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Diabetes and medicinal plants-A review

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Diabetes mellitus (DM), both insulin-dependent DM (IDDM) and non-insulin-dependent DM (NIDDM) is a common and serious metabolic disorder throughout the world. Traditional plant treatments have been used throughout the world for the therapy of diabetes mellitus. Among many medications and other alternative medicines, several herbs have been known to cure and control diabetes; additionally they have no side effects. The present paper is an attempt to list of the plants with anti-diabetic and related beneficial effects originating from different parts of world. 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 literature. There are 136 such plants described in this review which clearly shows the importance of herbal plants in the treatment of diabetes mellitus. The effects of these plants may delay the development of diabetic complications and provide a rich source for antioxidants that are known to prevent/delay different diseased states.

Key words: Diabetes mellitus, Medicinal plants, Hypoglycemic, Antioxidant

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1. INTRODUCTION

Diabetes mellitus is a common and very prevalent disease affecting the citizens of both developed and developing countries. It is estimated that 25% of the world population is affected by this disease. Diabetes mellitus is caused by the abnormality of carbohydrate metabolism which is linked to low blood insulin level or insensitivity of target organs to insulin [1]. Despite considerable progress in the treatment of diabetes by oral hypoglycemic agents, search for newer drugs continues because the existing synthetic drugs have several limitations. The herbal drugs with antidiabetic activity are yet to be commercially formulated as modern medicines, even though they have been acclaimed for their therapeutic properties in the traditional systems of medicine [2]. The plants provide a potential source of hypoglycemic drugs because many plants and plant derived compounds have been used in the treatment of diabetes. Many Indian plants have been investigated for their beneficial use in different types of diabetes and reports occur in numerous scientific journals.

Ayurveda and other traditional medicinal system for the treatment of diabetes describe a number of plants used as herbal drugs. Hence, they play an important role as alternative medicine due to less side effects and low cost. The active principles present in medicinal plants have been reported to possess pancreatic beta cells re-generating, insulin releasing and fighting the problem of insulin resistance [3]. Hyperglycemia is involved in the etiology of development of diabetic complications. Hypoglycemic herbs increase insulin secretion, enhance glucose uptake by adipose or muscle tissues and inhibit glucose absorption from intestine and glucose production from liver [4]. Insulin and oral hypoglycemic agents like sulphonylureas and biguanides are still the major players in the management but there is quest for the development of more effective anti-diabetic agents.

2. MEDICINAL PLANTS WITH ANTIDIABETIC AND RELATED BENEFICIAL PROPERTIES

2.1 Abelmoschus moschatus Medik (Malvaceae)

It is an aromatic medicinal plant, which is native to India. Myricelin, an active principle of *A. moschatus*, improves insulin sensitivity through increased post-receptor insulin signaling mediated by enhancements in IRS-1-associated PI3-kinase and GLUT 4 activity in muscles of obese Zucker rats. Myricetin might be used as a model substance for the development of antidiabetic compounds [5].

2.2 Acacia arabica (Lam) Wild. (Mimosaceae)

It is found all over India. The plant extract acts as an antidiabetic agent by acting as secretagouge to release insulin. It induces hypoglycemia in control rats but not in

alloxanized animals. Powdered seeds of *A. arabica* when administered (2, 3 and 4 g/kg body weight) to normal rabbits, induces hypoglycemic effect by initiating release of insulin from pancreatic beta cells [6].

2.3 Achyranthes aspera L (Amaranthaceae)

It is distributed throughout the tropical world. Oral administration of *A. aspera* powder produces a significant dose-related hypoglycemic effect in normal as well as in diabetic rabbits. The water and methanol extracts also decreases blood glucose levels in normal and alloxan diabetic rabbits. The acute toxicity study in rabbits does not reveal any adverse or side effects of this folk medicine at dosages up to 8 g/kg orally. The plant could act by providing certain necessary elements like calcium, zinc, magnesium, manganese and copper to the beta-cells [7].

2.4 Achyrocline satureioides (Less) DC (Asteraceae)

It is a medicinal plant symbol of Rio Grande do Sul state in Brazil. A new prenylated dibenzofuran, achyrofuran, a compound derived from *A. satureioides* significantly lowered blood glucose levels when administered orally at 20 mg/kg q.d [8]. The aqueous extract of the aerial parts of *A. satureioides* administered before bromobenzene (BB), at the dose of 300mg/kg, inhibited the increase of liver ALT and AST, whereas, the BB-induced liver shows increase of thiobarbituric acid reacting substances (TBARS) content. Also it significantly increases the depleted levels of liver glutathione and bile flow in rats. In addition, at the same dose, a significant increase in the bile flow of rats was found. The results obtained with the aqueous extract of *A. satureioides* support its use in popular medicine as a hepatoprotective and digestive agent, and the effects might be mediated through the antioxidant and choleretic activities [9].

2.5 Acosmium panamense Schott. (Leguminosae)

Oral application of water extracts at doses of 20 and 200 mg/kg and of butanol extracts at doses of 20 and 100 mg/kg significantly lowers the plasma glucose levels in diabetic rats within 3 h in streptozotocin (STZ)-induced diabetic rats [10].

2.6 Aegle marmelose (L) Corr. (Rutaceae)

A species of tree native to India, it is present throughout Southeast Asia as a naturalized species. A significant decrease in liver glycogen of diabetic rats is reversed to almost the normal level by the leaf extract and it also decreases the blood urea and serum cholesterol. A similar effect is seen with insulin treatment and the results indicate that the active principle in *A. marmelos* leaf extract has similar hypoglycemic activity to insulin treatment [11].

2.7 Agrimony eupatoria L. (agrimony) (Rosaceae)

Agrimony, when incorporated into the diet (62.5 g/kg) and drinking water (2.5 g/L) counters the weight loss, polydipsia, hyperphagia and hyperglycemia of STZ-diabetic mice. Aqueous extract (1mg/mL) stimulates insulin secretion from the BRIN-BDII pancreatic B-cell line, 2-deoxy-glucose transport, glucose oxidation and incorporation of glucose into glycogen in mouse abdominal muscle comparable with 0.1μM-insulin. These results demonstrate the presence of antihyperglycemic, insulin-releasing and insulin-like activity in *A. eupatoria* [12].

2.8 Ajuga iva L. Schreberr (Medit) (Lamiaceae)

A species native to Europe, Asia and Africa. Single and repeated oral administration of the water extract of *A. iva* L (AT) at a dose of 10 mg/kg produces a slight and significant decrease in plasma glucose levels in normal rats 6 h after administration and after 3 weeks of treatment. It continuously decreases thereafter and shows rapid normalization, which concludes *A.iva* possess a strong hypoglycemic effect in diabetic rats, and supports its traditional use in diabetes mellitus control [13].

