REVIEW ARTICLE

Survey on Anti-Diabetic Plants in Kashmir [India]

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ABSTRACT

Plants and their derivatives have been used in the treatment of diabetics for thousands of years. Herbal plants are important in the management of diabetes mellitus especially in developing countries where the resources are meager. Diabetes is a silent killer that kills every 10 seconds. India is having the highest number of diabetics in the world. Traditional plants medicines or herbal formulations give a natural way to decrease the diabetic complications. Approximately 80% of the populations of third world countries are dependent on traditional therapies for their health care and has been recommended by WHO to include traditional medicines in the primary health care level of these countries.

Diabetes mellitus is a major endocrine disorder which can cause renal failure, diabetic neuropathy abnormal metabolic control and people with diabetes are likely to develop cardiovascular diseases like atherosclerosis. Efforts are ongoing to understand and manage diabetes mellitus because the disease and disease related complications are increasing day by day. In spite of presence of large number of medicines in the pharmaceutical market, remedies from medicinal plants are used with success to treat this disease. There has been great demand for plant products due to low cost, easy availability and lesser side effects. There are about 45 plants described in this review which clearly shows the importance of herbal plants in the treatment of diabetes mellitus especially in Kashmir (India) where people have very little knowledge about these plants. The effect of these plants may delay the development of diabetic complications and provide a rich source of antioxidants that are known to prevent/ delay different diseased states.

Keyword: Diabetes mellitus, antidiabetic plants

INTRODUCTION

Diabetes is a metabolic disorder of carbohydrates, proteins and fats due to deficiency of insulin secretion. In the whole world, about 5% of the general populations are suffering from diabetes and this disease is taking the lives of people more than AIDS. The countries where people are suffering from this disease are India, USA, China, Japan, Indonesia, Pakistan, Brazil, Russia, Italy and Bangladesh. It has been seen that every fourth person with diabetes is an Indian and India is known as the Diabetes Capital of the world. Urban population is mostly affected. Study from Sheri Kashmir Institute of Medical Sciences (SKIMS, Soura) show that 2.5 to 8 % of the population is suffering from diabetes and 25 -26.5% people are in the prediabetic stage. Several drugs are available to decrease hyperglycaemia but these drugs have side-effects. So the search for new drug/compound is essential to overcome the diabetic problems. It is still a challenge to medical community. Plant drugs and herbal formulations are considered to be very less toxic and with lesser side-effects than the synthetic ones [1,2,3] Indian traditional medicinal system Ayurveda and Unani system in particular claim to cure the diabetes with the use of natural substances[4]

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Acorus calamus (Family: Acoraceae)

Local name: Sweet flag, Bach, Gora Bach, Vai Gander

The anti-hyperglycemic activity of methanol extract of *Acorus calamus* (AC) rhizome in streptozotocin (STZ) induced diabetic rats has been studied. Oral Glucose Tolerance Test (OGTT) has been performed in normal rats. Male albino rats were made diabetic by STZ (40 mg/kg, intraperitoneally). 200mg/kg of AC extract was administered orally to diabetic rats for 21 days to determine the anti-hyperglycemic activity by estimating various biochemical parameters. Oral administration of AC methanol extract showed significant restoration of the levels of blood glucose level. After 21 days of treatment, blood glucose, lipid profile (total cholesterol, LDL and HDL- cholesterol), glucose 6- phosphatase, fructose 1,6 bisphosphatase levels and hepatic markers enzymes (aspartate

aminotransferase, alanine aminotransferase, alkaline phosphatise) were decreased when compared with diabetic control. Plasma insulin, tissue glycogen, glucose-6-phosphate dehydrogenase levels were increased significantly compared to diabetic control. Concurrent histopathological studies of the pancreas showed comparable regeneration by extract which were earlier necrosed by STZ. The results exhibited that AC methanol extract possess potent anti-hyperglycemic activity in normal and STZ induced diabetic rats and so might be of useful in the management of diabetes. The phyto-treatment showed more efficient anti-hyperglycemic effect than the standard drug glibenclamide [5]

***Allium species* (*Family*: Liliaceae)**

Local name: Onion, Garlic, Piyaz, Lahsan

S-allyl cysteine sulphoxide (SACS), a sulphur containing amino acid of *Allium sativum L* (Garlic) that is the precursor of allicin and garlic oil, has been found to show significant antidiabetic effects in alloxan diabetic rats. Administration of a dose of 200 mg/kg significantly decreased the concentration of serum lipids, blood glucose and activities of serum enzymes like alkaline phosphatase, acid phosphatase and lactate dehydrogenase and liver glucose-6-phosphatase. It significantly increased liver and intestinal HMG CoA reductase activity and liver hexokinase activity. Oral administration of SACS to alloxan diabetic rats for a month ameliorated the diabetic conditions of treated rats comparable with rats treated with glibenclamide and insulin. In addition, SACS controlled lipid peroxidation better than the other two drugs. Furthermore, SACS significantly stimulated *in vitro* insulin secretion from beta cells isolated from healthy rats. Hence the beneficial effects of SACS could be due to its antioxidant and its secretagogue actions. The former effect is predominant and the latter is only secondary. The effect of feeding a 15 mg % capsaicin diet or 3 % freeze dried onion powder containing diet produced a significant reduction in the hyperglycaemic status of diabetic animals. This study revealed that onion feeding improves the metabolic status in diabetes probably because of its hypocholesterolemic as well as its hypoglycaemic effect [6]

