg curcumin daily for 3 months	Improved HbA1c, fasting blood glucose, and insulin sensitivity; reduced oxidative stress and inflammatory markers.	Ledyane Taynara Marton et al. Front Endocrinol (Lausanne). 2021.	[14]
3	Cinnamon (Cinnamomum verum)	Meta-analysis of 16 clinical trials	1–6 g/day for 40–90 days	Reduced fasting blood glucose, HbA1c, and triglyceride levels in patients with Type 2 diabetes mellitus.	Amir Hossein Moridpour et al. Phytother Res. 2024 Jan	[17]
4	Fenugreek (Trigonella foenum-graecum	Clinical trials	25 g seed powder/day	Improved glucose tolerance, reduced insulin resistance, and lowered cholesterol and triglyceride levels	Melina Haxhiraj et al. Int J Mol Sci. 2024.	[23]
5	Bitter Melon (Momordica charantia	Placebo-controlled clinical study	50 mL juice/day for 12 weeks	Reduced postprandial blood glucose levels and enhanced insulin secretion.	Soo Kyoung Kim et al. Complement Ther Med. 2020 Aug.	[27]
6	Jamun (Syzygium cumini)	Pre Clinical trial	2ml/day of jamun with sugar and stevia for 45 days on female rats	Improved glycemic control, increase body weight improves pancreatic and renal tissues	Saeed H, Shabbir MA, Rafi A, Din A, Khan MR, Gill P, Afzaal M, Ahmed F, Ahmad MF, Akram N, Hailu GG.	[32]

Clinical Evidence of Herbal Drugs with Metformin

Table No 5: Clinical Evidence of Herbal Drugs With Metformin.

Sr. No	Herb (Scientific name)	Study design and population	Combination and duration	Key findings	Author and year	References
1	Neem (Azadirachta indica)	Randomized, double-blind, placebo-controlled trial in 80 type 2 diabetic patients already on standard metformin	Neem leaf and twig aqueous extract 125, 250 or 500 mg twice daily with metformin for 12 weeks	Added to metformin, improved hyperglycemia, endothelial function, oxidative stress and systemic inflammation versus placebo at all doses; no effect on platelet aggregation or lipid profile.	Usharani Pingali et al. Diabetes Metab Syndr Obes. 2020.	[8]
2	Turmeric (Curcuma longa)	Open-label randomized trial in 60 male type 2 diabetic patients on metformin (500 mg twice daily)	Turmeric powder 2 g/day with metformin for 4 weeks (capsules taken 2 h after metformin)	Fasting glucose fell about 15% with turmeric versus 6% with metformin alone; HbA1c, LDL cholesterol, lipid peroxidation (MDA) and hsCRP improved; no adverse effects reported.	N Maithili Karpaga Selvi et al. Indian J Clin Biochem. 2015.	[40]
3	Curcumin (Curcuma longa)	Randomized, double-blind, placebo-controlled trial in 272 obese type 2 diabetic patients receiving metformin	Curcumin extract 1500 mg/day with metformin for 12 months	Improved beta-cell function (HOMA-β) and reduced fasting glucose and HbA1c compared with placebo.	Metha Yaikwawong et al. Nutr J. 2024.	[12]
4	Cinnamon (Cinnamomum verum)	Randomized controlled trial in newly diagnosed type 2 diabetic patients (30 on metformin alone, 27 on metformin + cinnamon)	Metformin 500 mg three times daily plus crude cinnamon powder 3 g/day for 12 weeks	Adding cinnamon gave a significant rise in 1,5-anhydroglucitol and ghrelin and a highly significant rise in adiponectin.	Shatha Mohammad et al. Jordan Med J. 2021.	[41]
5	Cinnamon (Cassia cinnamon)	Single-blind, placebo-controlled randomized trial in 60 type 2 diabetic patients on metformin or a sulfonylurea	Cinnamon cassia powder 1.5 g/day added to current therapy for 12 weeks	No significant difference from placebo in fasting glucose, HbA1c or lipid profile, so benefit is not consistent.	Suppapitiporn S et al. J Med Assoc Thai. 2006.	[42]
6	Fenugreek (Trigonella foenum-graecum)	Open-label randomized comparative study in 60 type 2 diabetic patients (30 per group)	Metformin 500 mg twice daily with or without fenugreek seed powder 1 g three times daily for 12	Fasting and postprandial glucose and HbA1c fell in both groups, with a significantly greater improvement in the metformin + fenugreek group.	Manmeet Kaur et al. Int J Basic Clin Pharmacol. 2016.	[43]

