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Role of Herbal Medicines in Management of Diabetes

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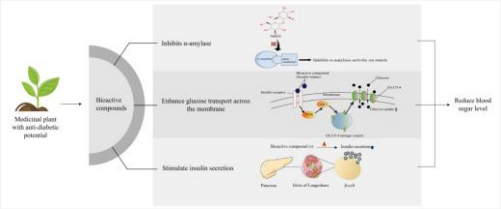
Abstract

Diabetes mellitus is a condition marked by elevated blood sugar levels, alterations in the metabolism of lipids, carbohydrates, and proteins, and over time, it can lead to complications affecting the eyes, kidneys, cardiovascular system, and neurological functions Many plants from throughout the world have been investigated for their potential to prevent diabetes. This review article aims to highlight some key medicinal plants with blood sugar-lowering effects supported by credible clinical and laboratory evidence, while also addressing the medicinal plants utilized in Iranian traditional medicine for diabetes treatment. The insights presented in this review were gathered from suitable articles found using the search terms diabetes mellitus, medicinal plants, type 1 diabetes, and medicinal plants. Diabetes mellitus is a condition marked by elevated blood sugar levels, alterations in the metabolism of lipids, carbohydrates, and proteins, and over time, it can lead to complications affecting the eyes, kidneys, cardiovascular system, and neurological functions. Many plants from throughout the world have been investigated for their potential to prevent diabetes. This review article aims to highlight some key medicinal plants with blood sugar-lowering effects supported by credible clinical and laboratory evidence, while also addressing the medicinal plants utilized in Iranian traditional medicine for diabetes treatmentA. The insights offered in this study were taken from suitable papers obtained using the search phrases diabetes mellitus, medicinal plants, type 1 diabetes, and medicinal plants. The insights offered in this study were taken from suitable papers obtained using the search phrases diabetes mellitus, medicinal plants, type 1 diabetes, and medicinal plants.

Graphical Abstract



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INTRODUCTION

Diabetes mellitus is a condition defined by high blood sugar levels, as well as alterations in the metabolism of fats, carbohydrates, and proteins [1]. Diabetes mellitus is the most prevalent chronic and metabolic disorder marked by elevated glucose levels resulting from either complete or partial insulin insufficiency. Complications affecting the eyes, kidneys, cardiovascular system, and neurological system are associated with this illness over time.

Additionally, it presents with symptoms including excessive urination, fatigue, unintended

weight loss, slow wound healing, blurred vision, and higher glucose levels in urine [2–4]. Without appropriate treatment, damage to the heart, blood vessels, nervous system, and kidneys, as well as neuropathy, can develop. The management involves a combination of diet, physical activity, and medication [5].

At present, insulin and hypoglycemic medications stand as the primary and efficient approach to managing diabetes; however, these substances are associated with numerous negative side effects. There are many reasons to increase the use of herbal remedies. A variety of plants from different parts of the world have been investigated for their abilities to lower blood sugar levels. This review article emphasizes several important medicinal herbs known for their glucose-reducing effects, supported by reliable clinical and laboratory studies, and also examines the herbs suggested in Iranian traditional medicine for diabetes treatment [6–8].

TYPES OF DIABETES MELLITUS

- Type 1 Diabetes (Insulin-dependent).
- Type 2 Diabetes (Non-insulin Dependent).

The details in this review were gathered from relevant articles found using search terms such as diabetes mellitus, medicinal plants related to type 1 diabetes, medicinal plants associated with type 2 diabetes, and the impact of extracts and essential oils from medicinal plants on diabetic tissues in the human body, indexed in databases including Iranmedex, Irandoc, ISI, Pub Med, Scopus, SID, Magiran, Google Scholar, among others.

Why Do We Need Herbal Drugs?

Given that the antidiabetic medications now on the market are dangerous and have serious side effects in different facets. More than 72.8% of diabetics are reportedly turning to herbal medications, dietary supplements, and other complementary essential medication cures. Acarbose causes gastrointestinal disturbances, Tolbutamide & Glyburide cause hypoglycemia & weight gain, and Pioglitazone is linked to liver toxicity and weight gain, to name a few common examples of currently accessible synthetic drugs. Nasopharyngitis, headaches, and nausea are caused by sitagliptin, saxagliptin, and linagliptin [9–13].

