

## AN OVERVIEW ON MEDICINAL PLANTS EXPLORED WITH ANTI-DIABETIC PROPERTIES

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### ABSTRACT

Diabetes mellitus is a common and serious metabolic disorder of the endocrine system throughout the world. This frightful disease is found in every part of the world and is becoming a serious threat to healthcare providers and leads to major cause of death. The number of person suffering from diabetes is increasing due to growth population, aging, urbanization, pollution, and increasing prevalence of obesity and lack of physical activity. It is a group of metabolic disorder characterized by high blood sugar levels that result from the deficiency or ineffective production of insulin by pancreas or action or both. There are lots of chemical agents available to control and treat diabetic patients. It may cause unwanted side effects, if these agents will be

used for longer duration. Thus, the need arises to cure this disease with potent drug causing fewer side effects. Alternative to these agents, many of the herbal plants are available across the world having anti-diabetic activity and show their action by different mechanism like stimulating or regenerating the  $\beta$  cell or extra pancreatic effect for hypoglycemic. It may delay the development of diabetic complications or correct the metabolic abnormalities. Numerous herbal plants have been investigated for their potential to treat different types of

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diabetes. This systemic review article focused on some reported anti-diabetic medicinal plants with their botanical name, common name, constituent, and mechanism of action.

**KEYWORDS:** Diabetes Mellitus, Pancreas, Insulin, Sugar, Medicinal Plants.

## INTRODUCTION

Diabetes mellitus is a common and very prevalent disease affecting the citizens of both developed and developing countries<sup>[1]</sup> and Asians make up more than 60% of the world's diabetic population.<sup>[2]</sup> It is considered a “modern day epidemic” and is rightly recognized as a global public health issue. The World Health Organization (WHO) reported that 300 million peoples would suffer from diabetes mellitus by the year 2025.<sup>[3,4]</sup> India is one of the leading countries for the number of people with diabetes mellitus and it is estimated that diabetes affects approximately 57 million people by the year 2025 in India.<sup>[5]</sup> India shall have the maximum number of diabetics in the world making it, the “Diabetic capital of the world.”<sup>[6]</sup> The prevalence of the disease in adult is 2.4 % in rural and 4.0 - 11.6 % in urban dwellers.<sup>[7]</sup>

Diabetes is a chronic metabolic disorder of proteins, fats and carbohydrate, affecting a large number of world populations in the world. It is characterized by the abnormality of carbohydrate metabolism which is linked to low blood insulin level or insensitivity of target organs to insulin or both.<sup>[8,9]</sup> The chronic hyperglycemia in diabetes is associated with long term damage, dysfunction and failure of various organs especially the heart, eyes, blood vessels, kidneys and nerves.<sup>[10]</sup> Long-term complications of diabetes include nephropathy, neuropathy, retinopathy, amputations, foot ulcers, autonomic neuropathy causing genitourinary, gastrointestinal and cardiovascular symptoms and sexual dysfunction. Diabetic subject have an increased incidence of peripheral arterial, atherosclerotic cardiovascular and cerebrovascular disease. Abnormalities of lipoprotein metabolism and hypertension are often found in diabetics. Impairment of insulin secretion and hyperglycemia characterized by symptom such as polyuria, polydipsia, weight loss, sometimes with polyphagia and blurred vision. Uncontrolled diabetes characterized with hyperglycemia with ketoacidosis or the nonketotic hyperosmolar syndrome is an acute life-threatening consequence.<sup>[11]</sup>

It can be classified into type I diabetes (Insulin-dependent diabetes mellitus) and type II diabetes (non-insulin-dependent diabetes mellitus). Type I Diabetes, previously called insulin-dependent diabetes mellitus (IDDM) or juvenile onset diabetes, may account for five percent to ten percent of all diagnosed cases of diabetes. Risk factors are less well defined for