			weeks			
7	Bitter Melon (Momordica charantia)	Retrospective hospital-record study of type 2 diabetic patients treated with bitter-melon powder alone or added to glibenclamide or metformin	Bitter-melon fruit powder (dose not stated in abstract) with metformin for at least 84 days	Fasting blood glucose fell by about 24 mg/dL with the metformin add-on; HbA1c was not affected. Retrospective design limits the evidence.	Puengjai Punikhom et al. J Thai Tradit Altern Med. 2016.	[44]
8	Jamun (Syzygium cumini)	Streptozocin induced rats were given powder with metformin for 8 weeks	Metformin 90mg/kg with jamun powder 200 mg /kg daily	Can be used as potential add on therapy with anti hyperglycemic effects.	Mulkalwar, Sarita, Vishwanath Kulkarni, Teja Deshpande, Harshavardhan Bhide, Abhi Patel, and A. V. Tilak. 2021	[45]
9	Aloe vera (Aloe barbadensis Mill.)	Randomized, double-blind, placebo-controlled trial in 60 hyperlipidemic type 2 diabetic patients not controlled on glyburide 10 mg/day and metformin 1000 mg/day	Aloe leaf gel 300 mg every 12 hours added to glyburide + metformin for 2 months	Significantly lowered fasting glucose, HbA1c, total cholesterol and LDL versus placebo, without significant changes in liver or kidney function tests.	Hasan Fallah Huseini et al. Planta Med. 2012.	[36]

The table below shows studies on humans where a herbal drug was used along with metformin (as an addition to regular metformin treatment or as a mixture), found in the literature review. It also includes different results on metformin combined with other herbal drugs to enhance health benefits.

Many of the studies included patients who were already taking metformin, so the results shown in the previous table indicate that these herbal medicines are used as additional treatments. Some of the trials were small, open-label, or looked back in time, while others had both large and small groups of participants, with different doses and herbal mixtures. As a result, the findings are initial, and these herbs should not be viewed as replacements for metformin.

DISCUSSION

When examining the studies in the combination table, curcumin/turmeric and neem provide the strongest proof for their use with metformin. The curcumin study was the largest, involving 272 participants, and lasted for 12 months, being both double-blind and placebo-

controlled. It showed better beta-cell function and lower fasting glucose and HbA1c in people taking metformin. Likewise, the neem study was also conducted in a double-blind and placebo-controlled way, showing improved blood sugar control, blood vessel function, and inflammation markers with metformin across all three doses tested. Fenugreek and turmeric powder also helped improve blood sugar levels when used with metformin; however, those studies were small, open-label, and brief (4 to 12 weeks), making their results less reliable. Cinnamon showed mixed results: one trial found improvements in adiponectin and related factors, while another found no significant effect on glucose or HbA1c levels. The evidence for bitter melon comes from a study that looked back and indicated a decrease in fasting glucose but no change in HbA1c. Aloe vera showed improvements in glucose and fat levels in a double-blind trial, but since participants were also taking glyburide along with metformin, it is not possible to separate its effect with metformin alone. For Jamun, the only supporting evidence in this review comes from an animal study with diabetic rats, where Jamun powder (200 mg/kg) was given with metformin (90 mg/kg) over 8 weeks, suggesting a possible additional blood sugar-lowering benefit. Since this is preclinical, it supports biological possibility but cannot be directly compared to human studies or used to determine correct doses for patients. No research has made direct comparisons of these herbs, and the differences in doses, preparations, and designs mean that no single herb can be clearly identified as the best to use with metformin. Thus, these conclusions are still uncertain.

CONCLUSION

The rising prevalence of diabetes worldwide necessitates the development of more effective, accessible, and economical treatment options. Herbal preparations can be a viable alternative or complement to conventional therapies. The anti-diabetic properties of Neem, Turmeric, Cinnamon, Fenugreek, Bitter Melon, Jamun, and Aloe vera have been investigated, highlighting their potential in improving glucose metabolism through diverse mechanisms of action, such as insulin mimicry, β-cell protection, enzyme inhibition, and antioxidant effects.

