Comprehensive Notes on Anti diabetic Potential of Medicinal Plants and Polyherbal Formulation

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Abstract

Diabetes mellitus is a common and serious metabolic disorder throughout the world. It is a dreadful disease found in all parts of the world and is becoming a serious threat to mankind health. Diabetes mellitus is a group of metabolic diseases characterized by high blood sugar levels that result from defects in insulin secretion, or action, or both. Traditional plants have been used throughout the world for the treatment of diabetes mellitus. Among many medications and polyherbal plants, several herbs have been known to cure and control diabetes; additionally they have no side effects. Although, synthetic oral hypoglycemic agents/insulin is the mainstream treatment of diabetes and effective in controlling hyperglycaemia, they have prominent side effects and fail to significantly alter the course of diabetic complications. This forms the main reason for an increasing number of people finding alternating therapies that may have less severe or no side effects. This article presents a review on some reported antidiabetic medicinal plants and plant based marketed polyherbal herbal formulations.

Keywords: Diabetes mellitus, Medicinal plants, glucose, polyherbal plants

1 Introduction

Diabetes is a heterogeneous metabolic disorder characterized by altered carbohydrate, lipid and protein metabolism which causes hyperglycemia resulting from insufficient insulin secretion, insulin action or both1. It is one of the refractory diseases identified by Indian council of medical research for which an alternative medicine is a need for the treatment. Diabetes mellitus has become a growing problem in the contemporary world2. The biochemical parameters (glucose, urea, creatinine, serum cholesterol, serum triglyceride, high density lipoprotein, low density lipoprotein, hemoglobin and glycosylated hemoglobin) of the polyherbal formulation were assessed in diabetic. The product showed its effectiveness in oral glucose tolerance test and antidiabetic activity, but it does not produce hypoglycemic effect. The present study supports the use of this product as an antidiabetic. The number of people with diabetes is increasing day by day the main cause of this problem is aging, urbanisation and increasing privilege of obesity and physical inactivity. Diabetes is a metabolic disorder where in human body does not produce or properly uses insulin, a hormone that is required to convert sugar, starches, and other food into energy3. Diabetes results in abnormal levels of glucose in the bloodstream.

In diabetes, hyperglycemia generates reactive oxygen species (ROS), which in turn cause lipid peroxidation and membrane damage and these free radicals play an important role in the production of secondary complications in diabetes mellitus (kidney, eye, blood vessel, and nerve damage)4. Currently available therapies for diabetes include insulin and various oral antidiabetic agents such as sulfonylureas, biguanides and glinides. Antioxidants have been shown to prevent the destruction of β- cells by inhibiting the peroxidation chain reaction and thus they may provide protection against the development of diabetes. Unfortunately, many of them have a number of serious adverse effects.

The aim of present review is to establish the use of plants, plant parts or extract in curing diabetes mellitus. It also collates available data on plants with hypoglycemic effects. In the present investigation, interest is focused on experimental studies performed on hypoglycemic plants and their bioactive components. A brief description is given about the, type of diabetes, related physiological
disorders and available herbal plants which can be further exploited for antidiabetic activity.

Additionally, in this review article an attempt was made to list out the herbal plants possessing antidiabetic activity by one or the other possible mechanisms. Different types of reported diabetes mellitus can be classified under following two categories

**Type 1 diabetes** (β-cell destruction, absolute insulin deficiency)

Type 1 is insulin-dependent diabetes mellitus (IDDM), in which the body does not produce any insulin. It most often occurs in children and young adults. Type 1 diabetes accounts for 5–10% of those with diabetes, results from a cellular-mediated autoimmune destruction of the β-cells of the pancreas.

**Type 2 diabetes** (ranging from predominantly insulin resistance with relative insulin deficiency to predominantly an insulin secretory defect with insulin resistance)

Type 2 is noninsulin-dependent diabetes mellitus (NIDDM), in which the body does not produce enough, or improper use of secreted insulin is the most common form of the disease, accounting for 90–95% of diabetes. Type 2 diabetes is nearing epidemic proportions, due to an increased number of elderly people, and a greater prevalence of obesity and sedentary lifestyles.

