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A REVIEW ON MEDICINAL PLANTS POTENTIAL WITH ANTIDIABETIC ACTIVITY

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ABSTRACT

Diabetes mellitus is a chronic metabolic disease. It causes number of complications, like retinopathy, neuropathy and peripheral vascular insufficiencies. The world wide prevalence of diabetes is expected to be more than 240 millions by the year 2010. In India more than 30 million people are with diabetes mellitus. There are lots of synthetic agents available to treat diabetes, but they have some undesirable side effects. Plant-based medicinal products have been known since ancient times and various medicinal plants and their products have been used to manage diabetes mellitus in the traditional medicinal systems of many countries in the world. Moreover, during the past few years many phytoconstituents which are responsible for antidiabetic activity have been isolated from the plant species. This review focuses mainly on selected plant species that have been reported for their antidiabetic properties using laboratory diabetic animal models in referred journals.

KEY WORDS: Diabetes mellitus, Medicinal plants, Antidiabetic, Herbal medicines.

INTRODUCTION

Diabetes Mellitus and Its Impact on Human Health

Diabetes mellitus is a chronic metabolic disorder, characterized by elevated blood glucose levels and disturbances in carbohydrates, fats and protein metabolism. These metabolic abnormalities resulting from defects in insulin secretion and/or insulin action (Fajans *et al*., 1997; George and Rudvid, 2000; Nyholm *et al*., 2000). There are two common forms of diabetes mellitus; Type-1 or Insulin Dependent Diabetes Mellitus (IDDM) and Type-2 or Non-Insulin Dependent Diabetes Mellitus (NIDDM) (Xie *et al*., 2002). IDDM is occurs due to complete loss of pancreatic β-islet cells and hence there is insulin deficiency. NIDDM is occurs due to insulin resistance (Agrawal and Paridhavi, 2007). Type-2 diabetes mellitus is much commoner than type-1, accounting for over 75% of all patients with diabetes in most population (Cantrill and Wood, 2005). The world wide prevalence of diabetes mellitus is expected to be more than 240 millions by the year 2010 (Chanrda *et al*., 2007). The countries with the largest number of diabetic people in the year 2025 will be India, China, United States (Ramachandran *et al*., 2002). In India more than 30 millions peoples are with diabetes mellitus (Shankar and Sundarka, 2001). In the next 25 years diabetes is being projected as the world's main disabler and killer (Edwin *et al*., 2006). The chronic hyperglycemia of diabetes is associated with damage, dysfunction and failure of various organs over long term (Lyra *et al*., 2006). It causes number of complications like retinopathy, neuropathy and peripheral vascular insufficiencies (Chehade and Moordian, 2000). A major complication of diabetes is loss of vision due to either to cataracts or to damage blood vessels of the retina. Sever kidney problems also may results from damage to renal blood vessels (Toratora and Grabowski, 2003). Diabetic patients typically have delayed or impaired wound healing and may develop chronic ulcers (Lateef *et al*., 2005). Type-2 diabetes is closely associated with obesity, obesity contributes to insulin resistance (Astrup and Finer, 2000; Kahn and Flier, 2000).

Diabetes and Existing Synthetic Drugs

Diabetes mellitus is still not completely curable by the present synthetic antidiabetic drugs. Insulin therapy is the only satisfactory approach in diabetes, even though it has several drawbacks like insulin resistance, brain

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atropy, anoresia and fatty liver in long term treatment (Piedrola *et al*., 2001; Weidmann, 1993). Several hypoglycemic agents such as biguanides and sulfonylureas are presently available to reduce hyperglycemia in diabetes mellitus. But these drugs have some undesirable side effects (Noor *et al*., 2008). Unfortunately after the introduction of these hypoglycemic agents about 50 years back, there is no major lead has been obtained in this direction of finding a proper drug for diabetes (Wadkar *et al*., 2008).

