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Review Paper

Cure of Diabetes mellitus by some medicinally important dioecious plants

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Abstract

In dioecious species, male and female reproductive structures occur on separate plants. In such plants, most studies have been conducted to identify sex of the plant before flowering stage. These plants also contain medicinal properties which have not been exploited at larger scale. Diabetes mellitus is a death causing disease and its prevalence is increasing at a very fast and alarming rate. Herbal drugs are preferred in diabetes treatment as conventional drugs have serious side effects. *Coccinia grandis*, *Trichosanthes dioica*, *Simmondsia chinensis*, *Garcinia indica*, *Momordica dioica* and *Celastrus paniculatus* are some of the dioecious plants with anti-diabetic properties. In these plants, several DNA fingerprinting studies have been done for gender identification but less research is done on their anti-diabetic potential. In the present work, focus is given on these medicinally important dioecious plants and their anti-diabetic properties have also been reviewed.

Keywords: Diabetes mellitus, Dioecious plants, *Coccinia grandis*, *Trichosanthes dioica*, *Simmondsia chinensis*, *Garcinia indica*, *Momordica dioica* and *Celastrus paniculatus*.

Introduction

Diabetes mellitus is a metabolic disorder characterized by abnormal increase in blood sugar levels resulting from partial or complete absence of insulin production by the body. Insulin is a hormone required to control glucose amount in the blood. In diabetes mellitus, body ineffectively uses insulin if produced. Symptoms of diabetes mellitus include frequent urination, weight loss, blurry vision, frequent urination, fatigue, extreme thirst and hunger and may result in complications like high blood pressure, kidney failure, blindness, heart diseases, stroke, foot and leg infections, sexual dysfunctions, pregnancy problems etc. Diabetes mellitus is mainly of three types, type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM) and gestational diabetes mellitus (GDM). T1DM is insulin dependent and is characterized by loss of the insulin producing beta cells of the islets of Langerhans in the pancreas leading to insulin deficiency. T2DM is non-insulin dependent and is characterized by insulin resistance and insufficient insulin production leading to hyperglycemia. In GDM, insulin receptors dysfunction leading to high blood glucose levels during pregnancy. T2DM is the most common form of diabetes and makes up more than 90% of all diabetes cases. In 2013, 382 million people were diabetic worldwide which is expected to be 592 million by 2035 resulting in an increase of 55%. People of Western Pacific were at the top with 138.2 million diabetic persons in 2013 followed by South East Asia and Europe. Mostly diabetic people belong to low and middle income countries and are of age between 40 and 59. India is at the second position after China in number of people with diabetes. India had 65.1 million diabetics in 2013 while China had 98.4 million. Diabetes and its complications are major causes of deaths in many of the countries. In 2013, diabetes mellitus caused 5.1 million deaths and 548 billion US dollars were expenditure globally for diabetes treatment^[1].

Dioecious plants in treatment of diabetes mellitus

Treatment of diabetes by herbal formulations is preferred over other approaches due to low costs and less side effects [2]. Traditional medicines have been proved to be better than conventional drugs in diabetes treatment [3]. Synthetic oral anti-diabetic agents are not safe for use during pregnancy [4] and can produce serious side effects [5]. More than 400 plant species have been shown containing hypoglycemic activity [6-8]. Dioecious plants have male and female reproductive organs borne on separate individuals of the same species. Only around 6% of angiosperms are dioecious [9]. In such plants, most studies have been conducted for sex identification at early seedling stages but focus should also be given to anti-diabetic potential of these plants. There are several dioecious plants which have been proved to be anti-diabetic like *Coccinia grandis*, *Trichosanthes dioica*, *Simmondsia chinensis*, *Garcinia indica*, *Momordica dioica* and *Celastrus paniculatus*. This review summarizes such anti-diabetic dioecious plants and their effectiveness in treatment of diabetes mellitus.

Trichosanthes dioica Roxb.