***Aralia cachemirica* (Family: Araliaceae)**

Local name: Aralia, Khoree

An aqueous and alcoholic extract of the roots of *Aralia cachemirica* were evaluated for hypoglycaemic activity in normal fasted and glucose induced hyperglycaemic rats. The aqueous and alcoholic extracts at a dose of 250 mg/kg showed statistically significant hypoglycaemic activity in glucose loaded animals, however, no effect was observed in normal fasted rats [7]

***Artemesia absinthium* (Family: Compositae)**

Local name: Sweet Sagewort, tethwan, worm wood

Artemesia absinthium administered in different doses (100,250 and 500 mg/kg) orally for 6 weeks. showed hypoglycaemic activity in normal and STZ induced diabetic rats. Blood sugar level, food intake and body weight changes were monitored periodically. At the end of the treatment period, the serum from diabetic animals was subjected to the estimation of lipid profile(high density lipoprotein, triglycerides and total cholesterol). Alanine transaminase (ALT), Aspartate tranaminase (AST), urea and creatinine and liver glycogen content was determined. Effect of *Artemisia absinthium* on glucose tolerance was carried out. A part of liver and pancreas was subjected to histopathological examination. *Artemisia absinthium* was found to produce significant hypoglycaemic activity in both normal and diabetic animals, which could be compared to Metformin (10 mg/kg).The food intake and body weight was increased with *Artemisia absinthium* treated diabetic rat. The elevated triglycerides, total cholesterol, ALT, AST, urea and creatinine levels were significantly reduced and high-density lipoprotein (HDL) levels were increased in diabetic rat after *Artemisia absinthium* treatment. The liver glycogen level was significantly increased. *Artemisia*

absinthium was found to increase the glucose tolerance. Histopathological examination showed that continuous treatment with *Artemisia absinthium* was found to produce the improved repair of the tissues after STZ induced injury. It was concluded that *Artemisia absinthium* can be effectively used in the treatment of diabetes mellitus [8]

Astragalus (Family: Leguminaceae)

Local name: Shatavani

The total of 136 early diabetic nephropathy patients were randomly divided into two groups. 50 cases in the conventional treated group and 86 in the extract treated group, the therapeutic course being 3 weeks. Levels of plasma endothein-1(ET-1), 24 hrs urinary albumin excretion rate (uAER),and platelet granule membrane protein (GMP-140), 6-keto-prostaglandin F1 alpha(6-keto-PGF 1 alpha), and thromboxane B2 (TXB2) before and after treatment were determined by radiommunoassay (RIA) and enzyme-linked immunosorbent assay (ELISA) respectively. Moreover, the above-mentioned criteria in 26 healthy subjects were also measured for control. The plasma ET-1, GMP-140, TXB2 and uAER levels in DN patients were higher, but keto-PGF1 alpha level was lower than those in healthy subjects. The above elevated criteria in diabetic nephropathy patients could be lowered by extract treatment. The pathogenesis and development of diabetic nephropathy might be closely associated with the changes of plasma ET-1 level and platelet function *Astragalus* could improve the above-mentioned changes in patients of early stage diabetic nephropathy.

In another study, the protective mechanism of *Astragalus* –IV (AGS-IV), a new glycoside of triterpene isolated from the root of *Astragalus* decreased the blood glucose concentration and HbAIC levels, and increases plasma insulin levels. AGS-IV increases the activity of glutathione peroxidase in nerves, depresses the activation of aldose reductase in erythrocytes, and decreases the accumulation of advanced glycation end products in both nerves and erythrocytes. Moreover, elevates Na+, K+ ATPase activity in both the nerves and erythrocytes of diabetic rats. These results indicate that AGS-IV exerts protective effects against the progression of peripheral neuropathy in STZ-induced diabetes in rats through several interrelated mechanisms [9, 10]

***Bauhinia variegate* (*Family*: Fabaceae)**

Local name: Orchid, Kachnara

Bauhinia variegate is a herbaceous medicinal plant, found throughout India. The leaves of the many *Bauhinia* species are used in antidiabetic treatments by many populations of the world. In India, stem bark is used as an antidiabetic in the Ayurvedic system of medicine.In in-vitro studies, the ethanolic extract of *B.variegate* and its major constituent, roseoside, have demonstrated enhanced insulin release from the beta-cell lines INS-I. Rats were divided into different groups. All normoglycaemic and hyperglycaemic rats orally received vehicle of the extract (distilled water) or *Bauhinia variegate* bark extract BVBE (200 and 400 mg/kg) or metformin (500mg/kg) as a reference standard for 7 days. Hyperglycaemia was induced in fasted rats by single intravenous dose of alloxan monohydrate. BVBE and metformin treatment significantly reduced the blood glucose levels in hyperglycaemic animals. The antihyperglycaemic effect of BVBE was comparable to metformin. Although the precise mechanism of the hypoglycaemic action of BVBE remains speculative, the extract may be acting like metformin [11]

