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A Review on Herbal Drug Therapy for Diabetes Mellitus

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ABSTRACT

This review focuses on the study of herbal drugs used in Diabetes mellitus treatment. Diabetes mellitus becomes a common metabolic disorder that poses a serious threat to the world's public health. Approximately 60 percent of the world's population use traditional medicines derived from medicinal plants. Due to lower side effects and low cost, herbal formulations are favoured. Synonymous with herbal medicine, phyto medicine or botanical medicine, plants are used for medicinal purposes. Herbal selection may depend on a number of factors, including the stage of diabetes progression, the types of co morbidities that patients have availability, affordability, and herbal safety profile. A list is compiled of medicinal plants with proven antidiabetic and related beneficial effects and herbal medicines used in diabetes treatment.

Key words:
Diabetes mellitus, herbal drugs, treatment, Insulin secretion, antidiabetic.

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INTRODUCTION

Diabetes is a chronic carbohydrate, fat, and protein metabolism disorder characterized by increased blood sugar levels and post-prandial fasting. This eventually leads to multiple body systems being damaged. Insulin is a protein hormone that controls insulin, fat, and protein metabolism in the body [8]. Any insulin production and action deficiency leads to severe metabolic problems. There are two types of diabetes, diabetes mellitus type 1 (T1DM) and type 2 (T2DM). T1DM is known as insulin-dependent diabetes mellitus (IDDM) and is due to insulin production being impaired. Nevertheless, T2DM is commonly associated with the cell's inability to respond to insulin (insulin resistance) and is therefore referred to as non-insulin-dependent diabetes mellitus (NIDDM). Diabetes mellitus is a complex metabolic disorder resulting from either insulin insufficiency or insulin dysfunction. In T1DM, β-cells of the pancreas are damaged, leading to a decreased insulin supply to the circulation. Patients will be fully dependent on exogenous insulin administration for existence. Contrary to this, T2DM was found in most diabetic patients (85 percent) resulting in peripheral insulin resistance, resulting in reduced insulin sensitivity to the skeletal muscles, adipose tissue and liver. Factors like aging, obesity, physical inactivity, population growth and urbanization can lead to a steady increase in the number of diabetes patients. Type II diabetes is the more common form of diabetes constituting 90% of the diabetic population. The global prevalence of diabetes is estimated to increase, from 4% in 1995 to 5.4% by the year 2025. WHO has predicted that the major burden will occur in developing countries.

Symptoms for both diabetic conditions may include

(i) High Levels Of Sugar In The Blood;
(ii) Unusual Thirst;
(iii) Frequent Urination;
(iv) Extreme Hunger And Loss Of Weight;
(v) Blurred Vision;
(vi) Nausea And Vomiting;
(vii) Extreme Weakness And Tiredness;
(viii) Irritability, Mood Changes Etc.

Common antidiabetic drugs

Many classes of pharmaceutical agents are currently used to treat diabetes by various mechanisms, such as inducing insulin release (e.g., sulfonylureas), decreasing hepatic glucose production, and enhancing peripheral glucose uptake (e.g. biguanidins) [27,28,29]. Some of the antidiabetes drugs commonly used include biguanides,e.g., metformin (via acting directly to influence insulin resistance), peroxisome proliferator activated receptor (PPAR) activators, e.g., thiazolidindiones (via improving insulin resistance), vidagliptin and other related "gliptins" (via blocking DPP-4, an enzyme that degrades the incretin GLP-1) and α-glucosidase inhibitors, e.g. acarbose and miglitol (via delaying the digestion of complex carbohydrates). Other diabetic agents target pancreatic beta-cell receptors by binding to the sulfonylurea receptor subunit, blocking the K^+-ATP channel to promote insulin release.

