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Medicinal Plants with Antidiabetic Effects – An Overview (Part 1)

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Abstract: Diabetes mellitus is one of the most common endocrine metabolic disorders. It caused significant mortality due to its complications. Insulin and oral antidiabetic drugs associated with a number of serious adverse effects. The search for more effective and safer hypoglycemic agents is one of the important areas of investigation. Medicinal plants possessed hypoglycemic effects by many mechanisms. The current review discussed the medicinal plants with antidiabetic effect with special focus on their mechanism of action.

Keywords: Diabetes, Insulin, Phytoconstituents, Pancrease, Blood glucose, Beta cell, Antidiabetic, Hypoglycaemic, Medicinal plant.

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I. INTRODUCTION

Diabetes mellitus is the most common endocrine disorder. It affected around 2.8% of the world's population and is anticipated to cross 5.4% by the year 2025. Medicinal plants were used for the treatment of diabetic mellitus in traditional medicine systems of many cultures throughout the world. The hypoglycemic activity of many medicinal plant products were evaluated and confirmed in animal models as well as in human beings. In some cases, the bioactive principles of the medical plants have been isolated and identified and the mechanism of antidiabetic effects was clarified. There are several possible mechanisms by which the medicinal plants induced hypoglycemia. These included: enhancing regeneration or revitalization of damaged pancreatic beta cells, and protecting against further damage, enhancing insulin synthesis and secretion from the beta-cells, decreasing glucose absorption from gastro-intestinal system, increasing insulin sensitivity of the tissues, possessing of insulin mimicking effects, and changing the activity of some enzymes involved in glucose metabolism[1]. This review discuss blood glucose-lowering effects of medicinal plants.

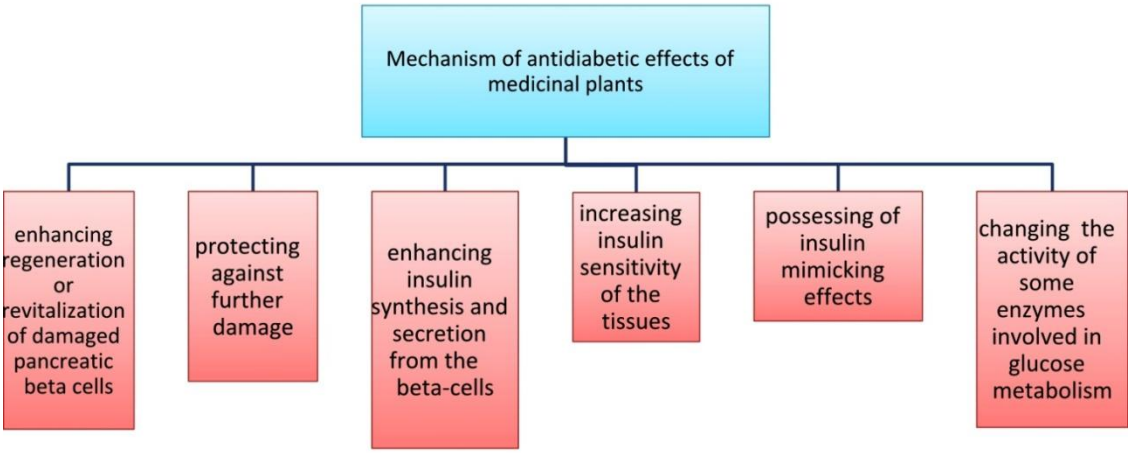

Fig 1: The mechanism of antidiabetic effects of medicinal plants

Medicinal plants with antidiabetic activity:

Achillea santolina

An acute administration of the aqueous extract of *Achillea santolina* (in a dose of 150 and 250 mg/kg body weight orally) resulted in significant reductions of serum glucose level in streptozotocin -induced diabetic rats. Chronic administration of the aqueous extract of *Achillea santolina* in a dose of 250 mg /kg orally for 28 days also showed marked hypoglycemic effects in streptozotocin -induced diabetic rats in comparison with diabetic control group [2].

Adiantum capillus-veneris

The alcoholic extract of *Adiantum capillus-veneris* showed significant hypoglycaemic effect in rabbit model, started after 30 min of administration of the extract and continued for 4 hours [3]. El-Tantawy *et al*., recorded the antidiabetic and diuretic effects of the alcohol and aqueous extracts of *Adiantum capillus-veneris* as well as its isolated mucilage [4].

Agrimony eupatoria

The effects of dietary administration of *Agrimony eupatoria* on streptozotocin (STZ)-diabetic mice and on *in vitro* glucose uptake, glucose metabolism and on insulin secretion by BRIN-BD11 cells were investigated. Agrimony incorporated into the diet (62.5 g/kg) and drinking water (2.5 g/l) countered the weight loss, polydipsia, hyperphagia and hyperglycaemia of STZ-diabetic mice. Aqueous extract of agrimony (1 mg/ml) stimulated 2-deoxy-glucose transport (1.4-fold), glucose oxidation (1.4-fold) and incorporation of glucose into glycogen (2.0-fold) in mouse abdominal muscle comparable with 0.1 microM-insulin. In acute 20 min tests, 0.25-1 mg/ml aqueous extract of agrimony evoked a stepwise 1.9-3.8-fold stimulation of insulin secretion from the BRIN-BD11 pancreatic B-cell line. This effect was abolished by 0.5 mM-diazoxide and previous exposure to extract did not adversely affect subsequent stimulation of insulin secretion by 10 mM-L-alanine, thereby indicating that there was no detrimental effect of the extract on cell viability. The effect of extract was glucose-independent and was not evident in BRIN-BD11 cells exposed to a depolarizing concentration of KCl. The ability of agrimony extract to enhance insulin secretion was dependent on use of heat during extract preparation. These results indicate the presence of antihyperglycaemic, insulin-releasing and insulin-like activity in *Agrimony eupatoria* [5].

Agropyron repens

The hypoglycaemic effect of an aqueous extract of *Agropyron repens* (*Triticum repens*) rhizomes was investigated in normal and streptozotocin (STZ) diabetic rats. After a single oral administration of the aqueous extract (20mg/kg) a significant decrease on blood glucose levels in STZ diabetic rats ($p<0.001$) was observed; the blood glucose levels were normalized after 2 weeks of daily oral administration of aqueous extract (20mg/kg) ($p<0.001$). Significant reduction on blood glucose levels were noticed in normal rats after both acute ($p<0.001$) and chronic treatment ($p<0.001$). In addition, no changes were observed in basal plasma insulin concentrations after treatment in either normal or STZ diabetic rats indicating that the underlying mechanism of this pharmacological activity seems to be independent of insulin secretion [6].

Allium cepa

The ethanol, chloroform and petroleum ether extracts of *Allium cepa* exerted hypoglycemic effects in alloxan, glucose and epinephrine induced diabetes in experimental animals [7-14]. The aqueous extract of onion , as well as its hypoglycemic effects, it improved the reduction in the antioxidant parameters (superoxide dismutase, catalase, glutathion peroxidase, and reduced glutathione) in alloxan induced diabetic rabbits [15]. In assessment of hypoglycemic activity of *Allium cepa* in type 1 and type 2 diabetic patients, ingestion of crude *Allium cepa* (100 g) caused a considerable reduction in fasting blood glucose levels by about 89 mg/dl in relation to insulin (145 mg/dl) in type 1 diabetic patients and it reduced fasting blood glucose levels by 40 mg/dl, compared to glibenclamide (81 mg/dl) in type 2 diabetic patients, 4 hours later. The same dose of crude *Allium cepa* produced a significant reduction in the induced hyperglycemia (GTT) by about 120 mg/dl compared to water (77 mg/dl) and insulin (153 mg/dl) in type 1 diabetic patients and considerably reduced GTT by 159 mg/dl in relation to water (55 mg/dl) and glibenclamide (114 mg/dl) in type 2 diabetic patients, after 4 hours [16]. The mechanisms that mediate the hypoglycemic effects of *Allium cepa* were included: Alyl propyl disulfide compounds competed with insulin for metabolism resulting in an increase of free insulin. *Allium cepa* also facilitated glycogen storage and increased glutathione peroxidase . Sulfur containing compounds such as dialkyl disulfides and their oxidized thiols can trap electrons from other systems and act as antiuoxidants. In addition , phenolic acids such as caffeic, chlorogenic ,ferulic, sinapic, p-coumaric, vanillic, syringic and p-hydroxy produced antioxidant activity [15-16].

Allium sativum

Garlic has been found to be effective in lowering serum glucose levels in streptozotocin and alloxan-induced diabetes in rabbits, rats and mice [17-19]. S-allyl cysteine sulphoxide, (allicin) in a dose of 200 mg/kg body weight was significant antidiabetic in rats [20-21]. However**,** both garlic oil and diallyl trisulphide produced hypoglycemic effects and improved glycaemic state in streptozotocin -induced diabetes in rats [22]. Orally administered garlic juice resulted in better utilization of glucose in glucose tolerance tests in rabbits. Allicin produced 60% of the activity of tolbutamide in alloxan-induced diabetic rabbits at a dose of 250 mg/kg [23]. Oral administration of garlic powder (800mg/day) to 120 patients for 4 weeks in a double-blind, placebo-controlled study decreased the average blood glucose by 11.6 % [24]**.**

Aloe vera

Aloe gel decreased blood sugar in diabetic and normal mice. It also decreased insulin resistance in mice [25-28]. In clinical trials, it appeared that orally administered *Aloe gel* (1-2 tablespoons twice daily) enhanced the hypoglycemic effect of glibenclamide [29-30].

Alpinia galanga

The administration of powdered rhizome of *Alpinia galanga* to the normal rabbits produced significant decrease in blood glucose level [31]. However Srividya *et al* found that the ethanolic extract of *Alpinia galanga* exerted antidiabetic effects in rats. The glucose uptake by rat hemi diaphragm was significantly more in all groups tested compared to control. 400 mg/kg b.wt treated group showed marked increase in body weight. Fluid intake (ml/day) was also increased when compared to the diabetic control. Serum glucose level (mg/dl) was found to decrease gradually from the date of administration of the extract to the end of the study when compared to the diabetic control. 400 mg/kg bw in diabetic rats showed potent serum glucose reducing capacity than 200 mg/kg bw. Total protein level was found to increase in the extract treated group when compared to diabetic control. Serum triglyceride level was found to be decreased when compared with diabetic control as well as diabetes treated with glibenclamide. Total cholesterol was also found to decrease drastically on the administration of the extract when compared with the diabetic control. The ethanolic extract of *Alpinia galanga* was found to be effective in inhibiting the α-Glucosidase when compared to Acarbose [32].

Althaea officinalis

Polysaccharide from the root of *Althaea officinalis* (Althaea mucilage-O) administered intraperitoneally to nondiabetic mice significantly reduced blood glucose [33]. Scopoletin (7-hydroxy-6-methoxy coumarin) is therapeutically evaluated in rats for hyperglycemia. Scopoletin (1.00 mg/kg, p.o.) administered daily for 7 days decreased the levels of serum thyroid hormones and glucose [34]**.**

Anchusa strigosa

The antidiabetic activity of aqueous extract of flowers of *A. strigosa* was examined in streptozotocin induced diabetic rats. The aqueous extract of *A. strigosa* flowers in a dose of 250 mg/kg and 500 mg/kg administered orally to diabetic rats for 30 days caused a dose-dependent fall in blood glucose and an improvement in serum insulin levels. Cholesterol and triglyceride levels showed significant reduction in comparison with diabetic control group. The extract treatment also showed significant increase in hepatic glycogen levels [35].

Anthemis nobelis

The effect of both a single dose and daily oral administration dose (20mg/kg body weight) for 15 days of the aerial part of *Chamaemelum nobile* aqueous extract on blood glucose concentrations and basal insulin levels in normal and streptozotocin-induced diabetic rats (STZ) were studied. Single oral administration of *C. nobile* aqueous extract reduced blood glucose levels from 6.0 ± 0.3 mmol/l to 4.9 ± 0.09 mmol/l ($P < 0.05$) 6h after administration in normal rats and from 21.1 ± 1.3 mmol/l to 14.5 ± 0.9 mmol/l ($P < 0.001$) in STZ diabetic rats. Furthermore, blood glucose levels were decreased from 6.1 ± 0.06 mmol/l to 4.6 ± 0.17 mmol/l ($P < 0.01$) and from 21.1 ± 1.31 mmol/l to 13.7 ± 0.9 mmol/l ($P < 0.01$) in normal and STZ diabetic rats, respectively, after 15 days of treatment. Basal plasma insulin concentrations remain unchanged after treatment in both normal and STZ diabetic rats , which means that the mechanism of this pharmacological activity seems to be independent of insulin secretion [36]. Flavonoid glucoside chamaemeloside, has been determined to have in vivo hypoglycaemic activity [37].

Arctium lappa

The antidiabetic effect of the ethanolic extract of the root of burdock (*Arctium lappa* L.) was investigated in streptozotocin- induced diabetic rats. Oral administration of the root ethanolic extract was significantly decreased blood glucose and increased insulin level in diabetic rats compared to the control diabetic group. Meanwhile, the levels of serum total cholesterol, triglycerides and low density lipoprotein in the root ethanolic extract treated diabetic rats were lower, and the high density lipoprotein level was higher than those index of the control diabetic rats. Furthermore, oral administration of root ethanolic extract was significantly decreased serum urea and creatinine as well as malondialdehyde levels of liver and kidney tissues, while body weight gain and tissue glycogen content were elevated in diabetic rat, all of which indicate an improvement in diabetic state. In addition, 400 mg/kg body weight of root ethanolic extract had a marked improvement of the glucose tolerance in normoglycemic rats [38]. Silver *et al* investigated the effect of burdock powder on normal and diabetic patients, and found out that burdock root possess hypoglycemic effects. The antidiabetic effect of burdock root was related to polysaccharides, the main component of the root. Root extract maintained the blood glucose level constant, therefore improving the tolerance to high glucose level [39].

Artemisia campestris

The effects of aqueous extracts of *A. campestris* leaf aqueous extract was examined on glycemic state, lipid profile, lipid peroxidation (MDA), protein carbonyl content (PCO), advanced oxidation protein products (AOPP), activities of both non-enzymatic and enzymatic antioxidants in alloxan-induced diabetic rats. The administration of *A.* campestris to diabetic rats at a dose of 200 mg/kg bw resulted in a significant reduction in glycemia, TC, TG, LDL-c, pancreas LPO, PCO and AOPP levels, CAT and GPx activities associated with an elevation of GSH content and SOD activity in comparison with diabetic group [40].

Asparagus officinalis

Streptozotocin-induced diabetic rats were treated with a methanolic extract of *Asparagus officinalis* seeds (250 and 500 mg/kg per d) or glibenclamide for 28 days. Treatment of the diabetic rats with the *Asparagus officinalis* extract at doses of 250 and 500 mg/kg suppressed the elevated blood glucose in a dose- and time-dependent manner. The 500 mg/kg, but not 250 mg/kg, dose significantly improved serum insulin levels in the diabetic rats. The insulin: glucose ratio was significantly increased at both doses in the *A. officinalis*-treated rats. Both qualitative and quantitative improvements in β-cell function were found in the islets of the *A. officinalis*-treated rats. The extract showed potent antioxidant activity in an *in vitro* assay and also improved the total antioxidant status *in vivo*. In most cases, the efficacy of *A. officinalis* (500 mg/kg) was very similar to a standard anti-diabetic drug, glibenclamide [41]. The hypoglycaemic effect of the aqueous extract of asparagus by-product (AEA) was evaluated in a streptozotocin (STZ)-induced diabetic rat model. Continuous administration of AEA for 21 days significantly decreased fasting serum glucose and triglyceride levels but markedly increased body weight and hepatic glycogen level in diabetic rats. In an oral glucose tolerance test, both the blood glucose level measured at 30, 60 and 120 min after glucose loading and the area under the glucose curve showed a significant decrease after AEA treatment [42].