***Berberis aristata* (Family: Berberidaceae,)**

Local name: Indian Berberry, Kashmiri Kawdach

Anti-hyperglycemic activity of root of *Berberis aristata* was studied in alloxan- induced diabetic rats. Five groups of albino Wistar rats were used each group having 6 rats. The two dose of 71.42 and 100mg/kg body weight ethanol extract of *B. aristata* were selected for anti-diabetic activity. Blood glucose levels were estimated in all the groups on 1st, 5th, 10th and 20th day of the treatment with *B. aristata*. The serum cholesterol, triglycerides, HDL, liver glycogen and

body weight were estimated on 20th day of treatment in all the groups compared against diabetic control group. The different extracts of root of *B. aristata* were also tested for glucose tolerance test in normal fasted rats. The ethanol extract of root of *B. aristata* 71.42 and 100mg/kg body weight showed a significant ($P<0.01$) reduction of serum glucose level in alloxan induced diabetic rats at 15th day as compared to diabetic control group. Cholesterol and triglycerides level were increased very significantly ($p<0.01$), in diabetic animal when compared with normal control group. The level of cholesterol and triglycerides reduced very significantly ($p<0.01$), when compared with diabetic control group. The level of HDL cholesterol was significantly ($p<0.05$) increased in the extract treated group when compared to diabetic control group. In oral glucose tolerance test, ethanol extract of *B. aristata* increase the glucose tolerance. It was observed that the ethanol extract of *B. aristata* possess anti-diabetic activity in alloxan induced diabetic rats [12]

***Brassica Juncea* (Family: Brassicaceae)**

Local name: Mustard, Sarsu

Hypoglycemic activity of *Brassica juncea* (seeds) aqueous extract at a dose of 250,350 and 450mg/kg body weight was evaluated on streptozotocin induced diabetic male albino rats. The serum insulin levels recorded a significant depletion in all groups, short term as well as long term diabetic animals, when compared to that of normal animals. A significant dosage dependent augmenting effect of the seed extract on the serum insulin was recorded in both short term as well as long term groups. The aqueous seed extract of *Brassica juneca* has potent hypoglycemic activity in male albino rat [13]

***Catharanthus roseus* (Family: Apocyanaceae)**

Local name: Vinca Periwinkle, Sadabahar

Oral administration of the aqueous fraction of an alcoholic extract of leaves of *Catharanthus roseus* led to marked lowering of glycaemia in normal and STZ induced diabetic rats. This effect was comparable with that of tolbutamide. Three suspension cultures of *C rosea* were obtained from three different cell lines. In the production medium, the first cell line produced 0.1% ajmalicine and the cell extract caused a 71% decrease in glycaemia in diabetic rats [14]

***Cichorium intybus* (Family: Asteraceae)**

Local name: chicory, Hand, Kasni.

Diabetes was induced in albino rat models with alloxan monohydrate (40 mg/kg) intravenously. Oxidative damage, impairment of oxidative defence and neuronal activity were investigated in cerebral hemispheres 48 hrs after alloxan administration. Diabetes caused an elevation of blood glucose, protein carbonyl content (PrC) and lipid peroxidation. The brain level of the antioxidant enzyme, catalase (CAT), reduced glutathione (GSH) and acetyl cholinesterase (AChE) exhibited significant decline in alloxan diabetes. Feeding with dried powder. leaves of *Cichorium intybus* decreased blood glucose level to near normal level. In another study, a dose of 125 mg of plant extract/kg body weight exhibits the most potent hypoglycaemic effect. Moreover, daily administration of *Cichorium intybus* (125 mg/kg) for 14 days to diabetic rats attenuates serum glucose by 20 %, triglycerides by 91% and total cholesterol by 16%. In addition, hepatic glucose-6-phosphatase activity markedly reduces by *Cichorium intybus* [15,16]

***Coriandrum sativum L* (Family: Umbelliferae)**

Local name: Coriander, Dhaniya

Coriandrum sativum L is grown as a spice crop all over the world. An ethanol extract of the seeds were investigated for effects on insulin release from the pancreatic beta cells in STZ induced diabetic rats. The results showed that administration of the ethanol extract (200 and 250 mg/kg,i.p) exhibited a significant reduction in serum glucose. Administration of STZ 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.The extract decreased serum glucose in STZ induced diabetic rats and increased insulin release from the beta cells of the pancreas[17]

