

REVIEW ON SIDDHA MEDICINAL PLANTS AND FORMULATIONS WITH ANTI DIABETIC ACTIVITY

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ABSTRACT

Diabetes is a metabolic syndrome characterized by hyperglycemia, hypercholesterolemia and hypertriglyceridemia. Several medicinal plants are employed in the treatment of diabetes through all over the world. This review presents the work taken up by different workers in different parts of the world which will help in finding new dimensions for discovery of antidiabetic products. Over the past decade, herbal medicines have been accepted universally, and they have an impact on both world health and international trade. This review gives some of the medicinal plants used in the treatment of diabetes, details of those plants and their recent researches are also given. They are *Aloe vera*, *Amaranthus caudatus*, *Amaranthus spinosus* and *Amaranthus viridis*, *Bignonia spida*, *Carissa carandas*, *Cassia auriculata*, *Coscinium*

fenestratum, *Costus igneus*, *Dalbergia sissoo*, *Foeniculum vulgare*, *Holoptelea integrifolia*, *Lagerstroemia speciosa*, *Luffa aegyptica*, *Mangifera indica*, *Melia azadirach*, *Mimosa pudica*, *Scoparia dulcis*, *Syzygium cumini*, etc. and some of the Siddha formulations are also discussed in this review.

KEYWORDS: Diabetes, medicinal plants, recent research, Siddha formulations.

INTRODUCTION

Diabetes is a metabolic syndrome characterized by hyperglycemia, hypercholesterolemia and hypertriglyceridemia. Diabetes is spreading in an alarming way throughout the world and three fourth of the world populations are rely upon the use of traditional medicine, which are largely derived from plants. Numbers of plants are used in treatment of diabetes all over the world. Hence, there is a need to search the antidiabetic drugs which apart from lowering the blood glucose levels can also modify the atherogenic lipid profile without producing many side effects.^[1] This review presents the works taken up by different workers in different part of the world which in turn will help in finding new dimension in discovery of antidiabetic product. Over the past decade, herbal medicines have been accepted universally, and they have an impact on both world health and international trade. Diabetes mellitus is a metabolic disorder in the endocrine system. This dreadful disease is found in all parts of the world and is becoming a serious threat to mankind health. There are lots of chemical agents available to control and to treat diabetic patients, but total recovery from diabetes has not been reported up to this date. Alternative to these synthetic agents, plants provide a potential source of hypoglycaemic drugs and are widely used in several traditional systems of medicine to prevent diabetes. In the present scenario herbal remedies gain more importance in various aspects. Some of the Siddha formulations are also discussed in this review article.

MATERIALS AND METHODS

Aloe vera:

Oral administration of *Aloe vera* leaf extract for 21 days in alloxan induced diabetic rabbits produced a significant reduction in fasting blood glucose levels and HbA1c in our study. Also there was significant decrease in serum levels of triglycerides(TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and a concomitant increase in high density lipoprotein cholesterol(HDL-C) in *Aloe vera* treated diabetic rabbit indicates the potential of *Aloe vera* as anti diabetic drug. The significant decrease in 'Atherogenic index' in *Aloe vera* treated group shows its protection against cardio vascular diseases.

Amaranthus caudatus, Amaranthus spinosus and Amaranthus viridis

To investigate the anti-diabetic and anti-cholesterolemic activity of methanol extracts of leaves of *Amaranthus caudatus*, *Amaranthus spinosus* and *Amaranthus viridis* in normal and streptozotocin (STZ) induced diabetic rats. In this method, the anti-diabetic and anti-cholesterolemic activity of methanol extracts of leaves of all three plants was evaluated by

using normal and STZ induced diabetic rats at a dose of 200 mg/kg and 400mg/kg p.o. daily for 21 days. Blood glucose levels and body weight were monitored at specific intervals, and different biochemical parameters, serum cholesterol, serum triglyceride, high density lipoprotein, low density lipoprotein and very low density lipoprotein were also assessed in the experimental animals. Histology of pancreas was performed. Results: it was found that all the three plants at 400mg/kg dose showed significant anti-diabetic and anti-cholesterolemic activity ($P < 0.01$), while 200 mg/kg dose less significant anti-diabetic activity ($P < 0.05$) was observed. Methanol extracts of *Amaranthus caudatus*, *Amaranthus spinosus* and *Amaranthus viridis* showed significant anti-diabetic and anti-cholesterolemic activity, which provides the scientific proof for their traditional claims.^[2]