Avena sativa

The treatment with *Avena sativa* caused an increase of insulin activity and improving sensitivity for normalizing blood glucose level and reduce glucose production by the liver [43]. The glycaemic and insulinaemic response to oat bread, oat bread with lingonberry fibre, oat-buckwheat bread and buckwheat porridge were tested in a small-scale clinical study (KHSHP E514/09). Nine healthy volunteers consumed test foods after overnight fasting. From samples taken at seven time points during 120 min. The mean glycaemic and C-peptide indexes (C-pepIs) were 32 and 100 for oat bread, 47 and 119 for oat-lingonberry fibre bread, 58 and 105 for oat-buckwheat bread and 71 and 77 for buckwheat porridge [44]. Oat and barley foods have been shown to reduce human glycaemic response, compared to similar wheat foods or a glucose control. Regression analysis on 119 treatments indicated that change in glycaemic response (expressed as incremental area under the post-prandial blood-glucose curve) was greater for intact grains than for processed foods. For processed foods, glycaemic response was more strongly related to the β-glucan dose alone ($r(2)=0.48$, $P<0.0001$) than to the ratio of β-glucan to the available carbohydrate ($r(2)=0.25$, $P<0.0001$). For processed foods containing 4 g of β-glucan, the linear model predicted a decrease in glycaemic response of 27 ± 3 mmol / min/l. Thus, intact grains as well as a variety of processed oat and barley foods containing at least 4 g of β-glucan and 30-80 g available carbohydrate can significantly reduce post-prandial blood glucose [45].

Ballota nigra

The hypoglycemic effect of *Ballota nigra* extract was investigated in alloxan-induced diabetes mellitus in rats. Administration of aqueous extract of *Ballota nigra* extract significantly reduced glucose in both healthy and diabetic rats [46].

Benincasa hispida

The stem chloroform extract of *Benincasa hispida* has significant hypoglycemic activity in normal male Wistar rats. The maximum reduction in blood glucose levels with stem extract of *Benincasa hispida* was recorded at a dose of 200 mg/kg bw [47].

Salad was prepared by using 100gm of ash gourd (*Benincasa hispida*) and one gram of curry leaves (10 curry leaves) and five grams of skimmed milk powder (made into curd) and pepper and salt are added for taste. This salad was freshly prepared every day and given to hyperlipidemic diabetic patients in mid morning for a period of three months to find out the therapeutic effect of supplementation of ash gourd and curry leaves. Supplementation of ash gourd and curry leaves had significant hypoglycemic and hypolidemic effect and it reduced the blood glucose level (both fasting and post prandial), within the period of three months [48, 49]. *Benincasa* hispida in a dose of 250 and 500 mg/kg in mice induced dose dependent decrease in glucose, triglyceride and insulin levels in plasma. It was also increased the glucose uptake from hemidiaphragm [50].

Brassica nigra

In streptozotocin induced diabetic rats treated with aqueous, ethanol, acetone and chloroform extracts of the seeds of *Brassica nigra*, the increase in serum glucose value between 0 and 1 hr of glucose tolerance test (GTT) was the least (29 mg/dl) in aqueous extract treated animals, while it was 54, 44 and 44mg/dl with chloroform, acetone and ethanol extracts respectively. In addition the effective dose of aqueous extract was found to be 200 mg/kg body weight in GTT. Administration of 200 mg/kg body weight of aqueous extract to diabetic animals once daily for one month brought down fasting serum glucose (FSG) levels . The glycosylated hemoglobin (HbA1c) and serum lipids in the treated group were much less than untreated diabetic controls [51]. Aqueous extract of *Brassica nigra* (AEBN) has been shown to have good antidiabetic effect along with significant decrease ($p<0.01$) of abnormal serum lipid levels. The mechanism of this effect was studied via investigation the effect of oral administration of AEBN for two months on glycolytic and gluconeogenic enzymes in liver and kidney tissues of rats with streptozotocin (STZ) induced diabetes mellitus. The activities of gluconeogenic enzymes were higher and of glycolytic enzymes were decreased in both the liver and kidney tissues during diabetes. However, in diabetic rats treated with AEBN for two months, decrease of serum glucose, increase of serum insulin and release of insulin from pancreas (shown in vitro from isolated pancreas) along with the restoration of key regulatory enzyme activities of carbohydrate metabolism and glycogen content were observed. The therapeutic role of AEBN in STZ induced diabetes can be attributed to the release of insulin from pancreas and change of glucose metabolizing enzyme activities to normal levels, thus stabilizing glucose homeostasis in the liver and kidney. The LD_{50} was found to be more than 15 times the effective dose (ED) implying higher margin of safety for AEBN [52].

Brassica rapa

The antidiabetic efficacy of turnip (*Brassica rapa*) roots ethanol extract (TE) was investigated in type 2 diabetic animals. C57BL/KsJ-db/db (db/db) mice and db/+ mice were used and the db/db mice were divided into control, TE (0.26 g/100g diet) and rosiglitazone (RG, 0.005 g/100g diet) groups. Despite hyperinsulinemia, the glucokinase activity was lower in the liver of the db/db mice than the db/+ mice, while the glucose-6-phosphatase activity was higher. TE and RG improved the glucose and insulin tolerance and lowered the blood glycosylated hemoglobin, plasma insulin, C-peptide and glucagon levels as well as reversed these hepatic glucose regulating enzyme activities in db/db mice. TE also increased the insulin/glucagon ratio and hepatic glycogen content. The plasma free fatty acid and plasma and hepatic cholesterol and triglyceride levels were higher in the db/db mice than db/+ mice. Interestingly, TE and RG lowered these plasma and hepatic lipids, and simultaneously reduced the hepatic phosphatidate phosphohydrolase, HMG-CoA reductase, ACAT, beta-oxidation and carnitine palmitoyl transferase activities. Furthermore, TE lowered the hepatic fatty acid synthase activity, hepatic lipid droplets accumulation, and adipose tissue weight and size [53].

Bryophyllum calycinum

The aqueous extract of *B. pinnatum* caused significant reductions in the blood glucose levels of the fasted normal and fasted streptozotocin –treated diabetic rats [54-56].

Caesalpinia crista

The seed powder, dissolved in water, showed hypoglycaemic activity in alloxanized hyperglycaemic rabbits. The aqueous extract of the seeds produced similar effects in rats [57]. *Caesalpinia crista* seed extract 300mg/kg orally produced significant anti hyperglycemic action , and decreased blood urea nitrogen levels significantly. It also induced hyperlipidemic effects significantly by lowering the elevated cholesterol and LDL level. The anti-hyperglycemic action of the extracts may be due to the blocking of glucose absorption [58]. The seed kernel powder was reported to have hypoglycaemic activity in experimental animals. Four extracts (petroleum ether, ether, ethyl acetate and aqueous) were tested for their hypoglycaemic potentials in normal and alloxan induced diabetic rats. In normal rats, only ethyl acetate and aqueous extracts showed minimum significant hypoglycaemic effect. In diabetic rats, the ether extract showed a marginal antidiabetic activity, while the petroleum ether extract failed to showed significant hypoglycaemic effect [59]. The antidiabetic activity of ethanolic and aqueous seed extracts of *Caesalpinia crista* were evaluated in streptozotocin induced diabetes in 2 days old pup's models. Both ethanolic and aqueous seed extracts of *Caesalpinia crista* showed antidiabetic activity, but the aqueous extract of *Caesalpinia crista* showed more significant effect as compared to the ethanolic extract. Both extracts caused significant decrease in serum glucose, cholesterol and triglyceride when compared with diabetic untreated group after 3 weeks treatment. Treatment with the extracts also affected the physical parameters; they decreased body weight, increase demand of food and water intake when compared with diabetic untreated group [60]. Hypoglycaemic, antihyperglycaemic and hypolipidemic activities of the aqueous and 50% ethanolic extracts of *Caesalpinia crista* seeds were studied in normal and streptozotocin - diabetic rats. In normal rats, both extracts exhibited hypoglycaemic activity as early as 4 h after administration at a lower dose (100 mg/kg). The hypoglycaemia produced by the aqueous extract was of prolonged duration as compared to ethanolic extract. In diabetic rats, both extracts produced significant ($P < 0.01$) antihyperglycaemic effect from day 5 onwards. Aqueous extract also exhibited antihypercholesterolemic and anti-hypertriglyceridemic effects in streptozotocin-diabetic rats [61]. The hydromethanolic extract was administered orally at a dose of 250 mg/kg of body weight per day to streptozotocin-induced diabetic rats for 21 days. The effects of hydromethanolic extract on the fasting blood glucose (FBG) level, activities of key carbohydrate metabolic enzymes like hexokinase, glucose-6-phosphatase, and glucose-6-phosphate dehydrogenase, and antioxidant enzymes like catalase and superoxide dismutase along with the effect on the lipid peroxidation level in hepatic tissues were studied. Glycogen levels were also assessed in hepatic and skeletal muscles and some toxicity parameters, such as serum glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, and alkaline phosphates activities were also measured. Treatment of the hydromethanolic extract of the seeds of *Caesalpinia crista* resulted in a significant ($P<0.05$) recovery in the activities of carbohydrate metabolic enzymes along with correction in FBG and glycogen levels as compared with the untreated diabetic group. The extract also caused significant ($P<0.05$) recovery in the activities of toxicity assessment enzyme parameters. The corrective effects produced by the extract were comparable to the standard antidiabetic drug, glibenclamide [62].

Calotropis procera

The root extracts of *Calotropis procera* were investigated for its anti-hyperglycemic effect in Male Wister Albino rats. Glibenclamide 500 µg/kg, petrolium ether, methanol and aqueous extracts of roots of *C. procera* were administered to streptozotocin induced diabetic rats at a dose of 250 mg/kg bw as a single dose per day for 15 days. It appeared that methanol and aqueous extracts were the most effective hypoglycemic extracts [63]. The protection effects of the dried latex of *Calotropis procera* against alloxan induced changes in rat kidney was evaluated. Daily oral administration of the aqueous suspension (100 and 400 mg/kg) in diabetic rats produced anti-hyperglycemic effect that was comparable to that of glibenclamide (10 mg/kg). Unlike glibenclamide, the aqueous suspension did not increase the serum insulin levels in diabetic rats. However, it produced a marked reduction in the levels of urinary glucose and protein and normalized the renal tissue levels of thiobarbituric acid-reactive substances (TBARS) and glutathione (GSH) in diabetic rats and the effect was comparable to that of glibenclamide. The protection afforded by the aqueous suspension was also evident from the histological analysis of the renal tissue [64]. Chronic administration of root methanol, stem methanol and leaf ethyl-acetate extracts of *Calotropis procera* for 2 weeks at 100 and 250 mg/kg doses were significantly ($p<0.01$) attenuated the diabetes induced mechanical hyperalgesia, thermal hyperalgesia, tactile allodynia and HbA1C% level in streptozotocin diabetic rats as compared to negative control rats. Furthermore, the root methanol extract of *Calotropis procera* in a dose of 100mg/kg enhanced the regeneration capability of β cells in the pancreas with significant ($p<0.01$) improvement in plasma insulin level in streptozotocin diabetic rats compared to untreated control rats [65]. The dry latex was evaluated for its antioxidant and antihyperglycemic effects in rats with alloxan-induced diabetes. Daily oral administration of dry latex at 100 and 400 mg/kg produced a dose-dependent decrease in blood glucose and an increase in hepatic glycogen. It also prevented the

body weight loss in diabetic rats and reduced the daily water consumption to values comparable with those of normal rats [66].

Canna indica

The polyphenolic compounds from *Canna indica* L. root increased glucose transport in cultured muscle cells [67].

Capparis spinosa

The antidiabetic hypolipidemic effect of *Capparis spinosa* fruit extract was studied in diabetic rats (200mg/kg and 400mg/kg bw) for 28 days, these doses caused nonsignificantly decreases in the glucose level at 60 and 120 min. However, *Capparis spinosa* extract exerted lipid lowering effects with the same extract [68]. The effects of *Capparis spinosa* fruit on histomorphological changes in pancreas in streptozotocin induced diabetes in male rats were studied . Histological assessments showed a significant increase in the number of β cells, diameter of islets, and amount of insulin in groups treated with hydroalcoholic extract of *Caparis Spinosa* compared to the diabetic control group [69-70].

Capsicum annuum and ***Capsicum frutescens***

Capsaicin exhibited a hypoglycaemic effect in dogs, it increased insulin release [71].

Carum carvi

The effect of single and repeated oral administration of the aqueous extract of *Carum carvi* fruits at a dose of (20mg/kg) on lipid metabolism was studied in normal and streptozotocin-induced diabetic rats (STZ). After a single oral administration, *Carum carvi* extract produced a significant decrease on triglycerides levels in normal rats ($p<0.05$). In STZ diabetic rats, cholesterol levels were decreased significantly 6h after *Carum carvi* treatment ($p<0.05$). On the other hand, repeated oral administration of *Carum carvi* extract exhibited a significant hypo-triglyceridemic and hypo-cholesterolemic activities in both normal ($p<0.01$) and STZ diabetic rats ($p<0.001$), 15 days after *Carum carvi* treatment [72]. The hypoglycemic effect of caraway ethanolic extract was investigated in normal and streptozotocin-induced diabetic rats. The results showed that the caraway ethanolic extract seeds at doses 0.2, 0.4 and 0.6 g/kg body weight significantly decreased serum glucose in diabetic rats in 3 and 5 h, but not in healthy rats [73]. To evaluate the effect of oral administration of caraway on the blood glucose level and the weight of diabetic rats. Diabetes was induced by intraperitoneal injection of 60 mg/kg body weight streptozotocin. Caraway was given orally at a dose of 1g/kg body weight daily. The results showed that oral administration of caraway caused a significant decrease in blood glucose level ($p=0.001$) and alleviated their body weight loss ($p=0.037$) [74]. The hypoglycaemic effect of aqueous extracts of *Carum carvi* was investigated in normal and streptozotocin (STZ) diabetic rats. Single dose or 14 days oral administration of the aqueous extracts (20 mg/kg) produced significant decrease in blood glucose levels in STZ diabetic rats ($P<0.001$); the blood glucose levels were nearly normalized 2 weeks after daily repeated oral administration of aqueous extracts (20 mg/kg) ($P<0.001$). No highly significant changes on blood glucose levels were noticed in normal rats after both acute and chronic treatments with extract. In addition, no changes were observed in basal plasma insulin concentrations after treatment with aqueous extract in either normal or STZ diabetic rats, which indicate that the underlying mechanism was doesn't depend of insulin secretion [75].

Carthamus tinctorius

The antidiabetic effect of *Carthamus tinctorius* was studied on fasting blood glucose and insulin levels in alloxan induced diabetic rabbits. Diabetic animals were treated with *Carthamus tinctorius* extract at doses of 200 and 300 mg/kg body weight. Extract were given orally for 30 days and the values for blood glucose levels were observed after 15th and 30th day of treatment. While insulin levels were checked at the end of the study. Animals were also observed for any gross toxicity during the study. Results revealed that *Carthamus tinctorius* exerted significant hypoglycemic effect at 200 mg/kg and 300mg/kg doses as compared to diabetic control group. Insulin levels were significantly increased in *Carthamus tinctorius* treated groups as compared to diabetic control [76]. The chemical components isolated from safflower seed (*Carthamus tinctorius* L.) were evaluated as α-glucosidase inhibitors. The compounds appeared as active α-glucosidase inhibitors were serotonin derivatives (e.g. N-p-coumaroyl serotonin and N-feruloyl serotonin). These compounds showed a potent inhibitory activity, the 50% inhibitory concentration values were calculated as 47.2 μm and 99.8 μm respectively, while that of the reference drugs acarbose and 1-deoxynojirimycin were estimated as 907.5 μm and 278.0 μm, respectively. Regarding the structure of the serotonin derivative, the existence of the hydroxyl group at 5-position in the serotonin moiety and the linkage of cinnamic acid and serotonin were essential for α-glucosidase inhibitory activities. The authors suggested that these results are helpful for the proper use of

safflower seed as traditional medicine for the treatment of diabetes, moreover, it could serve to develop medicinal preparations as supplements and functional foods for diabetics [77].

