

## A Review on Herbs Used in The Treatment of Diabetes Mellitus

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### ABSTRACT:

A serious threat to worldwide public health is posed by the metabolic disease known as diabetes mellitus. Despite the fact that there are substances and biochemical agents that can help control diabetes, there is no long-term cure that can allow a person to totally recover from this ailment. Through significant investigation, many conventional diabetic treatments have been uncovered. In the past, chemicals and extracts derived from different kinds of natural resources, particularly plants, have been an effective tool for controlling and treating diabetes and any potential problems. In order to help readers, comprehend the relevance of various herbal and polyherbal formulations that have been traditionally used to treat diabetes mellitus, this study has provided them with relevant information. Traditional medications derived from medicinal plants are used by about 60% of people. This article focuses on Indian herbal remedies and plants that are used to cure diabetes, notably in India. Diabetes is a serious condition that affects a large number of people globally from all walks of life. It has been shown to be a significant public health problem in India, particularly in urban areas. Although there are a number of strategies to minimize diabetes' negative effects and the difficulties that follow, herbal formulations are preferred since they are less expensive and have less adverse effects. A collection of medicinal plants with known antidiabetic characteristics is compiled, as well as herbal diabetes treatments. The use of traditional remedies derived from medicinal plants is estimated to be around 80%. These include *Momordica charantia*, *Withania somnifera*, *Phyllanthus amarus*, *Pterocarpus marsupium*, *Tinospora cordifolia*, *Allium sativum*, *Cinnamomum verum*, *Ocimum sanctum*, *Gymnema Sylvestre*, and *Trigonella foenum graecum*. Since free radical damage is one of the etiologic factors associated with the development of diabetes and its consequences, an anti-diabetic medication with antioxidant properties would be preferable. As a result, details about the antioxidant advantages of these medicinal herbs are also given.

**KEY WORDS:** Diabetes, Herbs, antidiabetic, antioxidant, extract; traditional medicine; polyherbal

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## **INTRODUCTION:**

A non-infectious endocrine disorder called diabetes mellitus alters how carbohydrates are digested and is associated with hypoglycemia [1] [2]. Numerous serious diseases, including microvascular (nephropathy, retinopathy, and nephropathy) and macrovascular (peripheral vascular disease and coronary heart problems) diseases, have been linked to the start of this condition [3]. Diabetes mellitus, generally known as diabetes, has been linked to "sweet urine" and muscle atrophy. The pancreas secretes the hormone insulin, which controls blood glucose levels. The pancreas releases insulin to keep the glucose level stable as these levels increase.

In diabetic patients, decreased or nonexistent insulin production results in hyperglycemia [4]. Diabetes mellitus has three different types. Type 1, type 2, and gestational diabetes. Insulin dependent diabetes mellitus is the name given to the condition as a result of the full loss of function of the pancreatic islets of Langerhans cells, which are present in Type 1 Diabetes mellitus. A temporary reduction of cell mass is a characteristic of type 2 diabetes, sometimes called insulin non-dependent diabetes mellitus. It is a hereditary propensity that is primarily associated with obesity, high blood pressure, and high cholesterol. Reduced insulin resistance and improved insulin production are required for the treatment of type 2 diabetes mellitus. Women who are pregnant who have gestational diabetes experience hyperglycemia as a symptom. It frequently appears in 2-4% of pregnancies during the second or third trimester [5]. Diabetes mellitus symptoms include polydipsia, polyuria, polyphagia, fatigue, nausea, vomiting, impotence in men, slow wound healing, and blurred vision [6]. There are 415 million people with diabetes globally, and that figure is projected to increase to 642 million by the year 2040, according to a survey done by the International Diabetes Federation (IDF) in 2016 [7]. Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels due to insufficient insulin production or impaired insulin utilization. Diabetes is a chronic condition that affects protein, lipid, and glucose metabolism (1, 2). It is characterized as an increase in blood sugar levels after ingesting any form of meal. Insulin that is either too little or too inefficient causes diabetes. The conventional treatment of diabetes often includes oral hypoglycemic agents and insulin injections. However, in recent years, there has been growing interest in alternative therapies, particularly the use of herbs, in managing diabetes. This review aims to explore the efficacy, safety, and mechanisms of action of various herbs commonly used in the treatment of diabetes mellitus (3). According to statistics, 2.8% of individuals globally suffer from this condition, and by 2025, that percentage is expected to reach more than 5.4% (3). Diabetes calls for early diagnosis, treatment, and dietary changes. Diabetes, a widespread ailment, is the fifth leading cause of death in the twenty-first century (4). Common diabetes complications have a wide range of aetiologies, a progressive course, and an urgent need for effective treatments (12). Today, a number of interventions, such as insulin therapy, medicine, and nutrition therapy, can be used to manage diabetes. Insulin deficiency or malfunction leads to diabetes mellitus, a serious metabolic disorder. Type I diabetes (insulin dependent) is caused by inadequate insulin synthesis because there are not enough beta cells. People with this illness are totally dependent on external sources of insulin, in contrast to Type II diabetes patients who can be treated with dietary changes, exercise, and medication. Type II diabetes, which is the more common form, affects 90% of those who have the disease. The following symptoms can be brought on by either type of diabetes: Some of the symptoms include high blood sugar levels, excessive thirst, frequent urination, extreme hunger and weight loss, impaired vision, nausea, and vomiting, as well as sudden weakness (13).