Blighia sapida

Extraction of the air-dried ground root of *Blighia sapida* (100 g) was done with 80mls distilled water for 2 h. The extract (ABRE) obtained was then administered at concentrations of 100mg/ml and 200mg/ml per 1000g body weight of the rats. The normoglycemic albino rats were employed. Qualitative phytochemical screening was carried out according to the standard methods of Trease and Evans (2006). The animals were fed ad libitum with vital finisher made up of maize and soya beans mainly. Fasting blood taken after 16h over night fasting was used in this study. The phytochemical screening of ABRE shows the presence of alkaloids, saponins, cardiac glycosides, reducing sugar, carbohydrates, flavonoids, phenol and tannin; while the test for protein showed negative results. Administration of the aqueous of *Blighia sapida* root bark at intervals of 48h for 21 days resulted in decrease in the blood glucose levels of rats. The findings of this study indicate that consumption of the ABRE exerts significant hypoglycemic effect in normoglycemic rats. These findings support the traditional use of ABRE for controlling diabetes. Further studies to isolate active principle(s) of the extracts as well as to elucidate their exact mechanism (s) of action are recommended.^[3]

Carissa carandas

In a study to investigate the effect of the orally administered aqueous extract of *Carissa carandas* on alloxan induced and normoglycemic Wister rats, the results showed that at the dose of 250 mg/kg body weight, the extract did not show any significant change in the blood glucose levels when compared to untreated control. Further, the doses of 500 and 1000 mg/kg body weight of extract showed a significant decrease in blood glucose levels after 4, 8 and 24 hours. In normoglycemic rats, the dose of 1000 mg/kg body weight of the extract

significantly decreased the blood glucose levels at 8 and 24 hours. The study concluded that the doses of extract had shown both significant hypoglycemic and antihyperglycemic effects in Wister rats.^[4]

Cassia auriculata

Aqueous extract of *Cassia auriculata* flowers was administered orally and different doses of the extract on blood glucose, haemoglobin, glycosylated haemoglobin, serum and tissue lipids, hexokinase and glucose- 6-phosphatase in streptozotocin-induced diabetic rats were studied. Glibenclamide was used as standard reference drug. *Cassia auriculata* flower extract (CFEt), at doses of 0.15, 0.30 and 0.45 g/kg body weight for 30 days, suppressed the elevated blood glucose and lipid levels in diabetic rats. *Cassia auriculata* at 0.45 g/kg was found to be comparable to glibenclamide.^[5]

Coscinium fenestratum

This work focused on the effect of *Coscinium fenestratum* ethanolic extract on plasma glucose concentrations in normal and streptozotocin (STZ)-induced diabetic rats, the stimulatory effect on insulin secretion from perfused rat pancreas and the inhibitory effects on rat intestinal-glucosidase enzymes, maltase and sucrase. In oral glucose, maltose and sucrose loading tests, the extract (250 - 1,000 mg/kg) significantly decreased plasma glucose concentrations in a dose-dependent manner. The extract (1,000 mg/kg) was most effective in decreasing plasma glucose concentrations and the response was closed to those of glibenclamide (5 mg/kg) and acarbose (3 mg/kg). In perfused rat pancreas, the extract (10µg/ml) stimulated insulin secretion in a biphasic pattern. However, the berberine at the same dose as the extract slightly increased insulin secretion by 1.33-fold over the basal control group. In addition, the extract inhibited the activities of both maltase and sucrase with the IC₅₀ of 3.89 and 11.22 mg/ml, respectively. Our findings suggest that the *Coscinium fenestratum* ethanolic extract exerted anti-hyperglycemic activity by stimulating insulin secretion and α-glucosidase inhibition.^[6]

Costus igneus

In a study to analyze the hypolipidemic effects of methanol extract of *Costus igneus* leaves in streptozotocin-induced diabetic rats, male diabetic rats were treated with 100 mg/kg/day of methanolic extract orally for 30 days. The experiment showed promising results by significantly decreasing cholesterol, triglycerides, free fatty acids and phospholipids in the liver, heart and kidney of diabetic treated rats. Lipoproteins restored normal levels in treated

group, significantly reducing serum total cholesterol and increasing High Density Lipoproteins (HDL)-cholesterol. Activity of lipoprotein lipase was enhanced in extract treated group. Glucose-6-phosphate dehydrogenase, LCAT and malic enzyme activities which were significantly lower in diabetic rats showed considerable increase in treated rats. The study, therefore, indicated that methanolic leaf extract of *Costus igneus* exerts potent hypolipidemic effects in diabetic rats. Hence the plant may also be useful in the cure and management of secondary complications of diabetes.^[7]