Diabetes and Herbal Medicines

Due to the adverse reaction and other undesirable side effects of synthetic drugs, there is an increasing demand by patients for the use of natural products and other dietary modulators with antidiabetic activity (Deb and Dutta, 2006). Therefore it is prudent to look for option in herbal medicines for the management of diabetes. Plant drugs are frequently considered to less toxic, free from side effects and relatively low costs than synthetic ones. Although, herbal medicines have long been used effectively for treating diseases in Asian communities and throughout the world (Bailey and Day, 1989; Eidi *et al*., 2006; Valiathan, 1998). According to the World Health Organization (WHO), an estimated 3.5 billion people in the developing world depends on the medicinal plants as part of their primary health care (Balick and Cox, 1996). Plants have been primary source of drugs and many of the presently available medicines have been derived directly or indirectly from plants. For example, the popular antihyperglycemic drug "metformin" (glucophage) is derived from *Galega officinalis* (Grover *et al*., 2002). For a long time diabetes has been treated with several medicinal plants or their extracts based on folklore medicine (Akhtar and Ali, 1980). A number of plant species are known to have hypoglycemic activity throughout the world (Kar *et al*., 2006; Kumar *et al*., 2006). Ehtnobotanical information indicates the more than 800 plants are used as traditional remedies for the treatment of diabetes (Pushparaj *et al*., 2000; Alarcon-Aguilara *et al*., 1998). About 600 traditional medicinal plants have been reported for diabetes till today (Edwin Jarald *et al*., 2008). In the Indian system of medicine, more than 100 medicinal plants are mentioned for the management of diabetes mellitus which are effective either alone or combinations (Kar *et al*., 2003). Alkaloids, amino acids, coumarins, flavonoids, steroids, triterpenoids, polysaccharides, glycopeptides, peptides, xanthone, lipids, iridoids, phenolics, guanidines, alkyl disulphides and inorganic ions are the phytoconstituents has been reported to have antididiabetic activity (Grover *et al*., 2002; Pulok *et al*., 2006).

In this review, the medicinal plant species which have been reported for their anti-diabetic properties, based on experimental animal models and reported in refereed journals are presented.

MEDICINAL PLANT SPECIES WITH ANTI-DIABETIC ACTIVITY

***Artanema sesamoides* (Family: Scrophuilariaceae)**

Artanema sesamoides Benth is a stout herb belongs to the family Scrophuilariaceae. It is distributed in southern Part of India, West Peninsula, Philippines, Malay, Sumatra, Java and Srilanka (Kritikar and Basu, 1975). Traditionally, this plant is used to treating diabetes in tribal people of Tamilnadu, India (Selven *et al.,* 2008). The anti diabetic activities of *Artanema sesamoides* have been reported by *Selvan et al*. In the study, the methanolic extract of *Artanema sesamoides* was found to have potent antidiabetic activity that reduces blood sugar level at 200 and 400mg/kg, p.o for 14 days in STZ-induced diabetic rats. The antidiabetic activity of *Artanema sesamoides* may be by sensitize the insulin receptor or stimulate the secretion of insulin from beta cells of Istets of Langerhans in pancreas (Selvan *et al.,* 2008). The seeds and root of *Artanema sesamoides* is reported to be medicinally important in traditional system of medicine. Decoction of root is given in diarrhea, rheumatism, stone, opthalmia and syphilis. Seeds are used for improve vitality, biliousness and favour conception (Kirtikar and Basu, 1975). The methanolic extract of *Artanema sesamoides* contains alkaloids, flavonoids and saponins (Selvan *et al*., 2008).