Type 1 diabetes than for Type 2 diabetes, but autoimmune, genetic, and environmental factors are involved in the development of this type of diabetes. Type 2 Diabetes was previously called non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes, which are mainly due to insulin resistance or abnormality in insulin secretion. Type 2 Diabetes may account for about 76 - 85 % of all diagnosed cases of diabetes. The risk of developing type 2 Diabetes in humans increases with age, obesity, cardiovascular disease (hypertension, dyslipidaemia), stress, rapid development of cities, substantial increase in purchase power, lifestyle ease, metro life, lack of physical activity, family history of diabetes and race/ethnicity.<sup>[12-16]</sup> The overall death rate in people with diabetes is about twice that of people without diabetes.<sup>[17]</sup>

Many allopathic medicines or oral hypoglycemic agents are available for the treatment of diabetes,<sup>[18]</sup> but these synthetic agents are associated with drawbacks such as rigid and multiple dosing regimen, high cost, inaccessibility and untoward effects like hypoglycaemia, nausea, vomiting, hyponatremia, flatulence, diarrhoea or constipation, alcohol flush, headache, weight gain, lactic acidosis, pernicious anaemia, dyspepsia, dizziness, joint pain.<sup>[19]</sup>

The cost of treating diabetes and associated complications exceeds \$100 billion per year and complications are far less common and less severe in people who have well controlled blood sugar levels.<sup>[20]</sup> Though there are various approaches to reduce the ill effects of diabetes and its secondary complications. In past few years, traditional medicine or herbal formulations are growing exponentially and these drugs are gaining popularity because of it is derived from natural origin and having minimum side effects.<sup>[21,22]</sup> Many traditional medicines are derived from medicinal plants, minerals and organic matter.<sup>[23,24]</sup>

The ethnobotanical information reports about 600-800 plants that may possess antidiabetic potential and several herbs have shown antidiabetic activity when assessed by using presently available experimental techniques.<sup>[25-27]</sup> One of the great advantages of medicinal herbs is that these are readily available and have always been an exemplary source of many of the currently available drugs has been derived directly or indirectly from them. The current review focuses on various medicinal plants possessing antidiabetic activity, their mechanisms of action and therapeutic efficiency, which can be beneficial for the mankind.

**Medicinal plants with anti-diabetic and another related beneficial properties*****Adansonia digitata***

*Adansonia digitata* or Baobab belongs to *Bombacaceae* family. African baobab also known as dead rat tree.<sup>[28]</sup> Baobab products (e.g. fruits, seeds, leaves, bark) are traditionally employed to the livelihood of many populations in Africa as it is a source of food, fibre and medicine. It is also named “the small pharmacy or chemist tree.”<sup>[29-31]</sup> The ethanolic extract of the Baobab bark produces antihyperglycaemic activities in alloxan induced diabetic female rats at doses of 250 and 500 mg/kg bwt, this effect may be produced by regeneration of  $\beta$ -cell of pancreas and potentiating the insulin secretion from surviving  $\beta$ -cells.<sup>[32]</sup> Apart from antidiabetic properties, the various parts of this plant have traditionally been used as immunostimulant, anti-inflammatory, antilipidaemic, analgesic, insect repellent and pesticidal.<sup>[33,34]</sup>

***Aegle marmelos***

*Aegle marmelos* belongs to family *Rutaceae* and also commonly known as Holy fruit tree, Bengal Quince and Bel. It showed the antidiabetic effects, which are more effective along with the oral hypoglycemic drug.<sup>[35,36]</sup> The leaf extract (10mg/kg bwt) showed effective hypoglycemic activity in streptozotocin induced diabetic rats. It increases utilization of glucose either by direct glucose stimulation or by acting like insulin for glucose uptake.<sup>[36-38]</sup> It may stimulate insulin secretion and increase glycogenesis and decrease glycogenolysis and gluconeogenesis.<sup>[39,40]</sup> The principle bioactive compounds like Aegelin,  $\alpha$  and  $\beta$  sitosterol, marmelosin and marmesin are responsible for anti-diabetic activity.<sup>[41]</sup> The presence of Aeglin, lupeol, eugenol, marmesinin constituents may prevent the myocardial damage due to diabetes mellitus. The antioxidant property of the leaf might be due to the presence of phenolic compounds such as flavonoids, phenolic acids and phenolic diterpenes.<sup>[42]</sup>

