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## Review Article

# Evaluating the Efficacy of Polyherbal Formulations in Diabetes Management

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### ABSTRACT

A chronic metabolic disease that needs to be effectively managed is diabetes mellitus. Although there are several pharmacologic treatments available to treat and control diabetes, there have not yet been reports of complete recovery from the disease. Numerous herbal remedies are useful in the treatment of diabetes. In contrast to synthetic and anti-diabetic medications, herbal medications with antidiabetic properties are widely developed commercially due to their ease of availability, affordability, and lack of adverse effects. 21000 are listed by the World Health Organization (WHO) and are used globally for medical purposes. The primary function of Ayurvedic formulations, which are primarily polyherbal, is to treat diabetes. The current study focused on diabetes, its treatment, and commercially available herbal treatments. Although synthetic oral hypoglycemic medications, such as insulin, are the standard of care for diabetes and are successful in reducing hyperglycemia, they have considerable adverse effects and do not appreciably change the progression of diabetic complications. This is the primary cause of the growing number of people looking for alternative treatments with less severe or nonexistent side effects. A list of herbal medications used to treat diabetes as well as medicinal plants with demonstrated antidiabetic and associated positive effects is compiled.

### INTRODUCTION

Insulin abnormalities in conjunction with impairments in glucose and lipid metabolism are connected to diabetes mellitus (DM). When the pancreas cannot make enough insulin or when the insulin is not used adequately, the disease occurs.<sup>[1]</sup>

Environmental and lifestyle factors that affect the formation of Type 1 and Type 2 diabetes include oxidative stress, obesity, inactivity, and heredity.<sup>[2]</sup> Diabetes's long-term effects include persistent hyperglycemia and abnormalities in the lipid profile due to disruptions in the metabolism of glucose, protein, and fat.<sup>[3]</sup>

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The development of safe and effective antidiabetic pharmaceuticals with fewer physiological adverse effects has been urgently needed due to the significant side effects of synthetic antidiabetic therapies. In order to determine the best herbal compositions that comprise powerful medicinal plants, experts have been studying medicinal flora in recent years.<sup>[4]</sup> In many nations, type 2 diabetes mellitus is the most dangerous illness, and the rising incidence of diabetic microvascular and macrovascular complications has raised serious concerns.<sup>[5]</sup> Diabetes mellitus is a systemic metabolic disease characterized by hyperglycemia, hyperlipidemia, hyperaminoacidemia, and hypoinsulinaemia it leads to decrease in insulin secretion and insulin action. Currently available therapies for diabetes include insulin and various oral antidiabetic agents such as sulfonylureas, biguanides,  $\alpha$ -glucosidase inhibitors and glinides. In developing countries products are expensive and not easily accessible<sup>[6]</sup> Diabetes is a diverse metabolic disease marked by changes in the metabolism of proteins, fats, and carbohydrates that lead to hyperglycemia from either insufficient insulin action or secretion, or both.<sup>[7]</sup> Diabetes mellitus is a severe medical condition with steadily rising incidence and death rates. The hallmark of diabetes mellitus is high plasma glucose levels brought on by either insulin resistance, inadequate insulin, or both, which results in aberrant protein, lipid, and carbohydrate metabolism. It may potentially result in acute or long-term consequences that cause microangiopathy, ketoacidosis, and other infections if left untreated. The two categories listed below can be used to group various forms of reported diabetes mellitus: Type 1: Insulin-dependent diabetes mellitus type 1 (IDDM) occurs when the body is unable to manufacture insulin. Young adults and children are most likely to experience it. Five to ten percent of cases of diabetes are type 1 diabetes.

Type 2: this diabetes, also known as noninsulin-dependent diabetes mellitus (NIDDM), is the most prevalent type of the disease, accounting for 90–95% of cases. It is caused by either insufficient insulin production or incorrect use of released insulin. Due to rising rates of obesity and sedentary lifestyles, as well as an aging population, type 2 diabetes is approaching pandemic proportions.

