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Research Article

A SYSTEMATIC REVIEW ON MEDICINAL PLANTS USED TO TREAT DIABETES MELLITUS

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ABSTRACT

Diabetes mellitus (DM), both insulin-dependent DM (IDDM) and non-insulin dependent DM (NIDDM) is a common and serious metabolic disorder throughout the world. Several oral hypoglycemic agents and insulin therapy are the primary forms of treatment for diabetes. However, prominent side effects of such drugs are the main reason for an increasing number of people seeking alternative therapies that may have less severe or no side effects. Several medicinal plants have been used to control diabetes in the traditional medicinal systems of many cultures worldwide. Many more medicinal plants have found potential use as hypoglycemic in the Indian system of medicines. In this review, there are 39 plants described. It clearly shows the importance of herbal plants in the treatment of diabetes mellitus. The present review profile-gives information about scientific name, common name, family and the parts of the plant used to treat diabetes.

Keywords: Diabetes mellitus, Medicinal plants.

INTRODUCTION

Diabetes mellitus is a syndrome of disordered metabolism, usually due to a combination of hereditary and environmental causes, resulting in hyperglycemia due to defects in either insulin secretion or insulin action in the body. Chronic hyperglycaemia during diabetes causes glycation of body proteins that in turn lead to secondary complications affecting eyes, kidneys, nerves and arteries[1].

The treatments of diabetes include diet, exercise, use of oral hypoglycemic agents and insulin is the primary forms of treatment for diabetes. Currently available synthetic antidiabetic agents besides being expensive produce serious side effects. Apart from currently available therapeutic options, many herbal medicines have been recommended for the treatment of diabetes mellitus, medicinal plants have the advantage of having no side effects[1]. Traditional plant treatments have been used throughout the world for the therapy of diabetes mellitus. History showed that medicinal plants have been used in traditional healing around the world for a long time to treat diabetes; this is because such herbal plants have hypoglycemic properties and other beneficial properties, as reported in scientific literatures[2]. This review clearly shows the importance of herbal plants in the treatment of diabetes mellitus.

Indian Medicinal Plants to Treat Diabetes Mellitus

India has an officially recorded list of 45,000 plant species and a various estimation of 7500 species of medicinal importance[3]. India has a rich history of using various potent herbs and herbal components for treating diabetes. Many Indian plants have been investigated for their beneficial use in different types of diabetes and reported in numerous scientific journals. In this review, there are 39 plants belonging to 30 families described about their uses in curing diabetes. The table 1 shows the information about scientific name, common name, family and the parts of the plant used to treat diabetes and the table 2 shows the pictures of the medicinal plants.

***Acorus calamus* (ACORACEAE) [Fig.1]**
Oral administration of methanolic extract of *A. calamus* rhizome restored the levels of blood glucose in Streptozotocin induced diabetic rats after 21 days. Further, lipid profile (total cholesterol, LDL and HDL-cholesterol), glucose 6-phosphatase, fructose 1,6 bis phosphatase levels and hepatic markers enzymes (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase) were decreased [4].

***Sclerocarya birrea* (ANACARDIACEAE) [Fig.2]**
The methylene chloride/methanol extract (150 and 300 mg/kg bw) of *S. birrea* stem bark significantly reduced the blood glucose level, plasma cholesterol, triglyceride and urea levels to the normal level and increased plasma insulin level in STZ induced diabetic rats[5].

***Annona squamosa* (ANNONACEAE) [Fig.3]**
Aqueous extract of *A. squamosa* root (at a dose of 250 mg/kg and 500 mg/kg bw) when given to STZ- induced diabetic rats reduced the blood glucose level from 285.52 to 208.81 mg/dl, 6 hours after oral administration of extract[6].

***Polyalthia longifolia* (ANNONACEAE) [Fig.4]**
Oral administration of the methanolic extract of *P. longifolia* bark (200 and 300 mg/kg bw) reduced the fasting blood glucose, moreover the elevated levels of SGOT, SGPT, ALP, triglycerides and total cholesterol were restored to near normal level in STZ induced diabetic rats[7].

***Ferula asafoetida* (APIACEAE) [Fig.5]**
The intraperitoneal injection of aqueous extract of *F. asafoetida* resin decreased the blood glucose level and increased the insulin secretion in the alloxan-induced diabetic rat model. The extract stimulated the changes of the functional state of pancreatic β-cells and had beneficial effect by partly preserved or restored pancreatic β-cell mass[8].

