

# Role Of Phyto Nutraceuticals In Management Of Hyperglycemia

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## Abstract

Due to the presence of therapeutically significant phytochemicals, medicinal plants have great promise in the treatment of a wide range of illnesses. Diabetic symptoms may be alleviated by a variety of drugs on the market, including insulin. However, these over-the-counter medications are costly and have several side effects. Herbal treatments are becoming more popular since they are both affordable and effective, with fewer adverse effects. This research includes information about diabetic-treating medicinal herbs. This review will summarise and classify research on medicinal plants with anti-diabetic properties, as well as prospective routes for additional investigation. A comprehensive search for medicinal plants with anti-diabetic properties was carried out using many search engines, such as Google Scholar, PubMed, Science Direct, and other online journals and books. Asian countries contain a vast array of plants that have been used by traditional practitioners to treat a wide range of illnesses. More than 80 plants that have been shown to have antidiabetic, anti-hyperglycemic, hypodiabetic, and insulin mimic properties have been gathered for this research. This review contains useful information on the different medicinal plants that are used to treat diabetes-related issues. Research on the plant's active compounds and mechanisms may be done.

**Keywords:** Diabetes, medicinal plants, antidiabetic, antihyperglycemic, hypoglycemic

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## Introduction

Medicinal herbs serve an essential part in the treatment of diabetes mellitus, a serious metabolic disorder. Traditional herbs have been discovered to offer significant anti-diabetic properties without any unwanted side effects. Anti-diabetic compounds present in these foods include flavonoids, alkaloids, phenolics, and tannins, which help the pancreas operate better by increasing insulin production or restricting glucose absorption via the intestinal tract. Diabetes has been treated with the use of 410 medicinal plants, but only 109 of these have been studied in depth for their mechanisms. Plant extracts

have been demonstrated to influence several metabolic processes including glycolysis, gluconeogenesis,

the Krebs cycle, glucose production/depletion, insulin synthesis, cholesterol production, and carbohydrate metabolism/absorption(1, 2). When it comes to the endocrine illness known as diabetes mellitus (DM), unusually high blood glucose levels are a symptom. Type 2 diabetes in adults is mostly caused by a shortage of insulin production in the pancreas' -Langerhans islet cells or a failure in insulin absorption in the peripheral tissues. Insulin hormone is released by the pancreas in response to a rise in blood glucose levels that occurs after eating. To lower blood sugar levels, insulin stimulates the liver to break down glucose, which is then eliminated from the bloodstream via fat digestion and muscle cell expulsion. Diabetics have high blood sugar levels due to the pancreas' inability or unwillingness to make adequate insulin. India is referred to be the "capital of diabetes" since it has more than 61 million people who suffer from the condition. As a result of inadequate health care, inadequate equipment, and other obstacles, India has difficulty efficiently managing diabetes and its repercussions. In the treatment of diabetes and its complications, herbal formulations are recommended over synthetic ones due to their lower risk of adverse effects and lower cost. Indian medicinal plants with anti-diabetic qualities are examined in this research, which relies on online electronic literature data(3-5).

### **Medicinal plants with antidiabetic activities**

#### **Aegle marmelos (L.) Corrêa (Wood apple)**

Wood apple (*Aegle marmelos* L.) Corrêa (Rutaceae) is a vital medicinal tree that grows in India's northern areas. As a laxative, the fruit of this tree has been used to treat dysentery and peptic ulcers, among other maladies. On an empty stomach every day, the Tripuri tribe in North East India drinks the juice of this fruit. Leaf paste is used to treat high fever caused by malaria. The fresh leaf decoction is used by the Theni district tribes of Tamil Nadu, India to calm the body and treat many diseases, including cough, eye problems, breast pain, and more. Streptozotocin-induced diabetic Wistar rats were treated twice daily for four weeks with oral aqueous extract of *A. marmelos* fruit, which significantly reduced blood sugar levels. The normal drug, glibenclamide, was less effective at this dosage. Streptozotocin-induced damage to pancreatic islets was partially restored by an aqueous fruit extract in a study conducted by Kamalakkannan and Prince (2005)(6-8). As with the leaf extract, the methanolic extract of the powdered callus of *A. marmelos* shows anti-diabetic properties. the aqueous seed extract of *A. marmelos* at a dosage of 250 mg/kg for 14 days decreased glycemic levels and stabilized lipid profiles in normal and severely diabetic rats. The glucose tolerance of diabetic and pre-diabetic rats was also enhanced. Supplementing diabetic rats with *A. marmelos* ethanolic extract (150 mg/kg for 30 days) may help avoid excess reactive oxygen species damage in streptozotocin-induced diabetic rats. Blood glucose and insulin levels were reduced, and insulin receptors were more sensitive to the hormones required to control blood sugar levels, in rats fed an aqueous fruit and leaf extract of *A. marmelos* (450 mg/kg for 21 days). An anti-diabetic and lipolytic compound (3,3-dimethylallyl) halfordinol has been found in the leaves of *A. marmelos*. The chloroform extract of *A. marmelos*, which included the terpene limonene, showed significant antiglycation properties when compared to the commonly used inhibitor aminoguanidine. These anti-hyperglycemic components, including aegelin and lupeol, have been found in the bark of *A. marmelos* and are hypoglycemic agents. Furthermore, diabetic rats' pancreatic beta cells were repaired by the bark extract. The aqueous fruit extract of *A. marmelos* was discovered to boost insulin sensitivity and restore beta-cell function in the pancreas by increasing the expression of

