MEDICINAL PLANTS AS ANTI-DIABETICS: A REVIEW
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ABSTRACT
Medicinal herbs as potential source of therapeutic aids have attained a significant role in health system all over the world for both humans and animals. Ayurveda and other Indian literature mention the use of plants in treatment of various human diseases. India has about 45000 plant species and among them, several thousands have been claimed to possess medicinal properties. The present paper aims to review various plant species from Indian origin and their constituents, which have been used in the traditional system of medicine and have shown hypoglycaemic activity.

KEY WORDS
Medicinal herbs, Hypoglycaemic activity

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INTRODUCTION

Diabetes is a metabolic disorder where in human body does not produce or properly uses insulin, a hormone that is required to convert sugar, starches, and other food into energy. Diabetes results in abnormal levels of glucose in the bloodstream. Herbal plants are very common in use in our day to day life. Either as a nutrient or as a source of food these herbs are being consumed by the patient as well as healthy person. Easy availability, raw consumption, least side effects and low cost makes the herbal preparations the king of all available therapies.\(^1\) Diabetes and herbs have got a long relation from the past. Thus, plants are a potential source of anti-diabetic drugs which can be proved by the ethnobotanical information reports about 800 plants that may possess anti-diabetic potential. Although, synthetic oral hypoglycemic agents/insulin are the mainstream treatment of diabetes and are effective in controlling hyperglycaemia, they have prominent side effects and fail to significantly alter the course of diabetic complications. This forms the main reason for an increasing number of people finding alternating therapies that may have less severe or no side effects.\(^2,3\)

The use of herbs as hypoglycemic is a major avenue in Indian perspectives particularly for treating diabetes, which require to be explored more effectively as there are so many literatures available on these aspects. The present review represents the profile of Indian medicinal plants commonly used in India that have been pharmacologically tested and proven to be effective as anti-diabetic drugs. The profile describes the scientific name, family, chemistry, activity and usage of the chemical constituents isolated from these medicinal plants for the treatment of diabetes.

PLANTS WITH ANTI-DIABETIC POTENTIAL

*Allium cepa* (Onion) and *Allium sativum* (Garlic) (Family: Liliaceae), is cultivated throughout India and is an important dietary constituent. It consists of alliiins, polysaccharides and saponins.\(^4,5\) The active components are believed to be sulfur-containing compounds – allyl propyl disulfide (APDS) in onions and diallyl disulfide (allicin) in garlic.\(^7\) In 2001, a significant decrease in glucose levels were reported in humans following garlic treatment.\(^8\) Studies have suggested that *A. sativum* controlled the blood glucose in serum and altered the activities of liver hexokinase glucose-6-phosphatase and haemoglobin coenzyme-A reductase towards normal and administering in the concentration of 10 ml/kg/day to rabbits significantly increased liver glycogen and free amino acids, which resulted in significant decrease in fasting blood sugar, triglycerides (in serum, liver and aorta) and liver serum proteins as compared to those in sucrose-fed group.\(^9\) Various ether soluble fractions of onion as a single oral dose (0.25 mg/kg) showed significant hypoglycemic effect in normal fasted rabbits and was reported to decrease hyperglycaemic peak in subcutaneous glucose tolerance tests conducted in rabbits and it was suggested that it can be a useful substitute for tolbutamide in controlling alloxan diabetes in rats.\(^10\)

*Aegle marmelos* (Family: Rutaceae), commonly known as Bael or Sirphal in hindi and Holy Fruit Tree in English, is a medium sized tree found wild, especially in dry forests and is also cultivated throughout India. The studied have reported that aqueous extract of the leaves (1 gm/kg for 30 days) significantly controlled blood glucose, urea, body weight, liver glycogen and serum cholesterol of alloxanized (60 mg/kg IV) rats as compared to controls and this effect was similar to insulin treatment. The extract was equi-effective in comparison to insulin in restoring blood glucose and body weight to normal levels.\(^10,11\) Consequently, the active principle of *A. marmelos* extract had similar hypoglycaemic effect to that of insulin.\(^11\)
**Murraya koeingii** (Family: Rutaceae), commonly known as Kurry patta in Hindi and curry leaf tree in English, is grown for its aromatic leaves and used extensively as a flavouring agent in curries and chutneys in India and other tropical countries. The oral feeding of *M. koeingii* leaves diet (10% w/w) for 60 days to normal rats showed hypoglycemic effect associated with increased hepatic glycogen content due to increased glycogenesis and decreased glycogenolysis and gluconeogenesis. Many enzymes of the liver including gluconeogenic enzymes have been reported to be affected by spice both in vitro cell culture systems as well as in vivo in experimental animals. The studies have depicted an interesting finding that suggests *M. koeingii* probably prevents the destruction of b cells of islets in the pancreas, it may have antioxidant or free radical scavenger properties in preventing these changes. Thus, *M. koeingii* may have a role in prevention of diabetes and its consumption should be encouraged in the early diabetic state.

