



# Role of medicinal plants in the management of diabetes mellitus: a review

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## Abstract

Medicinal plants have a vast potential in the treatment of various ailments due to the presence of therapeutically important phytochemicals. Diabetes is a serious metabolic disorder and several marketed medications are available to alleviate the symptoms of diabetes. However, these over the counter drugs are expensive and associated with several complications. Herbal medicines are gaining importance as they are cost-effective and also display improved therapeutic effects with lesser side effects. The present review includes the reports available on medicinal plants used for treating diabetes complications. The aim of the review is to categorize and summarize the available information on medicinal plants with anti-diabetic properties and suggesting outlooks for future research. A systematic search was performed on medicinal plants with anti-diabetic properties using several search engines such as Google Scholar, PubMed, Science Direct and other online journals and books. All the plants listed in this review are native to Asian countries and are routinely used by the traditional practitioners for the treatment of various ailments. Based on the literature data available, a total of 81 medicinal plants with anti-diabetic, anti-hyperglycemic, hypoglycemic, anti-lipidemic and insulin mimetic properties have been compiled in this review. This review provides useful information about the different medicinal plants for treating diabetes-associated complications. Further research can be carried out to study the active constituents and mechanism of these plants.

**Keywords** Diabetes · Medicinal plants · Antidiabetic · Antihyperglycemic · Hypoglycemic

## Introduction

Medicinal plants play a significant role in the treatment of diabetes mellitus which is a serious metabolic disorder. Traditional plants are reported to have significant anti-diabetic properties with no harmful side effects. They are rich sources of anti-diabetic compounds such as flavonoids, alkaloids, phenolic and tannins that improve the efficiency of pancreatic tissues by increasing the insulin secretion or decreasing the intestinal absorption of glucose (Kooti et al. 2016). Literature suggests that there are approximately 410

experimentally proven medicinal plants with anti-diabetic properties out of which the complete mechanism has been studied only for 109 plants. Several medicinal plant extracts have been shown to modulate the metabolic pathways such as glycolysis, gluconeogenesis, Krebs cycle, glycogen synthesis and their degradation, synthesis and release of insulin, cholesterol synthesis, carbohydrate metabolism and absorption (Prabhakar and Doble 2008). Diabetes mellitus (DM) is a chronic endocrine disorder which is characterized by high blood glucose levels that can interfere with carbohydrate, protein, and fat metabolism (Bastaki 2005). It is caused due to the deficit production of insulin by the  $\beta$ -Langerhans islet cells of the pancreas or due to defective insulin uptake in the peripheral tissues (Al-Goblan et al. 2014). An increase in the blood glucose level immediately after a meal triggers the release of insulin hormone from the pancreas. Insulin stimulates the liver to metabolize glucose and also stimulates the fat and muscle cells to remove glucose from the blood which results in a drop of blood sugar level to normal levels. If a person is diabetic, the blood sugar level remains high due to nil or ineffective production of insulin by the pancreas

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(Dean and McEntyre 2004). India has more than 61 million people living with diabetes and hence is considered to be the “capital of diabetes”. Effective treatment of diabetes and its associated complications still remains a major challenge for India due to several issues such as inadequate health care system, lack of proper facilities, etc. (Viswanathan and Rao 2013). Herbal formulations are favored over synthetic drugs to reduce the ill-effects of diabetes and its secondary complications due to lesser side effects and also being cost-effective (Modak et al. 2007). The present review aims to summarize some of the important Indian medicinal plants with anti-diabetic activities based on the electronic literature data available online.

## Medicinal plants with anti-diabetic activities

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

*Aegle marmelos* (L.) Corrêa (Rutaceae), commonly known as Bael or wood apple, is an important medicinal tree native to Northern India. The fruits of this tree are being routinely used for the treatment of dysentery, peptic ulcers, chronic diarrhea and as a laxative in various folk medicine (Baliga et al. 2011). Juice of this fruit is consumed on an empty stomach everyday by the Tripuri tribe in North East India for treating gastric problems. Leaf paste is used for high fever during malaria (Debbarma et al. 2017). The fresh leaf decoction is consumed twice a day for the treatment of a cough, eye problems, breast inflammation and as body coolant by the tribes of Theni district, Tamil Nadu, India (Jeyaprakash et al. 2011). Oral administration of aqueous extract of *A. marmelos* fruit (twice a day for 4 weeks) at a dosage of 250 mg/kg body weight resulted in significant reduction of blood sugar levels in streptozotocin-induced diabetic Wistar rats. This dosage showed effective results over the standard drug glibenclamide (Kamalakkannan and Prince 2003). In a similar study conducted by Kamalakkannan and Prince (2005), the aqueous fruit extract showed protective effects on the pancreas by partially reversing the damage induced by streptozotocin to the pancreatic islets. The methanolic extract of the powdered callus of *A. marmelos* is found to have analogous anti-diabetic potential as its leaf extract (Arumugam et al. 2008). Regular administration of the aqueous seed extract of *A. marmelos* at a dosage of 250 mg/kg for 14 days resulted in substantial reduction of blood glucose level and stabilization of lipid profile in normal and severely diabetic rats. The glucose tolerance was also found to be enhanced in the sub-diabetic and mild diabetic rats (Kesari et al. 2006). Ethanolic extract (150 mg/kg for 30 days) of *A. marmelos* modulates the antioxidant status in the diabetic rats thereby providing a strong defense against the damage caused due to reactive oxygen species