the peroxisome proliferator-activated receptor- $\gamma$  (PPAR $\gamma$ ). Extraction of Angelina marmelos leaves led to the discovery of various novel compounds, including anhydromarmeline and aegelineoside, which block  $\alpha$ -glucosidase to a high degree. Analyses of the enzyme  $\alpha$ -glucosidase revealed that anhydromarmeline was similarly very effective against it(9-11).

### **Coriandrum sativum L. (Coriander)**

Component of food Apiaceae family *Coriandrum sativum* L. offers both medicinal and nutritional properties. Extraction of ethanolic coriander stem and leaves extract from diabetic Wistar rats was shown to be hepatoprotective, hypoglycemic, hypolipidemic, and enhanced antioxidant capacity. Using an aqueous extract of coriander seeds, researchers were able to normalize blood glucose levels, decrease insulin resistance, and drop levels of total cholesterol and triglycerides in rats given a high-calorie diet(12-14). Using ethanol extract from coriander seeds (200 mg/kg body weight) to treat streptozotocin-induced diabetic rats, researchers were able to increase the insulin-releasing capacity of beta cells in pancreatic islets while simultaneously lowering blood glucose levels(15-17).

### **Zingiber officinale Roscoe (Ginger)**

Roscoe (ginger), a Zingiberaceae family member, has several health benefits. Asthma, gingivitis, toothache, high blood pressure, diabetes, sprains, and sprain-induced muscular soreness have all been traditionally treated with ginger rhizomes. The rhizomes of ginger have also traditionally been used to treat infectious diseases such as influenza and pneumonia. Ginger has been found to decrease blood sugar, enhance insulin sensitivity, reduce inflammation, and lower cholesterol and triglycerides by the use of the herb. Adding 3 grams of powdered ginger per day to the diet of type 2 diabetes for three months resulted in a better glycemic index and antioxidant status(18, 19). Insulin levels in type 2 diabetics were reduced by oral ginger supplementation (2 g/day), with no significant changes in fasting plasma glucose or glycated hemoglobin concentrations. In STZ-induced diabetic mice, hydroalcoholic ginger extracts significantly reduced heart structural abnormalities and improved blood leptin and apoprotein levels, as well as catechin G and homocysteine concentrations. Increasing insulin production and glucose absorption in muscles through cell surface presentation of GLUT-4 transporters and enhanced glycogen synthase 1 activity were all seen in diabetic mice treated with gingerol at a dose of 200 mg/kg/b.w. Ginger extract (500 mg/kg/b.w.) enhanced peripheral glucose absorption and corrected kidney and liver glycolytic deficits in diabetic rats by lowering gluconeogenic output(20-22).

### **Syzygiumcumini (L.) Skeels (Black plum)**

The Myrtaceae family includes *Syzygiumcumini* (L.) Skeels, a plant native to the Indian subcontinent, eastern Africa, and Southeast Asia. The Himalayan tribes of Sikkim and Darjeeling use a decoction of stem bark to treat diabetes mellitus. Diabetic Wistar rats received oral treatment of ethanolic and aqueous extracts of *S. cumini* bark (500 mg/kg for 21 days) and saw significant blood glucose-lowering effects. Extracts of *S. cumini*'s crude hydroalcoholic leaf extract were shown to protect against DNA damage and oxidative stress by exhibiting hypolipidemic and hypoglycemia properties, respectively. The phenolic and myricetin content of the leaf is to blame for these effects. 3T3-L1 and L6 myotubes were stimulated by the methanolic seed extract of *S. cumini*, which contained vitalboside A, an insulin

