

COMMON MEDICINAL PLANTS USED FOR THE MANAGEMENT OF DIABETES MELLITUS IN AYURVEDA, SIDDHA AND UNANI SYSTEM OF MEDICINE (ASU) IN INDIA: A REVIEW

Debajyoti Das¹, K. Prameela Devi¹, S. Asha¹, T. Maheswar²

Research Officer (Ay.)¹, Assistant Director²

Dr. Achant Lakshmipathi Research Centre for Ayurveda, VHS Campus, Taramani, Chennai-600113, Tamil Nadu, India

Email: debajyoti.das02@gmail.com

ABSTRACT

Diabetes Mellitus is a metabolic disorder affecting a large proportion of world's population. More than 300 million people of the world are suffering from this disease and the number is still increasing at a rapid rate as there is no permanent solution for the disease. Therefore, there is a need to develop safe and effective treatment modalities for diabetes. Ayurveda and other Indian literature mention the use of plants in treatment of various human ailments. India has about 45000 plant species and among them, several thousands have been claimed to possess medicinal properties. Out of them many herbal drugs stated to possess anti-diabetic activity. The present paper reviews some effective medicinal plants of ASU (Ayurveda, Siddha and Unani) drugs that are already proved experimentally, clinically for their anti-diabetic activity.

Keywords: Diabetes Mellitus (DM), Medicinal plant, Antidiabetic activity, ASU drugs.

INTRODUCTION

Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. It is a common and epidemic disease affecting the people of both the developed and developing countries. It is caused by the abnormality or dysfunction of carbohydrate metabolism ^[1]. World health organization (WHO) has defined diabetes Mellitus (DM) as a chronic disease caused by inherit-

ed and/or acquired deficiency in the production of insulin by the pancreas, or by the ineffectiveness of the insulin produced ^[2]. In India, the number of diabetic patients has increased from 31.7 million in 2000 to 69.1 million in 2016 ^[3]. A record increase of 117% has been noticed in diabetic patients in last 16 years and India has now been declared as "Diabetic Capital" of the world ^[4]. In high-income countries 85 to 95% of diabetes are of type 2 accounting for an even higher dominance in developing countries. It is intimately associated with improper utilization of insulin by target cells and tissues. It is currently a common and se-

rious health concern globally ^[5]. The World Health Organization (WHO) estimated that diabetes would be the seventh leading cause of death by the year of 2030, and suggested that healthy lifestyle and right medication and regular screening can prevent and avoid the consequence of diabetes, respectively ^[6]. The disease is associated with reduced quality of life and increased risk factors for mortality and morbidity. Many of allopathic medicines are available for the treatment of diabetes but somehow they have their own side effect & adverse effect like hypoglycaemia, nausea, vomiting, hyponatremia, flatulence, diarrhoea or constipation, alcohol flush, headache, weight gain, lactic acidosis, pernicious anaemia, dyspepsia, dizziness, joint pain. So, herbal drugs are a great choice which is having less or no side effects or adverse effects ^[7].

There is a growing interest in herbal remedies for the treatment of diabetes mellitus due to the side effects associated with the oral hypoglycemic agents (therapeutic agent). Source of the traditional herbal medicines are mainly planting which plays an important role in the management of diabetes mellitus ^[8]. About 70% of rural population relies on traditional medicinal system as their primary health care ^[9]. The successful treatment and management of diabetes are yet to be discovered. Within the Indian subcontinent, extensive research has been performed in ethno-medicine system to find out the possible uses of the plant as anti-diabetic agents ^[10]. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a large scale. India is the largest producer of medicinal herbs and is called as botanical garden of the world ^[11]. Now a day's medicinal plants are considered as an important therapeutic aid for reducing ailments of human being. Strong medicinal systems like Ayurveda, Unani and Siddha, are still promising and has been practiced over 1500 years. The people (>60-80%) from developed as well as developing countries depend on these medicinal systems for their health care requests ^[12]. More than 400 plant species having hypoglycemic activity have been

available in literature, however, searching for new antidiabetic drugs from natural plants is still attractive because they contain substances which demonstrate alternative and safe effects on diabetes mellitus. Most of plants contain glycosides, alkaloids, terpenoids, flavonoids, carotenoids, *etc.*, that are frequently implicated as having antidiabetic effect^[13]. Medicinal plants are being used for both prophylactic and therapeutic management of diabetes. Prophylactic action may be attributed to healthy organs and their cellular tissue especially beta cells of pancreas, hepatic tissue and preventive action on diabetic inducers. Therapeutic action may be due to curative action on affected tissue of pancreas, liver and organs related to diabetes ^[14]. These herbs are rich in antioxidants and phytochemicals. Phytochemicals increase antioxidant enzymes like catalase and glutathione, which suppress the high glucose levels and hence increase the insulin production in the body ^[15].

