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SHORT REVIEW

Anti-Diabetic Activity of Herbal Remedies

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Abstract

Herbal remedies, often known as herbal medicine or botanical medicine, are natural treatments that make use of the therapeutic capabilities of plants and plant-based extracts. Due to their apparent efficacy and lack of negative side effects, these treatments have been practiced for centuries in numerous civilizations all over the world. The usage of plant parts such as leaves, stems, flowers, roots, and seeds, as well as extracts made from plants, are just a few examples of the diverse practices that fall under the umbrella of herbal medicines. Numerous consequences are linked to diabetes, a long-term metabolic illness characterized by elevated blood sugar levels that affects millions of individuals worldwide. Many cultures have a long history of using herbal treatments to control diabetes, and this use is predicated on the idea that specific plants and plant extracts contain antidiabetic qualities. Garlic, neem, coriander, ivy gourd, papaya, jamun, tulsi, aloe vera, and many other plants are used in herbal therapies for diabetes. Since free radical damage is believed to have a part in the etiology of diabetes and its associated issues, an anti-diabetic drug having antioxidant qualities would be more successful. In conclusion, herbal remedies have shown promising anti-diabetic benefits and might be thought of as alternatives to or complements to current diabetes management strategies. To assess their efficacy, safety, and the best approach to use them in the management of diabetes, more research is needed. Before beginning therapy, it is crucial to consider the use of herbal products as diabetic therapies with a qualified medical expert due to the risk of interactions with other medications and the fact that every person's health is different. To ensure its trustworthiness in terms of both efficacy and safety, herbal products must be subjected to standardization and quality control.

Keywords: Anti-Diabetic, Antioxidant, India, Side Effects, Traditional Medicines

1. Introduction

Diabetes mellitus, an endocrine disorder that cannot be transmitted from person to person, is characterized by abnormalities in glucose metabolism and hyperglycemia. The occurrence of both micro-vascular (nephropathy, retinopathy, and nephropathy) and macro-vascular (peripheral vascular disease and coronary heart diseases) complications have been linked to it[1,2].

Type I diabetes is characterized by insulin insufficiency brought on by a deficiency of beta cells (insulin dependent). Type I diabetes (insulin dependence) should depend on exogenous insulin for continued existence, whereas individuals with Type II diabetes (insulin resistance) cannot react to insulin and can be controlled with dietetic modifications, work out, and medicines. Around 90% of all diabetics suffer with Type II diabetes, making it the most prevalent form of the disease. Both forms of diabetes have the following symptoms: Symptoms include (i) Elevated blood sugar levels (ii) Increased urine frequency (iii) Severe tiredness and weariness (iv) Intense thirst, intense appetite, and weight loss (v) Hazy vision (vi) Nausea and vomiting (vii) Irritability and mood swings, etc. Experimental evidence suggests that free radicals

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have a role in diabetes aetiology[3] and more prominently, the progression of diabetic complications[4-6], even though the biology of diabetes remains unexplained. DNA, proteins, and lipids are all vulnerable to damage from free radicals, which can affect normal cellular functions. As per the latest published reports, to prevent experimentally persuaded diabetes in animal models and to reduce the severe complications of diabetes, antioxidants which act by free radical neutralization are helpful[7,8]. The prevalence of diabetes in India has increased by 64% over the quarter century, says a November 2017 report by the Indian Council for Medical Research Institute for Health Metrics and Evaluation, and the Public Health Foundation of India. About 98 million Indians could have diabetes by 2030- these projections come from the International Diabetes Federation and the global burden of disease project. Currently, India is undergoing a rapid epidemiological transition with increased urbanisation. The current urbanization rate is 35% compared to 15% in the 1950s and this could have major implications on the present and future disease patterns in India with particular reference to diabetes and coronary artery disease[9]. About six times as many people in urban regions as in rural areas have diabetes. The primary causes of diabetes mellitus during the past 20 years have been decreased physical activity, increasing body weight and stress, dietary changes, malnutrition, alcohol consumption, and viral infection[10]. Female diabetic patients have a greater mortality rate than male diabetic patients due to differences in the way hormones and inflammation work in women. Diabetes is more prevalent among persons with less education[11]. The majority of those with diabetes live in developing countries[12,13].