in streptozotocin-induced diabetic rats (Narendhirakanan and Subramanian 2010). Treatment with aqueous fruit and leaf extract of *A. marmelos* (450 mg/kg for 21 days) resulted in significant lowering of blood glucose and insulin levels accompanied with enhanced insulin sensitivity in neonatal type 2 diabetic model rats (Mudi et al. 2017). A compound (3,3-dimethylallyl) halfordinol isolated from the leaves of *A. marmelos* exhibited anti-diabetogenic and lipolytic activities as well as decreased insulin resistance in treated mice models (Saravanan et al. 2014). Limonene, a terpene isolated from the chloroform extract of *A. marmelos* demonstrated potent anti-glycative properties at a 20-fold lower concentration than commonly used inhibitor aminoguanidine (Panaskar et al. 2013). The methanolic extract of the bark of *A. marmelos* demonstrated hypoglycemic effect which can be attributed to the presence of antihyperglycemic constituents—aegelein and lupeol. The study also further demonstrated the regenerative effects of the bark extract on the pancreatic beta cells in diabetic rats (Gandhi et al. 2012). The aqueous fruit extract of *A. marmelos* has shown to salvage the pancreatic beta cell function and improve insulin sensitivity by increasing the peroxisome proliferator-activated receptor- $\gamma$  (PPAR $\gamma$ ) expression (Sharma et al. 2011). A series of phenylethyl cinnamides including two novel  $\alpha$ -glucosidase inhibitors namely anhydromarmeline and aegelinosides have been isolated from the leaves of *A. marmelos* of which anhydroaegeline demonstrated high inhibitory activity against  $\alpha$ -glucosidase (Phuwapraisrisan et al. 2008).

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

*Coriandrum sativum* L., a member of the Apiaceae family, is a commonly used food ingredient possessing medicinal as well as nutritional properties (Laribi et al. 2015). Administration of ethanolic stem and leaves extract of coriander to alloxan-induced diabetic Wistar rats at a dosage of 200 mg/kg/b.w. resulted in hepatoprotective, hypoglycemic, hypolipidemic activities with improved antioxidant potential (Sreelatha and Inbavalli 2012). Sub-chronic administration of aqueous extract of coriander seeds to hyper-caloric diet fed Meriones shawi rats resulted in normalization of blood glucose levels with improved insulin resistance and decreased levels of total cholesterol and triglycerides (Aissaoui et al. 2011). Treatment of streptozotocin-induced diabetic rats with ethanol extract of coriander seeds (200 mg/kg body weight) resulted in decreased serum glucose and increased the insulin releasing capacity of beta cells of pancreatic islets (Eidi et al. 2009).

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

*Zingiber officinale* Roscoe, commonly known as ginger, belongs to the family of Zingiberaceae and is considered to be an important spice with innumerable health benefits. The rhizomes of ginger have been used traditionally for the treatment of hypertension, diabetes, arthritis, sprain, muscular aches, sore throats, fever, cramps, gingivitis, toothache, asthma and infectious diseases (Haniadka et al. 2013). Dietary ginger has been studied to exhibit hypoglycemic, anti-diabetic, anti-oxidant, hypocholesterolemic and hypolipidemic potential (Al-amin et al. 2006; Iranloye et al. 2008; Rani et al. 2012). Supplementation of powdered ginger (3 g/day) for 3 months in type 2 diabetic patients resulted in improved glycemic index and antioxidant status (Shidfar et al. 2015). In a similar study conducted on type 2 diabetic patients, oral ginger supplementation (2 g/day) was found to decrease the insulin levels with no significant changes observed in the fasting plasma glucose and glycated hemoglobin levels (Mahluji et al. 2013). Hydroalcoholic extract of ginger has found to significantly reduce the heart structural abnormalities in STZ-induced diabetic rats with improvement in serum leptin, apoproteins, cathepsin G and homocysteine levels (Ilkhanizadeh et al. 2016). Treatment of diabetic mice with gingerol, an active component of *Z. officinale*, at a dosage of 200 mg/kg/b.w. enhanced the secretion of insulin and also facilitated the uptake of glucose in skeletal muscles through cell surface presentation of GLUT4 transporters and augmentation of glycogen synthase 1 activity (Li et al. 2012b; Samad et al. 2017). Oral administration of ginger extract (500 mg/kg/b.w.) to diabetic rats facilitated the peripheral uptake of glucose and also corrected the impaired glycolytic process of kidney and liver by limiting the gluconeogenic formation (Abdulrazaq et al. 2012).

### ***Syzygium cumini* (L.) Skeels (Black plum)**

*Syzygium cumini* (L.) Skeels, commonly known as Jamun in India, belongs to the family of Myrtaceae and has a wide distribution in the Indian sub-continent, eastern Africa and Southeast Asian countries (Srivastava and Chandra 2013). Stem bark decoction is being consumed by the tribes of Sikkim and Darjeeling Himalaya, India, for the treatment of diabetes mellitus (Chhetri et al. 2005). Oral administration of ethanolic and aqueous extracts of the bark of *S. cumini* (500 mg/kg for 21 days) showed significant blood glucose lowering effects in diabetic Wistar rats (Tripathi and Kohli 2014). Crude hydroalcoholic leaf extract of *S. cumini* has shown to exhibit hypolipidemic and hypoglycemic properties rendering a defensive mechanism against DNA damage and damage caused due to oxidative stress. These properties can be attributed to the phenolic and myricetin content of the leaf (Baldissera et al. 2016). Vitalboside A, an insulin