Role of Herbal Drugs

Herbal plants represent a natural treasure of the nation. These herbal plants offer essential medical services to the communities in rural areas.

Ancient literature claims that over 800 herbs have anti-diabetic properties. Herbal treatments have been utilized for many years and are still widely used now all over the world. In the past few years, screening approaches that focus on mechanisms using biochemical or cellular targets have been employed to find various agents that come from natural sources, including lovastatin, pravastatin, and FK-506. Additionally, numerous natural substances, particularly those derived from plants used in medicine, are often found in assays designed according to conventional medical methodologies. It is estimated that approximately 80% of the global population depends on traditional herbal remedies for their essential health requirements [9–13].

Cause

Type 1 diabetes is classified as an autoimmune condition. It is thought that a mix of inherited traits and certain environmental influences lead the immune system to target and destroy the pancreatic cells responsible for insulin production. Obesity stands out as a primary factor contributing to insulin resistance, with roughly 90% of individuals diagnosed with type 2 diabetes being either overweight or obese. There is a higher likelihood that genetic components play a significant role in the development of type 2 diabetes. A family history of the condition heightens the chances of developing diabetes.

Signs and Symptoms

Typical signs and symptoms linked to diabetes encompass increased thirst, unintentional weight loss, tiredness, nausea, slow healing of wounds, skin infections, and issues related to hunger, among others [10].

Herbs or Plants Possessing Antidiabetic Effects

Indeed Diabetes and related disorders are treated by a large number of pharmacies. With 1300 plant species representing more than 750 rubrics throughout 190 families, the most recent NAPRALERT database covers everything from lower plants like fungus and algae to almost all kinds of sophisticated plants. In ethnopharmacology, many of these plants have been used to treat diabetes. While many of these plants have undergone experimental research to confirm their physiological activity, pharmacological and chemical components with anti-diabetic properties have received less attention. A variety of potentially bioactive compounds include complex polysaccharides, alkaloids, glycopeptides, terpenoids, peptides, amines, steroids, flavonoids, lipids, coumarins, sulfur-containing substances, and inorganic ions, which are encapsulated and linked together.

COMMON HERB-DRUG RELATIONS IN DIABETES

The simultaneous use of herbal antidiabetic remedies alongside pharmaceutical drugs might influence herb-drug interactions, potentially resulting in increased benefits (which could be favorable from a clinical perspective), diminished pharmacological actions, or negative medication events, such as low blood sugar levels. The upcoming section offers a concise overview of frequently used antidiabetic sauces and their relationships with antidiabetic medications. Research was carried out using standard databases to gather relevant literature up to the present time (Table 1).

Table 1. Herb–antidiabetic drug co-administration studies.

Herb	Co-administered Anti-Diabetic Drug	Findings
Aloe-vera	Glibenclamide	Improved effect on lowering the blood glucose.
Karela	Metformin	A decrease in serum glucose was found in the combination with fruit juice extract at half the normal dose of metformin.
Ginger	Glibenclamide	The Synergistic effect with ginger extract reduces blood glucose levels greater than glibenclamide as single
Neem	Azadiradione	It is a potent, multi-targeting compound from the neem tree with strong antioxidant, anti-inflammatory, and neuroprotective properties
Indian gooseberry/ Jamun	Jambosine	Traditionally used together in Ayurvedic medicine for their anti-diabetic properties
Holy basil	Ocimum sanctum	May have a synergistic effect when co-administered with conventional anti-diabetic drugs like glibenclamide
Tinospora cordifolia	Gliclazide	Combination with other diabetes medications to improve blood sugar control.
Cinnamon	Glibenclamide	It is recommended that it be taken together with diet and exercise
Acacia Arabica	Tannins	Based on their structure and exhibit properties such as antioxidant, anti-inflammatory, and astringent effects.
Gurmar	Gymnemagenin	Interact with glucose metabolism-related proteins, though it is currently for research

Aloe Vera: (Aloe barbadensis)

Among the over 400 varieties of aloe, aloe vera belongs to the Liliaceae family. Aloe's main constituents are galacturonic acid and carbohydrates. This factory has a wide range of clinical

applications, including cosmeceuticals, immunity, and organ care, according to traditional literature. Aloe vera reduces blood glucose levels in people with diabetes (Figure 1) [10–13].