Diabetes is a multifaceted condition that calls for a comprehensive treatment strategy. Diabetic patients either cannot produce sufficient insulin or their cells are resistant to it. When a person has a severe deficiency of insulin, they are given insulin. However, many different drugs are developed for situations when cells are not responsive to insulin, with potential issues with carbohydrate metabolism in mind. Post-prandial hyperglycemia can be treated digestively with glucosidase inhibitors like acarbose, miglitol, and voglibose. These prevent the digestion of carbohydrates, which reduces the cells' ability to take in glucose. For better glucose uptake by peripheral cells, a biguanide like metformin is recommended. Pancreatic cells can be stimulated to produce more insulin with the help of insulinotropic sulphonylureas like glibenclamide. Although many therapies are accessible, they are not without drawbacks due to expense and unwanted side effects which include low blood sugar, increased weight, gastrointestinal disorders, liver toxicity, and so on[14]. On the basis of current developments and the contribution of oxidative stress to the progression of diabetes mellitus, efforts are being undertaken to create appropriate anti-diabetic and antioxidant therapy.

Too far, over 400 conventional plant therapies for diabetes have been recorded; though, only a small fraction of these have been investigated systematically or medically to determine their effectiveness. The hypoglycemic outcome of several plant extracts has been demonstrated in both human and animal models of Type 2 diabetes. A major barrier to the widespread use of herbal therapy in modern medicine is the shortage of supporting scientific and clinical data. Herbal medicine needs more clinical research, as well as simple bioassays for biological standardization, pharmacological and toxicological assessment, and a wide range of animal models for toxicity and safety testing. Important too is identifying the active ingredient(s) in these plant extracts[15]. According to the Expert Committee on Diabetes of the World Health Organization, more study of traditional medicinal herbs is needed.

2. Medicinal Herbs with a Long History of Use as Anti-Diabetic Medicines

Anti-diabetic actions of medicinal plant and herb extracts are presently used. Several studies have exhibited that medicinal plant extracts have anti-diabetic effects and can restore pancreatic-cell function[16]. Summary of medicinal herbs and mechanism are shown in Table 1.

2.1 *Allium sativum* (Garlic)

Allium sativum, or garlic, is a member of the family Liliaceae[17]. There is evidence that a daily dose of garlic ethanolic extract (10 ml/kg/day) will reduce blood sugar levels. The anti-diabetic medication glibenclamide was compared to garlic extract and found to be less effective[18]. It was discovered that ethyl acetate, ethanol, and petroleum ether extract all had anti-diabetic effects in rats with Streptozotocin (STZ)-induced diabetes. Anti-platelet, antibacterial, blood pressure lowering, and cholesterol lowering are just few of the medicinal effects of garlic[19].

Table 1. Antidiabetic and other health benefits of traditional medicines

Plant Name	Common Name	Traditional medicine's anti-diabetic and other health benefits	References
Allium sativum	Garlic	Hypoglycemic, Anti-platelet, antibacterial, blood pressure lowering, and cholesterol lowering	18,19
Aloe barbadensis	Aloe vera	Enhance glucose tolerance, Hypoglycemic, anti-inflammatory, antioxidant, initiates insulin release from pancreatic beta cells	20-24
Acacia arabica	Babul	Stimulate insulin production and release	25
Azadirachta indica	Neem	Antihyperglycemic, anti-bacterial, anti-malarial, anti-fertility, hepato-protective, antioxidant	26,27
Catharanthus roseus	Bright eyes, Cape periwinkle, graveyard plant, Madagascar periwinkle, old maid, pink periwinkle, rose periwinkle	Increase insulin levels, hypolipidemic	28
Coriandrum sativum	Coriander	Antihyperglycemic increases glucose tolerance, hypoglycemic	29
Coccinia indica	Ivy gourd	Decrease glucose 6-phosphatase, decrease lactate dehydrogenase	30
Carica papaya	Papaya	Improve glucose and lipid metabolism	31
Eugenia jambolana	Jamun	Hypoglycemic, increase insulin secretion	32
Momordica charantia	Bitter gourd	Antihyperglycemic, hypoglycemic, increase glucose-6-phosphate dehydrogenase, decrease glucose-6-phosphatase	33,34
Mangifera indica	Mango	Hypoglycemic	35
Ocimum sanctum	Tulsi	Hypoglycemic, hypolipidemic	36-38
Pterocarpus marsupium	Malabar kino, Indian kino, Vijayasar, Venkai	Hypoglycemic, antihyperlipidemic, increase insulin secretion, increase glycogen levels	39,40
Tinospora cardifolia	Guduchi, Moonseed, Giloy	Over expression of Glut-4	41
Trigonella foenum graecum	Fenugreek	Stimulate insulin release, decrease glucose-6-phosphatase	42-44