Numerous clinical studies have demonstrated their capacity to reduce fasting and postprandial glucose levels, as well as hemoglobin A1c (HbA1c) and improve insulin sensitivity with minimal adverse effects. Herbal treatments can be used not only to manage acute hyperglycemia but also to prevent the development of diabetes-related complications. According to a randomized trial, Aloe vera combined with metformin showed more significant improvements in patients' glucose and lipid profiles; however, there is a lack of

clinical evidence for the adjunctive use of other herbal medications discussed in the article. Due to the risk of hypoglycemia and the potential for herbal products to be of inconsistent quality, these preparations must be used as supplements to mainstream diabetes therapies under the supervision of healthcare professionals.

Based on the available data, curcumin/turmeric and neem appear to be the most promising herbal supplements to be used in combination with metformin, as they were studied in randomized controlled trials (RCT) in patients on metformin therapy. The next in line are fenugreek and aloe vera, whereas the clinical benefits of cinnamon and bitter melon remain unsubstantiated. There is preliminary evidence from animal experiments for the adjunctive use of jamun in patients with T2DM; however, additional clinical studies are needed to confirm its efficacy and safety in humans and compare its effects to those of the other herbal supplements. As a result, these phytotheraupitic agents can be used as adjuncts to metformin to maximize the pro-homeostatic effects on glucose, lipids, oxidative stress, and inflammatory pathways in patients with DM but should not be used as a substitute for the first-line therapy. Larger interventional studies with extended follow-up are required to further elucidate the effects of these herbal treatments and establish their role in diabetes management.

Table No 6: Traditional Form Of Herbal Drugs and Use.

No.	Herb	Traditional form	Clinical form	References
1	Neem	Neem leaf juice or powder	500mg neem extract capsules daily	[8,10]
2	Turmeric	Mixed in warm milk, powder in food	1500mg curcumin/day	[13,15]
3	Cinnamon	Powder with water/tea	1 to 6 grams/day as capsule or added to diet	[18,20]
4	Fenugreek	Soaked seeds or powder	25 grams seed powder/day	[23,25]
5	Bitter melon	Juice, curry, capsule	50ml juice/day or 2 to 3 capsules daily	[27,29]
6	Jamun	Seed powder, fruit juice	5g seed powder twice a day after meals	[33,35]
7	Aloe vera	Fresh inner-leaf gel or juice (latex removed / decolorized)	300 mg aloe leaf gel capsule twice daily (every 12 h) for 2 months, alongside conventional therapy	[36,39]

REFERENCES

1. Banday MZ, Sameer AS, Nissar S. Pathophysiology of diabetes: An overview. Avicenna J Med., 2020 Oct 13; 10(4): 174-188. DOI: 10.4103/ajm.ajm_53_20. PMID: 33437689; PMCID: PMC7791288.
2. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels, Belgium: International Diabetes Federation; 2021. Available from: https://diabetesatlas.org

