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Review Article

Herbal Drugs with Anti-Diabetic Potential

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Abstract

Diabetes mellitus (DM), also known as insulin-dependent diabetes mellitus (IDDM) and non-insulin dependent diabetes mellitus (NIDDM), is a common and serious metabolic condition that affects people all over the world. Traditional herbal plants have been utilized to treat diabetes mellitus all throughout the world. Several herbs have been found to treat and control diabetes among numerous medicines and poly herbal plants; they also have no adverse effects. Diabetes mellitus is a horrible disease that affects people all over the world and is becoming a serious danger to humanity's health. Thus, herbal plants may be a possible source of anti-diabetic medicines, with ethno botanical data indicating that around 800 plants may have anti-diabetic potential. Although synthetic oral hypoglycemic agents/insulin are a popular diabetes therapy and are effective in controlling hyperglycemia, they have significant side effects and do not significantly modify the course of diabetic complications. This is the primary reason why an increasing number of individuals are looking for alternative medicines with fewer or no adverse effects. The botanical name, common name, component, and mechanism of action for anti-diabetic activity were provided in this review study, as well as plant-based commercial poly herbal formulations.

Keywords: Diabetes mellitus, Medicinal plants, glucose, poly herbal plants

INTRODUCTION

Diabetes is a metabolic disease characterized by alterations in glucose, lipid, and protein metabolism, resulting in hyperglycemia and inadequate insulin production, action, or both.[1,2] It is one of the stubborn illnesses recognized by the Indian Council of Medical Research for which a replacement drug is required for diabetic therapy. Diabetes mellitus is a major problem in today's world.[3] In diabetes, the biochemical parameters of the poly herbal formulation (glucose, urea, creatinine, serum cholesterol, serum triglyceride, high density lipoprotein, low density lipoprotein, hemoglobin, and glycosylated hemoglobin) were calculated. Although this product performed well in an oral glucose tolerance test, it does not have a hypoglycemic impact. The treatment of diabetic rats with herbal products resulted in substantial improvements in biochemical markers. According to the current study, the herbal substance can be used as an anti-diabetic.[4] The number of persons suffering from diabetes is steadily growing, Aging, urbanization, and the rising prevalence of obesity and physical inactivity are the primary causes of this disease. Estimate the diabetic burden and the number of people affected by diabetes; today and in the future, it is critical to have logical planning and allocation of resources for diabetes treatment and prevention. Diabetes is a metabolic condition in which the human body does not generate enough insulin, a hormone needed to convert sugar, starches, and other carbohydrates into energy.[5]

Diabetes is characterized by abnormal glucose levels in the bloodstream. Herbal plants may be found in abundance in our daily lives. These herbs are ingested by both the ill and the healthy individual as a nutrient or a source of nourishment. Herbal plans are widely available, may be consumed uncooked, have little adverse effects, and are inexpensive. Herbal medicines reign supreme over all other remedies.[6] The majority of diabetes cases fall into one of two basic etio pathogenic groups. The first is type 1 diabetes, which is characterized by an apparent lack of insulin secretion. On the other hand, much more widespread category is type 2 diabetes; the main cause is a combination of resistance to insulin action and an inadequate compensatory insulin-secretary response (American Diabetes Association, 2005). Now a day's available therapies of diabetes include insulin and various oral anti diabetic agents such as sulfonylurea's, biguanides and glinides.[7] They have a large number of serious side effects; therefore, in the search the more effective and safer hypoglycemic agents is one of the most important areas of investigation. In diabetes, the hyperglycemia give rise to reactive oxygen species (ROS), which result in lipid per oxidation and damage of membrane. These free radicals play a critical role in the development of diabetes mellitus secondary complications (kidney, eye, blood vessel, and nerve damage).[8,9] Antioxidants defend against the occurrence of diabetes by blocking the per oxidation chain reaction, which prevents the death of ß- cells.