***Cucumis sativus* (Family: Cucurbitaceae)**

Local name: Cucumber, Kheera

The different doses of ethanol extract were screened for their effects on serum glucose levels in STZ induced rats and lipid profile in blood were observed with histopathological studies. The oral administration of 200 and 400 mg/kg body weight of ethanol extracts of powder fruit of *Cucumis sativus* exhibited significant antidiabetic effects in STZ induced rats as compared to standard drug. In the same study the action of the extracts on diabetes induced hyperlipidemia was analyzed where the extracts significantly lowered the elevated cholesterol as well as LDL level. The drug has potential to act as antidiabetic as well as antihyperlipidemic. It was concluded that the ethanol extract at doses of 400 mg/kg body weight exhibited more significant antidiabetic activity [18]

***Daucus carota* (Family: Umbelliferae)**

Local name: Carrot, Gajar

Anti-oxidant agents have beneficial effects in diabetes mellitus. *Daucus carota* seeds extract has been shown to possess anti-oxidant activity. The effect of the methanolic extract of *Daucus carota* seeds on carbohydrate metabolism and morphology of pancreas was investigated in type I diabetic male rats. Diabetic rats were divided to 5 groups that received 100, 200 and 300 mg/kg of the extract, glibenclamide and distilled water daily for 6 days. Administration of all doses of *Daucus carota* seeds extract and glibenclamide for 6 days significantly decreased serum glucose levels, however, only 300 mg/kg of the extract as well as glibenclamide significantly increased insulin serum levels. *Daucus carota* seeds extract has hypoglycaemic effect by increasing insulin secretion and improvement of the pancreas.

In another study, male swiss mice were orally loaded with glucose after the extracts of *Daucus carota* had been given by oral loading. The extract of *Daucus carota* was prepared by boiling the dried material with water or macerating it with 80% ethanol. It was shown that the extract improved the glucose tolerance [19]

***Dioscorea dumetorum* Linn (Family: Dioscoraceae)**

Local name: Dioscorea, Kreench

The aqueous fraction of the methanolic extract of *Dioscorea dumetorum Linn* has an hypoglycaemic effect in healthy and alloxan diabetic rabbits when administered i.p (20 mg/kg). At a dose of 20 mg/kg, the fasting blood sugar in normoglycemic rabbits reduces from 112 mg/100 ml to 55 mg/100 ml after 4 hours. In alloxan diabetic rabbits, the blood sugar lowers from 520 mg/100 ml to 286 mg/ml at the same time interval. The aqueous fraction of the methanol extract produces comparable effects at 100 mg/kg. The hypoglycaemic effects are compared to those of tolbutamide [20, 21]

***Ephedra elata* (Family Ephedraceae)**

Local name: Ephedra, Ma Haung

Oral administration of an extract obtained from *Ephedra elata* to normoglycaemic rats produced a persistent hypoglycaemic effect when compared to Daonil [22]

***Equisetum myriochaetum (*Family: Equisetaceae)**

Local name: Mexican Giant Horsetail

The hypoglycemic effect of water as well as butanolic extracts prepared from aerial parts of *Equisetum myriohaetum* (Equisetaceae) were examined in streptozotocin induced diabetic rats. A single oral administration of the water extract (WE) at doses of 7 and 13 mg/kg and of the butanol extract (BE) at doses of 8 and 16 mg/kg significantly ($p < 0.001$) lowered the plasma glucose levels in diabetic rats after three hours of the administration. As a reference drug glibenclamide showed, at a dose of 3mg/kg, similar hypoglycemic effect like the tested extracts [23]

***Gentianalutea* (Family: Gentianaceae)**

Local name: Yellow Gentian

Gentiana lutea is a herbal species with a long term use in traditional medicine. The free radical scavenging activity of methanolic extracts of yellow gentian leaves and roots in two different systems using electron spin resonance (ESR) spectrometry were studied. Assays were based on the stable free radical 1,1- diphenyl-2-picrylhydrazyl (DPPH) and the superoxide radicals generated by the xanthine/ xanthine oxidase (X/XO) system. The results of gentian methanolic extracts were compared with the antioxidant capacity of synthetic antioxidant butylated hydroxyanisole (BHA).The study proved that yellow gentian leaves and roots exhibit considerable antioxidant properties expressed either by their capability to scavenge DPPH or superoxide radicals. This activity could also prove useful in the treatment of diabetes [24]

Ginkgo biloba (Family: Gingoaceae)

Local name: Maiden hair tree

Albino wistar rats with streptozotocin induced diabetes were divided into four groups of 10 animals each. Gum acacia, troglitazone 36 mg/kg. Ginkgo biloba 50 mg/kg and 100 mg/kg were administered to group I (control), group II (Standard),group III and group IV respectively. After 10 and 15 days of drug administration fasting blood sugar (FBS), blood glutathione (GSH) and serum ceruloplasmin were estimated. *Ginkgo biloba* in a high dose of 100 mg/kg produced a significant reduction in FBS of 31% and increase in blood GSH (57.6%) that is however much less than the fall in FBS produced by troglitazone (47%). However treatment with troglitazone and *Ginkgo biloba* at both doses did not alter the serum ceruloplasmin levels significantly. It was observed that the antidiabetic activity of *Ginkgo biloba* may be attributed to its antioxidant activity without having a role in metal ion mediated lipid peroxidation [25]

