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A Review on Antidiabetic Effect of Indian Medicinal Plants

Manjeera K*, Behera J and eRudra Bhavani JS

Department of Pharmacology, C.M.R. College of Pharmacy, India

***Corresponding author:** Kuchi Manjeera, M. Pharm. (Ph.D), Assistant Professor, Department of Pharmacology, C.M.R. College of Pharmacy, Kandlakoya, Medchal, Hyderabad, Telangana, 501401, India, Tel: +91 7396176659; Email: mkuchi@gitam.in

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Abstract

Diabetes mellitus is a growing global health concern, with rising incidence and mortality rates. Poor blood sugar control can have devastating health consequences. While conventional antidiabetic medications are effective, they often come with unwanted side effects. Medicinal plants offer a promising alternative, providing a natural source of antidiabetic compounds. Research highlights various plants with antidiabetic potential, backed by preclinical and clinical studies. The therapeutic benefits of these plants stem from the synergistic effects. Diabetes mellitus is a long-term metabolic disorder prompted by an insufficient supply of the hormone insulin. It is characterized by hyperglycaemia, altered protein, carbohydrate, and lipid metabolism & also an increased risk of vascular problems. In many parts of the world, diabetes affects around 5% of the population worldwide and now it is a serious health issue. According to estimates, there will be more than 300 million diabetics worldwide by 2025, and the expenses of treating the condition and complications might reach US$1 trillion annually.

Keywords: Diabetes Mellitus; Antidiabetic Activity; Medicinal Plants; Synergistic Effects; Diabetes Mellitus

Introduction

Diabetes mellitus is a complex clinical condition characterized by excessive blood sugar levels, resulting from insufficient insulin production, insulin resistance, or a combination of both. As the most prevalent endocrine disorder, it affects millions worldwide, with far-reaching consequences on multiple organ systems [1]. Diabetes, a chronic disease affecting 2-3% of the global population, remains a significant health challenge. Despite the introduction of sulfonylurea and metformin over 50 years ago, limited progress has been made in discovering new, effective treatments [2]. Traditional plant-based medicines, long used to manage diabetes, offer a promising source of new drug leads. In many countries, particularly in developing nations, plant extracts and folk preparations are widely prescribed by traditional practitioners and accepted by patients as a treatment for diabetes [3]. In diabetes, the body's cells fail to process sugar effectively due to impaired insulin function or insufficient insulin production. Insulin, a hormone regulating blood sugar, is either lacking or not utilized efficiently by the body. As a result, the pancreas cannot produce enough insulin, or the body becomes resistant to its effects. Consequently, the body begins to break down stored fat, protein, and glycogen to generate energy, leading to excessively high blood sugar levels [4]. Simultaneously, the liver produces excess ketones, toxic by-products that accumulate in the bloodstream Phytochemicals are perceived as a safer option compared to synthetic drugs, with minimal side effects. The appeal of herbal medicine is growing, driven by its affordability and lower toxicity, despite the existence of conventional treatments like oral hypoglycemic drugs and insulin [5]. The World Health Organization reports that a staggering 80% of the global population relies on herbal remedies for various ailments. However, with a vast array of approximately 400,000 plant species remaining understudied – only 6% have been investigated and 15% analyzed for phytochemicals – a systematic framework is urgently needed to assess the phytopharmacological potential of herbal medicines. Diabetes is brought on by the loss of these hormones' balanced impact, which is typically caused by decreased insulin production [6]. Sugar begins to build up in the blood, raising blood sugar levels, and sugar and other minerals pass via the urine. Hyperglycemia is a high blood sugar level, while glycosuria is the presence of sugar in the urine [7]. The pancreatic islets of Langerhans' β-cells secrete insulin, which is essential for the tissues' burning of sugar with oxygen's assistance. Therefore, diabetes mellitus is a collection of disorders that include polydipsia (drinking a lot of water), polyuria (excreting a lot of diluted urine), and glycosuria [8]. With a two-way link to diabetes mellitus, COVID-19 first became a pandemic in March 2020 and infected 254 million people globally until early November 2021. Severe metabolic consequences from pre-existing diabetes mellitus, such as hyperosmolarity and diabetic ketoacidosis necessitating massive dosages of insulin. The death rate for COVID-19 patients with diabetes mellitus is 36% in Italy [9]. Clinical recognition of the link between infection and diabetes mellitus has long existed. Diabetes weakens the immune system, increasing a person's vulnerability to diseases like COVID-19. Twelve Additionally, it encourages persistent inflammation, which raises the possibility of a major cytokine storm. Diabetes is associated with altered glucose metabolism because diabetic people have larger amounts of ACE2 receptors, which SARS-CoV-2 uses to enter cells.13. Diabetes also results in endothelial dysfunction [10].