***Catharanthus roseus* (APOCYNACEAE) [Fig.6]**
The administration of *C. roseus* leaf powder (100 mg/kg bw) lowered the plasma glucose and increased the plasma insulin were observed after 15 days in STZ induced diabetic rats. The significant enhancement in plasma total cholesterol, triglycerides, LDL and VLDL-cholesterol, and the atherogenic index of diabetic rats were normalized in extract treated diabetic rats[9].

***Ichnocarpus frutescens* (APOCYNACEAE) [Fig.7]**
Oral administration of the polyphenolic extract of *I. frutescens* (150 and 300 mg/kg bw) leaves significantly reduced the fasting blood glucose levels, hepatic HMG-CoA reductase activity decreased the total cholesterol, triglyceride, VLDL, HDL and LDL level in alloxan diabetic rats[10].

***Acanthopanax senticosus* (ARALIACEAE) [Fig.8]**
A hot water extract (85-95°C) of *A. senticosus* stem bark significantly decreased the plasma glucose level without affecting plasma insulin levels and inhibited α-glucosidase activity in diabetic mice. The addition of *A. senticosus* extract inhibited α-glucosidase activity but not α-amylase activity. Thus it would be useful as an ingredient of functional foods to improve postprandial hyperglycemia and prevent type II diabetes mellitus[11].

***Caralluma sinaica* (ASCLEPIADACEAE) [Fig.9]**
Treatment with alcoholic extract of *C. sinaica* (200 mg/kg bw) roots and aerial parts significantly reduced blood glucose level in STZ induced diabetic rat[12].

***Terminalia bellerica* (COMBRETACEAE) [Fig.10]**
The hexane (200mg/kg bw), ethylacetate (300mg/kg bw) and methanol (300 mg/kg bw) crude extracts of *T. bellerica* fruits significantly reduced the blood glucose level, total cholesterol, triglycerides, LDL cholesterol level, urea, uric acid, creatinine and serum total protein level while it increased the plasma insulin level of STZ induced diabetic rats[13].

***Costus speciosus* (COSTACEAE) [Fig.11]**
Oral administration of Eremanthin (a compound isolated from the plant *C. speciosus* rhizome) decreased the HbA_{1c}, serum total cholesterol, triglyceride, LDL-cholesterol level and at the same time markedly increased plasma insulin, tissue glycogen, HDL-cholesterol and serum protein of STZ induced diabetic rats. It also restored the plasma enzyme levels to near normal. Thus it –possessed a significant hypoclycemic and hypolipidemic activities and hence it could be used as a drug for treating diabetes[14].

***Vaccinium bracteatum* (ERICACEAE) [Fig.12]**
Intragastric administration of the aqueous and ethanolic extract of *V. bracteatum* leaves

significantly ameliorated the body weight, blood glucose, insulin and plasma lipid levels of STZ-induced diabetic mice[15]. The effect of *V. bracteatum* aqueous extract on the diabetic mice was superior to that of *V. bracteatum* ethanolic extract[15].

***Jatropha curcas* (EUPHORBIACEAE) [Fig.13]**

Oral administration of ethanolic extract of *J. curcas* leaves (250 & 500 mg/kg bw) significantly decreased the blood glucose level and can therefore be used as an alternative remedy for the treatment of diabetes mellitus and its complications[16].

***Securinega virosa* (EUPHORBIACEAE) [Fig.14]**

Intraperitoneal administration of (100, 300 and 600 mg/kg bw) methanol extract from *S. virosa* leaves significantly reduced the blood glucose level of STZ induced diabetic rats[17].

***Emblica officinalis* (EUPHORBIACEAE) [Fig.15]**

Oral administration of ethanolic extract of seed powder of *E. officinalis* decreased the blood glucose level and serum cholesterol level in alloxan induced diabetic rats[18].

***Trigonella foenum-graecum* (FABACEAEA) [Fig.16]**

Seeds of fenugreek have been shown to have multiple benefits in patients with diabetes such as reduction of blood glucose level and its complications[18-21]. Ethanolic extract of *T. foenum graecum* seed significantly decreased the blood glucose, serum cholesterol, SGOT and SGPT levels of alloxan induced diabetic rats[20-21]. Neveen *et al*[22] reported that alkaloid extract of fenugreek dried seeds significantly increased serum insulin level of STZ induced hyperglycemic rats.

