REVIEW ON ANTIDIABETIC MEDICINAL PLANTS

Hariprasad. R*, Kandasamy, C.S., Krishna Kumar, N, Shalavudeen Mohamed Akbar, S., Jegadeesh, S, and Venkatanarayanan, R.

Department of Pharmacognosy, R.V.S College of Pharmaceutical Sciences, Sulur, Coimbatore – 641402, TamilNadu, India.

ABSTRACT
Diabetes mellitus is common metabolic disorders. Since long back herbal medicines have been the highly respected source of medicine therefore, they have become a growing part of modern, high-tech medicine. The present review provides profiles of plants with hypoglycaemic properties, available through literature source from various database with proper categorization according to the parts used, mode of reduction in blood glucose and active phytoconstituents having insulin mimetics activity. From the review it was suggested that, plant showing hypoglycemic potential mainly belongs to the family Leguminoseae, Lamiaceae, Liliaceae, Cucurbitaceae, Asteraceae, Moraceae, Rosaceae and Araliaceae. The most active plants are, Gymnema sylvestre, Citrullus colocynthis, Trigonella foenum greacum, Momordica charantia, Allium sativum. The review describes some new bioactive drugs and isolated compounds from plants such as roseoside, epigallocatechin gallate, beta-pyrazol-1-ylalanine, cinchonain Ib, leucocyandin 3-O-beta-d-galactosyl cellobioside, leucopelargonidin-3- O-alpha-L rhamnoside, glycyrrhetinic acid, dehydrotrametenolic acid, strictinin, isostrictinin, pedunculagin, epicatechin and christinin-A showing significant insulinomimetic and antidiabetic activity with more efficacy than conventional hypoglycaemic agents. The antidiabetic activity of medicinal plants is attributed to the presence of polyphenols, flavonoids, terpenoids, coumarins and other constituents which show reduction in blood glucose levels.

KEYWORDS: Diabetes, Acacia, Alangium, Aloe vera, Panax.
INTRODUCTION

Diabetes mellitus, one of the most common endocrine metabolic disorders has caused significant morbidity and mortality due to microvascular complication. Human bodies possess enzymatic and non-enzymatic antioxidative mechanisms which minimize the generation of reactive oxygen species, responsible for many degenerative diseases including diabetes. The disease is rapidly increasing worldwide and affecting all parts of the world. Due to deficiency of the insulin people suffering from diabetes have high blood glucose level. Type 2 diabetes or non-insulin-dependent diabetes mellitus, is the most common form of the disease, accounting for cases in which the body does not produce enough insulin or properly use it. Currently available therapies for diabetes include insulin and various oral antidiabetic agents such as sulfonylureas, biguanides and glinides. Many of them have a number of serious adverse effects; therefore, the search for more effective and safer hypoglycemic agents is one of the important areas of investigation Aldose reductases, a key enzyme in the polyol pathway catalyze the reduction of glucose to sorbitol. Accumulation of sorbitol in the body causes various complications including cataract, neuropathy and nephropathy. The hypoglycemic effect of several plants used as antidiabetic remedies has been confirmed, and the mechanisms of hypoglycemic activity of these plants are being studied. Natural products having antidiabetic potential which acts through either insulinomimetic or secretagogues properties are reviewed here. This review also focuses on the role of traditional therapeutic and natural medicines from traditional medicinal plants for diabetes. Traditional medicines from readily available medicinal plants offer great potential for the discovery of new antidiabetic drugs.

Antihyperglycemic activity of the plants is mainly due to their ability to restore the function of pancreatic tissues by causing an increase in insulin output or inhibit the intestinal absorption of glucose or to the facilitation of metabolites in insulin dependent processes, in substances which demonstrate alternative and safe effects on diabetes mellitus. Most of plants contain glycosides, alkaloids, terpenoids, flavonoids, carotenoids, etc., that having antidiabetic effect.