Cassia occidentalis

The methanolic extract of *C. occidentalis* leaves was tested against alloxan-induced diabetic mice. The diabetes in the experimental mice was induced by a single intraperitoneal injection of alloxan. Treatment with *C. occidentalis* leaf extract at different doses (200 mg/kg, 300 mg/kg, and 450 mg/kg orally) significantly reduced the blood glucose level to normal in diabetic mice [78]. Methanol fraction of *C. occidentalis* leaves (COLMF) was tested against streptozotocin-induced diabetic rats. Oral administration of COLMF significantly and dose-dependently normalized hemoglobin, glycosylated hemoglobin, hepatic glycogen, lipid peroxidation, antioxidants (TBARS, HP, SOD, CAT, GPx VitC, VitE, GSH) and hepatic marker enzymes (ALT, AST, ALP, ACP) near to normal in STZ-diabetic rats ($p<0.05$). Histopathological examination showed that COLMF protected the pancreatic tissue from STZ-induced damage [79]. Aqueous extract of *C. occidentalis* produced a significant reduction in fasting blood glucose levels in the normal and alloxan-induced diabetic rats. Petroleum ether extract showed activity from day 14 and chloroform extract showed activity from day 7. Significant differences were observed in serum lipid profiles (cholesterol and triglyceride), serum protein, and changes in body weight by aqueous extract treated-diabetic animals, when compared with the diabetic control and normal animals. Concurrent histopathological studies of the pancreas of these animals showed comparable regeneration by extract which were earlier necrosed by alloxan [80]. Antidiabetic effect of the butanol (DTB) and aqueous (DTA) leaves extracts of *Cassia occidentalis* was evaluated in alloxan-induced diabetic mice. DTB group showed significant reduction in plasma glucose levels (95.2±7.46). DTA group showed significant reduction (119.6±29.03) but was less as compared with the DTB group. DTB group showed significant reduction in plasma cholesterol levels (186± 14.8). DTA group (190± 14.81) also showed significant reduction but slightly less as compared with the DTB group. DTB group showed significant reduction in LDL levels (99.7±7.3). Reduction in LDL levels in DTA group (111±5.1) was also significant as compared to DTB group. However, both extracts didn't induced significant changes in HDL and triglycerides levels [81].

Casuarina equisetifolia

The antidiabetic activity of *Casuarina equisetifolia* leaves ethanolic extract (EECE) was evaluated against streptozotocin (STZ) induced experimental rats. Blood glucose levels were determined on 0, 7th, 14th and 21st day after oral administration of ethanolic extracts of *Casuarina equisetifolia* (400mg/kg). An ethanolic extract of *C. equisetifolia* was found to reduce blood sugar in streptozotocin induced diabetic rats. Reduction in blood sugar could be seen from 7th day after continuous administration of the extract. The effect of extracts of *Casuarina equisetifolia* on serum lipid, total cholesterol, triglycerides, low density and high density lipoprotein were also measured in the diabetic and non diabetic rats. There was significant reduction in total cholesterol, LDL cholesterol, VLDL cholesterol and improvement in HDL cholesterol in diabetic rats [82]. The effect of *Casuarina equisetifolia* bark incorporated into rat feed at 10-40% on the lipid profiles and blood sugar of albino rats was investigated. The parameters studied were triacylglycerol (TGL), total cholesterol (TC), total lipid (TL), phospholipids (PHOS), high-density lipoprotein (HDL) and random blood sugar (RBS). There was no significant change ($P>0.05$) in the TGL levels of all the rats, including the control, as they all range between 0.18-0.22(mg/dl). The effects on TC and TL were irregular as they did not display any dose dependence. The mean plasma PHOS levels did not change significantly ($P>0.05$) between the control and the rats fed on 10% feed (0.19± 0.00 vs 0.18± 0.00 mg/dl), but was significantly lowered ($P<0.05$) at 20-40% feed content. The mean HDL level rose, although insignificantly ($P>0.05$) with the percentage contents of the bark in the feeds; by implication, the low-density lipoprotein (LDL) was decreasing with the increase in the bark contents of the feeds. The RBS also decreased as the percentage bark contents of the feeds increased, indication that it could have anti-diabetic properties [83].

Cicer arietinum

It was reported that the seeds reduced postprandial plasma glucose and were useful in the treatment of diabetes. The antihyperglycaemic activity of petroleum ether extract of *Cicer arietinum* (PEECA) seeds was evaluated at three different doses i.e. 100, 200 and 400 mg/kg po in alloxan (70 mg/kg iv) induced diabetic mice. In both acute and subacute studies serum glucose level (SGL) was measured. The change in body weight was noted during subacute study. Oral glucose tolerance test (OGTT) was performed in both diabetic and non-diabetic mice previously loaded with (2.5 g/kg po) glucose. Glyburide (10 mg/kg) was used as a standard drug. The maximum reduction in SGL was observed in PEECA (400 mg/kg) group at 6h (137.17 mg/dl) in acute study and on 21st day (217.79 mg/dl) in subacute study respectively. In glyburide treated mice the maximum reduction in SGL was observed at 6h (194.97 mg/dl) and on 21st day (267.40mg/dl) respectively. PEECA (400 mg/kg) and glyburide (10 mg/kg) prevented loss of body weight in diabetic mice. OGTT showed increased

glucose threshold in non-diabetic and diabetic mice. Accordingly, PEECA showed antihyperglycaemic activity comparable with glyburide [84].

Cichorium intybus

Ischemic manifestations and cerebral dysfunction have been demonstrated in diabetes. Otherwise, the impairment in the glycemic control is the basic mechanism causing inhibition of neuronal activity. Cerebral extract from alloxan diabetic rats significantly inhibited the brain AChE activity of normal animals, indicating the presence of an inhibiting factor in the cerebrum of diabetic rats. *Cichorium intybus* when fed for 10 days offered neuroprotection in diabetic rats by stimulating AChE activity [85-86].

The hypoglycemic and hypolipidemic properties of an ethanolic extract of *Cichorium intybus* (CIE) was studied in rats. Male Sprague-Dawley rats aged 9 weeks were administered with streptozotocin (STZ, 50mg/kg) intraperitoneally to induce experimental diabetes. The *Cichorium intybus* whole plant (CIE) was exhaustively extracted with 80% ethanol. Hypoglycemic effects of CIE were observed in an oral glucose tolerance test (OGTT). A dose of 125 mg of plant extract/kg bw exhibited the most potent hypoglycemic effect. Moreover, daily administration of CIE (125 mg/kg) for 14 days to diabetic rats attenuated serum glucose by 20%, triglycerides by 91% and total cholesterol by 16%. However, there was no change in serum insulin levels, which ruled out the possibility that CIE induced insulin secretion from pancreatic beta-cells. In addition, hepatic glucose-6-phosphatase activity (Glc-6-Pase) was markedly reduced by CIE when compared to the control group. The authors concluded that the reduction in the hepatic Glc-6-Pase activity could decrease hepatic glucose production, which in turn results in lower concentration of blood glucose in CIE-treated diabetic rats [87].

The effect of *Cichorium intybus* methanolic extract (CME) on glucose transport and adipocyte differentiation in 3T3-L1 cells was investigated by studying the radiolabelled glucose uptake and lipid accumulation assays. By performing detannification (CME/DT), the role of tannins present in CME on both the activitie`s was evaluated. CME and CME/DT exhibited significant glucose uptake in 3T3-L1 adipocytes with a dose-dependent response. CME inhibited the differentiation of 3T3-L1 preadipocytes but failed to show glucose uptake in inhibitor treated cells. The activity exhibited by CME/DT is exactly vice versa to CME. Furthermore, the findings from PTP1B inhibition assay, mRNA and protein expression analysis revealed the unique behavior of CME and CME/DT. Accordingly, the activities possessed by *Cichorium intybus* are highly desirable for the treatment of NIDDM because it reduces blood glucose levels without inducing adipogenesis in 3T3-L1 adipocytes [88].

The direct action of soluble fibers (chicory water-soluble extract and inulin) was investigated on the intestinal absorption of glucose in gut perfused rats. After equilibrium, both jejunal and ileal segments were simultaneously perfused with an isotonic electrolyte solution (pH 7.4) containing glucose (10 mmol/l) and chicory water-soluble extract (chicory extract) or inulin (10 g/l). Each test or control solution was perfused in random sequence, with perfusion times of 30 min. Chicory extract or inulin in the perfusate (10 g/l) inhibited the absorption of glucose from jejunum ($P<0.05$). The observed changes in glucose and water absorption caused by chicory extract or inulin were reversible after switching to a fiber free perfusate. Additionally, net water absorption changed to secretion upon addition of chicory extract or inulin. The authors concluded that the reduction in intestinal absorption of glucose observed after perfusion of chicory extract or inulin may be caused by viscosity-related increases in mucosal unstirred layer thickness [89].

In vitro experiments were designed to compare the effects of two hydroxycinnamic acids, caffeic and ferulic acids, to those obtained with a natural chicoric acid extract (NCRAE) (50 and 100 µg/ml) on the three major tissues implicated in glycemic regulation (pancreas, muscle and liver). *In vivo* experiments were performed in Wistar rats submitted to a daily intraperitoneal injection of natural chicoric acid extract NCRAE (3, 15 or 30 mg/ kg) for 4 days. On the fourth day, an intraperitoneal glucose tolerance test (IPGTT; 1 g/ kg) was carried out. Results showed that the three compounds used were able each to induce an original response. Caffeic acid mainly promoted a decrease in hepatic glycogenolysis. Ferulic acid elicited a clear increase of insulin release and a reduction of hepatic glycogenolysis. However, this compound induced an inhibition of muscle glucose uptake. NCRAE provoked an increase of insulin release and glucose uptake without any effect on hepatic glycogenolysis. None of these compounds implicated hepatic glucose 6-phosphatase in contrast to chlorogenic acid, known as an inhibitor of glucose 6-phosphatase and which is able to decrease glucose output from hepatocytes. *In vivo* experiments bring evidence that 4 daily ip administrations of NCRAE improve ip glucose tolerance in a dose-dependent manner and mainly via an insulin sensitizing effect [90].

The effects of a high-fructose diet supplemented with rutin and a chicory (*Cichorium intybus* L.) seed extract rich in caffeoylquinic acids (CQA) was tested on gut physiology and the development of disorders related to metabolic syndrome. A 28-days experiment was conducted on 32 young male Wistar rats. In comparison with control rats fed a standard corn starch diet (group C), the experimental group (group E) was fed a diet with an increased content of cholesterol and fructose (to 1% and 66% of the diet, respectively), as well as with oxidized soybean oil. Rats from the other two experimental groups were administered the same diet as

group E during the first 2 wks of feeding, whereas at the beginning of the last 2 wks, the diet was enriched with rutin (group ER) or the CQA-rich ethanol extract from chicory seeds (9.6% of CQA, group EC), so the amount of added phenolics was equal in both dietary groups (0.15%). The diet administered in group E caused hyperglycemia and increased blood serum atherogenicity in rats, but did not induce other manifestations of the metabolic syndrome, i.e., dyslipidemia and oxidative stress. Additionally, it affected gut physiology through increasing mucosal sucrase activity and disturbing fermentative processes in the cecum, such as the production of short-chain fatty acids and the activity of microbial enzymes. Similarly to rutin, the dietary addition of the chicory seed extract improved glycemia, which was comparable to that determined in group C. In addition, the extract was found to decrease the atherogenic index to the level observed in group C and to increase blood antioxidant status. Both dietary supplements reduced the content of thiobarbituric acid-reactive substances in kidney and heart tissue when compared with group E [91].

The effects of different chicory extracts on the blood glucose, total cholesterol (TC) and triglycerides (TG) was studied in hyperglycemic mouse model. It was found that the chicory alcohol soluble extract can decrease the blood glucose, TC and TG, which is more effective than the chicory alcohol deposit extracts [92].

Five intraperitoneal injection of cerulean (50 µg/ kg at 1 h intervals) in mice resulted in acute pancreatitis, which was characterized by edema, neutrophil infiltration, as well as increases in the serum levels of amylase and lipase in comparison to normal mice. Different doses of *Cichorium intybus* root (CRE) and aerial parts hydroalcoholic extract (CAPE) orally (50, 100, 200 mg/kg) and intraperitoneally (50, 100, 200 mg/kg) were administrated 1.0 and 0.5 h respectively before pancreatitis induction on separate groups of male mice (n=6). Control groups treated with normal saline (5 ml/ kg) similarly. Both extracts in greater test doses (100 mg/kg and 200 mg/kg, ip) were effective to decrease amylase (23-36%) and lipase (27-35%) levels. In oral route, the dose of 200 mg/ kg showed a significant decrease in levels of amylase (16%) and lipase (24%) activity while the greatest dose (200 mg/kg, ip) was only effective to diminish inflammatory features like edema and leukocyte infiltration in pancreatitis tissue ($P<0.01$) [93].

Cistanche tubulosa

The effects of *Cistanche tubulosa* on glucose homeostasis and serum lipids were studied in male mice model of type 2 diabetes. Different doses of *Cistanche tubulosa* (equivalent to 120.9, 72.6 or 24.2 mg verbascoside/kg) were administered orally once daily for 45 days to male db/db mice. *Cistanche tubulosa* significantly suppressed the elevated fasting blood glucose and postprandial blood glucose levels, improved insulin resistance and dyslipidemia, and suppressed body weight loss. However, *Cistanche tubulosa* did not significantly affect serum insulin levels or hepatic and muscle glycogen levels [94].

Acylated phenylethanoid glycosides, echinacoside and acteoside, the principal constituents in the stems of *Cistanche tubulosa*, inhibited the increased postprandial blood glucose levels in starch-loaded mice at doses of 250-500 mg/kg po. They also significantly improved glucose tolerance in starch-loaded mice after 2 weeks of continuous administration at doses of 125 and/or 250 mg/kg/day po without producing significant changes in body weight or increasing food intake. In addition, several constituents from *Cistanche tubulosa*, including echinacoside (IC_{50} = 3.1 µM), acteoside (1.2 µM), isoacteoside (4.6 µM), 2'-acetylacteoside (0.071 µM), tubulosides A (5, 8.8 µM), B (9, 4.0 µM), syringalide A 3-O-α-L-rhamnopyranoside (10, 1.1 µM), campneoside I (13, 0.53 µM), and kankanoside J1 (14, 9.3 µM), demonstrated potent rat lens aldose reductase inhibitory activity. The potency of 2'-acetylacteoside was similar to that of epalrestat (0.072 µM), a clinical aldose reductase inhibitor [95].

Citrullus colocynthis

The efficacy of *Citrullus colocynthis* (L.) Schrad fruit in 2 months clinical trial was conducted in 50 type II diabetic patients. Two groups of 25 each under standard antidiabetic therapy, received 100 mg *Citrullus colocynthis* fruit capsules or placebos three times a day, respectively. The patients were visited monthly and glycosylated hemoglobin (HbA1c), fasting blood glucose, total cholesterol, LDL, HDL, triglyceride, aspartate transaminase, alanine transaminase, alkaline phosphatase, urea and creatinine levels were determined at the beginning and after 2 months. The results showed a significant decrease in HbA1c and fasting blood glucose levels in *C. colocynthis* treated patients. Other serological parameters levels in both groups did not change significantly. No notable gastrointestinal side effect was observed in either group [96-97].

The direct *in vitro* effects of several distinct *Citrullus colocynthis* seed extracts was evaluated in glucose-stimulated insulin release from pancreatic islets isolated from rats. Six extracts were tested, a crude aqueous, defatted aqueous, ethyl acetate, H_2O-methanol, n-butanol extract and an extract containing a mixture of the major component (fraction A) identified by gel chromatography in the ethyl acetate, n-butanol and H_2O-methanol extracts. The majority of extracts exhibited a positive insulinotropic action when tested in the presence of 8.3 mM D-glucose [98].

Citrullus colocynthis possessed antidiabetic effect in rats at the dose of 50 and 100mg/kg bw for 28 days. Haematological and biochemical estimations were done at the end of experiment. Rats were then sacrificed and histopathological examinations were carried out . The results obtained showed that *Citrullus colocynthis* is safe for use as an antidiabetic remedy [99].

