

## A Review: Anti-Diabetic Activity of Herbal Drugs

**Dwiti Modak**

Ayurvedic Pharmacy, Lovely School of Pharmaceutical Sciences,  
Lovely Professional University, Phagwara, Punjab, India  
*dwiti.modak@rediffmail.com*



### ABSTRACT

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia resulting from increased hepatic glucose production, diminished insulin secretion and impaired insulin action. Though diabetes is a global problem so the present study aims to open new avenue to explore the antidiabetic activity of various medicinal plants on a firm scientific footing and different market formulation which add value as novel antidiabetic drug.

**Keywords:** Diabetes mellitus, insulin secretion, antidiabetic drug

### INTRODUCTION

**Anti-diabetic drugs** treat diabetes mellitus by lowering glucose levels in the blood. Traditional Medicines derived from medicinal plants are used by about 60% of the world's population. This review focuses on Indian Herbal drugs and plants used in the treatment of diabetes, especially in India. Diabetes is an important human ailment afflicting many from various walks of life in different countries. In India it is proving to be a major health problem, especially in the urban areas. Though there are various approaches to reduce the ill effects of diabetes and its secondary complications, herbal formulations are preferred due to lesser side effects, low cost and because of their natural origin. Though different types of oral hypoglycemic agents are available along with insulin for the treatment of diabetes, there is increased demand by patients to use the natural products with anti diabetic activity. It is a considerable discharge of urine, for the most part excessive, of a violent smell and sweet taste and attended with great thirst and general debility.<sup>[1]</sup>

In this disease, the animal salts are deficient in the urine, while sugar is secreted in considerable quantity, and these means are calculated to yield the former, and to counteract the later, at the same time that they are capable of correcting the morbid action of the digestive organs.

Diabetes mellitus is one of the common metabolic disorders characterized by hyperglycemia due to absolute or relative deficiency of insulin and results in significant morbidity and mortality. Diabetes, by

itself, increases the production of tissue damaging oxidative stress. Therefore, in diabetes the oxidative stress is referred as a case of double jeopardy for any beta cells that survive the disease.

### DIABETES

**Diabetes or Madhumeha** as per ayurveda is a disease in which there is improper functioning of insulin and as a result sugar level in the blood increase. Diabetes may cause heart problem, kidney failure, blurred vision if not treated timely.

Diabetes mellitus is increasing alarmingly worldwide and is defined as the abnormal glucose tolerance which affects pancreatic beta cells functions and sensitivity leading to progression of diabetes and its related complications. It is a chronic disorder of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar level and an increased risk of vascular complications. It is the most common endocrine disorder in men and women, and the major public health problem of epidemic proportions, once believed to be a disease of the west, is becoming an endemic to modernizing and urbanizing population in our country. Ayurvedic literature reveals that since the time of Charak and Sushrut many herbal medicines in different oral formulations have been recommended in Madhumeha (diabetes mellitus) and confident claims of cure are on record.<sup>[2]</sup>

**TYPES OF DIABETES:** Diabetes mellitus type 1 is a disease caused by the lack of insulin. Insulin must be used in Type I, which must be injected or inhaled.

Diabetes mellitus type 2 is a disease of insulin resistance by cells. Treatments include (1) agents which increase the amount of insulin secreted by the pancreas, (2) agents which increase the sensitivity of target organs to insulin and (3) agents which decrease the rate at which glucose is absorbed from the gastrointestinal tract.

Type I diabetes (insulin dependent) is caused due to insulin insufficiency because of lack of functional beta cells. Patients suffering from this are therefore totally dependent on exogenous source of insulin while patients suffering from Type II diabetes (insulin independent) are unable to respond to insulin and can be treated with dietary changes, exercise and medication. Type II diabetes is the more common form of diabetes constituting 90% of the diabetic population.

#### HOME REMEDIES FOR DIABETES

**Bilberry (*Vaccinium mytilus*) and Blueberry** are effective herbs that cure diabetes by lowering blood sugar and cholesterol levels.

**Bitter gourd (*Momordica charantia*)** fruit decoction in the morning in empty stomach at least for one month is helpful in bringing the blood sugar level to normal.