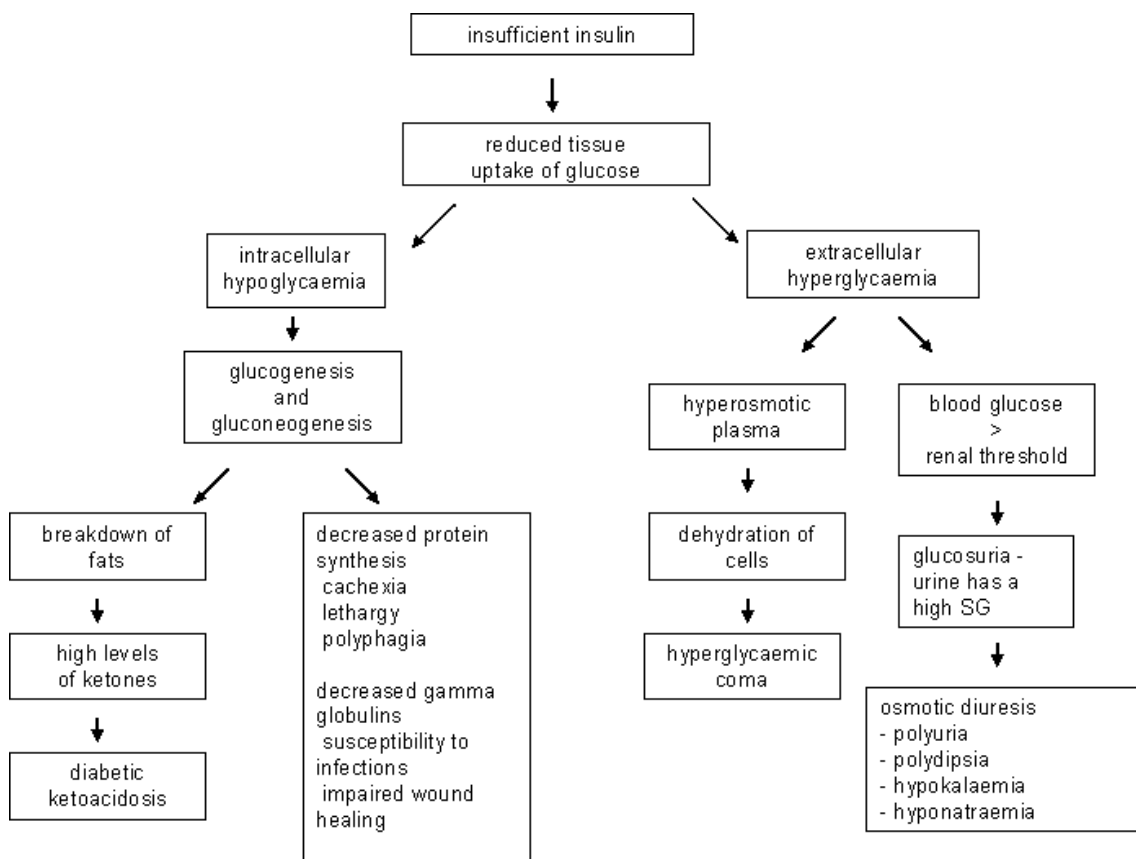
Once more, studies on the use of medicinal plants to treat diabetes are ongoing. Model chemicals discovered in medicinal plants have been used to produce numerous conventional drugs. Metformin is one instance of an efficient oral glucose-lowering drug. According to data from Aroma World, 61.3 million people in India have diabetes, with the majority of those affected being in the 20 to 79 age group.