***Clerodendron phlomoidis* (Family: Verbenaceae)**

Clerodendron phlomoidis L. is commonly known as 'Arni' in Hindi belongs to Verbenaceae family. It is distributed throughout India (Nadkarni, 1982; Kirtikar and Basu, 1999). The leaves of *Clerodendron phlomoidis* is used to treat diabetes in southern parts of India, especially tribals of Nilgiris. Oral administration of ethanol extract of leaves of *Clerodendron phlomoidis* at 200mg/kg dose level exhibited significant hypoglycemic activity in alloxan-induced diabetic rats. The ethanolic extract of leaves of *C. phlomoidis* is reported to contain several constituents such as alkaloids, phytosterols, glycosides, saponins, phenolic compounds, proteins and flavonoids (Dhanabal *et al.,* 2008). In traditional systems of medicine *Clerodendron phlomoidis* is also used to treat various disease viz., juice of leaves is used as bitter tonic and also given in neglected syphilitic complaints. The root decoction is used as a demulcent in gonorrhoea and also given during convalescence from measles (Nadkarni, 1982; Kirtikar and Basu, 1999).

***Curculigo orchioides* (Family: Hypoxidaceae)**

Curculigo orchioides Gaerth. is a well known plant in traditional Indian system of medicine, belongs to the family Hypoxidaceae (Amaryllidaceae). It is found in India, particularly in the sub-tropical Himalayas and in the Western Ghats (Chopra *et al.,* 1986). In Unani system of medicine, *Curuligo orchioides* is used for management of diabetes (Parrotta, 2001). The anti-hyperglycemic effect of *Curculigo orchioides* have been investigated by *Chauhan* and *Dixit*. In their study, the ethnolic extract of the rhizome at a dose of 100 and 200 mg/kg. p.o. produced the maximum glucose lowering in diabetic rats serum. The authors concluded that the ethanolic extract of *Curculigo orchiodes* rhizomes given orally at dose of 100mg/kg, possesses significant hypoglycemic in both normal and diabetic rats (Chauhan and Dixit, 2007). *Curuligo orchiodes* chiefly contains sterols, glycosides, alkaloids

saponins (Rao *et al*., 1978) and carbohydrates (Tiwari and Misra, 1976). Curulignin β-C, curculigosaponin-F has also been isolated from *Curuligo orchioides* (Xu *et al*., 1992).

***Ficus racemosa* (Family: Moraceae)**

Ficus racemosa Linn (Syn: *Ficus glomerata* Roxb) is a large deciduous tree, commonly known as 'Cluster fig', belongs to the family Moraceae. It is distributed throughout India, particularly in evergreen forests, moist localities (Kirtikar and Basu, 2001; Ramankutty and Nambair, 1996). *Ficus racemosa* is used to treat diabetes by the tribal of Chotanagpur (Patil, *et al*., 2006). The anti-hyperglycemic activity of *Ficus racemosa* is evaluated by *Tushar A Deshmukh et al*. The authors concluded that the petroleum ether extract of *Ficus racemosa* at the doses of 100, 200 and 400mg/kg, p.o daily for 35 days, causes the maximum reduction in serum glucose levels. They suggest, the dose of 200mg/kg showed the maximum reduction of serum glucose level in both acute and subacute studies (Tushar A Deshmukh *et al*., 2007). *Ficus racemosa* have been reported to contain gluanol acetate, hetriaconate, β-sitosterol, lypeiolacetate (Chandra *et al*., 1979, Merchant and Engineer, 1979). The fruit extracts of *Ficus racemosa* contain sterols, tannins, glycosides, triterpeniods, flavonoids and carbohydrates (Tushar A Deshmukh *et al*, 2007). The fruits of *Ficus racemosa* are also considered astringent, stomachic and carminative (Patil *et al*., 2006).

***Ichnocarpus frutescens* (Family: Apocynaceae)**

Ichnocarpus frutescens commonly known as 'black creeper' belongs to Apocynaceae family. It is distributed throughout India (Nadkarni, 2002). The roots and flowers of *Ichnocarpus frutescens* are used to treat diabetes in Madhya Pradesh and Uttara Kannada district of Karnakata (Yusuf-Shaw *et al*., 2004, Bhandary *et al*., 1995). The antidiabetic activity of *Ichnocarpus frutescens* have been reported by *Rakesh Barik et al*. The aqueous root extract of *Ichnocarpus frutescens* at doses of 250 and 500mg/kg, p.o for 15 days, produced significant reduction of fasting blood glucose levels in streptozotocin-nicotinamide induced type-II diabetic rats (Rakesh Barik *et al*., 2008). The roots of *Ichnocarpus frutescens* are also used as a diuretic and diaphoretic (Nadkarni, 2002). The leaves and stalks are used in the skin eruption and fever (Yoganarasimhan *et al*., 1982).