sensitizer isolated from the methanolic seed extract of *S. cumini* has shown to augment glucose transportation through IRb-triggered PI3K/Akt activation and allosteric inhibition of PTP1B in 3T3-L1 adipocytes and L6 myotubes (Thiyagarajan et al. 2016). Administration of aqueous extract of *S. cumini* seeds in high-fat-diet-streptozotocin-induced type 2 diabetic rats exhibited significant insulin sensitizing, anti-oxidant, anti-dyslipidemic, anti-inflammatory and  $\beta$ -cell protective effects by overexpression of PPAR $\alpha$  and PPAR $\gamma$  activity (Sharma et al. 2017). Oral administration of ethyl acetate fractions significantly modulated the serum glucose level, glucose tolerance, lipid profile, muscle and hepatic glycogen contents, hepatic hexokinase and glucose-6-phosphatase activities. An increase in the volume and size of the pancreatic islets was observed in the treated diabetic rats (Panda et al. 2009). The flavonoid-rich extract obtained from the seeds of *S. cumini* showed to increase the release of insulin from the pancreatic islets as well as decreased the levels of triglycerides and LDL in treated diabetic rats. These activities are a result of the dual upregulation of both the peroxisome proliferators-activated receptors (PPAR $\alpha$  and PPAR $\gamma$ ) (Sharma et al. 2008). Administration of ethanolic extract of the seeds of *S. cumini* significantly decreased the blood sugar level accompanied by an increased body weight in alloxan-induced diabetic rats (Singh and Gupta 2007). The aqueous seed extract of *S. cumini* (100 mg/kg for 21 days) exerts a modulatory effect on the hyperglycemic and inflammatory conditions observed in diabetes mellitus. It also exerts a protective effect against the pathophysiological manifestations triggered by the early stages of diabetes mellitus (Bitencourt et al. 2015). The presence of inorganic constituents such as chromium, potassium, sodium, vanadium in the seeds of *S. cumini* have also been studied to possess hypoglycemic and hypolipidemic activity (Ravi et al. 2004a, 2005). Oral administration of *S. cumini* kernel extract exhibited better hypoglycemic activity as compared to the whole seed extract in diabetic rats (Ravi et al. 2004b). Biosynthesized silver nano-particles from the seeds of *S. cumini* exhibited higher antioxidant activities as compared to the seed extract (Banerjee and Narendhirakannan 2011).

### ***Murraya koenigii* (L.) Spreng. (Curry tree)**

*Murraya koenigii* (L.) Spreng., a member of Rutaceae family, commonly known as curry leaf is an important medicinal plant native to India exhibiting diverse biological activities. Leaf decoction mixed with rice flour is used a treatment for indigestion and eye problems by the tribes of Theni district, Tamil Nadu, India (Jeyaprakash et al. 2011). Koenidine, a metabolically stable carbazole alkaloid isolated from the leaves of *M. koenigii* demonstrated a considerable reduction in the postprandial blood glucose level and improved insulin sensitivity in streptozotocin-induced diabetic rats

(Patel et al. 2016). Administration of ethanolic leaf extract of *M. koenigii* ameliorated the insulin sensitivity and glucose tolerance in dexamethasone-induced insulin-resistant mice. The glucose uptake and GLUT-4 translocation was augmented by the stimulatory effect of *M. koenigii* via insulin-mediated phosphorylation of AKT (Pandey et al. 2014). Oral administration of ethanolic extract of the leaves of *M. koenigii* significantly decreased the blood sugar levels in diabetic rats and also rendered protective effects against development of diabetic neuropathy (Tembhurne and Sakarkar 2010). Administration of aqueous extract of the leaves of *M. koenigii* (200 and 400 mg/kg for 30 days) considerably enhanced the antioxidant status and renal function in diabetic rats and also exhibited strong hypolipidemic and hypoglycemic action (Kesari et al. 2007; Yankuzo et al. 2011). Aqueous leaf extract of *M. koenigii* demonstrated better anti-hyperglycemic activity over the methanolic extract in treated alloxan-induced diabetes mice. Both the extracts are capable of regulating inflammatory cytokines, oxidative stress and prevention of the pancreatic islet damage in diabetic mice. The hypoglycemic property of the *M. koenigii* aqueous extract is based on its ability to elevate PON1 (paraoxonase 1 antioxidant enzyme) activity and subsequently decreasing hyperlipidemia. (Paul et al. 2011; Saha and Mazumder 2013). The extract of *M. koenigii* has been studied to exhibit cytoprotective effects on the pancreatic beta cell production. The effect of this extract on insulin secretion and islet protection was found to persist even after the discontinuation of treatment in diabetic mice (Dusane and Joshi 2012). Oral administration of ethanolic extract of *M. koenigii* (150 mg/kg b.w.) for 30 days in male albino rats resulted in increased levels of insulin, C-peptide, hemoglobin and protein with concomitant decrease in the levels of glycosylated hemoglobin and blood glucose. The presence of inorganic trace elements such as zinc, copper, chromium vanadium, nickel, iron, sodium and potassium in the leaves of *M. koenigii* could be responsible for improvement in managing impaired glucose tolerance and their indirect role in management in diabetes mellitus (Narendhirakannan et al. 2005, 2006).

### ***Gymnema sylvestre* (Retz.) R.Br. ex Sm.**

*Gymnema sylvestre* belonging to the family of Apocynaceae is an important medicinal plant with several pharmacological properties such as antidiabetic, anticarcinogenic and neuroprotective effects (Fabio et al. 2014). The leaves of this plant are dried and powdered and consumed orally with milk by the tribals in southern Western Ghats of Tamil Nadu, India, for alleviating the symptoms of diabetes mellitus (Ayyanar et al. 2008). *G. sylvestre* is popularly known as gurmar, exhibits sweet destroying property which is attributed to its phytoconstituents such as gymnemic acids, triterpenes, gymnema saponins, gurmarin (Tiwari et al. 2014).