The effect of root of *Citrullus colocynthis* on the biochemical parameters of normal and alloxan-induced diabetic was investigated in rats. Aqueous extract of roots of *Citrullus colocynthis* showed significant reduction in blood sugar level (58.70%) when compared with chloroform (34.72%) and ethanol extracts (36.60%) ($p<0.01$). The aqueous extracts showed improvement in parameters like body weight, serum creatinine, serum urea and serum protein as well as lipid profile and also restored the serum level of total and conjugated bilirubin, serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transminase and alkaline phosphatase [100].

The antidiabetic effect of *Citrullus colocynthis* on liver hexokinase and gluconeogenic enzymes such as glucose-6-phosphatase and fructose 1, 6-bisphosphatase was investigated in control and alloxan-diabetic rats. Oral administration of leaf suspension of *Citrullus colocynthis* (250 and 500mg /kg body weight) for 60 days resulted in momentous reduction in blood glucose (from 381 ± 34 to 105 ± 35 mg/ dl), glycosylated hemoglobin, a decrease in the activities of glucose-6 phosphatase and fructose 1, 6-bisphosphatase, and an increase in the activity of liver hexokinase. These findings further support the antidiabetic effect of *Citrullus colocynthis* [101].

A double-blind randomized placebo-controlled clinical trial using a parallel design was carried out to examine the safety and efficacy of *Citrullus colocynthis* topical formulation in patients with painful diabetic neuropathy. Sixty patients with painful diabetic polyneuropathy (PDPN) were randomly allocated to receive the topical formulation of *Citrullus colocynthis* (1:1 allocation ratio) or placebo for three months. The patients were evaluated before and after the intervention in terms of Neuropathic Pain Scale, electrodiagnostic findings, World Health Organization BREF quality of life scores and reported adverse events. The mean change in pain score was significantly higher in the *Citrullus colocynthis* group 3.89 than in the placebo group 2.28 ($P<0.001$). The mean changes in nerve conduction velocity of the tibial nerve, distal latency of the superficial peroneal nerve and sural nerve, as well as sensory amplitude of the sural nerve in the intervention group were significantly higher than in the placebo group ($P<0.001$). No significant differences were observed between the mean changes in other nerve conduction values. World Health Organization BREF quality of life scores, only showed significant improvement of the physical domain [102].

The effect of *Citrullus colocynthis* pulp extract on the structure of the liver was tested in diabetic rats at both light and scanning electron microscopic levels. Diabetes caused degenerative alterations in the form of disorganization of the hepatic cords, cytoplasmic vacuolization and pyknosis of the nuclei of hepatocytes and inflammatory cell infiltration. Scanning electron microscope examination of these livers revealed numerous lipid droplets within hepatocytes, damaged blood sinusoids and hemorrhage of erythrocytes between hepatocytes and inside Disse's spaces. The liver of *Citrullus colocynthis*-treated rats revealed minor histological changes versus the control animals [103].

Citrus species

To study the hypoglycemic effect of hexane extract of *Citrus limon* peel, diabetes was induced in rats by a single intraperitonial injection of alloxan (140mg/kg bw). Hexane extract (200mg/kg bw) of *Citrus limon* peel was administered orally, while metformine hydrochloride (175 mg/kg bw) was used as a standard drug. The results showed that hexane extract exerted significant hypoglycemic activity and the activity of extract was comparable to that of standard drug [104].

The effect of oral treatment with citrus peel extracts on wound repair of the skin was studied in diabetic rats. The extracts were estimated for vitamin C and total carotenoid contents prior to animal study. Diabetes mellitus was induced in rats by intraperitoneal injection of a single dose of streptozotocin (STZ, 75 mg/kg bw). One week after diabetes induction, full thickness excision wounds were made in hyperglycemic rats. The different test groups were treated with different citrus peel extracts orally at the dose of 400 mg/kg bw daily for 12 days. The blood glucose, body weight and rate of wound closure of each rat were measured every 3rd day during the experimental period. At the end of experiment, granular tissues of wounds were removed and estimated for hydroxylproline and total protein content. The results showed significant reduction in blood glucose and time to wound closure. Tissue growth and collagen synthesis were significantly higher as determined by total protein and hydroxylproline content [105].

Measurements of the effects of *Citrus medica* cv Diamante peel extract on the mouse insulinoma MIN6 β-cells indicated that it exerted direct stimulatory effects on the exocytotic release of insulin in a concentration-dependent manner. *Citrus medica* cv Diamante peel extract reduced plasma glucose concentration in mice [106].

The antidiabetic and hypolipidemic activity of petroleum ether extract of *Citrus medica* seeds was studied in streptozotocin (STZ) induced diabetic model in rats. Seed extract was given as (200 and 400 mg/kg, po.) The petroleum ether extract of *Citrus medica* seeds induced significant reduction ($p < 0.05$) of fasting blood glucose, serum cholesterol, serum triglycerides, LDL and VLDL in dose dependent manner after 15 days of drug administration. However, 200 mg/kg/day seed extract for 15 days was not showing any change in HDL level, while 400 mg/kg/day dose significantly increased HDL level in diabetic rats [107].

In vivo hypoglycemic, and antidiabetic activity of *Citrus medica* L. var. *Sarcodactylis* were confired in Sprague-Dawley-SPF rats and Wistar DIO rats. Insulin secretagogue effect of *Citrus medica* L. var. Sarcodactylis Hort fruits was confirmed by kinetic analysis on the hypoglycemic patterns of the intraperitoneal glucose tolerance and the insulin-glucose tolerance tests [108].

The antihyperglycemic activity of methanol extract of *Citrus limetta* fruit peel (MECL) was evaluated in streptozotocin-induced (STZ; 65 mg/kg bw) diabetic rats. Three days after STZ induction, diabetic rats received MECL orally at 200 and 400 mg/kg bw daily for 15 days. Glibenclamide (0.5 mg/ kg po) was used as reference drug. Blood glucose levels were measured on 0, 4^{th}, 8^{th}, and 15^{th} days of study. Serum biochemical parameters namely, SGOT, SGPT and ALP were also estimated. The TBARS and GSH levels of pancreas, kidney, and liver were determined. MECL significantly ($P<0.001$) and dose dependently normalized blood glucose levels and serum biochemical parameters, decreased lipid peroxidation, and recovered GSH as compared to those of STZ control [109].

The inhibitory effect of the aqueous *Citrus limetta* peel extract on the metabolism of carbohydrates was studied. The extract inhibited primarily the enzyme α-amylase by 49.6% at a concentration of 20 mg/ml and to a lesser extent the enzyme α-glucosidase with an inhibition of 28.2% at the same concentration. This inhibition was likely due to the high polyphenol content in the *Citrus limetta* peel (19.1 mg GAE/g). Antioxidant activity of the *Citrus limetta* peel demonstrated dose-dependent antioxidant activity , varying from 6.5% at 1.125 mg/ml to 42.5% at 20 mg/ml. The results showed that these polyphenolic compounds having both antihyperglycemic and antioxidant activities [110].

The anti-diabetic potential of orange peel and juice was attributed to anti peroxidation, inhibition of α-amylase enzyme activity responsible for the conversion of complex carbohydrates to glucose, increased hepatic glycogen content, stimulation of insulin secretion, and repair of secretory defects of pancreatic β-cells [111-112].

The effects of four different concentrations of peel extract from *Citrus sinensis* (CS) were investigated in male mice, the results revealed that they exerted glucose lowering and antiperoxidative activities. In a separate experiment their potential was evaluated with respect to the regulation of alloxan induced diabetes mellitus. While a single dose of alloxan (120 mg/kg) increased the serum levels of glucose and alpha-amylase activity, rate of water consumption and lipid peroxidation (LPO) in hepatic, cardiac and renal tissues with a parallel decrease in serum insulin level, administration of 25 mg/kg of CS was found to normalize all the adverse changes induced by alloxan, revealing the antidiabetic and anti peroxidative potential of tested fruit peel extracts [113].

Clerodendrum inerme

The anti-diabetic activity of *Clerodendrum inerme* was evaluated using *in vivo* streptozotocin-induced diabetes in mice, and *in vitro* studies. The leaves of *C. inerme* were extracted in petroleum ether, methanol followed by aqueous solvent. Methanolic extract of leaves of *Clerodendrum inerme* at 200 mg/kg showed a very significant and progressive reduction in glucose level [114-115].

Clitoria ternatea

The hypoglycemic effects of methanol, water, petroleum ether and chloroform extract of *Clitoria ternatea* leaves were evaluated in Streptozotocin induced diabetic rats for acute and subacute effects. The extract of *Clitoria ternatea* (200 and 400 mg/kg) significantly reduced blood glucose level in Streptozotocin induced diabetic rats. 400mg/kg possessed significant hypoglycemic effect, 200 mg/kg also decreased glucose level but not as 400mg/kg. The result of acute effect of the methanol extract , showed that 200 and 400 mg/kg exerted a very similar effect, but at the initial stage at the 30 min, 200mg/kg showed a fine decrease in blood glucose level. Subacute activity showed that on the long term use of extract the dose 200 mg/kg is much better to control the blood glucose level than the 400 mg/kg dose [116-117].

The hypoglycemic effects of methanol extract of *Clitoria ternatea* leaves (200 and 400 mg/kg) was investigated in alloxan induced diabetic rats. The extract of *Clitoria ternatea* significantly ($P<0.001$) reduced blood glucose level in alloxan induced diabetic rats twelve hours after administration [118].

The hypoglycemic effects of the aqueous extract of *Clitoria ternatea* leaves and flowers (50-500mg/kg) were investigated in alloxan-induced diabetes in rats. The aqueous extracts of *Clitoria ternatea* leaves and flowers (400 mg/kg bw) significantly ($P<0.05$) reduced serum glucose, glycosylated hemoglobin and

the activities of gluconeogenic enzyme, glucose-6- phosphatase, but increased serum insulin, liver and skeletal muscle glycogen and the activity of the glycolytic enzyme, glucokinase. For all the biochemical tests performed, the leaf extract-treated rat showed essentially the same profile as those treated with the flower extract [119-120].

The effect of combined leaf extracts of *Clitoria ternatea* (CTL) and *Trichosanthes dioica* (TDL) was evaluated on the streptozotocin (STZ) induced diabetic Wistar rats. The results revealed that the combined extracts significantly decreased ($p<0.05$) serum glucose after the 28-days treatment [121].

Encephalopathy is a major complication in juvenile diabetes mellitus which cripples the potential physiomorphological growth and development in early childhood. The alcoholic extract of roots of *Clitoria ternatea* was evaluated in preventing the possible complications related to brain hippocampal area CA3 and pancreatic tissue in juvenile diabetic rat experimental models. The diabetes was induced in 22 days (post natal) Wistar rats by giving intra peritoneal injection of Streptozotocin at a dose of 60 mg/kg body weight. After the confirmation of diabetic state, the treatment with oral administration of alcoholic root extract of *Clitoria ternatea* at a dose of 100 mg/kg bw/ day, was started immediately and continued for one month duration. At the end of 30 days treatment, the animals were sacrified, brain and pancreatic tissues were collected for gross and histological studies. On microscopy the brain tissue showed homogenous architecture, the hippocampal CA3 region neurons showed gross viable changes in the cell morphology. On the other hand, pancreatic tissue showed reduction in the cell with hypertrophy along with relatively less inflammatory changes in the islet cells of Langerhans of animals treated by alcoholic extract of roots of *Clitoria ternatea*. The authors concluded that alcoholic root extract of herb *Clitoria ternatea* significantly prevented the complications related to brain hippocampal area CA3 and pancreatic tissue in juvenile diabetic rat experimental models [122].

The effect of alcoholic root extract of *Clitoria ternatea* on the neurons of frontal cortex and dentate gyrus was studied in young diabetic rats. The diabetes was induced in 22 days (postnatal) Wistar rats by giving intraperitoneal injection of Streptozotocin at a dose of 60mg/kg body weight. Daily single oral treatment of 100 mg/kg bw of alcoholic root extract of *Clitoria ternatea* was started and continued for a month. At the end of treatment, the animals were sacrificed and brain tissue was subjected to histopathological studies. The preventive effect of the alcoholic root extract of *Clitoria ternatea* was confirmed by significant increase of viable neurons and the significant effect on the morphology of neurons of frontal cortex and dentate gyrus [123].

The inhibitory effect of the aqueous extract of *Clitoria ternatea* flower (CTE) was studied on fructose-induced formation of advanced glycation end products (AGEs) and protein oxidation. Inhibition of AGE formation is the imperative approach for alleviating diabetic complications. The various concentrations of CTE were incubated with BSA and fructose at 37°C for 28 days. The formation of fluorescent AGEs, the level of fructosamine, protein carbonyl content, and thiol group were measured. The *in vitro* antioxidant activity was measured by the 1,1-diphenyl 2-picrylhydrazyl (DPPH) scavenging activity, trolox equivalent antioxidant capacity (TEAC), ferric reducing antioxidant power (FRAP), hydroxyl radical scavenging activity (HRSA), superoxide radical scavenging activity (SRSA), and ferrous ion chelating power (FICP). The results demonstrated that CTE (0.25-1.00 mg/ml) significantly inhibited the formation of AGEs in a concentration-dependent manner. CTE also markedly reduced the levels of fructosamine and the oxidation of protein by decreasing protein carbonyl content and preventing free thiol depletion. In the DPPH radical scavenging activity and SRSA, CTE had the IC_{50} values of 0.47 ± 0.01 mg/ml and 0.58 ± 0.04 mg/ml respectively. Furthermore, the FRAP and TEAC values of CTE were 0.38 ± 0.01 mmol FeSO4 equivalents/mg dried extract and 0.17 ± 0.01 mg trolox equivalents/mg dried extract. However, CTE showed weak scavenging activity on hydroxyl radical and a weak antioxidant iron chelator. As conclusion, the results showed that CTE has strong antiglycation and antioxidant properties and might have therapeutic potentials in the prevention of AGE-mediated diabetic complications [124].

The pancreatic regeneration potential of diferent fractions of the ethanol extract of the aerial parts of *Clitoria ternatea* L. was studied. The antidiabetic and antihyperlipidemic potential was evaluated in streptozotocin-induced diabetic rats and correlated with its *in vivo* and *in vitro* antioxidant activity. The extract and its fractions were initially screened for acute and sub-chronic antidiabetic activity in the dose range of 100-200 mg/kg. The most potent extract and fractions were further evaluated for pancreatic β-cells regeneration activity along with antioxidant and antihyperlipidemic activity. The most significant pancreatic regeneration activity, antidiabetic and antihyperlipidemic activity was shown by ethanol extract and butanol soluble fraction at a dose level of 200 mg/kg [125].

Coriandrum sativum

Administration of coriander seeds (5g/day) to NIDDM patients for 60 days significantly decreased lipid peroxidation, protein oxidation, decreased activity of erythrocyte catalase (CAT), increased serum β carotene, vitamin A, E and C in NIDDM diabetics. The treatment was also increased the activity of erythrocyte antioxidant enzyme i.e. glutathione-S-transferase (GST) and reduced glutathione content (GSH) in the treated diabetics [126].

The hypoglycemic effect of *Coriandrum sativum* was studied clinically in patients with type-2 diabetes mellitus. After assaying fasting plasma and urinary glucose, 10 patients of type-2 diabetes mellitus with no previous medication, 10 patients of type-2 diabetes mellitus taking oral hypoglycemic agents with history of inadequate control and six control subjects were given low (2.5 g tid) and high (4.5 g tid) doses of aqueous and alcoholic extracts of *Coriandrum sativum* for 14 days. On 15^{th} day, blood and urine samples were taken for glucose estimation. *Coriandrum sativum* has significant hypoglycemic activity in high dose and can be successfully combined with oral hypoglycemic agents in type-2 diabetic patients whose diabetes was not controlled by oral hypoglycemic drug alone [127-128].

The hypoglycemic activity of methanolic extracts of leaves of *Coriandrum sativum* was evaluated in rats. The methanolic extract showed significant dose dependant decrease in blood glucose level at a dose of 200 and 400 mg/kg. It also decreased the lipid parameters such as total cholesterol, LDL, HDL, VLDL and TG when compared with diabetic control. SGOT and SGPT were reduced dose dependently [129].

