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An Overview on Some Recent Herbs Having Antidiabetic Potential.

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ABSTRACT

Diabetes mellitus, both insulin dependant and non-insulin dependent is a common and serious metabolic disorder throughout the world. Medicinal plants have been historically used for the treatment of diabetes throughout the world. Several herbs are known to cure diabetes and additionally they have no side effects. Many of the currently available drugs have been derived directly or indirectly from plants. There have been many studies on hypoglycemic plants, still a need to look for new drug as no drug has been shown to modify the course of diabetic complications. The present review presents the profiles of the plants with hypoglycemic properties reported in the literature from 2012 to 2013. This review has been presented in a very interactive manner the geographical source, plant part used, phytoconstituents responsible for particular action, solvent used for extraction and animals used for testing. There are 14 such plants described in this review which clearly shows the importance of herbal plants in the treatment of diabetes mellitus.

Keywords: Hyperglycemia , traditional herbs , Diabetes, Antidiabetic herbs

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INTRODUCTION

Diabetes mellitus is a global metabolic epidemic affecting essential biochemical activities in almost every age group. Diabetes mellitus is not a single disease but rather a group of metabolic disorders. Hyperglycemia in diabetes results from defect in insulin secretion and or insulin action. Conventionally insulin dependent diabetes mellitus is treated with exogenous insulin, and non-insulin dependent diabetes mellitus is treated with synthetic oral hypoglycemic agents like sulphonyl urea's and biguanides. Synthetic oral drugs produce adverse health effects. Different medicinal systems are using the active plant constituent which discovered as natural hypoglycemic medicine came from virtue of traditional knowledge. Herbal drugs are considered free from side effects than synthetic one [1].

A large diversity of animal models has been developed to better understand the pathogenesis of diabetes mellitus and new drugs introduced in market to treat this disease. This review also studied the animal model used in testing of drug [2]. Ayurveda and other traditional medicinal system for the treatment of diabetes describe a number of plants used as herbal drugs. The active principal present in medicinal plants have been reported to possess pancreatic beta cells regenerating, insulin releasing and fighting the problem of insulin resistance [3].

The ethanobotanical information reports about 800 plants that may possess antidiabetic potential and more than 1200 species of plants have been screened for activity on the basis of ethanopharmacology[4].

In India indigenous remedies have been used for treatment of diabetes mellitus since the time of charaka and sushruta. The World Health Organization has recommended the evaluation of tradiotnal plant treatments for the diabetes. Diabetes mellitus can be induced by pharmacological, surgical or genetic manipulations in several animal species. Most experiments in diabetes are carried out on rodents, although some studies are still performed in larger animals.

The aim of the present review is to focus on role of some traditional medicinal systems for the treatment of diabetes mellitus. Herbal drugs reported from 2012-2013 with antidiabetic potential have been reported here are *Annona squamosa* (Annonaceae), *Piper longum* (Piperaceae), *Annona reticulata* (Annonaceae), *Bauhinia purpurea* (Leguminosae), *Calamus erectus* (Arecaceae), *Momordica charantia* (Cucurbitaceae), *Kachure chooranam* (Arecaceae), *Zizyphus nummularia*(Rhamnaceae), *Tamarindus indica* seeds (Caesalpiaceae), *Tamarindus indica* fruit pulp (Caesalpiaceae), *Swertia chirata* (Gentianaceae), *Parmelia Perlata* (Parmeliaceae), *Gomphrena gobosa* (Amaranthaceae), *Psidium guvajava* (Myrtaceae) etc.

Annona Sqamosa (Annonaceae) [5]

The leaves are shown to have antidiabetic property. The effect of different fruit peel extract of *annonna sqamosa* on blood glucose and lipid profile have been studied in steptozocin induced diabetic rats and compared with glibanclamide, a reference drug. The administration of extract and standard drug was carried out every day for 21 days. Drug samples were collected through the tail vein just prior to and on days 0, 7, 14, and 21 after the drug administration. Evaluation of antidiabetic effect of text plant extract was done on six groups of rats and six rats in each group. The change in body weight was recorded during the study period. Significant decrease was observed in the body weight of diabetic rats compared to control rats. Treatment with extract of *annonna sqamosa* fruit peel shows significant increase in body weight and diminished blood glucose level on day 0, 7, 14, and 21. The untreated diabetic control rat group showed increase in blood glucose level through out the entire study period. Alcoholic extract of *annonna sqamosa* has shown maximum effect than petroleum ether and ethyl acetate.

