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APPRAISAL OF ANTIMICROBIAL MEDICINAL PLANTS WITH POTENTIAL THERAPEUTIC EFFECT ON DIABETES AND SICKLE CELL TRAIT

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ABSTRACT

Amidst unbearable side effects, and the expensive nature of imported drugs used in the management of sickle cell disease and diabetes, the search for attractive alternative with emphasis on availability and safety, will continue especially in resource poor countries. Again, it's not clear why there is sustained upsurge in diabetic and sickle cell disease despite efforts to clamp them down. The database on useful medicinal plants for treatment of diabetes and sickle cell was therefore improved. Other potential drugs suggested. Medicinal herbs can act as broad spectrum agents serving as anti-microbial, anti-diabetic and against sickle cell disease.

KEYWORDS

Medicinal herbs, Broad spectrum agents, Anti-microbial and Anti-diabetic.

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INTRODUCTION

Since ancient times, plants have been an exemplary source of medicine. Medicinal plants have the advantage of having no or minimum side effects when used as medicinal plants compared to imported synthetic alternatives. Metformin is most widely prescribed oral anti-diabetic drug used for the treatment of non-insulin-dependent diabetes mellitus (NIDDM) patients. It was first derived from a medicinal plant Galega officinal is, which was historically used for treatment of diabetes in medieval Europe. The effects of plants may delay the development of diabetic complications and

provide a rich source for antioxidants that are known to prevent/delay different diseased states.

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

Diabetes

Diabetes mellitus (DM) is a common and very prevalent disease in developed and developing countries. It is estimated that 25% of the world population is affected by this disease. Diabetes mellitus is a complex metabolic disorder resulting from either insulin insufficiency or insulin dysfunction. The disease is primarily classified as insulin-dependent diabetes mellitus (type 1 diabetes, IDDM), non-insulin-dependent diabetes mellitus (type 2 diabetes, NIDDM) and Gestational diabetes mellitus (GDM). Of the total diabetics, about 90% have NIDDM, which is characterized by post-prandial hyperglycaemia (PPHG) and associated with post-prandial oxidative stress. PPHG (increase in blood sugar level after a meal) plays an important role in the development of NIDDM, as well as in complications associated with the condition, including vascular diseases.

Insulin is a hormone secreted by the pancreas. It has to be secreted in adequate amount to transport glucose from blood into different cells of the body. Failure to produce insulin sufficiently or the produced insulin does not work efficiently, the glucose is not taken into the body but remains in the blood. This makes rise in blood sugar level causes hyperglycaemia. High blood sugar in diabetes produces polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger).

Sickle cell disease

Pathologic processes that cause hypoxia, acidosis, dehydration, hyperosmolality, and hypothermia, or elevated erythrocyte 2,3-DPG can transform silent sickle cell trait into a syndrome resembling sickle cell disease with vaso-occlusion due to rigid erythrocytes. Compound heterozygous sickle cell disease can be mistaken as uncomplicated sickle cell trait, particularly when an unusual globin variant is involved. People with uncomplicated sickle cell trait have a normal blood examination as assessed by conventional clinical methods, including normal red cell morphology indices, reticulocyte counts, and red blood cell survival by chromium labeling. Conventional methods of detecting hemolysis are negative, such as measurements of serum haptoglobin and bilirubin. Erythrocyte density distribution is normal, adherence to endothelium is not increased, altered membrane lipids and proteins are not detectable, cytoplasmic inside-out vesicles with high calcium content are absent, and permanently distorted erythrocytes are not observed.

Alternative therapy in the management of sickle cell disease (SCD)

The Role of Anti-Oxidants

It is still highly debated to date that nutrition has effect in the management of sickle cell disease and some preliminary studies to evaluate the effect of aged garlic extract on SCD patients showed a reduction in aggregates that adhere to red blood cells without significant changes to RBC, hemoglobin, and reticulocyte count. Many investigations are ongoing about the role of Thiocyanate in the management of sickle cell disease. Oxidative damage to cells may be responsible for activation of KCL-cotransport in sickled erythrocytes. The sickle cell erythrocytes are fragile and dehydrated and it is important that minerals and anti–oxidants are constantly supplied to maintain hydration and membrane integrity. Therefore many tropical plants (*M. charantia*,

Cymbropogoncitratus and *Camellia sinensis*, *Scopariadulcis, aged garlic* and *Picrorhizakurroa*) have been studied for their micronutrients and anti-oxidative properties.

Transgenic Animals in Sickle Cell Plants Research

Further studies with transgenic sickle cell mice showed that orally administered 5HMF inhibited the formation of sickle cells and significantly prolonged survival time under severe hypoxia, compared with untreated mice. A vanillin pro-drug, MX-1520, which is bio-transformed to vanillin in vivo, reduced the percentage of sickle cells under hypoxia in transgenic sickle mice. This demonstrates the potential of MX-1520 to be a new and safe anti-sickling agent for patients with SCD. The use of transgenic animals to effectively probe the usefulness of some of the plants with probable lead components in alleviating sickle cell crises has not been extensively undertaken by researchers in developing countries. Lack of adequate laboratory facilities and funding has hindered progress in this direction. With the vast natural resources available in these regions, provision of adequate funds and well equipped modern laboratories would go a long way towards actualizing the dream of these Scientists to solve their localized health problems without recourse to areas where some of these diseases are foreign.