Ayurveda is the major traditional system practiced in India. Many studies have confirmed the benefits of medicinal plants with hypoglycemic effects in the management of diabetes mellitus. The effects of these plants may delay the development of diabetic complications and even assist in correcting the metabolic abnormalities. Herbal medicines are popular remedies for diseases used by a vast majority of the world's population. Due to the popularity of indigenous medicinal systems, A separate ministry of Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy (AYUSH) has been constituted under the Government of India with a purpose to develop education and research in the indigenous medicinal system. Many herbal remedies were common in these indigenous systems of medicine, those reported for the treatment of diabetes. Diabetes Mellitus is referred by different names in Ayurveda, it is called as Madhumeha, in Siddha Medicine, Neerizhivu and Madhumegham and in Unani Medicine, Ziabetus Shakari.

In this review article, an attempt has been made to compile the pharmacologically reported and clinically effective antidiabetic plants available in ASU drugs which may be helpful to the health professionals, sci-

entists and scholars working in the field of pharmacology and therapeutics for further studies.

Materials and Methods

A review has been carried out to collect the information on anti-diabetic plants from the Ayurveda,

Siddha and Unani literature and published research articles. All the plants recorded were used for the treatment of diabetes. A variety of medicinal plants are prescribed in these literatures for the treatment of diabetes. A list of effective medicinal plants mostly used clinically to treat Diabetes Mellitus are tabulated.

Table 1: List of selected plants in ASU system of medicine having potent antidiabetic activity

Family	Botanical name	Ayurveda name	Unani name	Siddha name	Parts used	Active chemical constituents	Reference
Rutaceae	Aegle marmelos	bilva	bel	Vilvam	Leaf, Seed, Fruit	Aegeline 2, Coumarin, Flavonoid, Alkaloid	16.
Meliaceae	Azadirachta indica	Nimba	Neem	Vembu	Leaf, Seed	Nimbidin	
Solanaceae	Withania coagulans	-----	Paneerband	Ammukkura	Fruit	Milk-coagulating enzyme, Esterase, Fatty oil, Essential oil, Alkaloid	
Zingiberaceae	Curcuma longa	Haridra	-----	-----	Rhizome	Curcuminoid	
Asclepiadaceae	Gymnema sylvestre	Mesasringi	Gurmaar Booti	Sirukurinjan	leaf	Gymnemic acid, Gymnema, Saponin	
Cucurbitaceae	Momordica charantia	Karavellaka	Karela	Paakal	Fruit, whole plant	Charantin, Momordicin, Galactose - binding lectin Non -bitter, Diosgenin, Cholesterol, lanosterol, β - sitosterol, Cucurbitacin glycoside	
Cucurbitaceae	Coccinia indica	Bimbi	-----	Kovai	Leaf, fruit, root tuber,	B -amyrin, Lupeol, Cucurbitacin B	
Liliaceae	Aloe barbadensis	Kumari	Sibr	Katralai	Leaf pulp	Pseudoprototinosaponin AIII and prototinosaponins AIII	17.
Asclepiadaceae	Tinospora cordifolia	Guduci	Gilo	Seenthil	Stem	Tinosporin, berberine, tinosporinone	18
Leguminosae	Trigonella foenum-graecum	Methika	Hulbah	Venthayam	seed, whole plant	4-hydroxyisoleucine and hydroxyisoleucine	
Fabaceae	Pterocarpus marsupium	Asan	bijasar	Acamai, asanam	Bark, Heart	Pterocarpol, pterostilbene	19

					wood	
Myrtaceae	Syzygium cumini	Jambu	Jamun	Naval	Seed, fruit	Cuminy alcohol
Euphorbiaceae	Embllica officinalis	Amalaki	Amla	Nellikai	Fruit	Polyphenols: flavonoids, kaempferol, ellagic acid, gallic acid
Hippocrateaceae	Salacia reticulata	Saptarangi	-----	Kadalazhin-jil	Root, stem, leaf	polyphenol constituents - catechins, mangiferin, salacinol and kotalanol

Medicinal plants with Anti diabetic activity

Aegle marmelos: The oral administration of aqueous leaf extract on streptozocin (STZ) induced diabetic rats was proven to be equally potent as insulin in normalizing blood glucose and insulin levels. Its mode of action may be either due to stimulating glucose uptake or enhancing insulin secretion or both. In addition, it improved the functional state of the beta cells, regenerating the damaged pancreatic parts. However, oral and intraperitoneal administration of the fruit aqueous extract showed antidiabetic activity in STZ induced diabetic rats. It significantly reduced the blood-glucose level as well as glycosylated hemoglobin, while elevating both serum insulin and liver glycogen^[20].