There are many common herbs claiming to lower blood glucose levels, so the possibility of better glycemic control or being less dependent on insulin injections by taking herbal medicines is undoubtedly appealing. Nevertheless, herbal choice may rely on several factors, including the stage of diabetes development,

the types of co morbidities patients have, availability, affordability, and the herbal safety profile. Preclinical studies passed the laboratories ' threshold and entered the patients ' bedside. For the diagnosis of diabetes, medicinal plants are being looked up again. For medicinal plants, most modern medicines are extracted from prototypic molecules. Metformin is an effective oral glucose-lowering agent. The development was focused on diabetes treatment using Galega officinalis. Galega officinalis is rich in guanidine, the hypoglycemic component. Because guanidine is too toxic for clinical use, the alkyl biguanides synthalin A and synthalin B were introduced as oral anti-diabetic agents in Europe in the 1920s but were discontinued after insulin became more widely available. To date, over 400 traditional plant treatments for diabetes have been reported, although only a small number of these have received scientific and medical evaluation to assess their efficacy.

Medicinal Plants with Antidiabetic and Related Beneficial Effects

There are many suggested herbal remedies for diabetes and complications with diabetes. The main ingredients of these formulations are medicinal plants. A list of antidiabetic and related beneficial effects medicinal plants is presented in Table 1.

Plant Name	Ayurvedic/common name/herbal formulation	Antidiabetic and other beneficial effects in traditional medicine
Annona squamosa	Sugar apple	Hypoglycemic and antihyperglycemic activities of ethanolic leaf-extract, Increased plasma insulin level
Artemisia pallens	Davana	Hypoglycemic, increases peripheral glucose utilization or inhibits glucose reabsorption
Areca catechu	Supari	Hypoglycemic
Beta vulgaris	Chukkander	Increases glucose tolerance in OGTT
Boerhavia diffusa	punarnava	Increase in hexokinase activity,decrease in glucose-6-phosphatase and fructose bis-phosphatase activity, increase plasma insulin level, antioxidant
Bombax ceiba	Semul	Hypoglycemic
Butea monosperma	Palasa	Antihyperglycemic
Camellia sinensis	Tea	Anti-hyperglycemic activity, antioxidant
Capparis decidua	Karir or Pinju	Hypoglycemic, antioxidant, hypolipidaemic
Caesalpinia bonducella	Sagarghota, Fevernut	Hypoglycemic, insulin secretagogue, hypolipidemic
Coccinia indica	Bimb or Kanturi	Hypoglycemic
Emblica officinalis	Amla, Dhatriphala, a constituent of herbal formulation, “Triphala”	Decreases lipid peroxidation, antioxidant, hypoglycemic
Eugenia uniflora	Pitanga	Hypoglycemic, inhibits lipase activity
Ficus bengalenesis	Bur	Hypoglycemic, antioxidant

Acacia arabica: (Babhul);

It is found mostly in the wild habitat throughout India. The plant extract acts as an antidiabetic agent to release insulin by acting as a secretagouge. In control rats, but not in alloxanized animals, it induces hypoglycemia. When administered to normal rabbits, powdered seeds of Acacia arabica (2,3 and 4 g / kg body weight) induced hypoglycemic effect by initiating insulin release from pancreatic beta cells[16].

Aegle marmelos:

(Bengal Quince, Bel or Bilva) Aqueous leaf extract administration improves digestion and reduces blood sugar and urea, serum cholesterol compared to control in alloxanized rats. This extract, together with hypoglycemic activity, also prevented a peak increase in blood sugar at 1 hour in the oral glucose tolerance test [17].

Allium cepa: (onion)

Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits. Allium cepa is also known to have antioxidant and hypolipidaemic activity. Administration of a sulfur containing amino acid from Allium cepa, S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) to alloxan induced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues and normalized the activities of liver hexokinase, glucose 6-phosphatase and HMG Co A reductase [18, 19].

Allium sativum: (garlic)

This is a perennial herb that is grown all over India. Allicin is responsible for its pungent odor, a sulfur-containing compound, and substantial hypoglycemic activity has been shown. This effect is believed to be due to increased hepatic metabolism, increased release of insulin from pancreatic beta cells and/or insulin sparing effect.