It might have about doubled by 2030. India is thought to be the world's diabetes capital and it predominantly affects people in urban and rural areas [8]. Diabetes prevalence is steadily increasing in urban India. In urban regions, the prevalence of diabetes is almost six times higher than in rural areas. Over the past 20 years, reduced activity, increased weight and stress, dietary changes, malnutrition, alcohol consumption, and virus infections have been the main contributors to the growth in diabetes mellitus [1, 9]. Female diabetic patients are more adversely impacted than male diabetic patients because hormones and inflammation operate differently in women.

People with less education are more likely to have diabetes problems than people with higher education [10]. The majority of diabetes cases are seen in developing countries [11].

### DIAGNOSIS OF DIABETIC MELLITUS

Diagnosing diabetes can be done by checking blood sugar levels. Fasting blood sugar levels in a healthy male are 80 mg/dl, but postprandial levels can rise to 160 mg/dl. Several tests are performed in laboratories to identify diabetes, including the finger-prick blood sugar test, fasting blood sugar test, glucose tolerance diagnostic test, and glycohemoglobin [6].



**Figure 1:** Pathophysiology of Diabetes Mellitus

## **TYPE 2 DIABETES PATHOPHYSIOLOGY**

An important factor in the etiology of diabetes is oxidative stress.

Reactive oxygen species (ROS) production and the capacity of enzymatic or non-enzymatic antioxidants to neutralize them cause oxidative stress. Reactive oxygen species include both radical and non-radical species, including super oxide, hydroxyl, peroxy, and hydroperoxyl. Antioxidants are made up of super oxide dismutase, glutathione reductase, vitamins A, C, and E, carotene, glutathione, and trace elements.

When low density lipoprotein cholesterol is oxidized in the presence of reactive oxygen species, which are then taken up by hunter. receptors in scavenger cells, foam cells and arterial sclerosis plaques are produced. Numerous corrosive pathways that are important in the development of the diabetes disease can be stimulated by these ROS.

A few important mechanisms include the activation of protein kinase C, the sorbitol aldose reductase route, the electron transport chain, and the glucosamine pathway. The stimulation of these pathways and mechanisms of action can lead to amylin, atherosclerosis, programmed cell death, lipid peroxidation, development of advanced glycation end products (AGES), and loss of pancreatic cell function. It has been shown that nuclear factor erythroid derived 2 like 2 and their antagonist, like ECH associated protein 1, significantly protect cells from oxidative stress [12].

## **MEDICINES FOR DIABETES**

Diabetes mellitus illness can be prevented by managing blood sugar levels with a number of drugs, committing to various forms of exercise or yoga therapy, or adhering to a specific diet [9]. One of the many treatments for diabetes mellitus is insulin therapy. Other oral hypoglycemic drugs, such as sulphonylureas, thiazolidinedione's, and peptide analogs, are used to treat type 1 diabetes mellitus, Type 2 diabetes mellitus [4] [13]. Herbal preparations are frequently available over-the-counter. These herbal remedies are used to cure serious ailments. These drugs are also used when pharmacological treatments for illnesses prove ineffective. These drugs are risk-free and all-natural; they don't have any negative side effects. Herbal remedies permanently heal the patient and treat the sickness, in contrast to manufactured drugs, which do not permanently cure illnesses. Natural fruit, vegetable, and herb extracts are used in herbal treatments to treat a variety of ailments without generating any unfavorable side effects. On the other hand, chemical drugs are produced synthetically and also have drawbacks. Herbal preparations are less expensive when compared to allopathic drugs. Herbs are used to create natural compositions. Natural ingredients are used to make herbal cures, as opposed to natural ingredients being used to make allopathic medicines. Herbal formulations are available without a prescription, in contrast to all opathic drugs [15] [16].