Piper longum (Piperaceae) [6]

Antidiabetic and antihyperlipidemic activity of *piper longum* root aqueous extract was studied in sreptozocin induced diabetic rats. Estimation of blood glucose was carried out by glucose oxidase peroxidase method. Aqueous and methanolic extract produced significant antihyperglycemic activity at a dosage of 200 mg/kg body weight in diabetes treated rats.

Dose dependent study was carried out in which aqueous extracts at a dosage of 200mg/kg body weight has produced maximum antihyperglycemic activity in diabetic rats. The oral glucose tolerance test also confirmed blood glucose lowering activity of drug. The onset of antihyperglycemic action was observed from 60 min of the treatment and the steady state increase in the action continued up to 120 min. The loss in body weight observed in streptozocin induced diabetic rat group.

HbA1c is used as a marker for estimating the degree of protein glycation in diabetes mellitus. HbA1c was found to increase in patients with diabetes mellitus and the amount in increase is directly proportional to the fasting blood glucose level. In diabetic condition the excess glucose present in blood reacts with Hb to form HbA1c. Hence HbA1c level were elevated and total Hb level depleted in untreated diabetic rats. HbA1c level were well regulated near to normal in piper longum aqueous extract treated diabetic group, this could be due to an improvement in insulin secretion upon piper longum aqueous extract treatment.

***Annona Reticulata* L (Annonaceae) [7]**

Hypoglycemic and antidiabetic activity of ethanolic and water extract of leaf and stem bark of *Annona reticulata* was studied on Alloxan induced diabetic rats. Rats divided in to seven groups, each consisting of five rats. Administration of *Annona reticulata* (250mg/kg) to diabetic rat significantly decreased the level of blood glucose after 21 days treatment. The leaf ethanol extract was found to be more potent at a dose of 250mg/kg and it brought down the elevated blood glucose level in alloxan induced diabetic rats near to the normal.

***Bauhinia purpurea* (Leguminosae) [8]**

Invitro antidiabetic activity of stem bark of *Bauhinia purpurea* (Leguminosae) was studied by non enzymatic glycosylation of Hb assay, glucose uptake in yeast cell, and alpha amylase inhibition assay.

In non enzymatic glycosylation of Hb assay, Antidiabetic activity were investigated by estimating degree of non enzymatic hemoglobin glycosylation, measured by colorimetry at 520nm. Alpha-Tocopherol (Trolax) was used as a standard drug for assay. An increase in the glycosylation was observed on incubation of hemoglobin with the increasing concentration of glucose over a period of 72hrs. The plant extract was found to show significant inhibition of hemoglobin glycosylation which was indicated by presence of increasing concentration of hemoglobin.

In Glucose uptake in yeast cell test various concentrations of extracts were added to 1 ml of glucose solution and incubated together for 10 min at 37°C. Reaction was started by adding 100µl of yeast suspension, vortex and further incubated at 37°C for 60 min, the tubes were centrifuged and glucose was estimated in the supernant. Metronidazole was taken as standard drug. The percentage increase in glucose uptake by yeast cells was calculated.

The invitro α - amylase inhibition studies demonstrate that *Bauhinia purpurea* has well antidiabetic activity. α - amylase is enzyme that hydrolyses alpha-bonds of large alpha linked polysaccharides to yield glucose and maltose. α - amylase inhibitory activity was based on starch iodine method. The intestinal digestive enzyme α - amylase plays a vital role in the carbohydrate digestion. One antidiabetic therapeutic approach reduces the post prandial glucose level in blood by the inhibition of alpha amylase enzyme. The concentration dependant reduction percentage inhibition was studied. At a concentration of 20 microgram/ml of petroleum ether and hexane extract showed a significant percentage inhibition as compared to Acarbose, a standard drug.