Dalbergia sissoo

A research was performed to characterize the hypoglycemic effect of ethanolic leaf extract of *Dalbergia sissoo* L. leaves in alloxanized diabetic rats had findings indicating the hypoglycemic and potential antihyperglycemic nature of the extract. It was also found to be 12% more effective in reducing the blood glucose level compared to the standard drug Glibenclamide.^[8]

Foeniculum vulgare

Foeniculum vulgare Mill (F. Apiaceae) is an ancient common herb and spice known to the ancient Egyptians and Greeks, traditionally used as a carminative, a weak diuretic and lactation stimulant. To evaluate the essential oil of *Foeniculum vulgare* Mill for its hypoglycaemic effect and antioxidant activity in addition to histopathological study in streptozotocin induced diabetic rats. Rats were divided into 3 groups; normal control, diabetic control and diabetic group receiving orally *Foeniculum vulgare* Mill essential oil (30 mg/kg bw). The dose of essential oil was chosen according to its LD50. Serum glucose and whole blood glutathione peroxidase were measured in addition to histopathological study of rats kidney and pancreas. Ingestion of essential oil of *Foeniculum vulgare* Mill to diabetic rats corrected the hyperglycemia from (162.5 ± 3.19 mg/dl) to (81.97 ± 1.97 mg/dl) with p<0.05 and the activity of serum glutathione peroxidase from (59.72 ± 2.78 U/g Hb) to (99.60 ± 6.38 U/g Hb) with p<0.05. Also, improved the pathological changes noticed in their kidney and pancreas. Essential oil of *Foeniculum vulgare* Mill corrected the hyperglycemia and pathological abnormalities in diabetic induced rats, which could be in part through its antioxidative effect and restoring of redox homeostasis. This makes the possibility of its inclusion in antidiabetic drug industry.^[9]

Holoptelea integrifolia

The present study was aimed at pharmacological evaluation of *Holoptelea integrifolia* leaves. Methanol, Petroleum ether extract of leaves of *Holoptelea integrifolia* (Roxb.) was screened for Antidiabetic activity. Antidiabetic was compared with standard drug with Glibenclamide for Alloxan induced method. In all method both extract showed better results statistical significances.^[10]

Lagerstroemia speciosa

The leaves of *Lagerstroemia speciosa* (Lythraceae), a Southeast Asian tree more commonly known as banaba, have been traditionally consumed in various forms by Philipinos for treatment of diabetes and kidney related diseases. In the 1990s, the popularity of this herbal medicine began to attract the attention of scientists worldwide. Since then, researchers have conducted numerous in vitro and in vivo studies that consistently confirmed the antidiabetic activity of banaba. Scientists have identified different components of banaba to be responsible for its activity. Using tumor cells as a cell model, corosolic acid was isolated from the methanol extract of banaba and shown to be an active compound. More recently, a different cell model and the focus on the water soluble fraction of the extract led to the discovery of other compounds. The ellagitannin Lagerstroemin was identified as an effective component of the banaba extract responsible for the activity. In a different approach, using 3T3-L1 adipocytes as a cell model and a glucose uptake assay as the functional screening method, Chen et al. showed that the banaba water extract exhibited an insulin-like glucose transport inducing activity. Coupling HPLC fractionation with a glucose uptake assay, gallotannins were identified in the banaba extract as components responsible for the activity, not corosolic acid. Penta-O-galloyl-glucopyranose (PGG) was identified as the most potent gallotannin. A comparison of published data with results obtained for PGG indicates that PGG has a significantly higher glucose transport stimulatory activity than Lagerstroemin. Chen et al. have also shown that PGG exhibits anti-adipogenic properties in addition to stimulating the glucose uptake in adipocytes. The combination of glucose uptake and anti-adipogenesis activity is not found in the current insulin mimetic drugs and may indicate a great therapeutic potential of PGG.^[11]

Luffa aegyptica

The alcoholic and aqueous extract of *Luffa aegyptica* was studied for antidiabetic activity In alloxan induced diabetic rats by oral administration of extract 100mg/kg body weight for 15

days. The effect was compared with oral dose of 4.5mg/kg Glibenclamide. The alcoholic and aqueous extract of *Luffa aegyptica* leaves significantly decrease the blood glucose of hyperglycemic rats. Phytochemical study showed the presence of flavonoids. It is concluded that *Luffa aegyptica* leaf extract has significant antidiabetic activity, which lowered the fasting blood glucose level in alloxan induced diabetic rats.^[12]