Available medicinal plants[1-27]

Medicinal plants readily available for use in the tropics which needs further assessment for their activities against Microbial infections and also for their effect against sickle cells and diabetes are briefly summarized below. This summary is intended to expand the research horizon and update the data base for healthcare providers intending to use herbal medicines as attractive alternatives to increasing challenge of resistance posed by imported drugs.

Abelmoschusmoschatus Medik (Malvaceae)

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

Acacia arabica (Lam) Wild (Mimosaceae)

It is found all over India. The plant extract acts as an antidiabetic agent by acting as secret gouge to release insulin. It induces hypoglycemia in control rats but not in alloxanized animals. Powdered seeds of *A. Arabica* when administered (2, 3 and 4 g/kg body weight) to normal rabbits, induces hypoglycemic effect by initiating release of insulin from pancreatic beta cells.

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

Achyroclinesatureioides (Less) DC (Asteraceae)

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

effects might be mediated through the antioxidant and choleretic activities.

Lymphocytes extracted from peripheral-blood samples from each of six patients with newly diagnosed insulin-dependent diabetes mellitus were transplanted into athymic nude mice. At one or more sampling times (in the thirty-day study) blood-sugar was higher in the mice which had received lymphocytes from diabetic patients than in the control mice which had received lymphocytes from nondiabetic donors. Blood-sugar concentrations reached 260 mg/dl in some mice in the experimental group. This study demonstrates that lymphocytes may have an aggressive role in diabetogenesis. With this mouse experimental model mechanisms involved in diabetogenesis, and probably also in other disease in which lymphocytes are suspected of being involved in pathogenesis, could be investigated. The role of T lymphocytes in the production of islet cell injury resulting in diabetes has been suggested, in this instance by the transfer of lymphocytes from diabetic patients to mice. This killer T cell role was previously demonstrated using cultures of insulinoma cells exposed to lymphocytes from juvenile diabetes patients. The action of these cells in the etiopathogenesis of diabetes is speculative; perhaps they act against their targets when the suppressor cells are suppressed.

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Aegle marmelose (L) Corr. (Rutaceae)

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

Allium cepa L. (onion): (Liliaceae)

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

Allium sativum L. (garlic): (Liliaceae)

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

Aloe vera (L) Burm. (Asphodelaceae)

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

Andrographis paniculata Burm (Acanthaceae)

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

***Annona squamosal* L (Annonaceae)**

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

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

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

Astragalus membranaceus Bunge (Fisch) (Leguminosae)

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

Averrhoabilimbi L (Oxalidaceae)

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

Azadirachta-indica A. Juss. (Meliaceae)

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

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

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

Bauhinia forficate Link (Caesalpinaceae)

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

Bidens pilosa L (Asteraceae)

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

Biophytum sensitivum (L) DC. (Oxalidaceae)

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

Bixaorellana L. (Bixaceae)

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

Brassica nigra (L) Koch (Brassicaceae)

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

BryoniaalbaL. (Cucurbitaceae)

It is a flowering plant native to western Eurasia and adjacent regions, such as North Africa, the Canary Islands and South Asia. Administration of tri hydroxyl octa-decadienoic acids obtained from the roots of the native Armenian plant *B.alba* L. (0.05 mg/kg/day for 15 days. Lin.) restores the disordered

lipid metabolism of alloxan-diabetic rats. Metabolic changes induced in diabetes significantly restores towards their normal values with the exception of diminished triglyceride content of muscle which does not restores. Thus, they can influence the profile of the formation of stable prostaglandins by actions downstream of prostaglandin end peroxides.

Coriandrum sativum L (Apiaceae)

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

Cuminum cyminum L (Apiaceae)

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

Cuminum nigrum L (Apiaceae)

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

Cyamopsistetragonoloba (L) Taubert (Papilionaceae)

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

Dioscorea dumetorum (Kunth) Pax (Dioscoreaceae)

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

Ecliptaalba (L) Hassk (Asteraceae)

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

Emblica officinalis Gaertn (Euphorbiaceae)

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

Enicostema littoraleblume (Gentianaceae)

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

Ficusbengalensis L. (Moraceae)

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

Fraxinus excelsior L (Oleaceae)

The aqueous extract at a dose of 10 mg/kg/h produces a significant decrease in blood glucose levels in normal rats and more in diabetic rats. A potent increase of glycosuria concludes inhibition of renal glucose reabsorption. This renal effect might be at least one mechanism explaining the hypoglycemic activity of this plant in normal and diabetic rats.