Acacia Arabica

Acacia Arabica is used as home remedy in Indian system of medicine for reducing the complications of diabetes. It is found that this plant extract acts as an anti-diabetic agent by acting as secretagogue 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.[1]

Since ancient times, plants have been an exemplary source of medicine. Ayurveda and other Indian literature mention the use of plants in treatment of various human ailments. India has about 45,000 plant species and among them, several thousands have been claimed to possess medicinal properties. Research conducted in last few decades on plants mentioned in ancient literature or used traditionally for diabetes have shown anti-diabetic property. The present paper reviews 45 such plants and their products (active, natural principles and crude extracts) that have been mentioned/used in the Indian traditional system of medicine and have shown experimental or clinical anti-diabetic activity. Indian plants which are most effective and the most commonly studied in relation to diabetes and their complications are: Allium cepa, Allium sativum, Aloe vera, Cajanus cajan, Coccinia indica, Caesalpinia bonducella, Ficus bengalenesis, Gymnema sylvestre, Momordica charantia, Ocimum sanctum, Pterocarpus marsupium, Swertia chirayita, Syzigium cumini, Tinospora cordifolia and Trigonella foenum graecum. Among these we have evaluated M. charantia, Eugenia jambolana, Mucuna pruriens, T. cordifolia, T. foenum graecum, O. sanctum, P. marsupium, Murraya koeingii and Brassica juncea. All plants have shown varying degree of hypoglycemic and anti-hyperglycemic activity.[2]

The use of herbal drugs for the prevention and treatment of various health ailments has been in practice from time immemorial. Acacia arabica has been reported to be effective against a variety of disease including diabetes, skin disease and most concerning with cancer. The fresh plants parts of Acacia arabica is considered as astringent, demulcent, aphrodisiac, anthelmintic, antimicrobial, antidiarrhoeal, with good nutritional value in Indian traditional medicine system. This article briefly reviews the ethanobotanical as well as medicinal uses of Acacia arabica with plant description. This is an attempt to compile and document information on different aspect of Acacia arabica and its potential use. More studies are needed before the pharmacological properties of Acacia arabica can be utilized in therapy.[3] The powdered seeds of Acacla arabica and roots of Caralluma edulis were administered in doses of 2, 3 and 4 gm/kg body-weight to normal and alloxan-diabetic rabbits. The blood glucose levels were estimated before and 2, 4, 6 and 8 hours after the administration of plant suspension. The powdered seeds of Acacla Arabica exerted a significant (P <0.05)
hypoglycemic effect in normal rabbits. The hypoglycemic effect was not significant (P >0.01) in alloxan diabetic rabbits. The powdered roots of Caralluma edulls did not produce any significant (P >0.01) hypoglycaemic effect in normal as well as in alloxan diabetic rabbits. The doses used did not show any acute toxicity and behavioural changes. From this study it may be concluded that the powdered seeds of Acacia arabica act by initiating the release of insulin from pancreatic beta cells of normal rabbits. Moreover, Caralluma normal as well as in diabetic rabbits (JPMA 39:208, 1989).[4]

To investigate the role of Acacia Arabica extract as a hypoglycemic, antihyperlipidemic, and antioxidant agent in streptozotocin-induced diabetic rats. This is an animal experimental study conducted in King Fahd Research Center, King Abdulaziz University (KAU), Jeddah, Kingdom of Saudi Arabia from December 2012 to January 2013. Thirty-six female albino rats were divided into 2 equal groups; the first served as control, and the second was the streptozotocin-induced diabetic group. Each group was subdivided into 3 subgroups, each of 6 rats; the first was left untreated, the second and the third were treated with Acacia Arabica extract orally for 21 days (100 mg/kg for the second group and 200 mg/kg for the third group). On the twenty-first day, blood samples were withdrawn through the retro-orbital plexus of overnight fasted rats under light ether anesthesia for determination of serum glucose, insulin, total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), malondialdehyde (MDA), and coenzyme Q10 (Co-Q10). A significant decrease in levels of serum glucose, insulin resistance, TC, TG, LDL-C, MDA and a significant increase in HDL-C and Co-Q10 was observed in the treated diabetic groups when compared to the untreated diabetic group. The changes were dose dependent. The results found in this study indicate that Acacia Arabica extract has hypoglycemic, hypolipidemic, and antioxidant properties, therefore, it can be investigated for its efficacy in the treatment of diabetes in humans.[5]