***Allium cepa***

*Allium cepa* is commonly called as Onion belonging to family *Liliaceae* and probably native of South West Asia which is widely cultivated throughout the world. Bulb or whole plant is used for its therapeutic effect. The bulb part contains *s*-methyl cysteine sulfoxide, *s*-allyl cysteine sulfoxide has anti-diabetic activity. Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits.<sup>[43]</sup> Hypoglycemic activity reported in ether soluble fraction of onion (0.25mg/kg bwt) in streptozotocin induced rabbits. It normalizes the activities of liver hexokinase, glucose 6-phosphatase and HMG Co A reductase.<sup>[43,44]</sup> It is also known to have antioxidant and

hypolipidaemic activity.<sup>[45]</sup> When diabetic patients were given single oral dose of 50 gm of onion juice, it significantly controlled post-prandial glucose levels.<sup>[46]</sup>

### ***Allium sativum***

*Allium sativum* commonly known as garlic and belonging to family *Alliaceae*. It contains allicin, apigenin, allicin, s- allyl cysteine sulfoxide, which is responsible for hypoglycemic activity.<sup>[47-48]</sup> This effect is thought to be due to increased hepatic metabolism and increased insulin release from pancreatic beta cells and/or insulin sparing effect.<sup>[49-50]</sup> Garlic possesses many therapeutic benefits other than hypoglycemic as it exhibits anticoagulant, antioxidant, antimicrobial, hypocholesterolaemic and hypotensive activity.<sup>[51]</sup> Raw garlic possesses a beneficial potential in reversing proteinuria in addition to reducing blood sugar, cholesterol and triglycerides in diabetic rats.<sup>[52]</sup> Oral administration of aqueous homogenate of garlic (10 gm/kg bwt) to rabbits for two months significantly increased hepatic glycogen and free amino acid content as well as blood glucose and triglyceride levels in serum.<sup>[53]</sup>

### ***Aloe vera or Aloe barbedensis***

*Aloe vera* is commonly known as Burn plant or Gheekumari and belongs to *Liliaceae* family. It is a cactus like plant with green dagger fleshy spiny shaped leaves that filled with clearly viscous gel. The aqueous extract of *Aloe vera* (150mg/kg bwt) has the hypoglycemic effect in both IDDM and NIDDM.<sup>[54-55]</sup> Phytosterols (Lophenol/ Cycloartanol) present in plant that stimulate the biosynthesis and/or release of insulin as well as alter the activity of carbohydrate metabolizing enzymes.<sup>[56-58]</sup> *Aloe vera* gel also produces cardioprotective activity, reduces the increased TBARS, maintains the Superoxide dismutase and Catalase activity up to the normal level and increases reduced glutathione by four times in diabetic rats.<sup>[59,60]</sup>

### ***Andrographis paniculata***

*Andrographis paniculata* is commonly known as Kalmegh and belong to *Acanthaceae* family. This plant shows both antidiabetic and antioxidant effect.<sup>[61,62]</sup> Ethanolic leaf extracts (250 and 500 mg/kg bwt) possessed significant antihyperglycemic effect in streptozotocin induced diabetic rat which might be due to its islet cell restoring and regenerative ability as well as the upregulation of antioxidant enzymes.<sup>[63]</sup> The protective effect of leaf extract may be due to the andrographolide or other diterpenoids, flavonoids or polyphenols present in the plant.<sup>[64]</sup> Besides as anti-diabetic effect, *A. paniculata* had also been used as analgetic, antioxidants anti-malarial antibacterial and hepatoprotector.<sup>[65]</sup>

***Azadirachta indica***

*Azadirachta indica* is commonly called as Neem belonging to the family *meliaceae*. The powdered part, aqueous extract and alcoholic extract of *A. indica* show significant hypoglycemic activity.<sup>[66,67]</sup> Apart from having anti-diabetic activity, this plant also has anti-bacterial, antifungal, antimalarial, antifertility, anti-inflammatory, antiarthritic, antiulcer, hepatoprotective and antioxidant effects.<sup>[68-70]</sup> These properties may be due to the presence of phytochemical constituents like alkaloids, tannins, coumarin, proteins, stigmasterol, flavonoids, polyphenols and saponins.<sup>[71]</sup>