The active constituent of this plant includes gymnemic acid, gurmarin, tartaric acid, stigmasterol, betaine, glucose, calcium oxalate and choline which are responsible for the anti-obesity, anti-inflammatory and anti-diabetic properties of *G. sylvestre*. The possible mechanism for its hypoglycemic effects can be attributed to its ability to regenerate islet cells and inhibit glucose absorption from the intestine. It also acts by increasing the glucose utilization in the body and by increasing the activities of enzymes (phosphorylase enzyme) that are responsible for utilization of glucose (Kanetkar et al. 2007). Literature reports suggest that the leaves of *G. sylvestre* stimulates the pancreas due to which an increased insulin release is observed (Kanetkar et al. 2004).

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

*Phyllanthus emblica* L. (synonym: *Emblica officinalis* Gaertn.), commonly known as Amla belonging to the family of Euphorbiaceae is considered as a highly important medicinal plant in Ayurvedic medicine. The major bioactivities of this plant are attributed to its rich polyphenol content comprising mainly tannins and flavonoids. *E. officinalis* (*P. emblica*) exhibits anti-inflammatory, anti-cancer, immunomodulatory, anti-hyperglycemic properties and is also known to maintain glucose homeostasis and improve glucose metabolism (Yadav et al. 2017). It also aids in stimulating pancreatic insulin secretion and regeneration of beta cells (D'souza et al. 2014). Administration of aqueous extract of *E. officinalis* (*P. emblica*) in type 2 diabetic rats (1.25 g/10 mL/kg body weight) for 8 weeks significantly reduced the fasting serum glucose levels with improved oral glucose tolerance (Ansari et al. 2014). In a study conducted by Akhtar et al. (2011), diabetic volunteers treated with *E. officinalis* (*P. emblica*) powder at a dosage of 3 g/day exhibited a significant decrease in the total lipids with improved HDL cholesterol and lowered LDL cholesterol levels. Treatment with *E. officinalis* (*P. emblica*) fruit juice at a dosage of 1 mL/kg/b.w. orally for 8 weeks in type 1 diabetes-induced Wistar rats resulted in improved hyperglycemia, oxidative stress, hyperlipidemia and also augmented the myocardial antioxidant defense mechanisms thereby improving myocardial function in STZ-induced diabetic Wistar rats (Patel and Goyal 2011). Oral administration of a polyphenol-rich ethyl acetate extract fraction of *E. officinalis* (*P. emblica*) at a dosage of 10 or 20 mg/kg of b.w./day to streptozotocin-induced diabetic rats resulted in strong inhibition of glycosylated end products with increased body weight (Rao et al. 2005).

### ***Cinnamomum verum* J. Presl (Cinnamon tree)**

*Cinnamomum verum* J. Presl, belonging to the Lauraceae family is one of the most commonly consumed spices all



over the world. Cinnamon contains vital oils as well as active constituents such as cinnamic acid, cinnamaldehyde, cinnamate that are associated with several health benefits. Cinnamon exhibits a wide range of therapeutic effects such as antioxidant, anti-inflammatory, anti-cancer, anti-diabetic, anti-microbial and also known to have activities against neurological disorders (Rao and Gan 2014). Several polyphenols have been isolated from cinnamon that include rutin (90.06%), catechin (1.90%), quercetin (0.17%), kaempferol (0.02%), and isorhamnetin (0.10%) (Li et al. 2008; Yang et al. 2012). In a comparative study, the insulin potentiating effect of cinnamon was found to be 20-fold higher than many other spices (Broadhurst et al. 2000). Several literature reports reveal that cinnamon has blood glucose and cholesterol lowering activities (Mang et al. 2006; Crawford 2009). Cinnamon has been studied to induce GLUT4 translocation via the AMPK signaling pathway in 3T3-L1 adipocytes and C2C12 myotubes thus establishing its significant role in ameliorating the complications associated with type 2 diabetes mellitus (Shen et al. 2014). Cinnamon polyphenols have been reported to exhibit anti-diabetic activity by its mechanism that includes regulation of glucose levels, lipid metabolism, repair of pancreatic beta cells in STZ-induced high-fat diabetic mice and inhibition of iNOS, NF- $\kappa$ B activation (Li et al. 2013).

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

*Momordica charantia* L., belonging to the family of Cucurbitaceae has been used as a herbal medicine for several years due to its biological properties such as immunomodulation, hepatoprotection, anti-diabetes, anti-tumor and antioxidant (Zhang et al. 2016). A comparative study about the effect of charantin-rich extract (CEMC) of *M. charantia* on type 1 and type 2 diabetic animal models revealed that CEMC at a dosage of 200 mg/kg/day caused a significant decline in the body weight and non-fasting blood glucose level with decreased insulin resistance in high-fat-diet-induced diabetic KK/40HIJ mice. It also caused an increase in the plasma glucose tolerance, but no significant effect was observed on the insulin sensitivity of STZ-induced type 1 ICR 48 mice thus suggesting that CEMC has the potential of improving insulin sensitivity in T2D patients rather than protecting T1D patients against  $\beta$ -cell dysfunction (Wang et al. 2014). Oral administration of 3% bitter melon supplementation to high-fat-diet-induced male OLETF rats resulted in improved glucose tolerance and insulin sensitivity with significant down regulation of phospho-NF- $\kappa$ B (p65) (Ser536) and phospho-c-Jun N-terminal kinase (JNK) (Thr183/Tyr185) in liver, muscle and epididymal fats. It also significantly increased the levels of phospho-insulin receptor substrate-1 (Tyr612) and phospho-Akt (Ser473) and decreased activation of nuclear factor- $\kappa$ B (NF- $\kappa$ B) (Yang et al. 2015). Oral

administration of *Momordica* fruit extract (1.5 g/kg b.w.) for 28 days in STZ-induced Sprague Dawley rats resulted in increased bodyweight and elevated levels of superoxide dismutase, glutathione and catalase in the cardiac tissues thereby establishing its anti-hyperglycemic, cardio-protective and anti-oxidative properties (Abas et al. 2014). Oral administration of *M. charantia* juice to STZ-induced diabetic rats was found to regulate the uptake of glucose into the brush border vesicles of jejunum and also stimulated the uptake of glucose into muscle cells, a response similar to that of insulin (Ahmed et al. 2004).