Hibiscus rosa sinensis **(Family: Malvaceae)**

Local name: Shoe Flower, Jasund, Urhul, Gudhal

The antidiabetic and antioxidant activity of *Hibiscus rosa sinensis* was evaluated against STZ induced diabetic rats. The hypoglycaemic activity of *Hibiscus rosasinensis* extract was investigated in a dose dependent manner such as (125, 250 and 500 mg/kg b.w) by evaluating various biochemical parameters. The levels of blood glucose, carbohydrate metabolizing enzymes, TBARS, enzymatic and non-enzymatic antioxidants and lipid profiles were found to be significantly increased in diabetic rats when compared to control groups. Administration of extract in the treated groups showed altered changes in the above mentioned parameters and found that among the three doses, 250 mg/kg showed best result when compared to other two doses. It shows that *Hibiscus rosasinensis* possess antioxidant, hypoglycaemic and hypolipidemic activity against STZ induced diabetic rats [26]

Juniper Berries (Family: Cupressaceae)

Local name: Common juniper

The hypoglycaemic activity of a decoction from juniper berries was studied in both in normoglycemic and in STZ diabetic animals. Juniper decoction decreases glycemic levels in normoglycemic rats at a dose of 250 mg/kg. The administration of the decoction (125 mg total berries/kg) to STZ-diabetic rats for 24 days results in a significant reduction both in blood glucose levels and in the mortality index, as well as the prevention of the loss of body weight. This effect seems to be mediated by the peripheral action of juniper [27]

Lycium Barbarum **(Family Solanaceae)**

Local name: Wolfberry, gogi berry.

The hypoglycaemic activity of polysaccharide extracted from *Lycium barbarum* (LBP) was evaluated. The various parameters studied included body weight (b w) fasting blood glucose levels (FBG), total cholesterol (TC) and triglyceride (TG) in diabetic and

normal mice. LBP treatment (20, 40 mg/kg body weight) for 28 days resulted in a significant decrease in the concentration of FBG, TC, TG in diabetic mice. Furthermore, LBG significantly increased body weight. The data demonstrated LBP at the dose of 40mg/kg b.w exhibited the better effect [28]

***Marrubium vulgare* (*Family*: Labiateae)**

Local name: Gand Soi

Marrubium vulgare is used in traditional medicine in some countries such as Mexico in the treatment of diabetes. On the other hand, some studies reported the anti-oxidant effect of the extract due to its flavonoid content. The anti-diabetic activity of a daily single oral dose of 500mg/kg day of *M. vulgare* for 28 days was evaluated by measuring the fasting blood glucose and the peak of blood glucose level within 120 min of oral glucose tolerance test (OGTT) in diabetic rats. In addition, the effect of the extract on blood plasma insulin was measured as well as its effect on tissue glucogen contents in muscles and liver. *M. Vulgare* significantly reduced the blood glucose level. Furthermore, the extract of *M vulgare* showed significant increase in plasma insulin and tissue glycogen contents. The antidyslipidemic effect was demonstrated by a significant reduction in plasma total cholesterol (TC), triglycerides (TG), and low density lipoprotein-cholesterol (LDL-C),while the cardio-protective lipid high density lipoprotein (HDL-C) was increased. It was concluded that methanolic extract of *M. Vulgare* has antihyperglycemic with antidyslipidemic effect. The protective effect of the extract may be due to its antioxidant activity [29]

***Momordica charantia* (Family: Cucurbitaceae)**

Local name: Bitter gourd, Karela

Momordica charantia commonly known as bitter gourd or karela is a medicinal plant used in Ayurveda for treatment of diabetes mellitus. Various extract powders of the fresh and dried whole fruits have blood glucose lowering effect comparable to that of glibenclamide, a known synthetic drug. The aqueous extract powder of *Momordica charantia*, an edible vegetable, appears to be a safe alternative to reducing blood glucose. Charantin, isolated from M. Charantia fruits, produces prolonged hypoglycemia in varying doses in normal fasting rabbits, the fall being gradual and steady for 4 h and then recovering slowly. Charantin is found more active than equivalent doses of tolbutamide, and it was suggested that charantia acts at pancreatic as well as at extra pancreatic site [30]

***Morus alba* (Family: Moraceae)**

Local name: Mulberry,Tul

The effect of the methanol and aqueous extracts of *Morus alba* leaves was observed on fasting blood sugar levels in STZ induced diabetic rats. The methanolic and aqueous extracts significantly reduced the blood glucose levels in STZ induced diabetic rats. The antidiabetic activity of methanolic extract observed was better compared to same dose of aqueous extract. In diabetic albino rats, maximum percentage reduction was found to be 18.88 % and 9.91 % respectively for methanolic and aqueous extracts [31]