Natural antioxidants found in plants include tannins, flavanoids, vitamins C and E, and others. They can protect ß-cell function as well as the production of reactive oxygen species (ROS) caused by diabetes. We attempted to identify the herbal plants that have anti-diabetic action through two or more pathways in this review paper.[10, 11] Diabetes mellitus is defined by high blood glucose levels caused by inadequate insulin, insulin resistance, or both, resulting in metabolic abnormalities in carbohydrates, lipids, and proteins. It can develop to acute or chronic problems such as ketoacidosis, microangiopathy, and other infections if not treated or managed. The following two categories can be used to classify different kinds of diabetes mellitus:

Type 1 is a insulin-dependent diabetes mellitus (IDDM), in this type the body does not produce any Insulin secretion. It is commonly occur in children and young adults. In Type 1 diabetes 5–10% people are suffered from these types of Diabetes.

Type 2 is a noninsulin-dependent diabetes mellitus (NIDDM), in this type the body does not produce enough, or improper use of secreted insulin. It is the most common form of the disease, In Type 2 diabetes 90–95% people are suffered from this type of diabetes. The Type 2 diabetes is a epidemic proportions, because a large number of elderly people suffered from this type of diabetes, because have a greater prevalence of obesity and sedentary lifestyles.

Basis of Diabetes Mellitus treatment:

• Patient education from concerning the disease

• Physical exercise

• Diet and

• Hypoglycemic agents

Diabetes mellitus alone is because of its enormous incidence, morbidity, and mortality, diabetes has surpassed cancer as the third "killer" of mankind's health, behind cancer, cardiovascular, and cerebrovascular illnesses. As a result, once identified, it is successfully controlled with a variety of therapeutically effective medications. Apart from the fact that the treatment is based on chemotherapy drugs, the twentieth century has seen a shift toward naturopathy. Thus, medicinal plants have a significant role in the treatment or management of illnesses that prolong life, such as diabetes mellitus, particularly in poor nations with limited resources. Along with a slew of other illnesses that have infected otherwise healthy people. Using India's herbal integrity to treat such diseases is a viable option. The herbal plants can be utilized in part or whole to treat diabetes mellitus-related disorders. Furthermore, plant extracts can cure associated illnesses including polyuria, polydipsia, and glucosuria, as well as chronic diseases like diabetes mellitus.

Advantages[14, 15]

• Most of the herbal drugs are well tolerated by the patient, having fewer casual consequences and fewer side effects than traditional medicine, and it may be safer to use.

• Herbal drugs are more effective for long-standing health complaints and it don't respond well to traditional medicine

• Cost of herbal drugs is much less than prescription medications. Research, testing, and marketing add considerably to the cost of prescription medicines. Herbs tend to be inexpensive compared to drugs.

• Herbs are available without a prescription. Simple herbs, such as peppermint and chamomile, can be cultivated at home.

Life style for patient [16, 17]

• Some of the home and herbal remedies prescribed by Ayurveda are described below.

1. Turmeric and cinnamon are included in diets.

2. Oily, fried and starchy foodstuffs are avoided.

3. Coffee, sugar, refined flour and alcohol are avoided.

4. Eat smaller meals (low fat diet) five to six times a day instead of having three large meals.

5. Intake of vegetables like spinach, cucumber, tomatoes, onion, sprouts, beans, garlic

etc is increased.

6. Refrain from taking stress.

7. Regular exercise. Walk for at least 40 minutes a day.

8. Avoid red meat and excessive salt in your meals. Fish and soybean can be taken due to their good protein value.

9. Avoid white bread, rice, potatoes, sweet and sugary foods.

Recent Regulatory Developments:

Herbal medications, as defined by regulatory standards, are traditional medicines that predominantly employ medicinal plants in their therapeutic formulations. Traditional medicine (including herbal medicines) has lately been described by the World Health Organization as therapeutic techniques that have been in use for hundreds of years or more before the creation and spread of modern medicine, as well as others that are currently in use. In recent years, the FDA and EMEA have shown a great interest in botanical medicine research and have examined the regulatory frameworks controlling their use.. This heightened interest has given the natural goods industry a substantial boost, lowering the entry barriers for botanicals and allied items. These new rules are more crucial than ever before, since they ensure market exclusivity for botanicals and the approval of synergistic combinations of plant-derived bioactive products. India and China, both developing and developed countries, have a distinct inherent edge over the rest of the world.[18,19]

Mechanism of Action of Herbal Anti diabetics [20, 21]

The anti-diabetic activity of herbal plant are depends upon various mechanisms. The mechanism of action of herbal anti-diabetic can be grouped as:

• Adrenomimeticism, pancreatic beta cell potassium channel blocking, cAMP (2nd messenger) Stimulation.

