

**EXPLORING THE POTENTIAL OF CULINARY, NUTRACEUTICAL, AND
PHARMACOLOGICAL APPROACHES AS ADJUNCT THERAPY IN THE PREVENTION
OF DIABETES MELLITUS A REVIEW****Gauri D. Paithankar*, Vikram S. Sarukh, Nikita B. Shejwal Sakshi B. Gaikwad, Pooja B. Lasure, Ramdas Darade**

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ABSTRACT

Diabetes mellitus (DM) is a major global health challenge, with rising prevalence and limitations in current therapeutic options. Conventional medications, though effective, are often associated with side effects, high costs, and limited accessibility, necessitating safer adjunctive strategies. Emerging evidence highlights the potential of culinary practices, nutraceuticals, and pharmacological approaches in preventing and managing diabetes. Plant-derived bioactive compounds and functional foods have shown promise in regulating glucose metabolism, enhancing insulin sensitivity, and reducing oxidative stress. This review discusses the synergistic role of these adjunctive interventions in diabetes prevention, emphasizing their significance in promoting holistic and sustainable healthcare solution This review provides a complete overview of both traditional and modern medicinal plants with verified antidiabetic activities. Key botanicals include *Moringa oleifera*, *Trigonella foenumgraecum* (fenugreek), *Momordica charantia* (bitter gourd), *Syzygium cumini* (jamun), *Azadirachta indica* (neem), *Ocimum sanctum* (holy basil), *Nigella sativa* (black seed), and *Gymnema sylvestre*. Recent studies suggest pancreatic β -cell regeneration, improved glucose absorption through GLUT4, inhibition of α -amylase and α -glucosidase, regulation of PPAR- γ pathways, and lipid-lowering effects. This herbal approach confirms the value of including nutraceuticals into standard diabetic management, particularly in resource-constrained and rural settings. It encourages a transition from symptomatic therapy to preventive, personalised, and patient-friendly interventions. The combination of traditional plant knowledge and modern pharmacological research shows enormous promise for generating safer, more cost-effective, and long term diabetes prevention measures. The potential of several important medicinal plants used to make nutraceuticals for the treatment of diabetes mellitus is updated in this article, along with a suggestion of their biological mechanisms. By using natural bioactive ingredients to regulate blood glucose levels, plant-based nutraceuticals provide a promising new herbal approach to the effective control and treatment of diabetes mellitus.

KEYWORDS: Diabetes mellitus, Herbal Nutraceutical, Global health, blood glucose control, Natural therapy, medicinal plants.**O INTRODUCTION**

A metabolic disease is diabetes mellitus (DM). Chronic hyperglycemia is a symptom of diabetes mellitus (DM), a metabolic disorder that may have defects in insulin production and/or activity as a contributing factor.^[1,2] The multifactorial metabolic condition known as diabetes mellitus (DM) is among the top 10 causes of

death worldwide. Obesity and insulin resistance or insufficiency are the two primary causes of diabetes mellitus development.^[3] Because of aberrant glucose metabolism, diabetes mellitus (DM) results in hyperglycemia, which leads to kidney-related acute and long-term issues, irreversible damage to the retina, arteries, nerves, and bones harm.^[4] The hormone insulin,

which regulates blood sugar levels, is secreted by the pancreas. Diabetes impairs the body's ability to produce or use insulin effectively, leading to a number of short- and long-term issues. One of the most common endocrine (hormone-related) disorders worldwide, diabetes mellitus (DM) is a major public health concern that raises morbidity, mortality, and cost burden considerably.^[5] In 1995, there were an estimated 135 million persons with diabetes; by 2025, that figure is predicted to increase by 300 million.^[6] In 2011, 336 million people had diabetes; this number led to a dramatic change in the statistics, with fresh estimates indicating a dismal future with 552 million cases by 2030.^[7] Today, 175 million instances of diabetes go untreated, affecting almost half a billion people. Globally, 537 million people between the ages of 20 and 79 have diabetes, accounting for 10.5% of all adults. By 2030, this number is expected to rise to 643 million, and if current trends continue, it will reach 783 million by 2045. Go ahead. The burden of diabetes is not evenly distributed. Globally distributed, over 90% of persons with diabetes who are not diagnosed live in low- and middle-income countries.^[8]

Ayurveda, the traditional Indian medical system, classifies diabetes as "Madhumeha," a subgroup of Prameha, a category of urinary disorders. The primary objective of Ayurvedic treatment for Madhumeha is to restore the balance of the Doshas (Pitta, Kapha, and Vata). This is achieved by the use of herbal formulations, dietary changes, and lifestyle modifications. Numerous studies have examined the antidiabetic properties of herbal treatments derived from plants such as *Momordica charantia* (Karela), *Gymnema sylvestre* (Gurmar), *Trigonella foenumgraecum* (Methi), *Azadirachta indica* (Neem), and *Syzygium cumini* (Jamun). These treatments have demonstrated potential in reducing oxidative stress, improving insulin sensitivity, and lowering blood glucose levels.^[9,10]

□ Classification of diabetes mellitus

Within the year 1980, a United Nations body unveiled the first widely recognised classification of diabetes.^[11]

There are four basic forms of diabetes mellitus

1. Type 1 Diabetes (T1DM)

Diabetes type 1 (T1DM), an autoimmune illness, causes insulin insufficiency when the body's immune system mistakenly attacks and destroys the insulin-producing beta cells in the pancreas. This kind of diabetes is most frequently diagnosed in children, teenagers, and young adults, while it can occur at any age. People with type 1 diabetes must take insulin for the remainder of their life in order to manage their condition.^[12]

2. Diabetes Type 2 (T2DM)

The most prevalent kind of diabetes, type 2 diabetes (T2DM), accounts for about 90% of all instances of the disease. One of the main characteristics of type 2 diabetes is insulin resistance, which is the body's cells'

inefficient reaction to insulin. Furthermore, the pancreas may gradually lose its capacity to produce enough insulin to satisfy the body's needs. Type 2 diabetes is typically associated with age, obesity, sedentary lifestyles, and unhealthy lifestyle choices, such as poor eating habits.^[12]

3. GDM, or gestational diabetes mellitus

GDM, or diabetes mellitus during pregnancy, is a form of the disease that typically resolves after giving birth. Type 2 diabetes is more likely to develop in later life in women with a history of GDM. GDM is linked to a higher chance of problems for the growing foetus as well as the mother.^[12,13]

4. Other types of diabetes

These include diseases of the exocrine pancreas (like cystic fibrosis), genetic defects in insulin action, beta-cell function, and drug- or chemically-induced diabetes (like steroid-induced diabetes mellitus).