***Calamus erectus* (Arecaceae) [9]**

Hypoglycemic, hypolipidemic and antioxidant activity of fruit in streptozocin induced diabetic wistar rat was studied. Daily oral treatment with 400 mg/kg fruit extract for 14 days resulted in reduction of blood glucose. Glibanclamide was used as a reference standard. Antihyperglycemic effect of methanol extract was found to be more effective than reference standard. Diabetic rat showed significant increase in body weight during 14 days. Administration of methanol extracts shows decrease in body weight.

***Tamarandus indica* L [10]**

Antidiabetic effect of the *Tamarandus indica* Linn seeds in normal, type1, and type II model rats was studied. A total 250 rats were used to carry out the experiment. The animals were divided in to three groups with 6 to 8 rats in each group. *Tamarandus indica* Linn seeds powder was found to be more effective in type II diabetic rat model when fed 30 min before glucose load.

***Momordica Charantia* (Cucurbitaceae) [11]**

In review article of *Momordica charantia* so many intricate details of the plant and its applied aspects in medicine have been studied. It is a popular plant also known as bitter melon, karela used for treatment of diabetes. *M. charantia* is a tropical plant that is widely cultivated in Asia, India, East Africa and South America. It is climbing perennial that usually grow up to 5m and bear elongated fruits with knobbly surface. It is a useful medicinal and vegetable plant for human health and one of the most promising plant for diabetes. Bitter melon is powerful nutrient dence plant composed of bioactive chemicals, vitamins minerals and antioxidants which contribute to versatility in treating a wide range of illness. The main constituent of bitter melon which is responsible for antidiabetic effects are triterpine, steroids alkaloid, inorganic, lipid and phenolic compounds. It is proved to be versatile plant worthy of treating almost any disease inflicted on mankind, this is due to the fact that the plant possess over 225 different medicinal constituents. In relation to diabetes only charatin , insulin like peptide and alkaloid like extracts possess hypoglycemic properties.

***Phoenix dactylifera* L (Kachure chooranam) (Arecaceae) [12]**

Phoenix dactylifera linn (Arecaceae) commonly known as Date palm has been widely used in Siddha system of medicine for diabetes. Kachure chooranam is powder form of dried dates showed a significant inhibitory effect as a antidiabetic on alloxan induced diabetic rats. Glibanclamide 10mg/kg was used as reference standard. Albino rats of either sex weighing 210-230gm were usrd.28 days treatment with the test drug kachure chooranam significantly reduced the elevated blood glucose in alloxan induced diabetic rats, while it had no effect on blood glucose of normal rats.

***Zizyphus nummularia* (Rhamnaceae) [13]**

Antidiabetic activity of ethanolic and aqueous extract of leaves of *Zizyphus nummularia* (250mg/kg and 500mg/kg) was evaluated by dexamphithasone induced diabetic rats. In the experiment a total 42 overnight fasted rats were used. The 36 rats were rendered diabetic by the aqueous solution of dexmethasone (10mg/kg). Blood samples were subjected to glucose measurement and serum was used for the estimation of biochemical parameters TGL, HDL, LDL, VLDL and TG by a semi auto analyzer. Acute oral toxicity studies showed that both the extracts up to 500mg/kg are non toxic and safe. The body weight of normal and treated groups significantly differ from diabetic control. The treated group's animal body weight maintained through out the experiment.

***Swertia Chirata* (Gentianaceae) [14]**

It is medicinal plant indigenous to temperate Himalaya found in attitude of 1200-1300m from Kashmir to Bhutan and in Khasi hills at 1500m. Three main photochemicals mangiferin, amarogentin, and swertiamarin were identified in aqueous and 12% ethanolic extracts of all plant parts.

The antidiabetic activity of aqueous extract of *Swertia Chirata* in streptozocin induced diabetes in albino rats was studied and it was compared with standard drug Glibanclamide. In the study 24 male albino wistar rats were used divided in to 4 groups. *Swertia Chirata* aqueous extract at a dose of 200mg/kg body weight showed significant antidiabetic activity but less marked than standard drug.

