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Potent Indian herbs used for the cure and management of Diabetes

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Abstract: Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar levels. The global prevalence of diabetes is estimated to increase, from 4% in 1995 to 5.4% by the year 2025. The World Health Organization (WHO) has predicted that the major burden will occur in developing countries. The WHO has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called as botanical garden of the world. The current review focuses on medicinal plants used in the treatment of diabetes mellitus, a major crippling disease in the world leading to huge economic losses.

Keywords: Medicinal plant, Diabetes, Antidiabetic, Indian

Introduction:

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter.[1] A number of medicinal plants, traditionally used for over 1000 years named rasayana are present in herbal preparations of Indian traditional health care systems.[2] In Indian systems of medicine most practitioners formulate and dispense their own recipes.[3]

Diabetes mellitus is a chronic metabolic disorder of impaired carbohydrates, fat and protein metabolism, characterized by hyperglycemia, polyuria, polydipsia and weight loss, polyphagia, glycosuria, ketosis and acidosis which is due to insulin deficiency or insulin resistance which results in decrease utilization of carbohydrate and excessive glycogenolysis and gluconeogenesis from amino acid by fatty acids.[4, 5] The prevalence of diabetes is 6.4%, affecting 285 million adults, in 2010 and will increase to 7.7% and affecting the 439 million adults by 2030.[6] Chronic hyperglycemia often leads to microvascular complications that includes nephropathy, retinopathy, neuropathy and macrovascular complications that includes coronary artery disease, leading to myocardial infarction (heart attack) or angina, stroke (mainly ischemic type), peripheral vascular disease, which contributes to intermittent claudication (exertion-related foot pain) as well as diabetic foot and these complications leads to significant morbidity and mortality in patients with diabetes.[7-11] Diabetic nephropathy has been reported to occur in 25–40% of peoples with type I or type II diabetes and it increases by 6% per year[12] [9], where as diabetic neuropathy occurs in 50% to 66% of diabetic patients[13-16] while diabetic retinopathy with 5% is the fifth leading cause of blindness worldwide.[17]

It is a complex metabolic disorder resulting from either insulin insufficiency or insulin dysfunction. Type I diabetes (insulin dependent) is caused due to insulin insufficiency because of lack of functional beta cells. Patients suffering from this are therefore totally dependent on exogenous source of insulin while patients suffering from Type II diabetes (insulin independent) are unable to respond to insulin and can be treated with dietary changes, exercise and medication. Type II diabetes is the more common form of diabetes constituting 90% of the diabetic population. Symptoms for both diabetic conditions may include: (i) high levels of sugar in the blood; (ii) unusual thirst; (iii) frequent urination; (iv) extreme hunger and loss of weight; (v) blurred vision; (vi) nausea and vomiting; (vii) extreme weakness and tiredness; (viii) irritability, mood changes etc.[18]

Though pathophysiology of diabetes remains to be fully understood, experimental evidences suggest the involvement of free radicals in the pathogenesis of diabetes[18] and more importantly in the development of

diabetic complications.[19-21] Free radicals are capable of damaging cellular molecules, DNA, proteins and lipids leading to altered cellular functions. Many recent studies reveal that antioxidants capable of neutralizing free radicals are effective in preventing experimentally induced diabetes in animal models as well as reducing the severity of diabetic complications.[21-23]

Indian Medicinal Plants with Antidiabetic Effects:

Herbal medicines are the medicinal products that contain plant materials as their pharmacologically active components.[24] Medicinal plants are important for pharmacological research and drug development, not only when plant constituents are used directly as therapeutic agents, but also as starting materials for the synthesis of drugs or as models for pharmacologically active compounds. Herbal drugs are of three types based on the nature of the active metabolites. Drugs used in crude form are the first category. The active constituents isolated after the processing of plant extracts represent the second category of herbal drugs. These are pure molecules and generally pharmacologically more active. Herbal drugs for which data on acute and chronic toxicity studies in animals is available represent the third type.[25] It is estimated that about 25% of the drugs prescribed worldwide are derived from plants and 121 such active compounds are in use. Nearly 80% of African and Asian population depends on traditional medicines for their primary healthcare.[26] In India, about 80% of the rural population uses medicinal herbs or indigenous systems of medicine.[27]