***Caesalpinia bonducella***

*Caesalpinia bonducella* belongs to family *Caesalpinaceae* commonly known as Nata Karanja. These plants have the potential to act as antidiabetic as well as antihyperlipidemic.<sup>[72]</sup> The extracts of the seeds (300 mg/kg bwt) of this plant significantly lowered the blood sugar level in streptozotocin and alloxan induced diabetic rat.<sup>[72,73]</sup> The antihyperglycemic action of the extracts may be due to the blocking of glucose absorption. These extracts may also increase glycogenesis there by increasing liver glycogen content.<sup>[73]</sup> Barginin, caesalpinine A,  $\alpha$  and  $\beta$  amyryl and lupeol are the active principle that increases the release of insulin from pancreatic cells.<sup>[74]</sup> Apart from antihyperglycemic and hypolipidemic effect, it has also been used as antimalarial, antiamebic, antibacterial, anthelmintic, antipyretic, analgesic, anti-inflammatory, digestive, stomachic, liver tonic, expectorant, contraceptive, aphrodisiac and tonic.<sup>[75,76]</sup>

***Eugenia jambolana***

*Eugenia jambolana* popularly known as Jamun or Indian blackberry or Indian gooseberry, belong to *Myrtaceae* family. Antihyperglycemic effect produced by aqueous and alcoholic extract as well as lyophilized powder in both experimental models and clinical studies.<sup>[77]</sup> Extract of plant (100-400 mg/kg bwt) showed dose dependent decrease in blood glucose level in streptozotocin induced diabetes rats.<sup>[78]</sup> Insulin secretion may be stimulated on incubation of plant extract with isolated islets of Langerhans from normal as well as diabetic animals. These extracts also inhibit the insulinase activity from liver and kidney.<sup>[79]</sup> Apart from hypoglycemic effect, kernels or seed has been reported to have anti-inflammatory, neuropsychopharmacological, antibacterial, anti-HIV and antidiarrhoeal effects.<sup>[80]</sup>

***Ficus bengalensis***

*Ficus bengalensis* is commonly known as Banyan tree and belongs to *Moraceae* family. The extract of Banyan tree (100 mg/kg bwt), there is significant decrease in blood and urine sugar and increased blood insulin levels in normal and moderately alloxan induced diabetic animal.<sup>[81]</sup> Histopathology evidence showed the beta cytotropic activity of various parts of these plants. But the ethanolic extract of the fruit was found to exert a more pronounced antidiabetic activity than the ethanolic extract of the root or bark.<sup>[82]</sup> The mechanism of action of the principle may be related to its protective/inhibitory action against the insulin degradative processes.<sup>[83]</sup>

***Gymnema sylvestre***

*Gymnema sylvestre* commonly called Madhunashini or Gurmar belonging to family *Asclepidaceae*. The leaves are known for its antidiabetic activity which is rich in phytochemicals such as alkaloids, flavonoids, saponins and phenols.<sup>[84]</sup> Oral feeding of powdered leaves of *G. sylvestre* (500 mg/kg bwt) for 10 days significantly reduced the hyperglycaemia in rats. It changes the activity of gluconeogenic enzymes and reverses the pathological changes in the liver initiated during the hyperglycaemic phase. It helps the pancreas with insulin production in type 2 diabetes and increases the sensitivity to insulin in type 1 diabetics.<sup>[85]</sup> Hypoglycemic effect may be explained as the ability of gymnemic acids to delay the glucose absorption in the blood due to the atomic arrangement of gymnemic acid molecules which is similar to that of glucose molecules. These 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.<sup>[86,87]</sup> Apart from antihyperglycaemic effect, it is also known as anticancer, antimicrobial, anti-inflammatory, anodyne, thermogenic, digestive and liver tonic.<sup>[84]</sup>