sensitizer, to enhance glucose transport. Insulin sensitizing, anti-oxidant, anti-dyslipidemic, anti-inflammatory, and cell-protective activities were found in type 2 diabetic rats administered an aqueous extract of *S. cumin* seeds(23, 24). Oral administration of ethyl acetate fractions significantly altered blood glucose and cholesterol levels. Glycogen levels in the muscles and the liver were also significantly altered by the disease. Diabetic rats given therapy saw an increase in the volume and size of their pancreatic islets. Scientists found that an *S. cumin* seed extract rich in flavonoid flavonoids improved insulin release from the pancreatic islets in diabetic rats and decreased triglyceride and LDL levels in the blood. These activities are attributed to the dual upregulation of the peroxisome proliferator-activated receptors (PPAR $\alpha$  and PPAR $\gamma$ ). An ethanolic extract of *S. cumini* seed seeds decreased blood sugar levels while increasing body weight in diabetic mice treated with alloxan. *S. cumini* seed extract (100 mg/kg for 21 days) may help diabetics control hyperglycemic and inflammatory conditions. Diabetes Mellitus pathophysiological symptoms are also protected by it. The hypoglycemic and lipid-lowering activities of *S. cumin* seeds have been shown for chromium, potassium, sodium, and vanadium(25, 26). In diabetic rats, oral administration of *S. cumini* kernel extract demonstrated greater hypoglycemic activity as compared to the whole seed extract. Nanoparticles derived from the seeds of *S. cumini* have a higher antioxidant activity than the extract(27, 28).

#### ***Coccinia grandis* (L.) Voigt (Ivy gourd)**

For its hypoglycemic and antidiabetic effects on the human body, Cucurbitaceae plants like *CocciniaGrandis* Voigt and *CocciniaIndica* Wight & Arn. are well-known. Some research suggests that *C. grandis* (*C. indica*) fruit has renoprotective properties due to its ability to enhance diabetic rats' glucose tolerance as well as their urine sugar, albumin excretion, kidney index, and kidney glomerular filtration rate (GFR). *C. indica* (*C. grandis*) leaf extract has been shown to have anti-ureogenic, anti-hyperglycemic, antioxidant, hypoglycemic, and hypolipidemic activities in studies on diabetic rats(29, 30). Research on diabetic patients found that the dried extract of *C. indica* (*C. grandis*) had an insulin-mimicking effect by correcting elevated glycolytic pathway enzymes (G-6-p (ase) and LDH) and by restoring lipolytic pathway LPL activity. *C. grandis* fruit methanolic extract had an IC50 value of 6.12 g/mL and inhibited in vitro aldose reductase activity against partially purified bovine lens aldose reductase by 96.6 percent. This is due to the fruit's high phenolic and flavonoid content(31-33).

#### ***Allium sativum* L. (Garlic)**

On account of its high concentration of non-protein sulfur amino acids, garlic has long been recognized for its medicinal capabilities as a member of the *Allium* genus within the Alliaceae family. Diabetic rats given *A. sativum* extract with glibenclamide, a commercially available drug, gained weight and had better hypoglycemic effects. The antihyperlipidemic and improved glycemic control reported in a comparable experiment was in diabetic patients treated with commercially available drug metformin and garlic supplements(34, 35). Fresh garlic homogenate (250 mg/kg b.w.) for six weeks increased the antioxidant state of blood and cardiac tissues in diabetic Wistar rats. As a possible treatment for hypertension and nephropathy caused by overactive Ang II signaling, garlic extract was shown to lower the expression of the angiotensin AT1 receptor in STZ-induced diabetic rats' adrenal and renal tissues.

Anti-diabetic effects of garlic extract are superior to those of glibenclamide, a popular medication(36, 37).

