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Review Article

MANAGEMENT OF DIABETES MELLITUS WITH TRADITIONAL AYURVEDIC HERBS: A REVIEW

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ABSTRACT

Ayurvedic herbs have been used as a source of medicine since the dawn of humanity. There are over 21,000 herb species in India, and thousands of them have been claimed to have therapeutic characteristics. Ayurvedic herbs referenced in ancient literature or used historically for diabetes have been found to have anti-diabetic properties in studies undertaken in the last several decades. The current research examines ten such herbs that have been utilized in traditional medicine and have shown anti-diabetic effects in both experimental and clinical studies. The herbs mentioned in this review are *Ceratonia silliqua, Syzygium aromaticum, Verbena officinalis, Abelmoschus esculentus, Allium cepa, Coriandrum sativum, Lepidium sativum, Rosmarinus officinalis, Zingiber officinale, Eupatorium sp, Mangifera indica, Swertia chirayta, Ocimum sanctum, Azadirachta indica* and *Ablemoschus moschatus*. All these important ayurvedic plants have shown good responses against diabetes mellitus.

Keywords: Diabetes mellitus, Ayurvedic herbal drugs, Anti-diabetic, β-cells.

1. INTRODUCTION

Diabetes is a long-term carbohydrate, lipid, and protein metabolic disease condition marked by high fasting and postprandial blood sugar levels. Diabetes is expected to rise from 4% in 1995 to 5.4 percent by 2025, according to the World Health Organization, Type I and type II diabetes are the two most common kinds of diabetes. T1DM is a lifelong glucose homeostasis disorder characterized by destruction of the insulin-producing pancreatic -cell by the immune system, resulting in insulin insufficiency and hyperglycemia. New symptoms of T1DM have emerged in recent years, in addition to the typical symptoms (polyuria, polydipsia, polyphagia, and weight loss), such as diabetic ketoacidosis (DKA), which includes vomiting, abdominal pain and fatigue. This is an extremely fatal condition with a lot of comorbidities that need to be closely monitored. Because T1DM is a chronic illness, the best results are obtained when patients and their families take responsibility of their condition as part of a long-term, empowering relationship with it. People with this condition are completely reliant on exogenous insulin, whereas patients with Type II diabetes (insulin resistance) are unable to respond to insulin and can be managed with dietary changes, exercise and medication. Type II diabetes is the most common type of diabetes, accounting for the maximum number of diabetics [1, 2].

Despite recent advances in medical science, there are still a number of obstacles in the management of diabetes that necessitate special attention to developing hitherto unexplored sectors of medical knowledge. Medicines to regulate and treat diabetes have been produced by modern health systems; however, they are unable to provide comprehensive relief. Furthermore, they are linked to negative side effects like hypoglycemia [3]. Ayurveda's armamentarium could be a source of hypoglycemic medications that are generally safe, significantly effective, have few adverse effects and can improve quality of life [4]. Herbal therapies are also important in the management of diabetes mellitus type 2 according to the WHO. Diabetes Mellitus type 2 can be likened to *Madhumeha* in Ayurveda based on similar indications and symptoms. A list of 21,000 medicinal plants used around the world has been compiled by the World Health Organization (WHO). There are 2500 species in India, with 150 of them being utilized commercially on a regular basis. India is recognized as the world's botanical paradise and is the world's largest

producer of medicinal plants. The current study focuses on herbal medicinal preparations and plants used to treat diabetes mellitus, a terrible disease that costs billions of dollars worldwide [5].

2. TYPES OF DIABETES

Immunity-mediated T1DM is thought to be caused by an infectious or toxic insult to people whose immune systems are genetically prone to mount a strong autoimmune response against altered pancreatic β cell antigens or β cell molecules that resemble viral proteins (molecular mimicry). Damage produced by viruses like coxsackie B4 virus ormumps, poisonous chemical entities, or damaging cytotoxins and antibodies secreted by sensitized immunocytes are all extrinsic variables that alter β cell activity. Patients with certain HLA immune response genes are likely to be prone to a harmful autoimmune response (auto aggressiveness) against their own islet cells, mediated mostly by cytotoxic T cells. To treat hyperglycemia in these patients, an immuno-suppressive drug (such as cyclosporine) is given [6].