***Hibiscus rosa-sinensis***

*Hibiscus rosasinensis* commonly known as Gudhal or China rose belongs to the family of *Malvaceae*. It is a common Indian garden perennial flowering shrub. The flowers exhibited significant antidiabetic action in a dose and time dependent manner.<sup>[88]</sup> Extract of flower exhibits antihyperglycemic, antihyperlipidemic and antioxidant activities mainly at the dose of 250 mg/kg bwt without showing any toxic effects.<sup>[89]</sup> This plant also possesses various pharmacological activities other than antidiabetic properties such as radical scavenging,<sup>[90]</sup>

antibacterial, antipyretic and anti-inflammatory activities,<sup>[91]</sup> anti-tumor<sup>[92]</sup> and anti-convulsant.<sup>[93]</sup>

### ***Momordica charantia***

*Momordica charantia* is commonly known as bitter guard or bitter melon or vegetable insulin belonging to family *cucurbitaceae* and commonly used as an antidiabetic and antihyperglycemic agent.<sup>[94]</sup> The extracts from various components of this plant have been reported to have hypoglycemic effect in various animal models. Ethanolic extracts (200 mg/kg bwt) showed an antihyperglycemic effect in normal and streptozotocin induced diabetic rats. This may be because of inhibition of glucose-6-phosphatase besides fructose-1, 6-biphosphatase in the liver and stimulation of hepatic glucose-6-phosphate dehydrogenase activities.<sup>[95,96]</sup> Charantin, vicine and p-insulin are reported as the active principle of this plant. It was suggest that oral feeding of fruit juice may have a role in the renewal of  $\beta$  cell in streptozotocin diabetic rats. It increases the mitosis of pancreatic cells alternately may permit the recovery of partially destroyed  $\beta$  cell.<sup>[97]</sup> Apart from antidiabetic effect, there are various medicinal properties are claimed for *M. charantia* namely abortifacient, anthelmintic, contraceptive, antimalarial and laxative and also in galactogogue, jaundice, leprosy, pneumonia and rheumatism.<sup>[98,99]</sup>

### ***Ocimum sanctum***

*Ocimum sanctum* is commonly known as Tulsi. It belongs to family *Lamiaceae*. This plant has antidiabetic effect, the leaf extract (200 mg/kg bwt) showed the significant reduction in the plasma glucose level by approximately 9.06% on 15 days and 26.4% on 30 days of the experiment.<sup>[100]</sup> It may be due to the alteration of carbohydrate metabolism by effect on three enzymes of glucokinase, hexokinase and phosphofructokinase.<sup>[100,101]</sup> Eugenol, carvacrol, linalool, caryophylline and  $\beta$  sitosterol are the main active principles that have potent hypoglycemic and hypolipidemic effects in normal and diabetic rats. This plant also shows antioxidant, antibacterial, antifungal, antiviral, antiasthemic, antistress, antiasthemic antitumor, anti gastric ulcer activity, antimutagenic and immunostimulant activities.<sup>[102]</sup>

### ***Pterocarpus marsupium***

*Pterocarpus marsupium* is a deciduous moderate to large tree found in hilly region of India. It is commonly known as Indian Kino tree or Malabar Kino tree or Vijaysar and belongs to *Papilionaceae* family. An aqueous extract of wood (250 mg/kg bwt), shows significant hypoglycemic activity.<sup>[103]</sup> The active principle present in the plant is (-) Epicatechin, has

been found to be insulinogenic, enhancing insulin release and conversion of proinsulin to insulin *in vitro*. 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>[104]</sup> Marsupin, pterosupin and liquiritigenin obtained from this plant showed antihyperlipidemic activity.<sup>[105]</sup> Flavonoid fraction from *P. marsupium* has been shown to cause pancreatic beta cell regranulation.<sup>[106]</sup>