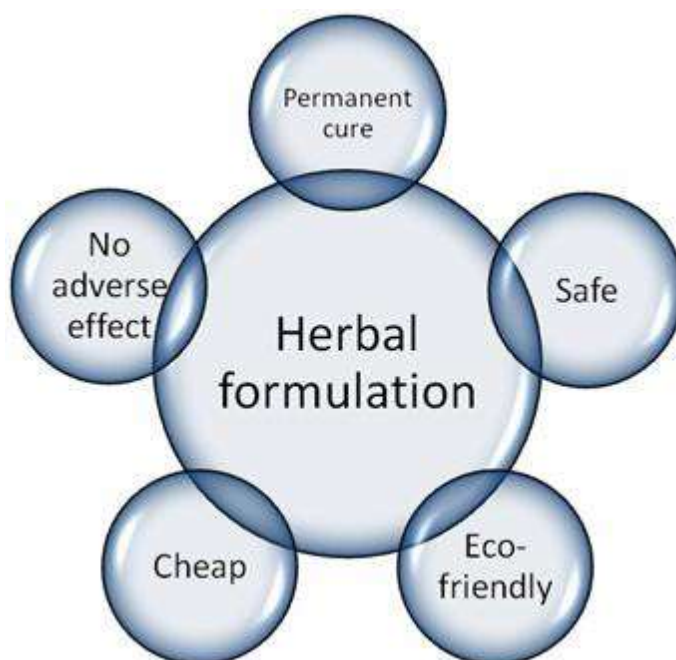
## **ORGANIC TREATMENT**

Finding a treatment for diabetes mellitus that has no adverse effects is the biggest issue facing medical practitioners. According to the world ethnobotanical, 800 medicinal plants are used to prevent diabetes mellitus. Only 450 medicinal plants have been clinically proven to have anti-diabetic properties, 109 of which have a comprehensive mode of action. Both experts and laypeople have used traditional medicinal herbs to treat diseases like diabetes, cancer, and heart disease for thousands of years. Native plants have been used for a very long time to treat diabetes in China and India. The Charaka Samhita and Susruta Samhita are two works that discuss the phytopharmacology aspects of diabetes and its detrimental effects [14].

Numerous side effects of synthetic diabetic drugs, such as nausea, vomiting, diarrhea, alcohol flush, migraines, edema, malignant anemia, and vertigo, have been reported. Herbal medicines have been demonstrated to be a better choice because they have less side effects and negative impacts than manufactured pharmaceuticals.

S.no	Category	Name of Drugs	Brand Name	Mode of action
1.	Insulin Rapid acting insulin Intermediate Acting Insulin Long acting	Regular Insulin, Insulin glulisine, Isophane Insulin Neutual protamine Hagedorn Extended insulin zinc insulin	Humulin R Apidra Humulin N Novolin N Ultralent	Decrease glucose production and Increase peripheral glucose uptake.
2.	Alpha glycosidase inhibitors	Acarbose Miglito	Precose Glyset	Decrease glucose absorption from intestine.
3.	Biguanides	Metformin, Phenformin	Glucophage DBI	Decrease insulin resistance.
4.	Sulfonylurea First generation agents Second generation agents	Tolbutamide Chlorpropamide Glipizide Glimepiride	Orinase Diabinese Glucotrol Amaryl	Block the ATP sensitive potassium channels.
5.	Peptide analogs Injectable incretin mimetics Glucagon like peptide -1 (GLP-1) Gastric inhibitory peptide analogs Injectable Amylin analogues	Exenatide Sitagliptin Saxagliptin linagliptin Pramlintide	Byetta Januvia Onglyza Tradjenta Symlin	Increase incretin levels which inhibit glucagon release and increases insulin secretion
6.	Glycosurics	Canagliflozin	Sulisent, Invokana	Inhibit reabsorption of glucose in the kidney and lower blood sugar level

**Table 1 Antidiabetic Drugs (5,14,16)**



**FIGURE 2** Advantages Of Herbal Formulation-

### **CONVENTIONAL DIABETES HERBAL REMEDIES**

Currently, extracts of medicinal plants and herbs are utilized to treat diabetes. Clinical studies have repeatedly shown that plant extracts from therapeutic plants have anti-diabetic activities and can restore the activity of pancreatic beta cells [17].