**Curry pâté, curry leaves (*Murraya koenigii*)** controls diabetes so is one of the important home remedies for diabetes. Hereditary diabetic patients also get the best benefit from its intake. Chewing (8-10) curry leaves in empty stomach is very effective for bringing sugar level in urine and blood to normal.

**Gooseberry, amla (*Emblica officinalis*)** is a natural herb that cures diabetes and brings the blood sugar to normal.

**Green tea (*Camellia sinensis*)** consumption has been used traditionally to control blood sugar in the body. It is associated with prevention of type 2 diabetes, lowering fasting blood levels of glucose, reducing triglycerides and free fatty acids, and enhancing ability of adipocytes to respond to insulin and absorb blood sugar. Its consumption also increases the body's ability to utilize blood sugar. Green tea polyphenols regulates the expression of genes involved in glucose uptake and insulin signaling.

**Gurmar (*Gymnema sylvestre*)** cures diabetes by lowering high sugar level in the blood and lead to proper functioning of insulin and also minimize the urge of taking sweets in the diabetes patients.

**Ispaghula husk (*Plantago ovata*)** is natural safe for treatment of diabetes.

**Maidenhair tree (*Gingo biloba*)** is very effective in controlling diabetes.

**Mango leaves (*Mangifera indica*)** are helpful in controlling diabetes. Take mango leaves, soak them in water and keep it over night then in an empty stomach take this liquid. Dry the leaves of mango trees and make its powder in a grinder. Mix the dry powder (1 teaspoon) of mango leaves in a glass of water and drink it every day. This is one of the useful home remedies for diabetes and good natural cure for diabetes.

**Papaya (*Carica papaya*)** are boiled and made into a paste and given with a pinch of common salt and jeera powder for six months to cure diabetes.

**Sweet potato leaves (*Ipomoea batatas*)** when taken with ash gourd or when taken with any herbal tea are effective in curing diabetes.<sup>[3, 4]</sup>

#### Traditional plant treatments for diabetes

##### Mushrooms

Research has shown the Maitake mushroom (*Grifola frondosa*) has a hypoglycemic effect, and may be beneficial for the management of diabetes. The reason Maitake lowers blood sugar is due to the fact the mushroom naturally acts as an alpha glucosidase inhibitor. Other mushrooms like *Reishi*, *Agaricus blazei*, *Agrocybe cylindracea* and *Cordyceps* have been noted to lower blood sugar levels to a certain extent, although the mechanism is currently unknown.

##### Cinnamon

The study on people published in 2003 conducted in the Department of Human Nutrition, NWFP Agricultural University, Peshawar, Pakistan concluded:

The results of this study demonstrate that intake of 1, 3, or 6 g of cinnamon per day reduces serum glucose, triglyceride, LDL cholesterol, and total cholesterol in people with type 2 diabetes and suggest that the inclusion of cinnamon in the diet of people with type 2 diabetes will reduce risk factors associated with diabetes

#### INDIAN MEDICINAL PLANTS WITH ANTI DIABETIC AND RELATED BENEFICIAL PROPERTIES

**Acacia arabica: (Babul)** The plant extract acts as an antidiabetic agent by acting as secretagogue to release insulin. It induces hypoglycemia in control rats but not in alloxanized animals. Powdered seeds of *Acacia arabica* when administered (2, 3 and 4 g/kg body weight) to normal rabbits induced hypoglycemic effect by initiating release of insulin from pancreatic beta cells.<sup>[5]</sup>

**Aegle marmelos: (Bengal Quince, Bel or Bilva)** Administration of aqueous extract of leaves improves digestion and reduces blood sugar and urea, serum cholesterol in alloxanized rats as compared to control. Along with exhibiting hypoglycemic activity, this extract also prevented peak rise in blood sugar at 1h in oral glucose tolerance test.