***Senna auriculata* (FABACEAEA) [Fig.17]**

Oral administration of the ethanolic extract of *S. auriculata* (at a dose of 150 mg/kg of bw) leaf significantly reduced the blood glucose level, SGOT, SGPT, ALP, total cholesterol, triglyceride and low density lipoprotein-cholesterol (LDL-C) levels to the normal level and significantly increased HDL-C and phospholipid (PL) level in alloxan induced diabetic rats[23]. *S. auriculata* leaf gained much importance in diabetic control as it has been used as a traditional medicine for diabetes; since the phytochemical analysis has shown the presence of potent phytochemicals like flavonoids, terpenoids, glycosides, steroids, saponin and phenols. Several authors reported that flavonoids, steroids/terpenoids, phenolic acids are known to be bioactive antidiabetic principles[24, 25].

Elavarasi *et al*[26] reported that the flowers of *C. auriculata* are used as an important ingredient in the poly herbal diabetic drug formulations prepared by Tribals of Kolli Hills, Tamilnadu to treat the diabetes.

***Ougeinia oojeinensis* (FABACEAEA) [Fig.18]**

The ethanolic extract of *O. oojeinensis* (200 mg/kg) bark significantly decreased the blood glucose level, triglycerides, LDL, VLDL and total cholesterol and increased high density lipoprotein level in alloxan induced diabetic rats[27].

***Cinnamonum zeylanicum* (LAURACEAE) [Fig.19]**

A compound Cinnamaldehyde isolated from *C. zeylanicum* bark. The oral administration of a Cinnamaldehyde compound (20 mg/kg) significantly decreased the HbA_{1C}, serum total cholesterol, triglyceride levels and at the same time markedly increased plasma insulin, hepatic glycogen and high density lipoprotein-cholesterol levels in STZ-induced diabetic rats[28]. It also restored the plasma enzyme reduction in blood glucose level[26].

***Allium cepa* (LILIACEAE) [Fig.20]**

Essential oil (100 mg/kg) obtained from the red onion significantly decreased the blood glucose level, serum lipids, lipid peroxide formation and serum nitric oxide level and increased the serum insulin level in STZ induced diabetic rats[29].

***Strychonous potatorum* (LOGANIACEAE) [Fig.21]**

Oral administration of the ethanolic extract of *S. potatorum* plant material significantly decreased the AST, ALT and ALP level along with reduction of blood glucose level of alloxan induced diabetic rats[30].

***Adansonnia digitata* (MALVACEAE) [Fig.22]**

Intraperitoneal administration of methanolic extract of *A. digitata* stem bark (100 mg/kg bw) significantly decreased the blood glucose level of STZ-induced diabetic Wistar rats[31].

***Hibiscus rosa sinensis* (MALVACEAE) [Fig.23]**

Treatment with the aqueous extract of *H. rosa sinensis* (500 mg kg^{-1}) aerial part reduced the blood glucose level, urea, uric acid and creatinine but increased the activities of insulin, C-peptide, albumin, albumin/globulin ratio and restored all marker enzymes to near control

levels of STZ-induced diabetic rats. Thus, it exhibited an antihyperglycaemic effect and consequently may alleviate liver and renal damage associated with STZ-induced diabetes mellitus in rats[32].
An Ethnobotanical survey of Elavarasi *et al*[26] stated that the *H. rosa sinensis* flowers used for treatment of diabetes.

***Ficus benghalensis* (MORACEAE) [Fig.24]**
The aqueous extract of *F. bengalensis* stem bark significantly reduced the blood glucose level of STZ induced diabetic rats[33].

***Ficus Glomerata* (MORACEAE) [Fig.25]**
The ethanolic extract of *F. Glomerata* leaves reduced the blood glucose, serum urea, creatinine and cholesterol level of alloxan induced diabetic rats[34].

***Ficus religiosa* (MORACEAE) [Fig.26]**
Oral administration of aqueous extract of *F. religiosa* bark significantly reduced the blood glucose level and increased the serum insulin level, glycogen content in liver and skeletal muscle in STZ-induced diabetic rats[35].