These unusual kinds of Both the severity of diabetes and the amount of therapy needed can vary.^[13,14]

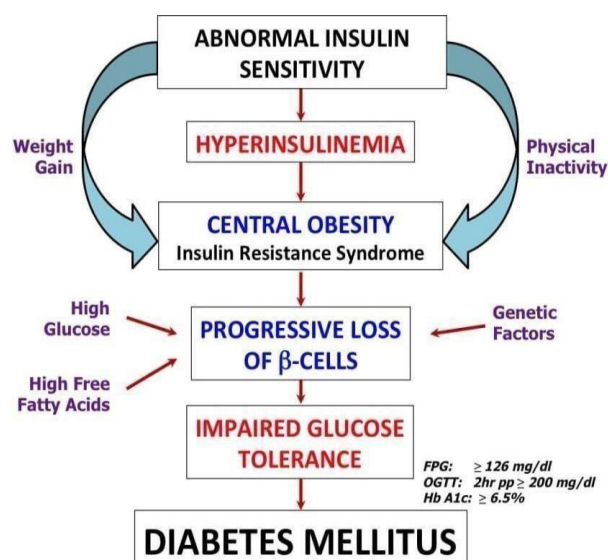


Fig. 1: Pathophysiology of Diabetes mellitus.

• Nutraceuticals

The term "nutraceuticals" was coined by Stephen Defelice, MD, founder and Foundation for Innovation in Medicine, by fusing the terms "nutrition" and "pharmaceuticals" to create "nutraceutical." The term describes products that are distinct from herbal products, dietary supplements (nutrients), specific diets, and processed meals such as cereals, soups, and beverages that are both a source of nourishment and medicine.

A new era of research to improve quality of life is brought about by nutraceuticals. It can reduce the likelihood of sickness by promoting immunity and preserving excellent health. In the US, the term "nutraceutical" refers to products that are regulated as

food ingredients, pharmaceuticals, and dietary supplements.

The term's meaning varies from country to country, but generally speaking, it refers to a food-derived substance that is usually sold in pharmaceutical forms that aren't usually associated with food. One way to characterise a product that contains nutraceuticals is as a substance that gives protection against chronic illnesses or physiological benefits.^[16] Nutraceuticals and functional foods have grown to be. multibillion dollar industries in the worldwide marketplace. Globally, the need to

appropriately label and evaluate the health effects of nutraceuticals is posing serious barriers to growth in this field. useful foods. Currently, the United States of America (USA) has the biggest and the world's fastest growing market for nutraceuticals and functional foods.^[17] These days, there is a lot of interest in nutraceuticals because of their possible medicinal, safety, and nutritional benefits. A study of the market It was recently suggested that the global nutraceuticals The market is growing and is expect to reach \$250 billion USD.

CLASSIFICATION OF NUTRACEUTICALS	
1. BASED ON NATURAL SOURCE	
Plant-based nutraceuticals	Curcumin (Turmeric), Resveratrol (Grapes), Allicin (Garlic)
Animal-based nutraceuticals	Omega-3 fatty acids (Fish oil), Glucosamine (Shellfish)
Microbial-based nutraceuticals	Probiotics (Lactobacillus, Bifidobacterium) Nisin
Marine-based nutraceuticals	Fucoidan (Brown algae) Red algae Astaxanthin (Red-sigae)
2. BASED ON CHEMICAL NATURE	
Polyphenols	Flavonoids, Tannins, Stilbenes
Terpenoids	Carotenoids (Lycopene, β -carotene) Saponins
Alkaloids	Caffeine, Berberine, Theobromine
Organosulfur compounds	Allicin, Sulforaphane
Fibers and Polysaccharides	Inulin, Pectin, Beta-glucan
Fatty acids	EPA, DHA, CLA (Conjugated linoleic acid)
4. BASED ON MECHANISM OF ACTION	
Antioxidant activity	Polyphenols, Vitamins C & E
Enzyme modulation	Berberine (AMPK activation) Curcumin (NF- κ B inhibition)
Hormonal modulation	Isoflavones (Estrogen-like effects) Flaxseed lignans
Gut microbiota regulation	Prebiotics & Probiotics
Forse con commercial formulation	Fortified foods (e.g. probiotic yogurt, omega-3 eggs)

By 2018 .[18]

• Fig 2: classification of Nutraceutical.

Classification of Nutraceutical

Nutraceuticals are general biological treatments intended to enhance health, avoid cancerous procedures and manage symptoms. They are categorised as follows:

- Why nutraceuticals used in diabetic mellitus

The word "nutraceuticals," which combines the words "nutrition" and "pharmaceuticals," refers to a food or component of a cuisine that offers therapeutic or health advantage encompassing both prevention and therapy of an illness.^[10]

Diabetes and diet are possibly the two diseases that are most closely related. Despite being a major factor in its development, diet is also one of the most effective techniques management of diabetes. Using dietary supplements in the management of diabetes, such as vitamins, minerals like chromium, vitamins C and B, and Herbs such as *Gymnema sylvestre* are known to be safe and efficient method for both prevention and blood sugar reduction of problems from diabetes. More significantly, when combined of a diabetic formula that has been clinically proven to work cooperatively for efficient diabetes care and associated issues.^[20] Important natural

products are botanicals, vitamins, minerals, antioxidants, lipids and amino acids (together known as “nutraceuticals” and dietary supplements). Sources of innovative therapies for type 2 diabetes and insulin resistance.^[21] Medicinal plants have the ability to create chemicals that could be used to treat diabetes mellitus.^[22] Traditional herbal medicines are employed as a safe alternative to standard hypoglycemic agents because synthetic treatments in NIDDM and insulin in IDDM have restricted functions and a high risk of adverse drug reactions. Tolerance, resulting in a dosage increase or prescription modification. By Ayurvedic herbs may serve as “potentiators” for these drugs and help diabetics

maintain their quality of life because they are rich in essential phytonutrients. Certain Ayurvedic medicinal plants have enormous potential, and Indian traditional medicine. CSIR has attempted a number of projects, Academics, DBT, and ICMR on the function of herbs nutritional supplements, nutraceuticals, and natural remedies for metabolic diseases such as Diabetes.^[23,24] Bitter melon, fenugreek, cinnamon, turmeric, and berberine are among the nutraceuticals that have demonstrated encouraging antidiabetic effects. Neutaceutical included in herbal dietary supplements have been shown to therapeutic benefits for Type 2 diabetes mellitus.^[25]