Coriander incorporated into the diet (62.5 g/kg) and drinking water (2.5 g/l, prepared by 15 min decoction) reduced hyperglycaemia of streptozotocin-diabetic mice. An aqueous extract of coriander (1 mg/ml) increased 2-deoxyglucose transport (1.6-fold), glucose oxidation (1.4-fold) and incorporation of glucose into glycogen of isolated murine abdominal muscle (1.7-fold) comparable with 10^{-8} M-insulin. In acute 20 min tests, 0.25-10 mg/ml aqueous extract of coriander evoked a stepwise 1.3-5.7-fold stimulation of insulin secretion from a clonal B-cell line. This effect was abolished by 0.5 mM-diazoxide. The effect of extract was potentiated by 16.7 mM-glucose and 10 mM-L-alanine but not by 1 mM-3-isobutyl-1-methylxanthine. Insulin secretion by hyperpolarized B-cells (16.7 mM-glucose, 25 mM-KCl) was further enhanced by the presence of extract. Activity of the extract was found to be heat stable, acetone soluble and unaltered by overnight exposure to acid (0.1 M-HCl) or dialysis to remove components with molecular mass<2000 Da. Activity was reduced by overnight exposure to alkali (0.1 M-NaOH). Sequential extraction with solvents revealed insulin-releasing activity in hexane and water fractions indicating a possible cumulative effect of more than one extract constituent [130].

Coriandrum sativum (CS) supplementation (1% and 3% w/w) to high fat diet (HFD) mice (for 12 weeks) significantly prevented HFD induced increment in body weight gain, food intake, feed efficiency, fasting blood glucose, plasma insulin, fasting insulin resistance index (FIRI), plasma and hepatic triglyceride (TG), total cholesterol (TC), plasma free fatty acid (FFA), adipocyte diameter and surface area along with decrement in adipocyte number. These set of changes were comparable to the rosiglitazone (0.05%) supplemented HFD fed mice [131].

The ethanol extract of *Coriandrum sativum* seeds was investigated for its effects on insulin release from the pancreatic beta cells in streptozotocin-induced diabetic rats. Pancreatic sections of 5 microm were processed for examination of insulin-releasing activity using an immunocytochemistry method. The results showed that administration of the ethanol extract (200 and 250 mg/kg, ip) exhibited a significant reduction in serum glucose. On the other hand, administration of streptozotocin decreased the number of beta cells with insulin secretory activity in comparison with intact rats, but treatment with the coriander seed extract (200 mg/kg) increased significantly the activity of the beta cells in comparison with the diabetic control rats [132].

The potential hypoglycemic activity of *Coriandrum sativum* (CS)-extract was investigated after a single oral dose and after daily dosing for 30 days (sub-chronic study) in normal and obese-hyperglycemic-hyperlipidemic (OHH) rats. A single dose of CS-extract or GLB suppressed hyperglycemia in OHH rats, and normoglycemia was achieved at 6h post dose; there was no effect on lipids, TG or insulin, but insulin resistance (IR) decreased significantly. The hypoglycemic effect was lower in normal rats. In the subchronic study in OHH rats, the effect of (CS-extract> glibenclamide) regarding reducing plasma glucose (causing normoglycemia on day 21), increasing insulin and decreasing IR, TC, LDL-cholesterol, and TG. Atherosclerotic index was decreased, while cardioprotective indices were increased by CS-extract, with no effect on body weight, urea or creatinine [133].

The antihyperglycaemic properties of the aqueous extract from the leaves and stems of *Coriandrum sativum* were evaluated in normoglycaemic rats, and on α-glucosidase activity from *Saccharomyces cerevisiae*. Rats were administered with the aqueous extract of the plant at 100, 300 and 500 mg/kg, to observe the effect on oral sucrose tolerance test. The aqueous extract exhibited significant antihyperglycaemic activity at the three tested doses. *In vitro* experiments with α-glucosidase exhibited a competitive-type inhibition [134].

The antidiabetic and antioxidant effects of *Coriandrum sativum* (CS) were studied in alloxan-induced diabetic rats. The extracts of CS in alloxan-induced diabetic rats were found to significantly lower blood glucose levels. Antidiabetic activity of the CS extracts was comparable with the clinically available drug glibenclamide. The levels of serum total cholesterol, triglycerides, and low-density lipoprotein cholesterol were lower in the extract-treated group and high-density lipoprotein cholesterol was higher than the diabetic control rats. The extracts of CS exhibited strong scavenging effect on 2, 2-diphenyl-2-picrylhydrazyl free radical and inhibited lipid peroxidation. The free radical scavenging effect of the extracts was comparable with that of the reference antioxidants. Furthermore, it also showed an improved antioxidant potential as evidenced by decreased lipid peroxidation and a significant increase in the activity of various antioxidant enzymes such as catalase, superoxide dismutase, and glutathione peroxidase in the liver of diabetic rats [135].

Cressa cretica

The antidiabetic activity of *Cressa cretica* was evaluated in alloxan induced diabetes in rats. The maximum glucose lowering effect of (11.86%) was observed at 12 hour after the administration of 300mg/Kg . Repeated oral treatment with ethanolic extract of *Cressa cretica* (EECC) (300mg/Kg/day) for two weeks significantly reduced blood glucose, serum cholesterol and improved HDL-cholesterol and albumin as compared to diabetic control group [136-137].

The antidiabetic potential of methanolic extract of *Cressa cretica* was studied in streptozotocin induced diabetic rats. The methanolic extract of *Cressa cretica* was administered orally at a dose of 100 mg/kg for 15 days to streptozotocin induced diabetic rats. Methanolic extract of *Cressa cretica* produced a significant reduction in fasting blood glucose level in diabetic rats. Significant differences were also observed in body weight in methnolic extract treated diabetic rats, when compared with diabetic control, normal control and standard drug treated rats. The authors postulated that phenolic compounds and flavonoids were responsible for antidiabetic activity [137-138].

Crocus sativus

The ameliorative effect of saffron aqueous extract on hyperglycemia and oxidative stress on diabetic encephalopathy was studied in streptozotocin induced diabetes mellitus in rats. Saffron at 40 and 80 mg/kg significantly increased body weight and serum TNF-α and decreased blood glucose levels, glycosylated serum proteins, and serum advanced glycation endproducts (AGEs) levels which triggered oxidative reaction [139-140].

Advanced glycation end products (AGEs) were causally correlated with diabetic vascular complications. AGEs triggered oxidative reaction then accelerated endothelial cell apoptosis which was a critical event in the process of vascular complications. Exposure of bovine endothelial cells (BEC) to 200 g/ml AGEs for 48h resulted in a significant increase in apoptotic rate, compared with control. Crocetin (a metabolite of crocin) prevented AGEs-induced BEC apoptosis, which correlates with crocetin attenuation of AGEs mediated increase of intracellular reactive oxygen species (ROS) formation and elevation of intracellular Ca^{2+} concentration ($[Ca^{2+}]i$) level ($P < 0.01$ versus AGEs group). These results demonstrate that crocetin prevents AGEs-induced BEC apoptosis through ROS inhibition and ($[Ca^{2+}]i$) stabilization and suggest that crocetin exerted a beneficial effect in preventing diabetes-associated vascular complications [141-142].

Cuminum cyminum

The orally administered seed powder (2 g/kg) lowered the blood glucose levels in hyperglycaemic rabbits [88-89]. The Antidiabetic effects of cumin seed, was examined in streptozotocin induced diabetic rats. An eight week dietary regimen containing cumin powder (1.25%) was found to be remarkably beneficial, as indicated by reduction in hyperglycaemia and glucosuria. This was also accompanied by improvement in body weights of diabetic animals. Dietary cumin also countered other metabolic alterations as revealed by lowered blood urea level and reduced excretions of urea and creatinine by diabetic animals [143-144].

Cuminaldehyde and cuminol were identified as potent insulinotrophic components. Cuminaldehyde and cuminol (25 µg/ml) showed 3.34- and 3.85-fold increased insulin secretion, respectively. The insulinotrophic action of both components was glucose-dependent and due to the closure of the ATP-sensitive K (K^+ -ATP) channel and the increase in intracellular Ca^{2+} concentration. An inhibitor of insulin secretion with potent β-cell protective action was also isolated from the same petroleum ether fraction. The authors concluded that *Cuminum cyminum* was able to lower blood glucose without causing hypoglycaemia or β-cell burn out [145].

The effect of methanolic extract of seeds of *Cuminum cyminum* (CC) on diabetes, oxidative stress and formation of advanced glycated end products (AGE) were investigated compared with glibenclamide. *In vitro* studies indicated that CC inhibited free radicals and AGE formation. Treatment of streptozotocin-diabetic rats with CC and glibenclamide for 28 days induced a reduction in blood glucose, glycosylated hemoglobin, creatinine, blood urea nitrogen and improved serum insulin and glycogen (liver and skeletal muscle) content

when compared to diabetic control rats. Significant reductions in renal oxidative stress and AGE were observed with CC when compared to diabetic control and glibenclamide. CC and glibenclamide also improved antioxidant status in kidney and pancreas of diabetic rats. Diabetic rats showed increase in rat tail tendon collagen, glycated collagen, collagen linked fluorescence and reduction in pepsin digestion [146].

The role of *Cuminum cyminum* supplementation on the plasma and tissue lipids was studied in alloxan diabetic rats. Oral administration of 0.25 g/kg body weight of *Cuminum cyminum* for 6 weeks to diabetic rats resulted in significant reduction in blood glucose and an increase in total haemoglobin and glycosylated haemoglobin. It also prevented a decrease in body weight. *Cuminum cyminum* treatment also resulted in a significant reduction in plasma and tissue cholesterol, phospholipids, free fatty acids and triglycerides. Histological observations demonstrated significant fatty changes and inflammatory cell infiltrates in diabetic rat pancreas, but supplementation with *Cuminum cyminum* to diabetic rats significantly reduced the fatty changes and inflammatory cell infiltrates. Moreover, *Cuminum cyminum* supplementation was found to be more effective than glibenclamide in the treatment of diabetes mellitus [147].

Cydonia oblonga

The antidiabetic activity of quince leaves hydro-ethanolic extract was studied in normal and streptozocin-induced diabetic rats. There was no significant effect on normal rats glucose, while, a significant reduction in the blood glucose levels was recorded in diabetic rats at a time period of 0 to 3 h [148-149].

Cynodon dactylon

The antidiabetic effect of ethyl acetate (70%) extract of *Cynodon dactylon* root and stem, was investigated in diabetes induced by a combination of ketamine (60 mg/Kg) and xylazine (10 mg/Kg) in mice, which induced a sustained hyperglycemia. Mice were treated with 50 and 100mg/Kg *Cynodon dactylon* extract. Both dosages of *Cynodon* dactylon extract had significant lowering effect on blood glucose level. The first dose was more effective than the second, and its impact was just like insulin [150].

250, 500 and 1000 mg/kg bw of aqueous extract of *Cynodon dactylon* were evaluated in diabetic rats and the dose of 500 mg/kg orally was the most effective dose. It lowered blood glucose level around 31% after 4 h of administration in normal rats [151-152].

Aqueous and non-polysaccharide fraction of *Cynodon dactylon* exhibited significant antihyperglycaemic activity in diabetic rats and decreased the glucose, cholesterol, triglyceride, high density lipoprotein, low density lipoprotein and urea levels [153].

The the antidiabetic activity of ethanolic extract of *Cynodon dactylon* root stalks was evaluated in streptozotocin induced diabetic rats. The study showed that the anti diabetic activity of ethanolic extract (500mg/kg) of *Cynodon dactylon* root stalks was comparable with the standard drug, tolbutamide [154].

The antidiabetic activity of aqueous *Cynodon dactylon* extracts was evaluated through an extensive in silico docking approach with PPARγ (Peroxisome Proliferator-Activated Receptor), GLUT-4 (glucose transporter-4) and SGLT2 (sodium glucose co-transporter-2). Interactions of these molecules with Gln 295 and Asp 294 residues of SGLT2 have been shown to compare well with that of the phase III drug, dapagliflozin. These residues have been proven to be responsible for sugar sensing and transport. This work showed that *Cynodon dactylon* extract was a potential SGLT2 inhibitor for diabetic neuropathy [155].

The antidiabetic, antioxidant and hypolipidemic efficacy of *Cynodon dactylon* were studied in alloxan-induced diabetic rats. A significant diminution of fasting blood sugar level with a significant increase in HDL and decrease ($p<0.05$) in cholesterol, triglyceride, LDL and VLDL were recorded after 15 days of treatment with 450 mg/kg bw *Cynodon dactylon* leaves extract. The investigation also revealed that the activities of AST, ALT, ALP, AP, LDH, and CPK were significantely ($p<0.05$) decreased in the extract- supplemented group. In the diabetic rats, the significant decrease in protein content and SOD, CAT, GPx, and GSH ($p<0.05$) activity and increase in LPO in plasma were found to be ameliorated after treatment with the plant extract [156].

The ability of the secondary metabolites of *Cynodon dactylon* to serve as an antagonist to angiotensin II type 1 receptor (AT_1) was studied. Twenty-four compounds were identified as the secondary metabolites of hydroalcoholic extract of *Cynodon dactylon* using the GCMS technique. Sixteen ligands showed effective binding with the target protein; diazoprogesteron, didodecyl phthalate, and 9,12-octadecadienoyl chloride and can be considered as compounds that could be used to bind with the active site sequence of AT_1. The authors concluded, that the metabolites of *Cynodon dactylon* could serve as a natural antagonist to AT_1 that could be used to treat diabetic retinopathy, so, activation of AT_1 expressed on retinal endothelial cells and pericytes has been implicated in contributing to the microvascular abnormalities in diabetic retinopathy [157].

Cyperus rotuntdus

The antidiabetic effect of of *Cyperus rotundus* was evaluated on alloxan induced hyperglycemia in rats. Oral daily administration of 500 mg/kg of the extract once a day for seven consecutive days, significantly lowered the blood glucose levels [158].

Cyperus rotundus (2.5 ml/kg, orally of 10% of the aqueous decoction of tuber parts) significantly decreased fasting serum glucose level in alloxan induced diabetic and normoglycemic rabbits. Hypoglycemic effects was appeared from the first week of the treatment, and tended to be increased with the continuation of the treatment [159].

The preventive role of ethanolic extract of *Cyperus rotundus* rhizomes (CRRE) was investigated on age associated changes in glucose in young and aged rats. CRRE was given as (500mg/kg bw) orally for 30 days. Age associated increase in serum glucose was observed in aged rats compared to young rats. Administration of CRRE to aged rats prevented the age associated changes in glucose level [160].

Dactyloctenium aegyptium

The anti-diabetic activity of different solvent extracts of *Dactyloctenium aegyptium* was in streptozotocin induced diabetic rats. All extracts under study shown significant decrease in serum glucose levels and antidiabetic potency of extracts was in the order of ethanolic extract > hydroalcoholic extract > aqueous extract > ethyl acetate extract > chloroform extract > n-hexane extract. The animals treated with ethanolic extract shown significant decrease in blood glucose, HbA1c, malondialdehyde levels and significant increase in insulin, Hb, SOD, catalase, reduced glutathione and body weight [161].

The antidiabetic effect of *n-hexane*, chloroform, ethyl acetate and methanolic fractions from ethanolic extract of *Dactyloctenium aegyptium* was investigated in streptozotocin induced diabetic rats. The methanolic fraction of ethanolic extract of *Dactyloctenium aegyptium* has favourable effect in bringing down the severity of diabetes. animals treated with MF shown significant decrease in blood glucose, HbA1c, malondialdehyde levels and significant increase in insulin, Hb, SOD, catalase, reduced glutathione and body weight [162].

Dalbergia sissoo

The ethanol, ethyl acetate,n-butanol and pet.ether extracts of the leaves of *Dalbergia sissoo* were investigated for antidiabetic activity in alloxan induced diabetic rats. The extracts produced a significant antidiabetic effect on first, third, fifth and seventh days at 300 mg/Kg body weight. Among all the extracts of *Dalbergia sissoo*, ethanol extract of leaves exhibited highly significant antidiabetic activity which is comparable with the standard drug, Glibenclamide [163].