**1.1 Basis of Diabetes Mellitus treatment:**

The American Diabetes Association has released condensed recommendations for Standards of Medical Care in Diabetes: A bridge for primary care providers for type 1 and 2 diabetes:

- Prediabetes
- Self-management education
- Nutrition
- Physical activity
- Smoking cessation
- Psychosocial care
- Immunizations
- Glycemic treatment
- Therapeutic targets
- Diagnosis and treatment of vascular complications
- Intensification of insulin therapy in type 2 diabetes

**1.2 Herbal drugs**

As a very common chronic disease, diabetes is becoming the third “killer” of the health of mankind along with cancer, cardiovascular diseases. Therefore once diagnosed, it is well regulated by means of various therapeutically effective drugs. Besides, the therapy based on chemotherapeutic agents, the present century has progressed towards naturopathy. Thus, medical plants have an ever emerging role to play in treatment or management of lifelong prolonging diseases like diabetes mellitus. The plants in parts or as full can be used for curing any disorder related with diabetes mellitus. Moreover, extracts of plants are self capable of treating the related disorders such as polyuria, polydipsia, glucosuria, etc. along with curing the chronic disorders such as diabetes mellitus.

Herbal plants are very common in use in our day to day life. Either as a nutrient or as a source of food these herbs are being consumed by the patient as well as healthy person. Easy availability, raw consumption, least side effects and low cost makes the herbal preparations the king of all available therapies. Plants contain natural antioxidants (tannins, flavonoids, vitamins C and E, etc.) that can preserve β-cell function and prevent diabetes induced ROS formation. Herbal preparations are obtained by subjecting whole plant, fragmented or cut plants, plants parts to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.

**1.3 Advantages of herbal drugs**

- Herbal drugs are well tolerated by the patient
- It is more effective for long-standing health complaints that don’t respond well to traditional medicine
- It is cheaper than prescription medications. Research, testing, and marketing add considerably to the cost of prescription medicines
- Herbal drugs are easily available. Simple herbs, such as peppermint and chamomile, can be cultivated at home

**1.4 Mechanism of action of herbal antidiabetic**

The antidiabetic activity of herbs depends upon variety of mechanisms. The mechanism of action of herbal anti-diabetic could be grouped as-

- Adrenomimeticism, pancreatic beta cell potassium channel blocking, cAMP (2nd messenger) stimulation
- Inhibition in renal glucose reabsorption
- Stimulation of insulin secretion from beta cells of islets or/and inhibition of insulin degradative processes
- Reduction in insulin resistance
Providing certain necessary elements like calcium, zinc, magnesium, manganese and copper for the beta-cells
Regenerating and/or repairing pancreatic beta cells
Increasing the size and number of cells in the islets of Langerhans
Stimulation of insulin secretion
Stimulation of glycogenesis and hepatic glycolysis
Protective effect on the destruction of the beta cells
Improvement in digestion along with reduction in blood sugar and urea
Prevention of pathological conversion of starch to glucose
Inhibition of β-galactocidase and α-glucocidase
Cortisol lowering activities
Inhibition of alpha-amylase

2 Medicinal plants with antidiabetic properties (Fig: 1)

Acacia arabica (Mimosaceae)
Feeding 94% seed to normal rats showed significant hypoglycemic effect. However, the same diet failed to show any hypoglycemic effect in alloxanized rats indicating that plant acts through release of insulin. Powdered seeds of Acacia arabica exerted a significant hypoglycemic effect in normal rabbits by initiating the release of insulin from pancreatic beta cells.12, 13

Achyranthes aspera (Amaranthaceae)
Oral administration of A. aspera powder produces a significant 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 plant also provides certain necessary elements like calcium, zinc, magnesium, manganese and copper to the beta-cells.13, 14

Allium cepa (Liliaceae)
Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits. It is also known to have antioxidant and hypolipidemic activity. Administration of a sulfur containing amino acid, S-methyl cysteine sulfoxide to alloxan induced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues.16. When diabetic patients were given single oral dose of 50 g of onion juice, it significantly controlled post-prandial glucose levels.