○ **Most effective Herbal plant (herbs) used in the treatment diabetes mellitus (DM)**

Sr no.	Plant Name	Botanical name	Family	Part used	Active compound	Mechanism of action	Why it's used
1	Moringa oleifera	Moringa oleifera	Moringaceae	Leaves	Quercetin, cholinergic acid	Improve insulin sensitivity Antioxidant effect	Reduce blood sugar, protect Pancreatic cells
2	Guava leaf tea	Psidium guajava	Myrtaceae	Leaves	Flavonoids Quercetin	Delayed glucose absorption, Antioxidant	Control postmeal sugar spike
3	Aloe Vera	Aloe barbadensis	Liliaceae	Gel, leaves	Aloin Emodin	Stimulates insulin secretion	Balance blood glucose levels
4	Fenugreek	Trigonella Foenumgraecum	Fabaceae	Seeds	4-Hydroxyisoleucine trigonelline	Delayed gastric emptying increase	Control appetite and sugar level
5	Bitter melon	Momordica charantia	Cucurbitaceae	Fruit	Charantin Polypeptides	Insulin mimetic action	Natural insulin like properties
6	Custard apple	Annona squamosa	Annonaceae	Leaves	Flavonoids Tannins	Antioxidant, improve glucose tolerance	Enhance insulin secretion
7	Peepal	Ficus religiosa	Moraceae	Leaves	Tannins phenols	Anti inflammatory, Regulate blood glucose metabolism	Traditional used in ayurvedic treatment
8	Holy basil	Ocimum sanctum	Lamiaceae	Leaves	Eugenol , Ursolic acid	Enhance insulin secretion, Antioxidant	Stabilizes blood glucose levels
9	Amla	Emblica officinalis	Ahyllantha ceae	Fruit	Ascorbic acid Tannins	Increase insulin sensitivity, Antioxidant	Rejuvenates Pancreatic cells
10	Cinnamon	Cinnamomum Zeylanicum	Lauraceae	Leaves Bark	Cinnamaldehyde Cinnamic acid	Increase glucose uptake, mimic insulin	Improve fasting blood sugar
11	Neem	Azadirachta indica	Meliaceae	Leaves bark	Nimbin Nimbidin	Improve insulin response, Antioxidant	Regulate glucose and lipid
12	Jamun	Syzygium cumini	Myrtaceae	Seeds fruit	Jamboline Ellagic acid	Slow starch breakdown enhance insulin activity	Control frequent urination and sugar level
13	Locorice	Glycyrrhiza glabra	Fabaceae	Root	Glycyrrhizin	Antioxidant Anti inflammatory	Reduce oxidative stress in

							Diabetes
14	Black seeds	Nigella sativa	Ranunculac eae	Seeds	Thymoquinone	Preserves beta cells integrity, Antioxidant	Prevent diabetes complications
15	Papaya leaves	Carica papaya	Caricaceae	Leaves	Flavonoids Papain	Improve insulin sensitivit y, Antioxidant	Helps regulate blood glucose levels

Moringa oleifera

Moringa oleifera (MO), also known as the "drumstick tree," belongs to the Moringaceae family. It is the most popular and widely used of the Moringa genus' thirteen species. It originated in the northeastern parts of India.

Bangladesh

Afghanistan, and Pakistan, near the southern Himalayas. Currently grown in tropical and subtropical parts of Asia,

America, and Africa. It is quickly expanding. A perennial tree with a maximum height of 12 meters and a high level of ecological flexibility. Because it can adjust to the most dissimilar soil, temperature, and precipitation conditions, it is exceptionally droughtresistant.^[26,27] Flowers, pods, seeds, and, most notably, leaves contain essential nutrients and nutraceuticals.^[28]



Fig. 3: moringa oleifera.

A growing body of research has indicated that MO may have advantageous roles in the metabolism of fats and carbohydrates.^[29] Nevertheless, there have only been a few clinical investigations on people with diabetes mellitus or glucose intolerance, and the findings have so far been mixed. A meal containing a single dosage of MO markedly increased glucose.^[30]

Numerous studies in sub-Saharan Africa and other regions of the world have documented Moringa oleifera's antidiabetic properties. M. oleifera leaves are appropriate source of leafy green vegetables to lower the risk of diabetes issues in people with diabetes (Giridhari et al., 2011). α amylase and α are inhibited by aqueous extract.

glucosidase; it enhances the antioxidant potential of glucose tolerance and the yeast cell's rate of glucose absorption. The Phytopharmaceuticals can be made from aqueous extract. As an adjuvant for the treatment of diabetes or by themselves.^[31]

Fenugreek

Fenugreek (Trigonella foenum graecum), a widespread annual plant in Egypt, India, and the Middle East, belongs to the Leguminosae family.^[32] Fenugreek seeds are used as a traditional remedy for diabetes and hypercholesterolaemia in Chinese medicine, Ayurveda (Indian medicine), and Unani (Arabic medicine).



Fig. 4: Fenugreek.

Trigonella foenum-graecum, often known as fenugreek, is a popular medical herb with demonstrated antidiabetic effects. Its seeds contain a lot of soluble fibre, especially galactomannan, which slows down the absorption and digestion of carbohydrates. Additionally, 4-hydroxyisoleucine, an uncommon amino acid found in fenugreek, is known to increase insulin production. Fenugreek supplementation has been shown in numerous human and animal trials to significantly lower HbA1c, postprandial glucose levels, and fasting blood glucose in patients with type 2 diabetes mellitus. Fenugreek also contains lipid-lowering properties and helps increase glucose tolerance, which makes it useful for managing metabolic diseases associated with diabetes in general.^[33]

The study by Madar et al. (1988) shown that the usage of powdered fenugreek may be useful in the treatment of diabetics who are not insulin-dependent. 15 g of fenugreek seed steeped in water was linked to

accompanied by a significant drop in postprandial sugar levels.^[34]

Guava leaf

The Myrtaceae family, which includes the common guava tree (*Psidium guajava* Linn.), is indigenous to tropical and subtropical regions. Its fruit is processed into jam and juice and is frequently consumed as food. Guava, or *Psidium guajava* Linn., is also frequently used in traditional medicine. In addition to these applications, Gutiérrez et al.^[35]

The biologically active ingredient or ingredients and underlying mechanisms of guava, which has been used to treat diabetes, have been investigated. The polysaccharides GP70 of guava were found to dramatically lower fasting blood levels and increase glucosylated serum protein (GSP) levels by 21% in individuals with type II.