Generally, in traditional medicine in Asian countries, many herbal drugs are combined in the form of a multi-herbal formula to enhance their functions. The herbal constituents are selected to emphasize the therapeutic actions or to reduce the toxicity or side effects of compounds from other herbal species in the mixture.[28] Oral hypoglycaemic agents like sulphonylureas and biguanides are still the major players in management of the disease but there is growing interest in herbal remedies due to side effects associated with the oral hypoglycaemic agents.[29] Nowadays, the use of complementary alternative medicine and

especially the consumption of botanicals have been increasing rapidly worldwide, mostly because of the less frequent side effects when compared to modern western medicine. Therefore there is a need to search more effective and safe herbal drugs for diabetes and its complications.[30, 31]

There are many herbal remedies suggested for diabetes and diabetic complications. Medicinal plants form the main ingredients of these formulations. A details of medicinal plants with antidiabetic and related beneficial effects is given bellow.

Allium cepa: (onion)

Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits. Allium cepa is also known to have antioxidant and hypolipidaemic activity. Administration of a sulfur containing amino acid from Allium cepa, S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) to alloxan induced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues and normalized the activities of liver hexokinase, glucose 6-phosphatase and HMG Co A reductase.[32, 33] When diabetic patients were given single oral dose of 50 g of onion juice, it significantly controlled post-prandial glucose levels.[34]

Allium sativum: (garlic)

This is a perennial herb cultivated throughout India. Allicin, a sulfur-containing compound is responsible for its pungent odour and it has been shown to have significant hypoglycemic hypoglycemic activity.[35] This effect is thought to be due to increased hepatic metabolism, increased insulin release from pancreatic beta cells and/or insulin sparing effect.[36] Aqueous homogenate of garlic (10 ml/kg/day) administered orally to sucrose fed rabbits (10 g/kg/day in water for two months) significantly increased hepatic glycogen and free amino acid content, decreased fasting blood glucose, and triglyceride levels in serum in comparison to sucrose controls.[37]

Aster koraiensis:

Aster koraiensis is widely distributed in the southern and the central part of Korean peninsula and Jeju Island. This herb has also

been utilized as pot plant, vegetable and medicinal plants in traditional Korean medicine for a variety of medical purposes, such as pertussis, chronic bronchitis and pneumonia.[38, 39] Oral administration of ethanolic extract of aerial parts of Aster koraiensis at a dose of 100, 200 mg/kg per day for 13 weeks in streptozotocin induced diabetic rats showed significant reduction in proteinuria and albuminuria and also prevented advanced glycation end products (AGEs) deposition and podocyte apoptosis. Furthermore expression of Bax and Bcl-2 (B-cell lymphoma 2) protein were restored by Aster koraiensis extract treatment in the renal cortex. Therefore results suggested that Aster koraiensis extract has an inhibitory effect of advanced glycation end products (AGEs) accumulation and anti-apoptotic effect in the glomeruli of diabetic rat. Aster koraiensis extract could be beneficial in preventing the progression of diabetic nephropathy.[40]

Aloe vera and Aloe barbadensis:

Aloe, a popular houseplant, has a long history as a multipurpose folk remedy. The plant can be separated into two basic products: gel and latex. Aloe vera gel is the leaf pulp or mucilage, aloe latex, commonly referred to as "aloe juice," is a bitter yellow exudate from the pericyclic tubules just beneath the outer skin of the leaves. Extracts of aloe gum effectively increases glucose tolerance in both normal and diabetic rats.[41] Treatment of chronic but not single dose of exudates of Aloe barbadensis leaves showed hypoglycemic effect in alloxanized diabetic rats. Single as well as chronic doses of bitter principle of the same plant also showed hypoglycemic effect in diabetic rats. This action of Aloe vera and its bitter principle is through stimulation of synthesis and/or release of insulin from pancreatic beta cells.[42] This plant also has an anti-inflammatory activity in a dose dependent manner and improves wound healing in diabetic mice.[43]

Azadirachta indica: (Neem)

Hydroalcoholic extracts of this plant showed antihyperglycemic activity in streptozotocin treated rats and this effect is because of increase in glucose uptake and glycogen deposition in isolated rat hemidiaphragm.[44, 45] Apart from having anti-diabetic activity, this plant also has anti-bacterial, antimalarial, antifertility, hepatoprotective and antioxidant effects.[46]

Artemisia dracunculus:

