



Review on Herbal Medication of Diabetes Mellitus

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Abstract

Chronic metabolic disease known as diabetes mellitus (DM) is defined by hyperglycemia brought on by insufficient insulin secretion, resistance to insulin action, or a combination of the two. In recent years, DM has spread like an epidemic both in the US and internationally. The morbidity and mortality associated with diabetes are anticipated to account for a substantial proportion of health care expenditures. Although there are several drug treatments currently available, the need for new herbal agents for the treatment of diabetes remains. Over the past 80 years, there has been a major evolution in the treatment objectives for diabetes patients, from preventing impending death to symptom relief to the now accepted goal of normalizing or approaching normal glucose levels in order to prevent diabetic complications. The results of a thorough literature search on natural plants investigated for anti-diabetic action during the past 80 years are summarized in the current review. The material has been summarized in an effort to draw attention to the chemical compounds and plant species that merit additional study as potential sources for new medication development. The researchers and businesspeople interested in diabetes should take note of the more than 100 plant species from a variety of families that have been included here. These plants contain different chemical classes of chemicals.

Keywords: Diabetes Mellitus types, management and treatment, herbal drug formulation.

Introduction

Diabetes is a long-term condition of the metabolism of carbohydrates, fats, and proteins marked by elevated fasting and postprandial blood sugar levels. By the year 2025, it is predicted that the global prevalence of diabetes will increase from 4% in 1995 to 5.4%. According to WHO, developing nations will shoulder the majority of the burden. Studies carried out in India over the past ten years have shown that not only is the prevalence of diabetes high, but it is also rising quickly among urban residents¹. In India, there are thought to be 33 million persons who have

diabetes. By 2025, this figure is probably going to rise to 57.2 million.

A complex metabolic condition known as diabetes mellitus is caused by either inadequate or dysfunctional insulin. Due to a deficiency in functioning beta cells, type I diabetes (insulin-dependent) is brought on by inadequate insulin production. Patients with this condition are consequently fully dependent on an exogenous source of insulin, in contrast to type II diabetes patients, who are insulin independent and can be treated with dietary changes, physical activity, and medication. 90% of people with diabetes have type II

diabetes, which is the more prevalent type. The anomalies induced in lipids and proteins are the main causative factors for the development of diabetes complications. The primary targets of free radicals in diabetic patients are extra-cellular and long-lived proteins such as elastin, laminin, and collagen. Due to hyperglycemia, these proteins are altered to create glycoproteins. The development of diabetic sequelae such as cataracts, microangiopathy, atherosclerosis, and nephropathy is linked to the alteration of these proteins, which are found in tissues like the lens, vascular wall, and basement membranes².

Free radicals oxidise lipoproteins when a person has diabetes. Additionally, very low density lipoprotein (VLDL), low density lipoprotein (LDL), and high density lipoprotein (HDL) all exhibit various anomalies in lipoprotein metabolism in diabetes. Increased oxidative stress in diabetes circumstances increases lipid peroxidation. Additionally, advanced glycation end products (AGEs) are created when proteins are glycosylated non-enzymatically. Atypical activities of cells and tissues are produced by AGE accumulation on long-lived molecules in tissues^{3,4}. Additionally, through binding to particular macrophage receptors, AGEs also contribute to enhanced vascular permeability in both micro- and macro-vascular structures. Free radicals are produced as a result, which causes endothelial dysfunction. AGEs can also form on histones and nucleic acids, which can result in gene expression changes and mutations.

Diabetes necessitates a diverse therapeutic approach due to the fact that it is a complex disease that causes several complications. Diabetes patients' cells either do not respond to insulin or do not produce enough of it. Patients receive insulin injections when they are completely insulin-deficient. Contrarily, numerous medications are being created to treat cells that do not respond to insulin while taking into account potential problems with carbohydrate metabolism. Acarbose, miglitol, and voglibose are a few examples of glucosidase inhibitors that are used to treat postprandial hyperglycemia at the digestive level.