**Allium cepa: (Onion)** Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits. Administration of a sulfur containing amino acid from *Allium cepa*, S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) to alloxan induced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues and normalized the activities of liver hexokinase, glucose 6-phosphatase and HMG Co A reductase. When diabetic patients were given single oral dose of 50 g of onion juice, it significantly controlled post-prandial glucose levels.<sup>[5]</sup>

**Allium sativum: (Garlic)** Allicin, a sulfur-containing compound is responsible for its pungent odour and it has been shown to have significant hypoglycemic activity. This effect is thought to be due to increased hepatic metabolism, increased insulin release from pancreatic beta cells and/or insulin sparing effect. Aqueous homogenate of garlic (10 ml/kg/day) administered orally to sucrose fed rabbits (10 g/kg/day in water for two months) significantly increased hepatic glycogen and free amino acid content, decreased fasting blood glucose, and triglyceride levels in serum in comparison to sucrose controls.

S-allyl cystein sulfoxide (SACS), the precursor of allicin and garlic oil, is a sulfur containing amino acid, which controlled lipid peroxidation better than glibenclamide and insulin. It also improved diabetic

conditions. SACS also stimulated *in vitro* insulin secretion from beta cells isolated from normal rats.<sup>[5,6]</sup>

**Aloe vera and Aloe barbadensis: (Ghritakumari)**

Aloe has a long history as a multipurpose folk remedy. The plant can be separated into two basic products: gel and latex. *Aloe Vera* gel is the leaf pulp or mucilage, aloe latex, commonly referred to as "aloe juice," is a bitter yellow exudate from the pericyclic tubules just beneath the outer skin of the leaves. Extracts of aloe gum effectively increases glucose tolerance in both normal and diabetic rats. Treatment of chronic but not single dose of exudates of *Aloe barbadensis* leaves showed hypoglycemic effect in alloxanized diabetic rats. Single as well as chronic doses of bitter principle of the same plant also showed hypoglycemic effect in diabetic rats. This action of *Aloe Vera* and its bitter principle is through stimulation of synthesis and/or release of insulin from pancreatic beta cells. Oral administration of *Aloe Vera* might be a useful adjunct for lowering blood glucose in diabetic patients.<sup>[5,6]</sup>

**Azadirachta indica: (Neem)** Hydroalcoholic extracts of this plant showed anti-hyperglycemic activity in streptozotocin treated rats and this effect is because of increase in glucose uptake and glycogen deposition in isolated rat hemidiaphragm.<sup>[7]</sup>

**Coccinia indica: (Ivy gourd)** Dried extracts of *Coccinia indica* (500 mg/kg body weight) were administered to diabetic patients for 6 weeks. These extracts restored the activities of enzyme lipoprotein lipase (LPL) that was reduced and glucose-6-phosphatase and lactate dehydrogenase, which were raised in untreated diabetics. Oral administration of 500 mg/kg of *C. indica* leaves showed significant hypoglycemia in alloxanized diabetic dogs and increased glucose tolerance in normal and diabetic dogs.

**Eugenia jambolana: (Indian gooseberry, Jamun)** In India decoction of kernels of *Eugenia jambolana* is used as household remedy for diabetes. This also forms a major constituent of many herbal formulations for diabetes. Antihyperglycemic effect of aqueous and alcoholic extract as well as

lyophilized powder shows reduction in blood glucose level. This varies with different level of diabetes. In mild diabetes (plasma sugar >180 mg/dl) it shows 73.51% reduction, whereas in moderate (plasma sugar >280 mg/dl) and severe diabetes (plasma sugar >400 mg/dl) it is reduced to 55.62% and 17.72% respectively. The extract of jamun pulp showed the hypoglycemic activity in streptozotocin induced diabetic mice within 30 min of administration while the seed of the same fruit required 24 h. The oral administration of the extract resulted in increase in serum insulin levels in diabetic rats.<sup>[12]</sup>