***Myristica fragrans* (Family : Myrtaceae)**

Local name: Nutmeg, Jaiphal

The hypoglycaemic and anti-diabetic activity of seeds of *Myristica fragrans* in normoglycaemic and alloxan-induced diabetic rats were evaluated. The petroleum ether extract of *Myristica fragrans* (PEMF) was administered orally in normal fasted, glucose fed (1.5 g/kg, p.o.) and alloxan (120 mg/kg, s.c.) –induced diabetic rats. The blood glucose levels were estimated. In addition, changes in body weight, organ (liver, kidney and pancreas) weight, serum lipid profile and blood parameter hemoglobin erythrocytes and different leukocytes) were assessed after two weeks in the extract treated diabetic rats. It has been found that, oral pre-treatment with PEMF at dose of 200mg/kg induced a significant ($p< 0.05$) decrease in blood glucose level,; i)from 56.5±3.19 (0 h) to 49.75±2.05 mg% (4 h) in normoglycaemic rats ii) from 145.75±9.65 to 81.5±4.03mg% in oral glucose tolerance test (OGTT) at ½ h compared to control

glucose fed rats, iii) from 305.8 ± 12.49 to 276.6 ± 6.11mg% after single dose treatment and from 326.25±7.05 to 268.0±9.6 mg% in alloxan-induced diabetic rats after daily treatment of PEMF for two weeks. After two weeks daily administration of PEMF, diabetic treated rats showed improvement in body weight, organ (liver and pancreas) weight, lipid profiles and haemoglobin content as compared to diabetic control rats. Thus *Myristica fragrans* possesses potential as an anti-diabetic [32]

Polygonatum officinale **Family: Liliaceae)**

Local name: Solomons seal

The hypoglycaemic effect of the rhizomes of *Polygonatum officinale* was investigated in both normal and streptozotocin-induced diabetic mice. The methanol extract of rhizomes of *Polygonatum officinale* (PO) (800 mg/kg) reduced the blood glucose of normal mice from 170+/- 3 to 136 +/- 5mg/100 ml 4 hours after intraperitoneal administration ($p<0.001$), and also significantly lowered the blood glucose of streptozotocin-induced diabetic mice from 696+/- 60 to 407+/-35mg/100ml under similar conditions ($p<0.01$). PO also suppressed epinephrine-induced hyperglycemia in mice. In addition, the n-butanol fraction of the methanol extract elicited a significant decrease in the blood glucose level of streptozotocin-induced diabetic mice after 4 hours ($p<0.05$) [33]

Psidium guajava **(Family: Myrtaceae)**

Local name: Guava, Amrud.

The anti-diabetic properties of an ethanol extract of the stem bark of *Psidium guajava* has been used to control diabetes in Indian System of Medicine. The anti- hyperglycaemic activity of this plant on blood glucose levels of normal, normal glucose loaded (OGTT) and alloxan-induced hyperglycaemic rats was evaluated. The results showed that ethanol stem bark extract exhibited statistically significant hypoglycaemic activity in alloxan-induced hyperglycaemic rats but was devoid of significant hypoglycaemic effect in normal and normal glucose loaded rats (OGTT)[34]

Punica granatum **(Family: Punicaceae)**

Local name: Pomegranate, Anar

The hypoglycaemic activity of *Punica granatum* Linn seed extract on rats made diabetic by streptozotocin (STZ) was investigated. The methanol extract of the seed at doses of 300 and 600 mg/kg, and chlorpropamide 200 mg/kg was administered to STZ diabetic rats. The seed extract (150,300, and 600 mg/kg, orally) caused a significant reduction of blood glucose levels in STZ induced diabetic rats by 47% and 52%, respectively, at the end of 12 h [35]

Salvia lavandulifolia (Family: Lamiaceae)

Local name: Spanish Sage

The hypoglycaemic activity of infusions and suspensions of *Salvia lavandulifolia* was studied in normoglycemic, hypoglycaemic and alloxan diabetic rabbits. Variations in circulating levels of insulin were also studied in normoglycemic animals. The greatest decrease in glucose levels (17-18%) were obtained with doses. 0.250 mg/kg in normoglycemic rabbits. In glucose induced hyperglycemia, antidiabetic activity was seen only when the *Salvia* infusion was administered simultaneously with glucose. In alloxan- diabetic rabbits, the daily administration of 0.250 mg/kg of infusion resulted in a 33% decrease in blood glucose levels [36]

Saussurea lappa (Family Asteraceae)

Local name: Costus root, Kuth, Kutha, Kut

The alcoholic extract of the root of *Saussurea lappa* were used on albino rats to investigate its effect on liver glycogen, blood glucose and plasma insulin. Treatment up to 7 days shows a significant hypoglycaemic response without an increase in plasma insulin [37]

Smilax glabra (Family: Smilacaceae)