Classification of Diabetes:

Diabetes Mellitus Type 1

The beta cells of the pancreatic islets of Langerhans, which are in charge of creating insulin, are destroyed in type 1 diabetes mellitus [DM]. Broadly T-cell-mediated auto-immune diseases' destructive effects As a result, it causes the blood's level of insulin to drop. There is just one preventive therapy for type 1 diabetes mellitus—insulin—and about 10% of cases are identified in North America and Europe. The majority of patients with type 1 diabetes mellitus are healthy, or, to put it another way, they were healthy at the time of beginning. In the early stages of treatment, almost everyone is responsive to insulin, but this sensitivity decreases over time. Juvenile diabetes is another name for type 1 diabetes, which affects youngsters more often than adults^[5].

Treatment of type 1 does not interfere with regular daytime and evening activities. If the patient is well informed, the required care and dosing are administered in a disciplined manner, and blood glucose levels are monitored, the patient may nevertheless feel slightly burdened by the treatments. Blood glucose levels in type 1 diabetes should be monitored as closely as feasible to normal levels (80-120 mg/dl), if at all possible. According to doctors, individuals who experience frequent hypoglycemia episodes should have their glucose levels checked every 140 to 150 ng/dl since any higher may cause frequent urination, which can cause dehydration. If untreated, ketosis, which happens when blood glucose levels exceed 300, can be fatal. In contrast, hypoglycemia, which can result in seizures and uncontrollable episodes, needs to be treated right away.

Diabetes Mellitus Type 2

The most prevalent kind of diabetes in the world is Type 2, commonly referred to as Non-Insulin Dependent Diabetes Mellitus [NIDDM] or adult-onset diabetes. The syndrome of type 2 diabetes is brought on by intricate interplay between inherited and environmental variables⁶. Type 2 diabetes mellitus has been attributed to a wide range of factors. It is believed that obesity—particularly abdominal obesity—is to blame for these patients'

poor insulin tolerance. The physiology of glucose is hampered by the hormone adipokines, which is secreted by hormonally active abdominal fat. Obesity is discovered in 50% of patients with type 2 diabetes. The ageing process and family history are other causes of type 2 diabetes. Anyone with type 2 diabetes who has had affected family members is likely to have this condition themselves. The percentage of children and adolescents has significantly increased over the past 20 years as a result of the rise in childhood obesity. Poor diet, a sedentary lifestyle, stress, drug-induced infections (staphylococcus), hypertension, and high levels of blood lipid and lipoprotein are additional causes of type 2 diabetes ^{7,8}.

Gestational Diabetes

The hormones necessary for the placenta's growth, which aids in the development of the foetus, also prevent the mother's insulin from working properly in her body. Insulin resistance is the issue at hand. A mother may require up to three times as much insulin during pregnancy for glucose to leave the blood and convert to energy. Gestational diabetes develops when the body becomes resistant to the effects of insulin. Hyperglycemia is the term for when blood glucose levels reach an elevated level ^{9,10}. In late pregnancy, gestational diabetes affects both the mother and the unborn child. Contrary to glucose and other nutrients, insulin does not pass the placenta. The placenta absorbs extra blood glucose,

which raises the baby's blood sugar levels. The baby's pancreas produces more insulin to lower the blood sugar as a result. The excess energy is stored as fat because the baby is receiving more energy than it need for growth and development. It may result in macrosomia, or a baby that is "fat." This obese newborn has respiratory issues from birth and may experience hypoglycemia because of an excess of insulin ¹¹.

Other Types

Classification efforts are still debatable because there are a number of uncommon causes of diabetes mellitus that do not fall into type 1, type 2, or gestational diabetes. Even when insulin levels are normal, which distinguishes it from type 2 diabetes, certain cases of diabetes are brought on by the body's tissue receptors failing to react to insulin. This type of diabetes is extremely rare. Defects in beta cell function can result from genetic alterations, whether they are autosomal or mitochondrial. In rare circumstances, abnormal insulin activity may also be genetically predetermined. Diabetes can result from any condition that severely damages the pancreas, such as cystic fibrosis and chronic pancreatitis. Diabetes can be brought on by conditions linked to increased secretion of insulin-antagonistic hormones, although it usually goes away once the excess hormone is eliminated. Numerous medications reduce insulin release, and certain toxins harm beta cells in the pancreas ¹²⁻¹⁹.