#### **Signs and Symptoms:**

The chance of acquiring problems from diabetes can be reduced by early detection and treatment. The following are common signs of diabetes. On the other hand, some individuals with type 2 diabetes have symptoms that are so subtle that they are overlooked. Typical signs of diabetes include: I'm so thirsty. Feeling really hungry despite eating. Extreme exhaustion blurry vision. v Slow-healing cuts and bruises. Despite eating more, you lose weight (Type 1). Hand or foot tingling, discomfort, or numbness (Type 2).<sup>[8]</sup>

#### **Basis of Diabetes Mellitus treatment:**

Patient education regarding the condition · Exercise · Nutrition · Drugs that lower blood sugar Due to its high frequency, morbidity, and mortality, diabetes is rapidly becoming the third "killer" of human health, after cancer, cardiovascular disease, and cerebrovascular illness. As a result, it is effectively managed with a variety of therapeutically effective medications after diagnosis. In addition to chemotherapeutic agent-based therapy, naturopathy has advanced in the current century. As a result, medicinal plants are becoming more and more useful in the management of chronic illnesses like diabetes mellitus, particularly in developing nations with limited resources. In healthy people, diabetes mellitus alone is associated with a number of other illnesses. Each of these illnesses can be treated by taking advantage of India's herbal resources. Any condition associated with diabetes mellitus can be cured by using the herbs, either whole or in



portions. Additionally, in certain instances, plant extracts can cure chronic conditions like diabetes mellitus and treat related conditions like polyuria, polydipsia, glucosuria, etc.

Benefits:

1. Herbal medications are often well tolerated by patients, may be safer to use, and have less side effects and unexpected consequences than traditional treatment.
2. Herbal medications work better for chronic illnesses that don't improve with conventional treatment.
3. Compared to prescription treatments, herbal remedies are significantly less expensive. Marketing, testing, and research
4. You can get herbs without a prescription. It is possible to grow simple herbs at home, like chamomile and peppermint.<sup>[9]</sup>

#### **The patient's way of life**

Below is a description of some of the herbal and home cures that Ayurveda recommends.

1. Incorporate diets containing cinnamon and turmeric.
2. Steer clear of fatty, fried, and starchy foods.
3. Steer clear of processed wheat, sugar, caffeine, and alcohol. Rather than eating three substantial meals a day, eat smaller meals five to six times a day (low fat diet).
5. Eat more vegetables, such as beans, garlic, sprouts, tomatoes, onions, cucumbers, and spinach.
6. Avoid taking on stress.
7. Frequent physical activity. Spend at least forty minutes each day walking.
8. Steer clear of red meat and too much salt in your meals. Because of their high protein content, fish and soy can be consumed.
9. Steer clear of sweet and sugary foods, rice, potatoes, and white bread.<sup>[10]</sup>

#### **Recent Regulatory Developments:**

Only traditional medicines that principally employ medicinal plant preparations for therapy are considered herbal pharmaceuticals, as specified by

regulatory regulations. According to a current WHO definition, traditional medicine (including herbal medications) includes therapeutic techniques that have been used for hundreds of years, before modern medicine developed and spread, as well as others that are still in use today. The regulatory frameworks controlling the research and use of botanical drugs have drawn significant attention from the FDA and EMEA in recent years. The natural products business has benefited greatly from this intense interest, which has also greatly reduced the barriers to entry for botanicals and allied items.<sup>[11]</sup>

#### **Mechanism of Action of Herbal Antidiabetics:**

Herbs' ability to lower blood sugar is dependent on a number of methods. Herbal anti-diabetic medications work in the following ways:

Reduction of insulin resistance; suppression of renal glucose reabsorption; stimulation of insulin production from islet beta cells or/and inhibition of insulin degradative processes; adrenomimeticism, blockage of pancreatic beta cell potassium channels, and cAMP (2nd messenger) stimulation. Enhancing the size and quantity of cells in the islets of Langerhans; supplying specific elements such as calcium, zinc, magnesium, manganese, and copper for the beta-cells; regenerating and/or repairing pancreatic beta cells; stimulating insulin secretion; stimulating glycogenesis and hepatic glycolysis; preventing beta cell destruction; improving digestion while lowering blood sugar and urea levels<sup>[12]</sup>