Mangifera indica

Mangifera indica (Anacardiaceae) stem bark contains a rich content of mangiferin and is used traditionally in Indian Ayurvedic system to treat diabetes. To investigate anti-diabetic and hypolipidemic effects of mangiferin in type 1 and type 2 diabetic rats models. Streptozotocin was used to induce type 1 and type 2 diabetic rats. Mangiferin (at a dose 10 and 20mg/kg) was administrated intra-peritoneally in type 1 and type 2 diabetic rats daily up to 30 days. Biochemical parameters notably fasting blood sugar, total cholesterol, triglycerides, low-density lipoprotein, very low-density lipoprotein and high-density lipoprotein were estimated. In addition, in vitro alpha amylase and alpha glucosidase inhibitory effects of mangiferin were performed and IC50 values were determined.

Mangiferin exhibited significant ($P < 0.05$) anti-diabetic as well as hypolipidemic effects by lowering FBS, TC, TG, LDL and VLDL levels; but also with elevation of HDL level in type 2 diabetic model rats. In addition, mangiferin showed appreciable alpha amylase inhibitory effect (IC50 value $74.35 \pm 1.9 \mu\text{g/ml}$) and alpha glucosidase inhibitory effect (IC50 $41.88 \pm 3.9 \mu\text{g/ml}$) when compared with standard drug acarbose (IC50 $83.33 \pm 1.2 \mu\text{g/ml}$). Mangiferin showed anti-diabetic as well as hypolipidemic potentials in type 2 diabetic model rats. Therefore, mangiferin possess beneficial effects in the management of type 2 diabetes with hyperlipidemia.^[13]

Mangifera indica leaves and kernel seeds were extracted with absolute alcohol and used for the study. The oral hypoglycaemic effect, glucose tolerance test and antidiabetic activity of the *Mangifera indica* kernel seeds extracts were studied at 100 and 200 mg/kg b.wt. The antidiabetic potential of *Mangifera indica* leaves and kernel seeds extract were compared with tolbutamide 500 mg/kg b.wt. The alcoholic extract of *Mangifera indica* leaves and kernel seeds at 200 mg/kg showed significant ($p < 0.01$) hypoglycaemic effect in the fasted normal rats after 3 h of drug administration, when compared with normal group. The *Mangifera indica* leaves and kernel seeds extracts were significantly increased insulin level at the dose level of 100, 200 mg/kg in aloxone induced diabetic rats. The alcoholic extract of

Mangifera indica leaves and kernel seeds having significant antidabetic effect against aloxone induced diabetes in Wistar rats and its stimulating insulin production in pancreas of Wistar rats.^[14]

Melia azadirach

In a study to evaluate the antidiabetic effect of *Melia azadirach* and its histological parameters in Alloxan induced diabetic albino rats, it was observed that oral administration of chloroform extracts of Melia leaf (250 and 500mg/kg body weight) for 30 days resulted in significant decrease of blood glucose from 298.62 ± 22.32 to 80.52 ± 04.71 and decrease in the activities of enzymes of liver. The results showed not only significant anti-hyperglycemic effect of Melia extracts in experimental model of diabetes mellitus but also indicated a dose dependant activity of the extracts. Histological studies of *Melia azadirach* in Alloxan induced albino rats, sampling and staining of pancreas, spleen, liver and kidney tissues of diabetic and normal rats showed strong antigenicity in beta-cells of the islets in control. Majority of the cells were apparently protected from light degeneration when treated with 25 and 50 ml/kg/bw of Melia and moderate antigenicity was noted in beta-cells of the islets of langerhans of the pancreatic tissue.^[15]

Mimosa pudica

In the present study attempts were made to study anti-diabetic activity of the leaves of *Mimosa pudica* Linn belonging to family Mimisace. Ethanolic and Petroleum ether extract of *Mimosa pudica* Linn use used and compared with Metformin as standard drug (500mg/kg). Wister strain of either sex were treated with Alloxan (150mg/kg) to induce diabetes. Glucose Oxidase/Perioxidase method was used for the determination of plasma glucose level. The ethanolic extract showed significant decrease in blood glucose level.^[16]