• Inhibition of urinal 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–glycosidase.

• Cortical lowering activities.

• Inhibition of alpha-amylase.

MEDICINAL PLANTS WITH ANTIDIABETIC AND RELATED BENEFICIAL PROPERTIES

Acacia Arabica (Mimosaceae)

Acacia Arabica is found and farmed across India. 94 percent of the seed meal was fed to normal rats, with a substantial hypoglycemic impact as compared to controls. However, the same diet had no influence on blood sugar levels in alloxanized rats (175 mg/kg SC) show that the herbal plant affects insulin release. In normal rabbits, powdered Acacia Arabica seeds given in dosages of 2, 3, and 4 gm/kg body weight induced the release of insulin from pancreatic beta cells, resulting in a significant (PB/0.05) hypoglycemic effect. At these dosages, no acute toxicity or behavioral abnormalities were detected. It may be found all across India. By functioning as a secretion to release of insulin, the plant extract serves as an anti-diabetic drug. In control rats, it causes hypoglycemia, but not in alloxanized animals. When normal rabbits are given powdered Acacia Arabica seeds (2, 3 or 4 g/kg body weight), it causes hypoglycemia via triggering insulin release from pancreatic beta cells.[22, 23]

Achyranthes aspera (Amaranthaceae)

This could be found all across the planet's tropical regions. Oral administration of Achyranthus aspera powder causes a significant dose-related hypoglycemia impact in both normal and diabetic rabbits. In both normal and alloxan diabetic rabbits, the water and methanol extracts lower blood glucose levels. At doses up to 8 g/kg orally, this herbal medication had no adverse or side effects in rabbits in an acute toxicity trial. Calcium, zinc, magnesium, manganese, and copper are some of the essential nutrients that the plant might provide to the beta-cell.[23, 24]

Allium cepa, Onion (Liliaceae)

Although Allium cepa is solely known from cultivation, similar wild species can be found throughout Central Asia. In diabetic rabbits, several ether soluble fractions as well as insoluble fractions of dried onion powder have anti-hyperglycemic effect. [25, 26] Allium cepa also has anti-oxidant and anti-lipidemic properties. S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) was given to alloxan-induced diabetic rats and was shown to dramatically reduce blood glucose and lipid levels in serum and tissues despite the fact that Allium cepa is only known from cultivation, comparable wild species may be found all across Central Asia. Several ether soluble fractions as well as insoluble fractions of dried onion powder exhibit anti-hyperglycemic effects in diabetic rabbits. Allium cepa have anti-oxidant and anti-lipidemic effects. S-methyl cysteine sulphoxide (SMCS) was administered to alloxan-induced diabetic rats at a dose of 200 mg/kg for 45 days, and it was shown to significantly lower blood glucose and lipid levels in serum and tissue. The activities of liver hexokinase, glucose 6-phosphatase, and HMG CoA reductase are all normalized. [27,28,29] When a diabetic patient was given a single oral dosage of 50 g onion juice, post-prandial glucose levels were considerably reduced. [29, 30]

Figure 1: *Acacia arabica*

Figure 2: *Allium cepa*

Allium Sativum, garlic (Liliaceae)