Fig. 5: Guava leaf.

^[16]By inhibiting tyrosine phosphatase, guava leaf extract significantly reduced the quantity of lipid droplets in the liver of people with type 2 diabetes.^[37] By inhibiting tyrosine phosphatase, an extract from *Psidium guajava* leaves has been shown to have strong anti-diabetic benefits. It can also reduce the quantity of lipid droplets in the liver of people with type 2 diabetes.^[38] Polysaccharides found in guavas have potent antioxidant properties.^[39]

Triterpenic acids and flavonoids, including avicularin and its 3-l-4-pyranoside, which have potent antibacterial properties, are found in guava leaves.^[40] Chronic metabolic disease is known as diabetes mellitus (DM).^[41]

Aloe Vera

Being a xerophyte, aloe vera thrives in extremely dry, desert environments, which are primarily found in

African nations.^[42] Prior to being moved to its own family, the Aloaceae, aloe was a member of the Lily family (Liliaceae).^[43]

The plant *A. vera* is used to manage and treat diabetes. Phytosterols found in the gel have been shown to lower FBGAm in diabetic mice.^[44,45]

Genus +e Aloe is a genus that contains over 450 species and grows in desert, tropical, and subtropical regions. It is a succulent plant that can reach heights of 60 to 100 cm and has either no stem or a short one. Its fleshy, thick, triangular, and spiky leaves^[46] give it the appearance of a cactus, although they are actually from of the lilac (Liliaceae) family. Because of its leaves' capacity to hold onto water, the plant may endure in areas that experience protracted drought, when most other flora withers away.^[47]



Fig. 6: Aloe Vera.

Among the 75 nutrients found in *A. vera* are minerals (calcium, magnesium, sodium, potassium, manganese, copper, zinc, chromium, and iron) and vitamins (folic acid, B12, C, E, and A). They also contain enzymes (carboxypeptidase, amylase, bradykinase, alkaline phosphatase, aliase, sterols, lipase, peroxidase, cellulase, and catalase), lignin, saponins, and salicylic acid.^[48]

These nutrients possess antiviral, anti-inflammatory, immunomodulatory, sugar, lipid, antioxidant, and musculerepairing properties. metabolism, antiseptic qualities, blood thinning, and pain relief.^[49]

Bitter melon

Momordica charantia (MC), commonly known as bitter melon, karela, balsam pear, or bitter gourd, is used by indigenous populations in Asia, South America, India, the Caribbean, and East Africa as a frequent treatment for disorders linked to diabetes.^[49–52] The fruits of bitter melon are consumed as food, but the entire plant—fruits, leaves, roots, and seeds—is used as medicine.



Fig. 7: Bitter Melon.

The chemical components of *Momordica charantia* (Karela) include alkaloids, momordicin and charantin (Figure 3), charine, cryptoxanthin, cucurbitins, cucurbitacins, cucurbitanes, cycloartenols, diosgenin, elaeostearic acids, erythrodil, galacturonic acids, gentisic acid, goyaglycosides, goyasaponins, and cycloartenols.

Lanosterol, lauric acid, linoleic acid, linolenic acid, hydroxytryptamines, gypsogenin, guanylate cyclase inhibitors, karounidiols, momordenol, momordicillin, momorcharaside, and momorcharins Myristic acid, nerolidol, momordicin, momordicosides, momordin, momordolo, oleanolic acid, oleic acid, oxalic acid, proteins, polypeptides, petroselinic acid, pentadecans, peptides, Trypsin inhibitors, uracil, vacine, v-insuline, verbascoside, vicine, zeatin, zeatinriboside, zeaxanthin, zeinoxanthin, rosmarinic acid, rubixanthin, spinasterol, steroidal glycosides, stigmastadiols, stigmasterol, taraxerol, trehalose, etc. Other amino acids include alanine, thscinne, glutamic acid, serine, and aspartic acid.

Citruline, elasterol, flavochrome, lutein, lycopene, pipecolic acid, ascorbigen, gamino butyric acid, and bsistosterol-dglucicide.^[53-54]

According to J. Viridi et al., giving fresh fruit juice orally to both normal and alloxandibetic rabbits at a dose of 6 c.c./kg body weight decreased blood sugar levels.^[55] The purported benefits of *Momardica charantia* fruit juice for diabetes were demonstrated by P. B. Aswar et al. The scientific foundation for the use of *Momardica charantia*

in the treatment of diabetes was established by the results of studies on the fruit extracts' anti-diabetic activity.^[56]

Karela, often known as bitter gourd (*Momordica charantia*), is a popular natural treatment for diabetes mellitus. It contains active ingredients that reduce blood glucose, such as polypeptidep, vicine, and charantin. These bioactive ingredients aid in lowering insulin resistance, increasing insulin production, and improving cellular absorption of glucose. Frequent intake of bitter gourd extracts or juice has been demonstrated to reduce postprandial and fasting blood sugar levels. Bitter gourd is frequently used in dietary and supplemental treatments for type 2 diabetes because of its hypoglycemic qualities.^[57]

Custard apple

Sitaphal, another name for the custard apple (*Annona squamosa*), is Ayurvedic and traditional medicine have traditionally used this herb to treat long-term conditions like diabetes mellitus. The leaves, seeds, and bark of the plant contain a variety of bioactive compounds, including flavonoids (quercetin, rutin), acetogenins (annonacin), alkaloids (anonaine), tannins, and phenolic acids. These active compounds have antidiabetic effects in a number of ways. They help lower blood glucose mostly by inhibiting the α amylase and α -glucosidase enzymes, encouraging peripheral glucose absorption, boosting insulin production, and controlling oxidative stress. The antioxidant and antiinflammatory properties of these phytochemicals also help to maintain the function of pancreatic β cells. Recent pharmacological study supports the traditional usage of *Annona squamosa*

as a possible natural medicine for type 2 diabetes prevention and treatment.^[58]