3. 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. Int J Mol Sci., 2020 Aug 30; 21(17): 6275. Doi: 10.3390/ijms21176275. PMID: 32872570; PMCID: PMC7503727.
4. Singh A, Shadangi S, Gupta PK, Rana S. Type 2 Diabetes Mellitus: A Comprehensive Review of Pathophysiology, Comorbidities, and Emerging Therapies. Compr Physiol., 2025 Feb; 15(1): e70003. Doi: 10.1002/cph4.70003. PMID: 39980164.
5. Kaul K, Tarr JM, Ahmad SI, Kohner EM, Chibber R. Introduction to diabetes mellitus. Adv Exp Med Biol., 2012; 771: 1-11. Doi: 10.1007/978-1-4614-5441-0_1. PMID: 23393665.
6. Vidhya Rekha U, Anita M, Bhuminathan S, Sadhana K. Known data on the therapeutic use of Azadiracta indica (neem) for type 2 diabetes mellitus. Bioinformation., 2022 Feb 28; 18(2): 82-87. Doi: 10.6026/97320630018082. PMID: 36420434; PMCID: PMC9649496.
7. Shashank M Patil, Prithvi S Shirahatti, Ramith Ramu, Azadirachta indica A. Juss (neem) against diabetes mellitus: a critical review on its phytochemistry, pharmacology, and toxicology, Journal of Pharmacy and Pharmacology, May 2022; 74(5): 681–710.
8. Pingali U, Ali MA, Gundagani S, Nutalapati C. Evaluation of the Effect of an Aqueous Extract of Azadirachta indica (Neem) Leaves and Twigs on Glycemic Control, Endothelial Dysfunction and Systemic Inflammation in Subjects with Type 2 Diabetes Mellitus – A Randomized, Double-Blind, Placebo-Controlled Clinical Study. Diabetes Metab Syndr Obes., 2020 Nov 17; 13: 4401-4412. Doi: 10.2147/DMSO.S274378. PMID: 33244247; PMCID: PMC7683773.
9. Alzohairy MA. Therapeutics Role of Azadirachta indica (Neem) and Their Active Constituents in Diseases Prevention and Treatment. Evid Based Complement Alternat Med., 2016; 2016: 7382506. Doi: 10.1155/2016/7382506. Epub 2016 Mar 1. PMID: 27034694; PMCID: PMC4791507.
10. Yarmohammadi F, Mehri S, Najafi N, Salar Amoli S, Hosseinzadeh H. The protective effect of Azadirachta indica (neem) against metabolic syndrome: A review. Iran J Basic Med Sci., 2021 Mar; 24(3): 280-292. Doi: 10.22038/ijbms.2021.48965.11218. PMID: 33995939; PMCID: PMC8087850.
11. Mokgalaboni K, Mashaba RG, Phoswa WN, Lebelo SL. Curcumin Attenuates Hyperglycemia and Inflammation in Type 2 Diabetes Mellitus: Quantitative Analysis

of Randomized Controlled Trial. Nutrients., 2024 Nov 30; 16(23): 4177. Doi: 10.3390/nu16234177. PMID: 39683570; PMCID: PMC11644433.

12. Yaikwawong M, Jansarikit L, Jirawatnotai S, Chuengsamarn S. Curcumin extract improves beta cell functions in obese patients with type 2 diabetes: a randomized controlled trial. Nutr J., 2024 Oct 1; 23(1): 119. Doi: 10.1186/s12937-024-01022-3. PMID: 39354480; PMCID: PMC11445938.
13. Hewlings SJ, Kalman DS. Curcumin: A Review of Its Effects on Human Health. Foods., 2017 Oct 22; 6(10): 92. Doi: 10.3390/foods6100092. PMID: 29065496; PMCID: PMC5664031.
14. Marton LT, Pescinini-E-Salzedas LM, Camargo MEC, Barbalho SM, Haber JFDS, Sinatora RV, Detregiachi CRP, Girio RJS, Buchaim DV, Cincotto Dos Santos Bueno P. The Effects of Curcumin on Diabetes Mellitus: A Systematic Review. Front Endocrinol (Lausanne)., 2021 May 3; 12: 669448. Doi: 10.3389/fendo.2021.669448. PMID: 34012421; PMCID: PMC8126655.
15. Urošević M, Nikolić L, Gajić I, Nikolić V, Dinić A, Miljković V. Curcumin: Biological Activities and Modern Pharmaceutical Forms. Antibiotics (Basel)., 2022 Jan 20; 11(2): 135. Doi: 10.3390/antibiotics11020135. PMID: 35203738; PMCID: PMC8868220.
16. Rao PV, Gan SH. Cinnamon: a multifaceted medicinal plant. Evid Based Complement Alternat Med., 2014; 2014: 642942. Doi: 10.1155/2014/642942. Epub 2014 Apr 10. PMID: 24817901; PMCID: PMC4003790.
17. Moridpour AH, Kavyani Z, Khosravi S, Farmani E, Daneshvar M, Musazadeh V, Faghfouri AH. The effect of cinnamon supplementation on glycemic control in patients with type 2 diabetes mellitus: An updated systematic review and dose-response meta-analysis of randomized controlled trials. Phytother Res., 2024 Jan; 38(1): 117-130. Doi: 10.1002/ptr.8026. Epub 2023 Oct 11. PMID: 37818728.
18. Silva ML, Bernardo MA, Singh J, de Mesquita MF. Cinnamon as a Complementary Therapeutic Approach for Dysglycemia and Dyslipidemia Control in Type 2 Diabetes Mellitus and Its Molecular Mechanism of Action: A Review. Nutrients., 2022 Jul 5; 14(13): 2773. Doi: 10.3390/nu14132773. PMID: 35807953; PMCID: PMC9269353.
19. Khan A, Safdar M, Ali Khan MM, Khattak KN, Anderson RA. Cinnamon improves glucose and lipids of people with type 2 diabetes. Diabetes Care., 2003 Dec; 26(12): 3215-8. Doi: 10.2337/diacare.26.12.3215. PMID: 14633804.