**Alangium salvifolium**

Methanolic extract of Alangium salvifolium leaves possesses antihyperglycemic and antihyperlipidemic effects in dexamethasone induced insulin resistance in rats, which may be due to the antioxidant and insulinotrophic effect of extract.[6]

The present study is aimed to investigate the antidiabetic, analgesic and anti-inflammatory effect of aqueous extracts of stem and leaves of Alangium Salvifolium (AEAS) and Pavonia Zeylanica (AEPZ). The antidiabetic activity was evaluated by measuring blood glucose level
in normal and streptozotocin (STZ) induced diabetic rats, the acetic acid induced writhing and hot plate methods in mice were used to assess analgesic activity and Carrageenan induced paw edema in rats, which is an acute model used to assess antiinflammatory activity. The results support the traditional usage of the plants of Alangium Salvifolium and Pavonia zeylanica by ayurvedic physicians for the control of diabetes, pain and inflammation.\[7\]

Alangium salvifolium is a commonly known herb in Indian system of medicine to treat various disorders including diabetes mellitus without any scientific evidences. Therefore this study was designed to investigate in vivo hypoglycemic and antidiabetic potential of methanol extract of fruits of Alangium salvifolium in glucose loaded animals and alloxan induced diabetic animals. In both the models Alangium salvifolium reduced the blood glucose level when compared to diabetic control group and exert a significant hypoglycemic and antidiabetic activity. However the potency of the herb was less than that of standard drug metformin.

Alangium salvifolium methanol extract also reduced the rate of body weight loss in normal and alloxan induced diabetic animals. The results of this study revealed the presence of a significant antidiabetic potential of methanol extract of Alangium salvifolium in alloxan induced diabetic rats. On the basis of this further research work is needed to investigate exact mechanism of action and also to isolate the active constituent/s responsible for the activity.\[8\]

The present study is aimed to investigate the effect of aqueous extract of stem and leaves of Alangium Salvifolium (AEAS) on blood glucose level in normal and alloxan induced diabetic rats. Oral administration of AEAS (200, 400 and 800mg/kg body weight) resulted in a significant reduction in blood glucose level. The effect was compared with 0.5mg/kg (I.P.) glibenclamide. The results support the traditional usage of the plant of Alangium Salvifolium by ayurvedic physicians for the control of diabetes.\[9\]

Alangium salvifolium is a medicinal plant, used by herbalist for treating various diseases, one of which is diabetes mellitus in Central India. However, its antidiabetic activity has not been scientifically validated so far. The aim of the present study was to evaluate the antidiabetic activity of ethanol extracts of leaves and barks of Alangium salvifolium against strepozotocin (STZ)-induced diabetic rats. The ethanol extracts of leaves and barks of Alangium salvifolium at doses of 200 and 400 mg/kg body weight was administered orally to diabetic rats. The blood glucose levels were monitored at specific intervals and found significantly
lowered the blood glucose level. Glibenclamide was used as a standard drug at a dose of 0.25 mg/kg. The effect of extracts on induced hyperlipidemia was analyzed where the extracts significantly lowered the elevated total cholesterol, triglycerides (TGL) and low density lipoprotein (LDL) level while increased the high density lipoprotein (HDL). Moreover, the decreased in body weight of rats after induction of diabetes, and increased in body weight of rats after treatment with extracts was observed. The experimental data exhibited that extract of leaves and barks of Alangium salvifolium has significant antidiabetic activity in streptozotocin-induced rats compared to standard drug. The ethanol extracts of leaves exhibited maximum antidiabetic activity as compared to barks extract.\textsuperscript{10}

**Aloe vera**

Hypoglycemic effect by bitter principle of Aloe vera in the rats is mediated through stimulation of synthesis or release of insulin from the beta-cells of Langerhans. Effect of pseudoprototinosaponin AIII and prototinosaponins AIII on glucose uptake and insulin release suggested their hypoglycaemic effects are due to actions on hepatic gluconeogenesis or glycogenolysis. Single as well as repeated doses of bitter principle of the Aloe vera showed hypoglycemic effect in diabetic rats, which was through stimulation of synthesis or release of insulin from pancreatic beta cells.\textsuperscript{11}