Figure 1: *Trichosanthes dioica*

Trichosanthes dioica Roxb., commonly known as pointed gourd is a member of Cucurbitaceae family and mainly cultivated as vegetable crop. This plant is perennial, dioecious and originated from Indo-Malayan regions and cultivated extensively in tropical and subtropical regions of the world. In India, it is extensively cultivated in the Eastern regions [10] mainly in Uttar Pradesh, West Bengal, Bihar, Orissa and Assam. Though plant produces well developed seeds but is also vegetatively cultivated due to poor germination, slow growth rate of seedlings and dioecious nature of the plant [11]. The plant is a rich source of carbohydrates, vitamin A [12], vitamin C, and contain trace elements like magnesium, potassium, copper, sulfur and chlorine and its leaves and stem contain many bioactive compounds with medicinal properties [13,14]. The plant is helpful in treatment of diseases like diabetes mellitus, alopecia, epilepsy, skin diseases [15] and contains hepatoprotective [16] and wound healing activities [17]. Plant extract is helpful in reduction of liver enzymes (Alanine transaminase and Alkaline phosphatase), serum creatinine and hence play important role in human physiology [18]. Its leaves are anthelmintic [19] and help in reducing blood cholesterol levels, blood sugar levels and blood phospholipid levels [20-23]. Leaves and seeds of this plant contain antidiabetic components [24]. Its fruits are easily digestible, diuretic [25], laxative [26], contain antiulcerous [27] and hypoglycemic properties [13,20]. Its fruits are also used in treatment of spermatorrhoea.

***Trichosanthes dioica* in diabetes mellitus treatment**

Sharma and Pant^[20] observed effect of raw deseeded fruit powder of *Trichosanthes dioica* on blood sugar, cholesterol, HDL, phospholipid and triglyceride levels in the normal albino rabbits. Role of *Trichosanthes dioica* seeds in normal and mild diabetic subjects in relation to lipid profile has also been evaluated by Sharma et al.^[21]. Sharmila et al.^[28], evaluated cholesterol lowering ability of aqueous fruit extract of *Trichosanthes dioica* in normal and streptozotocin diabetic rat. Rai et al.^[18], observed reduction in levels of blood glucose, postprandial glucose, urine protein and urine sugar, aspartate amino transferase, alanine amino transferase, alkaline phosphatase and creatinine, when doses of aqueous fruit extract of *T. dioica* was given in streptozotocin induced diabetic rats. Rai et al.^[24] evaluated the glycemic properties of *T. dioica* leaves, fruits and seeds extract. Antihyperglycemic activity of aqueous leaf extract has also been tested in normal and streptozotocin induced diabetic rats by Adiga et al.^[29] and observed reduction in blood glucose significantly. In 2012, potential of leaf extracts of *Trichosanthes dioica* and *Clitoria ternatea* combinedly was evaluated on streptozotocin induced diabetic and observed decrease in serum glucose significantly ($p < 0.05$)^[30]. In 2013, validation of antidiabetic activity of aqueous fruit extract of *Trichosanthes dioica* on normal, mild and severe diabetic models has also been done. A reduction in blood glucose level, urine sugar, total cholesterol and triglyceride levels were observed and body weight, total protein, HDL, hemoglobin levels were increased^[31]. Diabetes related studies of this plant have also been shown in Table 1.

***Coccinia grandis* (L.) Voigt.**



Figure 2: *Coccinia grandis*

Coccinia grandis (L.) Voigt is a climbing, perennial, dioecious, vegetatively propagated plant of Cucurbitaceae family, widely distributed in the tropical and sub-tropical regions of the world. Its native range extends from Africa to Asia^{[32][33]}. Its fruits are used as vegetable^[34] and are chewed to cure tongue sores^[35]. Each part of this plant is medicinally important and has been used in Ayurvedic and Unani practices in Indian subcontinent since ancient times^[36]. Several bioactive compounds such as alkaloids, glycosides, flavonoids, tannins, saponins are present in this plant. This plant is helpful in treatment of gonorrhoeae^[37], pyelitis, cystitis, strangury, snake bite, urinary gravel and calculi^[38]. Plant also contains antimutagenic^[39], hypolipidemic and hypoglycemic activities^[40-45]. Anti-diabetic^[46], anti-bacterial and hepatoprotective^[47] activities have been reported in leaves of this plant. Fruits extract of this plant contain antioxidant activities^[48], stem extract contains antispasmodic property and leaves aqueous extract contain anti-inflammatory properties^[49].