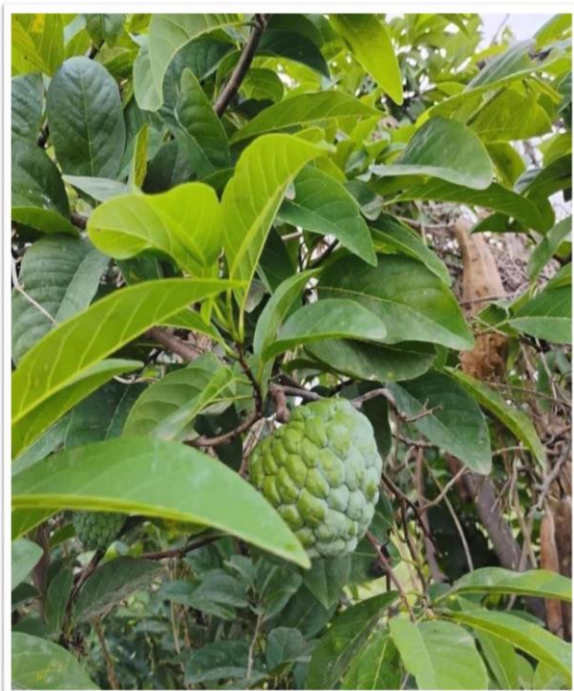


Fig. 8: Custard Apple.

Custard apple (*Annona squamosa* L.), is a popularly recognised fruit crop of India primarily in tropical regions. It is indigenous to the West Indies and is a member of the Annonaceae family (Porwal et al., 2011).^[59] The tropical fruit-bearing plant *Annona squamosa*, sometimes referred to as Sitaphal or custard

apple, is wellknown for its therapeutic qualities, especially in the treatment of diabetes. Its leaves and seeds have long been utilised to decrease blood sugar levels in traditional systems like Ayurveda. The plant's hypoglycemic impact is attributed to a number of pharmacologically active components, including flavonoids (quercetin, rutin), acetogenins, alkaloids, and tannins. These substances work by promoting insulin secretion, improving glucose uptake in peripheral tissues, and blocking digestive enzymes involved in the breakdown of carbohydrates. Furthermore, oxidative stress, a major contributor to diabetes problems, is prevented by the antioxidant action of its bioactive substances. *Annona squamosa* is a promising natural candidate for supplemental diabetes treatment because of scientific evidence supporting its antidiabetic properties.^[60]

Peepal

Due to its sacred association with both Buddhist and Hindu traditions, *F. religiosa*, also known as the "Bodhi tree" or "Tree of Life," is held in particular reverence throughout Southeast Asia, especially in the vicinity of temples. This species, which goes by names like the Sacred Tree and the Tree of Wisdom, offers significant therapeutic benefits. The tree's bark, leaves, seeds, fruits, roots, and latex are all employed for their medicinal properties, but the porous wood itself is not. Each of these components contributes to the plant's valued function in health and wellness and is frequently combined with other herbs for further advantages. They also each have a place in traditional medicine.^[61]



Fig. 9: Peepal.

Across the Indian plains, *Ficus religiosa* (L.), a large, long-lived tree with smooth bark when young, can be found flourishing at elevations of up to 170 meters in the Himalayan region. In Indian culture, this tree, which is frequently planted by roadsides and next to temples, has profound mythical, religious, and therapeutic importance. Across the Indian plains, *Ficus religiosa* (L.), a large, long-lived tree with smooth bark when young, can be found flourishing at elevations of up to 170 meters in the Himalayan region. In Indian culture, this tree, which is frequently planted by roadsides and next to temples, has profound mythical, religious, and therapeutic importance.^[62] β -sitosterol-D-glycoside, which has been linked to hypoglycemic effects, is found in the root bark of *F. religiosa*.^[63] Normal, glucoseloaded, and streptozotocin (STZ)-induced diabetic rats were given oral doses of *F. religiosa* bark extract at 25, 50, and 100 mg/kg. The data showed that blood glucose levels were significantly lower at all three doses, particularly at 50 and 100 mg/kg compared to 25 mg/kg. The bark extract also dramatically reduced serum triglyceride and total cholesterol levels in rats with STZ-induced diabetes, while increasing body weight, blood insulin levels, and the quantity of glycogen in the

liver and skeletal muscle. Furthermore, the pancreas of *F. religiosa* in diabetic rats induced with STZ had a notable antilipidperoxidative activity, indicating the bark's potent antidiabetic properties, especially in the aqueous extract.^[64]

Tulsi

An essential component of the Brahmanic spiritual ritual is the holy basil, or *ocimum sanctum*. On the other hand, "Tulsi" connotes the unmatched.

"Vishnupriya" is an extra name for the person who pleases Lord Vishnu.

This wonder has long been a part of our local culture and is grown in most Indian households and temples. Its botanical name is *Ocimum sanctum*, and it is referred to as Holy Basil in English. It is a member of the family Lamiaceae. There are two forms of tulsi: cultivated and forestland. It has dark leaves and fulfils the same function. Home remedies frequently employ tulsi to treat injuries, hepatic illnesses, respiratory issues, viral infections, earaches, spinal discomfort, hiccups, and conjunctival irritation in newborns.^[65,66]



Fig 10: Tulasi.

In India, the most revered houseplant is called tulsi. It is associated with Hinduism and Ayurveda as the goddess of wealth, well-being, and success. Four species are further classified as follows^[7]: *O. gratissimum* (Vanatulasi), *O.*

tenuiflorum (Krishna-tulsi), *O. sanctum* (Rama-tulsi), and *O. tenuiflorum* (Amrita-tulsi). Due to its potent antidiabetic, antioxidant, and anti-inflammatory properties, holy basil, also called tulsi, is a highly valued medicinal herb in Ayurveda that has long been used to treat diabetes mellitus. Eugenol, caryophyllene, ursolic

acid, rosmarinic acid, and flavonoids including luteolin and apigenin are the primary active ingredients in tulsi.