In the present investigation, the antidiabetic effect of Aloe vera leaf pulp extract was studied in vivo and in vitro as compared to glimiperide. Diabetes was induced experimentally in adult male albino rats by single-dose intraperitoneal injection of streptozotocin (50 mg/kg body weight). The in vitro study was performed using isolated islets of pancreas from adult female albino rats. Both aloe extract (10 ml/kg, p.o.) and glimiperide (10 mg/kg, p.o.) significantly decreased serum glucose and significantly increased serum insulin levels as compared to control diabetic rats. Serum levels of malondialdehyde (MDA) and superoxide dismutase (SOD) were significantly decreased while blood glutathione (GSH) was significantly increased by aloe treatment as compared to diabetic rats. Effect of aloe was better than the effect of glimiperide. Regarding the in vitro study, both aloe (10 μl/l) and glimiperide (10 μmol/l) significantly increased both basal and stimulated insulin secretion from the isolated islets of pancreas as compared to control. These results show a promising antidiabetic effect of aloe for further clinical trials regarding clinical use of aloe extract for treating type II diabetes.\textsuperscript{12}
An attempt was made to study the beneficial effects of Aloe vera (L.) Burm. fil. in streptozotocin-induced diabetic rats. In diabetic induced rats fed with A. vera (300 mg/kg body wt), the fasting plasma glucose levels were reduced to normal and body weight was found to be increased. In the pancreatic sections of diabetic rats fed with A. vera, the islets were comparable to normal rats. In liver, the changes caused after induction of diabetes are granular cytoplasm, dilated sinusoids, shrunken nuclei and inflammation, which was reduced after feeding with A. vera. Excess proliferation of epithelium in the small intestine was observed in diabetic rats, which was reduced after A. vera feeding. In diabetic rats and diabetic rats fed with A. vera, no change was noticed in the kidney and stomach.[13]

The plant Aloe vera is used in Ayurvedic, Homoeopathic and Allopathic streams of medicine and not only tribal com- munity but also most of the people for food and medicine. The plant leaves contains numerous vitamins, minerals, en- zymes, amino acids, natural sugars and other bioactive compounds with emollient, purgative, antimicrobial, anti in- flammatory, anti- oxidant, aphrodisiac, anti-helmenthic, antifun gal, antiseptic and cosmetic values for health care. This plant has potential to cure sunburns, burns and minor cuts, and even skin cancer. The external use in cosmetic primarily acts as skin healer and prevents injury of epithelial tissues, cures acne and gives a youthful glow to skin, also acts as extremely powerful laxative.[14]

The effects of processed Aloe vera gel (PAG) on the course of established diet-induced non- insulin-dependent diabetes mellitus (NIDDM) were studied in C57BL/6J mice. NIDDM was induced in C57BL/6J mice by feeding them a high-fat diet. Mice exhibiting diet-induced obesity (DIO) with blood glucose levels above 180 mg/dl were selected to examine the antidiabetic effects of PAG. Oral administration of PAG for 8 weeks reduced circulating blood glucose concentrations to a normal level in these DIO mice. In addition, the administration of PAG significantly decreased plasma insulin. The antidiabetic effects of PAG were also confirmed by intraperitoneal glucose tolerance testing. PAG appeared to lower blood glucose levels by decreasing insulin resistance. The administration of PAG also lowered triacylglyceride levels in liver and plasma. Histological examinations of periepididymal fat pad showed that PAG reduced the average size of adipocytes. These results demonstrate that the oral administration of PAG prevents the progression of NIDDM-related symptoms in high-fat diet-fed mice, and suggest that PAG could be useful for treating NIDDM.[15]
Panax ginseng

Ginseng polypeptides isolated from the root of Panax ginseng, when injected subcutaneously at daily doses of 50 and 100 mg/kg for 7 successive days in mice resulted in decreased blood glucose, increased liver glycogen level and stimulated insulin secretion. The aqueous ethanolic extract of Korean red ginseng significantly evoked a insulin release in a glucose-independent manner.[16]