***Psidium guajava* (MYRTACEAE) [Fig.27]**
A hot water extract of *P. guajava* unripe fruit peel (400 mg/kg) significantly decreased the triglyceride, total cholesterol, alkaline phosphatase, asperate amino transferase, alanine amino transferase and creatinine levels of STZ induced diabetic rats[36].

***Syzygium cumini* (MYRTACEAE) [Fig.28]**
Mycaminose a compound isolated from the plant *S. cumini* seed extract. Oral administration of a compound (50 mg/kg), ethyl acetate (200 mg/kg) and methanol extracts (400 mg/kg) of fruits and leaves of *S. cumini* reduced the blood glucose level of STZ-induced diabetic rats[37]. *S. cumini* seed powder and ethanol extract *S. cumini* seed have potential antihyperlipidemic effect in type 2 diabetic model rats[38]. Elavarasi *et al*[26] reported that the seed powder of *S. cumini* reduced the blood glucose level.

***Biophytum sensitivum* (OXALIDACEAE) [Fig.29]** Oral administration of the ethanolic extract of *B. sensitivum* whole plant significantly decreased the blood glucose level, serum cholesterol level and increased the total protein level of alloxan induced diabetic rats[39].

***Phyllanthus reticulatus* (PHYLLANTHACEAE) [Fig.30]**
Treatment with petroleum ether and ethanolic extracts of *P. reticulatus* (1000 mg/kg) leaves significantly reduced the blood glucose level of alloxan induced diabetic rats[40].

***Rumex patientia* (POLYGONACEAE) [Fig.31]**
Seed powder supplementation of *R. patientia* showed reduction in serum glucose level, LDL cholesterol level and increased the HDL-cholesterol level of STZ induced diabetic rats[41].

***Posidonia oceanica* (POSIDONIACEAE) [Fig.32]**
The aqueous ethanolic extract of *P. oceanica* leaves (150 and 250 mg/kg bw) significantly decreased the blood glucose level, ALP, GSH, SOD, GPx, CAT, GPT and nitric oxide level to the normal level in alloxan induced diabetic rats[42].

***Bruguiera gymnorrhiza* (RHIZOPHORACEAE) [Fig.33]**
Oral administration of ethanolic extract of *B. gymnorrhiza* root (400 mg/kg b.wt) significantly reduced the blood sugar level, total cholesterol, triglycerides, VLDL and LDL and significantly increased the HDL level of STZ induced diabetic rats[43].

***Aegle marmelos* (RUTACEAE) [Fig.34]**
The methanolic extract of leaf and callus powder of *A. marmelos* significantly decreased the blood sugar level of STZ induced diabetic rabbits[44]. *A. marmelos* would act like insulin in the restoration of blood sugar and body weight to normal levels in rat and was therefore recommended as a potential hypoglycemic agent[45].
Elavarasi *et al*[26] reported that the leaves of *A. marmelos* are used by Tribals of Kolli Hills as an important ingredient in the poly herbal diabetic drug formulations.

***Salvadora oleoides* (SALVADORACEAE) [Fig.35]** Oral administration of ethanolic extract of *S. oleoides* (1 and 2 g/kg bw) aerial parts significantly reduced the blood glucose level and improves lipid profile in euglycemic as well as alloxan induced diabetic rats[46].

***Selaginella tamariscina* (SELAGINELLACEAE) [Fig.36]** The ethanolic extracts of *S. tamariscina* whole plant ameliorated the fasting blood glucose level and improved oral glucose tolerance in STZ induced diabetic rats[47]. It significantly lowered the total cholesterol (TC), triglyceride (TG), LDL-c, free fatty acids (FFA), tumor necrosis factor (TNF), ALT, AST, blood urea nitrogen (BUN) and malondialdehyde (MDA) levels of diabetic rats[47].

***Solanum xanthocarpum* (SOLANACEAE) [Fig.37]**

The methanolic extract of both the leaves (field grown and in vitro raised) of *S. xanthocarpum* at a dose of 200 mg/kg given orally, significantly reduced the blood glucose level, urea, uric acid and creatinine level and increased the serum insulin level in alloxan induced diabetic rats[48].