The hypoglycemic effect of ethanolic extract of Dalbergia sissoo leaves was evaluated in alloxanized diabetic rats. The ethanolic extract of Dalbergia sissoo leaves was administered orally at different doses (250 and 500 mg/kg) to normal rats. The dose of 500 mg/kg was found to be more effective dose in oral route and it decreases blood glucose level (BGL) by 38.2 % in normal healthy rats after 1 day of administration. After daily treatment with the both dose (250 and 500 mg/kg) of ethanolic Dalbergia sissoo extract for 21 days to severely diabetic (FBG 300- 350 mg/dl) rats, the BGL reduced to 125 mg/dl by 250 mg/kg and 104 mg/dl by 500 mg/kg. It is more effective when compare with the standard drug Glibenclamide. It reduces blood glucose level up to 189.2, 115.2, 104.6 mg/dl at successive days of 7, 14, 21, at the dose of 500 mg/kg compare with standard drug which reduces blood glucose level up to 250.2, 141.2, 120.4 mg/dl. In comparison to glibenclamide, the extract was 12% more effective in reducing blood glucose level [164].

The antidiabetic potential of alcoholic and aqueous stem bark extract of Dalbergia sissoo and their fractions was studied on streptozotocin-nicotinamide induced type 2 diabetic rats. The study also included estimations of blood glucose levels, lipid profile, liver glycogen, body weight and antioxidant status in normal and diabetic rats. The results showed that alchohalic extracts (250 and 500mg/kg respectively) and aqueous extract (400mg/kg) significantly reduced the blood glucose level ($P<0.05$) where as hexane soluble extract and butane soluble extract did not reduced the blood glucose level significantly. Alcoholic extracts and aqueous extracts significantly restored the lipid profile and showed improvement in liver glycogen, body weight and antioxidant status in diabetic rats [165].

The antidiabetic effect of ethanolic extract of Dalbergia sissoo (DS) bark (250 and 500 mg/kg) was investigated in alloxan (AL) induced diabetic rats. The two doses caused significant reduction in blood glucose levels. The effect was more pronounced in 500mg/kg than 250 mg/kg. DS also showed significant increase in body weight and glycogen content in liver of AL-induced diabetic rats while there was significant reduction in the levels of serum triglyceride and total cholesterol. DS also showed significant improvement in the pancreas of AL-induced diabetic rats [166].

Datura fastuosa

The seed powder of the plant was tested for its hypoglycemic activity in normal and alloxan-induced diabetic rats. 25, 50 and 75 mg/kg, of the seed powder orally produced significant reduction in blood glucose at the 8 h in both normal and diabetic rats . The effect was found to be dose dependent with all treatments at the doses administered [167].

Daucus carota

A dichloromethane (DCM) extract of carrot roots stimulated insulin-dependent glucose uptake (GU) in adipocytes in a dose dependent manner. Bioassay-guided fractionation of the DCM extract resulted in the isolation of the polyacetylenes falcarinol and falcarindiol. Both polyacetylenes were significantly stimulated basal and/or insulin-dependent GU in 3T3-L1 adipocytes and porcine myotube cell cultures in a dose-dependent manner. Falcarindiol increased peroxisome proliferator-activated receptor (PPAR)γ-mediated transactivation significantly at concentrations of 3, 10 and 30 μM, while PPARγ-mediated transactivation by falcarinol was only observed at 10 μM. Falcarindiol was linked to the ligand binding domain of PPARγ with higher affinity than falcarinol and that both polyacetylenes exhibited characteristics of PPARγ partial agonists. Falcarinol was shown to inhibit adipocyte differentiation as evident by gene expression studies and Oil Red O staining, whereas falcarindiol did not inhibit adipocyte differentiation, which indicates that these polyacetylenes have distinct modes of action [168].

The effect of the methanol extract of D. carota (wild carrot) seeds (100, 200 and 300 mg/kg bw orally for 6 days), was studied on the serum levels of lipids and biochemical indices of kidney and liver function in streptozocin-induced diabetic (type I) rats. Administration of *D. carota* seeds extract in diabetic rats for six days, at all doses significantly decreased serum levels of total cholesterol, triglycerides and creatinine. Furthermore, oral administration of extract (200 and 300 mg/kg) significantly decreased serum levels of Low density lipoprotein cholesterol (LDL-C), aspartate amino transferase (AST) and urea. Also, extract (300 mg/kg) decreased alanine aminotransferase (ALT) serum levels ($P < 0.05$) [169].

Desmostachia bipinnata

The effect of hydroalcoholic extract of Desmostachya bipinnata was evaluated in glycemic status in non- diabetic rats. The results showed that the hydroalcoholic extract has no effect on euglycemic levels with minimal insignificant alterations. But, the supplementation of this extract in hypoglycemic (food deprivation or swim exercise induced) rats reduced the extent of hypoglycemia significantly. In addition, this extract reduced the degree of hyperglycemia induced by exogenous administration of dextrose significantly [170].

The antidiabetic activity of ethanolic extract of Desmostachya bipinnata whole plant (EDB) was studied in alloxan induced diabetes in rat. The extract showed significant antidiabetic activity at 200 and 400mg/kg, it was significantly ($P<0.05$) decreased blood glucose, cholesterol, TG, SGOT, SGPT, ALP, urea, uric acid and Creatinine [171].

***Digitalis* species**

Digitonin, a saponin from the seeds of *Digitalis purpurea*, improved the glucose tolerance and had beneficial effects on serum lipids by improve antioxidant activity in rats [172].

Dodonaea viscose

Dodonaea viscose leaves extracts (A-M) were evaluated in normal and alloxan-diabetic rabbits. Blood glucose levels were determined after oral administration of 250 and 500 mg/kg of *D. viscosa* leaves extracts. These doses of the leaves significantly reduced blood glucose in normal and significantly in alloxan-diabetic rabbits. It was also found that blood glucose levels of rabbits treated with aqueous: methanolic extract of *D. viscosa* leaves 500 mg/kg body weight was decreased significantly at 2, 4 and 6 h. Then oral glucose tolerance test was carried out in rabbits treated orally with A-M extract (500 mg/kg). Blood glucose of A-M extract treated rabbits was significantly decreased after oral glucose load. In addition, simultaneous administration of A-M extract and exogenous human insulin (3 units/kg body weight) reduced more potently the blood glucose levels of treated diabetic rabbits than those treated with the A-M extract only. Furthermore, oral administration of A-M extract of D. viscosa (250 and 500 mg/kg) continuously for 30 days produced significant reduction of blood glucose levels in diabetic rabbits compared with controls [173].

The methanolic extract of leaves of Dodonaea viscosa (D.viscosa) was evaluated for antidiabetic activity. The antidiabetic activity was studied using the Glucose uptake by isolated rat hemi-diaphragm in vitro model. The value of glucose uptake by rat hemi-diaphragm for D. viscosa was 13.80 ± 0.1697 compared to control (5.34 ± 0.12) and insulin 15.45 ± 0.12 mg/g/min [174].

The ethyl acetate extract (DEA) and methanolic extract (DME) of Dodonaea viscosa leaves were administered orally at different doses (200 and 400mg/kg bw) to normal as well as STZ- diabetic rats. DME

produced significant hypoglycemic effect in normal rats after 6h of administration. After acute treatment DME 400mg/kg produced marked fall (30.87%) after 6h of administration. DME 200mg/kg and 400mg/kg both showed improvement in glucose tolerance. Treatment of diabetic rats for 28 days with DME reduced the fasting glucose level by 43.81% than their pretreatment level. It brought about fall in level of total cholesterol by 36% and 38.89% and HbA1c by 29.44% and 35.6%. The increase in glycogen level was found to be 68.97% after treatment with DME 400mg/kg bw. It also normalized the elevated level of MDA in diabetic rats. DME 200mg/kg and 400mg/kg brought about the decreased level of GSH to near normal. The level of SGOT, SGPT were also found to be decreased which is comparable to the standard [175].

The different extracts of the Dodonaea viscosa were tested for anti-diabetic activity, by glucose tolerance test in normal and alloxan induced diabetic rats. Aqueous ethanol and butanol extracts had shown significant protection and lowered the blood glucose levels to normal limit in glucose tolerance test. In alloxan induced diabetic rats, the maximum reduction in blood glucose was observed after 3h at a dose of 250 mg/kg of bw. The percentage of glucose reduction by aqueous ethanol and butanol extracts were 30 and 48% respectively [176].

Methanol and chloroform extract of Dodonaea viscosa were administered to alloxan induced diabetic albino rats. Blood glucose, triglycerides, cholesterol, protein, urea, creatinine, SGPT, SGOT were checked. Histological changes in pancreas and liver of the animal were also examined. Extract treated groups shown reduction in blood glucose level to normal limit. Increased levels of all other biochemical parameters like SGPT, SGOT, Triglycerides, Cholesterol, Protein, Creatinine and Urea with alloxan treatment have been significantly reduced by extracts. Histological changes associated with alloxan induction was also attenuated by extracts [177].

Dolichos lablab

The antidiabetic activity of methanolic extract of Dolichos lablab seeds was studied in Streptozotocin-Nicotinamide induced diabetic rats. The methanolic extract of the seeds of Dolichos lablab was given by oral route at doses of 200 and 400mg/kg bw. MEDL dose dependely ($P<0.001$) reduced blood glucose levels, total cholesterol, triglycerides, SGPT, SGOT levels compared to untreated diabetic rats. MEDL 400 mg/k bw possessed more promising antidiabetic activity compared to 200mg/kg bw [178].

The anti hyperglycaemic activity of Dolichos Lablab methanol extract (MEDL) was studied in normal and streptozotocin - nicotinamide induced diabetic rats. MEDL was administered at doses of 200mg/kg and 400mg/kg, per oral to diabetes induced and normal rat for 14 days [179].

The antidiabetic effect of ethanolic extract of Dolichos Lablab leaves and seedswas investigated in alloxan induced diabetic rat. Alcoholic extracts of dried leaves of Dolichos lablab was given orally administered for 7 days . The oral administration of extracts at doses of 200 mg/ kg lead to a significant blood glucose reduction [180].

The antihyperglycemic properties of methanol extract of beans (fruits containing seeds) of Lablab purpureus was investigated using oral glucose tolerance test (OGTT). Administration of methanol extract of beans led to dose-dependent and significant reductions in blood glucose levels in glucose-loaded mice. At doses of 50, 100, 200 and 400 mg per kg body weight, the extract reduced blood glucose levels by 16.4, 39.1, 40.1, and 54.8%, respectively compared to control animals [181].

Echinochloa crusgalli

The anti-diabetic activity of the Echinochloa crusgalli (L.)P. Beauv grains 70% hydroalcoholic (HAEC) extract was studied in normal and alloxan (ALX) induced diabetic rats. A single dose was studied in the normal rats for 12 hrs. Oral glucose tolerance test (OGTT) was performed in normal rats after receiving glucose orally (2g/kg). Diabetes was induced by ALX (120mg/kg, ip) three different doses of HAEC (200, 400 and 600mg/kg, po) were administered orally to experimental diabetic induced rats for 21 days. Glibenclamide (5mg/kg p.o.) was used as standard reference. Fasting blood glucose levels, changes in body weight and organ weight, serum albumin, urea, total protein, creatinine, total lipid profile, haemoglobin, GSH, SOD and TBARS were evaluated. Histopathological examination of pancreas was also performed. Oral glucose tolerance test clearly indicate that 400 and 200mg/kg po HAEC significantly reduced blood glucose levels. Single dose of HAEC on normal rats showed a significant decrease in the fasting blood glucose levels when compared with the normal control rats. In diabetic rats, treatment with the 400, and 200mg/kg, po showed significant reduction in the fasting blood glucose levels, serum cholesterol, serum triglycerides, LDL-C and VLDL-C levels. A significant escalation was seen in the levels of HDL-C, haemoglobin, body weight and liver weight. The anti-oxidant TBARS, GSH and SOD levels were improved compared with untreated diabetic rats [182].

***Ephedra* species**

Alcoholic extract of *E. alata* exerted hypoglycemia one hour after administration to fasting rats. The same extract failed to reduce blood glucose levels in alloxanized rats compared to the positive control, glibenclamide [183].

Equisetum arvense

The methanolic extract of *Equisetum arvense* (50, 100, 250 and 500 mg/ kg daily for 5 weeks) was investigated for its antidiabetic activity in streptozotocin-induced diabetic rats. The results showed that different doses of methanolic extract significantly lowered blood. Also the weights of methanolic-extract treatment group were significantly higher. Concurrent histological studies of the pancreas of these animals showed comparable regeneration by methanolic extractwhich were earlier, necrosed by streptozotocin [184-186].

Eryngium creticum

The hypoglycemic activity of an aquous decoction of plant arial parts of *E. creticum* was tested in normoglycemic and streptozocin-hyperglycemic rats. Results indicate that those extract caused significant reductions in blood glucose concentrationin in normoglycemic rats (20%), and streptozocin-hyperglycemic rats (64.2%) when given orally [187].

The hypoglycemic effects of the aqueous extracts of *Eryngium creticum* aerial parts were examined in normal, glucose loaded and alloxan diabetic experimental animals. Eryngium creticum exhibited a potent and significant hypoglycemic effects in normal-fed, glucose loaded and and alloxan diabeticanimals [188-190].

The pancreatic and extrapancreatic effects of crude aqueous extracts (AE) of *Eryngium creticum* was studied using bioassays of β-cell proliferation and insulin secretion as well as glucose diffusion as possible modes of actions. Similar to L-alanine insulinotropic efficacy in MIN6 β-cell, glucose-stimulated Ca^{2+} regulated- insulin secretion was potentiated by AE s of *E.creticum* (0.01 mg/ml). Comparable to glucagon-like peptide-1-enhanced β-cell proliferation in 2-day treatment wells, a dose dependent augmentation of bromodeoxyuridine incorporation was obtained with the *E. creticum* AE (0.1, 0.5 and 1 mg/ml) [191].

***Eucalyptus* species**

The anti-hyperglycemic activity of the ethanolic extract of *Eucalyptus camaldulensis* leaves was studied on oral glucose tolerance test (OGTT) on albino rats. The administration of the ethanolic extract at a dose of 500 mg/kg of body weight showed a highly significant reduction in blood glucose when compared with control ($P<0.001$) [192].

Euphorbia hirta

The ethanol extract of *Euphorbia hirta* showed a significant decreased blood glucose level on alloxan-induced diabetic rats [193].

The antidiabetic effect of ethanolic extract of leaf, flower and stem of *Euphorbia hirta* was investigated in streptozotocin induced diabetic mice. Oral administration of all extracts induced significant reduction in blood glucose level at the 15^{th} day of the study [194].

Ethanol extract and ethylacetate fractions showed α-glucosidase inhibition activity. Based on the in vitro and in vivo test, *Euphorbia hirta* ethanolic extract and ethyl acetate anti-diabetes mechanism was related to its antioxidant capacity and also to its α-glucosidase inhibitory properties [195].

Foeniculum vulgare

The antiglycation properties of methanolic extracts of 23 fennel samples were evaluated in the bovine serum albumin (BSA)/glucose system. The level of glycation, conformational alterations and protein binding to RAGE receptors were assessed by Congo red binding assay and a brown staining method. Some samples showed high anti-glycative activity[196].

Fumaria officinalis

The antidiabetic effects of *Fumaria officinalis* was studied in an animal model of DM2. Diabetes was induced in male Wistar rats by feeding 21% fructose in drinking water for 8 weeks. They were treated with aqueous extracts (10%) of the plant for 8 weeks. *Fumaria officinalis* treated group did not show any significant changes in the blood glucose, plasma insulin, urine glucose and urine volume between the 8th and the 16th week[197].