Artemisia dracunculus or Russian tarragon is a perennial herb that belongs to the Asteraceae family. Many edible and medicinal uses have been attributed to this species and it is commonly used for flavoring food in many traditional recipes.[47] An ethanolic extract of Artemisia dracunculus L. having antidiabetic activity was examined as a possible aldose reductase (ALR2) inhibitor, a key enzyme involved in diabetic complications that is caused by the enhanced activation of the polyol pathway during hyperglycemia. The four compounds such as 4, 5-di-O-caffeoylquinic acid, davidigenin, 6-demethoxycapillarisin and 20, 40-dihydroxy-4-methoxydihydrochalcone was isolated from the Artemisia dracunculus that inhibit the activity of ALR2. At 3.75µg/mL, the ethanolic extract of A. dracunculus shoots inhibited the human recombinant ALR2 enzyme activity and therefore evaluates its potential for treatment of diabetic complications.[48]

Acacia arabica: (Babhul)

It is found all over India mainly in the wild habitat. The plant extract acts as an antidiabetic agent by acting as secretagouge to release insulin. It induces hypoglycemia in control rats but not in alloxanized animals. Powdered seeds of Acacia arabica when administered (2,3 and 4 g/kg body weight) to normal rabbits induced hypoglycemic effect by initiating release of insulin from pancreatic beta cells.[49]

Aegle marmelos: (Bengal Quince, Bel or Bilva)

Administration of aqueous extract of leaves improves digestion and reduces blood sugar and urea, serum cholesterol in alloxanized rats as compared to control. Along with exhibiting hypoglycemic activity, this extract also prevented peak rise in blood sugar at 1h in oral glucose tolerance test.[50]

Bacopa monnieri:

Bacopa monnieri Linn is belong to a family Scrophulariaceae (vernacular; Brahmi), is an annual creeping plant and it is found throughout India, Nepal, Srilanka, China and Taiwan. Oral administration of aqueous ethanolic extract of whole plant of Bacopa monnieri to diabetic rats at a dose of 50, 125 and 250mg/kg body weight once a day for 15 days showed significant retrogression of disturbed antioxidant status and peroxidative

damage and hence reveals its potential to play a crucial role in defence against free radicals. Significant increase in SOD (Superoxide dismutase activity), CAT (Catalase activity), GPx (Glutathione peroxidase) activity and levels of GSH (Reduced glutathione) and reduction in the level of MDA (Malondialdehyde) was observed in extract treated diabetic rats. Thus, Bacopa monneiri appears to have a potential to inhibit the neuronal and renal complications due to diabetes.[51]

Corni fructus:

Corni fructus comprised the major iridoid glycosides, loganin and morroniside and loganin containing iridoid glycoside exhibited a renoprotective effect in streptozotocin-induced type 1 diabetic rats.[52] Loganin was isolated from Corni fructus and it has been shown that oral admintration of loganin to diabetic mice at a dose of 20 or 100 mg/kg body weight daily for 8 weeks exhibits protective effects against hepatic injury and diabetic complications associated with abnormal metabolic states and inflammation caused by oxidative stress and advanced glycation end product formation. Loganin treatment suggesting that it could improve the hyperglycemia and dyslipidemia in type II diabetes and have protective effects against diabetic cardiovascular complication by reduced the levels of serum glucose, triglyceride, and LDL/ VLDL(Low density lipoprotein/Very low density lipoprotein) cholesterol in db/db mice and enhanced HDL (High density lipoprotein) cholesterol and enhanced oxidative stress was alleviated by loganin through a decrease in thiobarbituric acid-reactive substances and reactive oxygen species .The marked lipid-regulatory effect of loganin was exerted in the liver of type II diabetic mice via suppressing mRNA expressions related to lipid synthesis and adjusting the abnormal expression of peroxisome proliferator-activated receptor a and sterol regulatoryelement binding protein in the nucleus. Furthermore, loganin also inhibited advanced glycation end product formation and the expression of its receptor and nuclear factor-kappa B-induced inflammation in the hepatic tissue of db/db mice.[53]

Carum carvi (Black zeera):

Caraway commonly known as black zeera, member of aromatic umbelliferous plants. In ancient time, Caraway has been used for the treatment of digestive disorders. The major

constituents of its seeds are carvone, flavonoids and limonone, whereas it's minor constituents are myrcene, beta-caryophyllene, thujone, anethole and pinene. Co-treatment of Carvi aqueous seed extract (30 and 60mg/kg bwt) for 60 days prevent the streptozotocin induced diabetic nephropathy by reducing the level of serum glucose, urea, creatinine, total urinary protein and total albumin excretion in diabetic rats. The overall renoprotective of Carum carvi is probably due to its antioxidant effect.[54]