#### **Polyherbal Formulation**

According to studies, several individual plants had high levels of phenolics and flavonoids, and when combined with green tea, their polyherbal mixture produced the highest level of antioxidant activity of any extract.<sup>[13]</sup> Because of their synergism and fewer adverse effects, polyherbal herb combinations are preferred in most traditional approaches for managing diabetes.<sup>[14]</sup> Similar to the conventional silver sulphadiazine cream,



diabetic foot ulcers were reported to be effectively and safely healed by diabetic wound cream made with a polyherbal formulation.<sup>[15]</sup> Using carrageenan-induced rat paw edema and cotton pellet granuloma methods, the anti-inflammatory properties of the polyherbal formulation, which contains *Allium cepa*, *Allium sativum*, *Aloe vera*, *Cajanus cajan*, *Coccinia indica*, *Caesalpinia bonducella*, *Ficus bengalensis*, *Gymnema sylvestre*, *Momordica charantia*, *Ocimum sanctum*, *Pterocarpus marsupium*, *Swertia chirayita*, *Syzgium cumini*, *Tinospora cordifolia*, and *Trigonella foenum graecum* were tested in rats for acute and sub-acute models of inflammation using oral doses of 300 mg/kg and 600 mg/kg, respectively. In all experimental models, the formulation demonstrated significant anti-inflammatory effect that was on par with that of the common medication, indomethacin.<sup>[16]</sup>

#### **Herbal medications that have antidiabetic effects:**

1) Fenugreek, or *Trigonella foenum graecum*:

It may be found all over India, and one of the main ingredients in Indian spices is often fenugreek seeds. In both rats and humans, 4-hydroxyleucine, a new amino acid derived from fenugreek seeds, enhanced the release of insulin by isolated islet cells in response to glucose stimulation. In both normal and diabetic rats, oral treatment of 2 and 8 g/kg of plant extract resulted in a dose-dependent drop in blood glucose levels. In diabetic rats, fenugreek seed administration also enhanced glucose metabolism and restored normal creatinine kinase activity in the liver, skeletal muscle, and heart. Additionally, it decreased the activity of fructose-1, 6-biphosphatase and glucose-6-phosphatase in the liver and kidneys. Additionally, this plant exhibits antioxidant action.<sup>[17]</sup>

2) *Aloe barbadensis* and *Aloe vera*: The leaf is aloe vera gel. The Journal of Phytopharmacology 46 Aloe latex, sometimes known as "aloe juice," is a

bitter yellow fluid that comes from the pericyclic tubules directly beneath the leaves' outer skin. Aloe gum extracts successfully improve glucose tolerance in both healthy and diabetic rats. In alloxanized diabetic rats, administration of *Aloe barbadensis* leaf exudates on a chronic but not a single dose resulted in a hypoglycemic effect. In diabetic rats, both single and repeated dosages of the bitter component of the same plant had a hypoglycemic effect. *Aloe vera*'s bitter principle works by encouraging the production and/or release of insulin from beta cells in the pancreas.<sup>[18]</sup>

3) *Mangifera indica*: The mango plant's leaves are employed in Nigerian traditional medicine as an antidiabetic medication, despite the fact that oral aqueous extract did not change blood glucose levels in rats with normoglycemia or streptozotocin-induced diabetes. However, when the extract and glucose were given together, as well as when the extract was given to the rats 60 minutes prior to the glucose, antidiabetic effect was observed. The findings suggest that *Mangifera indica* aqueous extract has hypoglycemic properties. An intestinal decrease in absorption could be the cause of this.<sup>[19]</sup>

4) *Acacia arabica*, often known as Babhul, is primarily found in its natural habitat in India. The plant extract functions as a secretagogue to release insulin, which lowers blood sugar levels. Control rats experience hypoglycemia, whereas alloxanized animals do not. When given to healthy rabbits at doses of 2, 3, and 4 g/kg body weight, powdered *Acacia arabica* seeds caused a hypoglycemic effect by triggering the release of insulin from the pancreatic beta cells.<sup>[20]</sup>

5) *Allium cepa*: Onion: In diabetic rabbits, different ether-soluble and insoluble fractions of dried onion powder exhibit anti-hyperglycemic effect. It is also well known that *Allium cepa* has hypolipidemic and antioxidant properties.[5] Alloxan-induced diabetic rats were



given 200 mg/kg of S-methyl cysteine sulphoxide (SMCS), an amino acid containing sulfur from *Allium cepa*, for 45 days. This resulted in a significant reduction in blood glucose levels and lipids in serum and tissues, as well as a normalization of the activities of liver hexokinase, glucose 6-phosphatase, and HMG Co A reductase. Postprandial glucose levels were dramatically reduced in diabetic patients who received a single oral dosage of 50 g of onion juice.<sup>[21]</sup>

