



Indian traditional medicinal plants for the treatment of Diabetes Mellitus (DM): Review

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Abstract

Diabetes is a metabolic problem recognized by a hyperglycemic condition from improper secretion and action of insulin. Traditionally, several medicinal plants have been used in India for the prevention and treatment of diabetes. Medicinal plants are a significant source for antidiabetic therapy. This review is based on the compilation and evaluation of the present information related to medicinal plants, their parts, and their bioactive compounds with antidiabetic properties, emphasizing their significance for further research and drug development.

Keywords: Madhumeha, antidiabetic, medicinal plants, bioactive compounds, remedies

Introduction

Diabetes mellitus (DM) is generally referred to as “Madhumeha” in Ayurveda. DM is a global health problem, but many people in developing countries are more affected. According to the study of the international diabetes federation (IDF), about 415 million youth below the age of 70 years had DM in 2015 [24] (Ogurtsova *et al.*, 2017). This study highlights its status as a global health problem, and it is expected to reach another 200 million by 2040 (Zheng *et al.*, 2018) [54]. It is a common metabolic problem described by the deficiency of glucose homeostasis arising from defective insulin synthesis and action (Banday *et al.*, 2020) [5]. Insulin is a hormone produced by the islets of Langerhans in the pancreas. DM disturbs the metabolism of carbohydrates, proteins, fats, electrolytes, and water, leading to effect many organs and organ systems. Uncontrolled diabetes leads to various complications, which can be classified into microvascular complications, such as neuropathy, nephropathy, and retinopathy, and macrovascular complications, including cardiovascular disease, strokes, and peripheral vascular diseases (Chawla *et al.*, 2016) [13]. Diabetes mellitus is primarily classified into two types: type- 1 and type- 2 diabetes (Panja *et al.*, 2006).

Type 1: diabetes, which is known as insulin-dependent diabetes mellitus, is classified by an insufficient or incomplete absence of the production of insulin, requiring daily administration of insulin. It mostly occurs in children and young adults.

Type 2: diabetes is described as non-insulin-dependent diabetes mellitus, which is caused by ineffective insulin action due to either less secretion of insulin from the pancreas or improper utilization by the body. It is more prevalent in older adults, but recently, younger adults or children have also been affected by type 2. Genetic factors, obesity, unhealthy diet, insufficient physical activity, stress, and lifestyle factors are commonly risk factors for the development of type 2 diabetes (Inzucchi *et al.*, 2015) [24]. There is another class of diabetes present- Gestational diabetes, which primarily results from glucose intolerance,

from the start of pregnancy. Although this is temporary, this condition may increase the long-term risk of diabetes (Bellamy *et al.*, 2009) [6]. There are many drugs and medicines used to control or prevent diabetes, biguanides, sulfonylureas, meglitinides, peroxisome proliferator-activated receptor- γ agonist (glitazones), α -glucosidase inhibitors, DPP-4-inhibitors, SGLT2 inhibitors, dopamine-2 agonists, etc. are some of them. But effective treatment against diabetes is still needed to search (Inzucchi *et al.*, 2015) [24]. A healthy diet, yoga, exercises, meditation, routine medical checkups, following doctors and treatments are so many ways to cure DM. Many researchers are still doing their best to find alternative therapies and herbal medicines to treat diabetes.

Indian flora is full of plants with medicinal properties. Recently, the trend of use of herbal remedies is rapidly growing globally because they are considered safer, more effective, and also cost-friendly. Our Vedic literature, like “Charak-Sanhita,” already mentions the importance of plants and their derivative for the treatment of DM (Ekor, 2014) [14]. Many plant species are used in folk medicines because of their antidiabetic properties (Grover *et al.*, 2002) [17]. In India, several native remedies have been used to treat diabetes mellitus since ancient times of “Charak and Shushruta”. According to reports of ethnobotanical information, it can be estimated that about 800 plants may have antidiabetic properties (Gaonkar & Hullatti, 2020) [16]. Also, bioactive compounds found in these trees show antidiabetic properties. After a thousand years of research on the therapeutic effects of these herbal remedies on human health problems, minimal experimental data are present on these treatments (Kaushal *et al.*, 2019) [25]. Most common, easily available and effective antidiabetic herbal plants as garlic (*Allium sativum*), onion (*Allium sepa*), kalmegha (*Andrographis paniculata*), ghrita kumara (*Aloe vera*), erect spiderling (*Boerhaviadiffuse*), tea (*Camellia sinensis*), avaarai (*Cassia auriculata*), ivy gourd (*Cocciniaindia*), turmeric (*Curcuma longa*), gurmara (*Gymnema sylvestre*), gudhal (*Hibiscus rosa-sinensis*), arandi-castor (*Ricinus communis*), brown mustard (*Brassica juncea*) etc., are rich sources of phytochemicals and