Caesalpinia bonducella:

Caesalpinia bonducella is widely distributed throughout the coastal region of India and used ethnically by the tribal people of India for controlling blood sugar. Both the aqueous and ethanolic extracts showed potent hypoglycemic activity in chronic type II diabetic models. These extracts also increased glycogenesis thereby increasing liver glycogen content.[55] Two fractions BM 169 and BM 170 B could increase secretion of insulin from isolated islets. The aqueous and 50% ethanolic extracts of Caesalpinia bonducella seeds showed antihyperglycemic and hypolipidemic activities in streptozotocin (STZ)-diabetic rats. The antihyperglycemic action of the seed extracts may be due to the blocking of glucose absorption. The drug has the potential to act as antidiabetic as well as antihyperlipidemic.[56]

Capparis deciduas:

This is found throughout India, especially in dry areas. Hypoglycemic effect was seen in alloxanized rats when the rats were fed with 30% extracts of Capparis decidua (C. decidua) fruit powder for 3 weeks. This extract also reduced alloxan induced lipid peroxidation significantly in erythrocytes, kidney and heart. C. decidua was also found to alter superoxide dismutase and catalase enzyme levels to reduce oxidative stress.[57] C. decidua additionally showed hypolipidaemic activity.[58]

Coccinia indica:

Dried extracts of Coccinia indica (C. indica) (500 mg/kg body weight) were administered to diabetic patients for 6 weeks. These extracts restored the activities of enzyme lipoprotein lipase (LPL) that was reduced and glucose-6- phosphatase and lactate dehydrogenase, which were raised in untreated diabetics. Oral administration of 500 mg/kg of C. indica leaves showed

significant hypoglycemia in alloxanized diabetic dogs and increased glucose tolerance in normal and diabetic dogs.[59]

Enicostemma littorale blume:

Enicostemma littorale blume is a glabrous perennial herb belonging to the family Gentianaceae. The plant is used in flok medicine to treat the diabetes mellitus, rheumatism, abdominal ulcers, hernia, swelling, itching and insect poisoning.[60] Methanolic extract of whole plant of Enicostemma littorale blume (EL) was studied to assess its protective effects in alloxaninduced diabetic neuropathy in male Charles foster rats. An intragastrically administration of extract at a dose of 2.5g/kg body weight for 45 days were significantly restored the changes in lipid peroxidation status and anti-oxidant enzymes (super-oxide dismutase, glutathione peroxidase and catalase) levels in diabetic rats. Decrease in Na+-K+ ATPase (Sodium-Potassium Adenosine Triphosphatase) activity was also significantly restored by Enicostemma littorale blume (EL).Therefore Protective effect of Enicostemma littorale blume (EL) against neuropathy could be due to controlling hyperglycemia and reducing oxidative stress.[61]

Eugenia jambolana: (Indian gooseberry, jamun)

In India decoction of kernels of Eugenia jambolana is used as household remedy for diabetes. This also forms a major constituent of many herbal formulations for diabetes. Antihyperglycemic effect of aqueous and alcoholic extract as well as lyophilized powder shows reduction in blood glucose level. This varies with different level of diabetes. In mild diabetes (plasma sugar >180 mg/dl) it shows 73.51% reduction, whereas in moderate (plasma sugar >280 mg/dl) and severe diabetes (plasma sugar >400 mg/dl) it is reduced to 55.62% and 17.72% respectively.[62] The extract of jamun pulp showed the hypoglycemic activity in streptozotocin induced diabetic mice within 30 min of administration while the seed of the same fruit required 24 h. The oral administration of the extract resulted in increase in serum insulin levels in diabetic rats. Insulin secretion was found to be stimulated on incubation of plant extract with isolated islets of Langerhans from normal as well as diabetic animals. These extracts also inhibited insulinase activity from liver and kidney.[63]

Ginger:

Ginger (Zingiber officinale Roscoe, Zingiberacae) is widely used around the world in foods as a spice. For centuries, it has been an important ingredient in Chinese, Ayurvedic and Tibb- Unani herbal medicines for the treatment of catarrh, rheumatism, nervous diseases, gingivitis, toothache, asthma, stroke, constipation and diabetes.[64] Diabetic rats received the Ginger powder at 5% of their consumed food daily in streptozotocin induced diabetic nephropathy for 8 weeks significantly reduces the extent of lipid peroxidation, which is measured in terms of malondialdehyde (MDA) levels and improves plasma antioxidant capacity. Therefore Ginger causes a decrease in lipid peroxidation, an increase of plasma antioxidant capacity and a reduction in renal nephropathy.[65]