2.9 Allium cepa L. (onion): (Liliaceae)

Allium cepa is known only in cultivation but related wild species occur in Central Asia. Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits. *A. cepa* also known to have antioxidant and hypolipidemic activity. Administration of a sulfur containing amino acid, S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) to alloxan induced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues. It normalizes the activities of liver hexokinase, glucose 6-phosphatase and HMG Co A reductase [14, 15]. When diabetic patients were given single oral dose of 50 g of onion juice, it significantly controlled post-prandial glucose levels [16].

2.10 Allium sativum L. (garlic): (Liliaceae)

It is a perennial herb cultivated throughout India. Oral administration of the garlic extract significantly decreases serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, AST and ALT levels, while increases serum insulin in diabetic rats but not in normal rats when compared with antidiabetic drug glibenclamide. The antidiabetic effect of the extract was more effective than glibenclamide. It is concluded that the plant must be considered as excellent candidate for future studies on diabetes mellitus [17].

2.11 Aloe barbadensis Mill.(Liliaceae)

The species has been widely cultivated throughout the world. Treatment of chronic but no single dose of exudates of *Aloe barbadensis* leaves shows hypoglycemic effect in

alloxanized diabetic rats. Single as well as chronic doses of bitter principle of the same plant also show hypoglycemic effect in diabetic rats. This action is through stimulation of synthesis and/or release of insulin from pancreatic beta cells [18].

2.12 Aloe vera (L) Burm.(Asphodelaceae)

It grows in arid climates and is widely distributed in Africa, India and other arid areas. *Aloe vera* gel at 200 mg/kg 1possessessignificant antidiabetic, cardioprotective activity, reduces the increased TBARS, maintains the Superoxide dismutase and Catalase activity up to the normal level and increases reduced glutathione by four times in diabetic rats [19]. The leaf pulp extract showed hypoglycemic activity on IDDM and NIDDM rats, the effectiveness being enhanced for type II diabetes in comparison with glibenclamide [20].

2.13 Andrographis paniculata Burm. (Acanthaceae)

It is a herbaceous plant native to India, Sri Lanka and widely cultivated in southern Asia. Oral administration of andrographis significantly increases the activity of SOD and Catalase. Also decreases blood glucose levels due to its antioxidant properties [21]. The ethanolic extract of *A. paniculata* possesses antidiabetic property and may be attributed at least in part to increase glucose metabolism. Its hypotriglyceridemic effect is also beneficial in the diabetic state [22].

2.14 Annona squamosa L (Annonaceae)

It is a small well-branched tree or shrub, grows at lower altitudes. Administration of 15 mg/kg/day of isolated juercetin-3-O-glucoside from *Annona squamosa* leaves for 10 consecutive days to the hyperglycemic animals reverse these effects and simultaneously inhibits the activity of hepatic GIucose-6-phosphatase. It further decreases the hepatic and renal lipid peroxidation with a concomitant increase in the activities of antioxidative enzymes, such as Catalase and Superoxide dismutase as well as glutathione content, indicating its safe and antiperoxidative effects [23].

2.15 Artemisia herba-alba Asso (Med).(Asteraceae)

It is a perennial shrub that grows commonly on the steppes of Northern Africa, Arabian Peninsula, Western Asia and Southwestern Europe. Oral administration of 0.39 g/kg body weight of the aqueous extract of the leaves or barks produces a significant reduction in blood glucose level, while the aqueous extract of roots and methanolic extract of the aerial parts of the plant produce almost no reduction in blood glucose level. The extract of the aerial parts of the plant seem to have minimal adverse effect and high LD50 value [24].

2.16 Artemisia dracunculus L. (Asteraceae)

Commonly known as "dragon herb". It is native to a wide area of the Northern Hemisphere from easternmost Europe across central and eastern Asia to India, western North America, and south to northern Mexico. At doses of 50-500rag/kg/day, the hypoglycemic activity of the extract enhances 3-5-fold with the bio-enhancer Labrasol, making it comparable to the activity of the anti-diabetic drug metformin [25]. Tarralin, an ethanolic extract lowers elevated blood glucose levels by 24% relative to control animals. The extract also increases the binding of glucagon-like peptide to its receptor in vitro. These results indicate that tarralin has antihyperglycemic activity and plays a potential role in the management of diabetic status [26].

2.17 Astragalus membranaceus Bunge (Fisch.): (Leguminosae)

It is used in traditional Chinese medicine. The protective mechanism of AGS-IV, a new glycoside of cycloartane-type triterpene isolated from the root of *A. membranaceus* (Fisch.) decreases the blood glucose concentration and HbAlC levels, and increases plasma insulin levels. AGS-IV increases the activity of glutathione peroxidase in nerves, depress the activation of aldose reductase in erythrocytes, and decreases the accumulation of advanced glycation end products in both nerves and erythrocytes. Moreover, elevates Na+, K+-ATPase activity in both the nerves and erythrocytes of diabetic rats. These results indicate that AGS-IV exerts protective effects against the progression of peripheral neuropathy in STZ-induced diabetes in rats through several interrelated mechanisms [27].

2.18 Averrhoa bilimbi L (Oxalidaceae)

The plant is mainly found in Asia and in some other parts of the world. At a dose of 125-mg/kg-body weight, the aqueous fraction (AF), butanol-soluble fraction (BuF) and the reference drug metformin (500 mg/kg body weight), produces significant blood glucose-lowering effect in the diabetic rats when compared to the vehicle (distilled water). Also Hepatic glucose-6-phosphatase activity in AF- and metformin-treated groups is lower, but not in BuF-treated groups, compared to that in vehicle-treated group. These results indicate that AF is more potent than BuF in the amelioration of hyperglycemia in STZ-diabeiic rats and is a potential source for the isolation of new orally active agent(s) for anti-diabetic therapy [28].

2.19 *Azadirachta-indica* A. Juss. (Meliaceae)

Commonly known as Neem. It is a tree native to India, Burma, Bangladesh, Sri Lanka, Malaysia and Pakistan, growing in tropical and semi-tropical regions. A low (0.5g tid) and high (2g tid) doses of powdered part, aqueous extract and alcoholic extract of *A. indica* shows significant hypoglycemic activity in high dose and can be successfully

combined with oral hypoglycemic agents in type-2 diabetic patients whose diabetes is not controlled by these agents [29].

2.20 *Bauhinia candicans* Benth (Leguminosae)

A medicinal plant indigenous to sub-tropical regions of Argentina and southern Brazil. The effect of different fractions of methanolic extract of *B. candicans* leaves (8 mg/kg) shows hypoglycemic activity along with a reduced urinary glucose excretion. Among the fractions, the butanolic fraction (fraction III) exhibits highest activity. Moreover, fraction III reduces plasma glucose level in normal, as well as, glucose loaded rabbits. These results suggest that *B. candicans* increases the peripheral metabolism of glucose [30].