6) Garlic, or *Allium sativum*, is a perennial herb that is grown all over India. Its strong smell is caused by the sulfur-containing chemical allicin, which has also been demonstrated to have strong hypoglycemic effects.<sup>[22]</sup> Higher hepatic metabolism, higher insulin release from pancreatic beta cells, and/or the insulin sparing effect are the three possible causes of this impact. When given orally to rabbits fed sugar (10 g/kg/day in water for two months), an aqueous homogenate of garlic (10 ml/kg/day) dramatically raised the amount of hepatic glycogen and free amino acids, decreased fasting blood glucose, and lowered serum triglyceride levels when compared to sucrose controls.<sup>[23]</sup>

7) The bitter gourd, *Momordica charantia*, belongs to the Cucurbitaceae family. Kaattu pagar-kai is the local name. Bitter guard is the common name for the plant, which comes in a variety of forms. In India and other Asian nations, *Momordica*

*charantia* is frequently used as an antidiabetic and antihyperglycemic medication. In several animal models, it was demonstrated that extracts of fruit pulp, seeds, leaves, and the entire plant had a hypoglycemic impact. When given subcutaneously to humans and langurs, polypeptide p, which was extracted from the fruit, seeds, and tissues of *M. charantia*, had a notable hypoglycemic impact. In both normal and STZ diabetic rats, ethanolic extracts of *M. charantia* (200 mg/kg) demonstrated both hypoglycemic and antihyperglycemic effects. In addition to fructose-1, 6-biphosphatase, glucose-6-phosphatase may be inhibited in the liver, while hepatic glucose-6-phosphate dehydrogenase activities may be stimulated.<sup>[24]</sup> Generally grown throughout India, the plant is a climbing shrub. Along with food, unripe fruits are consumed orally. Dosage: Take two to three fresh, unripe fruits every day for three months.<sup>[25]</sup>

8) Hydroalcoholic extracts of *Azadirachta indica*, also known as neem, demonstrated antihyperglycemic action in rats treated with streptozotocin. This effect was caused by an increase in glucose absorption and glycogen deposition in the isolated rat hemidiaphragm. This plant has antibacterial, antimalarial, antifertility, hepatoprotective, and antioxidant properties in addition to its anti-diabetic action.<sup>[26]</sup>

Sr. No.	Herbs	Chemical Constituents
1.	Peepal	tannins, saponins, polyphenolic compounds, flavonoids, and sterols
2.	Jamun	anthocyanins, glucoside, ellagic acid, isoquercetin, kaempferol, myricetin, and hydrolysable tannins
3.	Bitter gourd	vicine, charantine, and triterpenoids
4.	Tulsi	flavonoids, saponins, tannins, triterpenoids, rosmarinic acid, apigenin, isothymusin, isothymonin, cirsimaritin, orientin, and vicenin
5.	Indian kino tree	terpenoids and phenolic compounds: $\beta$ -sitosterol, lupenol, aurone glycosides, epicatechins, and iso-flavonoids
6.	Fenugreek	Saponins, 4-hydroxyisoleucine, and trigonelline, an alkaloid
7.	Garlic	allicin, allixin, ajoene, and other organosulphur compounds