2.2 *Aloe barbadensis* (Aloe vera)

The common houseplant *aloe vera* has been used for centuries as a home remedy for a wide range of medical problems. Gel and latex are the two main components of the plant. The *aloe vera* gel comes from the leaf's mucilage or pulp, while the aloe latex, sometimes called "aloe juice," is a bitter yellow secretion from the pericyclic tubules just under the leaf's outer epidermis. Extracts of aloe gum enhance glucose tolerance in both diabetic and non-diabetic rats[20]. The exudates from *Aloe barbadensis* leaves had a hypoglycemic effect on alloxanized diabetic rats when given in chronic dosages, but not when given in single doses. Bitter principle extracted from the same plant exhibited a hypoglycemic effect when administered in both single and chronic doses to diabetic rats. In order for *aloe vera* and its bitter component to have any effect, the beta cells in the pancreas need to have their insulin production or release stimulated[21]. This herb promotes faster healing of wound in diabetic mice and has an anti-inflammatory impact that is dose-reliant, according to the research[22]. Blood glucose levels were significantly lowered after administering extract of *aloe vera* leaf in water orally[23]. Anti-diabetic, antioxidant, and a four-fold increase in glutathione levels in diabetic rats are only some of the therapeutic benefits of *aloe vera* gel[24].

2.3 *Acacia arabica* (Babul)

It occurs naturally over the entire country of India. The plant extracts combat diabetes by stimulating the body's natural insulin production. While alloxanized rats do not experience hypoglycemia, control rats do. Normal rabbits were fed *Acacia arabica* seed powder (2, 3, or 4 g/kg body weight) and experienced hypoglycemia due to the resulting liberation of insulin from pancreatic beta cells[25].

2.4 *Azadirachta indica* (Neem)

Extracts of *Azadirachta indica* in water and alcohol displayed anti-hyperglycemic action in rats treated with streptozotocin, with the augmented glucose absorption and glycogen accumulation in separated rat hemidiaphragm being the likely mechanism(s) at work. In addition to its anti-diabetic characteristics, this plant possesses anti-bacterial, anti-malarial, anti-fertility, hepato-protective, and antioxidant activities[26,27].

2.5 *Catharanthus roseus* (Bright Eyes, Cape Periwinkle, Graveyard Plant, Madagascar Periwinkle, Old Maid, Pink Periwinkle, Rose Periwinkle)

For centuries, people have turned to the *Catharanthus roseus* Linn (Apocynaceae) plant as a natural remedy for diabetes. Diabetic and control rats were administered a 100 mg/kg body weight/day/60 day oral administration of a *C. roseus* leaf powder suspension in 2 ml distilled water. Insulin levels dropped as glucose levels rose continuously in the diabetic rats' plasma. After 15 days of treatment, plasma glucose in the diabetic group decreased, while plasma insulin levels increased. At the end of the experiment, plasma glucose had nearly returned to normal, while insulin levels remained elevated. Rats with diabetes had a rise in the atherogenic index and plasma total cholesterol, triglycerides, LDL, and VLDL levels, but these values returned to normal in diabetic-treated rats. In contrast to diabetic control rats, which showed a decrease in hepatic and muscular glycogen content and changes in the activity of glucose metabolism enzymes (glucose-6-phosphate dehydrogenase, glycogen phosphorylase, hexokinase, phosphofructokinase, and pyruvate kinase), *C. roseus* administration reversed these effects. As our results show, *C. roseus* has antidiabetic and lipid lowering actions, it may be useful as herbal medicine for the treatment of diabetes[28].