**Gymnema sylvestre** (Family: Asclepiadaceae), called gurmar or Merasingi, is a woody, climbing plant, native to India. The main constituents are gymnemic acid, gurmarin, a polypeptide of 35 amino acids and saponins. Investigation of the hypoglycaemic activity of saponin constituents from gymnemic acid, a crude saponin fraction of *G. sylvestre*, identified not only two new saponins, gymnemosides a and b, but also gymnemic acid V as the active principle. Its triterpene glycosides isolated from plant inhibited glucose utilization in muscles and Gymnemic fractions also inhibit glucose uptake in the intestine. According to a study, *G. sylvestre* enhances the production of endogenous insulin. The studies have revealed that the drug acts indirectly through stimulation in insulin secretion of the pancreas, as it has no direct action on the carbohydrate metabolism and it significantly reduced glucose levels in the hyperglycemic rats, it had no effect on normal rats. It was found that gymnemic acid molecules prevent activation of taste buds by sugar molecules, curbing the sugar craving by filling the receptor locations on the taste buds. Similarly, gymnemic acid molecules fill the receptor location in the absorptive external layers of the intestine thereby preventing the sugar molecules absorption by the intestine, which results in low blood sugar level. It was also found that the *G. sylvestre* aqueous extract of leaves stimulates insulin secretion from mouse cells and isolated human islets in vitro, without compromising cell viability and the crude extracts and its isolated compound dihydroxy gymnemic triacetate shows hypoglycaemic effect against streptozotocin induced diabetic rats in dose and time dependent manner.

**Ficus bengalenesis** (Family: Moraceae), commonly known as Indian Banyan tree or Bur, is a very large tree distributed throughout India from sea level to 1,200 m. It yields latex containing Caoytchoue (2.4%), Resin, Albumin, Cerin, Sugar and Malic acid. A glucoside isolated from the bark of *F. bengalenesis* showed more potent hypoglycaemic action as compared to crude ethanolic extract and the activity was half of tolbutamide. Glycoside of leucopelargonidin isolated from the bark of *F. bengalenensis* exerts significant hypoglycaemic, hypolipidemic and serum insulin raising effects in moderately diabetic rats with close similarities to the effects of a minimal dose of glibenclamide. In addition, pelargonidin was more potent than leucocyanidin in stimulating in vitro insulin secretion by beta cells. Leucodelphinidin (250 mg/kg) also showed hypoglycemic action equal to that of glibenclamide (2 mg/kg) in normal and alloxan-diabetic rats.

**Ocimum sanctum** (Family: Labiatae), commonly known as Tulsi in Hindi and Holy basil in English, is a herb found throughout India, up to an altitude of 1,800 m. in the Himalayas and its cultivated in temples and gardens. Oral administration of an alcoholic extract of leaves of *O. sanctum* reduced glycaemia in normoglycaemic, glucose-fed hyperglycaemic and
streptozotocin-induced diabetic rats. Furthermore, the extract potentiated the action of exogenous insulin in healthy rats. Administration of leaf powder to healthy and diabetic rats resulted in reduction of fasting blood glucose after one month.\[9,10,13\]

**Panax ginseng** (Family: Araliaceae) are slow-growing perennial plants with fleshy roots. The root of ginseng has been used for over 2,000 years in the Far East for its health-promoting properties. It is found to contain triterpene glycosides, or saponins, commonly referred to as ginsenosides, polysaccharides, peptides, polyacetylenic alcohol, and fatty acids.\[5,15,17\] Ginseng polypeptide, isolated from the root of *P. ginseng*, was demonstrated to decrease the level of blood sugar and liver glycogen when injected intravenously to rats. The aqueous extract of root of *P. ginseng* showed a remarkable hypoglycemic activity on administration to mice.\[9\] It increases insulin production, reduces death of pancreatic β-cells and insulin resistance, improves postprandial glycemia in diabetic patients.\[8\] Ginseng also elevated mood, improved psychophysiological performance and physical activity, and reduced body weight.\[7\]