Garlic (Allium sativum Linn):

Garlic is probably one of the earliest known medicinal plants. Garlic is commonly known as Allium sativum and belongs to the family liliaceace. Studies have shown that intraperitoneal administration of aqueous Garlic bulbs extract at a dose of 100mg/kg may prevent vascular complication of diabetes mellitus by lowered the serum angiotensin converting enzyme activity in nondiabetic and streptozotocin diabetic rats.[66]

Gymnema montanum:

Gymnema species are traditionally used to treat disorders such as diabetes, high cholesterol, wounds, inflammation and gastrointestinal ailments.[67, 68] Gymnema montanum hook is one of such endemic plant species that belongs to Asclepiadaceae family and it is found mainly in the Shola forests of Western Ghats in India. Ethanolic extract of Gymnema montanum was tested to evaluate the reno-protective effect in alloxan-induced diabetic rats. An oral dose of 200 mg/kg body weight of the ethanol extract of leaves of Gymnema montanum was administered in rats for 3 weeks that significantly normalized the elevated blood glucose, renal markers including urea, creatinine and uric acid and lipid peroxidation markers including thiobarbituric reactive substances (TBARS) and hydroperoxides and increased the antioxidant enzymes levels such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and

glutathione-S-transferase (GST) in diabetic kidney. Thus Gymnema montanum ethanolic leave extract was found to be more effective in reducing oxidative stress and it confirming the ethnopharmacological use of Gymnema montanum in protecting diabetes and its complications.[69]

Hibiscus sabdariffa Linnaeus:

Hibiscus sabdariffa linnaeus (local name Roselle) belongs to family Malvaceae and is usually used as a beverage in Southeast Asia. The constituents in the flowers of Hibiscus species are polyphenolic acids, flavonoids, and anthocyanins. Aqueous extract of dried flowers of Hibiscus sabdariffa L. at a dose of 100 mg/kg and 400 mg/kg for 8 weeks ameliorate the diabetic nephropathy in streptozotocin induced type I diabetic rats by reducing lipid peroxidation, increasing catalase and glutathione activities significantly in diabetic kidney and decreasing the plasma levels of triglyceride. Further it also improves the hyperglycemia caused osmotic diuresis in renal proximal convoluted tubules in diabetic rats and regulating the Akt/Bad/14- 3-3g signaling. Therefore Hibiscus sabdariffa extract possessed the potential effects to ameliorate diabetic nephropathy via improving oxidative status and regulating Akt/Bad/14-3-3g signalling.[70]

Lindera strychnifolia (Sieb. and Zucc.) :

F. Villar is belongs to Lauraceae family and Uyaku is the common name for Lindera strychnifolia.[71-75] The roots of Lindera strychnifolia (Sieb. and Zucc.) F. Villars (Lauraceae) was used in Chinese folk medicine as acesodyne and antispasmodic termed Linderae Radix (LR). It has been shown that the oral administration of aqueous extract of roots of Lindera strychnifolia at a dose of 730 mg/kg/day for 12 weeks to diabetic mice showed glomeruli with greater area and cell population, smaller glomerular sclerotic index, and less fibrosis in glomeruli, where apoptotic rate of glomerular cells were decreased. Furthermore, renal TGF-h1 expression was decreased in the Lindera strychnifolia extract-treated group. Therefore these findings suggested that the Lindera strychnifolia therapy can be a novel therapeutic approach against diabetic nephropathy.[76]

Momordica charantia: (bitter gourd)

Momordica charantia is commonly used as an antidiabetic and antihyperglycemic agent

in India as well as other Asian countries. Extracts of fruit pulp, seed, leaves and whole plant was shown to have hypoglycemic effect in various animal models. Polypeptide p, isolated from fruit, seeds and tissues of M. charantia showed significant hypoglycemic effect when administered subcutaneously to langurs and humans.[77] Ethanolic extracts of M. charantia (200 mg/kg) showed an antihyperglycemic and also hypoglycemic effect in normal and STZ diabetic rats. This may be because of inhibition of glucose-6-phosphatase besides fructose-1, 6- biphosphatase in the liver and stimulation of hepatic glucose- 6-phosphate dehydrogenase activities.[78]