***Coccinia grandis* in diabetes mellitus treatment**

Hypoglycemic property of *C. indica* have been evaluated by Brahmachari et al.^[42], Mukherjee et al.^[43], Kumar et al.^[50]. Khan et al.^[51] observed the efficiency of *C. grandis* in treatment of diabetes mellitus patients. Anti-diabetic activity of *Coccinia indica* has also been evaluated in dogs^[52,53]. Doss and Dhanabalan^[54], evaluated anti-hyperglycaemic and insulin release potential of *Coccinia grandis* aqueous leaves extract in normal and alloxan diabetic rats. The changes in body weight, serum lipid profiles, blood glucose and cholesterol levels were analyzed and found that aqueous extracts of this plant was efficient in reducing blood glucose, urea, protein and cholesterol levels. In 2003, protective

effect of *Coccinia indica* on fatty acid composition changes in streptozotocin induced diabetic rats was reported [48]. In 2008, Kuriyan et al. [55] evaluated the potential of *C. grandis* in diabetes treatment. Munasinghe et al. [56], conducted double blind phase 1 experiment to check the efficiency of *Coccinia grandis* leaves in reducing blood sugar levels in healthy individuals. Diabetes related studies in this plant have also been shown in Table 1.

***Simmondsia chinensis* (Link) Schneider**



Figure 3: *Simmondsia chinensis*

Simmondsia chinensis (Link) Schneider, commonly known as jojoba is a member of Simmondsiaceae family and native to Southern Arizona, Sonora and Baja California. This plant is dioecious, woody, perennial, evergreen and is cultivated mainly for its seeds. Its seeds contain oil known as jojoba wax composed of linear wax esters [57,58]. Jojoba oil is non-toxic, biodegradable and is used as high temperature and high pressure lubricant in heavy machineries [59]. Jojoba oil is also a source of biodiesel [60-62] and has antifeedant effect [63-65]. Jojoba oil also helps in reducing blood cholesterol level and altering lipo-protein patterns [66]. Jojoba oil is also helpful in reducing weight loss, improve liver functions, cancer remediation and enhancing hair growth [67]. Jojoba oil also has properties like anti-acne, skin emollient [68,69], antipsoriasis [70] and anti-inflammatory [71].

***Simmondsia chinensis* in diabetes mellitus treatment**

Shahwan [72] evaluated the effect of oral administration of 70% ethanol seeds extract of Jojoba on lipid profile in rabbits. A drop in serum cholesterol and triglycerides levels was observed. The tissues lipids profiles of heart muscle and liver showed similar reduction in serum lipids. This study proved antihyperlipidemic activity of seeds extract of this plant. Diabetes related studies in this plant have also been shown in Table 1.

***Momordica dioica* Roxb. Ex. Wild.**

Momordica dioica Roxb. Ex. Wild., a member of cucurbitaceae family is a perennial, dioecious climber. This plant originated in Indo-Malayan regions [73,74] and is cultivated for its fruits which are used as vegetable [75]. This plant is rich in vitamin C [76], carotene, protein and carbohydrate [73]. The whole plant is medicinally important and used in treatment of poisoning, eye diseases and fever [77].

Its tuberous roots, leaves and fruits are used in India as a folk remedy for diabetes^[78]. Roots of this plant are used in treatment of piles, urinary and bowel complaints^[79] and contain antimicrobial, antifungal, spermicidal and anthelmintic activity. Its leaves are antihelminthic, aphrodisiac and are used in treatment of jaundice, asthma, bronchitis, hepatic damages and urinary retention. The infusion of its fruit powder produces errhine effect in nostrils and promotes sneezing and increased discharges^[80,81].