### ***Ocimum tenuiflorum* L. (Holy basil)**

*Ocimum tenuiflorum* L. (synonym: *Ocimum sanctum* L.), commonly known as tulsi or holy basil belongs to the family of Lamiaceae and is considered as a sacred and important medicinal herb in India. Oral administration of ethanolic leaf extract of *O. sanctum* (*O. tenuiflorum*) (500 mg/kg b.w.) for 15 days resulted in decreased levels of blood glucose, glycosylated hemoglobin, free fatty acids, lipid peroxide and low density lipoproteins and had significantly beneficial effects on HDL synthesis. The mechanism behind the lipid-lowering action of *O. sanctum* (*O. tenuiflorum*) can be attributed to its ability to reactivate lecithin cholesterol acyl transferase, hepatic lipoprotein lipase enzymes and post-heparin lipolytic enzymes (Husain et al. 2015). A tetracyclic terpenoid [16-hydroxy-4,4,10,13-tetramethyl-17-(4-methyl-pentyl)-hexadecahydro-cyclopenta[a]phenanthren-3-one] isolated from the hydro alcoholic extract of the aerial parts of *O. sanctum* (*O. tenuiflorum*) exhibited potential anti-diabetic properties by ameliorating glucose levels, total cholesterol, low and high density lipoprotein cholesterol and triglycerides parameters (Patil et al. 2011). Fixed oil extracted from the leaves of *O. sanctum* (*O. tenuiflorum*) significantly lowered the blood glucose and lipid parameters while increasing serum insulin levels. It also exhibited nephro-protective activity by suppression of high TBARs level and enhancement of various antioxidative enzymes present in the renal tissues of diabetic Wistar rats. This property may be attributed to  $\alpha$  linolenic acid present in the fixed oil (Suanarunsawat et al. 2016). Oral administration of aqueous extract of *O. sanctum* (*O. tenuiflorum*) mixed with diet for 8 weeks showed a significant reduction in fasting blood glucose, lipid peroxidation products, serum lipid profile and improvement in glucose tolerance (Hussain et al. 2001). In a study carried out by Hannan et al. 2006, ethanol, butanol, aqueous and ethylacetate fractions of *O. sanctum* (*O. tenuiflorum*) leaves stimulated insulin secretion from the damaged rat pancreas, isolated rat islets and in clonal pancreatic  $\beta$ -cells. Administration of *O. sanctum* (*O. tenuiflorum*) seed oil (0.8 g/day b.w.) for 4 weeks demonstrated hypocholesterolemic and

**Table 1** Medicinal plants with anti-diabetic properties

S. no.	Botanical name	Common name(s)	Family	Part(s) used for the study	Activities	References
1	<i>Abelmoschus esculentus</i> (L.) Moench	Lady's finger	Malvaceae	Seeds, fruit	Antidiabetic, antioxidant and antihyperlipidemic	Sabitha et al. (2011) and Mishra et al. (2016)
2	<i>Acacia nilotica</i> (L.) Delile	Gum arabic tree	Leguminosae	Leaves	Antioxidant, antidiabetic, antihyperlipidemic	Hegazy et al. (2013)
3	<i>Allium cepa</i> L.	Onion	Amaryllidaceae	Bulb	Hypoglycemic, anti-diabetic, anti-hyperlipidemic	Eldin et al. (2010) and Ikechukwu and Ifeanyi (2016)
4	<i>Aloe vera</i> (L.) Burm.f.	Aloe	Asphodelaceae	Leaves	Anti-hyperglycemic, anti-hypercholesterolemic, hypoglycemic, hypolipidemic	Huseini et al. (2012) and Kim et al. (2009)
5	<i>Annona squamosa</i> L.	Sugar apple	Annonaceae	Leaves, fruit pulp	Hypoglycemic, anti-diabetic, anti-lipidemic	Shirwaikar et al. (2004), Gupta et al. (2005) and Gupta et al. (2008)
6	<i>Artemisia pallens</i> Wall. ex DC.	Artemisia	Asteraceae	Aerial parts	Hypoglycemic	Subramoniam et al. (1996), Ruikar et al. (2011)
7	<i>Averrhoa bilimbi</i> L.	Bilimbi	Oxalidaceae	Leaves, roots, fruit	Anti-hyperglycemic, antihyperlipidemic, hypoglycemic, anti-diabetic	Tan et al. (2005), Xu et al. (2014) and Kurup and Mini (2017)
8	<i>Azadirachta indica</i> A. Juss	Neem tree	Meliaceae	Leaves, seeds	Hypoglycemic, $\beta$ -cell regeneration	McCallia et al. (2016) and Khosla et al. (2000)
9	<i>Berberis vulgaris</i> L.	Barberry	Berberidaceae	Root, fruit	Hypoglycemic, anti-diabetic	Meliani et al. (2011)
10	<i>Beta vulgaris</i> L.	Beet	Amaranthaceae	Leaves, fruit	Anti-hyperglycemic, hypoglycemic	Bolkent et al. (2000) and Kabir et al. (2015)
11	<i>Biophytum sensitivum</i> (L.) DC.	Little tree plant	Oxalidaceae	Leaves	Hypoglycemic	Puri (2001) and Ananda et al. (2012)
12	<i>Brassica juncea</i> (L.) Czern.	Brown mustard	Brassicaceae	Seeds	Hypoglycemic	Yadav et al. (2004) and Thirumalai et al. (2011)
13	<i>Bryophyllum pinnatum</i> (Lam.) Oken	Life plant, miracle leaf	Crassulaceae	Leaves	Antidiabetic, hypoglycemic	Ojewole (2005)
14	<i>Boerhavia diffusa</i> L.	Spreading hogweed	Nyctaginaceae	Leaves	Anti-diabetic	Pari and Satheesh (2004) and Singh et al. (2011)
15	<i>Bombax ceiba</i> L.	Cotton tree	Bombacaceae	Leaves	Antihyperglycemic, antihyperlipidemic	Guang-Kai et al. (2017)
16	<i>Caesalpinia bonduc</i> (L.) Roxb	Fever nut	Caesalpinaceae	Seeds, root bark	Hypoglycemic, antihyperglycemic, antihypercholesterolemic, antihypertriglyceridemic hypolipidemic	Sharma et al. (1997), Chakrabarti et al. (2005) and Sayed and Wadkar (2018)
17	<i>Cajanus cajan</i> (L.) Millsp.	Pigeon pea	Fabaceae	Leaves, seeds	Hypoglycemic	Jaiswal et al. (2008) and Uchegbu and Ishiwu (2016)