It's a perennial herb that's grown all throughout India. It is widely used as a food additive. In alloxan diabetic rabbits (150 mg/kg IV), oral treatment of 0.25 gm/kg ethanol, petroleum ether, and ethyl ether extract of Allium sativum caused 18.9, 17.9, and 26.2 percent decrease in blood sugar. In slightly diabetic rabbits (glucose levels ranging from 180 to 300 mg percent), oral treatment of 0.25 gm/kg allicin (isolated from A. sativum) induced hypoglycemia equivalent to tolbutamide, whereas it had no such effect in severely diabetic animals (blood sugar-/350 mg percent). Oral administration of aqueous garlic homogenate (10 ml/kg/day) to sucrose-fed rabbits (10 gm/kg/day in water for 2 months) In comparison to sucrose controls, there was a substantial increase in hepatic glycogen and free amino acid content, as well as a decrease in fasting blood sugar, triglyceride levels in serum, liver, and aorta, and protein levels in serum and liver. When compared to the anti diabetic medication glibenclamide, oral treatment of garlic extract significantly lowers blood glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, AST and ALT levels while increasing serum insulin in diabetic rats but not in normal rats. The extract's anti-diabetic efficacy was superior to that of glibenclamide. The plant should be regarded a good option for future diabetes mellitus research, according to the researchers.[31, 32]

Aloe barbadensis, Aloe gibberellins (Liliaceae)

It thrives in arid conditions and is found throughout Africa, India, and other dry regions. In diabetic rats, aloe Vera gel at 200 mg/kg exhibited substantial anti diabetic and cardio protective action, reducing elevated TBARS, maintaining Superoxide dismutase and Catalase activity at normal levels, and increasing reduced glutathione by four times.[33] The extract's leaf pulp had hypoglycemic action in IDDM and NIDDM rats, with the efficacy for type II diabetes being higher than glibenclamide. In STZ diabetic mice, both Aloe Vera and (at doses ranging from 2-100 mg/kg) suppress inflammation and enhance wound healing in a dose-dependent manner.[34] Both clinically and experimentally, the dried sap of the plant (half a tablespoon daily for 4-14 weeks) has demonstrated a substantial hypoglycemic impact.

Aloe Vera (Liliaceae)

It looks like a cactus and has green dagger-shaped leaves that are fleshy, tapering, spiky, and packed with sticky gel. The hypoglycemic activity of Aloe Vera aqueous extract was administered orally at a dosage of 150mg/kg of body weight. Treatment of chronic but no single dosage of exudates of Aloe barbadensis leaves exhibits hypoglycemic effect in alloxanized diabetic rats. In diabetic rats, single and chronic dosages of bitter principle from the same plant had a hypoglycemic impact. This is accomplished by stimulating insulin production and/or release from pancreatic beta cells.[35, 36]

Andrographis paniculata (Acanthaceae)

It's a herbaceous plant native to India and Sri Lanka that's commonly grown in southern Asia. SOD and Catalase activities are considerably increased when andrographis is taken orally. Its antioxidant qualities also help to lower blood glucose levels. The ethanolic extract of A. paniculata has anti-diabetic properties, which may be due to an increase in glucose metabolism. In diabetics, its hypotriglyceridemic action is also helpful. It's a herbaceous plant native to India and Sri Lanka that's commonly grown in southern Asia. SOD and Catalase activities are considerably increased when andrographis is taken orally. Its antioxidant qualities also help to lower blood glucose levels. [37, 38]

Figure 3: *Allium sativum*

Figure 4: *Aloe Vera*

Figure 5: *Andrographis paniculata*

Annona squamosa (Annonaceae)

It thrives at lower altitudes and is a tiny, well-branched tree or shrub. The hyperglycemic mice were given 15 mg/kg/day of isolated juercetin-3-O-glucoside from Annona squamosa leaves for 10 days, which reversed these effects while also inhibiting hepatic GIucose-6-phosphatase activity. The blood glucose level in STZ-induced diabetic rats was decreased from 285.52 to 208.81 mg/dl 6 hours after oral administration of an aqueous extract of A. squamosa root (at doses of 250 mg/kg and 500 mg/kg bw). It also reduces hepatic and renal lipid per oxidation while simultaneously increasing the activity of anti oxidative enzymes like Catalase and Superoxide dismutase, as well as glutathione levels, showing that it is safe and antiperoxidative.[39, 40]

Azadirachta-indica (Meliaceae)