Table no.1 Few Medicinal Plants with Beneficial Effects on Diabetes and Other Conditions

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
Capparis decidua	Karir or Pinju	Hypoglycemic, antioxidant, hypolipidaemic
Emblica officinalis	Amla, Dhatriphala, a constituent of herbal formulation, "Triphala"	Decreases lipid peroxidation, antioxidant, hypoglycemic
Ficus bengalensis	Bur	Hypoglycemic, antioxidant

Management and Treatment

Knowing everything there is to know about diabetes is crucial because, while it cannot be completely cured, DM can be successfully managed. The patient is ultimately responsible for managing their food, exercise routine, and medication in order to control their diabetes. Better methods for managing diabetes and treating its complications have emerged as a result of advancements in diabetes research.

- External and implantable insulin pumps, along with new, better insulin, have made significant advancements in managing high blood sugar levels without allergic responses.
- Oral hypoglycemic medications regulate type 2 diabetes.
- Hemoglobin A1c laboratory testing and new, better blood glucose monitors [new gadget for personal blood glucose monitoring] are both used to assess blood glucose control during the last three months.
- Effective accessibility to treatments for diabetes-related organ damage.

Due to the fact that DM is a chronic condition, there is sadly no complete treatment. Diabetes can only be managed with appropriate medication, exercise, diet restriction, and monitoring of blood glucose levels within the acceptable range, all of which do not alter normal physiology. Therefore, the patient needs to be informed about all diabetes-related complications, whether they are short-term or long-term.

Although there is just one treatment option for type 1 DM—insulin—and oral hypoglycaemics are only useful in type 2 DM. Diabetes carries a number of cardiovascular risks, although these can be adequately managed with the right lifestyle choices and medication if required.

Exercise and a healthy diet can successfully monitor cholesterol-related complications. The only way to treat type 1 diabetes is by external insulin delivery. This could involve either natural insulin (insulin) or artificial insulin (Humalog, Novolog). Today, however, there are insulin pumps that can detect the blood glucose level and release the appropriate amount of insulin to maintain a healthy blood glucose level.

Table no .2 Formulated Herbal Drugs with Anti Diabetic Properties

Drug	Company	Ingredients
Diabecon	Himalaya	Gymnema sylvestre, Pterocarpus marsupium, Glycyrrhiza glabra, Casearia esculenta, Syzygium cumini, Asparagus racemosus, Boerhavia diffusa, Sphaeranthus indicus, Tinospora cordifolia, Swertia chirata, Tribulus terrestris, Phyllanthus amarus, Gmelina arborea, Gossypium herbaceum, Berberis aristata, Aloe vera, Triphala, Commiphora wightii, shilajeet, Momordica charantia, Piper nigrum, Ocimum sanctum, Abutilon indicum, Curcuma longa, Rumex

		maritimus
Diasulin		Cassia auriculata, Coccinia indica, Curcuma longa, Emblica officinalis, Gymnema sylvestre, Momordica charantia, Scoparia dulcis, Syzygium cumini, Tinospora cordifolia, Trigonella foenum graecum
Pancreatic tonic 180 cp	ayurvedic herbal supplement	Pterocarpus marsupium, Gymnema sylvestre, Momordica charantia, Syzygium cumini, Trigonella foenum graecum, Azadirachta indica, Ficus racemosa, Aegle marmelos, Cinnamomum tamala
Ayurveda alternative herbal formula to Diabetes	Chakrapani Ayurveda	Gurmar (Gymnema sylvestre) Karela (Momordica charantia) Pushkarmool (Inula racemosa) Jamun Gutli (Syzygium cumini) Neem (Azadirachta indica) Methika (Trigonella foenum graecum) Guduchi (Tinospora cordifolia)
Bitter gourd Powder	Garry and Sun natural Remedies	Bitter gourd (Momordica charantia)

Indian Medicinal Plants with Beneficial Effects for Diabetes and Other Conditions

Numerous herbal treatments are recommended for diabetes and its consequences. The majority of these compositions' constituents come from medicinal plants.