By enhancing insulin sensitivity, increasing insulin synthesis, and encouraging peripheral tissues to absorb glucose, these compounds aid in hypoglycemic activity. Tulsi also lowers blood glucose levels by inhibiting the liver's processes of gluconeogenesis and glycogenolysis. Additionally, it protects pancreatic β cells from damage caused by oxidative stress. Tulsi supplementation dramatically lowers fasting and postprandial blood glucose levels in both clinical and experimental settings, according to scientific studies.^[68,69] Through a number of biochemical mechanisms, tulsi aids in the treatment of diabetes mellitus. It increases the body's availability of insulin by improving the release of insulin from pancreatic β -cells. Additionally, tulsi increases the sensitivity of insulin receptors in target tissues, such as muscles and adipose tissue, facilitating improved absorption and utilisation of glucose. Additionally, it suppresses the hepatic enzymes that are in charge of glycogenolysis and gluconeogenesis, so hence lowering glucose synthesis in the liver. Its active components' antioxidant properties shield pancreatic β -cells from oxidative stress, maintaining their functionality and halting further harm. Additionally, Tulsi improves glycaemic control by controlling important enzymes involved in the metabolism of carbohydrates. When combined, these measures significantly lower diabetics' postprandial and fasting blood glucose levels.^[69]

° Amla

In traditional Ayurvedic medicine, amla (*Emblica officinalis*), sometimes referred to as Indian gooseberry, is a highly valued medicinal plant that has demonstrated encouraging outcomes in the treatment of diabetes. Vitamin C, tannins, and polyphenolic compounds—all of which have strong antioxidant and antidiabetic effects—are abundant in it. Amla increases insulin secretion, improves glucose absorption, and shields beta cells in the pancreas from oxidative stress, all of which contribute to lowering blood glucose levels. Alphaamylase and aldose reductase, two enzymes involved in the metabolism of carbohydrates, are inhibited by its active constituents, emblicanin A and B, gallic acid, and ellagic acid.

These combined benefits make amla an effective natural treatment for improving glycaemic control and reducing diabetic complications.^[70] The scientific name for amla, which is used in Indian medicine to cure a number of conditions, is *Emblica officinalis* (Eo) or *Phyllanthus emblica*. Amla is a member of the small Euphorbiaceae genus *Emblica*. It can be found growing in tropical and subtropical areas of the Malay Peninsula, China, Indonesia, India, and Sri Lanka.^[71]

Aldose reductase contributes to secondary complications of diabetes, such as cataracts. Amla inhibits aldose reductase and contains antihyperglycemic effects.^[72]



Fig. 11: Amla.

° Cinnamon

The dried inner bark of the Lauraceae family's *Cinnamomum verum* (genuine cinnamon) or

Cinnamomum cassia (Chinese cinnamon) is used to make cinnamon, which has long been used medicinally. Cinnamaldehyde, cinnamic acid, and polyphenols are the

main active ingredients in cinnamon that contribute to its hypoglycemic effects in people with diabetes mellitus. Increased insulin receptor activation, increased cellular uptake of glucose, GLUT-4 translocation stimulation, and inhibition of hepatic gluconeogenesis comprise the mechanism of action (MOA). By stimulating insulin receptors and raising insulin sensitivity, it also functions similarly to insulin. These consequences help lower blood sugar levels. Because of its bioactive components, cinnamon helps treat diabetes by enhancing insulin signalling and lowering inflammation and oxidative stress, two factors that lead to insulin resistance in type 2 diabetes.^[73]



Fig. 12: cinnamon.

Four of the more than 300 plants in the genus *Cinnamomum* are used to make the spice "cinnamon".^[18]

Chinese Cassia (*Cinnamomum aromaticum*) and Ceylon "True" (*Cinnamomum zeylanicum*) are the most widely available varieties of cinnamon.^[74] The most significant components of cinnamon are cinnamonaldehyde and trans-cinnamaldehyde (Cin), which are found in the essential oil and contribute to the scent and many biological activities associated with cinnamon.^[75] In rats with diabetes caused by streptozotocin, cinnamon bark has been shown to have anti-diabetic effects; a component of cinnamon has been dubbed "insulin-potentiating factor" (IPF).^[76]

Cells, which improves endogenous insulin output. Furthermore, neem's antioxidant capacity decreases diabetic complications by neutralising free radicals and decreasing lipid peroxidation. The processes support the use of neem as a herbal supplement for the treatment of type 2 diabetes mellitus (DM).^[77]

° Neem

A popular Ayurvedic herb, neem (*Azadirachta indica*) is used extensively for its antiinflammatory, antidiabetic, and antioxidant properties. Neem's ability to regulate blood glucose levels and enhance insulin sensitivity has shown promise in hypoglycemic advantages for those with diabetes mellitus.

The key bioactive molecules causing these effects include nimbin, nimbidin, azadirachtin, and quercetin. These substances promote glucose absorption, block α -glucosidase and α -amylase enzymes, and protect pancreatic β - cells from oxidative stress. Neem extracts have been proven to repair injured pancreas.



Fig. 13: Neem.

One of the main chronic degenerative diseases is diabetes, which is marked by uncontrolled blood glucose levels (Hieronymus & Griffin, 2015; Joshi et al., 2010; Shori & Baba, 2013; Upreti, Ali, & Basir, 2013). By 2030, diabetes is predicted to rank as the eleventh leading cause of mortality worldwide (Mathers and Loncar, 2006). As the illness worsens, individuals must deal with lifelong financial and physical hardships, which calls for less expensive therapies. The use of neem extracts in pharmacotherapies and other procedures is growing (Al Akeel et al., 2017; Joshi et al., 2010; Mathers & Loncar, 2006).

In a nutshell, there are two types of diabetes. Studies on the impact of neem extracts on both forms of diabetes have produced conflicting findings. As neem extracts are still being studied for their effects and toxicity, we advise against using them directly.^[78] Hyperglycemia, decreased insulin action, and impaired systemic insulin synthesis are the hallmarks of diabetes, a serious public health issue.^[79]

° Jamun

Jamun (*Syzygium cumini*) is also called as traditional medicinal plant used to treat diabetes mellitus. Its seeds, leaves, bark, and fruit pulp provide antidiabetic effects. The primary active ingredients responsible for its medicinal actions are jamboline (an alkaloid), ellagic acid, gallic acid, anthocyanins, quercetin, and flavonoids. Jamboline is known to block starch conversion into sugar, which regulates blood glucose levels. Jamun seeds' polyphenolic constituents protect pancreatic β cells from oxidative damage and improve insulin sensitivity.^[80]



Fig. 14: Jamun illnesses and complications.^[81]

Mycaminose, a component of *Syzygium cumini* Linn. seed kernels, was discovered to have an antidiabetic effect on streptozotocin-induced diabetic rats in Kumar's study. Rats with streptozotocin-induced diabetes were given mycaminose (50 mg/kg), ethyl acetate (200 mg/kg), and methanol extracts of *Syzygium cumini* Linn. seeds (400 mg/kg). Significantly lower blood glucose levels were seen.