**Juglans regia: (Walnut)** It is one of the medicinal plants used in tradition Indian medicine as a treatment for diabetes, but little scientific documentation supports its anti diabetic action. The scientists at Isfahan University, Isfahan, Iran evaluated the anti diabetic effect of ethanolic walnut leaf extract. During experiment twenty four male Wister rats were divided into four groups: non diabetic rats, alloxan-induced diabetic rats treated with ethanolic extracts of walnut (200mg/kg) and alloxan –induced diabetic rats treated with glibenclamide (0.6mg/kg). Fasting blood sugar decreased meaningfully in diabetic rats treated with walnut leaves and diabetic rats treated with glibenclamide. Insulin level increased and glycosylated hemoglobin decreased significantly in diabetic groups receiving either glibenclamide or *J. regia* compared with the diabetic group with no treatment. The histological study revealed that the size of islets of Langerhans enlarged consequentially as compared to diabetic rats with no treatment. Effects of administering glibenclamide or extract of walnut on all parameters discussed above showed no difference and both tended to bring the values to near normal. Thus, the ethanolic extract from this plant leaves has a dramatic antidiabetic effect on diabetes –induced rats.<sup>[8]</sup>

**Leucas lavandulifolia** The plant *Leucas lavandulifolia* Sm. of family Labiatae was evaluated for its antidiabetic activity in alloxan induced diabetic rats as well as for its in vitro antioxidant property. It was observed that Methanolic extract of *L. lavandulifolia* exhibited significant antidiabetic activity in dose dependent manner, but not better than glibenclamide.<sup>[9]</sup>

**Mangifera indica: (Mango)** The leaves of this plant are used as an antidiabetic agent in Nigerian folk medicine, although when aqueous extract given orally did not alter blood glucose level in either normoglycemic or streptozotocin induced diabetic rats. However, antidiabetic activity was seen when the extract and glucose were administered simultaneously and also when the extract was given to the rats 60 min before the glucose. The results indicate that aqueous extract of *Mangifera indica* possess hypoglycemic activity. This may be due to an intestinal reduction of the absorption of glucose.<sup>[5]</sup>

**Momordica charantia: (Bitter gourd)** It is commonly used as an antidiabetic and antihyperglycemic agent in India as well as other Asian countries. Extracts of fruit pulp, seed, leaves and whole plant was shown to have hypoglycemic effect in various animal models. Polypeptide p, isolated from fruit, seeds and tissues of *M. charantia* showed significant hypoglycemic effect when administered subcutaneously to langurs and humans. Ethanolic extracts of *M. charantia* (200 mg/kg) showed an antihyperglycemic and also hypoglycemic effect in normal and STZ diabetic rats.<sup>[10]</sup>

**Ocimum sanctum: (Holy basil, Tulsi)** Since ancient times, this plant is known for its medicinal properties. The aqueous extract of leaves of *Ocimum sanctum* showed the significant reduction in blood sugar level in both normal and alloxan induced diabetic rats. Significant reduction in fasting blood glucose, uronic acid, total amino acid, total cholesterol, triglyceride and total lipid indicated the hypoglycemic effects of tulsi in diabetic rats. Oral administration of plant extract (200 mg/kg) for 30 days led to decrease in the plasma glucose level by approximately 9.06 and 26.4% on 15 and 30 days of the experiment respectively. Renal glycogen content increased 10 fold while skeletal muscle and hepatic glycogen levels decreased by 68 and 75% respectively in diabetic rats as compared to control.<sup>[11]</sup>

**Phyllanthus amarus: (Bhuiamala)** Traditionally it is used in diabetes therapeutics. The whole plant extract also reduced the blood sugar in alloxanized diabetic rats.

**Pterocarpus marsupium: (Indian kino tree)** Pterostilbene, a constituent derived from wood of this plant caused hypoglycemia in dogs showed that the hypoglycemic activity of this extract is because of presence of tannates in the extract. Flavonoid fraction from *Pterocarpus marsupium* has been shown to cause pancreatic beta cell regeneration. Marsupin, pterosupin and liquiritigenin obtained from this plant showed antihyperlipidemic activity. Like insulin, (-) epicatechin stimulates oxygen uptake in fat cells and tissue slices of various organs, increases glycogen content of rat diaphragm in a dose-dependent manner. <sup>[13]</sup>

**Trigonella foenum graecum: (Fenugreek, Methi)** 4-hydroxyleucine, a novel amino acid from fenugreek seeds increased glucose stimulated insulin release by isolated islet cells in both rats and humans. Oral administration of 2 and 8 g/kg of plant extract produced dose dependent decrease in the blood glucose levels in both normal as well as diabetic rats. Administration of fenugreek seeds also improved glucose metabolism and normalized creatinine kinase activity in heart, skeletal muscle and liver of diabetic rats. <sup>[6]</sup>