Neem is the common name for this plant. It is a tropical and semi-tropical tree native to India, Burma, Bangladesh, Sri Lanka, Malaysia, and Pakistan. In type-2 diabetic patients whose diabetes is not controlled by oral hypoglycemic agents, low (0.5g tid) and high (2g tid) doses of powdered part, aqueous extract, and alcoholic extract of A. indica show significant hypoglycemic activity in high dose and can be successfully combined with these agents..[41]

Catharanthus roseus (Apocynaceae)

Oral treatment of 0.5, 0.75, and 1.0 mL/kg body weight decreased blood glucose levels in normal and diabetic rabbits to levels equivalent to glibenclamide, a typical medication. The results show that C. Roseus has a long-lasting effect on blood glucose reduction, and the active compounds method of action is most likely mediated by increased insulin production from Langerhans betacells or by an extrapancreatic mechanism.[44]

Figure 6: *Azadirachta indica*

Figure 7: *Catharanthus roseus*

***Momordica charantia* L. (Cucurbitaceae)**

Vegetable insulin is made from M. charantia (bitter melon). In a 30-minute oral sucrose tolerance test, administration of aqueous extract (AE), methanol fraction (MF), or methanol insoluble fraction (MIF) all considerably lower plasma glucose levels than control. Furthermore, in the oral sucrose tolerance test, the plasma insulin level at 30 minutes after MF administration is lower than the control, demonstrating that bitter melon reduces postprandial hyperglycemia via inhibiting glycosidase activity.[45]

***Panax ginseng* (Araliaceae)**

The roots are used to treat type 2 diabetes when taken orally. In the liver and muscle, extracts of ginseng species have anti hyperglycemic action, which is linked to enhanced peroxisome proliferator-activated receptor gamma expression and activation of adenosine monophosphate-activated protein kinase. P. ginseng root taken orally enhances insulin sensitivity and may be utilized as an adjunct treatment for diabetic individuals with insulin resistance.[46, 47, 48]

***Ocimum sanctum* L. (Lamiaceae)**

Tulsi is the popular name for it. This herb has been used for therapeutic purposes since ancient times. [49, 50] The hypoglycemic and hypolipidemic benefits of tulsi in diabetic rats were demonstrated by significant reductions in fasting blood glucose, uronic acid, total amino acid, total cholesterol, triglyceride, and total lipid.[51, 52] The plasma glucose level is reduced after 30 days of oral administration of plant extract (200 mg/kg). In diabetic rats, renal glycogen content rises tenfold, whereas skeletal muscle and hepatic glycogen levels fall by 68 and 75 percent, respectively, when compared to control rats. Antioxidant, antibacterial, antifungal, antiviral, antiasthemitic, antistress, anticancer, stomach antiulcer activity, antimutagenic, and immunostimulant properties have also been observed in this plant. [53, 54]

***Tinospora cordifolia* (Menispermaceae)**

Guduchi is the common name for a herbaceous vine native to India, Myanmar, and Sri Lanka's tropical regions. Blood glucose and brain lipids are significantly reduced in alloxan diabetic rats after oral treatment of an aqueous T. cordifolia root extract. Despite the fact that the aqueous extract at a dosage of 400 mg/kg has a substantial anti hyperglycemic effect in many animal models, its impact is only one unit/kg of insulin.[55, 56]

Figure 8: *Tinospora cordifolia*

Figure 9: *Ocimum sanctum*

Table 1: Some Plants Having Hypoglycemic Activities.[57]