The isolated chemical "Mycaminose" and its extracts (ethyl acetate and methanol) have been shown to have antidiabetic actions on streptozotocin-induced diabetic rats.^[82]

° Liquorice

Liquorice, also known as Mulethi, is derived from the root and stolons of *glycyrrhiza glabra* Linn., a member of the Fabaceae family. This perennial herb, native to Southern Europe and parts of Asia, is well known for its sweettasting root, which is mostly owing to the presence of the chemical glycyrrhizin. Liquorice has long been used in conventional medicinal systems including.

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(TCM) due to its antiinflammatory, antioxidant, and antidiabetic effects. Licorice's active ingredients, including glycyrrhizin, glabridin, and liquiritigenin, contribute to its medicinal applications, particularly in liquorice.^[83]

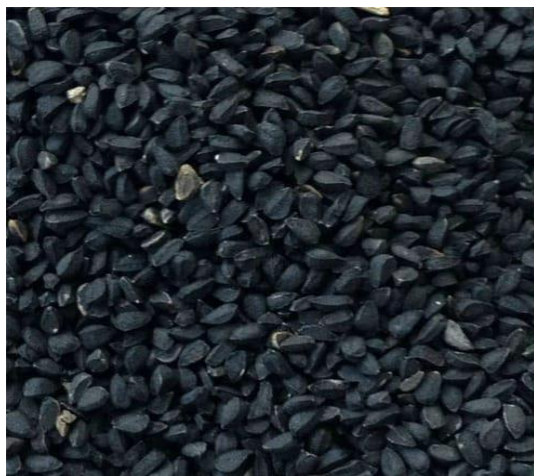


Fig 15: Liquorice.

Liquorice (*Glycyrrhiza glabra*) has demonstrated promising antidiabetic efficacy due to the presence of many bioactive ingredients, including glycyrrhizin, glabridin, liquiritigenin, and isoliquiritigenin. Due to its antiinflammatory and antioxidant qualities, glycyrrhizin shields pancreatic β -cells from oxidative damage, a significant issue in diabetes. One important flavonoid, glabridin, improves insulin sensitivity and controls glucose metabolism by activating PPAR- γ . By inhibiting the α -amylase and α -glucosidase enzymes, liquorice extracts slow down the breakdown of carbohydrates and lower postprandial hyperglycemia.

Liquorice flavonoids promote better glycaemic management by increasing insulin secretion and decreasing pro-inflammatory cytokines including TNF- α .

and IL-6. The potential of liquorice as a natural medicine to treat type 2 diabetes mellitus is supported by these integrated pathways.^[83]



° Black seeds

The herb *Nigella sativa*, also known as black seeds, belongs to the Ranunculaceae family. Chronic conditions like diabetes, hypertension, cancer, obesity, and more have all been treated using *N. sativa*.^[84]



Fig 16: Black seeds.

Thymoquinone, nigellone, flavonoids, tannins, and saponins are among the bioactive components found in its seeds that support its anti-diabetic effects. The most potent of these substances is thymoquinone, which is well known for its hypoglycemic, anti-inflammatory, and antioxidant qualities. By enhancing insulin release from pancreatic β -cells, improving peripheral tissue insulin sensitivity, and lowering oxidative stress, which shields β -cells from damage, black seed enhances the treatment of diabetes. Additionally, it decreases intestinal glucose absorption, which lowers blood sugar levels after meals. Regular use of *Nigella sativa* (typically 1-3 grammes of powder or 500 mg capsules twice daily) has been shown in clinical research to significantly reduce fasting blood glucose and HbA1c levels while also improving lipid profiles. *Nigella sativa* supplementation for 12 weeks improved glycaemic control in individuals with type 2 diabetes, according to a study published in the Saudi Journal of Biological Sciences (Bamosa et al., 2015). As a result, black seed exhibits promise as a natural supplement for the management and prevention of diabetes.^[85]

° Papaya plant

Papaya (*Carica papaya* L.) is called as tropical plant belonging to the family Caricaceae. The biological source of papaya includes the fresh or dried parts of its fruit, seeds, and milky latex. It is prized for its nutritional and therapeutic qualities and is extensively grown in tropical and subtropical areas. In addition to being high in vitamins A, C, and E, papaya fruit also contains papain, a proteolytic enzyme that facilitates digestion and is frequently used to treat indigestion and other gastrointestinal issues. Papaya seeds have long been used to get rid of intestinal worms because of their anthelmintic qualities. Papaya leaves have also drawn notice for their hypoglycemic properties, which may help

treat diabetes mellitus by reducing blood glucose levels. Additionally, the plant has antiinflammatory, antioxidant, and wound-healing qualities, which make it beneficial for skin care and conventional wound and acne treatments.

Moreover, papaya leaf juice is popularly used in some regions for managing dengue fever due to its ability to increase platelet count. Overall, papaya is a versatile plant widely used in folk medicine and modern research supports many of its health benefits.^[86]



Fig 17: papaya plant.

The chemical composition and distribution of bioactive substances vary significantly among leaves, pulp, seed, and fruit.^[87] It has been discovered that some papaya tree parts contain antihyperglycemic properties. Aqueous and ethanolic papaya leaf extracts effectively reduced hyperglycemia in rats receiving streptozotocin (STZ) and alloxan, two diabetic drugs.^[88-91] For three or seven days, extracts were administered at low or high doses to rats with alloxan-induced diabetes (180 mg/kg), along with glimepiride at 0.2 and 0.4 mg/kg and metformin at 50 and 100 mg/kg body weight, respectively. At 5 mg/kg bodyweight, papaya leaf extracts produced results similar to those of metformin (50 mg/kg) and glimepiride (0.2 mg/kg), although with a delayed onset of action. Combining papaya leaf extract with high dosages of glimepiride considerably increased its onset impact ($p < 0.01$) when compared to glimepiride monotherapy. Additionally, the decrease in blood glucose at 24 hours was highly significant ($p > 0.001$), and the effect persisted for 72 hours, with the exception of the low glimepiride low papaya leaf combination. This suggests that papaya leaf extract can interact with cells directly or in a complementary way to produce a hypoglycemic effect.^[92]