Aloe barbadensis (Aloe vera): Extracts of aloe gum effectively increases glucose tolerance in both normal and diabetic rats. Single dose of exudates of Aloe barbadensis leaves showed hypoglycemic effect in alloxanized diabetic rats. Single as well as chronic doses of bitter principle of the same plant also showed hypoglycemic effect in diabetic rats. This action of Aloe vera and its bitter principle is through stimulation of synthesis and/or release of insulin from pancreatic beta cells. This plant also has an anti-inflammatory activity in a dose dependent manner and improves wound healing in diabetic mice.^[21]

Azadirachta indica: Hydroalcoholic extracts of this plant showed antihyperglycemic activity in streptozocin treated rats and this effect is because of increase in glucose uptake and glycogen deposition in isolated rat hemidiaphragm. Apart from having anti-diabetic activity, this plant also has antibacterial, antimalarial, antifertility, hepatoprotective and antioxidant effects.^[22]

Withania coagulans: It exhibited hypoglycaemic activity which is an effective and safe alternative treatment for diabetes. Hypoglycemic activity of Withania coagulans was exhibited in streptozocin induced rats. Significant improvements in symptoms and signs were observed and euglycemia was attained in diabetes mellitus type 2. A withanolide, named coagulanolide isolated from Withania coagulans fruits has anti-hyperglycemic activity in rats^[23].

Curcuma longa: Rhizome powder of curcuma longa in the dose of 200mg/Kg was identified as the most effective dose with significant decrease in the levels of blood glucose & lipid profile. Both turmeric and curcumin decrease blood sugar level in alloxan-induced diabetes in rat. Curcumin also decreases advanced glycation end products induced complications in diabetes mellitus^[24].

Gymnema sylvestre: Alcoholic extract of Gymnema sylvestre stimulated insulin secretion from the rat islets of Langerhans and several pancreatic beta cell lines. In another study, oral administration of a water-soluble leaves extract of Gymnema sylvestre at 400 mg/day, p.o. to 27 IDDM patients on insulin therapy lowered fasting blood glucose and insulin requirements. Oral administration of Gymnema sylvestre to diabetic rats increased the number of pancreatic islet and beta cells, as well as insulin levels, suggesting a possible repair or regeneration of the endocrine pancreas. Water-soluble extracts of Gymnema sylvestre leaves release insulin probably by causing regeneration of pancreatic beta cells both in vivo and in vitro^[25].

Momordica charantia: It is commonly used as an antidiabetic and antihyperglycemic agent in India as well as other Asian countries. Extracts of fruit pulp,

seed, leaves and whole plant was shown to have hypoglycemic effect in various animal models. Polypeptide p, isolated from fruit, seeds and tissues of *M. charantia* showed significant hypoglycemic effect when administered subcutaneously to langurs and humans. Ethanolic extracts of *M. charantia* (200 mg/kg) showed an antihyperglycemic and hypoglycemic effect in normal and STZ 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. [26]

***Coccinia indica*:** It is widely used in traditional treatment of diabetes mellitus in sub-Saharan Africa and Southeast Asia. Pectin isolated from the fruits of *C. indica* has hypoglycemic activity. Alcoholic extract of plant was found to be active in reducing blood glucose level, then this extract was subjected to further fractionation to evaluate its biochemical parameters effecting diabetes and results suggested toluene as an active fraction. The action of these principles may be due to their β -cell restorative properties against alloxan induced damage. [27]

***Trigonella foenum graecum*:** It is found all over India and the fenugreek seeds are usually used as one of the major constituents of Indian spices. 4-hydroxyleucine, a novel amino acid from fenugreek seeds increased glucose stimulated insulin release by isolated islet cells in both rats and humans. Oral administration of 2 and 8 g/kg of plant extract produced dose dependent decrease in the blood glucose levels in both normal as well as diabetic rats. Administration of fenugreek seeds also improved glucose metabolism and normalized creatinine kinase activity in heart, skeletal muscle and liver of diabetic rats. It also reduced hepatic and renal glucose-6-phosphatase and fructose -1, 6- biphosphatase activity. This plant also shows antioxidant activity. [28]

***Tinospora cordifolia*:** The isoquinoline alkaloid rich fraction from stem, includes palmatine, jatrorrhizine, and magnoflorine which have been reported for insulin mimicking and insulin releasing effect both in vitro (using rat pancreatic β -cell line, RINm5F) and in vivo. Another isoquinoline alkaloid 'berberine' has

been tested and used successfully in experimental and human diabetes. It lowers elevated glucose level as effectively as metformin. Besides, tinosporin, isocolumbin, palmatine, tinocordiside, cordioside and β -sitosterol compounds present in stem and root which are also reported to possess antidiabetic, antihyperlipidemic and antioxidant properties. [29]