Table 1 (continued)

S. no.	Botanical name	Common name(s)	Family	Part(s) used for the study	Activities	References
18	<i>Camellia sinensis</i> (L.) Kuntze	Tea plant	Theaceae	Leaves	Anti-hyperglycemic, antihyperglycemic and antidiabetic	Ankolekar et al. (2011) and Abeywickrama et al. (2011) and Satoh et al. (2015)
19	<i>Capparis decidua</i> (Forssk.) Edgew.	Karira	Capparidaceae	Fruit, flowers, bark	Anti-diabetic, hypolipidemic	Chahlia (2009) and Sharma et al. (2010)
20	<i>Capsicum annuum</i> L.	Capsicum	Solanaceae	Fruit	Insulinotropic	Islam and Choi (2008)
21	<i>Centaurium erythraea</i> Rafn	Common centaury	Gentianaceae	Leaves	Antihyperglycemic	Stefkov et al. (2014)
22	<i>Catharanthus roseus</i> (L.) G. Don	Madagascar periwinkle	Apocynaceae	Leaves	Anti-diabetic, hyperlipidemic, anti-hyperglycemic	Rasineni et al. (2010) and Al-Shaqha et al. (2015)
23	<i>Citrullus colocynthis</i> (L.) Schrad.	Bitter apple, wild gourd	Cucurbitaceae	Fruit, seeds, root	Hyperglycemic, antihyperglycemic	Abdel-Hassan (2000), Barghamdi et al. (2016), Hussain et al. (2014)
24	<i>Clausena anisata</i> (Willd.) Hook.f. ex Benth.	Horsewood	Rutaceae	Root	Hyperglycemic	Ojewole (2002)
25	<i>Cocos nucifera</i> L.	Coconut	Arecaceae	Spadix, drupe, coconut water	Anti-hyperglycemic, antihyperglycemic, hypoglycemic	Naskar et al. (2011) and Pinto et al. (2015)
26	<i>Cheilocostus speciosus</i> (J.Koenig) C.D.Specht	Cane-reed	Costaceae	Root, leaves	Antihyperglycemic, hypoglycemic, hypolipidemic	Bavarva and Narasimhacharya (2008) and Eliza et al. (2009)
27	<i>Curcuma longa</i> L.	Turmeric	Zingiberaceae	Rhizome	Antioxidant, antidiabetic, hepatoprotective	Ahmad et al. (2014)
28	<i>Cyclocarya paliurus</i> (Batalin) Hjmsk.	Wheel wingnut	Juglandaceae	Bark	Hyperglycemic, anti-ti-hyperglycemic, anti-hyperlipidemic	Li et al. (2011), Xiao et al. (2017) and Wang et al. (2013)
29	<i>Dillenia indica</i> L.	Elephant apple	Dilleniaceae	Leaves	Antidiabetic, hypolipidemic	Kumar et al. (2011)
30	<i>Eucalyptus globulus</i> Labill.	Blue-gum	Myrtaceae	Leaves	Anti-hyperglycemic	Ahlem et al. (2009)
31	<i>Embelia ribes</i> Burm.f.	False black pepper	Myrsinaceae	Berries	Anti-hyperglycemic, antidiabetic	Bhandari and Ansari (2008) and Durg et al. (2017)
32	<i>Eugenia uniflora</i> L.	Brazilian cherry	Myrtaceae	Fruit	Antihyperglycemic, antidiabetic, antihyperglycemic, antidiabetic	de Souza Cardoso et al. (2017)
33	<i>Ficus benghalensis</i> L.	Banyan tree	Moraceae	Bark, aerial roots	Anti-diabetic	Singh et al. (2009)
34	<i>Ficus religiosa</i> L.	Sacred fig	Moraceae	Bark	Anti-diabetic	Pandit et al. (2010)
35	<i>Helicteres isora</i> L.	Indian screw tree	Sterculiaceae	Root	Antidiabetic, hypolipidemic, antihyperglycemic	Chakrabarti et al. (2002) and Venkatesh et al. (2004)
36	<i>Hibiscus rosa-sinensis</i> L.	Chinese hibiscus, shoe black plant	Malvaceae	Flower, leaves	Hyperglycemic, antidiabetic	Sachdeva and Khemani (2003) and Kumar et al. (2013)
37	<i>Ipomoea batatas</i> (L.) Lam	Sweet potato	Convolvulaceae	Leaves, root	Hyperglycemic	Oki et al. (2011), Mohanraj and Sivasankar (2014)
38	<i>Juniperus communis</i> L.	Common juniper	Cupressaceae	Berries	Hyperglycemic	de Medina et al. (1994), Gori-dien et al. (2009)