Figure 1. Aloe vera.

Karela—Momordica Charantia

Momordica charantia, also known as karela, is a bitter melon whose juice contains a number of chemical ingredients, such as sterols, glucoside fusions, and charantin polypeptides. Karela has been the focus of numerous clinical investigations when it is used alongside standard antidiabetic medications. In one particular study, a mixture of 400 mg of chloroform/benzene karela extract was administered along with half the regular clinical doses of either metformin or glibenclamide in patients with non-insulin-dependent diabetes mellitus (NIDDM). The findings suggested that this combination produced a weaker hypoglycemic effect compared to the full doses of metformin or glibenclamide on their own, indicating a possible additive impact. Comparable results have been observed in animal studies, where treatments using both metformin and karela juice/extract collectively exhibited a diminished hypoglycemic effect in diabetic rat models in comparison to each treatment separately (Figure 2) [10–13].

Figure 2. Karela.

Ginger—Zingiber Officinale

Ginger is commonly utilized both as a spice and as a medicinal agent in various instances. Raw ginger comprises approximately 9 percent lipids or glycolipids and 5 to 8 percent oleoresin. The pungent compounds, which make up about 25 percent of the oleoresins, primarily include gingerols and related phenolic substances. The water extract is known to have antidiabetic properties in several countries. It is thought that the antidiabetic properties of ginger can be linked to its capabilities as an antioxidant and its anti-glycation functions, in addition to its role in enhancing the expression of the glucose transporter known as Glut 4. In a study using a diabetic rat model triggered by streptozotocin (STZ), the combined

treatment of ginger extract (25 or 50 mg/kg) alongside glibenclamide (5 mg/kg) resulted in notable reductions in non-fasting blood sugar levels by 26 and 25%, respectively, in contrast to the 7. 9% decrease seen with glibenclamide on its own (Figure 3).

Figure 3. Ginger—Zingiber Officinale.

Azadirachta Indica: (Neem)

Neem is a plant that thrives in tropical regions and originates from India and Asia. Every aspect of the neem plant offers healing and disinfectant properties. Traditionally, neem has been significant in ancient healing practices in India and China. Almost every component of the neem tree—its foliage, blossoms, seeds, fruits, roots, and outer skin—have been used in various treatments over the years. Some clinical research indicates that certain compounds derived from Azadirachta indica (Neem) may aid in regulating blood sugar levels in individuals with diabetes mellitus. An alcoholic extract from neem has shown anti-hyperglycemic effects in rats treated with streptozotocin, which is attributed to its ability to enhance glucose uptake and increase glycogen storage in the hemidiaphragm of insulated rats (Figure 4) [14–28].

Figure 4. Azadirachta Indica: (Neem).

Eugenia Jambolana: (Indian Gooseberry/ Jamun)

Every part of the neem tree possesses medicinal and cleansing qualities. Historically, neem has played an important role in traditional medicinal practices in both India and China. Virtually every element of the neem plant—its leaves, flowers, seeds, fruit, roots, and bark Both the aqueous and alcoholic extracts, along with the lyophilized powder, demonstrated a decrease in blood glucose levels. The extract from the pulp of Eugenia jambolana showed a hypoglycemic effect in diabetic mice induced by streptozotocin within 30 minutes of application, while the seeds of the jambolana fruit took 24 hours. When taken by mouth, the extract led to a considerable rise in serum insulin levels among diabetic rats. (Figure 5) [13–17].

Ocimum Sanctum (Holy Basil)

Known commonly as tulsi, this plant has been recognized for its medicinal benefits since ancient times. Holy basil is related to the more commonly used culinary species and is referred to in the Ayurvedic tradition as tulsi; it has been deemed the "Queen of Sauces" since the days of ancient Indian civilizations. The water-based extract obtained from the foliage of Ocimum sanctum caused a