Garcinia kola Heckel (W and C Afr) (Clusiaceae)

It is found in Africa mainly in subtropical or tropical moist lowland forests. The extract decreases the activity of microsomal glucose-6-phosphatase and lipid peroxidation (LPO) products. At a dose of 100 mg/kg, the fasting blood sugar in normoglycemic rabbits reduces from 115 mg/100 mL to 65 mg/100 mL after 4 h. In alloxan diabetic rabbits, the blood sugar lowers from 506 mg/100 mL to 285 mg/100 mL at 12 h. Kolaviron, a mixture of C-3/C-8 linked biflavonoids obtained from Garcinia kola produces significant hypoglycemic effects. 56.

Gongronema latifolium Endl. (Asclepiadaceae)

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

Helicteresisora L., As. (Sterculiaceae)

Distributed widely in forests throughout India. The hot water extract of fruit of *H. isora*exhibits significant antioxidant activity and moderate antidiabetic activity, at 200 mg/mL dose it shows glucose uptake activity and found to be active comparable with insulin and metformin. The ethanolic extract has insulin-sensitizing and hypolipidemic activity and has the potential for use in the treatment of type-2 diabetes. *Hypoxis Hemerocallidea* Conn Corm (African potato) (Hypoxidaceae). At a dose of 800 mg/kg, the plant extract causes 30.20% and 48.54% reductions in the blood glucose concentrations of fasted normal and STZ-treated diabetic rats. Thus, possesses hypoglycemic activity.

Inula Racemosa Hook. F. (Asteraceae)

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

Lagerstroemia Speciosa (L) Pers. (Lythraceae)

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

that the soft gel formulation has a better bioavailability than a dry-powder.

Lepidium Sativum L. (Brassicaceae)

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

Mangifera Indica L. (Anacardiaceae)

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

Momordica Charantia L. (Cucurbitaceae)

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

Morinda Lucida Benth. (Rubiaceae)

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

Myrcia Uniflora Barb., Rods. (Myricaceae)

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

Nigella Sativa L (Ranunculaceae)

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

Ocimum Sanctum L. (Lamiaceae)

It is commonly known as Tulsi, this plant is known for its medicinal properties. The aqueous extract of leaves shows significant reduction in blood sugar in both normal and alloxan induced diabetic rats. Significant reduction in fasting blood glucose, uronic acid, total amino acid, total cholesterol, triglyceride and total lipid indicate the hypoglycemic and hypolipidemic effects of tulsi in diabetic rats. Oral administration of plant extract (200 mg/kg) for 30 days leads to decrease in the plasma glucose. Renal glycogen content increases 10 fold while skeletal muscle and hepatic glycogen decreases by 68 and 75% in diabetic rats as compared to control. This plant shows anti: oxidant, bacterial, fungal, viral, asthemitic, stress, tumor, gastric ulcer, mutagenic and immunostimulant activities.

Origanum Vulgare L. (Lamiaceae)

It is native to warm-temperate western and southwestern Eurasia and the Mediterranean region. Oral administration of the aqueous extract (20 mg/kg) produces significant decrease on blood glucose levels in STZ diabetic rats. However, the blood glucose levels gets normalised from the

fourth day after daily repeated oral administration of aqueous OV extract (20 mg/kg). This concludes that an aqueous extract of *O. Vulgare* exhibits anti-hyperglycemic activity in STZ rats without affecting basal plasma insulin concentrations. The known compound bakuchiol, isolated from an extract of *O. pubescens* reduces blood glucose levels in a dose dependent fashion in db/db mice and displays no hypoglycemic effect in lean mice at 250 mg/kg q.d. An oral dose of bakuchiol at 150 mg/kg q.d. in the fat-fed, streptozotocin (STZ)-treated rat, a new rodent model for type 2 diabetes, significantly lowers plasma glucose and triglyceride levels.

Paeonia Lactiflora Pall. (Paeoniaceae)

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

Panax Ginseng C. Meyer. (Araliaceae)

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

Phyllanthus Amarus Schum and Thonn (Euphorbiaceae)

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

Psidium Guajava L. (Myrtaceae)

An indigenous medicinal plant used to control diabetes in India. Ethanol stem bark extract exhibits statistically significant hypoglycemic activity in alloxan-induced hyperglycemic rats but devoid of hypoglycemic effect in normal and glucose loaded rats (OGTT). Aqueous extract shows hypolipidaemic activity in addition to its hypoglycemic and antidiabetic activity.

Pterocarpus Marsupium Roxb. (Papilionaceae)

It is widely used in 'Ayurveda' as 'Rasayana' for management of various metabolic disorders. An aqueous extract of *P. marsupium* wood, at an oral dose of 250 mg/kg, shows statistically significant hypoglycemic activity. Marsupin, pterosupin and Iiquiritigenin obtained from this plant show antihyperlipidemic activity. 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.

CONCLUSION

Conclusively, with the present policy on poverty alleviation in developing countries, it is hoped that herbs mentioned in this work and others too numerous to be mentioned could be explored as potential sources of drug production. Finally, natural products are becoming more important in modern day society, as man is moving away from synthetic products which can be detrimental to the environment and human health. This review has highlighted some herbs used by the local people to control sickle cell anaemia and diabetes mellitus. These plants reviewed though does not eradicate these health problems but help to control and enables patients to live stable lives.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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