### ***Rubia cordifolia***

*Rubia cordifolia* belongs to family *Rubiaceae*. It is also known as Indian Madder and majit or manjit. The roots of this plant show the anti-hyperglycemic and anti-oxidant properties.<sup>[107-111]</sup> While aerial parts of this plant also shows hypoglycemic effect.<sup>[112]</sup> Oral administration of alcoholic extract of roots of *R. cordifolia* (200 mg/kg bwt) in alloxan induced diabetic rats for two weeks, the blood glucose reduced by 27.1 %, serum total cholesterol by 19.8 % and serum triglyceride by 16.6% as compared to diabetic control group.<sup>[109]</sup> The antihyperglycaemic effect might be due to increased insulin secretion in diabetes. In ancient world, this plant is reputed as an efficient blood purifier and hence is extensively used against blood, skin and urinary diseases.<sup>[113]</sup>

### ***Terminalia chebula***

*Terminalia chebula* also known as harad, haritaki, belong to family *Combretaceae*. It is used in ayurvedic medicine for treating the complications of diabetes mellitus.<sup>[114,115]</sup> Oral administration of aqueous and ethanolic extract of fruits of *T. chebula* (200 mg/kg bwt) reduced the levels of blood glucose in streptozotocin induced experimental diabetic rats.<sup>[116]</sup> An *in vitro* studies with pancreatic islets showed that the insulin release was nearly two times more than that in untreated diabetic animals.<sup>[117]</sup>

### ***Tinospora cordifolia***

*Tinospora cordifolia* belonging to the family *Menispermaceae* is commonly known as Guduchi and Giloya. It is widely used in ayurvedic medicine for treating diabetes mellitus.<sup>[118-121]</sup> The aqueous extract of *T. cordifolia* root (400 mg/kg bwt) could elicit significant antihyperglycemic effect in different animal models.<sup>[122]</sup> Main chemical constituents are berberine, giloin, tinosporaside, tinosporin, tinosporic acid and tinosporol.<sup>[123]</sup> It is also used in venereal disease as well as antileprotic, antiperiodic, anti-inflammatory, antiallergic, antispasmodic, antipyretic and diuretic.<sup>[124]</sup>

***Trigonella foenum graecum***

*Trigonella foenum graecum* is commonly known as Fenugreek and Methi, is a member of family *Fabaceae*. The beneficial effects of this plant have been demonstrated in both insulin dependent and non insulin dependent diabetic animals.<sup>[125]</sup> The plant extract (2 and 8 gm/kg bwt) produces dose dependent decrease in the blood glucose levels in both normal as well as diabetic rats.<sup>[126]</sup> Fenugreek seeds have a novel 4-hydroxyisoleucine amino acid, which increased the insulin release by isolated islet cells in both rats and humans.<sup>[127]</sup> It also reduced hepatic and renal glucose-6-phosphatase and fructose -1, 6-biphosphatase activity.<sup>[128]</sup> This plant also shows antioxidant activity.<sup>[129,130]</sup> Administration of fenugreek seeds improves glucose metabolism and normalizes creatinine kinase activity in heart, skeletal muscle and liver of diabetic rats. Apart from these activities leaves and seeds are used as anti inflammatory antipyretic and immunomodulatory effect.<sup>[131]</sup>

***Withania somnifera***

*Withania somnifera* is a perennial plant, commonly known as Ashwagandha, belonging to the family *Solanaceae*. The root and leave *W. somnifera* produces hypoglycaemic and hypolipidaemic effects in diabetic rats.<sup>[132,133]</sup> It is also used in Ayurvedic and Unani systems for treatment of tumors and tubercular glands. An aqueous extract of this plant (200 and 400 mg/kg bwt) produdes hypoglycemic activity in streptozocine induced diabetic rats. The pharmacological effects of *W. somnifera* are attributed to the presence of withanolides.<sup>[132]</sup>

**CONCLUSION**

The prevalence of diabetes mellitus continues to rise worldwide. It is associated with decreased insulin production or resistance towards its action. There are many modern synthetic drugs are available to treat the diabetic patients. But due to unwanted harmful side/toxic effect, patients are relying on alternative therapies with hypoglycemic properties. Recently lot of research work carried out to justify the role of herbs for prevention and treatment of diabetes and its ailments. 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 aim of present review is to establish the use of plants, plant parts or extract in curing 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 by scientists and scholars in the field of pharmacology and therapeutics to develop anti-diabetic drugs.

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