***Lagerstroemia speciosa* (Family: Lythraceae)**

Lagerstroemia speciosa is a Southeast Asian tree more commonly known as 'banaba', belongs to the family Lythraceae. Traditionally, *Lagerstroemia speciosa* has been consumed in various forms by Philippines for treatment of diabetes (Guy Klein *et al*., 2007). *Kakuda et al*., studied the antidiabetic activity of *Lagerstroemia speciosa* by preparing water and methanol extracts of the plant. After feeding the extract to hereditary type-2 diabetic KK-Ay/Ta Jcl mice, they found that food containing either 3% of methanol extract or 5% of water extract was effective in reducing blood glucose and insulin levels (Kakuda *et al*., 1996). *Lagerstroemia speciosa* contains Corosolic acid (2α-hydroxyursoloic acid) (Murakami *et al*., 1993) and Lagerstroemin (Hayashi *et al*., 2002). *Lagerstroema speciosa* it has become relatively popular in the form of health-promoting tea products in United States and Eastern Asia (Guy Klein *et al*., 2007).

***Parkinsonia aculeata* (Family: Cesalphineaceae)**

Parkinsonia aculeata L. is a medium tree belongs to the family Cesalphineacea. It is found in semi-arid area in Northeast of Brazil. Traditionally, the infusion of the aerial parts of *Parkinsonia aculeata* has been used to manage diabetes-related complications in Northeast Brazil (Almeida *et al*., 2005). In a study undertaken to evaluate the antidiabetic potential of the water soluble fraction of aerial parts from *Parkinsonia aculeata* at a dose of 125 or 250mg/kg, p.o for 16 days, exhibited a significant reduction in serum and urinary glucose in alloxan-induced diabetic rats (Leite *et al*., 2007). *P. aculeata* contains C-glycosylflavones (Besson *et al*., 1980) and Luteolin 7, 4'-dimethyl ether 6-C-glucoside (El-sayed *et al*., 1991).

***Paspalum scrobiculatum* (Family: Poaceae)**

Paspalum scrobiculatum Linn is a tufted perennial grass, commonly known as 'Kodomillet', belongs to the family Poaceae. It is distributed in Madhya Pradesh, Chattisgarh and Karnataka in India (Singh, 1999). The use of the grains of *Paspalum scrobiculatum* for the management of diabetes mellitus has been reported in the texts of Ayurveda (Sanchan Kumar, 2004). Scientifly, the anti-diabetic activity of *Paspalum scrobiculatum* is evaluated by *Sanjay Jain et al*. The authors concluded that the ethanolic extract at 500 mg/kg dose, orally administered for 15 days produced the maximum reduction in fasting blood glucose and increase in serum insulin level in alloxan-induced diabetes. The hypoglycemic action of *Paspalum scrobiculatum* may be by potentiating the insulin effects of plasma by increasing either the pancreatic secretion of insulin from the existing beta cells or by its release from the bound form (Sanjay Jain *et al*., 2009). The grains of *Paspalum scrobiculatum* are also useful in controlling inflammation, hepatopathy, haemorrhages, and general debility (The Wealth of India, 2003).

***Salvadora oleoides* (Family: Salvadoraceae)**

Salvadora oleoides Decne. is an oil-yielding medicinal and multipurpose tree, belongs to the family Salvadoraceae. It is commonly known in India as 'meetha jal' (Singh *et al*., 1996). The hypoglycemic activity of *Salvadora oleoides* has been reported. The oral administration of ethanolic extract of the aerial parts *S. oleoides* at the doses of 1g and 2g/kg, per 21 days, produced significant reduction in blood glucose levels in alloxan-induced diabetic rats (Yadav *et al*., 2008). *Salvadora oleoides* leaves are said to possess anti-inflammatory, anti-ulcer, and analgesic activity (Anonymous, 1972).