Aloe vera and Aloe barbadensis

Aloe, a popular houseplant, as a multi-purpose folk remedy, has a long history. Two essential substances can be isolated from the plant: gel and latex. Aloe vera gel is the pulp of the leaf or mucilage, aloe latex, commonly known as "aloe juice," is a bitter

yellow exudate from the pericyclic tubules just below the leaves ' outer skin..

Azadirachta indica: (Neem)

Hydroalcoholic extracts from this plant demonstrated anti-hyperglycemic activity in rats treated with streptozotocin and this effect is due to increased glucose uptake and deposition of glycogen in isolated rat hemidiaphragm. This plant also has antibacterial, antimalarial, antifertility, hepatoprotective and antioxidant effects as well as anti-diabetic activity.

Caesalpinia bonducella

Caesalpinia bonducella is common throughout India's coastal region and used ethnically by India's tribal people to control blood sugar. For chronic type II diabetic models, both the aqueous and ethanolic extracts displayed strong hypoglycemic activity. These extracts also increased glycogenesis, increasing the content of liver glycogen.

Capparis decidua

This can be found all over India, especially in dry areas. In alloxanized rats, hypoglycemic effect was observed when the rats were fed 30% of Capparis decidua (C. decidua) fruit powder extracts for 3 weeks. This extract also significantly reduced lipid peroxidation caused by alloxan in erythrocytes, kidneys and heart. C. Decidua was also found to alter the enzyme levels of superoxide dismutase and catalase to reduce oxidative stress.

Coccinia indica

Coccinia indica (C. indica) dried extracts (500 mg / kg body weight) were given for 6 weeks to diabetic patients. Both extracts also restored the reduced enzyme lipoprotein lipase (LPL) and glucose-6-phosphatase and lactate dehydrogenase activities that have been elevated in untreated diabetics. Oral administration of 500 mg/kg of C. indica leaves showed significant hypoglycemia in alloxanized diabetic dogs and increased glucose tolerance in normal and diabetic dogs.

Eugenia jambolana: (Indian gooseberry, jamun)

Eugenia jambolana kernel decoction is used as a household remedy for diabetes in India. This is also a major component of many diabetes herbal formulations. Antihyperglycemic activity of both aqueous and alcoholic extract and lyophilized powder has lowered blood glucose levels. Such extracts have inhibited liver and renal insulinase function.

Mangifera indica: (Mango)

The leaves of this plant are used in Nigerian folk medicine as an antidiabetic agent, although in normoglycemic or streptozotocin-induced diabetic rats, aqueous extract given orally did not alter blood glucose levels. Antidiabetic activity was observed, however, when the extract and glucose were administered simultaneously and when the extract was administered to the rats 60 minutes before the glucose. The results indicate that aqueous extract of Mangifera indica possess hypoglycemic activity. This may be due to an intestinal reduction of the absorption of glucose.

Momordica charantia: (bitter gourd)

Momordica charantia is commonly used as an antidiabetic and antihyperglycemic agent in India as well as other Asian countries. Extracts of fruit pulp, seed, leaves and whole plant was shown to have hypoglycemic effect in various animal models. Polypeptide p, isolated from fruit, seeds and tissues of M. charantia showed significant hypoglycemic effect when administered subcutaneously to langurs and humans. Ethanolic extracts of M. charantia (200 mg/kg) showed an antihyperglycemic and also hypoglycemic effect.

Ocimum sanctum: (holy basil)

It's commonly referred to as Tulsi. This plant has been known for its medicinal properties since ancient times. Ocimum sanctum's aqueous leaf extract showed a significant decrease in blood sugar levels in both normal and alloxan-induced diabetic rats. There was a significant decrease in blood glucose, uronic acid, total amino acid, total cholesterol, triglyceride and total lipid indicated the hypoglycemic and hypolipidemic effects of tulsi in diabetic rats. Oral administration of plant extract (200 mg/kg) for 30 days led to decrease in the plasma glucose level by approximately 9.06 and 26.4% on 15 and 30 days of the experiment respectively.