***Tamarandus indica* L (Caesalpinaceae) [15]**

Antidiabetic and hepatoprotective activities of *Tamarandus indica* Linn. Fruit pulp in alloxan model was studied. *Tamarandus indica* Linn known as tamarind is a well known plant of Indian medicinal system. The

pulp of fruit shows antidiabetic activity. Male wistar albino rats weighing between 180-250gms were used for study. Fresh fruits of *Tamarandus indica* Linn were cut in to small pieces and pulp was used for the preparation of extract for testing serum glucose and lipid profile. Antidiabetic effect of *Tamarandus indica* extract was found significant when compared to alloxan treatment group and it also decreased the elevated cholesterol, LDL, VLDL and TGs and significantly increased HDL levels.

Parmelia Perlata Ach (Permeliaceae) [16]

Antidiabetic And Antihyperlipidemic effect of *parmelia perlata* in alloxan induced diabetic rats was studied. The aqueous extract of the selected plant was administered at dose levels of 200mg and 400mg/kg body weight for 60 days. After the experimental period the blood and tissue samples were collected and subjected to various biochemical and enzymic parameters. There were profound alteration in fasting blood glucose, serum insulin, glycosylated hemoglobin (HbA1C) and liver glycogen levels in alloxanized rats. Glucose-6-phosphatase, glucokinase, and fructose 1-6 bisphosphatase activity were also altered in diabetic rats. Administration of plant extract significantly ($P < 0.05$) reduced the fasting blood glucose and HbA1C level and increased the level of plasma insulin. The activities of glucose metabolizing enzymes were also resumed to normal. There was a profound improvement in serum lipid profiles by reducing serum triglyceride, cholesterol, LDL, VLDL, free fatty acids, phospholipids and increasing the HDL level in a dose dependent manner. Healthy adult wistar strain of albino rats of either sex, weighing 150-200 g was used as experimental models. The effect of leaf extract was compared with standard drug Glibenclamide (600microgram/kg bw). The result indicate that *Parmella perlata* could be good natural source for developing an antidiabetic drug that could be maintained the blood glucose level and the lipid profile near to normal values.

Gomphrena gobosa (Amaranthaceae) [17]

The whole plant of *Gomphrena gobosa* (Amaranthaceae) was used for preparation of extracts. Methanolic n-Hexane, chloroform, Carbon tetrachloride and aqueous extracts were subjected to evaluate hypoglycemic activity test by glucose tolerance test. Among all fractions n-Hexane soluble fractions at a dose of 400mg/kg body weight lower the blood glucose level significantly in mice model when compared with the standard drug Glibenclamide. Swiss albino mice of 6-8 weeks age were divided in to six groups with five mice in each group. GRI-control with Tween80 in DMSO and normal saline solution, GRII - standard drug, GRIII-methanolic extract, GRIV-n-Hexane, GRV-chloroform extract, GRVI-carbon tetrachloride extract.

Psidium guvajava (Myrtaceae) [18]

The evaluation of hypoglycemic and hypolipidemic potential of ethanolic extract of leaf of *psidium guvajava* was studied on normal and alloxan induced diabetic rats. Male albino rats 6-8 weeks in age weighing 150-180g were used and divided into four groups, six rats in each group. Group I was treated with normal saline solution, Gr II with alloxan, Gr III with ethanolic extract and Gr IV with alloxan and ethanolic extract. Administration of ethanolic extract shown marked reduction in blood glucose level.

DISCUSSION

Diabetes mellitus is one of the chronic disease and is associated with hyperglycemia, hyperlipidemia, obesity and hypertension. Streptozocin selectively destroys pancreatic insulin secreting β -cells causing diabetes close to type II diabetes of humans. The loss in body weight observed in STZ induced diabetic rat group, may be due to muscle wasting and loss of tissue proteins upon induction of diabetes with STZ. In this study, the hypoglycemic activity of 14 drugs have been overviewed. In most of the studies diabetes was induced by Streptozocin or Alloxan. The hypoglycemic activity of the various extract was studied by *in vivo* or *in vitro* method. There have been many studies on hypoglycemic plants and great variety of compounds have been isolated. But very few compounds have been isolated that would be of direct beneficial to patient. The present review listed some of the plants that have been pharmacologically tested and shown to be of some value in diabetes mellitus.