Type 2 diabetes is a broad category that encompasses milder versions of the disease that primarily affect adults but can also affect youngsters. More than 90 percent of diabetics fall into this category. Circulating endogenous insulin is sufficient to prevent ketoacidosis, but it is insufficient to prevent hyperglycemia in the face of increasing demands due to tissue insensitivity. In the vast majority of cases, the cause of this kind of diabetes is unknown. Tissue insulin sensitivity has been seen in the majority of Type 2 patients, independent of weight, and has been connected to a variety of factors [7].

The pancreatic cells' response to glucose is also reduced. Hyperglycemia appears to aggravate both tissue resistance to insulin and defective cell responsiveness to glucose, and treatment that lowers hyperglycemia to normal levels appears to alleviate both abnormalities. According to the preponderance of epidemiologic research, Type 2 diabetes has significant genetic consequences. Although a link to a gene on chromosome 2 that codes for calpain-10, a cysteine protease, has been discovered in a Mexican-American population, the genetic factors that cause Type 2 diabetes have yet to be discovered [8]. Diabetes mellitus has been classified into some other specific types (Fig. 1).

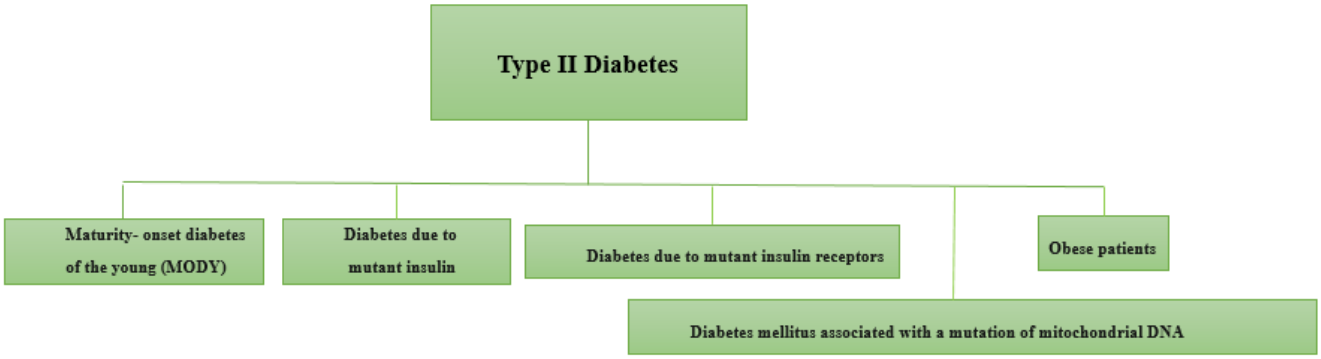

Fig. 1: Classifications of Type II Diabetes

2.1. Maturity- onset diabetes of the young (MODY)

This is a relatively uncommon monogenic illness defined by non-insulin-dependent diabetes, autosomal dominant heredity, and beginning age of 25 years or less. Patients are non-obese, and their hyperglycemia is caused by insulin secretion that is impaired by glucose [9].

2.2. Diabetes due to mutant insulin

This is an extremely unusual non-obese Type 2 diabetes variant. Diabetes was mild and demonstrated autosomal dominant genetic transmission because affected people were heterozygous and had one normal insulin gene [10].

2.3. Diabetes due to mutant insulin receptors

Defects in one of the insulin receptor genes have been found in more than 40 patients with diabetes.

2.4. Diabetes mellitus associated with a mutation of mitochondrial DNA

Diabetes has been linked to a mitochondrial DNA mutation that prevents the transfer of leucine or lysine into mitochondrial proteins. The majority of patients

have a moderate form of diabetes that is treated with oral hypoglycemics. Hearing loss affects two-thirds of individuals with this kind of diabetes, while a lesser percentage experience a syndrome of encephalopathy, lactic acidosis, myopathy, and stroke-like episodes (MELAS) [11].

2.5. Obese patients

Extra pancreatic factors cause insensitivity to endogenous insulin, which is the most frequent form of diabetes. Nonketotic moderate diabetes develops when a malfunction in insulin synthesis prevents effective correction for insulin resistance. The main issue is a "target organ" condition that causes poor insulin action and, as a result, can affect pancreatic β cell function. Late clinical manifestations of diabetes mellitus include a variety of pathologic changes affecting small and large blood vessels, cranial and peripheral nerves, and the lenses of the eyes. These lesions cause hypertension, renal failure, blindness (retinopathy), autonomic and peripheral neuropathy, lower-extremity amputations, myocardial infarction, and cerebrovascular accidents [12].