***Guazuma ulmifolia* (STERCULIACEAE) [Fig.38]** Treatment with *G. ulmifolia* bark induced the glucose uptake in insulin-resistant adipocytes, in addition to its lack of pro-adipogenic or anti-adipogenic effects in murine 3T3-F442A preadipose cell line[49]. It exerted its anti-diabetic effects by stimulating glucose uptake in both insulin sensitive and insulin-resistant adipocytes without inducing adipogenesis[49].

***Vitex negundo* (VERBANACEAE) [Fig.39]**

Idopyranose is a compound isolated from the leaves of *V. negundo* (50mg/kg bw) reduced the blood glucose level, serum urea, and cholesterol level in STZ-induced diabetic rats. It helped to regenerate the damaged pancreas and protected the pancreatic ß cells and hyperglycemic in nature against STZ-induced diabetic rats[50].

Elavarasi *et al*[26] made an Ethnobotanical study in the Kolli hills of Tamil Nadu, through an oral interview to investigate the medicinal plants used in the treatment of diabetes. They reported 16 species of plants belonging to 14 families were commonly used by the tribal peoples to treat diabetes and its related illness. Among the 16 plant species, *Cassia auriculata*, *Hibiscus rosa sinensis, Syzygium cumini* and *Aegle marmelos* were also reported their antidiabetic activity by several authors[23,32,37 & 44].

Diabetes mellitus is a metabolic disorder attributed to diminished production of insulin or resistance to its action. In order to prevent this alarming health problem, the development of research in to new hypoglycaemic and potentially antidiabetic agents is of great interest.

The present review revealed the plant species belonging to Euphorbiaceae (3 species), Moraceae (3 species), Fabaceae (3 species), Annonaceae (2 species), Malvaceae (2 species) and Myrtaceae (2 species) families have most potent hypoglycaemic effects. The most commonly used studied species are *Trigonella foenum graecum, Senna auriculata, Cinnamonum zeylanicum, Hibiscus rosa sinensis, Syzygium cumini* and *Aegle marmelos.*

The methods used in the experiments are diverse. The diabetic model that was most commonly used was the streptozotocin- and alloxan-induced diabetic rats or mouse to obtain diabetic models. Scientific validation of several Indian medicinal plant species has proved the efficacy of the botanicals in reducing the sugar level. From the reports on their potential effectiveness against diabetes, it is assumed that the botanicals have a major role to play in the management of diabetes, which needs further exploration for necessary development of drugs and nutraceuticals from natural resources.

In conclusion, this paper has presented a list of anti-diabetic plants used in the treatment of diabetes mellitus. It showed that these plants have hypoglycemic effects. Many new bioactive drugs isolated from plants having hypoglycaemic effects showed antidiabetic activity equal and sometimes even more potent than known oral hypoglycaemic agents. However, many other active agents obtained from plants have not been well characterized. More investigations must be carried out to evaluate the mechanism of action of medicinal plants with antidiabetic effect. The toxic effect of these plants should also be elucidated.

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Table 1: Medicinal plants used to treat diabetes