Acacia Arabica: (Babul)

It is primarily found in untamed habitats in India. By acting as an insulin secretagogue, the plant extract counteracts diabetes. In control rats, it causes hypoglycemia, but not in alloxanized animals. When normal rabbits received 2, 3, and 4 g/kg of powdered *Acacia arabica* seeds, the release of insulin from the pancreatic beta cells resulted in a hypoglycemic effect³¹.

Marmelo Aegle: (Bengal Quince, Bel or Bilva)

In comparison to control, giving alloxanized rats aqueous extract of the leaves improves digestion and lowers blood sugar, urea, and serum cholesterol. This extract not only showed hypoglycemic action but also reduced the peak rise in blood sugar at 1 hour in the oral glucose tolerance test³².

The Onion Cepa (onion)

Different ether-soluble fractions of dried onion powder as well as its insoluble fractions exhibit anti-hyperglycemic effect in diabetic rabbits.

Additionally, the antioxidant and hypolipidemic properties of *Allium cepa* are well documented. S-methyl cysteine sulphoxide (SMCS), an amino acid from the *Allium cepa* family that contains sulphur, was administered to alloxan-induced diabetic rats for 45 days at a dose of 200 mg/kg. This treatment significantly reduced serum and tissue lipid levels and normalised the activities of the enzymes liver hexokinase, glucose 6-phosphatase, and HMG-CoA reductase^{33,34}. One oral dose of 50 g of onion juice significantly reduced post-prandial glucose levels in diabetic patients³⁵.

Aloe Barbadosis and Aloe Vera

Popular indoor plant aloe has a long history of use as a variety of folk remedies. Gel and latex are the two fundamental compounds that can be extracted from the plant. Aloe latex, sometimes known as "aloe juice," is an exudate from the pericyclic tubules just below the outer epidermis of the leaves and is a bitter yellow liquid. Aloe vera gel is the leaf pulp or mucilage. In both normal and diabetic rats, aloe gum extracts efficiently enhance glucose tolerance³⁶. Exudates from *Aloe barbadensis* leaves had a hypoglycemic impact on alloxanized diabetic rats but not on single doses of treatment. In diabetic rats, single and repeated dosages of the bitter component of the same plant also had hypoglycemic effects.

Aloe vera's activity and bitter principle stimulate the production and/or release of insulin from pancreatic beta cell [37]. Additionally, this plant improves wound healing in diabetic mice and has dose-dependent anti-inflammatory activity [38].

Azadirachta Indica: (Neem)

In streptozotocin-treated rats, hydroalcoholic extracts of this plant exhibited antihyperglycemic activity. This effect is due to an increase in glucose absorption and glycogen deposition in isolated rat hemidiaphragm [39,40]. This herb not only contains anti-diabetic properties, but also anti-bacterial, anti-malarial, anti-fertility, hepatoprotective, and antioxidant ones [41].

Capparis Deciduas

This is found throughout India, especially in dry areas. When rats were fed fruit powder containing 30% extract of the Capparis decidua (*C. decidua*) plant for three weeks, the rodents' blood sugar levels decreased. Additionally, in erythrocytes, kidney, and heart, this extract greatly reduced lipid peroxidation caused by alloxan. In order to lessen oxidative stress, *C. Decidua* was also found to change the levels of the enzymes catalase and superoxide dismutase [42]. *C. Decidua* also demonstrated hypolipidaemic activity [43].

Coccinia Indica

Patients with diabetes received dried extracts of *Coccinia indica* (*C. indica*) (500 mg/kg body weight) for six weeks. In diabetics who had not received treatment, these extracts reversed the lowered and elevated activity of the enzymes glucose-6-phosphatase, lactate dehydrogenase, and lipoprotein lipase (LPL) [44]. administering 500 mg/kg of *C* orally. In alloxanized diabetic pups, *indica* leaves significantly reduced blood sugar levels and enhanced glucose tolerance in both healthy and diabetic dogs.