Phyllanthus amarus: (bhuiawala)

It is a herb of up to 60 cm in height from the Euphorbiaceae family. It is commonly referred to as Bhuiamala. It is scattered all over India's hotter parts, mainly Deccan, Konkan, and southern Indian states. It is traditionally used in the treatment of diabetes. Phyllanthus amarus methanolic extract has been found to have potent antioxidant activity. This extract also reduced the blood sugar in alloxanized diabetic rats. The plant also shows antiinflammatory, antimutagenic, anticarcinogenic, antidiarrhoeal activity.

Pterocarpus marsupium:

It is a moderate to large deciduous tree found primarily in the hilly region of India. Pterostilbene, a component derived from this plant's wood that caused hypoglycemia in dogs, showed that this extract's hypoglycemic activity was due to the presence of tannates in the extract. Pterocarpus marsupium flavonoid fraction has been shown to cause regranulation of pancreatic beta cells .Marsupin, pterosupin and liquiritigenin obtained from this plant showed antihyperlipidemic activity .

Trigonella foenum graecum: (fenugreek)

It is found all over India and the fenugreek seeds are usually used as one of the major constituents of Indian spices. 4-hydroxyleucine, a novel amino acid from fenugreek seeds increased glucose stimulated insulin release by isolated islet cells in both rats and humans. It also reduced hepatic and renal glucose-6-phosphatase and fructose −1, 6-biphosphatase activity . This plant also shows antioxidant activity.

Tinospora cordifolia: (Guduchi)

It is a large, glabrous, deciduous shrub of the Menispermaceae family. It is widespread across India and is commonly referred to as Guduchi. For 6 weeks, oral administration of the Tinospora cordifolia extract (T. cordifolia) roots resulted in a significant reduction in blood and urine glucose and in serum and tissue lipids in alloxan diabetic rats.The extract also prevented a decrease in body weight. T. cordifolia is widely used in Indian ayurvedic medicine for treating diabetes mellitus

Herbs and Compounds That Regulate Insulin Resistance Amorfrutins and Licorice

Licorice, the common name for the plants that comprise the genus Glycyrrhiza, is utilized as herbal medicine for a wide range of diseases. The ethanol extract of G. uralensis was found to reduce blood glucose, fat weight, and blood pressure in rodent models.

Dioscorea Polysaccharides and Dioscorea

The rhizome of Dioscorea is used as a traditional Chinese medicine for asthma, abscesses, chronic diarrhea, and ulcers. Dioscorea extract reduced blood glucose in high fat diet-induced rats.

Anthocyanins and Blueberry

Blueberry (Vaccinium spp.) was demonstrated to lower systolic and diastolic blood pressure and lipid oxidation and improves insulin resistance, diabetes, diabetic complications, and digestion [. Notably, blueberries contain powerful antioxidants that can neutralize free radicals that cause neurodegenerative disease, cardiovascular disease, and cancer. Accordingly, phenolics and anthocyanins were proposed as active compounds for diabetes and insulin resistance.

Astragalus Polysaccharides and Astragalus

Astragalus membranaceus root has been used as a Chinese medicine for a long time and has antioxidant, antidiabetic, antihypertensive and immunomodulatory activities. A's extract. Membranaceus has been shown to treat diabetes and complications of diabetes. In addition, treatment with Astragalus polysaccharides improved glycemic control in diabetic rodents through increased insulin sensitivity.

Gastrodia elata

G. elata has been utilized as Chinese medicine for blood circulation and memory. More recently, the extract of G. elata has been reported to improve insulin resistance. Vanillin and 4-hydroxybenzaldehyde were proposed as the active compounds.

Cinnamon

All common cinnamon (Cinnamomum verum and C. zeylanicum) and cassia (C. aromaticum) have been used in beverages and medicines worldwide for a long time as flavoring agents. Traditionally, cinnamon was used for rheumatism, wounds, nausea, headaches, and colds. Extensive studies on the effect of cinnamon on diabetes and metabolic syndrome have been carried out recently. Cinnamon was shown to reduce blood glucose via reduction of insulin resistance and increase of hepatic glycogenesis. Cinnamon phenolics were proposed to be the active compounds in modulation of insulin signaling.