We evaluated antihyperglycemic and anti-obese effects of Panax ginseng berry extract and its major constituent, ginsenoside Re, in obese diabetic C57BL/6J ob/ob mice and their lean littermates. Animals received daily intraperitoneal injections of Panax ginseng berry extract for 12 days. On day 12, 150 mg/kg extract–treated ob/ob mice became normoglycemic (137 ± 6.7 mg/dl) and had significantly improved glucose tolerance. The overall glucose excursion during the 2-h intraperitoneal glucose tolerance test decreased by 46% (P < 0.01) compared with vehicle-treated ob/ob mice. The improvement in blood glucose levels in the extract-treated ob/ob mice was associated with a significant reduction in serum insulin levels in fed and fasting mice. A hyperinsulinemic-euglycemic clamp study revealed a more than twofold increase in the rate of insulin-stimulated glucose disposal in treated ob/ob mice (112 ± 19.1 vs. 52 ± 11.8 μmol · kg⁻¹ · min⁻¹ for the vehicle group, P < 0.01). In addition, the extract-treated ob/ob mice lost a significant amount of weight (from 51.7 ± 1.9 g on day 0 to 45.7 ± 1.2 on day 12, P < 0.01 vs. vehicle-treated ob/ob mice), associated with a significant reduction in food intake (P < 0.05) and a very significant increase in energy expenditure (P < 0.01) and body temperature (P < 0.01). Treatment with the extract also significantly reduced plasma cholesterol levels in ob/ob mice. Additional studies demonstrated that ginsenoside Re plays a significant role in antihyperglycemic action. This antidiabetic effect of ginsenoside Re was not associated with body weight changes, suggesting that other constituents in the extract have distinct pharmacological mechanisms on energy metabolism.[17]

Despite a lack of medical evidence to support its therapeutic efficacy, the use of herbal medicine has increased considerably. Ginseng, one of the most widely used herbs, is hypothesized to play a role in carbohydrate metabolism and diabetes mellitus. We therefore undertook a preliminary short-term clinical study to assess whether American ginseng (Panax quinquefolius L) affects postprandial glycemia in humans.[18]

Antihyperlipidemic and antihyperglycemic effects of Red Ginseng (RG, steamed and dried root of Panax ginseng C. A. Meyer, family Araliaceae), major component of which is
ginsenoside Rg3, and Bifidodoterium-fermented RG (FRG), major component of which is
ginsenoside Rh2, were investigated. Orally administered RG and FRG potently reduced the
serum triglyceride levels in corn-oil-induced hypertriglycemidemic mice as well as total
cholesterol and triglyceride levels in Triton WR-1339-induced hyperlipidemic mice. Of the
saponin and polysaccharide fractions of RG and FRG, the polysaccharide fraction inhibited
postprandial blood glucose elevation of maltose- or starch-loaded mice and reduced the blood
triglyceride levels in corn-oil-induced hypertriglycemidemic mice. The saponin fraction and
its ginsenosides Rg3 and Rh2 reduced blood triglyceride and total cholesterol levels in Triton
WR1339-induced hyperlipidemic mice. The inhibitory effect of FRG and its main
 constituents against hyperlipidemia and hyperglycemia in mice were more potent than those
of RG. These findings suggest that hypolipidemic and hypoglycemic effects of RG can be
enforced by Bifidus fermentation and FRG may improve hyperlipidemia and
hyperglycemia.\[19]\n
A hypoglycaemic principle, panaxan B, obtained from the roots of Panax ginseng, was shown
to be a peptidoglycan with Mₚ of about 1 800 000. Physico-chemical and chemical studies
indicated panaxan B to be mainly composed of α-1,6 linked D-glycopyranose residues with
branching at the C-3 position, the ratio of terminals, branching positions and intermediate
units being about 1:1:1.8.\[20]\n
**Catharanthus roseus**