20. Ranasinghe P, Galappaththy P, Constantine GR, Jayawardena R, Weeratunga HD, Premakumara S, Katulanda P. Cinnamomum zeylanicum (Ceylon cinnamon) as a potential pharmaceutical agent for type-2 diabetes mellitus: study protocol for a randomized controlled trial. Trials., 2017 Sep 29; 18(1): 446. Doi: 10.1186/s13063-017-2192-0. PMID: 28962661; PMCID: PMC5622575.
21. Luo W, Deng J, He J, Yin L, You R, Zhang L, Shen J, Han Z, Xie F, He J, Guan Y. Integration of molecular docking, molecular dynamics and network pharmacology to explore the multi-target pharmacology of fenugreek against diabetes. J Cell Mol Med., 2023 Jul; 27(14): 1959-1974. Doi: 10.1111/jcmm.17787. Epub 2023 May 31. PMID: 37257051; PMCID: PMC10339091.
22. Cortez-Navarrete M, Pérez-Rubio KG, Escobedo-Gutiérrez MJ. Role of Fenugreek, Cinnamon, Curcuma longa, Berberine and Momordica charantia in Type 2 Diabetes Mellitus Treatment: A Review. Pharmaceuticals (Basel)., 2023 Mar 30; 16(4): 515. Doi: 10.3390/ph16040515. PMID: 37111272; PMCID: PMC10145167.
23. Haxhiraj M, White K, Terry C. The Role of Fenugreek in the Management of Type 2 Diabetes. Int J Mol Sci., 2024 Jun 26; 25(13): 6987. Doi: 10.3390/ijms25136987. PMID: 39000103; PMCID: PMC11240913.
24. Kim J, Noh W, Kim A, Choi Y, Kim YS. The Effect of Fenugreek in Type 2 Diabetes and Prediabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Int J Mol Sci., 2023 Sep 12; 24(18): 13999. Doi: 10.3390/ijms241813999. PMID: 37762302; PMCID: PMC10531284.
25. Qiu D, Hu J, Zhang S, Cai W, Miao J, Li P, Jiang W. Fenugreek extract improves diabetes-induced endothelial dysfunction via the arginase 1 pathway. Food Funct., 2024 Apr 2; 15(7): 3446-3462. Doi: 10.1039/d3fo04283a. PMID: 38450419.
26. Sur S, Ray RB. Bitter Melon (Momordica Charantia), a Nutraceutical Approach for Cancer Prevention and Therapy. Cancers (Basel)., 2020 Jul 27; 12(8): 2064. Doi: 10.3390/cancers12082064. PMID: 32726914; PMCID: PMC7464160.
27. Kim SK, Jung J, Jung JH, Yoon N, Kang SS, Roh GS, Hahm JR. Hypoglycemic efficacy and safety of Momordica charantia (bitter melon) in patients with type 2 diabetes mellitus. Complement Ther Med., 2020 Aug; 52: 102524. Doi: 10.1016/j.ctim.2020.102524. Epub 2020 Jul 22. PMID: 32951763.
28. Mahwish, Saeed F, Sultan MT, Riaz A, Ahmed S, Bigiu N, Amarowicz R, Manea R. Bitter Melon (Momordica charantia L.) Fruit Bioactives Charantin and Vicine

Potential for Diabetes Prophylaxis and Treatment. Plants (Basel)., 2021 Apr 8; 10(4): 730. Doi: 10.3390/plants10040730. PMID: 33918062; PMCID: PMC8070166.