3. DIAGNOSIS DATA

47.5 % of the diabetic patients in the survey had T2DM, while 52.5 % had T1DM. For 14.3 %, 61.2 %, 22.5 %, and 2%, diabetes was diagnosed within a year, 1-15 years, 16-30 years, and above 30 years, respectively [13].

4. ETHNOBOTANICAL DATA

Medicinal plants were usually used in conjunction with conventional treatment for diabetics. Patients think of this use as a way to augment their diabetic treatment. Various surveys gathered information around West Bengal state as well as all of India showed more than 20 species which can be useful in diabetes. Three of these plants were used just for T1DM, while the other five were used for both T1DM and T2DM [14].

5. AYURVEDIC HERBS USED IN MANAGEMENT OF DIABETES

5.1. *Ceratonia silliqua* (Shimbibhed)

Hot and cold extracts from the leaves of *Ceratonia silliqua* (Fam. Fabaceae) better known as carob or locust bean, a traditional ayurvedic herb, have shown promising anti-diabetic action in rats and other animal studies. The plant can reach a height of 7-12 metres. This perennial green tree is typically hermaphrodite, with flower clusters and pinnately shaped leaves. They have droopy pod fruits with plumpy sheaths that are 10-30 cm in length. Within the pod, there are 12-16 firm seeds [15]. The biochemical and histological findings of this study revealed that both the hot hydrous extract and the cold extract of *Ceratonia siliqua* leaves have hypoglycemic effects on rats, and that both extracts had significant hypoglycemic effects in alloxan-induced diabetic rats with no change in body weight. It was also suggested that the renewal or repair of pancreatic islet-cells after damage caused by alloxan could be the primary explanation for alloxan-injected guinea pigs recovering from the drug's effects [16].

5.2. *Syzygium aromaticum* (Lavangaha)

EtOH extract of clove (*Syzygium aromaticum* flower buds); an important ayurvedic spice, has been demonstrated to drastically reduce blood glucose levels. *Syzygium aromaticum* (Fam. Myrtaceae, is an evergreen tree that grows to be 8-30 meters tall. Canopy is modest in size, and the crown base is low. Branches are semi-erect and plentiful. The lower side of the leaves is glabrous, with many oil glands. Each peduncle produces 3-4 stalked flowers at the end, and the flowers are tiny and in terminal cymose clusters. Sepals have little triangular projections on them [17]. *Syzygium aromaticum* extract was found to have therapeutic effects in decreasing blood sugar, oxidative stress, plasma cholesterol, triglycerides and LDL levels in this investigation. *Syzygium aromaticum* also decreases liver tissue damage and boosts blood insulin levels, making it useful in lowering diabetes-related tissue damage [18].

5.3. *Verbena officinalis* (Bhantaka)

Simpler's joy, or *Verbina officinalis*, is a perennial herb and a traditional medicine native to Europe that belongs to the Verbenaceae family. It can reach a height of 70 cm and has an erect habit. The serrated lobed leaves have clusters of two-lipped mauve blooms, and the delicate spikes have clusters of two-lipped mauve flowers [19]. It is a historically important medicinal plant that has been linked to the treatment of type 1 diabetes and a variety of other pharmacological effects [20].

5.4. *Abelmoschus esculentus* (Bhindaka)

In medicine, *Abelmoschu sesculentus* Linn. (Fam. Malvaceae); often known as okra, is used to treat diabetes mellitus. It belongs to the mallow family and is

a blooming plant. Its delicious green seed pods are prized. Minerals, vitamins, antioxidants and fibre are all abundant in it. Okra's origins are debated, with enthusiasts claiming West African, Ethiopian and South Asian roots. Herbs, undershrubs, and tiny trees are all Abelmoschus species. Simple prickly or stellate hairs on the branches. Leaves alternating, palmately lobed or palmilobed, sagittate to hastate with to-parted segments or pennilobed, edges crenate-dentate, seldom whole, coriaceous, and petiolate. Axillary or terminal inflorescence, single or in cymes [21]. The antidiabetic efficacy of *Abelmoschus esculentus* is mediated by boosting insulin secretion, increasing insulin sensitivity, and limiting carbohydrate absorption in the gut; however, it was unable to block the enzymes α-glucosidase and α-amylase [22].