antidiabetic activity. Every herb contains its own active ingredients that help lower blood sugar and control diabetes complications (R. Gupta *et al.*, 2007)^[47].

Review

The review work involved a comprehensive search of research articles from online databases, including Google Scholar, Science Direct, etc. In addition, studies of systematically validated medicinal plants with significant antidiabetic properties were also collected and analyzed.

Plants having antidiabetic properties

1. *Brassica juncea* (Brassicaceae), Mustard / Rai (Common Name)

It is known as Chinese mustard or brown mustard, a commonly used spice in many Indian foods. It is distributed mainly in Europe, Africa, North America, and Asia. Triterpenes, Saponins, alkaloids, flavonoids, proteins, and carbohydrates are active biochemical compounds found in this plant (Parikh & Khanna, 2014)^[36]. It has antiscorbutic, diuretic, stimulant, stomachic, anthelmintic, antidiabetic, diaphoretic, antiarthritic, and hypoglycemic properties, and because of these properties, it is pharmacologically very important. It is also used for abscesses, bladder inflammation, or hemorrhage in many countries (Parthiban *et al.*, 2015)^[37]. Thirumalai *et al.* 2011^[49] suggested hypoglycemic activity of the aqueous seed extract of the plant at a particular dose in streptozotocin-induced diabetic male albino rats (Thirumalai *et al.*, 2011)^[49]. Kumar *et al.* in 2019 experimented for 21 days and suggested the anti-hyperglycemic and anti-oxidative properties of the methanolic extract of *B. juncea* by observing decreased blood sugar level, decreased lipid peroxidation (LPO), nitric oxide (NO), and enhanced superoxide dismutase (SOD) and glutathione (GSH) in liver, kidney, pancreas, and muscle tissues on day 21. They showed no difference in cholesterol and triglyceride levels on day 21 (A. Kumar *et al.*, 2019)^[28].

2. *Helicteres isora* (Malvaceae), Indian screw tree/Marodphali (Common Name)

This plant has various common names, such as Marodphali, Marorphali, Enthani, because its fruit has a screw-like appearance (N. Kumar & Singh, 2014)^[29], and is also known as “Avartani” in Sanskrit. It is widely distributed all over India. Many bioactive compounds like antioxidants, proteins, phenols, flavonoids, alkaloids, glycosides, carotenoids, and tannins are present in this plant. It has diverse medicinal properties, including expectorant, antidiarrhoeal, antidiabetic, antispasmodic, and hemostatic. The antidiabetic activities of the aqueous bark extracts of *Helicteres isora* on streptozotocin-induced diabetes. Biochemical dysregulation was corrected after 2 weeks of treatment with the bark extract of *H. isora*, resulting in restoration of fasting blood glucose levels to normal ranges, decreased polyphagia and polydipsia, and weight gain in diabetic-treated rats. Zareen *et al.* (2019) demonstrated an experiment on streptozotocin-induced diabetic rats and observed a significant reduction in blood glucose levels, triglycerides, and cholesterol after the oral administration of butanoic extract of *H. isora* roots. They proved the hypoglycemic and hypolipidemic properties of this extract at the acute and chronic dosing of 125 mg/kg and 250 mg/kg (N *et al.*, n.d.).