Fumaria parviflora

The hypoglycaemic effects of methanolic extract of *Fumaria parviflora* [125 mg and 250 mg/ kg/ day, ip for seven days] was evaluated in normal and streptozotocin-induced diabetic rats. Administration of

methanolic extract of *Fumaria parviflora* extract showed potent glucose lowering effect only on streptozotocin induced diabetic rats below 100 mg/dl [P<0.001]. However, no significant differences in the blood glucose levels were recorded between diabetic rats received 125 or 250 mg/kg of plant extracts [198].

The effect of oral consumption of *Fumaria parviflora* [6.25%, orally after injection of streptozocin for five weeks] was assessed on serum glucose and lipid levels in streptozocin diabetic rats. Serum levels of glucose, triglyceride, total cholesterol, HDL and LDL were evaluated before and three and six weeks after the treatment. The results revealed that there was no significant difference in the glucose level between diabetic rats treated with *Fumaria parviflora* and untreated diabetic rats at third and sixth weeks. However there was a significant decrease in triglyceride level in *Fumaria parviflora* treated group as compared to untreated diabetic rats at third and sixth weeks. In *Fumaria parviflora* treated group, serum total cholesterol, showed a significant decrease and HDL cholesterol showed a significant increase at sixth week [199].

The antidiabetic effect of various doses of the powdered *Euphorbia prostrata* was investigated on blood glucose levels of the normal and alloxan-diabetic male albino rabbits. *Fumaria parviflora* produced significant hypoglycaemic effects in the normal rabbits only. Moreover, acute toxicity studies and records of behavioural patterns carried out in rabbits and rats, respectively showed no adverse effects in the dosages tested. It was conceivable that the plant contained some hypoglycaemic principles which act probably by initiating the release of insulin from the pancreatic beta cells of normal rabbits [200-201].

Glossostemon bruguieri

The root mucilages of Glossostemon bruguieri possessed remarkable hypoglycemic activity, it decreased the blood glucose level in diabetic rats by 54.5% within 15 days[202].

Glycyrrhiza glabra

The effects of long-term glycyrrhizin treatment (2.7, 4.1 g/kg diet) on diabetic symptoms were studied using genetically non-insulin dependent diabetic model mice (KK-Ay). The elevation of blood glucose concentration was almost entirely suppressed in mice fed the 0.41% glycyrrhizin diet 7 weeks after the beginning of test feeding, although it was not suppressed in mice fed the control diet or the 0.27% glycyrrhizin diet. Water intake in the control and 0.27% glycyrrhizin diet groups increased gradually, whereas, this was not true in the 0.41% glycyrrhizin diet group. Glycyrrhizin treatment significantly lowered blood insulin level. Throughout the experiment, glycyrrhizin did not affect the food intake or body weight. The mice fed the 0.41% glycyrrhizin diet also improved their tolerance to oral glucose loading 9 weeks after the beginning of test feeding[203].

The effect of glycyrrhizin was studied on streptozotocin (STZ)-induced diabetic changes and associated oxidative stress, including haemoglobin-induced free iron-mediated oxidative reactions. Glycyrrhizin treatment improved significantly the diabetogenic effects of STZ, it modulated blood glucose level, glucose intolerant behaviour, decreased serum insulin level including pancreatic islet cell numbers, increased glycohaemoglobin level and enhanced levels of cholesterol and triglyceride. The treatment significantly reduced diabetes-induced abnormalities of pancreas and kidney tissues. Oxidative stress parameters, serum superoxide dismutase, catalase, malondialdehyde and fructosamine in diabetic rats were reverted to respective normal values after glycyrrhizin administration. Free iron in haemoglobin, iron-mediated free radical reactions and carbonyl formation in haemoglobin were pronounced in diabetes, and were counteracted by glycyrrhizin. Effects of glycyrrhizin and glibenclamide treatments appeared comparable[204].

***Gossypium* species**

The inhibitory effect of aqueous extract of different parts (bark, leaf, and flower) of cotton plant (*Gossypium herbaceum)* on key enzymes linked with type 2 diabetes and oxidative stress was studied in rat pancreas *in vitro*. The ability of the extract to inhibit the activity of α-amylase and α-glucosidase as well as activities of pro-oxidant Fe^{2+}-induced lipid peroxidation was determined spectrophotometrically. The results revealed that the extracts were able to inhibit the activity of α-amylase and α-glucosidase in rat's pancreas in a dose dependent manner (0–88.8 mg/ml). Incubation of pancreas tissue homogenate in the presence of Fe^{2+} caused a significant increase (233.3%) in the malondialdehyde (MDA) content of pancreas homogenate, nevertheless, the introduction of the aqueous extract inhibited MDA production dose dependently (0–33.33 mg/ml) and also exhibited further antioxidant properties represented by their high radical scavenging and Fe^{2+} chelating abilities[205].

Anti-diabetic and hypolipidemic effects of seed of Gossypium herbaceum and its aqueous and ethanol extracts were investigated in alloxan-induced diabetic rabbits. Gossypium herbaceum powder, its aqueous (GHA) and ethanol (GHE) extract significantly (P<0.05) reduced normoglycemia, serum cholesterol, triglyceride and urea in a dose dependent order (200→300 mg/kg of body weight) in normal rabbits. Gossypium herbaceum and GHE ameliorated completely the alloxan effect on serum levels of glucose, cholesterol,

triglyceride, creatinine and urea in alloxan-induced diabetic rabbits. Histopathological examination confirmed the protective effect of Gossypium herbaceum , GHA and GHE against alloxan-induced destruction of β-cells of pancreas in diabetic rabbits[206].

The hypoglycemic and hypolipidemic effect of ethyl ether and ethanol extracts of Gossypium Herbaceum (200mg/kg) leaves was evaluated in alloxan induced diabetes in rat, with measurements of biochemical parameters. The extracts showed significant ($p<0.01$) antihyperglycemic and hypolipidemic activity as compared to diabetic control. The extracts showed beneficial effects on blood glucose level in alloxan model. It also reduced the elevated biochemical parameters such as triglycerides, low density lipoprotein, very low density lipoprotein, Total Cholesterol and increased the reduced level of high density lipoprotein[207].

Helianthus annuus

The antihyperglycemic effect of ethanol seed extract (250mg/kg and 500mg/kg, po) was studied in normal, glucose loaded hyperglycemic and streptozotocin (STZ) induced Type2 diabetic rats. Alcoholic seed extract of *Helianthus annuus* showed less significant changes in blood glucose level of normoglycemic rats ($P<0.05$), while, it caused much reduction in blood glucose levels ($P<0.01$) in diabetic rats. Administration of extract in streptozotocin-nicotinamide induced diabetic rats, significantly decreased the blood glucose level ($P<0.001$), restored the lipid profile, showed improvement in body weight, liver glycogen content, glycosylated haemoglobin, plasma malondialdehyde, glutathione level and serum insulin levels[208-209].

The crude methanol extract of *Helianthus annuus* was separated into fractions and evaluated for antidiabetic effect. The extract yielded thirteen fractions. Bioactivity screening of the fractions (60 mg/kg) using alloxan-induced hyperglycemic rats showed that fraction 8, 9, 10 and 13 caused various degrees of reduction in FBG in time-dependent manner. The activities of the fractions were compared to the crude extract (600 mg/kg). The crude extract (HAE), glibenclamide, fractions 8, 9, 10 and 13 caused 66.74%, 57.43%, 61.36%, 59.80%, 70.63% and 78.03% reductions in FBG, respectively, at 6 h[210].

The antidiabetic, oral glucose tolerance test (OGTT), and antioxidant effects of methanol extract of H. annuus leaves were investigated using alloxan-induced diabetic rats. The extract (150, 300, and 600 mg/kg) showed a significant ($p < 0.05$) dose- and time-dependent decrease in blood glucose level of alloxan-induced diabetic rats. At 6 h posttreatment, there was a significant ($p < 0.05$) decrease in blood glucose level at 600 mg/kg (66.74 %) extract compared with the negative control group (10 mg/kg distilled water). The OGTT in normoglycemic rat showed no significant ($p > 0.05$) difference in blood glucose level among the treatment groups. In diabetic OGTT, the blood glucose level of the extract (600 mg/kg)-treated group was significantly ($p < 0.05$) lower when compared to the that of the negative control group at 120 min post glucose load, but there was no significant ($p > 0.05$) difference between the extract- and glibenclamide (2 mg/kg)-treated groups. The extract also produced a concentration-dependent increase in antioxidant activity[211].

Among three plants, the sunflower sprout Helianthus annuus exhibited the strongest inhibitory effects against the formation of advanced glycation end products (AGEs). At a concentration of 1.0 mg/ml, its inhibitory rate achieved 83.29%, which was stronger than that of aminoguanidine (1 mM), a well-known synthetic antiglycative agent (with an inhibitory rate of 80.88%). The antioxidant capacity of H. annuus was also much stronger than other sprout samples in terms of free radical scavenging and reducing properties.An active ingredient contributing to these activities was identified as cynarin (1,5-dicaffeoylquinic acid). Sunflower sprout H. annuus rich in cynarin may be regarded as a beneficial food choice for diabetic patients[212].

Helianthus tuberosus

The ethanol extracts of tubers of *Helianthus tuberosus* (250 and 500 mg/kg bw) showed antidiabetic effect in streptozotocin induced diabetic rats, it also showed
an inhibitory effect on kidney tissue TBARS levels (24.5%)[213-214].

Hibiscus cannabinus

The antidiabetic activity of methanolic extract of Hibiscus cannabinus leaves was evaluated in streptozotocin induced diabetic rats. The alcoholic extract was orally administered at a dose of 400mg/kg bw for 15 days. The result showed that the alcoholic extract of Hibiscus cannabinus leaves significantly lowered the blood glucose in hyperglycemic rats[215-216].

Hibiscus rosa-sinensis

The antidiabetic effect of ethyl acetate fraction of Hibiscus rosa sinensis petals (EHRS) was evaluated in experimental diabetes at a dose of 25 mg/kg bw and compared with metformin. The elevated levels of serum glucose (398.56 ± 35.78) and glycated haemoglobin (12.89 ± 1.89) in diabetic rats were significantly decreased (156.89 ± 14.45 and 6.12 ± 0.49, respectively) by (EHRS) administration. Hepatotoxicity marker enzyme levels

in serum were normalized, the glycogen content was restored by regulating the activities of glycogen metabolizing enzymes. It significantly modulated the expressions of marker genes involved in glucose homeostasis signalling pathway. Histopathological analysis of liver and pancreas supported the biochemical findings[217].

The anti-diabetic effects of aqueous ethanolic extract of Hibiscus rosa sinensis was investigated in streptozotocin-induced diabetic rats. Oral administration of H. rosa sinensis (500 mg/kg) aqueous extract to diabetic rats for 4 weeks significantly reduced blood glucose, 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. Accordingly, *H. rosa sinensis* extract has an antihyperglycaemic effect and alleviated liver and renal damage associated with streptozotocin-induced diabetes mellitus in rats[218].

The hypoglycemic activity of the ethanol extract of Hibiscus rosa-sinensis was studied in rats. After a single dose of the extract, a slight but insignificant hypoglycemic effect was observed at 30 and 90 min. At 120 min it was mild but significant. After repeated administration of the extract (once a day for seven consecutive days) a statistically significant ($P < 0.001$) reduction in blood glucose levels was observed at 30, 90 and 120 min after glucose loading. The average hypoglycemic activity, after repeated administration of 250 mg/kg leaf extract was 81%, under similar conditions average activity of tolbutamide was 96%. At 250 mg/kg the efficacy of the extract was found to be 84% of tolbutamide (100 mg/kg). Repeated treatment of animals either with tolbutamide a sulphonylurea or H. rosa-sinensis caused a 2-3-fold improvement in glucose tolerance as compared to those receiving only once[219].

The antidiabetic effect of Hibiscus rosa sinensis flower powder was studied in type II diabetic patients. 2g flower powder of Hibiscus rosa sinensis , daily for 60 day significantly decrease level, mean fasting blood glucose, post prandial blood glucose level, mean glycosylated Hb level , mean total cholesterol, triglyceride level, total LDL and total VLDL cholesterol Level[220].

Because fraction-3 (F3) and fraction-5 (F5) were more effective fractions among 5 fractions obtained from the ethanolic extract of H. rosa sinensis leaves, they were used to study their anti-diabetic properties in non obese diabetic mice. Serum glucose, glycosylated hemoglobin, triglyceride, cholesterol, blood urea, insulin, LDL, VLDL, and HDL were estimated. Both fractions F3 and F5 (100 and 200 mg/kg body weight) demonstrated insulinotropic nature and protective effect in non obese diabetic mice[221].

The hypolipidimic activity of flowers extract of *Hibiscus rosa sinensis* was studied in alloxan induced diabetic rats oral administration of flowers extract in doses 50,100,200 mg/kg po, showed significant improvement in dyslipidemia caused by diabetes mellitus as evidenced by reduced level of total cholesterol, triglycerides, VLDL, LDL and elevated in HDL levels significantly[222].

The effect of ethanolic extract of *Hibiscus rosa-sinensis* (EHBS) leaves on alloxan-induced diabetes with dyslipidemia was studied in rats. Treatment of alloxan-induced diabetic rats with 2.0 mg/kg bw of EHBS for 1 week significantly reduced glucose level, TC, TG and LDL-C, and increased HDL-C and weight of kidney, pancreas and liver compared with diabetic rats. A similar results were obtained when the treatment of alloxan-induced diabetic rats continued for 4 weeks. EHBS leaves extracts , in comparison with metformin, possessed profound hypoglycemic and hypolipidemic activities[223].

The antidiabetic, hypolipidimic, antioxidant and histopathological effects of Hibiscus rosa sinensis were investigated in Alloxan induced diabetes in rats. HEFHR (Hydroalcoholic extract of flower *Hibiscus rosa-sinensis*) (50-200 mg/kg bw) possessed significant and sustained oral antidiabetic activity, comparable with the hypoglycemic effect of glibenclamide and sulphonylurea. Flower extract of HRS was more efficacious in lipid lowering effect and in antioxidative activity than glibenclamide. After 28 day treatment with flower extract, size of islets was significantly increased and necrosis and atrophy of islets were significantly improved; also increase in number and diameter of cell islets compared to the diabetic group[224].

Blood glucose and total lipid levels were determined in streptozotocin induced diabetic rats after oral administration of an ethanol flower extract of Hibiscus rosa sinensis. Ethanol flower extract possessed hypoglycemic effect after 7 and 21 days of oral administration of the extract. Maximal diminution in blood glucose (41-46%) was noticed after 21 days. The extract lowered the total cholesterol and serum triglycerides by 22 and 30%, respectively. HDL-cholesterol was much higher increased (12%) by the extract compared to glibenclamide (1%). The hypoglycemic activity of this extract is comparable to that of glibenclamide but is not mediated through insulin release[225].

Hibiscus sabdariffa

The inhibitory effect of aqueous extracts of two varieties (red and white) of *Hibiscus sabdariffa* (Roselle) calyces on carbohydrate hydrolyzing enzymes (α-amylase and α-glucosidase) was studied. as a possible mechanism for their antidiabetes properties. The extracts caused inhibition of α-amylase and α-glucosidase activities *in vitro*.The IC_{50} revealed that the red variety (25.2 µg/ml) exhibited higher α-glucosidase inhibitory activity than the white variety (47.4 µg/ml), while the white variety (90.5 µg/ml) exhibited higher α-

amylase inhibitory activity than the red variety (187.9 μg/ml). However, the α-glucosidase inhibitory activities of both calyces were higher than that of their α-amylase[226].

The antidiabetic and antioxidant effects of purple roselle extract were studied in streptozotocin(STZ)-induced diabetes in rats. After 21 treatment, roselle extract had the ability to lower blood sugar (both curative and preventive), increase of antioxidant capacity, and improve insulin production[227].