**Momordica charantia** (Family: Cucurbitaceae), commonly known as bitter melon, bitter gourd or karela, is grown in tropical countries of Asia, Africa and South America. It is a very common folklore remedy for diabetes and the blood sugar-lowering action of the fresh juice or unripe fruit has been established in animal experimental models as well as human clinical trials. The major compounds isolated from this plant and identified as hypoglycemic agents are Charantin, polypeptide-P and vicin.\[1,9]\] Various studies have shown hypoglycemic effect in various animal models using extract of fruit pulp, seed, leaves and whole plant of *M. charantia*.\[17,18\] Alcohol-extracted charantin from *M. charantia* consists of mixed steroids and was found to be more potent than the oral hypoglycemic agent tolbutamide in an animal study. Bitter melon also contains an insulin-like polypeptide, polypeptide- P, similar in structure to bovine insulin. It was found to decrease blood sugar levels when injected subcutaneously into type 1 diabetic patients and appears to inhibit gluconeogenesis and is believed to improve glucose tolerance in Type II diabetes.\[11,13,16\] Fried karela fruits consumed as a daily supplement to the diet produced a small but significant improvement in glucose tolerance in diabetic subjects without any increase in serum insulin levels.\[7\]

**Eugenia jambolana** (Family: Myrtaceae), commonly known as Jamun or black plum, is being widely used to treat diabetes by the traditional practitioners over many centuries. It is a large evergreen tree growing up to 30 m high found widely in India.\[3,5\] Preliminary studies on seeds and decoction of dry leaves of *E. jambolana* have shown anti-hyperglycemic activity.\[10,12,16\]

The oral administration of the pulp extract of the fruit resulted in the enhancement of insulinemia in normoglycaemic and diabetic rats. The incubation of isolated pancreatic islet cells of normal and diabetic animals with this plant extracts resulted in increased insulin secretion. In addition, the extract inhibited insulinase activity from liver and kidney.\[11\] Oral administration of dried alcoholic extract of the seeds caused hypoglycemia and reduced glycosuria. In addition, the treatment also partially restored altered hepatic and skeletal muscle glycogen content and hepatic glucokinase, hexokinase, glucose-6-phosphate and phosphofructokinase levels.\[10,13\]

**Picrorrhiza kurroa** (Family: Scrophulariaceae), commonly known as Kutki in India, is a small herb found in the Himalayan region from Kashmir to Sikkim. Dried rhizomes of the plant are being used for medical treatment. Recently, it has been known that alloxan induces its diabetogenic activity mainly by inducing oxygen free radicals and thereby damaging the
pancreas. *P. kurroa* extract was found to reduce the glucose level in normal, glucose loaded animals and in animals made diabetic with alloxan. It was reported earlier that *P. kurroa* extract can act as a free radical scavenger in vitro and it indicates that administration of *P. kurroa* can reduce the level of serum lipid peroxides as well as ameliorate the destruction of WBC and confirms the possibility that the major function of the extract is on the protection of vital tissues including the pancreas, thereby reducing the causation of diabetes in these animals.\[^{12,13}\] Alcoholic extract of *P. kurroa* (75 mg extract/kg) reduced serum glucose that was maximum 2 h after the dose. It also showed antihyperglycemic effect in alloxanized diabetic rats.\[^{10}\]

*Psidium guajava* (Family: Myrtaceae), commonly known as Guava or Amrood, is a semi deciduous tropical tree in north India and is widely grown throughout India for its fruits. It is found to contain a high percentage of vitamin C, carotene, vit B\(_1\), B\(_2\), B\(_6\), and free sugars (glucose, fructose and sucrose).\[^{3,22,23}\] The oral administration of aqueous leaves extract of *P. guajava* at the dose of 500mg/kg b.w for 15days have shown beneficial effect not only on blood glucose but also on body weight, glucose and ketone level of urine and tissue of pancreas in streptozotocin induced adult albino diabetic rats. Methanolic extract (51%) of *P. guajava* leaves showed hypoglycemic effect in type 2 diabetes.\[^{11}\] Flavonoid glycosides such as strictinin, isostrictinin and pedunculagin are the effective constituents, which have been used in clinical treatment of diabetes to improve the sensitivity of insulin. A glycoprotein was also identified as active component for anti-diabetes.\[^{18}\]