***Pterocarpus marsupium*:** The reports on hypoglycemic activity of *P. marsupium* is related to Pterostilbens, 3 – 4 dimethexystilbene. Mukherjee and Ray reported that *P. marsupium* had hardly any hypoglycemic activity confirmed the antihyperglycemic property with the extract of *P. marsupium*. Antidiabetic activity. [30]

***Syzygium cumini*:** Suspensions of seed kernel of *S. cumini* 4g / dose level was found to show maximum antidiabetic effect (42.64%) in rabbits 3h after medication. Nair and Santhakumar stated that like tolbutamide, drug of *S. cumini* may also be promoting endogenous release of insulin. It produced a significant decrease in the blood sugar level (17.04%) in alloxan diabetic rats. [30]

***Embellica officinalis*:** The aqueous fruit extract of *Phyllanthus emblica* showed effect on type-II diabetes, triglycerides and liver specific enzyme, alanine transaminase. It was shown that aqueous fruit extract in a dose of 200mg/kg body weight, significantly decreased the blood glucose level. [31]

***Salacia reticulate*:** Reported that compounds such as Salcinol and kotalanol isolated from *Salacia reticulate* possess α -glucosidase inhibiting activity. *S. reticulata* and *Catharanthus roseus* L mixtures showed hypoglycemic and hypolipidemic effects in diabetic induced rats. Further report that herbs decreased blood glucose level when compared to control in diabetic induced rats. The decreased blood glucose level is mainly due to the inhibition of pancreas lipase enzyme, aldose and glucosidase. [32]

Mechanism of Action of Antidiabetic plants [33]

The antidiabetic activity of herbs depends upon variety of mechanisms. The mechanism of action of herbal antidiabetic could be grouped as-

- Adrenomimeticism, pancreatic beta cell potassium channel blocking, cAMP (2nd messenger) stimulation,
- Inhibition in renal glucose reabsorption,
- Stimulation of insulin secretion from beta cells of islets or/and inhibition of insulin degradative processes,
- Reduction in insulin resistance,
- Providing certain necessary elements like calcium, zinc, magnesium, manganese and copper for the beta-cells,
- Regenerating and/or repairing pancreatic beta cells,
- Increasing the size and number of cells in the islets of Langerhans,
- Stimulation of insulin secretion,
- Stimulation of glycogenesis and hepatic glycolysis,
- Protective effect on the destruction of the beta cells,
- Improvement in digestion along with reduction in blood sugar and urea,
- Prevention of pathological conversion of starch to glucose,
- Inhibition of β -galactocidase and α -glucocidase,
- Cortisol lowering activities,
- Inhibition of alpha-amylase.

DISCUSSION

The evaluation of traditional medicinal plants, which are considered to be excellent for oral diabetic therapy, has been recommended by the World Health Organization (WHO) as they are effective, non-toxic and with less or no side effects as were noted by World Health Organization (1980). Before the discovery of insulin and hypoglycemic drugs, diabetic patients were treated with medicinal plants and traditional treatments.

Many traditional plants and their derived bioactive compounds are used for treatments of diabetes through various mechanisms of actions and there has been increased scientific interest in medicinal plants research that has been reported to be used traditionally

to manage diabetes. These plants are natural antioxidants and their anti-diabetic compounds, such as flavonoids, tannins, phenolic, and alkaloids that improve the performance of pancreatic tissues by increasing the insulin secretion or decreasing the intestinal absorption of glucose.

203 Indian medicinal plants are identified for diabetes from 355 articles which are extracted from 15631 articles using text data mining approach. Among of them 22 plants are frequently used to cure and prevent diabetes mellitus. Evaluation has been taken the frequency of Indian medicinal plants for diabetes to understand which specific plants are mostly preferred among Indian medicinal plants for diabetes. It is found that six plants (*Momordica charantia*, *Syzygium cumini*, *Gymnema sylvestre*, *Trigonella foenumgraecum*, *Tinospora cordifolia*, *Aegle marmelos*, *Pterocarpus marsupium*, and *Azadirachta indica* etc.) highly explored for the metabolic disorder (≥ 20 frequencies).^[34] This result suggests that these plants are important for the treatment and prevention of diabetes which are mentioned in Ayurveda, Siddha and Unani system of medicine (ASU) in India.

CONCLUSION

Many traditional plants are empirically used throughout the world to treat the disease because they are considered as less toxic and free from side effects than synthetic drugs. Several reviews on the plants used in the management of diabetes have been reported earlier. However current review highlights certain common plants commonly used in ASU system of medicine for the treatment of diabetes mellitus. These drugs have no proven side effects and can help in reduce the cost of the treatment of diabetes mellitus. Further studies are needed to find out the suitable formulations in ASU system of medicine which is cost effective and more beneficial for the treatment of Diabetes Mellitus.

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