Dichloromethane-methanol extract of leaves and twigs of Catharanthus roseus in
carbohydrate metabolism, showed to enhance secretion of insulin. The extract was also found
to be helpful in prevention of damage caused by oxygen free radicals.\[21]\n
The aim of this study was to evaluate the hypoglycemic activity of extracts from the flower,
leaf, stem, and root in normal and alloxan-induced diabetic mice. Methods. Roots, leaves,
flowers, and stems were separated to obtain organic and aqueous extracts. The blood glucose
lowering activity of these extracts was determinate in healthy and alloxan-induced
(75 mg/Kg) diabetic mice, after intraperitoneal administration (250 mg/Kg body weight).
Blood samples were obtained and blood glucose levels were analyzed employing a
 glucometer. The data were statistically compared by ANOVA. The most active extract was
fractioned. Phytochemical screen and chromatographic studies were also done. Results. The
aqueous extracts from C. roseus reduced the blood glucose of both healthy and diabetic mice.
The aqueous stem extract (250 mg/Kg) and its alkaloid-free fraction (300 mg/Kg)
significantly reduced blood glucose in diabetic mice by 52.90 and 51.21%. Their hypoglycemic activity was comparable to tolbutamide (58.1%),. Conclusions. The best hypoglycemic activity was presented for the aqueous extracts and by alkaloid-free stem aqueous fraction. This fraction is formed by three polyphenols compounds.[22]

The need for the novel pharmaceutical products out from the plant has attained a great interest in the present research world due to the cost and the higher side effects that are associated with the chemically manufactured drugs. Catharanthus roseus, which is a potent medicinal plant many of the pharmacological actions such as antimicrobial, antioxidant, anthelmintic, antifeedant, antisterility, antidiarrheal, antidiabetic effect etc. That is used to treat many of the fatal diseases. Alkaloids were the major phytochemical constituent of the above medicinal plant and have different types possessing various medicinal uses. The pharmacology of the plant was found to be associated mostly especially with the alkaloids that occupies almost most of the parts of the plant. In this review, an attempt has been made to summarize the pharmacological effect of the above plant against various disease starting from the antimicrobial to that of the antineoplastic diseases in a precise way to help the scientist and learners to understand the basis medicinal value of the plant.[23]

Herbal medicinal plants are boon for human being as treatment of existing and new diseases are being developed either direct or indirect usage of plants. But availability of such plants and their properties also play an important role. Catharanthus roseus is a very important medicinal herb in this direction as availability and its property both are fortunate thing for humankind. This plant is used in treatment of several diseases like diabetes, cancer, high blood pressure, asthma, inflammation, dysentery, brain imbalance, angiogenesis, malaria and other diseases that occur due to potent micro organisms. Though it's a native of Madagascar but it is found most parts of the world. It is also appreciated for its long flowering period throughout the year. Its roots, plant stems and flowers having active constituents to inhibit the growth of disease and other micro organism. Extracts from the dried or wet flowers and leaves of plants are applied as a paste on wounds in some rural communities. The substances vinblastine and vincristine extracted from the plant are used in the treatment of leukemia and Hodgkin's lymphoma. The fresh juice from the flowers of C. roseus is used to treat various skin problems e.g. dermatitis, eczema and acne. Therefore, the main active constituents present in this plant are alkaloids, flavonoids, steroids and phenolic acid. As C roseus has mammoth potential to heal many syndrome due to its phytopharmaceuticals assets and it's
intact fractions i.e. root, leaf, stem and flower are drug compliant. Still further research is required to find main utility in healing of diseases arises due to deadly viruses.[24]

Catharanthus roseus G.Don of the family Apocynaceae is a native of Madagascar and now found commonly throughout India. The species has been cultivated for herbal medicine as well as a garden plant. It is a rich source of alkaloid constituents. The alkaloids vinblastine and vincristine extracted from the plant are used in the treatment of leukemia and Hodgkin's disease. The entire plant is used in many disorders like diabetes, malaria, hypertension, heart disease in many countries. This plant is commonly found with pink and white flower variety everywhere. The present investigation deals with microscopic evaluation of white and pink forms of Vinca rosea root. Both these plants have same medicinal value so in this study we observe if there any differential characters are present or not particularly in the root. A detailed pharmacognostic study of drug samples was carried out which highlighted certain diagnostic macro and microscopic characters useful for their identification. Such a study would serve as a useful gauge in standardization of the root material and ensuring quality formulations.[25]

REFERENCE