significant drop in blood glucose levels in both healthy and alloxan-induced diabetic rats. Giving the water extract (200 mg/kg) orally for a duration of 30 days led to a decrease in blood sugar levels by nearly 9. 06% and 26. 4% at the 15-day and 30-day intervals of the study, respectively. In diabetic rats, the content of renal glycogen increased tenfold, while the levels of glycogen in skeletal muscle and the liver were decreased by 68% and 75%, respectively, in comparison to the control group. Around 67 percent of the world's population uses traditional healing methods that stem from herbal plants. In Bangladesh and India, Tulsi (O. sanctum) has a wide range of applications (Bhattacharya et al., 1997; Chattopadhyay, 1993, 1999; Vats et al., 2002; Grover et al., 2002; Kar et al., 2003; Gholap and Kar, 2004; Narendhirakannan et al., 2006; Modak et al., 2007; De et al., 2015) [2, 4, 5, 21, 8, 15, 7, 23, 20, 6]. It may affect alterations in glycogen levels and carbohydrate metabolism in animals caused by streptozotocin (Vats et al., 2004a). One study indicates that Tulsi can be used as an adjunct to dietary therapy and pharmacological treatment in cases of mild to severe non-insulin dependent diabetes mellitus (NIDDM) (Agrawal et al., 1996) (Figure 6) [19].

Figure 5. Eugenia Jambolana: (Indian gooseberry/ Jamun).

Figure 6. Ocimum sanctum: (holy basil).

Tinospora Cordifolia (Guduchi)

Guduchi is a large, rough climbing shrub that tends to be short-lived. It is a highly effective spice used in Ayurveda to manage diabetes and maintain the harmonious function of various organs, and it belongs to the Menispermaceae family. This plant is commonly cultivated throughout India and is widely referred to as Guduchi. Administering the extract of Tinospora cordifolia (T.cordifolia) roots orally for 6 weeks resulted in a notable decrease in blood and urine glucose levels as well as serum lipids in diabetic rats induced by alloxan. Additionally, the extract helped to prevent a reduction in body weight (Figure 7) [20].

Figure 7. Tinospora cordifolia: (Guduchi).

Cinnamon

Cinnamon is a scented spice obtained from the bark of the Cinnamonum Zylanicum tree. It is commonly utilized as a component in numerous recipes. Research conducted on humans has indicated that cinnamon may enhance glucose levels, insulin production, insulin sensitivity, and lipid profiles in the bloodstream. Additionally, it serves as an antioxidant. A different research indicated that taking a cinnamon supplement might lead to lowered fasting blood sugar levels, a decrease in overall cholesterol and "bad" low-density lipoprotein cholesterol, higher amounts of "good" high-density lipoprotein cholesterol, reduced triglycerides, and enhanced insulin sensitivity. A different research indicated that taking a cinnamon supplement might lead to lowered fasting blood sugar levels, a decrease in overall cholesterol and "bad" low-density lipoprotein cholesterol, higher amounts of "good" high-density lipoprotein cholesterol, reduced triglycerides, and enhanced insulin sensitivity (Figure 8).

Figure 8. Cinnamon.

Acacia Arabica

The animal study took place at the King Fahd Research Center at King Abdulaziz University in Jeddah, Saudi Arabia, during the period from December 2012 to January 2013. A total of thirty-six female albino rats were separated into two equal groups; the first served as the control group, while the second group was induced with diabetes using streptozotocin. Each group was then further subdivided into three subgroups, each containing six rats; the first subgroup received no treatment, whereas the second and third subgroups were administered Acacia Arabica extract orally for a duration of 21 days at dosages of 100 mg/kg and 200 mg/kg, respectively. On the twenty-first day, blood samples were obtained from rats that had fasted overnight through the retro-orbital plexus while they were under ether anesthesia to evaluate serum glucose, insulin, triglycerides, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, malondialdehyde, and coenzyme Q10. The results revealed a significant decrease in insulin resistance, serum glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol, and malondialdehyde levels, along with a substantial rise in high-density lipoprotein cholesterol and coenzyme Q10 levels in the diabetic groups that received treatment in contrast to the diabetic group that did not receive treatment. The extract of Acacia Arabica exhibited hypoglycemic, hypolipidemic, and antioxidant effects, suggesting it could be explored further for diabetes treatment in humans (Figure 9) [22–25].

Figure 9. Acacia Arabica.