### **Momordica charantia L. (Bitter melon)**

It has long been used in herbal medicine for its immunomodulatory, hepatoprotective, anti-diabetic, anti-tumor, and antioxidant properties of *Momordica charantia* L., a member of the Cucurbitaceae family of plants. CEMC at 200 mg/kg/day resulted in considerable weight loss and decreased non-fasting blood glucose levels, as well as a reduction in insulin resistance, according to the findings of research on type 1 and type 2 diabetic rats. Type 1 ICR 48 mice that were infected with STZ showed an increase in insulin sensitivity, but their plasma glucose tolerance was unaffected. This shows that instead of protecting T2D patients from  $\beta$ -cell malfunction, CEMC may help enhance insulin sensitivity in T2D individuals. Male OLETF rats were given a 3% bitter melon supplementation orally to increase their glucose tolerance and insulin sensitivity(38, 39). Additionally, there was an improvement in blood glucose tolerance as well as insulin sensitivity in the blood as a consequence of this treatment. Insulin receptor substrate-1 phosphorylation (Tyr612) and phosphorylation of Akt (Ser473) were both significantly enhanced, although nuclear factor- $\kappa$ B activation (NF- $\kappa$ B) was decreased. For 28 days, rats administered *Momordica* fruit extract (1.5 g/kg b.w.) increased their body weight and had greater levels of superoxide dismutase, glutathione, and catalase in their cardiac tissues, demonstrating the extract's anti-hyperglycemic, cardioprotective, and anti-oxidative qualities. In STZ-induced diabetic mice, *M. charantia* juice produced a response akin to insulin, reducing glucose absorption into brush border vesicles in the jejunum and increasing glucose uptake in muscle cells. This was observed(40, 41).

### **Phyllanthus Emblica L. (Indian gooseberry)**

*Phyllanthus Emblica* L. (synonym: *Emblica Officinalis* Gaertn. ), a member of the Euphorbiaceae family, is often known as Amla and plays an important role in Ayurvedic medicine. The bulk of its biological activity is attributed to its high polyphenol content, primarily in the form of tannins and flavonoids. Anti-inflammatory, anticancer, immunomodulatory, and anti-hyperglycemic properties of the herb *E. Officinalis* (also known as *P. emblica*) have been examined for their ability to stabilize glucose levels and promote glucose metabolism(42, 43). This supplement also aids insulin secretion and  $\beta$ -cell regeneration. Fasting blood glucose levels were decreased and oral glucose tolerance was raised in type 2 diabetic rats (1.25 g/10 mL/kg body weight) after eight weeks of treatment with *E. Officinalis* (*P. emblica*). Participants in the Akhtar et al. (2011) experiment who took 3 g of *E. officinalis* (*P. emblica*) powder daily reported significant decreases in total lipids, an increase in HDL cholesterol, and a drop in LDL cholesterol. Eight weeks of therapy with 1 mL/kg/b.w. of fruit juice from *E. Officinalis* (*P. emblica*) decreased excessive hyperglycemia, oxidative stress, hyperlipidemia, and improved cardiac antioxidant defense mechanisms in STZ-induced diabetic Wistar rats. Polyphenol-rich extracts of *E. officinalis* (*P. emblica*) ethyl acetate were shown to strongly suppress the synthesis of glycosylated end products in streptozotocin-induced diabetic mice(44-46).

### **Gymnemasylvestre (Retz.) R.Br. ex Sm.**

For its anti-cancer, anti-disease, and neuroprotective properties, *Gymnema Sylvestre* is an important medicinal plant in the Apocynaceae genus. To treat diabetes mellitus, people in the southern Western Ghats of Tamil Nadu in India consume the dried and powdered leaves of this plant with milk. In *G. Sylvestre*, often known as gurmar, gymnemic acids, triterpenes, *Gymnema saponin*, and other phytoconstituents are assumed to be responsible for the herb's sweet-destruction characteristics(47-49). Anti-obesity and anti-inflammatory and anti-diabetic properties are attributed to the plant's gymnemic acid, gurmarin, tartaric acid, stigmasterol, betaine, and choline components. Its hypoglycemic effects may be because it regenerates islet cells and decreases gastrointestinal glucose absorption. The supplement also increases glucose intake and enzyme activity (phosphorylase), both of which are necessary for glucose utilization. When the pancreas is stimulated by *G. Sylvestre*, insulin production increases(50-52).

### **Conclusion**

Diabetes, the most common endocrine disease, affects about 100 million people worldwide. In the recent decade, the number of diabetics in India, traditionally regarded as the world's diabetes capital, has increased substantially. Medicinal breakthroughs including the discovery of biguanides, thiazolidinediones, and insulin paved the way for the development of several medications. These drugs, despite their hypoglycemic benefits, typically induce adverse effects such as renal issues, tiredness, nausea, vomiting, and diarrhea. Since herbal medicine has fewer adverse effects and greater therapeutic results, it is being reinvented for these reasons. This research summarises the list of Asian medicinal herbs with anti-diabetic activity. Native peoples throughout the world have used these plants for generations to treat a wide range of ailments. Several pharmacological studies have demonstrated that these medicines may be useful in the treatment of diabetes mellitus because of their hypoglycemic, antilipidemic, and insulin mimicking properties. Anti-diabetic plant active components and possible avenues for future research are discussed in this review.

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