***Momordica dioica* in diabetes mellitus treatment**

Evaluation of antidiabetic activity of various organic fruits extracts (chloroform, ethyl acetate and alcohol extracts) of *M. dioica* in alloxan-induced diabetic rats has been done by Reddy *et al.*^[82]. Fruits extracts of ethyl acetate and ethanol showed significant anti-diabetic activity. Investigation of antidiabetic activity of *Momordica dioica* fruits extract in streptozotocin-diabetic rats using diabetes-oxidative damage in kidney has been conducted by Gupta *et al.*^[83] and found its kidney protective role in diabetes. Rao and Mohan^[84], evaluated the effect of methanolic seed extract of *Momordica dioica* on lipid profile in streptozotocin induced diabetic rats. Diabetes related studies in this plant have also been shown in Table 1.

***Garcinia indica* Choisy**

Garcinia indica Choisy, also known as kokam, is a member of Clusiaceae family and originated from tropical Asian, African and polynesian countries^[85]. The plant is dioecious^[86] but according to Rawat and Bhatnagar^[87], the nature of the plant is gynodioecious with female and bisexual flowers occurring on different plants. This plant is mainly cultivated for its fruits which contain enormous medicinal properties. Its fruits contain anticholesterol^[88,89], antidiabetic^[90], anti-oxidant and anti-glycation activities^[91,92]. *Garcinia indica* fruits extracts contain many medicinal compounds like ascorbic acid^[93], flavonoids and phenolic acids, citric acid, malic acid, polyphenols, carbohydrates, anthocyanin pigments^[93,94], camboginol and isoxanthochymol and poly-isoprenylated benzophenones^[95].

***Garcinia indica* in diabetes mellitus treatment**

Kirana and Srinivasan^[96] studied the effect of fruits aqueous extract of *Garcinia indica* in type 2 diabetic rats. Significant decrease in fasting and postprandial blood glucose was observed along with restoration of erythrocyte glutathione which is an intracellular anti-oxidant in diabetes. Diabetes related studies in this plant have also been shown in Table 1.

***Celastrus paniculatus* Willd.**

Celastrus paniculatus Willd. also known as Malkangoni, is a large, woody, climbing, usually dioecious shrub found all over in India, Sri Lanka and Maldives^[97]. The plant is helpful in treatment of diseases like epilepsy, insomnia, rheumatism, cognitive dysfunction, gout, dyspepsia^[98], diarrhoea and haemorrhage^[99]. Seeds of this plant are helpful in treatment of various diseases since ancient times^[100] such as paralysis, leprosy, gout, rheumatism and sores^[101]. Oil obtained from seeds of this plant has memory enhancing ability^[102] and is helpful in treatment of abdominal disorders, beri-beri, sores^[103], muscle relaxation and intestinal disorders^[104]. Free-radical-scavenging properties and anti-oxidant properties are exhibited by its seeds methanolic extract^[105].

***Celastrus paniculatus* in diabetes mellitus treatment**

Patil *et al.*^[106] observed hypolipidemic effect of methanolic seeds extract of *C. paniculatus* in hypercholesterolemic rats. A decrease in cholesterol levels was observed which may be due to increase in the serum HDL levels and increase in lipoprotein lipase and plasma LCAT activities which are involved in transport of tissue cholesterol to liver for its excretion. Reduction in activities of glucose 6-phosphate dehydrogenase, HMG-CoA reductase and malate dehydrogenase were also observed. Diabetes related studies in this plant have also been shown in Table 1.