Mangifera indica: (Mango)

The leaves of this plant are used as an antidiabetic agent in Nigerian folk medicine, although when aqueous extract given orally did not alter blood glucose level in either normoglycemic or streptozotocin induced diabetic rats. However, antidiabetic activity was seen when the extract and glucose were administered simultaneously and also when the extract was given to the rats 60 min before the glucose. The results indicate that aqueous extract of Mangifera indica possess hypoglycemic activity. This may be due to an intestinal reduction of the absorption of glucose.[79]

Ocimum sanctum: (holy basil)

It is commonly known as Tulsi. Since ancient times, this plant is known for its medicinal properties. The aqueous extract of leaves of Ocimum sanctum showed the significant reduction in blood sugar level in both normal and alloxan induced diabetic rats.[80] Significant reduction in fasting blood glucose, uronic acid, total amino acid, total cholesterol, triglyceride and total lipid indicated the hypoglycemic and hypolipidemic effects of tulsi in diabetic rats.[81, 82] Oral administration of plant extract (200 mg/kg) for 30 days led to decrease in the plasma glucose level by approximately 9.06 and 26.4% on 15 and 30 days of the experiment respectively. Renal glycogen content increased 10 fold while skeletal muscle and hepatic glycogen levels decreased by 68 and 75% respectively in diabetic rats as compared to control.[83] This plant also showed antiasthemitic, antistress, antibacterial, antifungal, antiviral, antitumor, gastric antiulcer activity, antioxidant, antimutagenic and immunostimulant activities.

Phellodendri cortex:

Phellodendri cortex is the dried trunk bark of Phellodendron amurense ruprecht and it contains a number of alkaloids such as berberine, palmatine and jatrorrhizine. Crude extract obtained from Phellodendri cortex (PC) was studied in male sprague-dawley rats for their ability to prevent the diabetic nephropathy in streptozotocin-induced diabetic rats by its beneficial effects for correcting the hyperglycemia, antioxidant enzyme system and renal dysfunctions. Oral administration of aqueous extract of the peel of PC at a dose of 379mg/kg body weight once daily for 4 weeks showed significant reduction in tubular epithelial changes (such as Armanni-Ebstein cells) and oxidative stress through the restoration of enzymatic antioxidative defense system. Therefore treatment with PC extract can prevent the development of diabetic nephropathy by a reduction in renal damage through the restoration of enzymatic antioxidative defense system.[84]

Picrorhiza scrophulariiflora:

Picrorhiza is a perennial herb belonging to the family of Scrophulariaceae. The dried rhizomes of Picrorhiza have long been used to treat inflammatory diseases such as arthritis and asthma in Southeast Asia. Oral administration of ethanol extract of dried rhizomes of Picrorhiza scrophulariiflora at a dose of 400 mg/kg per day for 5 or 10 weeks in streptozotocin induced diabetic rats significantly attenuated oxidative stress in the diabetic kidney by a reduction in NADPH (nicotinamide adenine dinucleotide phosphate) oxidase-dependent superoxide generation and decreased expression of malondialdehyde and advanced oxidation protein products in renal tissue. This was accompanied by an improvement in renal inflammation, including decreased macrophage influx and downregulated expression of chemokines such as CCL2 (chemokine (C-C motif) ligand 2) and transforming growth factor-ß1 (TGF-ß1). These data suggest that Picrorhiza scrophulariiflora might improve diabetic nephropathy, probably through inhibition of redox-sensitive inflammation.[85]

Phyllanthus amarus: (bhuiawala)

It is a herb of height up to 60 cm, from family Euphorbiaceae. It is commonly

known as Bhuiamala. It is scattered throughout the hotter parts of India, mainly Deccan, Konkan and south Indian states. Traditionally it is used in diabetes therapeutics. Methanolic extract of Phyllanthus amarus was found to have potent antioxidant activity. This extract also reduced the blood sugar in alloxanized diabetic rats.[86] The plant also shows antiinflammatory, antimutagenic, anticarcinogenic, antidiarrhoeal activity.