***Syzigium cumini* (Family: Myrtaceae)**

Syzigium cumini Linn is a large evergreen tree, commonly known as 'Jamun' tree belongs to the family Myrtaceae. *Syzigium cumini* is native to India, thrives easily in tropical climate and is found in many parts of our sub-continent as well as countries of Asia and Eastern

Africa (Samba-Murthy and Subramanyam, 1989; Indira and Mohan Ram, 1992). The seeds of Jamun have been used by natives in treatment of diabetes (Chopra *et al.*, 1958). The seeds of *Syzigium cumini* have been considered as an indigenous source of medicines with hypoglycaemic (Mahapatra *et al.*, 1985), antipyretic (Ghosh *et al.*, 1985) and anti-inflammatory (Chaudhuri *et al.*, 1990) actions. The anti-diabetic activity of *Syzigium cumini* has been reported by *Stanely Mainzen Prince et al.* In the study, that the oral administration of alcoholic seeds extract of *Syzigium cumini* at dose of 100mg kg^{-1} daily for 42 days, resulted in a significant reduction in blood glucose, urine sugar and also lipids in serum and tissues in alloxan-induced diabetic rats (Stanely Mainzen Prince *et al*., 2004).

***Tinospora cordifolia* (Family: Menispermaceae)**

Tinospora cordifolia Miers is a glabrous climbing succulent shrub, belongs to the family Menispermaceae. It is native to India and also occurs in Burma and Ceylon. *Tinspora cordifolia* is widely used in Ayurredic medicine in India for treating diabetes mellitus and metabolic disorders (Nadkarni, 1954, Chopra *et al.*, 1958). The anti diabetic activity of stem, leaves and roots of *Tinospor cardifolia* have been evaluated in various experimental models (Gupta *et al*., 1967; Noreen *et al*., 1992; Stanely *et al.*, 2000). The effect of aqueous extract of *Tinospora cordifolia* root on diabetes has been reported by *Stanely et al.* The extract at the doses of 2.5 and 5.0 gm kg^{-1} possess significant antidiabetic activity. The hypoglycaemic action of *Tinospora cordifolia* may be potentiating the insulin effect of plasma by increasing either the pancreatic secretion of insulin from the β-cells of islets of Langerhans or its release from bound insulin (Stanely *et al.*, 2000).

***Tridax procumbens* (Family: Compositae)**

Tridax procumbens Linn. is a weed, commonly known as 'Ghamra' and in English popularly called 'Coat buttons' belongs to the family Compositae. It is distributed throughout India and is employed as indigenous medicine for a variety of ailments (Saraf and Dixit, 1991; Ali *et al.*, 2001). Traditionally, it is used to treat diabetes in the Mandesh region. The traditional claim of Mandesh region with regard to *Tridax procumbens* for its anti-diabetic activity is evaluated by *Durgacharan et al*. In the study, that the aqueous and alcoholic extracts from *Tridax procumbens* leaves (200 mg/kg) orally administered for 7 days produced a significant decrease in the blood glucose level in the model of alloxan-induced diabetic rats (Durgacharan A Bhagwat *et al.*, 2008). In Indian traditional medicine, *Tridax procumbens* is extensively used as anti-coagulant, anti-fungal and in insect repellent, in bronchial catarrh, diarrhoea and dysentery (Ali *et al.*, 2001). Moreover, it exhibits wound healing activity and promotes hair growth (Saraf *et al.*, 1991).