5.5. *Allium cepa* (lashunam)

The onion, *Allium cepa* of the Amaryllidaceae family, an important ayurvedic herb, has been demonstrated to be beneficial in both forms of diabetes. It is a vegetable that belongs to the genus Allium and is the most extensively farmed species. Garlic, scallion, leek, chive and Chinese onion are all close relatives. The Japanese bunching onion (*Allium fistulosum*), the tree onion, and the Canada onion are among the species in this genus that are commonly known to as onions and are farmed for food (*Allium canadense*). Although the term "wild onion" is used to describe a variety of Allium species, *A. cepa* is only known from cultivation. Although escapes from cultivation have become entrenched in some areas, its primordial wild form is unknown. Although the onion is a biennial or perennial plant, it is often handled as an annual and harvested during its first growing season. The onion plant has a fan of hollow, bluish-green leaves, and when a specific day-length is achieved, the bulb at the base of the plant begins to swell. The bulbs are made up of underground stems that have been reduced and compressed, encircled by mushy modified scale (leaves) that encase a central bud at the tip of the stem. The foliage dies down in the autumn (or spring in the case of overwintering onions) and the outer layers of the bulb become increasingly dry and brittle [23]. In alloxan-induced diabetic rats, various studies showed potential hypoglycaemic and hypolipidaemic action. It's hypoglycemic and hypolipidemic actions may operate as a preventive mechanism against the development of hyperglycemia and hyperlipidemia, both of which are hallmarks of diabetes [24].

5.6. *Coriandrum sativum* (Vitunnaka)

Coriander or *Coriandrum sativum*, belongs to the Apiaceae family and have been traditionally used to treat diabetes as mentioned in ancient ayurvedic texts. It is a culinary and medicinal herb that can become weedy if not grown properly. The Global Compendium of Weeds classifies it as an "agricultural weed, casual foreign, cultivation escape, garden thug, naturalised, sleeper weed, weed," and it is classified as a weed in Israel, Lebanon, Morocco and Taiwan. It's an annual with erect, 1 to 3 foot tall, slender, branching stems. The lower leaves are stalked and pinnate, with roundish or oval leaflets that are somewhat lobed. The leaf segments at the top are more divided and linear. By enhancing and rebuilding pancreatic β cells and suppressing the α -glucosidase enzyme in the small intestine, the leaves demonstrated anti-diabetic effect. (Table 1) [25, 26].

5.7. *Lepidium sativum* (Ahaleeva)

Garden cress, *Lepidium sativum* of the Brassicaceae family, a famous ayurvedic herb is commercially produced in England, France, the Netherlands and Scandinavia. They are a fine-taproot annual herb. The stem is erect, simple to densely branched, and glabrous or coated with minute hairs, reaching a height of 70 cm. Leaves are petioled, sparsely pubescent, up to 10 cm long, pinnati- or bipinnatipartite, with 2-4 pairs of lateral lobes; lobes are linear, lanceolate, or oblanceolate (even obovate in lower leaves), up to 3 cm long; uppermost leaves are serrate. Fruits are siliculae elliptic in outline, 4.5-6.5 mm long, 3-4 mm broad, with prominent apical wings, deeply emarginate; style distinct, with stigma completely within or just level with the top of the sinus, with seeds wingless, reddish brown, 2-3 mm long, 1.5 mm broad; style distinct, with stigma completely within or just level with the top of the sinus; style distinct, with stigma completely within or just level with the top of Lepidium controls diabetes by increasing antioxidants and improving lipid profiles, as well as reducing oxidative damage and modulating antioxidant enzymes, and potentiating pancreatic insulin secretion from the remaining islet β cells due to blood glucose, cholesterol, triglyceride, and urea suppression [27, 28].

5.8. *Rosmarinus officinalis* (Rusmari)

The Mediterranean plant *Rosmarinus officinalis* (Family Lamiaceae) is widely known as rosemary. The

branching, bushy evergreen shrub can reach a height of two meters. Rosemary is a plant that thrives in harsh climates where it is exposed to sun and heat. It grows in the sun amid dry scrub and rocky cliffs, frequently near the sea. The woody stems are angular and densely covered in narrow, needle-shaped leaves. The leaves are glossy green on top and coated with small hairs underneath, curving downwards. Light blue, pastel violet, white, and pinkish rosemary blossoms are among the many colours available. Flowers appear in bunches of two or more at the plant's higher ends. Their shape, which resembles a mouth's upper and lower lip, is similar to that of other plants in the mint family, also known as Labiatae, which means "having lips." A significant amount of pharmacological research has shown that rosemary extract and its phenolic constituents, particularly carnosic acid, rosmarinic acid, and carnosol, can significantly improve diabetes mellitus by regulating glucose metabolism, lipid metabolism, anti-inflammation, and anti-oxidation (Table 1), indicating rosemary extract and its phenolic compounds, particularly carnosic acid, rosmarinic acid, and carnosol, help ameliorate diabetes mellitus by controlling glucose levels [29, 30].