### **THE SATIVUM ONION**

Locally referred to as "garlic," this plant belongs to the Liliaceae family, which also includes *Allium sativum* [18]. A 10 ml/kg/day solution of garlic extract in ethanol frequently produces hypoglycemic effects [2]. Glibenclamide, an anti-diabetic drug, was outperformed by garlic extract [19]. Extracts of petroleum ether, ethanol, and ethyl acetate were found to have anti-diabetic effects in rats given STZ. Garlic has a range of health benefits, including compounds that reduce blood pressure, cholesterol, and microbes [20].

### **ALOE BORBADENSIS**

It belongs to the Liliaceae family and is known as Ghikanvar. It resembles a cactus plant due to its hefty, narrowing, hairy, and viscid clear gel-filled green blade-shaped leaves. Blood sugar levels are significantly lowered when aloe vera aqueous extract is administered orally in a dosage of 150 mg/kg of body weight [18]. In diabetic rats, aloe vera gel increased glutathione levels by four times, and it also contains anti-diabetic and antioxidant characteristics [4]. Aloe Vera gel is commonly known for its wound-healing properties, but it may also help manage diabetes. Studies have suggested that Aloe Vera consumption may decrease fasting blood glucose levels and improve lipid profiles (7). However, excessive consumption of Aloe Vera may cause gastrointestinal disturbances, warranting caution in its use (8).

### **AZADIRACHTA INDICA**

Locally, it is referred to as "neem" and is a plant belonging to the Liliaceae family.

It is accessible to both Burma and India [18]. High doses of the ethanolic and aqueous extracts of *Azadirachta indica* show a reduction in blood glucose levels. It can be taken with such medications in type 2 diabetics whose diabetes is not only controlled by allopathic treatments [2]. Numerous patients over the world are treated with neem pills comprised of natural elements. Its extract improves blood circulation and aids in reducing blood glucose levels in the body by expanding blood vessels [21].

### **EARLY BRASSICA**

It belongs to the cruciferae family and is known as Rai. It frequently serves as a seasoning in a variety of dishes. In diabetic rats caused by alloxan, the aqueous seed extract was shown to reduce blood sugar levels. 450, 350, and 250 mg/kg of extract have hypoglycemic effects [22].

### **PAPAYA TREE**

It belongs to the caricaceae family and is known as papaya. A seed and leaf extract improves wound healing and reduces blood sugar and fat levels in rats with diabetes caused by alloxan [23].

### **CATHARANTHUS ROSE**

It belongs to the Apocynaceae family and is known by the name *Vinca roseus*.

Methanolic extract of leaves and twigs shows a drop in blood sugar levels in diabetic rats treated with alloxan. When oral doses of 500 mg/kg of leaves and twig extract were administered to animals, their blood sugar levels were lowered [18].

The mechanism of action of *Catharanthus roseus* is increased insulin synthesis from Langerhans cells [2].

### **THE HERB CORIANDER**

It belongs to the Apiaceae family and is primarily known as coriander.

It frequently serves as a seasoning in a variety of dishes. 200 mg/kg seed extract often increases the activity of the Langerhans cells, reduces blood sugar levels, and stimulates the generation of insulin from the pancreatic beta cells in rats with alloxan-induced diabetes. The *Coriandrum sativum* extract has the ability to produce insulin and lower blood sugar levels [2].

### **VERONICA JAMBOLANA**

It is referred to as jamun and is a member of the Myretaceae family. It has dried seeds from *Eugenia jambolana* and mature fruits. Its active components are malvidin 3-laminaribioside and ferulic acid.