2.21 *Bauhinia forficate* Link. (Caesalpinaceae)

Commonly known as Pata de Vaca, native to Brazil and Peru. Oral administration of kaempferilrin , a major flavonoid compound of the n-butanol fraction from *B. forficata* leaves leads to a significant hypoglycemic effect in normal and in alloxan-induced diabetic rats. In normal rats, kaempferitrin lowers blood glucose only with the higher dose of (200 mg/kg) at 1 h after treatment and also shows antioxidant properties [31]. Administraton of aqueous, ethanolic and hexanic extracts daily for 7 days at doses of 200 and 400 mg/kg, p.o., to the alloxan-diabetic rats shows significant reductions in plasma glucose, triglycerides, total cholesterol and HDL-cholesterol after treatment with the extracts and glibenclamide (standard drug) as compared to the diabetic controls [32].

2.22 *Bidens pilosa* L (Asteraceae)

It is known as Spanish Needle. The butanol fraction *of B. pilosa* inhibits the differentiation of naive helper T (ThO) cells into Thl cells but enhances their transition into type II helper T (Th2) cells, thus can prevent diabetes pausibly via suppressing the differentiation of ThO cells into Thl cells and promoting that of ThO cells into Th2 cells, thus preventing autoimmune diabetes in non-obese diabetic mice [33].

2.23 *Biophytum sensitivum* (L) DC. (Oxalidaceae)

The annual perennial herbaceous plant is a traditional medicine in Nepal. Initial dose-response studies shows a dose of 200 mg/kg body weight is optimum for hypoglycemia. In 16-h fasted non-diabetic rabbits, a single administration brings about a 16.1% fall in fasting plasma glucose at the end of 1 and 2 h, and the hypoglycemic effect persists at the end of 6 h (13.8% fall). Serum insulin levels shows a significant rise in the treated animals, which suggests a pancreatic mode of action (i.e. insulinotropic effect), suggesting that the hypoglycemic response of *B. sensitivum* may be mediated through stimulating the synthesis/release of insulin from the beta cells of Langerhans [34].

2.24 *Bixa orellana* L. (Bixaceae)

It is a shrub or small tree from the tropical region of the Americas. This annatto extract decreases blood glucose levels in fasting normoglycaemic and streptozotocin-induced diabetic dogs. In normal dogs, it suppresses the postprandial rise in blood glucose after an oral glucose load and also causes an increase in insulin-to-glucose ratio in normal dogs. Increased insulin levels were not due to increased insulin synthesis as after 1h residence time and half-hour postprandial, decreases C-peptide levels. It is concluded that *B. orellana* (annatto) lowers blood glucose by stimulating peripheral utilization of glucose, and it is possible that this glucose-lowering extract might be of pharmacological importance [35].

2.25 *Brassica nigra* (L) Koch (Brassicaceae)

It is an annual weedy plant cultivated for its seeds and is native to the southern Mediterranean region of Europe. Administration of 200 mg/kg body weight of aqueous extract to diabetic animals daily once for one month brings down fasting serum glucose (FSG) levels while in the untreated group FSG remains at a higher value. In the treated animals the increase in glycosylated hemoglobin (HbAlc) and serum lipids is much less when compared with the levels in untreated diabetic controls [36].

2.26 *Bryonia alba* L.(Cucurbitaceae)

It is a flowering plant native to western Eurasia and adjacent regions, such as North Africa, the Canary Islands and South Asia. Administration of trihydroxyoctadecadienoic acids obtained from the roots of the native Armenian plant *B. alba* L. (0.05 mg/kg/day for 15 days. Lin.) restores the disordered lipid metabolism of alloxan-diabetic rats. Metabolic changes induced in diabetes significantly restores towards their normal values with the exception of diminished triglyceride content of muscle which does not restores. Thus, they can influence the profile of the formation of stable prostaglandins by actions downstream of prostaglandin endoperoxides [37].

2.27 *Bumelia sartorum* Mart. *(Sapotaceae)*

It has been mentioned in Brazilian folklore for its reputed use in the treatment of diabetes mellitus and inflammatory disorders. Bassic acid, an unsaturated triterpene acid isolated from ethanol extract *of B. sartorum* root bark, elicits significant hypoglycemic activity and increases plasma insulin levels significantly in alloxan-diabetic rats and alters the pattern of glucose tolerance in these animals [38]. Besides hypoglycemic activity, the extract also elicits significant anti-

inflammatory activity, but shows no significant effects on blood pressure, respiration or on the various isolated tissue preparations [39].

2.28 *Caesalpinia bonducella* (L) Roxb. (Caesalpinaceae)

The oral administration of the extracts (300 mg/kg) produces significant antihyperglycemic action as well as lowers the BUN levels significantly. The action of the extracts on diabetes induced hyperlipidemia significantly lowers the elevated cholesterol as well as LDL level. The antihyperglycemic action of the extracts may be due to the blocking of glucose absorption. The drug has the potential to act as antidiabetic as well as antihyperlipidemic [40].

2.29 *Cajanus cajan* (L) Millsp. (Papilionaceae)

Single doses of unroasted seeds (60% and 80%) on administration to normal as well as alloxanized mice shows significant reduction in the serum glucose levels after 1-2 hr and a significant rise at 3 hr. In case of roasted seeds, on other hand serum glucose levels increases during 3 hr experimental period. It is therefore concluded that roasting of seeds at high temperature for half an hour period results in the total loss of hypoglycemic principle but not the hyperglycemic principle present in the seeds [41].

2.30 *Carum carvi* L.(CC) (Apiaceae) / *Capparis spinosa* L. (CS) (Capparidaceae)

(CC) is a biennial plant native to western Asia, Europe and Northern Africa and (CS) is native in Israel and eastern part of Mediterranean. After a single dose or 14 daily doses, oral administration of the aqueous CC and CS extracts (20 mg/kg) produces a significant decrease on blood glucose levels in STZ diabetic rats, and brings down to nearly normal after 2 weeks. There is no high significant change on blood glucose levels or basal plasma insulin concentrations in normal rats after both acute and chronic treatments with CS and CC [42].

2.31 *Casearia esculenta* Roxb. (Flacourtiaceae)

Casearia esculenta root (Roxb.) is widely used in traditional system of medicine to treat diabetes in India. Oral administration of aqueous extract of root (300 mg/kg body weight) for 45 days results in a significant reduction in blood glucose and in the activities of glucose-6-phosphatase and fructose-1,6-bisphosphatase and an increase in the activity of liver hexokinase. However, in the case of 200 mg/kg body weight of extract, it shows less activity. The study clearly shows that the root extract of *C. esculenta* possesses potent antihyperglycemic activity but weaker than that of glibenclamide [43].

2.32 *Cassia auriculata* L.(Caesalpinaceae)

It occurs in the dry regions of India and Sri Lanka. Oral administration of CLEt- to mildly diabetic (MD) and severely diabetic (SD) rats at a dose of 400 mg/kg once a day for 15 days shows significant reduction in fasting blood glucose, also enhances the activity of hepatic hexokinase, phosphofructokinase, suppresses glucose-6-phosphatase and fructose-l,6-bisphosphatase in both MD and SD rats. Histopathological examination of pancreatic sections reveals increased number of islets and beta-cells in CLEt-treated MD as well as SD rats [44].