Pterocarpus marsupium:

It is a deciduous moderate to large tree found in India mainly in hilly region. Pterostilbene, a constituent derived from wood of this plant caused hypoglycemia in dogs[87, 88] showed that the hypoglycemic activity of this extract is because of presence of tannates in the extract. Flavonoid fraction from Pterocarpus marsupium has been shown to cause pancreatic beta cell regranulation [47].[89] Marsupin, pterosupin and liquiritigenin obtained from this plant showed antihyperlipidemic activity.[90] (−) Epicatechin, its active principle, has been found to be insulinogenic, enhancing insulin release and conversion of proinsulin to insulin in vitro. Like insulin, (−) epicatechin stimulates oxygen uptake in fat cells and tissue slices of various organs, increases glycogen content of rat diaphragm in a dose-dependent manner.[91]

Propolis:

Propolis is a resinous hive product collected by honeybees from many plant sources.[92] Oral administration of ethanolic extract of Brazilian green Propolis in doses of 100, 200 & 300 mg/ kg body weight for 40 days in streptozotocin induced diabetic rats improved the body and kidney weights, serum glucose, lipid profile, MDA (Malondialdehyde) and renal function tests in a dose dependent manner. Significant increase in SOD (Superoxide dismutase activity), CAT (Catalase activity) and levels of GSH (Reduced glutathione) and reduction in the level of MDA (Malondialdehyde) was observed in extract treated diabetic rats. Those results may suggested a strong antioxidant effect of Propolis which can ameliorate oxidative stress and delay the occurrence of diabetic nephropathy in diabetes mellitus.[93]

Salvia miltiorrhizae:

Salvia miltiorrhizae radix is a traditional Chinese herbal medicine that has been used for many years in China, Japan, and Korea

for the treatment of diabetic complications. Lithospermic acid B (LAB) was isolated from Salvia miltiorrhizae and is known to have multiple pharmacological activities such as antihypertensive effect[94,] beneficial effects on renal injury[95] protective effect on hepatitis[96] and antioxidant effect.[97]The effect of Lithospermic acid B (LAB) on the prevention of diabetic nephropathy was studied in type 2 diabetic OLETF (Otsuka Long- Evans-Tokushima Fatty) rats. Further oral dose of 20 mg/kg of the LAB was administered once daily to10-week old male OLETF rats for 28 weeks that attenuated the development of diabetic nephropathy by significantly lowered the levels of lipid peroxidation, monocyte chemoattractant protein-1 (MCP-1), and transforming growth factor-ß1 (TGF-ß1) expression.[98]

Trigonella foenum graecum: (fenugreek)

It is found all over India and the fenugreek seeds are usually used as one of the major constituents of Indian spices. 4-hydroxyleucine, a novel amino acid from fenugreek seeds increased glucose stimulated insulin release by isolated islet cells in both rats and humans.[99] Oral administration of 2 and 8 g/kg of plant extract produced dose dependent decrease in the blood glucose levels in both normal as well as diabetic rats.[100] Administration of fenugreek seeds also improved glucose metabolism and normalized creatinine kinase activity in heart, skeletal muscle and liver of diabetic rats. It also reduced hepatic and renal glucose-6-phosphatase and fructose –1,6-biphosphatase activity.[101] This plant also shows antioxidant activity.[102, 103]

Tinospora cordifolia: (Guduchi)

It is a large, glabrous, deciduous climbing shrub belonging to the family Menispermaceae. It is widely distributed throughout India and commonly known as Guduchi. Oral administration of the extract of Tinospora cordifolia (T. cordifolia) roots for 6 weeks resulted in a significant reduction in blood and urine glucose and in lipids in serum and tissues in alloxan diabetic rats. The extract also prevented a decrease in body weight.[104] T. cordifolia is widely used in Indian ayurvedic medicine for treating diabetes mellitus.[105-108] Oral administration of an aqueous T. cordifolia root extract to alloxan diabetic rats caused a significant reduction in blood glucose and brain lipids. Though the aqueous extract at a dose of 400 mg/kg could elicit significant antihyperglycemic effect in different animal

models, its effect was equivalent to only one unit/kg of insulin. It is reported that the daily administration of either alcoholic or aqueous extract of T. cordifolia decreases the blood glucose level and increases glucose tolerance in rodents. [109]

Conclusion:

The present review has focused the selected medicinal plants used in the treatment of diabetic complications. It shows that the plants highlighted above have potent role in diabetic complications. Most of the plant extracts and its isolated constituents exhibited hypolipidemic and antioxidant effects, which may be helpful to treating diabetes and its associated complications. Thus many different plants have been used for treatment of diabetes and its complications. Efforts are now being made to investigate mechanism of action of some of these plants using model systems.

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