29. Cortez-Navarrete M, Pérez-Rubio KG, Escobedo-Gutiérrez MJ. Role of Fenugreek, Cinnamon, Curcuma longa, Berberine and Momordica charantia in Type 2 Diabetes Mellitus Treatment: A Review. Pharmaceuticals (Basel)., 2023 Mar 30; 16(4): 515. Doi: 10.3390/ph16040515. PMID: 37111272; PMCID: PMC10145167.
30. Hsu PK, Pan FFC, Hsieh CS. mcIRBP-19 of Bitter Melon Peptide Effectively Regulates Diabetes Mellitus (DM) Patients' Blood Sugar Levels. Nutrients., 2020 Apr 28; 12(5): 1252. Doi: 10.3390/nu12051252. PMID: 32354072; PMCID: PMC7281988.
31. Das G, Nath R, Das Talukdar A, Ağagündüz D, Yilmaz B, Capasso R, Shin HS, Patra JK. Major Bioactive Compounds from Java Plum Seeds: An Investigation of Its Extraction Procedures and Clinical Effects. Plants (Basel)., 2023 Mar 7; 12(6): 1214. Doi: 10.3390/plants12061214. PMID: 36986906; PMCID: PMC10057433.
32. Saeed H, Shabbir MA, Rafi A, Din A, Khan MR, Gill P, Afzaal M, Ahmed F, Ahmad MF, Akram N, Hailu GG. Assessment of Diabetes Mellitus Retrieving Potential of Low Caloric Jamun (Syzygium cumini) Drink Through Animal Modeling. Food Sci Nutr., 2025 May 5; 13(5): e70251. Doi: 10.1002/fsn3.70251. PMID: 40330204; PMCID: PMC12053304.
33. Ayyanar M, Subash-Babu P, Ignacimuthu S. Syzygium cumini (L.) Skeels., a novel therapeutic agent for diabetes: folk medicinal and pharmacological evidences. Complement Ther Med., 2013 Jun; 21(3): 232-43. Doi: 10.1016/j.ctim.2013.03.004. Epub 2013 Apr 25. PMID: 23642956.
34. Stanely Mainzen Prince P, Kamalakkannan N, Menon VP. Syzigium cumini seed extracts reduce tissue damage in diabetic rat brain. J Ethnopharmacol., 2003 Feb; 84(2-3): 205-9. Doi: 10.1016/s0378-8741(02)00316-1. PMID: 12648817.
35. Benherlal PS, Arumughan C. Chemical composition and in vitro antioxidant studies on Syzygium cumini fruit. J Sci Food Agric., 2007 Nov; 87(14): 2560-9. Doi: 10.1002/jsfa.2957. PMID: 20836162.
36. Huseini HF, Kianbakht S, Hajiaghaee R, Dabaghian FH. Anti-hyperglycemic and anti-hypercholesterolemic effects of Aloe vera leaf gel in hyperlipidemic type 2 diabetic patients: a randomized double-blind placebo-controlled clinical trial. Planta Med., 2012 Mar; 78(4): 311-6. Doi: 10.1055/s-0031-1280474. PMID: 22198821.

37. Suksomboon N, Poolsup N, Punthanitisarn S. Effect of Aloe vera on glycaemic control in prediabetes and type 2 diabetes: a systematic review and meta-analysis. J Clin Pharm Ther., 2016 Apr; 41(2): 180-8. Doi: 10.1111/jcpt.12382. PMID: 27009750.
38. National Center for Complementary and Integrative Health. Aloe Vera: Usefulness and Safety. Available from: https://www.nccih.nih.gov/health/aloe-vera
39. Mayo Clinic. Aloe. Available from: https://www.mayoclinic.org/drugs-supplements-aloe/art-20362267
40. Selvi NMK, Sridhar MG, Swaminathan RP, Sripradha R. Efficacy of Turmeric as Adjuvant Therapy in Type 2 Diabetic Patients. Indian J Clin Biochem., 2015 Apr; 30(2): 180-6. Doi: 10.1007/s12291-014-0436-2. PMID: 25883426.
41. Mohammad S, Fadhil N, Mahmood M. Effects of metformin and cinnamon on 1,5 anhydroglucitol, adiponectin and ghrelin on newly diagnosed type 2 diabetes mellitus patients. Jordan Med J., 2021; 55(4).
42. Suppapitiporn S, Kanpaksi N, Suppapitiporn S. The effect of cinnamon cassia powder in type 2 diabetes mellitus. J Med Assoc Thai., 2006 Sep; 89 Suppl 3: S200-5. PMID: 17718288.
43. Kaur M, Singh N, Sharma G, Singh D. To study the efficacy and tolerability of fenugreek seed powder as add-on therapy with metformin in patients of type-2 diabetes mellitus. Int J Basic Clin Pharmacol., 2016; 5(2): 378-83. Doi: 10.18203/2319-2003.ijbcp20160748.
44. Punikhom P, Tiyaworanant S, Suriyakrai S. The Glucose-lowering Effects of the Powder of Momordica charantia L. Fruits on Type 2 Diabetic Patients. J Thai Tradit Altern Med., 2016; 14(1).
45. Mulkalwar, Sarita, Vishwanath Kulkarni, Teja Deshpande, Harshavardhan Bhide, Abhi Patel, and A. V. Tilak. "Anti hyperglycemic Activity of Syzygium Cumini (Jamun) in Diabetic Rats". Journal of Pharmaceutical Research International, 2021; 33(35A): 12-19.
46. Rena G, Hardie DG, Pearson ER. The mechanisms of action of metformin. Diabetologia., 2017 Sep; 60(9): 1577-1585. Doi: 10.1007/s00125-017-4342-z. Epub 2017 Aug 3. PMID: 28776086; PMCID: PMC5552828.
47. Lorenzetti B, Zucco C, Miglietta S, Lamberti F, Bruno G. Oral Hypoglycemic Drugs: Pathophysiological Basis of Their Mechanism of Action. Pharmaceuticals (Basel).,