Table 1 (continued)

S. no.	Botanical name	Common name(s)	Family	Part(s) used for the study	Activities	References
39	<i>Lantana camara</i> L.	Big-sage, wild-sage	Verbenaceae	Fruits	Anti-hyperglycemic, anti-diabetic	Venkatachalam et al. (2011)
40	<i>Lithocarpus polystachyus</i> (Wall. ex A.DC.) Rehder	Sweet tea	Fagaceae	Leaves	Hyperglycemic	Hou et al. (2011)
41	<i>Phyla nodiflora</i> (L.) Greene	Capeweed	Verbenaceae	Whole plant	Anti-hyperlipidemic, anti-hyperglycemic	Balamurugan et al. (2011)
42	<i>Mangifera indica</i> L.	Mango	Anacardiaceae	Leaves, fruit	Anti-diabetic, hypoglycemic	Gondi et al. (2015) and Ganog-pichayagrai et al. (2017)
43	<i>Memecylon umbellatum</i> Burm. f.	Iron wood	Melastomataceae	Leaves	Anti-diabetic	Sunil et al. (2017)
44	<i>Morus alba</i> L.	White mulberry	Moraceae	Fruit, leaves	Anti-hyperglycemic, anti-hyperlipidemic, anti-glycemic	Naowaboot et al. (2009) and Jiao et al. (2017)
45	<i>Mucuna pruriens</i> (L.) DC.	Velvet bean	Fabaceae	Seeds	Anti-diabetic	Majekodunmi et al. (2011)
46	<i>Musa × paradisiaca</i> L.	Plantain	Musaceae	Stem, leaves, infructescence stalks, fruit	Antidiabetic, antihyperlipidemic, anti-hyperglycemic	Dikshit et al. (2012) and Jaber et al. (2013)
47	<i>Nelumbo nucifera</i> Gaertn.	Indian lotus	Nelumbonaceae	Seeds, leaves	Hyperglycemic, antihyperlipidemic	Mani et al. (2010) and Liu et al. (2013)
48	<i>Olea europaea</i> L.	Wild olive	Oleaceae	Leaves	Antihyperglycemic, hypolipidemic, hypoglycemic	Wainstein et al. (2012)
49	<i>Ophiopogon japonicus</i> (Thumb.) Ker Gawl.	Dwarf lilyturf	Asparagaceae	Root	Anti-diabetic, hypoglycemic	Li et al. (2012a)
50	<i>Opuntia streptacantha</i> Lem.	Prickly pear cactus	Cactaceae	Leaves (cladode)	Anti-hyperglycemic	Andrade-Cetto and Wiedenfeld (2011)
51	<i>Phyllanthus niruri</i> L.	Stonebreaker	Phyllanthaceae	Aerial parts	Anti-diabetic	Beidokhti et al. (2017)
52	<i>Picrorhiza kurroa</i> Royle ex Benth.	Yellow gentian	Plantaginaceae	Rhizome	Anti-diabetic	Chauhan et al. (2008)
53	<i>Piper nigrum</i> L.	Black pepper	Piperaceae	Fruit	Anti-hyperglycemic	Atal et al. (2012)
54	<i>Prosopis glandulosa</i> Torr.	Honey mesquite	Fabaceae	Pods	Anti-diabetic	George et al. (2011)
55	<i>Psidium guajava</i> L.	Guava	Myrtaceae	Fruit, leaves	Anti-hyperglycemic, anti-hyperlipidemic	Deguchi and Miyazaki (2010) and Huang et al. (2011)
56	<i>Pterocarpus marsupium</i> Roxb.	Indian kino tree	Fabaceae	Bark	Hyperglycemic, anti-hyperglycemic, inhibition of aldose reductase activity	Dhanabal et al. (2006), Mishra et al. (2013) and Xu et al. (2018)
57	<i>Punica granatum</i> L.	Pomegranate	Punicaceae	Leaves, fruit	Anti-diabetic, anti-hyperlipidemic, anti-glycation	Das and Barman (2012) and Kumagai et al. (2015)
58	<i>Salacia reticulata</i> Wight	Marking nut tree, kotalahimbatu	Celastraceae	Root, stem, leaves	Anti-diabetic, anti-hyperlipidemic	Stohs and Ray (2015)
59	<i>Semecarpus anacardium</i> L.f.	Marking nut	Anacardiaceae	Nut	Anti-hyperlipidemic, hypoglycemic and antihyperglycemic	Arul et al. (2004) and Khan et al. (2013)



Table 1 (continued)