S. No.	Botanical name	Common name	Family	Parts used
1.	*Acorus calamus*	Sweet flag	Acoraceae	Rhizome
2.	*Sclerocarrya birrea*	Jelly plum	Anacardiaceae	Stem bark
3.	*Annona squamosa*	Sugar apple	Annonaceae	Roots
4.	*Polyalthia longifolia*	Buddha tree	Annonaceae	Bark
5.	*Ferula asfoetida*	Stinking gum	Apiaceae	Resin
6.	*Catahranthus roseus*	Rose peri winkle	Apocyanaceae	Leaves
7.	*Ichnocarpus frutescens*	Black creeper	Apocyanaceae	Leaves
8.	*Acanthopanax senticosus*	Siberian ginseng	Araliaceae	Stem bark
9.	*Caralluma sinaica*	Caralluma	Asclepiadaceae	Root&aerial parts
10.	*Terminalia bellerica*	Belliric myrobalan	Combretaceae	Fruits
11.	*Costus speciosus*	Crepe ginger	Costaceae	Rhizome
12.	*Vaccinium bracteatum*	Sea bilberry	Ericaceae	Leaves
13.	*Jatropha curcas*	Physic nut	Euphorbiaceae	Leaves
14.	*Secrinega virosa*	White berry bush	Euphorbiaceae	Leaves
15.	*Emblica officinalis*	Indian Gooseberry	Euphorbiaceae	Seed
16.	*Trigonella foenum graecum*	Fenu greek	Fabaceae	Seeds
17.	*Senna auriculata*	Tanner's cassia	Fabaceae	Leaves
18.	*Ougeinia oojeinensis*	Sandan	Fabaceae	Bark
19.	*Cinnamonum zeylanicum*	Cinnamon	Lauraceae	Bark
20.	*Allium cepa*	Onion	Liliaceae	Essential oil of red onion
21.	*Strychonous potatorum*	Clearing nut tree	Loganiaceae	Whole plant
22.	*Adansonnia digitata*	Baobab	Malvaceae	Stem bark
23.	*Hibiscus rosa sinensis*	Chinese hibiscus	Malvaceae	Aerial parts & flower
24.	*Ficus benghalensis*	Indian fig	Moraceae	Stem bark
25.	*Ficus glomerata*	Cluster fig tree	Moraceae	Leaves
26.	*Ficus religiosa*	Sacred tree	Moraceae	Bark
27.	*Psidium guajava*	Guava	Myrtaceae	Unripe fruit peel
28.	*Syzygium cumini*	Java plum	Myrtaceae	Fruits & leaves
29.	*Biophytum sensitivum*	Siker pud	Oxaildaceae	Whole plant
30.	*Phyllanthus reticulates*	Black honey shrub	Phyllanthaceae	Leaves
31.	*Rumex patientia*	Garden patience	Polygonaceae	Seed
32.	*Posidonia oceanic*	Neptune grass	Posidoniaceae	Leaves
33.	*Bruguirea gymnorrhiza*	Black mangrove	Rhizoporaceae	Roots
34.	*Aegle marmelos*	Bael tree	Rutaceae	Leaf&callus
35.	*Salvadora oleoides*	Salvadora	Salvadoraceae	Aerial parts
36.	*Selaginella tamariscina*	Resurrection fern	Selaginellaceae	Whole plant
37.	*Solanum xanthocarpum*	Yellow berried night shade	Solanaceae	Leaves
38.	*Guazuma ulmifolia*	Bay cedar	Sterculiaceae	Bark
39.	*Vitex negundo*	Five leaved chaste tree	Lamiaceae	Leaves

Fig.1: *Acorus calamus*

Fig.2: *Sclerocarya birrea*

Fig.3: *Annona squamosa*

Fig.4: *Polyalthia longifolia*

Fig.5: *Ferula asafoetida*

Fig.6: *Catharanthus roseus*

Fig.7: *Ichnocarpus frutescens*

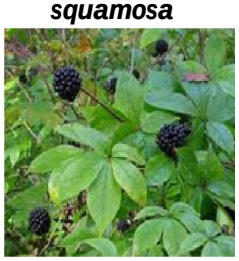

Fig.8: *Acanthopanax senticosus*

Fig.9: *Caralluma sinaica*

Fig.10: *Terminalia bellerica*

Fig.11: *Costus speciosus*

Fig.12: *Vaccinium bracteatum*

Fig.13: *Jatropha curcas*

Fig.14: *Securinega virosa*

Fig.15: *Emblica officinalis*

Fig.16: *Trigonella foenum graecum*

Fig.17: *Senna auriculata*

Fig.18: *Ougeinia oojeinensis*

Fig.19: *Cinnamonum zeylanicum*

Fig.20: *Allium cepa*

Fig.21: *Strychonous potatorum*

Fig.22: *Adansonnia digitata*

Fig.23: *Hibiscus rosa sinensis*

Fig.24: *Ficus benghalensis*

Fig.25: *Ficus glomerata*

Fig.26: *Ficus religiosa*

Fig.27: *Psidium guajava*

Fig.28: *Syzygium cumini*

Fig.29: *Biophytum sensitivum*

Fig.30: *Phyllanthus reticulatus*

Fig.31: *Rumex patientia*

Fig.32: *Posidonia oceanica*

Fig.33: *Bruguiera gymnorrhiza*

Fig.34: *Aegle marmelos*

Fig.35: *Salvadora oleoides*

Fig.36: *Selaginella tamariscina*

Fig.37:*Solanum xanthocarpum*

Fig.38: *Guazuma ulmifolia*

Fig.39: *Vitex negundo*

Plate 1: Medicinal plants with potential of antidiabetic activities

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