The effects of *H. sabdariffa* UKMR-2 (HSE) variety (100 mg/kg/bw orally for 28 consecutive days) on sperm functioning of streptozotocin-induced diabetic was studied in rats. Administration of HSE significantly lowered the level of fasting blood glucose and increased plasma insulin level in group as. Sperm quality was improved with significantly higher sperm concentrations ($p<0.05$) and sperm motility ($p<0.001$) as well as lower percentage of sperm abnormality ($p<0.05$) as compared to the diabetic group. Plasma follicle-stimulating hormone (FSH) level was significantly elevated ($p<0.05$) in HSE group than in diabetic group while no significant alteration in plasma testosterone and luteinizing hormone (LH) level were seen between groups[228]. The effect of oral administration of aqueous extract of Hibiscus sabdariffa (HS, at a 12 hr interval, daily for 7, 14 and 21 days, respectively) on blood glucose, serum sodium and serum potassium concentrations was eevaluated in albino rats. The results revealed a significant decrease ($P<0.05$) in blood glucose level after 21 days of administration of HS and a significant decrease ($P<0.05$) in serum sodium concentration at 7 and 14 days of administration[229].

The mechanism underlying the antidiabetic effect of ethanolic extract of H. sabdariffa calyxes (HS-EE, 0.1 and 1.0 g/kg/day, respectively, for 6 weeks) was investigated in streptozotocin-induced diabetic rats. HS-EE 1.0 g/kg/day significantly decreased the blood glucose level by 38 ± 12% in diabetic rats but not in normal rats. In normal rats, treatment with 1.0 g/kg HS-EE increased the basal insulin level significantly as compared with control normal rats (1.28 ± 0.25 and 0.55 ± 0.05 ng/ml, respectively). Diabetic rats treated with 1.0 g/kg HS-EE also showed a significant increase in basal insulin level as compared with the control diabetic rats (0.30 ± 0.05 and 0.15 ± 0.01 ng/ml, respectively). Microscopic histological examination showed that HS-EE 1.0 g/kg significantly increased the number of islets of Langerhans in both normal rats (1.2 ± 0.1 and 2.0 ± 0.1 islet number/10 low-power fields (LPF) for control and HS-EE treated group, respectively) and diabetic rats (1.0 ± 0.3 and 3.9 ± 0.6 islet number/10 LPF for control and HS-EE treated group, respectively)[230].

The effect of *Hibiscus sabdariffa* polyphenol extract (HPE) was investigated in streptozotocin (STZ) induced diabetic nephropathy. The results revealed that HPE reduced kidney mass induced by STZ significantly, as well as improving hydropic change of renal proximal convoluted tubules in the rats. HPE also significantly reduced serum triglyceride, total cholesterol and LDL in STZ induced rats. Treatment with HPE significantly increased the activity of catalase and glutathione and reduced lipid peroxidation (thiobarbituric acid-reactive substances)[231].

The protective effect of H. sabdariffa polyphenolic extract (HPE) was investigatedin type 2 diabetic rat model. Treatment with HPE reduced hyperglycemia and hyperinsulinemia, especially at the dose of 200 mg/kg. HPE decreased serum triacylglycerol, cholesterol, and the ratio of low density lipoprotein/high density lipoprotein (LDL/HDL). Diabetes promoted plasma advanced glycation end product (AGE) formation and lipid peroxidation, while HPE significantly reduced these elevations. Immunohistological observation revealed that HPE inhibited the expression of connective tissue growth factor (CTGF) and receptor of AGE (RAGE), which was increased in type 2 diabetic aortic regions. HPE also recovered the weight loss found in type 2 diabetic rats[232].

The possible protective effects of Hibiscus sabdariffa calyxes aqueous extract (HSL,100mg/kg/day, orally for 28 consecutive days), as an antidiabetic and antioxidant agent against oxidative liver injury in streptozotocin-induced diabetic were investigated in rats. Supplementation of HSL significantly lowered the level of fasting blood glucose and increased plasma insulin level compared to negative control ($p<0.05$). Alanine aminotransaminases and aspartate aminotransferase level were found to be significantly reduced in the treated group compared with negative control[233].

The antidiabetic, hypolipidimic, antioxidant and histopathological effects of hydroalcoholic extract of flower *Hibiscus rosa-sinensis* (HEFHR) were studied in alloxan induced diabetes in rats. HEFHR possessed significant and sustained oral antidiabetic activity, comparable with the hypoglycemic effect of glibenclamide and sulphonylurea. Flower extract of HRS was more efficacious in lipid lowering effect and in antioxidative activity than glibenclamide. After 28 day treatment with flower extract, size of islets was significantly increased and necrosis and atrophy of islets were significantly improved[234].

The effects of Hibiscus sabdariffa (HSE) on diabetic nephropathy was tested in streptozotocin induced type 1 diabetic rats. HSE was capable of reducing lipid peroxidation, increasing catalase and glutathione activities significantly in diabetic kidney, and decreasing the plasma levels of triglyceride, low-density lipoprotein and increasing high-density lipoprotein value. In histological examination, HSE improved hyperglycemia-caused osmotic diuresis in renal proximal convoluted tubules in diabetic rats. The results also

showed that it up-regulated Akt/Bad/14-3-3γ and NF-κB-mediated transcription. Accordingly, HSE ameliorated diabetic nephropathy via improving oxidative status and regulating Akt/Bad/14-3-3γ signaling[235].

***Hyoscyamus* Species**

The anti-diabetic potential of methanolic leaves extract of *Hyoscyamus albus* (was evaluated in diabetic rats. Streptozotocin-induced diabetic rats, were administered (100 and 200 mg/Kg bw) for 30 days. The oral administration of both doses of methanolic leaves extract of *Hyoscyamus albus* significantly reduced the levels of blood glucose and glycosylated hemoglobin in diabetic rats. Determination of plasma insulin levels revealed that the extract possessed insulin stimulating action[236].

Calystegines, polyhydroxylated alkaloids extracted from Hyoscyamys albus seeds were investigated for their in-vivo antidiabetic effect on Streptozotocine induced diabetes in mice. They markedly reduced blood glucose levels and lipid parameters of diabetic mice to normal concentrations after 20days of treatment at 10mg/kg and 20mg/kg ($p<0.05$). Histopathological study of diabetic mice pancreas indicated that calystegines of Hyoscyamus albus have minimized streptozotocine damages on β-cells of islets of Langerhans, stimulated β-cells regeneration and improved with this insulin secretion[237].

Jasminum sambac

The antidiabetic potential of flower extract of *J. sambac* was evaluated using oral glucose tolerance test, alloxan induced diabetes and streptozotocin induced diabetes models inrats. The blood glucose levels of test extract treated animals were found to be significantly less in all the models compared to diabetic control[238].

The antidiabetic effects of ethyl acetate and water extracts of leaves of *Jasminum sambac* at a dose of 300mg/kg, orally, for 21 days were evaluated in alloxan induced diabetic rats. Aqueous extract showed significant ($p<0.01$) reduction of elevated blood glucose level, while, ethyl acetate extract was less active compared to aqueous extract[239-240].

Juglans regia

Treatment with *J. regia* extracts in the experimental animal samples resulted in a significant decrease in blood glucose, glycosylated hemoglobin, low-density lipoprotein (LDL), triglyceride and total cholesterol and a significant increase in insulin and high-density lipoprotein (HDL) level[241]. The antidiabetic effect of *J. regia* leaves in type 1 diabetes was evaluated in streptozotocin induced diabetes in rats. Treatment with the *J. regia* extracts resulted in a significant decrease in blood glucose, glycosylated hemoglobin, LDL, triglyceride, and total cholesterol, and a significant increase in insulin and HDL level [242].

The effect of a 30-day oral administration of aqueous extract of walnut leaf (10, 50, 150, 300, and 500 mg/day) was studied in comparison with glibenclamide in normal and diabetic rats. Administration of all doses and over 10 mg/kg significantly lowered the blood glucose level in normal rat and diabetic rats, compared with dose and duration-dependent control groups. This effect was higher for doses of 50 and 150 mg/kg in normal rats and for doses of 300 and 500 mg/kg in diabetic rats, which was similar to glibenclamide (4 mg/kg)[243].

The mechanism of hypoglycemic action of *Julans regia* leaves methanolic extract (JRLME) was studied in rats. After three weeks of treatment, the plant extract had a significant hypoglycemic action in both short and long term models. There was also permanent blood glucose reduction in treated groups, the *in vitro* assay of α-glucosidase activity displayed inhibitory action of JRLME, like Acarbose, but less effectively[244].

The antidiabetic effect of ethanolic walnut leaf extract (200 mg/kg) was evaluated in nondiabetic, alloxan-induced diabetic rats. Fasting blood sugar decreased meaningfully in diabetic rats treated with *J. regia*. Insulin level increased and glycosylated hemoglobin decreased significantly in diabetic groups receiving *J. regia* compared with the diabetic group without treatment. Size of islets of Langerhans enlarged consequentially in *J. regia* treated rats[245].

The hypoglycemic effect of oral methanolic extracts of leaf and fruit peel (200 mg/kg for both) of walnut was evaluated in alloxan induced diabetic rats. Four weeks later, blood was collected for biochemical analysis and pancreases were removed for β-cells counts in histological sections. Diabetes increased fast blood sugar (FBS) and HbA1c, and decrease β-cell number and insulin. FBS decreased only in leaf extract group. HbA1c decreased in leaf extract and insulin groups. The β-cells number increased in leaf and peel extract groups. Insulin increased moderately in all treatment groups[246].

The antihyperglycemic properties of the Juglans regia leaf extract was investigated in streptozotocin-nicotinamide induced diabetic rats. One week after induction of diabetes, oral treatment started with extract of Juglans regia and Metformin and continued for 4 weeks. Fasting blood sugar, body weight, serum lipids and insulin level were measured in different groups. A significant reduction of glucose, HbA1c, total cholesterol and serum triglycerides were detected after 4 weeks in rats treated with Juglans regia leaves

compared to the control groups. Juglans regia extract treatment showed potential hypoglycemic and hypolipidemic effects in type 2 diabetic rats[247].

The effects of the Juglans regia leaf extract on hyperglycemia lipid profiles in type II diabetic patients were investigated clinically using 61 patients, suffering from type II diabetes with fasting blood glucose (FBG) between 150 and 200mg/dl, glycated hemoglobin (HbA1c) between 7% and 9%. First group received 100mg Juglans regia leaf extract in capsules form two times a day for 3 months and other group received 100mg placebo capsule with the same dosage. The standard anti-diabetic therapy (metformin and glibenclamide, and nutritional regimen) was continued in both groups. The results indicated that FBG, HbA1c, total cholesterol and triglyceride levels in Juglans regia treated patients significantly decreased after 3 months compared with the baseline and with placebo group. Patients in Juglans regia group were significantly satisfied with Juglans regia treatment compared with the placebo group. No liver, kidney and other side effects were observed in the groups, except more GI events (specially a mild diarrhea) associated with extract treatment at the beginning of the study[248].

Fifty eight Iranian male and female patients with type 2 diabetes were enrolled in a clinical trial, received J. regia leaves extract for two months for determination of HbA1c and blood glucose level as a main outcome and insulin, SGOT, SGPT, and ALP level as secondary outcome. The results revealed that serum fasting HbA1C and blood glucose levels were significantly decreased and the insulin level was increased in patients in the *J. regia* group[249].

A pilot study was carried out to determine the efficacy and safety of walnut hydrosol (WH) in patients with type 1 diabetes. Eight patients with diabetes mellitus (DM) type 1 were enrolled in the study. They were advised to drink 250 ml WH after meals twice a day for four weeks. WH can control the glycemic level in people with diabetes, but it may be associated with minor and major side effects. The average daily blood sugar level and insulin dose decreased in seven subjects. Two subjects developed generalized pruritic erythematous skin rash. One patient presented hypoglycemic coma[250].

The effect of Juglans regia ethanolic leaf extract on lumbo-sacral spinal cord was evaluated in 18 and 20 days old fetus of diabetic mother rats. Female rats became diabetic by intraperitoneal injection of streptozotocin (50 mg/kg). In their first day of pregnancy, they received walnut leaf extract at a dose of 250 mg/ kg. After formation of the nervous system, two fetuses were obtained after anesthezing animals on 18^{th} and 20^{th} gestational days. The animals were euthanized, their birth weight were recorded and the lumbo-sacral spinal cord samples were taken and fixed. Significant decrease in the transverse diameter, vertical diameter, and the number of neurons in the spinal cord gray matter of the spinal cord at days 18 and 20 of pregnancy in the diabetic group compared to other groups was observed ($p \leq 0.05$) and a significant difference in the number of neurons in the spinal cord white matter was observed on day 18 of pregnancy ($p \leq 0.05$). The result confirmed the ameliorative effects of ethanolic extract of walnut leaves in controlling the metabolic disorders in diabetic pregnancy on the fetus's central nervous system[251].

Juniperus communis

Orally administered juniper decoction showed significant hypoglycemic activity in normal rats after single doses equivalent to 250-500mg juniper/kg and in streptozotocin-induced diabetic rats after 24-day treatment with doses equivalent to 125mg juniper/kg. The effects could be attributed to an increase in peripheral absorption of glucose, independent of plasma insulin levels[252-253].

Juniperus communis was evaluated for the antidiabetic and antihyperlipidemic activity on Streptozotocin(STZ)-nicotinamide induced diabetic rats. The methanolic extract of *Juniperus communis* (100 and 200mg/kg bw) was administered orally in diabetic rats. The extract showed significant ($P<0.01$) reduction in blood glucose levels total cholesterol, triglyceride, LDL, VLDL, with elevation of HDL levels in diabetic rats. The effects were dose dependent[254].

Juniperus Communis Lynn (JCL) (50, 100, 200 mg/kg JCL oil for 30 days were given to hypercholesterolemic rats to determine their o of hypolipidemic effects. The administration of cholesterol increased the TC level significantly with a significant increase in Ox-LDL levels, but the administration of JCL together with cholesterol prevented these changes[255].

Juniperus oxycedrus

The hypoglycaemic and antidiabetic activities ethanol and water leaves extracts of Juniperus oxycedrus subsp. oxycedrus (Joso), were evaluated using normal, glucose-hyperglycemic and streptozotocin-induced diabetic rats. Through in vivo bioactivity-guided fractionation processes, a nonpolar fraction was separated from the n-hexane subextract by silica gel column chromatography as the main active fraction. Subfractions of this fraction was found to possess antidiabetic activity and their chemical composition revealed that fatty acids, such as palmitic, linoleic and linolenic acid were the major compounds in subfractions[256-257].

The hypoglycaemic activity of Juniperus oxycedrus ssp, oxycedrus oils was investigated through the inhibition of α-amylase. The results revealed that oil obtained by hydrodistillation from *J. oxycedrus* ssp. *oxycedrus* wood exhibited α-amylase inhibitory activity with IC_{50} of 3.49 µl/ml[258].
The hypoglycaemic and antidiabetic activities ethanol and water leaves extracts of Juniperus oxycedrus subsp. oxycedrus (Joso), were evaluated using normal, glucose-hyperglycemic and streptozotocin-induced diabetic rats. Through in vivo bioactivity-guided fractionation processes, shikimic acid, 4-O-β-d-glucopyranosyl ferulic acid and oleuropeic acid-8-O-β-d-glucopyranoside were isolated from the n-butanol sub extract as the main active ingredient of the active subfraction. After 8 days administration of the major compound shikimic acid, blood glucose levels were decreased (24%), malondialdehyde levels in kidney tissues were decreased (63-64%) and liver enzymes (AST, ALT, ALP) of diabetic rats were significantly decreased[259].

Jussiaea repens

Ethyl acetate extract (50mg kg bw) reduced significantly the elevated glucose level of alloxan-diabetic rats in comparison with glibenclamide which proved its significant antidiabetic activity[260-261].

***Kochia scoparia* (*Bassia scoparia*)**

The methanolic extract of kochia scoparia was found to inhibit the increase in serum glucose-loaded rats. Through bioassay-guided separation, momordin Ic and its 2'-O-beta-D-glucopyranoside, with three new saponins named scoparianosides A, B, and C were isolated as the active principles. Momordin Ic and its 2'-O-beta-D-glucopyranoside, were found to potently inhibit glucose and ethanol absorption in rats[262-263].

II. Conclusion

Diabetes mellitus is one of the most common endocrine metabolic disorders. It caused significant mortality due to its complications. Medicinal plants possessed hypoglycemic effects by many mechanisms. The current review discussed the medicinal plants with antidiabetic effect with special focus on their mechanism of action.

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