Allium sativum (Liliaceae)
Oral administration of ethanol, petroleum ether, ethyl ether extract of Allium sativum causes reduction in blood sugar in alloxan-diabetic rabbits. Aqueous homogenate of garlic administered orally to sucrose fed rabbit’s significantly increased hepatic glycogen and free amino acid contents, decreased fasting blood sugar, triglyceride levels in serum, liver and aorta and protein levels in serum and liver. 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. It is concluded that the plant must be considered as excellent candidate for future studies on diabetes mellitus.17, 18

Aloe barbadensis (Liliaceae)
Aloe vera had significant antidiabetic and cardioprotective activity and reduces the increased TBARS and 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. The dried sap of the plant has shown significant hypoglycemic effect.19, 20

Andrographis paniculata (Acanthaceae)
The ethanolic extract of Andrographis paniculata significantly increases the activity of SOD and catalase. Also decreases blood glucose levels due to its antioxidant properties.21

Annona squamosa (Annonaceae)
Aqueous extract of A. squamosa root when given to STZ-induced diabetic rats reduced the blood glucose level. Further, 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.22, 23

Artemisia dracunculus (Asteraceae)
The ethanol and aqueous extracts of aerial and root of Artemisia dracunculus has significant antihyperglycemic activity in Streptozotocin-induced rats the extracts significantly lowered the elevated total cholesterol, triglycerides (TGL) and low density lipoprotein (LDL) level while increased the High density lipoprotein (HDL)24.

Azadirachta indica (Meliaceae)
Aqueous 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.25
Acacia Arabica
Achyranthes Aspera
Allium Cepa
Allium Sativum
Aloe Barbadensis
Andrographis paniculata
Annona Squamosa
Artemisia dracunculus
Azadirachta indica
Bryonia Alba
Catharanthus roseus
Euphorbia hirta
Ficus racemosa
Momordica charantia
Panax ginseng
Ocimum sanctum  Mangifera indica  Stephania hernandifolia

Tinospora cordifolia  Trigonella foenum-graecum  Ougeinia ooejinensis

**Fig 1: Different Medicinal plants of antidiabetic properties**

**Bryonia alba (Cucurbitaceae)**

Administration of trihydroxyoctadecadienoic acids obtained from the roots of *B. Alba* 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 restores26.

**Catharanthus roseus (Apocynaceae)**

Oral administration of *C. roseus* reduced the blood glucose of both normal and diabetic rabbits. Prolonged action in reduction of blood glucose by *C. roseus* and the mode of action of the active compound(s) is probably mediated through enhance secretion of insulin from the betacells of Langerhans or through extra pancreatic mechanism27.

**Euphorbia hirta (Euphorbiaceae)**

An ethanolic extract of *Euphorbia hirta* was found to reduce blood sugar in streptozotocin induced diabetic rats from 7th day after continuous administration. There was significant reduction in total cholesterol, LDL cholesterol, VLDL cholesterol and improvement in HDL cholesterol in diabetic rats28.

**Ficus racemosa (Moraceae)**

Methanol extract of leaves of *Ficus racemosa* has significant antidiabetic activity in Streptozotocin-induced rats. The effect of the extracts on diabetes 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)29.

**Momordica charantia L. (Cucurbitaceae)**

Aqueous extract and methanol fraction of *M. charantia* significantly suppresses plasma glucose levels. It suppresses postprandial hyperglycemia by inhibition of α glucosidase activity30.

**Panax ginseng (Araliaceae)**

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. *P. ginseng* root also improves insulin sensitivity and may be used as an adjuvant therapy for treating diabetic patients with insulin resistance31,32.

**Ocimum sanctum L. (Lamiaceae)**

Aqueous extract of leaves shows significant reduction in blood sugar level 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 rats33.

**Mangifera indica (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 indicates that the aqueous extract of the leaves of *M. indica* possess hypoglycemic activity35.

**Stephania hernandifolia** (Menispermaceae)

The ethanolic extract exhibited more significant antidiabetic and antioxidant activity in Streptozotocin (STZ)-induced diabetic rats. The antioxidant activity in vitro was measured by means of the 1, 1-diphenyl-2-picrylhydrazyl (DPPH) and Superoxide-free radical scavenging assay36.

**Tinospora cordifolia** (Menispermaceae)

Root extract of *T. cordifolia* shows significant reduction in blood glucose and brain lipids in alloxan diabetic rats36.