***Vernonia anthelminticum* Willd (Family: Asteraceae)**

Vernonia anthelminticum Willd is a well-known plant in traditional Indian system of Ayurvedic medicine belongs to the family Asteraceae. It is found in the tropical wild forest in India, Pakistan, Nepal, Srilanka and Myanmar (Warrier, 1994). In the Unani system of medicine, it is used for treating diabetes (Parrotta, 2001). Scientifially, the antidiabetic activity of *Vernonia anthelminticum* is evaluated by *Karthikeyan et al.* The ethanolic extract of *Vernoia anthelminticum* seeds, given orally at a dose of 500mg/kg, possesses significant hypoglycemic activity. The anti-hyperglycaemia produced by the extract may be due to increased uptake of glucose at tissue level or increase in pancreatic beta-cell function or due to inhibition of intestinal absorption of glucose (Karthikeyan *et al*., 2008). The ethanolic, benzene and acetone extract of seeds of *Vernonia anthelminticum* chiefly contain two novel and known steroids. It has also been identified as (24 alpha/R)-stigmasta-7-en-3-one (**1**), (24 alpha/R)-stigmasta 7, 9 (11)-dien-3-one (**2**), (24 alpha/R) stigmasta-5, 22-dien-3-Beta-01 (**3**) and (24 alpha/s)-stigma-7, 22, -dien-3-beta-01 (**4**) (Metha and Parashar, 1996). *Vernovia anthelminticum* is also useful for treating asthma, skin disease, pruritus, hecoderma, dyspepsia, fever, opthalmopathy and are very specific for round worm and thread worm (Warrier, 1994).

***Vitex megapotamica* (Family: Verbenaceae)**

Vitex megapotamica is a tree that grows to a height of 20m, belongs to the Verbenaceae family (Lorenzi, 1998). The hypoglycemic effect of *Vitex megapotamica* has been evaluated by *Leila Zanatta et al.* In their study, oral administration of crude extract of *Vitex magapotamica* leaves, at doses of 400 and 800 mg/kg significantly reduces serum glucose level in both normal and diabetic animals. The ethylacetate as well as n-butanol fractions were able to diminish glycemia in diabetic animals. The ethyl acetate fraction at the dose 400 and 800 mg/kg produced the maximum hypoglycemic effect (28 and 20%, respectively) in diabetic rat and the same dose of the n-butanol fraction reduced the hyperglycemia only by 11% at 1h after treatment. The authors concluded that the crude extract of *Vitex megapotamica* leaves was effective in decreasing the serum glucose level in normal and diabetic rats and that neither the extract nor the fraction acted by reducing intestinal absorption (Leila Zanatta *et al.*, 2007). Previous studies have reported the isolation of pterosteron, polyodin B, phytoecdysones and ecdysonatiges steroids and iridoids (Rimpler, 1969, 1972).

***Zygophyllum gaetulum* (Family: Zygophyllaceae)**

Zygophyllum gaetulum Emb & Maire, belongs to the family Zygophyllaceae. It is widely used in Moroccan folk medicine for the management of diabetes mellitus (Jaouhari *et al.*, 2000). The antidiabetic activity of this plant was evaluated by *Skim et al*. They reported that the oral or intraperitoneal administration of *zygophylum gaetulum* to normal or alloxan-induced diabetic rats significantly decreases the blood glucose level and increased the plasma insulin level (Skim *et al.*, 1998). It was also found that the aqueous extract of *Zygophyllum gaetulum* was more effective than glucohage retard (biguandie) and effective as glipizide (Sulphonylurea) in NIDDM volunteer patients (Lazrek *et al.*, 1994). The aqueous infusion of the aerial parts of *Zygophyllum gaetulum* (1g/kg) caused significant reduction in blood glucose concentration (Jaouhari *et al.*, 2000).

CONCLUSION

This review has presented a list of anti-diabetic plants in the management of diabetes mellitus. It showed that these plants have anti-diabetic properties. The potency of herbal medicine is significant and they have negligible side effects than existing synthetic antidiabetic drugs. Recently, herbal products have started gaining importance as complementary and alternative medicine to treat diabetes mellitus. However, many other active constituents obtained from plant species have not been well characterized. More investigations must be found out to evaluate the mechanism of action of herbal medicines with antidiabetic activity.

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