Diabetes patients are treated using dried seed extract (200 mg/kg) [21].

### **SYLVESTRE THE FITNESS NEMA**

This Asclepidaceae family member is known by the name Gudmar, which translates as "sugar destroying." *G. sylvestre* leaf extract (3.4/13.4 mg/kg) effectively reduced blood sugar levels in streptozotocin-induced rats. In Indian ayurvedic treatments, it is mostly used to treat diabetes. Alkaloids, flavonoids, saponins, and sugars make up *G. Sylvester's* active components. Inflammation, cancer, and a number of microbiological illnesses are also treated with it [20].

**MANNIFERA SP.**

It usually goes by the name "mango" and is a member of the Anacardiaceae family.

In rats with alloxan-induced diabetes, oral treatment of an aqueous extract did not affect blood glucose levels, whereas leaves extract (250 mg/kg) showed anti-diabetic effectiveness [24].

**MOMORDICA CHARANTIA**

It is usually referred to as bitter melon (karela) and is a member of the Cucurbitaceae family. *Momordica charantia*, commonly known as cucurbitacin B, contains momordic I and momordica II. Diabetes is treated using it. It contains lectins with insulin-like action. The non-protein lectin interacts with insulin receptors. This lectin decreases blood sugar by acting on peripheral tissues [25]. A 200 mg/kg dose of *M. charantia* fruit extract has hypoglycemic effects. Bitter melon has a long history of traditional use in treating diabetes. Studies have shown that the active compounds in bitter melon, including charantin and polypeptide-p, help reduce blood glucose levels by increasing glucose uptake and improving insulin sensitivity. While the evidence is promising, more clinical trials are needed to establish its long-term efficacy and safety (4).

**FENUGREEK (TRIGONELLA FOENUM-GRAECUM):** Fenugreek seeds have demonstrated hypoglycemic effects in various animal and human studies. The high fibre content in fenugreek may slow down carbohydrate absorption, contributing to better blood sugar management. Moreover, fenugreek may stimulate insulin secretion from the pancreas, aiding in glucose utilization (5).

**SACRED SPACE**

It belongs to the Labiateae family and is known as tulsi. It is abundantly available all over India. It is used to treat a range of ailments in Indian ayurvedic medicines. Numerous animal studies have revealed that aqueous extract of *Ocimum sanctum* leaves (200 mg/kg) has hypoglycemic effects in streptozotocin-induced rats. Additionally, it is used to treat stomach ulcers, reduce stress, and manage tumors [26]. It is also used to treat fungal infections and manage tumors.

**HEART-SHAPED TINOSPORA**

It is a member of the Menispermaceae family and is known as guduchi. The active ingredients of *T. cardifolia* are diterpene compounds, such as tinosporone, tinosporic acid, Syringen, berberine, and giloin [27]. Oral administration of *T. cardifolia* root extract (50-200mg/kg) causes a decrease in blood and urine sugar levels over the course of six weeks in streptozotocin-induced diabetic mice. In Indian ayurvedic treatments, it is mostly used to treat diabetes. Root extract also prevents weight loss [24].

Generally speaking, diverse plant parts like roots, stems, leaves, and fruits are extracted via maceration, infusion, percolation, decoction, and soxhlet extraction. Ethanol, methanol, and petroleum ether are the solvents that are used the most frequently.

**❖ HERBAL REMEDIES FOR DIABETES MELLITUS ARE AVAILABLE.**

There are currently numerous multi herbal formulations for the treatment of diabetes on the Indian market, including Vati, Churna, Arkh, and Quath [9]. These formulations could contain powdered or liquid extracts of several diabetes-treating plant components. These formulations



are referred to as poly herbal formulations since they contain 3 to 25 herbs in their composition [13].

### **AEGLE, MARMELO**

It is known as Bael and belongs to the Rutaceae family. It was developed in India, where ayurveda and other conventional treatments for a variety of ailments use various plant parts, including leaves, bark, roots, and fruits. The mixed, powdered leaves of neem, tulsi, and A. marmelos are taken three times daily for fifteen days. Animal studies have shown that aegle marmelos (100, 200, and 500 mg/kg) is effective in treating a range of ailments, including cancer, many viral infections, and various microbial diseases [24].