*Trigonella foenum graecum* (Family: Leguminosae), commonly known as Methi or Fenugreek seeds, are found as a wild plant and also cultivated in Northern India.\[^{25}\] It is found to contain mucilages, proteins, proteinase inhibitors, steroid saponins and saponin- peptide esters, sterols, flavonoids, nicotinic acid, coumarin, trigonelline and volatile oil.\[^{8,18}\] The effect of fenugreek seed on blood glucose and the serum lipid profile was reported in insulin-independent (type 1) diabetes patients.\[^{9}\] Administration of the defatted seed (1.5-2.0 g/kg daily) to both normal and diabetic dogs reduced fasting and postprandial blood levels of glucose, glucagon, somatostatin, insulin, total cholesterol, and triglycerides, and increased HDL-cholesterol levels. The intake of seed fiber of *T. foenumgraecum* reduces the rate of glucose absorption and may delay gastric emptying, thereby preventing the rise in blood sugar levels following a meal. Seed’s fiber also stimulates insulin receptor sites to burn cellular glucose at high fiber diet.\[^{8,10}\] Mechanism of action of fenugreek seeds as an orally active hypoglycemic effect may be mediated through stimulating insulin synthesis and or secretion from the beta pancreatic cells of Langerhans. The therapeutic role of Trigonella seed powder in type 1 diabetes is due to change of glucose and lipid metabolizing enzyme activities to normal values, thus stabilizing glucose homeostasis in the liver and kidney.\[^{7,9}\]

*Lawsonia inermis* (Family: Lythraceae), commonly known as Henna or Mhendi, is a much branched glabrous shrub or small tree, cultivated for its leaves is found to constitute carbohydrates, proteins, flavonoids, tannins and phenolic compounds, alkaloids, terpenoids, quinones, coumarins, xanthones and fatty acids. Ethanol (70 %) extract of *L. inermis* showed significant hypoglycaemic and hypolipidaemic activities in alloxan induced diabetic mice after oral administration.\[^{20}\] Decreased concentration of glucose, cholesterol and triglycerides to normal was seen by feeding of 0.8 g/kg of *L. inermis* extract.\[^{2}\] Methanol (95 %) extract of leaves of *L. inermis* was found to possess significant in-vitro antihyperglycemic effect.\[^{3}\]

*Cinnamomum zeylanicum* (Family: Lauraceae), commonly known as Cinnamon, is harvested by growing the tree for two years then coppicing it. The mainly constitute volatile oils, containing cinnamaldehyde. Cinnamon ingestion reduced total plasma glucose responses
as measured by area under the curve (AUC) to oral glucose ingestion as well as improved insulin sensitivity.\textsuperscript{[2]} Cinnamon supplementation may thus be important to \textit{in vivo} glycaemic control and insulin sensitivity in humans and they also appear to be sustained for 12 hour. Cinnamon also significantly delayed gastric emptying and profoundly lowered postprandial glycaemic response without any significant effect on satiety.\textsuperscript{[6, 5]}

\textit{Tinospora cordifolia} (Family: Menispermaceae), commonly known as Gaduchi, is found in forests throughout India and is widely used in Ayurveda as tonic, vitalizer and as a remedy for diabetes and metabolic disorders.\textsuperscript{[4]} The main constituents are found to be alkaloids, diterpenoid lactones, glycosides, steroids, Sesquiterpenoid, phenolics, aliphatic compounds and Polysaccharides.\textsuperscript{[24]} Leaves of this plant are rich in protein (11.2\%) and are fairly rich in calcium and phosphorus.\textsuperscript{[19]} Oral administration of the aqueous extract of \textit{T. cordifolia} root produced a significant reduction in blood glucose, brain lipid level, hepatic glucose-6-phosphatase, serum acid phosphatase, alkaline and lactate dehydrogenase and increase in body weight, total haemoglobin and hepatic hexokinase in alloxanized diabetic rats.\textsuperscript{[10,11]}

It is reported that the daily administration of either alcoholic or aqueous extract of \textit{T. cordifolia} decreases the blood glucose level and increases glucose tolerance in rodents. Ethyl acetate extract of its roots has afforded a pyrrolidine derivative with hypoglycemic activity in rabbits.\textsuperscript{[19]} Another study suggests that oral administration of the extract for 6 weeks results in significant reduction in blood and urine glucose and in lipids in serum and shows its hypoglycemic action.\textsuperscript{[9]}

**CONCLUSION**

The prevalence of diabetes mellitus continues to rise worldwide and treatment with oral hypoglycemic drugs ends with numerous side effects and huge monetary expenditure. There is increasing demand by patients to use the natural products with antidiabetic activity. This paper has presented various anti-diabetic plants that have been pharmacologically tested and shown to be of some value in treatment of Diabetes Mellitus. The effects of these plants may delay the development of diabetic complications and correct the metabolic abnormalities. However, more investigations must be carried out to evaluate the mechanism of action of medicinal plants with antidiabetic effect.

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