Medicinal Plants with reported Antidiabetic Effect on experimental models

Sr. No.	Plant(Family)	Part of plant used	Material	No. of animals used	Drug induced diabetes	Result	Reference
1	Annona Sqamosa (Annonaceae)	Fruit peel	Alcohol, ether,ethyl acetate	36 rats	Strptozotocin	significant increase in body weight and diminished blood glucose level	Ashok Sharma et al
2	Piper longum (Piperaceae)	Root	Aqueous and ethanolic extract	albino rats	Strptozotocin	HbA1c level were well regulated near to normal in piper longum aqueous extract treated diabetic group	Shalik Abdul Nabi et al
3	Annona ReticulataL.(Annonaceae)	Leaves and stem bark	Ethanolic and aqueous extract	35 albino rats	Alloxan	brought down the elevated blood glucose level	Kalyani Pathak et al
4	Bauhinia purpurea (Leguminosae)	Stem bark	Petroleum ether, ethanol,hexane	Nil	non enzymatic glycosylation of Hb assay, glucose uptake in yeast cell, and alpha amylase inhibition assay.	Significant antiproteinase activity, inhibition of glycosylation, shows good glucose uptake by yeast cells.	Bhoomi B Joshi et al
5	Calamus erectus (Arecaceae)	fruit	Methanolic extract	wistar rat	streptozocin induced	Reduction of blood glucose level and body weight	Mitali Ghosal et al
6	Tamarandus indica Linn	Seeds	Aqueous extract	250 rats	streptozocin induced	effective in type II diabetic rat model	Anzana Parvin et al
7	Momordica Charantia (Cucurbitaceae)	Plant	----	-----	-----	Alcoholic extract lower the blood sugar level	Baby Joseph
8	kachure chooranam , Phoenix dactylifera linn (Arecaceae)	dried dates	Aqueous extract	24 rats	Alloxan	reduction in blood glucose level	
9	Zizyphus nummularia (Rhamnaceae)	Leaves	aqueous and 12% ethanolic	male albino wistar rats	dexamethasone	reduction in blood glucose level and body weight maintained	
10	Swertia Chirata (Gentianaceae)	Whole plant	aqueous and 12% ethanolic extracts	24 male albino wistar rats	Alloxan	Significant antidiabetic activity	
11	Tamarandus indica Linn (Caesalpinaceae)	Fruit pulp	ethanolic extracts	Swiss albino rats	Alloxan	Antidiabetic effect	Narendra Koyaguru et al
12	Parmelia Perlata. Ach (Permeliceae)	leaves	Aqueous extract	Swiss albino rats	Alloxan	reduced the fasting blood glucose and HbA1C level and increased the level of plasma insulin	Jothi g and Brindha p
13	Gomphrena gobosa (Amaranthaceae)	whole plant	Methanolic n-Hexane, chloroform, Carbon tetrachloride and aqueous extracts	30 Swiss albino mice	Glucose tolerance test	lower the blood glucose level	Hamiduzzaman Md.
14	Psidium guvajava (Myrtaceae)	Leaves	Ethanolic extract	24 rats	Alloxan	reduction in blood glucose level	Shakira Banu M. et al

CONCLUSION

Long before the use of insulin became common, indigenous remedies were used for the treatment of Diabetes mellitus. There has been an increasing demand from patients for the use of natural products with antidiabetic activity. This is largely because insulin can not be used orally and insulin injections are associated with the risk of hypoglycaemia and impairment of hepatic and other body functions. The undesirable side effects and contraindications of synthetic drugs and the fact that they are not suitable for the use during pregnancy, have made scientists look towards hypoglycaemic agents of plant origin [19].

In spite of presence of known antidiabetic medicines in the market, remedies from the medicinal plants are used with success to treat this disease possibly because they are considered to be less toxic and free from side effects compared to synthetic one. [20] The current paper was aimed at providing a review on research carried out on traditional medicinal plants and current research carried out on antidiabetic herbs. So a number of medicinal plants have been proven antidiabetic and related beneficial effects in treatment of diabetes are compiled.

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