Eugenia Jambolana: (Indian Gooseberry, Jamun)

A decoction made from *Eugenia jambolana* kernels is a common home treatment for diabetes in India. This also makes up a significant portion of several herbal

diabetes medications. A decrease in blood glucose level is indicated by the antihyperglycemic effect of aqueous and alcoholic extracts as well as lyophilized powder. This changes with different stages of diabetes. It indicates a 73.51% reduction in mild diabetes (plasma sugar >180 mg/dl), but only 55.62% and 17.72% reductions in moderate and severe diabetes (plasma sugar >280 mg/dl and >400 mg/dl, respectively) [45]. In streptozotocin-induced diabetic mice, the extract of jamun pulp displayed hypoglycemic action within 30 minutes of treatment, whereas the extract of jamun seed took 24 hours. administration of the extract orally. In streptozotocin-induced diabetic mice, the extract of jamun pulp displayed hypoglycemic action within 30 minutes of treatment, whereas the extract of jamun seed took 24 hours. When the extract was given orally to diabetic rats, the serum insulin levels rose. The incubation of plant extract with isolated islets of Langerhans from normal as well as diabetic rats was reported to enhance insulin secretion. These extracts also inhibited insulinase activity in the liver and kidney [46].

Herbal Drug Formulations

Admark Herbals Ltd.'s Dia-Care is marketed as having an 18-month cure rate for both Type 1 and Type 2 diabetes after 90 days of treatment. Insulin users will finally be freed from their reliance on it. The entire course of treatment is completed in six phases, each lasting 90 days. A little over 5 grammes of powder, or about 1 tea spoon, is combined with 1/2 glass of water, thoroughly swirled, and left overnight. The only thing that needs to be consumed in the morning on an empty stomach is water, not sediment. Fresh water is added to the remaining medication, kept overnight, and swallowed 30 minutes before dinner. The medication has an extremely bitter flavour. It is an all-natural formula. with no negative consequences.

A special natural solution called Diabetes-Daily Care, produced by Nature's Health Supply, effectively and safely enhances sugar metabolism. All the natural substances indicated in Table 2 are included in Diabetes Daily Care™, which was created

specifically for type 2 diabetics, in the ratio that is best for the body to use.

With a mix of effective immunomodulators, anti-hyperlipidemics, anti-stress, and hepatoprotective qualities of plant origin, DIABETA, a formulation of Ayurvedic Cure that is available in pill form, is an anti-diabetic. The Diabeta formulation is based on ancient Ayurvedic references, which are further supported by current research and clinical testing. Diabetes affects many body regions in various strategies for controlling elements and routes efficiently leading to diabetes mellitus. It targets a number of factors, which triggered the diabetes and treats the diabetic complications that cause degenerative issues. Diabeta is safe and effective in managing Diabetes Mellitus as a single-agent supplement to synthetic anti-diabetic drugs.

Diabeta helps overcome resistance to oral hypoglycemic drugs when used as an adjuvant in cases of uncontrolled diabetes. Diabeta confers a sense of well-being on patients and promotes symptomatic relief of complaints like weakness, giddiness, pain in the legs, body ache, polyuria, and pruritis. Fenugreek seed extracts are found in the Plethico Laboratory product Syndrex. For more than a thousand years, fenugreek has been a component in conventional recipes. Currently, animal models and cultured islet cells are being used to understand the mechanism of this anti-diabetic medication. As a result, a wide variety of plants have been utilised singly or in combination with other ingredients to treat diabetes and its consequences. One of the primary concerns with this herbal composition is that the active components are not properly defined. The active ingredients and their molecular interactions must be understood in order to standardise the product and analyse its therapeutic efficacy. The mechanism of action of some of these plants is now being studied using model systems.

Conclusion

Hyperglycemia brought on by insufficient insulin production, resistance to insulin action, or a combination of the two is what diabetes mellitus (DM), a chronic metabolic condition, is characterised

by. DM has become an epidemic in recent years, both domestically and abroad. The goals of treatment for diabetes patients have undergone a significant development over the past 80 years, moving from averting impending mortality through symptom relief to the current acknowledged target of stabilising or near normal glucose levels in order to prevent diabetic complications. In the current review, the findings of a thorough literature search on natural plants examined for anti-diabetic effect during the past 80 years are compiled. The information has been condensed in an effort to highlight the substances and plant species that demand more research as potential sources for the creation of novel medications. Different chemical classes are present in these plants.

Acknowledgement

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