Scoparia dulcis

Scoparia dulcis L. of family Scrophulariaceae has been documented as a traditional treatment of diabetes. The effect of this plant may delay the development of diabetic complications and correct the metabolic abnormalities using variety of mechanisms. This review focuses mainly on the antidiabetic activity of this ethno medicinal plant *Scoparia dulcis* L. and the phytochemicals responsible for this bioactivity isolated from this hypoglycaemic plant.^[17]

Syzygium cumini

Syzygium cumini (Myrtaceae) is widely used traditional system of medicine to treat diabetes in India. The present study was carried out to isolate and identify the putative antidiabetic compound from the *Syzygium cumini* seed. A compound, mycaminose was isolated from *Syzygium cumini* seed extract. The isolated compound mycaminose (50 mg/kg) and ethyl acetate and methanol extracted compounds of *Syzygium cumini* (seed (200 and 400 mg/kg) was undertaken to evaluate the anti-diabetic activity against streptozotocin (STZ)- induced diabetic rates. The compound 'Mycaminose' and ethyl acetate and methanol extracted produced significant ($p < 0.05$) reduction in blood glucose level. The standard drug, glibenclamide (1.25 mg/kg) also produced significant ($p < 0.05$) reduction in blood glucose level against STZ-induced diabetic rats. The results of this experimental study indicate that isolated compound 'Mycaminose', ethyl acetate and methanol extracts possess anti-diabetic effects against STZ-induced diabetic rats.^[18]

Compound Formulation

Aqueous extract of the formulation, prepared from powder of plants, *Toddalia asiatica* (Linn.) Lam., *Terminalia chebula* Retz.; CB Clarke in part, *Terminalia bellirica* Roxb., *Eclipta alba* (Linn.) Hassk., *Enicostemma littorale* Blume, named as Pan-Five powder was subjected to phytochemical test and pharmacological screening for antidiabetic and diuretic activities. At different dose level of 100mg/kg and 200mg/kg weight, the formulation showed significant activity when compared to respective standard.^[19]

SIDDHA FORMULATIONS FOR DIABETES

1. *Kadhali Nei*
2. *Saga Vallathagi*
3. *Mathumega Pattai Thool*
4. *Mathumega Chooranam*
5. *Thoothuvalai Usitham*
6. *Saamai Usitham*
7. *Atthi Usitham*
8. *Satthuma Usitham*
9. *Neerizhivu Usitham*
10. *Vizhuthu Usitham*
11. *Mahaa Vinthathi Kuligai*

12. *Vitthathi Chooranam*
13. *Megathi Usitham*^[20]
14. *Vilaampazha Sarbatth*
15. *Vilaampazha Dhavagam*
16. *Vilaampazha Bhaanam*
17. *Raja Vallaathi*
18. *Narasimma Ilagam*^[21]
19. *Sarabaraaja Maththirai*
20. *Lagu Chanthirothaya Chendhooram*
21. *Kaala Kanda Mega Naarayana Chendhooram*
22. *Lagu Vaanama Mezhugu*^[22]
23. *Linga Kattu*^[23]
24. *Swarna Loga Chendhooram*^[24]
25. *Vallarai Chooranam*^[25]
26. *Sahala Megatthirkum Ennai*
27. *Karpoora Kalappu Thool*
28. *Sagala Mega Nei*
29. *Ashuvagenthi Kalappu Thool*
30. *Amirtha Sanjeevi Chooranam*
31. *Vilvathy Ilagam*
32. *Koozhpaanda Nei*
33. *Perum Poosani Nei*
34. *Aavaarai Nei*
35. *Kadhali Kanthaga Nei*
36. *Thaaipaal Nei*
37. *Megathy Vadagam*
38. *Abhraga Chendhooram*
39. *Chandhrodhaya Chendhooram*
40. *Suyamaakini Chendhooram*
41. *Santhanaathi Thylam*
42. *Kurunthotti Thylam*^[26]

CONCLUSION

Diabetes is a syndrome characterized by deranged carbohydrate metabolism resulting in abnormally high blood sugar level (hyperglycemia). Number of plants is used in different part of the world for curing diabetes.^[27] Management of diabetes without any side effect is still a challenge to the medical field. There is continuous search for alternative drugs; therefore it is prudent to look for options in herbal medicine for diabetes as well. Traditional antidiabetic plants might provide new oral hypoglycemic compounds which can counter the high cost and poor availability of the present day drugs for the rural population especially in developing countries.^[28]

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