Gymnema Sylvestre (Gurmar)

Gymnema sylvestre, known as "sugar destroyer" in Hindi, has been the focus of much research due to its antidiabetic qualities. The primary bioactive ingredients, gymnemic acids, share structural similarities with glucose molecules. These chemicals may interfere with the intestinal absorption of glucose and block the receptors for sweet flavors. Research has shown a noFigure decrease in HbA1c, blood sugar levels after meals, and fasting blood sugar in individuals with both type 1 and type 2 diabetes (Figure 10).

Figure 10. Gymnema sylvestre (Gurmar).

Advance Technologies in Dibetis Mallitus

The area of diabetes management is evolving quickly as innovative research, technology, and therapies that can enhance the health and quality of life for individuals with diabetes are consistently being developed [27].

Non-Invasive Glucose Monitoring Sensors

For individuals with diabetes, using a capillary blood glucose meter for self-monitoring has historically been the sole method to assess their blood glucose management. This self-monitoring provides an incomplete view of glycemic control (open to interpretation) and primarily enables the patient to adjust their insulin dosages accordingly. Non-invasive connected sensors that continuously monitor interstitial glucose have improved in accuracy, slowly liberating themselves from the need for calibration [28].

Connected Insulin Pens

Novo Nordisk has recently revealed its intentions to launch a connected ("smart") insulin pen that will automatically track the amount of insulin that was administered. For individuals who require multiple daily injections, this innovation eliminates the need for logs, reduces the chances of missing doses or unintentionally stacking insulin, and provides access to the same computer-produced reports that assist in identifying patterns and enhancing treatment, similar to the experience of insulin pump users. The latest connected pens (NovoPen 6TM and NovoPen Echo PlusTM) are designed to be reused, received approval in Europe (CE marked), and are equipped with a small display that shows the most recent dose [28].

Intelligente Insulin Pumps

Investigations utilizing the intraperitoneal method of administration have been performed. This approach reduces the occurrence of serious hypoglycemia and enhances HbA1c levels in contrast to the subcutaneous method. Certain bio-artificial pancreases currently make use of the external layer of the peritoneum, indicating it as a potential site (for instance, BAirTM, Beta-O2 Technologies, and MailPanTM [for the macrocapsulation of pancreatic islets], Defymed Company) [28].

Artificial Pancreas for Glycemic Management

Using Artificial Pancreas to Control Blood Sugar The "artificial pancreas," often known as the "diabetes patient's dream," has recently emerged as a result of the development of all the technologies

we have just witnessed. Since its effectiveness in ambulatory care was demonstrated in 2015, a recent meta-analysis of 24 studies involving 585 patients has confirmed a significant improvement in the amount of time spent in the target, a decrease in mean blood glucose and HbA1c, and a decrease in hypoglycaemia [28].

Artificial Intelligence for Diabetes Management

In recent times, various informatics tools and methods, such as data analysis applications, knowledge structures, and algorithms based on Artificial Neural Networks, have been created and utilized to enhance the management of chronic conditions. These advancements or methods are collectively known as "telemedicine 3. 0" assistance and artificial intelligence. Three clinical data sets hold particular significance for this context:1) the attributes of the patients; 2) the digital health records of the patients, which encompass documentation from medical practitioners, laboratory findings, and additional information regarding diseases and treatments, and epidemiology that could be useful for association studies and prognostic and medication response prediction modeling; and 3) knowledge of the literature, including guidelines for managing diabetes [28].

CONCLUSION

Across the globe, herbal remedies are increasingly recognized and utilized for managing diabetes. Various herbs are employed to address different forms of diabetes and their associated issues. A range of medicinal plants has been evaluated for their potential blood sugar-lowering effects, and researchers have conducted preliminary studies on these plants. The scientific validation of numerous Indian botanical species has demonstrated their effectiveness in lowering glucose levels, suggesting they may hold therapeutic significance. Consequently, a wide array of plants has been utilized alone or in combinations to treat diabetes. The interaction between antidiabetic herbs and medications can lead to either opposing or synergistic effects. The increase in glucose reduction carries the risk of inducing hypoglycemia, thus necessitating the monitoring of possible side effects when these compounds are combined. However, in spite of the risks involved, the combination of these herbal treatments with antidiabetic drugs has generally shown favorable clinical outcomes, as it may enhance blood sugar reduction, allowing for a decrease in the dosage of antidiabetic medications and consequently reducing their side effects. Herbal treatments could be a beneficial approach in the control of diabetes.

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