Fenugreek

Fenugreek seeds (Trigonella foenum-graecum) are used as a food supplement and have a long history of labor induction medicine, aiding digestion and improving metabolism and nutrition. Animal studies have shown that fenugreek seed extract can decrease blood glucose levels. Fenugreek is thought to be a promising diabetes agent and its complications. The glucose-lowering action of this plant involves reduction of insulin resistance.

Lychee

Lychee (Litchi chinensis) is an evergreen fruit tree. Its seeds are used as a Chinese herbal medicine for pain, gastrointestinal diseases, and others. Recently, lychee seed was reported to have antidiabetic activity in rats and human patients. Lychee seed extract exerts its action through reduction of insulin resistance. In addition, oligonol from lychee fruit showed anti-oxidative activity and, thus, protected the liver and kidney in T2D animal models.

Herbs and Compounds with Multiple Antidiabetic Actions

Some plants and plant compounds can target multiple metabolic pathways.

Berberine

Berberine was first isolated from Berberis vulgaris, an isoquinoline alkaloid. This compound has multiple functions ranging from inhibition of inflammation and cancer suppression to metabolic syndrome reduction and other activities. With respect to T2D, this compound lowered hyperglycemia, increased insulin resistance, stimulated pancreatic -cell regeneration, and decreased lipid peroxidation in a mouse model of T2D. Thus, it may be useful for treatment of T2D and other types of diabetes.

Bitter Melon

Bitter melon, the fruit of the plant Momordica charantia is used in Ayurvedic medicine [156]. The biochemistry and bioactivities associated with the antidiabetic effect of the extracts of bitter melon and M. charantia as a whole have been extensively studied.. Modes of action of bitter melon and M. charantia include insulin secretion, inhibition of glucose reabsorption in guts, preservation of islet cells and their functions, increase of peripheral glucose utilization, and suppression of gluconeogenic enzymes.

Capsaicin and Chili Pepper

Chili peppers, the fruits of the Capsicum plants, are commonly used as food and medicine. Chili pepper extract exerts an insulinotropic action, implying its action on cells. Capsaicin, a pungent component of chili pepper, activates AMPK in 3T3-L1 preadipocytes

Ginseng

In oriental medicine, ginseng (Panax ginseng) was seen as a panacea. In rodent models, P. ginseng and North American ginseng (P. quinquefolius) have been shown to reduce blood glucose. In humans and/or rodents, roots, berries and/or leaves have been found to be effective against T2D. Both ginsengs ' glucose-reduction mechanisms may involve a reduction in insulin resistance and-cell function.

Turmeric

Curcumin is a major component of turmeric rhizomatous powder (Curcuma longa) and is widely used in Southern Asia as food and medicine. Curcumin and turmeric rhizomes have a number of bioactivities, including antioxidant, anti-inflammatory, antidiabetic, and immunomodulatory activities. T2D has been treated with curcumin. Overall, turmeric is likely to exercise antidiabetic action through insulin regulation, -cell function, and gut absorption.

Ginger

Zingiber officinale, is commonly used as an ingredient in foods and medicine. Compelling data show that ginger extract has hypoglycemic, insulinotropic, and sensitizer effects on healthy humans and on experimental animals. More recently, Li and colleagues reported that ginger extract enhanced insulin release and reduced insulin resistance. One clinical study reported that consumption of ginger powder, 3 g per day for 30 days, significantly reduced blood glucose and lipids in T2D patients. Gingerol and shogaol are the main active compounds in ginger extract.

CONCLUSION:

The use of plants is one of the ancient traditions, the urge to evaluate the mechanism of their underlying pharmacological action and its associated benefits and adverse effects is imposed on the present society. Thus, the use of herbal medicines for the prevention, well-being and treatment of diabetes is still being continued in modern society. As a result, many herbs have demonstrated antidiabetic activity by regulating insulin secretion, cell sensitivity to insulin, glucose abruption, etc.

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