3. *Murraya koenigii* (Rutaceae), Curry Leaves / Curry Patta (Common Name)

It is known as the “Curry Patta” plant, widely used because of its leaves. Leaves of this plant enhance the flavors of foods. It is found in India and many tropical countries. The main bioactive compounds present in this plant are α -pinene, β -pinene, β -caryophyllene, limonene, bornyl acetate, terpinen-4-ol, γ -terpinene, and α -humulene, with numerous medicinal properties, such as anti-bacterial, anti-fungal, and anti-protozoal. Different parts of *Murraya koenigii* have long been utilized in conventional or ethnobotanical medicine for the treatment of various diseases like rheumatism, traumatic injury, and snakebite, and studies have displayed that it has antioxidant, anti-diabetic, and anti-dysenteric activities. Traditionally, Curry leaf is utilized as a stimulant, an antidiabetic, and for the control of diabetes mellitus. In 2015^[24], Vijayanand stated that extracts derived from the plant leaves resulted in a significant glucose-lowering effect in alloxan-induced diabetic albino rats at the doses of 250 and 500 mg/kg (Vijayanand, 2015)^[42]. Al-Ani *et al.* investigated the antidiabetic effects and renal and endocrine protective effects of the aqueous crude extracts of curry leaves in STZ-induced diabetic rats (Al-Ani *et al.*, 2017)^[1].

4. *Acacia arabica* (Fabaceae) or *nilotica*: Gum Arabic Tree / Babul (Common Name)

It is commonly known as babool, and is cultivated throughout India. This plant has various chemical compounds present, like phenolics, gallic acid, protocatechuic acid, pyrocatechol, catechin, epigallocatechin-7-gallate, quercetin, iso-quercetin, etc. (Roqaiya *et al.*, 2015)^[42]. This plant is medically used as an antioxidant, anti-abortion, and anti-inflammatory, and has killing activities against bacteria, fungi, viruses, malaria, etc. The gum is used in diabetes as a tonic, sauteed in ghee, and used in the formation of sweetmeat (K.M Nadkarni, 1910)^[26]. Consuming the mucilage of Babool gum leads to sugar passing in urine in diabetes mellitus. Wadood *et al.* reported that babul seeds contain a substance(s) which reduce the blood glucose level in normal glycemia instead of alloxan-diabetic rabbits, resulted that the mechanism of action involving the release of insulin from pancreatic beta-cells (Wadood *et al.*, 2007)^[52]. Rechanger showed the coagulating activity of the stem bark of the babul plant. It is administered as a decoction (20 mg/kg), resulting in a notable lowering in blood glucose levels in mild alloxanized diabetic rabbits fasted for 18 hrs. (Rechanger, 2010)^[40]. In 2010, Yasir *et al.* discovered that the aqueous extract of the plant exhibits increased antihyperglycemic activity in diabetic and normal rats at a significant dose of 400 mg/kg (Yasir *et al.*, 2010)^[53]. In 2013^[21], Hegazy *et al.* observed that the extract of these plants showed considerable glucose-lowering activity in albino rats when using doses of 100 mg/kg and 200 mg/kg (Hegazy *et al.*, 2013)^[21].

5. *Ficus religiosa* (Moraceae), Sacred Fig / Peepal tree (Common Name)

It has been reported to be used for the treatment of diabetes in the traditional system of Ayurveda (Simmonds & Howes, 2006). Herbal extract prepared from the bark for the treatment of diabetes (Bouché *et al.*, 2004)^[8]. The plant contains numerous bioactive compounds, including tannins,

glycosides, polyphenolic compounds, flavonoids, sterols, and furanocoumarin derivatives, namely, bergapten and bergapton, which may play a role in its antidiabetic activity. Sitosterol-d-glucoside extract from the bark of pipal is used to elicit glucose-lowering activity in rabbits. Bouche *et al* reported that the aqueous extract of *Ficus religiosa* was administered orally for 21 days, resulting in significant hypoglycemic activity and increased insulin levels (Bouché *et al.*, 2004)^[8]. Grover *et al* observed that the peepal extract has therapeutic properties to decrease muscle and hepatic glycogen in diabetes (Grover *et al.*, 2002)^[17].