Local name: Chinaroot, sarsaparilla

The hypoglycemic effect of the rhizomes of *Smilax glabra* was investigated in normal and KK-Ay mice, one of the animal models of non-insulin dependent diabetes mellitus (NIDDM) with hyperinsulinemia. The methanol extract of rhizomes of *Smilax glabra* (100mg/kg body weight) reduced the blood glucose of

normal mice 4 h after intraperitoneal administration ($p<0.05$), and also significantly lowered the blood glucose of KK-Ay mice under similar conditions ($p<0.001$). *Smilax glabra* suppressed epinephrine-induced hyperglycemia in mice. *Smilax glabra* treated KK-Ay mice significantly decreased the blood glucose in an insulin tolerance test. The hypoglycemic effect of *Smilax glabra* raised insulin sensitivity [38]

***Swertia Species* (Family: Gentianaceae)**

Local name: Swertia

The hypoglycaemic activity of an aqueous ethanolic extract of *Swertia japonica* and its ethyl acetate, n-butanol, water soluble fractions, together with ether soluble and insoluble fractions of ethyl acetate soluble fraction was observed in streptozotocin induced hyperglycaemic rats. It was found that an aqueous ethanolic extract was more effective than a mixture of tolbutamide and buformine, and an ethanolic extract of another species of this plant, *S. chirayita* in lowering the blood glucose level. Furthermore, an ethyl acetate soluble fractions of *S. japonica* and its ether insoluble fraction showed a potent hypoglycaemic activity. It was also observed that the hexane fraction of *S. chirayita* shows hypoglycaemic activity and this is due to insulin releasing activity[39,40,41]

***Syzygium cumini* (Family: Myrtaceae)**

Local name: Clove, Laung

The ethanolic extract of seeds is *S. cumini* increased body weight and decreased blood sugar level in alloxan diabetic albino rats. Level of significance for decrease in blood sugar after feeding alcoholic extract of *S. cumini* seeds in various doses was highly significant. The extract feeding showed definite improvement in the histopathology of islets. The most important finding is that the blood sugar level, which once dropped to normal levels after extract feeding was not elevated when extract feeding was discontinued for 15 days. Oral administration of 2.5 and 5.0 g/kg body weight of the aqueous extract of the seed for 6 weeks results in significant reduction in blood glucose and an increase in total haemoglobin, but in the case of 7.5 g/kg body weight the effect is not significant. The aqueous extract also decreases free radical formation which clearly shows the antioxidant property. Thus the study shows that *Syzigium cumini* seed extract has hypoglycaemic action [42, 43]

***Tribulus terrestris* (Family: Zygophyllaceae)**

Local name: Small Caltrops, Chota Gokhru

The methanol extract of *Tribulus terrestris* significantly decreases fasting glucose level in diabetic rats. After 4 and 6 hrs it shows significant reduction in glucose level. It also shows significant decrease in the levels of glycosylated haemoglobin, total cholesterol, triglycerides and LDL-cholesterol [44]

***Trigonella foenum graecum* (Family: Papillionaceae: Flabaceae)**

Local name: Fenugreek, methi

In insulin dependent diabetic patients, the fenugreek diet significantly reduced fasting blood glucose and improved the glucose tolerance test. There was a 54 % reduction in the 24 hr urinary glucose excretion. The results showed the usefulness of fenugreek seeds in the management of diabetes. Oral administration of *T. foenum graecum* to healthy and alloxan induced diabetic rats (2 and 8 g/kg) produced a significant fall in blood glucose level (BGL) both in the normal as well as diabetic rats. The hypoglycaemic effect was dose related. On the other hand, the aqueous extract of fenugreek leaf when given to both healthy and alloxan diabetic rats, produced a significant reduction in BGL. However, an ethanolic extract of fenugreek leaf produced no reduction in BGL in healthy rats but i.p administration of 0.8 gm/kg of the ethanolic leaf extract to diabetic rats produced a significant reduction of BGL. When steroid saponins extracted from the seed of fenugreek were administered chronically mixed with food (12.5 mg/day per 300 gms body weight) to healthy and STZ induced diabetic rats, food intake and the motivation to eat in healthy rats were significantly increased and the food consumption in diabetic rats was also stabilized. In both healthy and diabetic rats,

steroid saponins decreased total plasma cholesterol without any change in triglycerides. It has been shown that the disrupted free radical metabolism in diabetic animals may be normalized by fenugreek seed supplementation in the diet. Moreover, fenugreek significantly decreased the blood glucose levels [45,46]

***Vinca rosea* (*Family*: Apocyanaceae)**

Local name: Periwinkle, Sadabahar

The anti-diabetic activity of *Vinca rosea* methanolic whole plant extracts in alloxan induced diabetic rats for 14 days were evaluated. The methanolic whole plant extracts at high dose (500mg/kg) exhibited significant anti-hyperglycaemic activity than whole plant extract at low dose (300mg/kg) in diabetic rats. The methanolic extracts also showed improvement in parameters like body weight and lipid profile as well as regeneration of B-cells of pancreas in diabetic rats. Histopathological studies reinforce the healing of pancreas, by methanolic *Vinca rosea* extracts, as a possible mechanism of their anti-diabetic activity [47]