1.	Peepal	tannins, saponins, polyphenolic compounds, flavonoids, and sterols
9.	Leaf-flower	Corilagin, gallic acid and macatannin B
10.	Cinnamon	Tannins, flavonoids, glycosides, terpenoids, coumarins and anthraquinones
11.	Black seed	Flavonoids, unsaturated fatty acids, nigellone, thymoquinone (TQ), p-cymene and carvone
12.	China aster	Apigenin, apigenin-7-O- $\beta$ -D- glucoside, hyperin, kaempferol, kaempferol-7-O- $\beta$ -D- glucoside
13.	Basil	Cardiac glycosides, flavonoids, glycosides, reducing sugars, saponins, steroids and tannins
14.	Jute	Caffeic acid, chlorogenic acid and isorhamnetin
15.	Mistletoe fig	Vitexin, isovitexin, proanthocyanidin, flavonoids, 3-flavanol monomers and flavones glycosides
16.	Bitter oleander	Gallic acid and quercetin
17.	Olive	Oleuropein, hydroxytyrosol, oleuropein aglycone, and tyrosol
18.	Soybean	Phenolic compounds
19.	Vinca	Carbohydrate, flavinoid, saponin, alkaloids, Vindogentianine
20.	Bitter melon	Momordicin, charantin, and galactose-binding lectin
21.	Fennel	50–60% anethole and 20% de-fenchone
22.	Astragalus	saponins, polysaccharides, flavonoids, amino acids, and trace elements
23.	Baobab	protein (19.84 $\pm$ 0.022%), fat (3.72 $\pm$ 0.014%), fibre(4.16 $\pm$ 0.014%), ash (8.66 $\pm$ 0.014%), Moisture (9.86 $\pm$ 0.00%), and Carbohydrate (53.78 $\pm$ 0.05%).
24.	Berberine	isoquinoline alkaloid
25.	Black Cohosh	hydroxycinnamic acids, caffeic acid (3), ferulic acid (4), and isoferulic acid
26.	Bloodroot	alkaloids, primarily sanguinarine. Others include chelerythrine, berberine
27.	Burdock root	Fructooligosaccharides are inulin compounds
28.	Bitter Melon	Charantin, momordicosides, and cucurbitacins
29.	Holy Basil	Eugenol, methyl eugenol, and $\beta$ -caryophyllene
30.	Java Plum	Jamboline, jambosine, and gallic acid
31.	Deodar	Cedrol, cedrene
32.	Tarwar	Auriculatin, cassiaurin
33.	Punarnava	Punarnavine, boerhavine
34.	Shatavari	Asparagosides, racemosides
35.	Guduchi	Tinosporin, cordifolin
36.	Curry Leaf	Volatile oils, alkaloids
37.	Jambu	Jamboline, jambosine, gallic acid
38.	Amla	Ascorbic acid, ellagic acid, gallic acid
39.	Arjuna	Arjunolic acid, arjungenin
40.	Ashwagandha	Withanolides, alkaloids
41.	Ginseng	Ginsenosides, ginseng saponins
42.	Aloe vera	Aloin, aloe-emodin, acemannan

43.	Acacia	gallic acid, dicatechin, quercetin, robidandiol, $\beta$ -amyryn, hentriacontane, betulin
44.	Alfalfa	saponins, essential oils, polysaccharides, flavonoids, and alkaloids
45.	Blueberry	chlorogenic acid, flavonids, alpha-linolenic acid, pterostilbene, resveratrol, and vitamins
46.	Flaxseed	phenolic acids, flavonoids and lignans
47.	Guava leaves	lavonoid, sesquiterpene, triterpenoid, coumarin, alkaloid, and tannin
48.	Mint	menthol and menthone
49.	Mustard seed	1,8-cineole, and limonene
50.	Cumin	cuminlaldehyde (19.9–64.31 %), p-cymene (6.1 %–47.08 %), cuminal (36.31 %)

### Severity of Diabetes:

In this study, the following criteria were used to generate the diabetes severity score: the presence of cardiovascular disease (CVD); longer duration of diabetes; diabetes-related renal complications (chronic kidney disease, CKD); or the complexity of diabetes medications (use of insulin or multiple OHAs). The diabetes severity score was determined by adding the points from each feature, which was represented by a total of 0–5. A diabetes severity score of 1 was noted if at least three OHAs were used, and if the diabetes had been present for at least five years. An estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m<sup>2</sup> was considered chronic kidney disease (CKD).[27]

### CONCLUSION:

Diabetes has been effectively treated with herbal medicine all around the world. Diabetes types I and II, as well as associated complications, are managed using herbs. Diabetes mellitus is becoming more and more common around the world, and using oral hypoglycemic medications to treat it can have a lot of negative side effects and cost a lot of money. Patients' desire to use natural medications with antidiabetic properties is growing. Several anti-diabetic plants that have undergone pharmacological testing and been found to have some potential for treating diabetes mellitus are discussed in this paper. These plants

have the potential to cure metabolic imbalances and postpone the onset of diabetes consequences. The researchers have conducted some preliminary investigations and have taken into consideration the potential hypoglycemic effects of the plants described above. Herbal formulations' medicinal value is determined by their effects. As a result, numerous plants have been utilized either alone or in combination to treat diabetes.

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