5.9. *Zingiber officinale* (Singabera)

Zingiber officinale, also known as ginger, is a perennial ayurvedic herb that is widely grown in the tropics and occasionally naturalizes in it. Because many varieties don't blossom or are sterile, it usually spreads vegetatively. *Zingiber officinale* is thought to have originated in India. It's a popular commercial crop in South and Southeast Asia, tropical Africa (particularly Sierra Leone and Nigeria), Latin America, the Caribbean (particularly Jamaica) and Australia. The rhizome (underground stem) of ginger is thicker and branching, giving it the appearance of a bloated hand. The rhizome has a brown corky outer covering (which is typically removed before usage) and a pale yellow centre with a pungent lemon smell. Annually, shoots (pseudostems) grow up to 1.2 m tall from buds on the rhizome. The long (up to 7 cm), narrow (up to 1.9 cm wide), mid-green leaf blades are positioned alternately on these pseudostems, which are made up of a series of leaf bases (sheaths) wrapped tightly around one another. The flowering heads are cone-shaped spikes made up of a series of greenish to yellowish leaf-like bracts that are borne on distinct shorter stalks. Flowers are pale yellow in colour with a purple lip with yellowish spots and striations that protrude just beyond the outer edge of the bracts. Cultivated plants rarely, if ever, generate flowering stems [31]. It works by increasing the expression and translocation of the GLUT-4 glucose transporter to the cell's plasma membrane, removing excess glucose from the blood (Table 1) [32].

5.10. *Eupatorium sp.* (Ayapana)

Eupatorium sp. is a flowering plant genus in the Asteraceae family, with between 36 and 60 species depending on the categorization system. The majority are herbaceous perennials that develop to a height of 0.5-3 m (1.6-9.8 ft). Thoroughwort or boneset are two common names for them. *In vitro*, an aqueous extract of *Eupatorium* stimulated insulin production in the BRIN-BD11 pancreatic beta cell line [33, 34].

5.11. *Azadirachta indica* (Nimba)

Azadirachta indica is an evergreen tree of family Meliaceae, commonly known as Neem. It is a tropical and semi-tropical tree that grows in Bangladesh, India, Sri Lanka, Malaysia and Pakistan. The powder version of the leaf acts as a potent antidiabetic agent. In high doses, aqueous and alcoholic extracts have considerable hypoglycemic action, lowering serum glucose levels. Antibacterial, antimalarial, antifertility, hepato-protective, and antioxidant actions are all possible with this herb [35, 36].

5.12. *Swertia chirayita* (Kirata)

Swertia chirayita is a plant of family Gentianaceae, better known as Chirata, known to significantly increased the levels plasma insulin and reduce blood sugar [37]. Swerchirin, the most prominent phytochemical ingredient present in the aerial sections of the plant, induced considerable depletion of aldehyde fuchsin stained beta granules after a single oral treatment to rats [38].

5.13. *Mangifera indica* (Aamram)

Mangifera indica common ayurvedically important plant of family Anacardiaceae commonly known as Mango, play an important role in antidiabetic effects. When compared to an oral dose of chlorpropamide, the aqueous extract of the leaves displays substantial hypoglycemic activity by effectively scavenging blood glucose levels, but had no effect on streptozotocin-induced diabetic mice under the same conditions [39].

5.14. *Ocimum sanctum* L. (Tulasi)

Ocimum sanctum, very common ayurvedic herb of family Lamiaceae, commonly known as Tulsi, widely found in India, Bangladesh and many parts of Asia. This herb has been used for therapeutic purposes since ancient times. In both normal and alloxan-induced diabetic rats, the aqueous extract of leaves exhibits substantial effectiveness in lowering blood sugar levels [40]. In diabetic rats, it also lowers fasting blood glucose, uric acid, total cholesterol, hypoglycemic, and hypolipidemic levels [41].