***Vitis vinifera* (Family: Vitaceae)**

Local name: Common grapevine, Kawdach

Diabetic peripheral neuropathy (DPN) is one of the most common diabetic chronic complications. Grape seed proanthocyanidins extracts (GSPE) as therapeutic agents against DPN were studied in STZ induced diabetic rats. GSPEs (250mg/kg body weight/d) were administered to diabetic rats for 24 wk. Motor nerve conductive velocity (MNCV) and mechanical hyperalgesia were determined in the rats. Serum glucose, glycated haemoglobin, advanced glycation end products (AGEs), and tissue malondialdehyde (MDA) and superoxide dismutase (SOD) were determined. GSPE significantly increased the MNCV, mechanical hyperalgesia and SOD of diabetic rats associated nerval damage. This study provided a new recognition of natural medicine for the treatment of DPN[48]

***Withania somnifera* (Family: Solanaceae)**

Local Name: Winter Cherry, Ashwagandh

Withania somnifera is an important medicinal plant, which is used in traditional medicine to cure many diseases. Hypoglycaemic and hypolipidaemic effects of root and leaf extracts WSREt and WSLEt were also investigated in alloxan induced diabetic rats. WSREt and WSLEt and the standard drug glibenclamide were orally administered daily to diabetic rats for eight weeks. After the treatment period, urine sugar, blood glucose, haemoglobin (Hb), glycosylated haemoglobin(HbA1C), liver glycogen, serum and tissue lipids, serum and tissue proteins, liver glucose-6-phosphatase (G6P) and serum enzymes like aspartate tranaminase (AST), alanine transaminase (ALT), acid phosphatase (ACP) and alkaline phosphatase (ALP) levels were determined. The levels of urine sugar, blood glucose, HbA1C, G6P, AST, ALT, ACP, ALP, serum lipids except high density lipoprotein bound Cholesterol (HDL-c) and tissues like liver, kidney and heart lipids were significantly increased, however Hb, total protein, albumin, albumin- globulin (A-G) ratio, tissues protein and glycogen were significantly decreased in alloxan induced diabetic rats. Treatment of the diabetic rats with WSREt, WSLEt and glibenclamide restored the changes of the above parameters to their normal level after eight weeks of treatment, indicating that WSREt and WSLEt possess hypoglycaemic and hypolipidaemic activities in alloxan induced diabetes mellitus(DM) rats [49]

***Zea mays* (*Family*: Gramineae)**

Local name: Maize, Makkai

The effect of corn silk-*Zea mays* on glycaemic metabolism was studied in alloxan and adrenaline induced hyperglycaemic mice. The effect of corn silk on blood glucose, glycohaemoglobin, (HbAIc) insulin secretion, damaged pancreatic beta cells, hepatic glycogen and gluconeogenesis in hyperglycaemic mice were studied. After the mice were orally administered with corn silk extract, the blood glucose and HbAIc were significantly decreased in alloxan induced hyperglycaemic mice, while the level of insulin secretion was markedly elevated in alloxan

induced hyperglycaemic mice. The alloxan damaged pancreatic beta cells of the mice were partly recovered gradually after the mice were administered with corn silk extract 15 days later. Also, the body weight of the alloxan induced hyperglycaemic mice was increased gradually. However, it also increased the levels of hepatic glycogen in alloxan induced hyperglycaemic mice. Corn silk extract markedly reduced hyperglycaemia in alloxan induced diabetic mice. The action of corn silk extract on glycaemic metabolism was by increasing insulin level as well as recovering the injured beta cells. The results show that corn silk extract may be used as a hypoglycaemic food or medicine for hyperglycaemic people in terms of this modern pharmacological study [50]

***Zingiber officinale* (Family: Zinzeberaceae)**

Local name: Ginger, Adrak

The hypoglycaemic effects of *Zingiber officinale* dried rhizomes ethanol extract (ZOE) in mice and rats were studied. Hypoglycaemic effects of the plant extract were investigated in rats, using streptozotocin (SIZ)-induced diabetes mellitus models. Chlorpropamide (250 mg/kg) was used as reference drug for comparison. ZOE (50-800mg/kg i.p) produced dose-dependent, significant ($p<0.05$-0.001) hypoglycaemic effect in normal (normoglycaemic) and diabetic rats which indicate that *Zingiber officinale* rhizomes ethanol extract possesses hypoglycaemic properties [51, 52]

CONCLUSION

Scientific validations of several Indian plant species have proved the efficacy of herbal drugs in treating hyperglycemia. This needs further exploration for necessary development of drugs from natural sources. Diabetes is becoming the third killer of the health of mankind along with cancer, cardiovascular and cerebrovascular diseases because of high prevalence, morbidity and mortality. Laboratories are conducting research on the medicinal plants in a scientific manner for the development of alternative drugs and strategies for the better management of diabetes. The main aim of the present review was to collect the available data on medicinal plants with antidiabetic and hypoglycaemic effect with reference to Jammu and Kashmir which may be useful to researchers as well as practitioners.

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CONFLICT OF INTEREST STATEMENT

We declare that we have no conflict of interest.

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