S. no.	Botanical name	Common name(s)	Family	Part(s) used for the study	Activities	References
60	<i>Senna auriculata</i> (L.) Roxb.	Avaram senna, styptic weed, Matara tea	Fabaceae	Leaves, flower	Antihyperglycemic, hypolipidemic, antihyperlipidemic	Gupta et al. (2009) and Rajendran et al. (2017)
61	<i>Solanum virginianum</i> L.	Yellow-fruit nightshade	Solanaceae	Leaves	Anti-hyperglycemic	Poongothai et al. (2011)
62	<i>Sweritia chirayita</i> (Roxb.) Buch.-Ham. ex C.B. Clarke	Clearing nut tree, bitter stick	Gentianaceae	Whole plant	Anti-diabetic	Phoboo et al. (2013)
63	<i>Symplocos cochinchinensis</i> (Lour.) S. Moore	Laurel sapphire berry	Symplocaceae	Leaves	Anti-diabetic, anti-lipidemic	Sumil et al. (2011) and Sumil et al. (2012)
64	<i>Tetraena alba</i> (L.f.) Beier & Thulin	White bean-caper	Zygophyllaceae	Whole plant	Antihyperglycemic and antihyperlipidemic	Ghoul et al. (2013)
65	<i>Tinospora sinensis</i> (Lour.) Merr.	Malabar gulbel, Chinese tinospora	Menispermaceae	Root	Hypoglycemic and hypolipidemic	Stanely Mainzen Prince and Menon (2003)
66	<i>Trigonella foenum-graecum</i> L.	Fenugreek	Fabaceae	Seeds	Hypoglycemic, hypocholesterolemic, anti-hyperglycemic	Xue et al. (2007) and Kumar et al. (2012)
67	<i>Urtica dioica</i> L.	Stinging nettle	Urticaceae	Aerial parts	Anti-hyperglycemic	Bnouham et al. (2003)
68	<i>Vitex negundo</i> L.	Chinese chastetree, horseshoe vitex	Lamiaceae	Leaves	Anti-hyperglycemic	Sundaram et al. (2012)
69	<i>Viscum album</i> L.	Mistletoe	Viscaceae	Leaves	Antihyperglycemic, insulinotropic	Eno et al. (2008)

antioxidant effects in cholesterol-fed rabbits (Gupta et al. 2006).

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

*Allium sativum* L., commonly known as garlic, belongs to the *Allium* genus in the family Alliaceae that are known to contain a high concentration of non-protein sulfur amino acids that are responsible for their medicinal features (Ovesná et al. 2015). Administration of *A. sativum* extract along with the commercially available drug glibenclamide resulted in increased weight and exhibited better hypoglycemic effect in streptozotocin-induced diabetic rats (Poonam et al. 2013). Similar results were observed in a study where diabetic patients when treated with combination of commercially available drug metformin and garlic supplementation exhibited improved glycemic control in addition to antihyperlipidemic activity (Ashraf et al. 2011). Treatment with fresh garlic homogenate (250 mg/kg b.w.) for 6 weeks resulted in better modulation of antioxidant status in blood and cardiac tissues of streptozotocin-induced diabetic-induced Wistar rats (Naderi et al. 2015). Administration of garlic extract resulted in reduction of blood glucose concentration accompanied by downregulation of the adrenal and renal expression of angiotensin AT1 receptor in STZ-induced diabetic rats which explains its potential in reversing the harmful consequences of excessive Ang II signaling, manifested by the development of hypertension and nephropathy (Mansour et al. 2013). The anti-diabetic effect of garlic extract has been reported to be more effective than the standard drug glibenclamide (Eidi et al. 2006).

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

*Coccinia grandis* (L.) Voigt (synonym: *Coccinia indica* Wight & Arn.) belonging to the family of Cucurbitaceae is an important medicinal plant known for its anti-diabetic and hypoglycemic properties. *C. indica* (*C. grandis*) fruits have been studied to exhibit renoprotective effect as it has been reported to ameliorate glucose tolerance, urine sugar, albumin excretion, kidney index, and glomerular filtration rate as well as exhibited beneficial effects on the antioxidant enzymes of the kidney in diabetic rats (Gurukar et al. 2013). *C. indica* (*C. grandis*) leaf extract possesses anti-ureogenic, anti-hyperglycemic (Baizid Alam Shibib et al. 2012), antioxidant (Venkateswaran and Pari 2003), hypoglycemic and hypolipidemic (Pari and Venkateswaran 2003) effects as reported by several studies carried out on diabetic rats. In a study carried out on diabetic patients *C. indica* (*C. grandis*) dried extract was found to exhibit insulin mimicking activity by correcting the elevated enzymes (G-6-p (ase) and LDH) in the glycolytic pathway and by restoring the LPL activity in lipolytic pathway (Kamble et al. 1998). Methanolic

extract of *C. grandis* fruit exhibited 96.6% in vitro aldose reductase inhibitory activity against partially purified bovine lens aldose reductase with an IC<sub>50</sub> value of 6.12 µg/mL. This activity can be attributed to the high percentage of phenolic and flavonoid content of the fruit (Kondhare and Lade 2017).

Few medicinal plants with anti-diabetic potential are tabulated in Table 1.

## **Conclusion**

Diabetes is the most common endocrine disorder that affects nearly 100 million people worldwide. India, also known as the diabetes capital of the world has witnessed an alarming increase in the number of diabetics over the past decade. Advancement in modern medicine has resulted in the development of several pharmaceutical drugs such as biguanides, thiazolidinediones, biguanides, and insulin. Even though these drugs show hypoglycemic activities, they are often associated with several complications such as nephrological disorders, fatigue, upset stomach, diarrhea, etc. All these reasons have stimulated the rework on herbal medicine to find suitable alternatives that will have lesser side effects and improved therapeutic effects. The present review has summarized the list of medicinal plants of Asian countries that are known to possess anti-diabetic properties. These plants are traditionally used by various tribal people for the treatment of several ailments. Pharmacological studies have reported their hypoglycemic, anti-hyperglycemic, insulin mimicking, anti-lipidemic properties and hence when administered in proper dosages can be beneficial for ameliorating the various complications associated with diabetes mellitus. This review provides the scope for the readers to further explore the active constituents of anti-diabetic plants and its possible mechanisms for future research.

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## **Compliance with ethical standards**

**Conflict of interest** The authors have declared no conflict of interest.

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