S.no.	Common name	Botanical name and family	Parts used	Therapeutic action
1	Asiatic ginseng	Panax ginseng (Araliac)	Roots	Reduces blood glucose levels via slowing the absorption of carbohydrates, enhancing glucose transport, and modulating insulin secretion.
2	Ashwagandha, winter cheery	Withania somnifera (Solanaceae)	Roots	Reduced blood sugar levels
3	Asiatic sweet leaf	Symplocos Paniculata (Symplocaceae)	Leaves/ stems	1 and 2 inhibitors of protein tyrosine phosphatase 1B (PTP1B)
4	Banana	Musa sapientum Kuntz (Musaceae)	Fruits/flowers	Blood glucose and glycosylated hemoglobin levels are reduced.
5	Banyan tree	Ficus bengalensis (Moraceae)	Bark	Insulinase activity in the liver and kidneys is inhibited, and insulin secretion is stimulated.
6	Barbados	Aloe barbadensis Mill. (Liliaceae)	Leaves	Insulin production and release are stimulated.
7	Betal, betal wine	Piper betle (Piperaceae)	Leaf	glucose metabolism, anti-hyperglycemic
8	Bilwa, bael fruit	Aegle marmelos (Rutaceae)	Leaf Extract	Decrease cholesterol and blood urea level
9	Bitter kola, false kola	Garcinia kola (Clusiaceae)	Seed	Hypoglycemic and Hypolipidemic
10	Black tea	Camellia sinensis (Theaceae)	Leaves	Leaves help to lower blood sugar levels.

Table 2: Marketed Herbal Anti diabetic Products

S.no.	Product	Manufacturer	Mechanism	Ref
1	Sharang Dyab-Tea	Plant Med lab Pvt. Ltd.	Insulin synthesis should be encouraged.	[61]
2	Herbal hills jambu	Isha Agro Developers	Blood and urine sugar levels should be lowered.	[62]
3	Stevia-33	Vitalize Herbs Pvt. Ltd.	Beta cells in the pancreas should be activated.	[63]
4	Diab-FIT	Herbal FIT	Maintain a normal blood sugar level.	[64]
5	Madhumar capsule	Kangrd Hills Care and Products	Control diabetes mellitus in people who have it for a long time.	[65]
6	Daya Stone Powder	Jignesh and Co.	Reduce your blood glucose level.	[66]
7	Blue berry	Hikma FZCO	Antidiabetic	[67]
8	Episulin	Varuna Biocell Pvt. Ltd.	Antidiabetic	[68]

Figure 10: Stevia 33

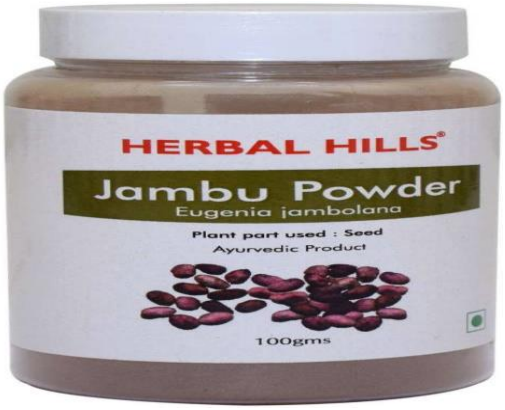

Figure 11: Herbal hills jambu powder

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CONCLUSION

The most prevalent and dangerous endocrine disease is diabetes mellitus. This illness affects more than 300 million people throughout the world. As a result, medicines based on western medical principles (allopathic) are generally ineffective, have a high risk of side effects, and are prohibitively expensive, especially in poor countries. Diabetes mellitus is becoming more common across the world, and treatment with oral hypoglycemic medications comes with a slew of adverse effects and a hefty price tag. Patients are increasingly requesting natural medicines with anti-diabetic properties. Various anti-diabetic herbs have been pharmacologically examined and proven to be of some use in the treatment of Diabetes Mellitus in this study. These plants' properties may help to postpone the onset of diabetes problems and rectify metabolic imbalances. However, further research is needed to determine the mechanism of action of medicinal herbs having anti-diabetic properties.

The purpose of this review is to determine whether plants, plant parts, or extracts may be used to treat diabetes mellitus. It also compiles information on plants that have hypoglycemic properties. Experimental research on hypoglycemic plants and their bioactive components are the focus of the current inquiry. The kind of diabetes, associated physiological problems, and accessible herbal plants that might be further explored for anti-diabetic action are all briefly described. Overall, the profiles of plants with hypoglycemic characteristics documented in the literature are presented in this review. All of the herbal medicines that have been mentioned.

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