### **C. ALLIUM**

It is a member of the Liliaceae family and is referred to as onion or pyaz locally. That of *Allium cepa*. ether has anti-hyperglycemic activity ether-soluble and -insoluble components of dried onion powder. It contains the chemical component allyl propyl disulfide, known as APDS, it prevents the destruction of insulin by the liver and cause the pancreas to produce insulin. which raises insulin concentration and lowers the blood sugar levels for glucose. collected critical oil (100mg/kg) red onion frequently exhibits antihyperglycemic and anti-statin action Its anti-oxidant effects in diabetic rats produced by alloxan. The most effective percentage for treating hyperglycemia is 300 mg/kg. likewise, hyperlipidemia. According to data from several human trials and animal studies, onions are used to treat cancer, diabetes, asthma, and various viral infections.

### **ISSUES WITH INDIAN HERBAL MEDICINE**

Herbs have medical value, yet some people have questioned using them. These include the necessity for uniformity, the fact that patients aren't always given a specified dosage or schedule, and the possibility of variable levels of the active ingredient due to an unstandardized production method. The current problem is "how to prepare these herbal medicines to dispel the aforementioned criticisms and contend with pharmaceutical drugs." It will need in-depth analysis that separates and classes the main components of the medicinal plants. Few illnesses have also been successfully treated with either conventional medicine or even unconventional remedies. By researching the plant world and the logic underlying their potentials through linked research, it is vital to consider alternative treatment techniques [24, 25].

### **THE POTENTIAL FOR HERBAL DIABETES TREATMENTS**

People use a range of herbal remedies, and contemporary medicines usually incorporate various local pharmaceuticals. Nearly 80% of the population in developing countries, especially in rural regions, rely on conventional medical care for their medical requirements. Due to the broad preference for products made from natural sources, herbal medicines have experienced a resurgence of interest in wealthy countries. Therefore, it is important to distinguish between herbal remedies that are easily accessible for self-medication and those that are prescribed by a medical practitioner. Diabetes mellitus is a dangerous physical condition that is escalating in prevalence worldwide. More recently developed active treatments with greater anti-diabetic efficacy than oral hypoglycemic drugs used in confirmed therapy have been generated from plants. The identification of plants with anti-diabetic qualities that may benefit people has recently attracted people's attention. Additionally, it might provide support for the creation of a novel oral diabetic treatment [20-40].



Figure 3 Pictures of Herbal Plants Used for Diabetes Mellitus

## CONCLUSIONS

Diabetes mellitus, the most common endocrine disease, affects millions of people worldwide. Hyperglycemia caused by deficits in insulin secretion, action, or both characterizes a group of metabolic diseases like this one. The shift in research toward traditionally available medications with low side effects and a wide range of bio activity and do not require time-consuming pharmaceutical synthesis is due to the limited number of commercially available diabetes medications that still have many side effects and other problems like unwanted hypoglycemic effect. These elements are what are causing this transition, combined with the rise in resistance and patient populations who may be at danger. Researchers, scientists, and academics may use the information in this review article to develop evidence-based complementary therapy for a variety of diabetes conditions. Substances and extracts derived from various natural resources play a key role in the development of drugs and the treatment of hyperglycemic problems in diabetes mellitus.

The use of herbs in the treatment of diabetes mellitus is an intriguing area of research. While several herbs have shown promising results in lowering blood glucose levels and improving insulin sensitivity, further investigations are needed to establish their long-term efficacy, safety, and appropriate dosages. It is crucial for individuals with diabetes to consult their healthcare providers before incorporating herbs into their treatment regimen to avoid potential interactions with other medications. Integrating evidence-based herbal remedies with conventional therapies may offer a holistic approach to managing diabetes and improving overall well-being. Because of their anti-diabetic components, such as flavonoids, tannins, phenolic acids, and alkaloids, which improve the function of pancreatic tissues by raising insulin secretion or lowering intestinal glucose absorption, plants are effective natural antioxidants and herbal remedies. To determine the components of plants that are therapeutically useful and the molecular connections between their compounds, more research is needed.

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