2.33 *Catharanthus roseus* (L)G.Don.(Apocynaceae)

Oral administration at dose-dependent of 0.5, 0.75 and 1.0 mL/kg body weight reduced the blood glucose of both normal and diabetic rabbits comparable with that of the standard drug, glibenclamide. The results indicate a prolonged action in reduction of blood glucose by *C. roseus* and the mode of action of the active compound(s) is probably mediated through enhance secretion of insulin from the beta-cells of Langerhans or through extra pancreatic mechanism [45].

2.34 *Chamaemelum nobile* (L) All. (Asteraceae)

It is a low perennial plant found in dry fields and around gardens in Europe, North America, and Argentina. Single oral administration at a dose of 20mg/kg body weight of *C. nobile* aqueous extract reduces blood glucose levels after 6h in normal rats and in STZ diabetic rats. After 15 days of treatment, Basal plasma insulin concentrations remain unchanged [46].

2.35 *Cichorium intybus* L.(Asteraceae)

A bushy perennial herbaceous plant, which lives as a wild plant on roadsides in its native Europe, and in North America and Australia. A dose of 125 mg of plant extract/kg body weight exhibits the most potent hypoglycemic effect. Moreover, daily administration of *Cichorium intybus* (C1E) (125 mg/kg) for 14 days to diabetic rats attenuates serum glucose by 20%, triglycerides by 91% and total cholesterol by 16%. In addition, hepatic glucose-6-phosphatase activity (Glc-6-Pase) markedly reduces by CIE [47].

2.36 *Clausena anisata* (Willd) Benth. (Rutaceae)

At a dose of 800 mg/kg p.o., *Clausena anisata* (Wild) Hook (CAME) reduces the mean basal blood glucose concentrations of fasted normal and fasted diabetic rats by 57.52 and 51.30%, respectively [48].

2.37 *Coccinia indica* Wt & Arn. (Cucurbitaceae)

An indigenous plant used in Ayurvedic medicine in India. Dried extracts of *C. indica* (500 mg/kg body weight) administered to diabetic patients for 6 weeks restores the activities of enzyme lipoprotein lipase (LPL), glucose-6-phosphatase and lactate dehydrogenase, which rises in untreated diabetics [49].

2.38 *Coriandrum sativum* L (Apiaceae)

An annual herb native to southern Europe and North Africa to southwestern Asia. Coriander seed extract (200 mg/kg) significantly increases the activity of the beta cells in comparison with the diabetic control rats and decreases serum glucose in streptozotocin-induced diabetic rats and releases insulin from the beta cells of the pancreas [50]. The extract shows antihyperglycemic, insulin-releasing and insulin-like activity [51].

2.39 *Cuminum cyminum* L (Apiaceae)

A flowering plant native from the East Mediterranean to East India. The seeds extract of *C. cyminum* (CC) causes a reduction in blood glucose, glycosylated hemoglobin, creatinine, blood urea nitrogen and improved serum insulin and glycogen (liver and skeletal muscle) content. It shows significant reduction in renal oxidative stress and AGE when compared to diabetic control and glibenclamide. CC and glibenclamide improved antioxidant status in kidney and pancreas of diabetic rats [52].

2.40 *Cuminum nigrum* L (Apiaceae)

It grows mainly in Central Asia and India. Oral administration of the flavonoid contents of the plant causes hypoglycemic effect at a dose range of 0.5 to 1.5 g/kg, both in normal and alloxan-diabetic rabbits [53]. Curcumin promotes AMPK activation and glucose uptake with increased insulin sensitivity in muscle cells as a potential anti-diabetic therapeutic agent [54].

2.41 *Cyamopsis tetragonoloba* (L) Taubert. (Papilionaceae)

The species are distributed across Africa, Asia and the Pacific. The aqueous extract of beans at 250 mg/kg body wt. significantly lowers blood glucose levels in alloxan-induced diabetic rats within 3 h of administration. Continuation for 10 days produces statistically significant reduction in the blood glucose levels while shows marginal activity is in normal and glucose-loaded rats [55].

2.42 Dioscorea dumetorum (Kunth) Pax.(Dioscoreaceae)

It is mainly found in West and Central Africa. At a dose of 20 mg/kg, the fasting blood sugar in normoglycemic rabbits reduces from 112 mg/100 mL to 55 mg/100 mL after 4h. In alloxan diabetic rabbits, the blood sugar lowers from 520 mg/100 mL to 286 mg/100 mL at the same time interval. The aqueous fraction of the methanol extract produces comparable effects at 100 mg/kg. Whereas, chloroform fraction rises the fasting blood sugar of normal rabbits to 196 mg/100 mL after 6h. The hypoglycemic effects are compared to those of tolbutamide [56].

2.43 Eclipta alba (L) Hassk. (Asteraceae)

It is widely distributed throughout India, China, Thailand, and Brazil. Oral administration of leaf suspension of *E. alba* (2 and 4 g/kg body weight) for 60 days results in significant reduction in blood glucose, glycosylated hemoglobin HbA(l)c. The extract decreases the activities of glucose-6-phosphatase and fructose-1,6-bisphosphatase, and increase the activity of liver hexokinase. Thus, oral administration of *E. alba* possess potent antihyperglycemic activity [57].

2.44 Emblica officinalis Gaertn. (Euphorbiaceae)

Different solvent extracts of *E. officinalis* acts as α-amylase and α-glucosidase inhibitor. Significant antiglycation activity also confirms the therapeutic potential of these extracts against diabetes. Methanol extracts significantly inhibits the oxidation of LDL under in vitro conditions [58].

2.45 Enicostema littorale blume (Gentianaceae)

Dried plant equivalent extract of 1.5 g/100 g body weight causes significant decrease in glycosylated haemoglobin, liver glucose-6-phosphatase activity and increase in serum insulin levels of the diabetic rats. There is no toxicity parameter of extract treated diabetic rats as compared to diabetic control rats. The above results suggest that *E. littorale* is a potent antidiabetic agent without any toxic effect [59].

2.46 Ficus bengalensis L. (Moraceae)

A reputed plant commonly known as "banyan tree" in Ayurvedic literature. At a dose of 100 mg/kg for one month, there is significant decrease in blood and urine sugar, certain lipid components in serum, tissues and glucose-6-phosphatase activity in liver, but increase in body weight, the activities of hexokinase and HMG-COA reductase in tissues as compared to diabetic control. The mechanism of action of the principle may be related to its protective/inhibitory action against the insulin degradative processes [60].

2.47 Fraxinus excelsior L. (Oleaceae)

The aqueous extract at a dose of 10 mg/kg/h produces a significant decrease in blood glucose levels in normal rats

and even more in diabetic rats. A potent increase of glycosuria concludes inhibition of renal glucose reabsorption. This renal effect might be at least one mechanism explaining the hypoglycemic activity of this plant in normal and diabetic rats [61].