2010 Sep 15; 3(9): 3005–3020. doi:10.3390/ph3093005. PMID: 27713388; PMCID: PMC4034109.

48. Das, Aurobinda & Mostofa, Mahbub & Hoque, ME & Das, Shobhan & Sarkar, Kamal. COMPARATIVE EFFICACY OF NEEM (AZADIRACHTA INDICA) AND METFORMIN HYDROCHLORIDE (COMET®) IN STREPTOZOTOCIN INDUCED DIABETES MELLITUS IN RATS. Bangladesh Journal of Veterinary Medicine, 1970; 8: 75-80. 10.3329/bjvm.v8i1.8353.
49. Di Magno L, Di Pastena F, Bordone R, Coni S, Canettieri G. The Mechanism of Action of Biguanides: New Answers to a Complex Question. Cancers (Basel)., 2022 Jun 30; 14(13): 3220. Doi: 10.3390/cancers14133220. PMID: 35804992; PMCID: PMC9265089.
50. Solana D, Rossi L, Schianca GP, Maffioli P, Bigliocca M, Mella R, Corlianò F, Fra GP, Bartoli E, Derosa G. Sulfonylureas and their use in clinical practice. Arch Med Sci., 2015 Aug 12; 11(4): 840-8. Doi: 10.5114/aoms.2015.53304. Epub 2015 Aug 11. PMID: 26322096; PMCID: PMC4548036.
51. Bayanati M, Ismail Mahboubi Rabbani M, Sirous Kabiri S, Mir B, Rezaee E, Tabatabai SA. Dipeptidyl Peptidase-4 Inhibitors: A Systematic Review of Structure-Activity Relationship Studies. Iran J Pharm Res., 2024 Oct 29; 23(1): e151581. Doi: 10.5812/ijpr-151581. PMID: 40066124; PMCID: PMC11892788.
52. Hsia DS, Grove O, Cefalu WT. An update on sodium-glucose co-transporter-2 inhibitors for the treatment of diabetes mellitus. Curr Opin Endocrinol Diabetes Obes., 2017 Feb; 24(1): 73-79. Doi: 10.1097/MED.0000000000000311. PMID: 27898586; PMCID: PMC6028052.
53. Lebovitz HE. Thiazolidinedione: the Forgotten Diabetes Medications. Curr Diab Rep., 2019 Nov 27; 19(12): 151. Doi: 10.1007/s11892-019-1270-y. PMID: 31776781; PMCID: PMC6881429.
54. Lu H, Xie T, Wu Q, Hu Z, Luo Y, Luo F. Alpha-Glucosidase Inhibitory Peptides: Sources, Preparations, Identifications, and Action Mechanisms. Nutrients., 2023 Oct 5; 15(19): 4267. Doi: 10.3390/nu15194267. PMID: 37836551; PMCID: PMC10574726.