**Tinospora cordifolia: (Guduchi)** Oral administration of the extract of *Tinospora cordifolia* roots for 6 weeks resulted in a significant reduction in blood and urine glucose and in lipids in serum and tissues in alloxan diabetic rats. The extract also prevented a decrease in body weight. *T. cordifolia* is widely used in Indian ayurvedic medicine for treating diabetes mellitus. Oral administration of an aqueous *T. cordifolia* root extract to alloxan diabetic rats caused a significant reduction in blood glucose. Though the aqueous extract at a dose of 400 mg/kg could elicit significant anti-hyperglycemic effect in different animal models, its effect was equivalent to only one unit/kg of insulin. It is reported that the daily administration of either alcoholic or aqueous extract of *T. cordifolia* decreases the blood glucose level and increases glucose tolerance in rodents. <sup>[6]</sup>

#### MARKET PRODUCT FOR FORMULATED HERBAL DRUGS WITH ANTI DIABETIC PROPERTIES

Many formulations are in the market and are used regularly by diabetic patients on the advice of the physicians.

**Diabeccon manufactured by 'Himalaya'** is reported to increase peripheral utilization of glucose, increase hepatic and muscle glucagon contents, promote B cells repair and regeneration and increase c peptide level. It exerts an insulin like action by reducing the glycated hemoglobin levels. It minimizes long term diabetic complications.

**Epinsulin marketed by Swastik formulations** contains epicatechin, a benzopyran, as an active principle. Additionally it has an insulin-mimetic effect on osmotic fragility of human erythrocytes and it inhibits Na/K ATPase activity from patient's erythrocytes. It is reported to be a curative for diabetes, Non Insulin Dependant Diabetes Mellitus (NIDDM) and a good adjuvant for Insulin Dependant Diabetes Mellitus (IDDM), in order to reduce the amount of needed insulin. It is advised along with existing oral hypoglycemic drugs and is known to prevent diabetic complication.

**Pancreatic Tonic (Ayurvedic herbal supplement):** Pancreas Tonic is a botanical mixture of traditional Indian Ayurvedic herbs currently available as a dietary supplement.

**Bitter gourd powder marketed by Garry and Sun.** It lowers blood and urine sugar levels. The Bitter gourd is specifically used as a folk medicine for diabetes. It contains compounds like bitter glycosides, saponins, alkaloids, reducing sugars, phenolics, oils, free acids, polypeptides, sterols, 17-amino acids including methionine and a crystalline product named p-insulin. It is reported to have hypoglycemic activity.

**Dia-Care manufactured by Admark Herbals Ltd.** is claimed to be effective for both Type 1, Type 2 diabetes within 90 days of treatment and cures within 18 months. Persons taking insulin will eventually be liberated from the dependence on it. The whole treatment completes in 6 phases, each phase being of 90 days. Approx. 5 grams (1 tea spoon) powder is mixed with 1/2 glass of water, stirred properly and kept overnight. Only the water and not the sediment must be taken in the morning on empty stomach. To the remaining medicine fresh water is added and kept for the whole day and is consumed half an hour before dinner. The taste of the drug is very bitter. It is a pure herbal formula without any side effects.

**Gurmar powder manufactured by Garry and Sun** is an anti-diabetic drug, which suppresses the intestinal

absorption of sacharides, which prevents blood sugar fluctuations. Gurmar stimulates insulin secretion and has blood sugar reducing properties. It blocks sweet taste receptors when applied to tongue in diabetes to remove glycosuria. It deadens taste of sweets and bitter things like quinine (effects lasts for 1 to 2 hours).