2.48 Garcinia kola Heckel (W & C Afr)((Clusiaceae)

It is found in Africa mainly in subtropical or tropical moist lowland forests. The extract decreases the activity of microsomal glucose-6-phosphatase and lipid peroxidation (LPO) products [62]. At a dose of 100 mg/kg, the fasting blood sugar in normoglycemic rabbits reduces from 115 mg/100 mL to 65 mg/100 mL after 4 h. In alloxan diabetic rabbits, the blood sugar lowers from 506 mg/100 mL to 285 mg/100 mL at 12 h. Kolaviron, a mixture of C-3/C-8 linked biflavonoids obtained from Garcinia kola produces significant hypoglycemic effects [63].

2.49 Gongronema latifolium Endl. (Asclepiadaceae)

The origin of the plant is traced to Nigeria in West Africa. The aqueous extract of *G. latifolium* is able to significantly increase the activities of hepatic hexokinase and decrease the activities of glucokinase, but does not produce any change in the hepatic glycogen and both hepatic and blood glucose content of diabetic rats [64]. The effects of oral administration of aqueous and ethanolic leaf extracts increase the activity of superoxide dismutase and the level of reduced glutathione. The aqueous extract further increases the activity of glutathione reductase while the ethanolic extract causes a significant increase in the activity of glutathione peroxidase and glucose-6-phosphate dehydrogenase and a significant decrease in lipid peroxidation. These results suggest that the extracts from *G. latifolium* leaves could exert their antidiabetic activities through their antioxidant properties [65].

2.50 Helicteres isora L., As.(Sterculiaceae)

Distributed widely in forests throughout India. The hot water extract of fruit of *H. isora* exhibits significant antioxidant activity and moderate antidiabetic activity [66], at 200 mg/mL dose it shows glucose uptake activity and found to be active comparable with insulin and metformin [67]. The ethanolic extract has insulin-sensitizing and hypolipidemic activity and has the potential for use in the treatment of type-2 diabetes [68].

2.51 Hypoxis hemerocallidea conn Corm (African potato) (Hypoxidaceae)

At a dose of 800 mg/kg, the plant extract causes 30.20% and 48.54% reductions in the blood glucose concentrations of fasted normal and STZ-treated diabetic rats respectively. Thus, possesses hypoglycemic activity [69].

2.52 Inula racemosa Hook.f.(Asteraceae)

It grows in the temperate and alpine western Himalayas. The petroleum ether extract of roots lowers plasma insulin and glucose levels within 75 min of oral administration to albino rats and it significantly counteracts adrenaline-induced hyperglycemia in rats. The extract further shows negative inotropic and negative chronotropic effects on frog heart. All these findings indicate that one of the constituents of *I. racemosa* may have adrenergic beta-blocking activity [70].

2.53 Lagerstroemia speciosa (L) Pers.(Lythraceae)

L. speciosa standardized to 1% corosolic acid (Glucosol) at daily dosages of 32 and 48mg for 2 weeks shows significant reduction in the blood glucose levels. Glucosol in a soft gel capsule formulation shows a 30% decrease in blood glucose levels compared to 20% drop with dry-powder filled hard gelatin capsule formulation, suggesting that the soft gel formulation has a better bioavailability than a dry-powder formulation [71].

2.54 Lepidium sativum L. (Brassicaceae)

It is a fast-growing, edible herb. The aqueous LS extract at a dose of 10 mg/kg/h causes a potent inhibition of renal glucose reabsorption which in turn reduces blood sugar. This renal effect is at least one mechanism explaining the hypoglycemic activity of this plant in normal and diabetic rats [72].

2.55 Mangifera indica L.(Anacardiaceae)

The aqueous extract produces reduction of blood glucose level in normoglycemic and glucose-induced hyperglycemia, but does not have any effect on streptozotocin-induced diabetic mice under the same conditions when compared with that of an oral dose of chlorpropamide. The result indicates that the aqueous extract of the leaves of *M. indica* possess hypoglycemic activity [73].

2.56 Momordica charantia L. (Cucurbitaceae)

M. charantia (bitter melon) is commonly known as vegetable insulin. An oral sucrose tolerance test reveals that administration of aqueous extract (AE), methanol fraction (MF) or methanol insoluble fraction (MIF) each significantly suppresses plasma glucose levels at 30 min as compared with control. In addition, the plasma insulin level at 30 min also lowers after MF administration than the control in the oral sucrose tolerance test, these results demonstrates that bitter melon suppresses postprandial hyperglycemia by inhibition of α-glucosidase activity [74].

2.57 Morinda lucida Benth.(Rubiaceae)

The extract demonstrates a significant and dose-dependent hypoglycemic activity within 4 h after oral administration in normal rats. In hyperglycemic rats, the extract produces a significant anti-diabetic effect from day 3 after oral administration, with 400 mg/kg extract-treated animals. These results suggest that the leaves of *M. lucida* have a strong glucose lowering property when administered to streptozotocin-treated rats [75].

2.58 Myrcia uniflora Barb., Rods.(Myricaceae)

A plant is widely used in northern Brazil for treatment of diabetes. The aqueous extracts of Myrcia has a beneficial effect on the diabetic state, mainly by improving metabolic parameters of glucose homeostasis which reduces hyperglycemia, polyphagia, polydipsia, urine volume and the urinary excretion of glucose and urea. Also, Myrcia administration for 3 weeks has no effect on the weight of epididymal and retroperitoneal adipose tissue, or on the concentrations of pancreatic and serum insulin [76].

2.59 Nigella sativa L (Ranunculaceae)

Oral administration of ethanol extract of *N. sativa* seeds (300 mg/kg body weight/day) to streptozotocin induced diabetic rats for 30 days significantly reduces the elevated levels of blood glucose, lipids, plasma insulin and improved altered levels of lipid peroxidation products (TBARS and hydroperoxides) and antioxidant enzymes like catalase, superoxide dismutase, reduced glutathione and glutathione peroxidase in liver and kidney. The results confirm the antidiabetic activity of *N. sativa* seeds extract [77].

2.60 Ocimum sanctum L. (Lamiaceae)

It is commonly known as Tulsi. Since ancient times, this plant is known for its medicinal properties. The aqueous extract of leaves shows significant reduction in blood sugar level in both normal and alloxan induced diabetic rats [78]. Significant reduction in fasting blood glucose, uronic acid, total amino acid, total cholesterol, triglyceride and total lipid indicate the hypoglycemic and hypolipidemic effects of tulsi in diabetic rats [79]. Oral administration of plant extract (200 mg/kg) for 30 days leads to decrease in the plasma glucose level. Renal glycogen content increases 10 fold while skeletal muscle and hepatic glycogen levels decreases by 68 and 75% respectively in diabetic rats as compared to control [80]. This plant also shows antioxidant, antibacterial, antifungal, antiviral, antiasthemitic, antistress, antitumor, gastric antiulcer activity, antimutagenic and immunostimulant activities.

2.61 Origanum vulgare L. (Lamiaceae)

It is native to warm-temperate western and southwestern Eurasia and the Mediterranean region. Oral administration of the aqueous extract (20 mg/kg) produces significant decrease on blood glucose levels in STZ diabetic rats. However, the blood glucose levels gets normalised from the fourth day after daily repeated oral administration of aqueous OV extract (20 mg/kg). This concludes that an aqueous extract of *O. Vulgare* exhibits anti-hyperglycemic activity in STZ rats without affecting basal plasma insulin concentrations [81].