Table 1: Studies related to anti-diabetic activities of some dioecious plants

<i>Coccinia grandis</i> (L.) Voigt	Leaf extract of <i>Coccinia grandis</i> in treatment of diabetes and its complications in streptozotocin induced diabetes	Krishnakumari et al. 2011 ^[107]
	Assessment of efficiency of leaves of <i>Coccinia grandis</i> as a hypoglycaemic agent in healthy individuals and to identify common short-term adverse effects	Munasinghe et al. 2011 ^[56]
	Anti-hyperglycaemic and insulin release effects of aqueous extracts of leaves of <i>Coccinia grandis</i> in normal and alloxan diabetic rats	Doss and Dhanabalan, 2008 ^[54]
	Influence of <i>Coccinia indica</i> on enzymes involved in glycolytic and lipolytic pathway in human diabetes	Kamble et al. 1998 ^[108]
<i>Trichosanthes dioica</i> Roxb.	Evaluation of antihyperglycaemic effectiveness of combined leaf extracts of <i>Trichosanthes dioica</i> and <i>Clitoria ternatea</i> in STZ-induced diabetic rats.	Sharmila et al. 2007 ^[28] , Daisy and Rajathi, 2009 ^[111] , Kavitha and Premalakshmi, 2012 ^[115]
	Hypoglycemic potential of aqueous extract of <i>T. dioica</i> leaves in streptozotocin (STZ) induced sub and mild diabetic rats	Chandrasekhar et al. 1988 ^[112] , Rai et al. 2008 ^[18] , Rai et al. 2008 ^[24]
	Effect of aqueous leaf extract of <i>T. dioica</i> on serum glucose level in glucose loaded, normal and hyperglycemic rats	Adiga et al. 2010 ^[29]
	Extracts of seeds, fruits and dried leaves of <i>Trichosanthes dioica</i> are used in treatment of diabetes mellitus	Sharma and Pant, 1988 ^[20] , Sharma et al. 1990 ^[13]
	Influence of alcoholic extract of whole fruit of <i>Trichosanthes dioica</i> on blood sugar	Sharma and Pant, 1992 ^[113]
<i>Momordica dioica</i> Roxb. Ex. Wild.	Evaluation of anti-hyperlipidemic efficiency of methanolic extract from <i>Momordica dioica</i> seeds in Streptozotocin (STZ) induced diabetic rats	Rao and Mohan, 2014 ^[84]
	Investigation of antidiabetic and renal protective effect of <i>Momordica dioica</i> fruits extract in streptozotocin diabetic rats using diabetes oxidative damage in kidney.	Gupta et al. 2011 ^[83]
	Evaluation of antidiabetic activity of chloroform, ethyl acetate and alcohol extracts of <i>M. dioica</i> fruits in alloxan-induced diabetic rats	Reddy et al. 2006 ^[82]
	Evaluation of fruits, leaves and tuberous roots used in India as a folk remedy for diabetes	Sadyojatha and Vaidya, 1996 ^[78]
<i>Garcinia indica</i> choisy	Evaluation of antihyperglycemic activity of methanolic extract of <i>Garcinia indica</i> on streptozotocin induced diabetic rats	Swathi et al. 2015 ^[114]
	Effect of aqueous extract of <i>G. indica</i> on GSH in type 2 diabetic rats	Kirana and Srinivasan, 2010 ^[96]
	Diabetes treatment by decoction of <i>G. indica</i> fruits	Agnivesha, 2001 ^[90]
	Whole fruit extract potential of <i>Garcinia indica</i> in lowering blood glucose levels in streptozotocin induced hyperglycemic rats	Yamaguchi et al. 2000 ^[91]
<i>Simmondsia chinensis</i> (Link) Schneider	Evaluation of antihyperlipidemic effect of seeds extract of <i>Simmondsia chinensis</i> in rabbits	Shahwan, 2014 ^[72]
<i>Celastrus paniculatus</i>	Evaluation of hypolipidemic potential of methanolic seeds extract of <i>Celastrus paniculatus</i> in experimentally induced hypercholesterolemic rats.	Patil et al. 2010 ^[106]
	Potential of <i>Celastrus paniculatus</i> seeds extract in hypolipidaemic activity in cholesterol fed rabbits	Mathur et al. 1993 ^[97]

Conclusion

Diabetes mellitus is one of the major causes of death throughout the world and its influence is increasing very rapidly. In 2014, 4.9 million individuals died due to this disease worldwide. Conventional drugs for diabetes treatment have several serious side effects. Therefore, herbal medicines are being preferred these days with less or no side effects. There are few medicinally important dioecious plants like *Coccinia grandis*, *Trichosanthes dioica*, *Simmondsia chinensis*, *Garcinia indica*, *Momordica dioica* and *Celastrus paniculatus*, whose anti-diabetic potential have not been exploited properly. In this study, few medicinally important dioecious plants and their anti-diabetic potentials have been reviewed. Proper research on anti-diabetic properties of these plants may help in development of effective anti-diabetic herbal drugs.

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