6. *Eugenia jambolana* (Myrtaceae), Indian Blackberry/ Jamun (Common Name)

In India jamun plant has been utilized in various complementary and alternative medicine systems. The decoction of jamun seeds prepared in boiling water is useful in numerous conventional medicines of treatment in India (Baliga *et al.*, 2013)^[4]. The plant consists of various bioactive chemical compounds, including anthocyanins, kaempferol, myricetin, glucoside, ellagic acid, isoquercetin, and hydrolysable tannins. The alkaloid and glycoside jamboline are often found in the seed, which helps in the reduction of the conversion of starch into sugar (Ayyanar & Subash-Babu, 2012)^[3]. The bark of jamun also consists of important components, such as quercetin, betulinic acid, β -sitosterol, eugenin, ellagic acid, and gallic acid (Chaudhuri *et al.*, 1990)^[12], bergenin (Bhatia & Bajaj, 1975)^[7], tannins, and flavonoids. Even leaves of jamuns contain acylated glycosylated flavanols, quercetin, myricetin, and tannins. The hypoglycemic effect of *Eugenia jambolana* resulted in the regulated secretion of insulin, or downregulating the insulin degradation (Aybar *et al.*, 2001)^[2]. Singh and Gupta reported a significant reduction in blood sugar level in alloxan-induced diabetic rats after administration of the seed powder of jamuns (N. Singh & Gupta, 2007)^[47].

7. *Momordica charantia* (Cucurbitaceae), Bitter melon / Bitter gourd (Common Name)

In Asia, South America, and East Africa regions, *M. charantia* is one of the most effective fruits utilized as therapeutic purpose for the treatment of diabetes, cardiovascular diseases, and related conditions. It is normally used as a vegetable included in the diet. Bitter gourd has several bioactive compounds, including vicine, charantin, and triterpenoids, with some antioxidants with antidiabetic properties (Krawinkel & Keding, 2006)^[27]. The bitter melon has glucose-lowering and lipid-lowering properties (Inayat-ur-Rahman *et al.*, 2009)^[22]. Studies show that *Momordica charantia* has the potential to repair damaged β -cells, thereby increasing insulin secretion and enhancing insulin sensitivity (Saxena & Vikram, 2004)^[44]. The main components of bitter melon with considerable antidiabetic properties are triterpenes, proteins (M. Saeed *et al.*, 2010)^[43], steroids, alkaloids, inorganic compounds, lipids, and phenolic compounds (Budrat & Shotipruk, 2008)^[9]. Ethnomedical uses are confirmed by modern scientific evidence. *M. charantia* is represented as a highly promising plant for its antidiabetic properties (Cefalu *et al.*, 2008; Leung *et al.*, 2009)^[10, 31].

8. *Ocimum sanctum* (Lamiaceae), Holy basil / Tulsi (Common Name)

Holy basil is a medicinal plant with immense potential because of its nutritional and chemical composition.

Eugenol, the active component extracted from the plant *O. sanctum*, has much therapeutic potential (Pattanayak *et al.*, 2010)^[39]. The extract derived from the leaves of *O. sanctum* has been shown to activate the insulin secretion pathway (Hannan *et al.*, 2006)^[20]. Chattopadhyay demonstrated that oral consumption of the alcohol-based extract of leaves of *O. sanctum* resulted in decreased blood sugar levels in normal and glucose-fed hyperglycemic diabetic rats, and regulation of the action of exogenous insulin in normal rats (Chattopadhyay, 1993)^[11]. Patil *et al* observed that the chloroform extracts obtained from the aerial parts of Tulsi restored the raised level of serum glucose (R. N. Patil *et al.*, 2011a).

9. *Trigonella foenum-graecum* (Fabaceae), Fenugreek / Methi (Common Name)

Fenugreek has been shown to have strong antidiabetic benefits through research employing a range of experimental models (P. Kumar *et al.*, 2012; Roberts, 2011)^[30, 41]. In humans and mice, the blood sugar level can be reduced by fenugreek leaf, seed, and seed mucilage (A. Gupta *et al.*, 2001; Vats *et al.*, 2002)^[17, 18]. It may be found all over India, and Indian spices usually include the seeds as one of their key ingredients. Fenugreek seeds have a novel amino acid, 4-hydroxyleucine, which stimulates glucose activity. Inegbedion *et al* investigated the effect of aqueous extract of fenugreek seeds on some kidney function parameters of albino rats. They observed that exposing the rats to fenugreek seed aqueous extract did not significantly change serum urea, creatinine, and uric acid levels compared to the control (Inegbedion *et al.*, 2022)^[23]. It is concluded that fenugreek seed aqueous extract is safe to be used as an effective remedy against kidney diseases at some doses, but higher doses may not be safe. Singh *et al* experimented to observe the antidiabetic effect of 4-HIL in type 2 diabetic and healthy Sprague Dawley rats. This experiment demonstrated the ameliorative effect of 4-HIL by lowering the altered blood glucose level in hyperglycemic rats, as well as not changing the normal level of glucose in healthy rats, without any toxic effects *in vitro* and *in vivo* (P. Singh *et al.*, 2022)^[48]. Also, the result provided strong scientific evidence for the antidiabetic potential of 4-HIL to manage diabetes and associated secondary complications.