2.62 Otholobium pubescens L. (Papilionaceae)

The known compound bakuchiol, isolated from an extract of *O. pubescens* reduces blood glucose levels in a dose-dependent fashion in db/db mice and displays no hypoglycemic effect in lean mice at 250 mg/kg q.d. An oral dose of bakuchiol at 150 mg/kg q.d. in the fat-fed, streptozotocin (STZ)-treated rat, a new rodent model for type 2 diabetes, significantly lowers plasma glucose and triglyceride levels [82].

2.63 Paeonia lactiflora Pall.(Paeoniaceae)

Paeoniflorin and 8-debenzoylpaeoniflorin isolated from the dried root of *P. lactiflora* pall produces a significant blood sugar lowering effect in streptozotocin-treated rats and has a maximum effect at 25 min after treatment and this hypoglycemic action is also observed in normoglycemic rats only at 1 mg/kg. Plasma insulin does not change in paeoniflorin-treated normoglycemic rats indicating an insulin-independent action [83].

2.64 Panax ginseng C. Meyer. (Araliaceae)

The roots are taken orally in the treatment of type II diabetes. Extracts of ginseng species shows antihyperglycemic activity associated with increased peroxisome proliferator-activated receptor gamma expression and adenosine monophosphate-activated protein kinase phosphorylation in liver and muscle [84]. Oral administration of *P. ginseng* root improves insulin sensitivity and may be used as an adjuvant therapy for treating diabetic patients with insulin resistance [85].

2.65 Phyllanthus amarus Schum & Thonn. (Euphorbiaceae)

A traditional Ayurveda herb used in southern India. Methanolic extract of P. *amarus* has potential anti-oxidant activity as it could inhibit lipid peroxidation, and scavenge hydroxyl and superoxide radicals in vitro. This extract also reduces the blood sugar in alloxanized diabetic rats [86].

2.66 Psidium guajava L. (Myrtaceae)

An indigenous medicinal plant used to control diabetes in Indian System of Medicine. Ethanol stem bark extract exhibits statistically significant hypoglycemic activity in

alloxan-induced hyperglycemic rats but devoid of hypoglycemic effect in normal and glucose loaded rats (OGTT) [87]. Aqueous extract shows hypolipidaemic activity in addition to its hypoglycemic and antidiabetic activity [88].

2.67 Pterocarpus marsupium Roxb.(Papilionaceae)

It is widely used in 'Ayurveda' as 'Rasayana' for management of various metabolic disorders. An aqueous extract of *P. marsupium* wood, at an oral dose of 250 mg/kg, shows statistically significant hypoglycemic activity [89]. Marsupin, pterosupin and Iiquiritigenin obtained from this plant show antihyperlipidemic activity [90]. (-)Epicatechin, its active principle, has been found to be insulinogenic, enhancing insulin release and conversion of proinsulin to insulin in vitro. Like insulin, (-)epicatechin stimulates oxygen uptake in fat cells and tissue slices of various organs, increases glycogen content of rat diaphragm in a dose-dependent manner [91].

2.68 Retama raetam (RR) (Forssk) Webb. (Papilionaceae)

The aqueous extract of RR at a dose of 20mg/kg significantly reduces the blood glucose in normal rats 6h after a single oral administration and two weeks after repeated oral administration. This hypoglycemic effect is more pronounced in streptozotocin (STZ) diabetic rats. The aqueous extract of RR has no effect on basal plasma insulin levels [92]. Also causes a potent inhibition of renal glucose reabsorption [93]. These findings suggest that the aqueous extract of RR possess significant hypoglycemic effect in both normal and STZ diabetic rats.

2.69 Salacia reticulate W. (Celastraceae)

Supplementation of 0.01 % solution of the extract as drinking water prevents the elevation of the plasma glucose level and intestinal α-glucosidase activities in type 1 diabetic mice. This treatment also prevents the elevation of the plasma, pancreatic, and kidney lipid peroxide levels, lowering of the plasma insulin level, and elevation of the kidney aldose reductase activities in diabetic mice. These results suggest that the water extract of the leaves of *S. reticulata* could be a beneficial food material for the prevention of diabetes and obesity because of its multiple effects [94].

2.70 Spergularia purpurea (SP) (Pers) G, Donf.(Caryophyllaceae)

The aqueous extract at a dose of 10 mg/kg produces a significant decrease in blood glucose levels in normal rats, and even more in diabetic rats. This hypoglycemic effect might be due to an extra-pancreatic action of the aqueous extract of SP, since the basal plasma insulin concentrations unchange after SP treatment. This concludes that aqueous extract perfusion of SP inhibits endogenous glucose production in mice [95].

2.71 Suaeda fruticosa (SF) Euras (Chenopodiaceae)

The aqueous extract at a dose of 192 mg/kg produces a significant decrease in blood glucose levels in normal rats, and even more in diabetic rats. This hypoglycemic effect might be due to an extra-pancreatic action of the aqueous extract of SF, since that the levels of plasma insulin unchange between the values before and after treatment. The effect of the aqueous extract on the plasma cholesterol is significant in both normal and diabetic rats but, there is no significant effect of SF on plasma triglycerides in both groups [96].

2.72 Syzigium cumini (L) Skeels.(Myrtaceae)

Commonly known as 'Jamun', is widely used in Indian folk medicine for the treatment of diabetes mellitus. Oral administration of 2.5 and 5.0 g/kg body weight of the aqueous extract of the seed for 6 weeks results in significant reduction in blood glucose and an increase in total haemoglobin, but in the case of 7.5 g/kg body weight the effect is not significant. The aqueous extract also decreases free radical formation which clearly shows the antioxidant property. Thus the study shows that Jamun seed extract (JSEt) has hypoglycemic action [97].

2.73 Tamarindus indica L. (Caesalpinaceae)

Aqueous extract of seed of *T. indica* when given to mild diabetic (MD) and severe diabetic (SD) rats at the dose of 80 mg and 120 mg/0.5 mL distilled water/100 g body weight/d respectively for 14 days, the extract shows attenuation of hyperglycemia and hyperlipidemia in streptozotocin-induced diabetic rats [98].

2.74 Telfaria occidentalis Hook. (Cucurbitaceae)

It is a tropical vine grown in West Africa as a leaf vegetable and for its edible seeds. The aqueous extract given orally in 1 g/kg to the mice 60 minutes before glucose administration reduces the blood glucose level from day two when compared with that of chlorpropamide (200 mg/kg) under the same conditions. The results of this study indicates that the aqueous extract of the leaves of *T. occidentalis* possess hypoglycemic activity [99].