2.6 *Coriandrum sativum* (Coriander)

Coriander is the most common name for the plants in the Apiaceae family. It's a common seasoning for a broad range of dishes. The blood sugar level significantly rose after the streptozotocin injection. This increase was blunted by the administration of *Coriandrum sativum* seed extract, and it was even more muted by prolonged administration. HbA1C levels were similarly reduced, although no improvement in blood sugar control was seen. Metformin, in contrast to the placebo, was more successful in lowering BSL. *Coriandrum sativum* seed extract, given orally at a dosage of 40 mg/kg, showed glucose lowering activity in streptozotocin-induced diabetic rats. Therefore, *Coriandrum sativum* may have great therapeutic efficacy as an anti-diabetic medication, and it may be prescribed as a dietary supplement[29].

2.7 *Coccinia indica* (Ivy gourd)

Diabetic patients were given dried extracts of *Coccinia indica* (*C. indica*) (500 mg/kg body weight) for 6 weeks. These extracts reversed increased glucose-6-phosphatase and lactate dehydrogenase and normalized decreased Lipoprotein Lipase (LPL) activity in untreated diabetics. Alloxanized diabetic dogs treated orally with 500 mg/kg of *C. indica* leaves displayed substantial glucose lowering activity and improved glucose tolerance[30].

2.8 *Carica papaya* (Papaya)

The caricaceae family includes the papaya tree and its fruit. Using an alloxan model, researchers found that extract from the seeds and leaves improved glucose and lipid metabolism and sped recovery in alloxan-induced diabetic rats[31].

2.9 *Eugenia jambolana* (Jamun)

It is a common practice in India to treat diabetes at home with a decoction made from the kernels of the *Eugenia jambolana* tree. This is an important component in many diabetes herbal therapies. Extracts in water and alcohol, as well as lyophilized powder, have been shown to have hypoglycemic effects, bringing down blood sugar levels. The extent to which these shifts occur depends on the state of the diabetes. The jamun pulp extract had a hypoglycemic effect in streptozotocin-persuaded diabetic rats 30 min after injection, while the seed of the same fruit needed 24 hrs. When the extract was given orally to

diabetic rats, blood insulin levels increased. Plant extract incubated with isolated Langerhans islets from normal and diabetic rats increased insulin secretion[32].

2.10 *Momordica charantia* (Bitter gourd)

Momordica charantia is widely used as an anti-diabetic and anti-hyperglycemic medicine in India and other Asian nations. All parts of the plant, including the pulp, the seeds, the leaves, and the stalks, have been displayed to have a hypoglycemic outcome in animal models. The subcutaneous administration of polypeptides isolated from *M. charantia* fruit, seeds, and tissues exhibited a profound hypoglycemic effect on both langurs and humans. Anti-hyperglycemic and hypoglycemic effects of *M. charantia* ethanolic extracts (200 mg/kg) were seen in both normal and STZ induced diabetic rats. This might be because hepatic glucose-6-phosphate dehydrogenase activity is increased, while hepatic glucose-6-phosphatase is inhibited[33,34].

2.11 *Mangifera indica* (Mango)

Plant leaves are utilized as an anti-diabetic treatment in Nigerian traditional medicine, despite the fact consumption of aqueous extract orally had no effect on blood glucose levels in normoglycemic or streptozotocin-pursuaded diabetic rats. Nonetheless, anti-diabetic effect was observed when the extract and glucose were given to the rats simultaneously, as well as when the extract was given to the rats 60 mins before the glucose. The results raise the possibility that the aqueous extract of *Mangifera indica* has hypoglycemic effects. The explanation may lie in a diminished intestinal absorption of glucose[35].