○ Mechanism of action of herbal nutraceutical

Herbal medications and nutraceuticals often exhibit multi-target, multichannel, and synergistic characteristics due to the diverse elements found in each natural product. Herbal medications and nutraceuticals may help manage diabetes and associated vascular consequences by targeting multiple pathways. Herbal medications have been used in traditional Chinese, Ayurvedic, and Unani medicinal practices for ages to treat various diseases, as evidenced by clinical records. Herbal medicines and nutraceuticals offer safe and effective alternatives to pharmaceutical medications, which often have limited therapeutic efficacy and undesirable side effects. Since the majority of claimed therapeutic effects depend on practitioner experience and historical records, the effectiveness, safety, and purity of herbal medicines have emerged as major concerns. Natural products are manufactured using a particular recipe and are frequently sold without a prescription. Scientific testing of efficacy and mechanism of action is frequently lacking. The quality of a natural preparation cannot be reliably determined by the pharmaceutical method of analysing a single component. Quality control methods that adopt a comprehensive approach to complementary medicine must be developed in order to assess the chemical basis of herbal remedies and nutraceuticals.^[93]

Plant-based nutraceuticals have received attention for their ability to modify blood glucose levels through a variety of pathways, potentially providing additional benefits in diabetes care. The mechanism includes.

1. Enhancing insulin secretion

Herbs like *Gymnema sylvestre* and *Panax ginseng* stimulate β -cells in the pancreas, increasing endogenous insulin synthesis.

Gymnemic acids imitate glucose molecules and interact with taste receptors and pancreatic β -cells to increase insulin production.

2. Improving insulin sensitivity

Berberine (from *Berberis aristata*) and catechins (from green tea) enhance insulin receptor sensitivity and diminish insulin resistance in peripheral tissues.

They activate the AMP-activated protein kinase (AMPK), which increases glucose absorption and fatty acid oxidation.

3. Preventing Carbohydrate Digestion and Absorption

Plants such as *Salacia reticulata* and *Momordica charantia* inhibit α -glucosidase and α -amylase enzymes, which slows carbohydrate digestion and absorption. 5. Increasing Glucose Uptake.

Compounds in *Moringa oleifera* and *Trigonella foenum-graecum* (fenugreek) promote GLUT4 translocation, which improves peripheral glucose absorption by muscle and adipose tissues.

4. Antioxidant and anti-inflammatory effects

Numerous herbal nutraceuticals, including *Embolia officinalis* (amla) and *Curcuma longa* (turmeric), reduce inflammation and oxidative stress linked to diabetes-related issues. Curcumin lowers proinflammatory cytokines and inhibits NF- κ B.

5. Regeneration of Pancreatic β -cells

In experimental studies, several herbs (such as *Tinospora cordifolia* and *Ocimum sanctum*) have demonstrated the ability to repair or preserve pancreatic islet cells.^[94-99]

Advantages of herbal conventional therapy for nutraceuticals

Plant-based nutraceuticals have several distinct advantages over traditional antidiabetic treatments. Most synthetic medications used to treat diabetes, such as sulfonylureas or metformin, are associated with side effect such as gastrointestinal pain, hypoglycemia, or long-term organ damage. Nutraceuticals sourced from natural sources, particularly medicinal plants, are generally more tolerable and have fewer adverse effects. They provide multi-targeted activity by altering glucose metabolism, increasing insulin sensitivity, lowering oxidative stress, and inhibiting inflammation. This comprehensive approach is especially effective for chronic disorders such as type 2 diabetes, which involve intricate metabolic processes. Furthermore, herbal nutraceuticals are frequently less expensive and more widely available, making them appropriate for long-term

use in low-resource situations. Furthermore, they are more culturally acceptable and can be incorporated into regular meals as functional foods or drinks. However, greater standardisation and clinical validation are required to assure efficacy and safety across populations.

- 1) Compared to synthetic drugs like metformin or sulfonylureas, nutraceuticals have less adverse effects, such as hepatic, renal, and gastrointestinal problems.
- 2) Multi-Targeted Mechanism of Action: Chemicals derived from plants control oxidative stress, lower inflammation, and increase insulin sensitivity.
- 3) Enzyme Inhibition Activity: By inhibiting enzymes that hydrolyse carbohydrates, such as α -amylase and α -glucosidase, herbal remedies might reduce postprandial glucose levels.
- 4) Pancreatic β -Cell Support – Herbs like *Gymnema sylvestre* help regenerate and function insulin-secreting β -cells in the pancreas.
- 5) Improved Lipid Profile – Nutraceuticals can control dyslipidaemia by lowering LDL, triglycerides, and increasing HDL, reducing cardiovascular risk.
- 6) Preventive and Therapeutic Roles: - Nutraceuticals can prevent disease progression in prediabetics and those with metabolic syndrome, in addition to treating diabetes.
- 7) Low Risk of Hypoglycemia: These medicines are safe for long-term usage, particularly in elderly or polypharmacy patients, as they do not induce abrupt reductions in blood glucose levels.
- 8) High in Antioxidant and anti-inflammatory compound. Polychemicals. Such as polyphenols and flavonoids help to lower oxidative stress and inflammation which are key contributors to diabetes.^[100-104]

CONCLUSIONS

Traditional herbal remedies play an important role in alternative medicine. Herbal nutraceuticals, a safe, natural, and multitargeted substitute for conventional pharmacotherapy, have become a promising therapeutic approach in the management of diabetes mellitus. These nutraceuticals have strong antidiabetic effects and are made from medicinal plants that are abundant in bioactive compounds like flavonoids, alkaloids, polyphenols, saponins, and terpenoids.

Despite their potential, the therapeutic use of herbal nutraceuticals is hindered by plant composition diversity, a lack of dosage standardisation, and a scarcity of large-scale clinical trials. Addressing these gaps through scientific validation, regulatory backing, and quality assurance methods will be critical for incorporating herbal nutraceuticals into standard diabetic care.

Finally, herbal nutraceuticals provide a holistic and integrative approach to diabetes control, combining traditional medical knowledge with modern healthcare demands.

They will play a significant role in the future of individualised and preventive diabetic care because of their capacity to slow the progression of the disease, lessen complications, and enhance quality of life. The main anti-hyperglycemic qualities of plants and their substances are highlighted in this review. All of the findings reported here lend credence to the medicinal potential of antidiabetic plants and their constituents, which may be utilised as nutraceuticals to reduce the symptoms of diabetes and enhance quality of life. The use of Ayurvedic herbs as a safer and more effective nutraceutical supplement for diabetes has been examined and validated by hundreds of experimental and clinical studies.

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