2.75 Tinospora cordifolia Miers. (Menispermaceae)

Commonly known as Guduchi, an herbaceous vine indigenous to the tropical areas of India, Myanmar and Sri Lanka. Oral administration of an aqueous *T. cordifolia* root extract to alloxan diabetic rats causes a significant reduction in blood glucose and brain lipids. Though the aqueous extract

Table 1
Medicinal plants with antidiabetic and their reported effect on experimental models

Botanical Name	Family	Antidiabetic and other beneficial effects	References
Achiliea santolina L.	Asteraceae	Hypoglycemic, antioxidant	[103]
Artemisia patterns	Asteraceae	Hypoglycemic, increases peripheral glucose utilization	[104]
Areca catechu L.	Arecaceae	Hypoglycemic	[105]
Beta vulgaris L.	Chenopodiaceae	Increases glucose tolerance in OGTT	[106]
Boerhaavia diffusa L.	Nyctaginaceae	Decreases blood glucose level and increases plasma insulin levels, antioxidant	[107]
Bombax ceiba L.	Malvaceae	Hypoglycemic	[108]
Butea manosperma (Lam)	Caesalpinaceae	Anti-hyperglycemic	[109]
Carum carvi L.	Apiaceae	Potent anti-hyperglycemic	[110]
Capparis spinosa L.	Capparidaceae		
Cogniauxia podoleana Baillon Bail Ion	Cucurbitaceae	Hypoglycemic and anti-hyperglycemic	[111]
Commelina communis L.	Conimelinaceae	Anti-hyperglycemic, management of non-insulin-dependent diabetes.	[112]
Croton cajucara Benth	Euphorbiaceae	Anti-hyperglycemic	[113,114]
Curcuma longa L.	Zingiberaceae	Hypoglycemic, plays a role in PPAR-gamma activation	[115]
Cynodon dactylon Pers	Poaceae	Anti-hyperglycemic	[116]
Enicostemma littorale Blume	Gentianaceae	Decreases plasma glucose level, glycosylated haemoglobin and glucose-6-phosphatase activity in liver	[117]
Eriobotrya japonica Lindl.	Rosaceae	Hypoglycemic	[118]
Gentiana olivieri L.	Gentianaceae	Hypoglycemic, anti-hyperlipidemic	[119]
Ginkgo biloba L.	Ginkgoaceae	Hypoglycemic, increases pancreatic beta-cell in NIDDM	[120,121]
Globularia alypum L.	Globulariaceae	Hypoglycemic, increases plasma insulin levels	[122]
Glycyrrhiza uralensis Fish.	Papilionaceae	PPAR-gamma ligand-binding activity, decreases the blood glucose levels	[123]
Gymnema nwntanum Hook	Asclepiadaceae	Anti-peroxidative, antioxidant, may prevent the cholinergic neural and retinal complications of hyperglycemia in diabetes	[124]
Gymnema sylvestre R. Br.	Asclepiadaceae	Hypoglycemic. Hypolipidemic	[125]
Hintonia standleyana	Rubiaceae	Anti-hyperglycemic	[126]
Ibervillea sonorae S.	Cucurbitaceae	Acute and chronic hypoglycemic	[127]
Ipomoea aquatic Forsk.	Convolvulaceae	Decreases serum glucose concentration by 29.4% in Type II diabetic patients. hypoglycemic	[128]
Kalopanax pictus Thumb.	Araliaceae	Anti-diabetic activity, hypocholesterolmic and hypolipidemic	[129]
Lagerstroemia speciosa L.	Lythraceae	Insulin-like actions, glucose uptake, anti-adipogenesis	[130,131]
Medicago saliva L.	Fabaceae	Anti-hyperglycemic, insulin-releasing and insulin-like activity	[132]
Morus alba L.	Moraceae	Protects pancreatic beta cells from degeneration anddiminishes lipid peroxidation	[133]
Morus indica. L.	Moraceae	Hypoglycemic	[134,135]
Morus inignis L.	Moraceae	Hypoglycemic	[136]
Murraya koenigii L.	Rutaceae	Hypoglycemic, increases glycogenesis,decreases gluconeogenesis and glycogenolysis	[137]
Nelumbo nucifera L.	Neluntbonaceae	Improves glucose tolerance and potentiates the action of exogenouslyinjected insulin	[138]
Nigella saliva Gaertn.	Ranunculaceae	Decreases oxidative stress and preserves pancreatic beta-cell integrity.	[139]
Ocimum gratissinuim L. Var.	Lamiaceae	Hypoglycemic	[140]
Pandanus odorus Ridl.	Pandanaceae	Hypoglycemic, increases serum insulin levels and liver glycogen	[141]
Parmentieru edulis A.DC	Bignoniaceae	Hypoglycemic	[142]
Phyllanthus sellowianus Mull.Arg.	Euphorbiaceae	Hypoglycemic	[143]
Psacalium decompositum (Gray) H.	Asteraceae	Hypoglycemic	[144]
Psacalium peltatum (Kunth)	Asteraceae	Anti-hyperglycemic	[145]
Punica granatum L.	Punicaceae	Improves postprandial hyperglycemia in type 2 diabetes and obesity by inhibiting intestinal alpha-glucosidase activity	[146]
Solaria oblonga	Celastraceae	Hypoglycemic and possess anti-oxidant activity	[147]
Sambucus nigra L.	Adoxaceae	Insulin-releasing and insulin-like activity	[148]
Sanguis draxonis	Apocynaceae	Increase insulin sensitivity and improve the development of insulin resistance in rats	[149]
Sclerocarya birea (A.Rich)	Anacardiaceae	Hypoglycemic	[150]
Scoparia dulcis L.	Scrophariaceae	Hypoglycemic, antihyperlipidemic, antidiabetic	[151,152]
Swertia chirayita (Roxb)	Gentianaceae	Stimulates insulin release from islets	[153]
Syzygium alternifolium (Wt) Walp.	Myrtaceae	Hypoglycemic, antihyperglycemic and antihyperlipidemic	[154.155]
Terminalia bellirica (Gaertn)	*Combretaceae*	Stimulates insulin secretion. Enhances insulin action andinhibits both protein glycation and starch digestion	[156]
Terminalia chebula Retz.	Combretaceae	Dose-dependent glucose lowering effect, antidiabetic and renoprotective,decreases hepatic and skeletal muscle glycogen content, increases insulin release from the pancreatic islets	[157-159]
Teucriumpolium	Lamiaceae	Increases insulin release, antioxidant and hypoglycemic	[160]
Tinospora cordifolia Miers..	Menispermaceae	Hypoglycemic	[161]
Tinospora crispa (L) Hook.	Menispermaceae	Anti-hyperglycemic, stimulates insulin release from islets	[162]
Urtica dioica L.	Urticaceae	Anti-hyperglycemic	[163]
Urtica pilulifera L.	Urticaceae	Hypoglycemic	[164]
Vinca rosea L.	Apocynaceae	Anti-hyperglycemic	[165]
Withania soimifera (L) Dunal	Solanaceae	Hypoglycemic, antioxidant, diuretic and hypocholesterolemic	[166,167]
Withania coagulans Dunal	Solanaceae	Anti-hyperglycemic, anti-hyperlipidemic and hypoglycemic	[168,169]
Zizyphus sativa Gaertn	Rhamnaceae	Hypoglycemic	[170]
Zizyphus spina-christi L.	Rhamnaceae	Insulinotropic, hypoglycemic anddepressant effect on the central nervous system	[171]
Zygophyllum gaetulum Emb	Zygophyllaceae	Hypoglycemic, increases plasma insulin levels	[172]