2.12 *Ocimum sanctum* (Tulsi)

Tulsi is the name most people use to refer to it. This plant has a long history of therapeutic usage. An aqueous extract of *Ocimum sanctum* leaves was found to significantly lower blood sugar levels in both normal and alloxan-induced diabetic mice. Fasting blood sugar, uronic acid, total amino acid, total cholesterol, triglyceride, and total lipid were all significantly decreased in diabetic rats, demonstrating the hypoglycemic and hypolipidemic actions of Tulsi. By the end of the trial's on 15th and 30th days, participants who were given plant extract orally (200 mg/kg) had reduced their plasma glucose concentrations by 9.06% and 26.4% respectively. Renal glycogen content in diabetic rats was increased by a factor of ten, while glycogen concentrations in skeletal muscle and the liver were reduced by 68% and 75% respectively[36-38].

2.13 *Pterocarpus marsupium* (Malabar kino, Indian kino, Vijayasar, or Venkai)

This medium-to-large deciduous tree is endemic to the mountainous regions of India. This extract's hypoglycemic effects are likely due to pterostilbene, a chemical generated from the wood of this plant, given that tannates are present in the extract and cause hypoglycemia in dogs. Regranulation of pancreatic beta cells is induced by the flavonoid fraction of Pterocarpus marsupium. Antihyperlipidemic substances such as ligeritigenin, pterosupin, and marsupin can be found in this plant. (-) Epicatechin, the active component, has been shown to be insulinogenic in in vitro tests, meaning that it increases insulin secretion and proinsulin conversion. Similar to the effects of insulin, (-) epicatechin increases glycogen levels in the rat diaphragm and speeds up oxygen absorption in fat cells and tissue segments from a variety of organs[39,40].

2.14 *Tinospora cardifolia* (Guduchi, Moonseed, Giloy)

The well-known herb *Tinospora cordifolia* has many medicinal uses, including as an effective anti-diabetic treatment. Examining the mechanism of action of *Tinospora cordifolia* and its active component in L6 cells, which are differentiated myocytes, is the focus of this study. In addition to being a critical indicator of diabetes in cells, the insulin-reliant glucose transporter-4 (Glut-4) is responsive to exogenous drugs and is up to five times over-expressed by *Tinospora cordifolia* and four times over-expressed by palmatine. PPAR, in addition to Glut-4, is the most critical protein involved in regulating glucose metabolism, and its expression was also increased. In addition, inhibitors of the insulin pathway suppressed the glucose absorption falicitated by *Tinospora cordifolia* and palmatine, suggesting that insulin is a major mediator of this activity[41].

2.15 *Trigonella foenum graecum* (Fenugreek)

Fenugreek seeds are a staple ingredient in Indian spices and are widely available throughout the country. 4-hydroxyleucine, a novel amino acid isolated from

fenugreek seeds, improved glucose-stimulated insulin release by islet cells in both rats and humans. Plant extracts at 2 and 8 g/kg when orally administered reduced blood glucose levels in both normal and diabetic rats. Heart, skeletal muscle, and liver glucose metabolism were all improved after diabetic rats were given fenugreek seeds. The enzymes glucose-6-phosphatase and fructose-1, 6-biphosphatase were both inhibited in the liver and kidneys as a result[42-44].

3. The Challenges of Herbal Medicines in India

There are a number of factors that can compromise the safety, efficacy, and incorporation of herbal medications into modern healthcare practices, despite their long history of usage and potential advantages. Quality control issues, a lack of regulation, the loss of traditional expertise, patent disputes, and drug interactions are only some of the problems that need to be solved. Quality control is a significant challenge in the herbal medicine industry. Herbal products can vary greatly in their composition, potency, and purity due to factors such as plant species, growing conditions, harvesting practices, and processing methods. There are concerns about contamination with pesticides, heavy metals, and other contaminants, as well as adulteration with synthetic drugs. Poor quality control can lead to inconsistent therapeutic effects, potential harm to patients, and loss of trust in herbal medicines as a viable healthcare option. Lack of regulation is another challenge in the herbal medicine industry. In many countries, herbal medicines are classified as dietary supplements or traditional medicines, which are often subject to less stringent regulation compared to pharmaceutical drugs. This can result in variations in manufacturing standards, labelling requirements, and quality control measures for herbal products. The lack of standardized regulations can make it difficult for consumers and healthcare practitioners to assess the quality and safety of herbal medicines. Traditional knowledge loss is a significant challenge associated with herbal medicines. Traditional knowledge about herbal remedies is often passed down through generations in indigenous communities and local cultures. However, this knowledge may be at risk of loss due to various factors, such as changing lifestyles, globalization, and urbanization. As a result, there is a risk of losing valuable traditional knowledge about the safe and effective use of herbal medicines, as well as the sustainable harvesting and conservation of medicinal plants. Patent issues pose challenges for herbal medicines. Many herbal remedies are derived from traditional knowledge and have been used for centuries in local communities. However, the process of obtaining patents for herbal medicines, especially in Western countries, can be complex and may not always take into account traditional knowledge or the rights of indigenous communities. This can lead to issues of bio piracy, where the commercialization of herbal remedies may result in the unfair appropriation of traditional knowledge and resources from indigenous communities without their consent or fair compensation. Interactions with other medicines are also a concern when using herbal remedies. Herbal medicines contain bioactive compounds that can interact with other medications, leading to potential adverse effects or reduced efficacy of both the herbal medicine and the conventional medicine. These interactions can be complex and may not always be well understood, particularly due to the lack of standardized regulation and limited scientific research on herbal medicine interactions.