**DIABETA, a formulation of Ayurvedic Cure**, available in the capsule form is an anti-diabetic with combination of proven anti-diabetic fortified. The formulation of Diabeta is based on ancient Ayurvedic references, further corroborated through modern research and clinical trials. Diabeta acts on different sites in differing ways to effectively control factors and pathways leading to diabetes mellitus. It attacks the various factors, which precipitate the diabetic condition, and corrects the degenerative complications, which result because of diabetes. Diabeta is safe and effective in managing Diabetes Mellitus as a single agent supplement to synthetic anti-diabetic drugs. Diabeta helps overcome resistance to oral hypoglycemic drugs when used as adjuvant to cases of uncontrolled diabetes.

**Syndrex manufactured by Plethico Laboratory** contains extracts of germinated fenugreek seed. Fenugreek is used as an ingredient of traditional formulations over 1000 years. We are currently studying the mechanism of this antidiabetic drug using animal model on one hand and cultured islet cells on the other.

Thus many different plants have been used individually or in formulations for treatment of diabetes and its complications. One of the major problems with this herbal formulation is that the active ingredients are not well defined. It is important to know the active component and their molecular interaction, which will help to analyze therapeutic efficacy of the product and also to standardize the product. Efforts are now being made to investigate mechanism of action of some of these plants using model systems.

**Antidiabetic Activity of a Herbal Formulation from *Tinospora cordifolia* stem and *Plumbago rosea* root** PRTC contains the medicinal herbs, *P. rosea* and *T. cordifolia* is widely used in ayurveda to treat diabetes. Guduchi Satwa, a starchy water extract prepared from it is recommended as an anti diabetic tonic. Antioxidant properties of *T. cordifolia* have

also been reported. Therefore the significant antioxidant effects exhibited by PRTC herein may partly be due to the presence of the *T. cordifolia* component. It is also reported to decrease levels of plasma lipid per oxidation in alloxan diabetic rats. In consonance with the results, *T. cordifolia* ameliorated cyclophosphamide induced toxicity, due to its free radical scavenging activity.

*T.cordifolia* is reported to contain sitosterol, terpenoids, lignans etc. Sitosterol may be attributed to its antidiabetic activity. PRTC was relatively non toxic. This is not surprising as its two herbal components (*P. rosea* and *T. cordifolia*) are extensively used in several Ayurvedic formulations. The present herbal formulation therefore warrants further research as a novel antidiabetic herbal drug.<sup>[14]</sup>

#### DIABETES SYMPTOMS

- Loss of weight indicates that there is a problem in the blood sugar level and functioning of insulin
- Blurred vision
- Frequent urination is one of the major symptom of diabetes
- Severe hunger pain or emptiness stress and irritation also give sign of diabetes.
- Nausea and vomiting
- Extreme weakness and tiredness
- Unusual thirst
- Mood change, etc.

#### DIABETES CAUSES

- Hereditary and genetics leads to diabetes
- It also cause due to increase production of glucose level in the blood vessels and less production of glucose in the body. Also caused due to infections caused by viruses.
- Stress, obesity, increased cholesterol level, excess intake of oil and sugar and no physical exercise are some other cause of diabetes.
- According to Ayurveda it is caused by vitiation of all the three dosha but vata is to most vitiate out of the three.

#### DOs & DON'Ts FOR DIABETES

- Controlling diet and eating right is very important for diabetic patients and their health.
- Low fat diet and vegetables like spinach, cucumber must be taken as they are good for controlling diabetes. Onion, sprouts, beans, garlic in the diet of

diabetics low down the sugar level in the blood. Tomatoes, vegetable salad, fruits and milk products like cheese should be taken.

- Starchy food products like white bread, rice, potatoes should be avoided as they are not easily digestible.

- Diabetic patient should not be scared of eating sugar rich fruits. These are safe and do not increase insulin production.

- Less amount of oil should be taken and coffee, sugar refined flour, alcohol, heavy metals should be avoided.

- Meals should be small as the foods are easily digestible and are good for the health of diabetics.

- Taking stress should be avoided as it worsens the conditions.

- Avoiding mutton, excess salt in the meal will help in controlling the body weight and diabetes. Avoiding junk food and oily food will control the level of cholesterol, lowers the blood pressure level and diabetes.

### CONCLUSION

In the present review an attempt has been made to investigate the antidiabetic herbal plants and marketed formulations which may be useful to the health professionals and scholars for further scientific research in the field of pharmacology and therapeutics.

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