Table 1: Detail of plants used in Diabetes

Name of the plant	Part of the plant used	Family	Common name	Mechanism of action
Ceratonia silliqua	Leaves	Fabaceae	Carob	The renewal or repair of pancreatic islet-cells after damage.
Syzygium aromaticum	Flower	Myrtaceae	Clove	Decreasing blood sugar, oxidative stress, plasma cholesterol, triglycerides, and LDL levels.
Verbena officinalis	Flower	Verbenaceae	Simpler's Joy	-
Abelmoschus esculentus	Pods	Malvaceae	Okra	Boosts insulin secretion, increase insulin sensitivity, and limit carbohydrate absorption in the gut
Allium cepa	Root	Amaryllidaceae	Onion	Operate as a preventive mechanism against the development of hyperglycemia and hyper-lipidemia
Coriandrum sativum	Seeds	Apiaceae	Coriander	Regenerate the β cell in pancreas and inhibiting the α-glucosidase enzyme in small intestine
Lepidium sativum	Tree pods	Brassicaceae	Garden cress	Potentiate pancreatic insulin secretion from the remaining islet β cells due to blood glucose.
Rosmarinus officinalis	Flower	Lamiaceae	Rosemary	Regulation of glucose metabolism, lipid metabolism
Zingiber officinale	Rhizome	Zinziberaceae	Ginger	Increase the expression and translocation of the GLUT-4 glucose transporter to the cell's plasma membrane
Eupatorium sp.	Leaves	Asteraceae	Ayapan	Stimulation of insulin production
Azadirachta indica	Leaves	Meliaceace	Neem	Significant hypoglycemic activity in high dose by decreasing serum glucose level
Swertia chirayta	Aerial part	Gentianaceae	Chirata	The aerial parts of the plant, to rats caused decreasing blood glucose with marked depletion of aldehyde fuchsin stained beta granules
Mangifera indica	Leaves	Anacardiaceae	Mango	Effective scavenging of glucose molecule by the extract.
Ocimum sanctum	Leaves	Lamiaceae	Tulsi	Significant activity of decrease in blood sugar level
Ablemoschus moschatus	Fruits	Malvaceae	Musk dana	Improves insulin sensitivity through increased post receptor insulin signaling mediated by enhancements in IRS-1-associated PI3- kinase and GLUT 4 activity

5.15. *Abelmoschus moschatus* (Lata Kasturi)

Abelmoschus moschatus is an aromatic medicinal plant of family Malvaceae commonly known as musk dana, found in all south Asian nations especially India. Myricelin, which is contained in the fruit of this plant, enhances insulin sensitivity by increasing post-receptor insulin signalling, which is mediated by increases in IRS-1-associated PI3-kinase and GLUT 4 activity in the muscles of obese Zucker rats [42].

The leaves, fruits, and roots are the most commonly used plant components from the mentioned plants. Fig. 2 depicts the plant parts used in the treatment of diabetes and their frequency.

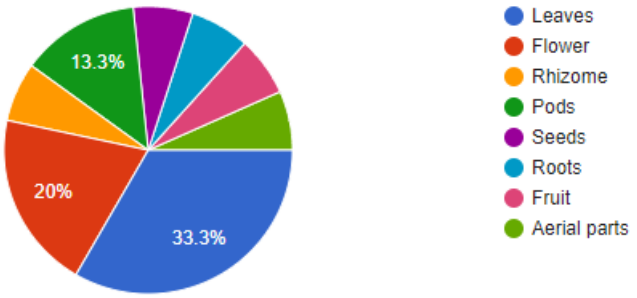

Fig. 2: Percentage occurrence of herbal parts used for diabetes treatment

6. CONCLUSION

Diabetes is a disease in which blood sugar levels are abnormally high. The condition affects millions of people around the world. A chronic illness in which the pancreas generates little or no insulin is known as type I diabetes. Diabetes research is undertaken in order to improve clinical management. Diabetic patients were treated with ayurvedic herbs and traditional remedies before the discovery of insulin and hypoglycemic medicines. Multiple ayurvedic herbal medications have been found to have beneficial benefits in lowering blood glucose levels or preventing hyperglycemia-related problems. Some of them have shown great effect in controlling both Type I as well as in Type II diabetes as well by different mechanisms. In this review some of the some important effective and common ayurvedic herbs and trees and their mechanism in management of diabetes have been mentioned. Further researches regarding the clinical prospects of these plants needed to be explored.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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