**Trigonella foenum-graeceum** (Leguminoseae)

Trigonella foenum-graeceum bark significantly decreased the blood glucose level, triglycerides, LDL, VLDL and total cholesterol and increased high density lipoprotein level in alloxan induced diabetic rats36-40.

**Ougeinia oojeinensis** (Fabaceaea)

The ethanolic extract of *O. oojeinensis* bark significantly decreased the blood glucose level, triglycerides, LDL, VLDL and total cholesterol and increased high density lipoprotein level in alloxan induced diabetic rats36-40. The ethanolic extract of *O. oojeinensis* bark significantly decreased the blood glucose level, triglycerides, LDL, VLDL and total cholesterol and increased high density lipoprotein level in alloxan induced diabetic rats36-40.

**Solanum xanthocarpum** (Solanaceae)

Methanolic extract of *S. xanthocarpum* significantly reduced the blood glucose level, urea, uric acid and creatinine level and increased the serum insulin level in alloxan induced diabetic rats41.

3 Herbal drug formulations

Diabecon manufactured by ‘to increase peripheral utilization of glucose, increase hepatic and muscle glucagon contents, promote B cells repair and regeneration and increase c peptide level.

3.1 Epinsulin

Marketed by Swastik formulations, contains epicatechin, a benzopyran, as an active principle. Epicatechin increases the cAMP content of the islet, which is associated with increased insulin release. It plays a role in the conversion of proinsulin to insulin by increasing cathepsin activity. Additionally it has an insulin-mimetic effect on osmotic fragility of human erythrocytes and it inhibits Na/K ATPase activity from patient’s erythrocytes. It corrects the neuropathy, retinopathy and disturbed metabolism of glucose and lipids. It maintains the integrity of all organ systems affected by the disease. It is reported to be a curative for diabetes, NIDDM and a good adjuvant for IDDM, in order to reduce the amount of needed insulin. It is advised along with existing oral hypoglycemic drugs and is known to prevent diabetic complications. It has gentle hypoglycemic activity and hence induces no risk of being hypoglycemic42-46.

4 Polyherbal Formulations *Annona squamosa* and *Nigella sativa*

Polyherbal formulation of *Annona squamosa* and *Nigella sativa* decreased blood glucose, plasma insulin, tissue lipid profile, and lipid peroxidation in streptozotocin induced diabetic rats. Aqueous extract of polyherbal formulation was administered orally (200 mg/kg body weight) for 30 days. The different doses of polyherbal formulation on blood glucose and plasma insulin in diabetic rats were studied and the levels of lipid peroxides and tissue lipids were also estimated in streptozotocin induced diabetic rats. The effects were compared with tolbutamide. Treatment with polyherbal formulation and tolbutamide resulted in a significant reduction of blood glucose and increase in plasma insulin47,48.

4.1 Polyherbal Formulation of Kashore guggulu

Triphala and giloya are cut into small pieces manually or into a pulverizer. They are dipped overnight into water. In the morning, this water is boiled until 1/4th of water is left. Then, decoction is prepared by filtering this water. In this decoction of triphala and giloya, purified guggul gum is added and this mixture is heated slowly so that we get syrup like liquid of hard consistency. Now, powders of herbs are added and this mixture is pounded (stricken again and again) either by hand or in a mortar and pestle or in chattu machine. Processing this mixture for some hours decreases the particle size and increases the bioavailability of the mixture. Thereafter, tablets are made from this gum like mixture either by hand or by tablet machine. The average size varies between 250-500 mg per tablet. It is taken with milk or water or herbal decoction48.

5 Conclusions

The prevalence of diabetes mellitus continues to rise worldwide and treatment with oral hypoglycemic drugs ends with numerous side effects and huge monetary expenditure. There is increasing demand by patients to use the natural products with antidiabetic activity. This paper has presented various anti-diabetic plants that have been pharmacologically tested and shown to be of some value in treatment of diabetes Mellitus. The effects of these plants may delay the development of diabetic complications and correct the metabolic abnormalities. However, more investigations must be carried out to evaluate the mechanism of action of medicinal plants with antidiabetic effect.
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7 Competing interest

None

8 Author’s contributions

US and SPT carried out literature review and draft the manuscript. AR participated in collection of data. All authors read and approved the final manuscript.

9 Reference


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