A number of initiatives are underway to solve these issues by creating quality control standards, regulatory frameworks, and intellectual property protection for herbal medicines. There is a rising awareness of the importance of protecting medicinal plants and supporting sustainable harvesting methods. The safe and effective use of herbal medicines in contemporary healthcare practices can be ensured by collaboration between traditional knowledge holders, herbal medicine practitioners, researchers, and regulatory organizations. The requirement for uniform rules, quality assurance procedures, and the safeguarding of indigenous knowledge is brought into focus by these difficulties. To ensure the safe and successful use of herbal medicines in healthcare practices, more research, collaboration, and advocacy is needed[45-47].

4. The Future of Herbal Medications for Diabetes Mellitus

Numerous herbal medicines are used, and new indigenous drugs are constantly being incorporated into conventional medicine. Approximately 80% of the population in developing countries, especially in rural areas, uses alternative medicine to treat illness. The growing demand for products with natural ingredients

has led to a revival of the herbal medicine industry in developed nations. Therefore, it's critical to differentiate between herbal medications prescribed by a doctor and over-the-counter herbal therapies. As the prevalence of diabetes mellitus rises, it represents a major health risk for people everywhere.

It has lately come to light that plant-based medications with anti-diabetic efficacy surpass that of oral hypoglycemic pharmaceuticals used in established treatment. Anti-diabetic plants have recently come to the forefront of scientific interest. There is a chance it could also help with the development of a better oral medication for treating diabetes[48].

5. Conclusion

The potential anti-diabetic benefits of herbal products have been recognized, providing a non-pharmaceutical option to traditional medications for diabetes management. Herbal medications are gaining popularity due to their perceived safety and little side effects; these advantages have led to their traditional use in many cultures all over the world for the treatment of diabetes. The potential of herbal medications to increase insulin production, improve insulin sensitivity, and decrease insulin resistance is a major reason for their success as anti-diabetic agents. Promising findings in the management of blood sugar levels suggest that herbal treatments may complement standard anti-diabetic medications. Moreover, herbal drugs also possess additional health benefits, including antioxidant, anti-inflammatory, and lipid-lowering properties, which can potentially help in managing complications associated with diabetes such as oxidative stress, inflammation, and dyslipidaemia. However, there are challenges associated with the use of herbal drugs for diabetes management. One of the major challenges is the lack of standardization and quality control of herbal products, which can result in variable efficacy and safety profiles. Herbal drugs can also interact with other medications, leading to potential adverse effects or reduced efficacy. Long-term benefits on glycaemic control and other diabetes-related outcomes are not well-established, and the safety and efficacy of many herbal medications is not well-established. In conclusion, herbal medications' anti-diabetic effects have been found to be promising, suggesting that they may be taken into account alongside conventional treatments for diabetes. However, more study is required to determine their reliability, effectiveness, and best application in diabetes care. It is crucial to consult a healthcare professional before using herbal drugs as anti-diabetic agents, considering potential interactions with other medications and individual health conditions. Standardization and quality control of herbal products should be ensured to ensure consistent efficacy and safety.

6. References

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