Table 2
Synthetic drugs and their side effects

Agent	Mechanism	Site of action	Advantages	Side effects
Sulphonylureas	Stimulating insulin production by inhibiting the K-ATP channel	Pancreatic beta cells	Effective and inexpensive	Hypoglycemia and weight gain.
Metformin	Decreases insulin resistance	Liver	Weight loss Does not cause hypoglycemia	Nausea and diarrhea. Hypoglycemia occurs when combined with sulfonylurea or insulin.
Thiazolidinediones	Reduce insulin resistance by activating PPAR-γ	GI tract	Low risk	Increased liver enzymes, weight gain,edema, mild anemia.
α-glucosidase inhibitors	Reduces intestinal glucose absorption	Fat, muscle	Decreases postprandial plasma triglyceride levels	Diarrhea, abdominal pain, flatulence; Serum levels of transaminases increases at doses.

at a dose of 400 mg/kg could elicit significant antihyperglycemic effect in different animal models, its effect is equivalent to only one unit/kg of insulin [100].

2.76 Trigonella foenum graecum L. (fenugreek) (Papilionaceae)

Used both as an herb (the leaves) and as a spice (the seed) and cultivated worldwide as a semi-arid crop. Oral administration of 2 and 8 g/kg of plant extract produces dose dependent decrease in the blood glucose levels in both normal as well as diabetic rats [101]. Administration of fenugreek seeds improves glucose metabolism and normalizes creatinine kinase activity in heart, skeletal muscle and liver of diabetic rats. It also reduces hepatic and renal glucose-6-phosphalase and fructose -1, 6-biphosphatase activity [102].

3. SYNTHETIC DRUGS AND HERBAL MEDICINE

Oral hypoglycemic drugs are used only in the treatment of type 2 diabetes which is a disorder involving resistance to secreted insulin. Type 1 diabetes involves lack of insulin and requires insulin for treatment. There are now four classes of hypoglycemic drugs: These drugs are approved for use only in patients with type 2 diabetes and are used in patients who have not responded to diet, weight reduction, and exercise. They are not approved for the treatment of women who are pregnant with diabetes.

Sulfonylureas are the most widely used drugs for the treatment of type 2 diabetes and appear to function by stimulating insulin secretion. The net effect is increased responsiveness of ß-cells (insulin secreting cells located in the pancreas) to both glucose and non-glucose secretagogues, resulting in more insulin being released at all blood glucose concentrations. Sulfonylureas may also have extra-pancreatic effects, one of which is to increase tissue sensitivity to insulin, but the clinical importance of these effects is minimal (Table 2).

Metformin is an oral antidiabetic drug in the biguanide class. It is the first-line drug of choice for the treatment of type 2 diabetes, in particular, in overweight and obese people and those with normal kidney function. It is effective only in the presence of insulin. But, in contrast to sulfonylureas, it does not directly stimulate insulin secretion. Its major effect is to increase insulin action. One important effect appears to be suppression of glucose output from the liver.

Thiazolidinediones or TZDs act by binding to PPARs (peroxisome proliferator-activated receptors), a group of receptor molecules inside the cell nucleus, specifically *PPARγ* (gamma). The ligands for these receptors are free fatty acids (FFAs) and eicosanoids. When activated, the receptor migrates to the DNA, activating transcription of a number of specific genes. TZDs reverse insulin resistance by acting on muscle, fat and to a lesser extent liver to increase glucose utilization and diminish glucose production and are also effective when given in combination with metformin.

Alpha-glucosidase inhibitors inhibit the upper gastrointestinal enzymes that convert dietary starch and other complex carbohydrates into simple sugars which can be absorbed. The result is to slow the absorption of glucose after meals. Alpha-glucosidase inhibitors are used to establish greater glycemic control over hyperglycemia in diabetes mellitus type 2, particularly with regard to postprandial hyperglycemia. They may be used as monotherapy in conjunction with an appropriate diabetic diet and exercise or with other anti-diabetic drugs.

Herbs have been used for healing purposes and to promote wellness since from the ancient times and are not categorized as medicines but treated as food since they are natural products. Nowadays, herbal medicines, health and dietary supplements are flooding the markets. The use in the right way provides effective and safe treatment for many ailments and the effectiveness is mostly subjective to the patient. The potency varies based on the genetic variation, growing conditions, timing and method of harvesting, exposure to air, light, moisture, and type of preservation of the herbs. Herbal medicines can be used for healing purposes and to promote wellness and are not addictive or habit forming, but are powerful nutritional agents that support the body naturally. They promote health and serve as excellent healing agents without side effects. Chinese herbs are taken as tonics to enhance physical and mental well-being and can nourish the body's deepest and most basic elements. They are

also safe and effective for health, healing, weight loss/gain/maintenance.

Herbal medicines are great body balancers that help regulate body functions, can be used to support balance process of our body and offer the nutrients that the body fails to receive due to poor diet or environmental deficiencies in the soil and air. They can be used to treat many diseases such as diabetes, asthma, eczema, premenstrual syndrome, rheumatoid arthritis, migraine, menopausal symptoms, chronic fatigue, and irritable bowel syndrome, etc., and can be used for maintaining general health. Herbal preparations are best when taken under the guidance of a trained professional. When used correctly, herbal medicines are considered safer than conventional medications. People are greatly concerned about the efficacy and side effects of many synthetic drugs, and hence choose herbal medicines for providing a safe and natural alternative treatment for many health problems. The use is widespread and growing, In fact, herbs are always the alternative medicine and primary source. The advantages of using herbal medicines are numerous. They tend to be more effective for long-standing health complaints that don't respond well to traditional medicine. Herbs typically have fewer side effects, and may be safer to use over time.

4. CONCLUSIONS

Diabetes is a serious metabolic disorder. Differences in social structure, psychic stress, obesity, hormonal imbalance and heredity are optimizing the growth of pandemic. At present, the treatment of diabetes mainly involves a sustained reduction in hyperglycemia by the use of biguanides, thiazolidinediones, sulphonylureas, D-phenylalanine derivatives, meglitinides and α-glucosidase inhibitors in addition to insulin. However, due to unwanted side effects the efficacies of these compounds are debatable and there is a demand for new compounds for the treatment of diabetes [173,174]. Hence, plants have been suggested as a rich, as yet unexplored source of potentially useful antidiabetic drugs. However, only a few have been subjected to detailed scientific investigation due to a lack of mechanism-based available in vitro assays [175-177]. These efforts may provide treatment for all and justify the role of novel traditional medicinal plants having anti-diabetic potentials.

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