10. *Azadirachta indica* (Meliaceae), Neem (Common Name)

Indica is a tropical evergreen and widely distributed plant in Asia. Whole plant parts are important in medicine. It may have hypoglycemic qualities, according to several findings (El-Hawary & Kholief, 1990; Mahdi *et al.*, 2003)^[15, 32]. *A. indica* leaf and bark extract can significantly reduce glucose levels in the blood. Shrivastava *et al* studied the blood sugar-lowering effects of the extract of leaf and bark of the *A. indica* plant. They showed that diabetic Charles foster rats fed a high-fat diet had raised blood glucose levels, which were subsequently returned to normal levels following treatment with leaf extract from *A. indica* (Shrivastava *et al.*, 2012)^[45]. This implies that leaf extract from *A. indica* has potential antidiabetic qualities. Patil *et al* found good results after administration of 800 mg/kg of 70% alcoholic neem root bark extract (NRE) to diabetics (P. Patil *et al.*, 2013)^[38].

Discussion

Diabetes mellitus is a health problem that is mainly described by hyperglycemia, a high blood sugar level caused by improper insulin secretion and action. It is mainly recognized into two types, type I and type II diabetes. Because of the high-risk factor of diabetes, researchers are growing interested in the search for new antidiabetic agents. Traditionally Several therapeutic plant families have been used as an antidiabetic medicine in different forms, such as their plant bodies, leaves, fruits, water extracts, and so on. Some of the plant families, such as Brassicaceae, Malvaceae, Rutaceae, Fabaceae, Moraceae, Cucurbitaceae, and Amaryllidaceae, have significant antidiabetic potential. Among the most extensively studied species are *Brassica juncea*, *Murraya koenigii*, *Acacia arabica*, *Ficus religiosa*, *Eugenia jambolana*, *Momordica charantia*, *Ocimum sanctum*, *Trigonella foenum-graecum*, and *Azadirachta indica*. Traditionally, a wide range of experimental methods and clinical trials have been done to understand their antidiabetic properties. Transient hyperglycemia is commonly induced using the oral glucose tolerance test (OGTT), whereas streptozotocin- and alloxan-induced diabetic rat or mouse models are frequently used to simulate type I diabetes.

Most clinical findings support the beneficial role of medicinal plants in reducing blood glucose levels and managing diabetes mellitus. Various mechanisms have been proposed to explain their hypoglycemic effects, including stimulation of pancreatic β -cell function, enhancement of insulin secretion, protection against insulin degradation, and improvement of insulin sensitivity or insulin-like activity. Other mechanisms involve better regulation of glucose homeostasis through increased peripheral glucose utilization, enhanced hepatic glycogen synthesis, reduced glycogen breakdown, inhibition of intestinal glucose absorption, and modulation of carbohydrate metabolism. Together, these effects may contribute to the prevention or reduction of diabetic complications.

Conclusion

India has a rich diversity of medicinal plants traditionally used to treat diabetes. The current study on the antidiabetic activity of several herbs helps to clarify the therapeutic potential of these herbs through mechanisms such as decreased glucose absorption, enhanced insulin action, and antioxidant effects. These medicinal properties are due to the presence of several bioactive components, including alkaloids, flavonoids, and phenolic compounds. Herbal medicines are significantly more secure and economical than synthetic medicines. However, more experimental studies and proper clinical evaluation are needed to standardize the mechanisms of action of medicinal plants and to confirm their safety and effectiveness. The information discussed here regarding therapeutic herbs may be helpful for further diabetes research.

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