This review also focus on the emphasizes the significance of traditional therapies and natural medicines derived from medicinal plants in managing diabetes. The use of readily available medicinal plants in traditional medicine presents a promising avenue for the development of innovative antidiabetic treatments [11].

Classification of Diabetes Mellitus

Diabetes mellitus is categorized into various types based on its underlying causes, but it is generally acknowledged that the disease primarily manifests in two distinct forms: Type 1 and Type 2 diabetes. Type 1 Diabetes Mellitus (DM) was formerly known as juvenile diabetes due to its prevalence in children, but it can actually affect individuals of all ages, including both children and adults [12]. While adults often maintain adequate insulin secretion to prevent ketoacidosis for many years, younger people usually have a faster rate of beta-cell death and present with ketoacidosis. There is a fluctuating risk of diabetic ketoacidosis because to their insulinopenia. Insulin therapy will eventually be necessary for all people with type 1 diabetes in order to maintain normoglycemia. For more details, go to the chapters that go into great length about the pathophysiology of type 1 diabetes [13].

Type 2 Diabetes Mellitus (DM), also known as non-insulin-dependent DM, is the most prevalent form of the disease, accounting for approximately 90-95% of all DM cases. This type of diabetes is largely influenced by lifestyle factors and genetic predisposition, and can often be managed through dietary changes and regular physical activity [14]. A common sign of type 2 diabetes is postprandial hyperglycaemia, which is defined as an unusual increase in blood sugar levels after a meal. f Inhibiting the hydrolysis of carbohydrates by α-glucosidase and α-amylase can cause type II diabetes by delaying the digestive tract's absorption of glucose [15]. Furthermore, blocking these enzymes lengthens the time needed for Inhibiting the hydrolysis of carbohydrates by α-glucosidase and α-amylase can cause type II diabetes by delaying the digestive tract's absorption of glucose [16].

Gestational Diabetes Mellitus (GDM)

Diabetes is the most prevalent medical complication during pregnancy, compounded by the fact that nearly half of all pregnancies worldwide are unplanned. For women with gestational diabetes, uncontrolled high blood sugar can have serious consequences for both mother and baby, increasing the risk of: birth defects pregnancy loss, early labor, pregnancy-related hypertension complicated deliveries, mortality birth-related injuries [17]. The number of pregnant women with diabetes has skyrocketed, with gestational diabetes and pre-existing type 1 or type 2 diabetes affecting nearly 10% of women under 30. Specifically, pregnancies complicated by type 1 diabetes have risen by 33-44%, while those complicated by type 2 diabetes have seen a staggering increase of 90-111% [18].

Treatment of Diabetes mellitus

Insulin and Oral Hypoglycaemic Drugs

Insulin therapy aims to replicate the body's natural insulin regulation, effectively managing postprandial hyperglycaemia and preventing hypoglycaemia [19]. Various insulin preparations are available, including human, beef, and pork insulin. However, insulin therapy can have complications and adverse effects, such as weight gain and hypoglycaemia, typically resulting from incorrect dosing or mismatched meals and insulin injections [20]. Sulfonylureas, a class of medications for type 2 diabetes, work by binding to receptors on pancreatic beta cells, stimulating insulin release. They also increase peripheral glucose uptake and reduce hepatic glucose output by 20-30%. Additionally, sulfonylureas may impair glucose absorption in the gut, further contributing to their therapeutic effect [21]. Researchers have explored various injectable and oral medications to enhance insulin treatment for type 1 diabetes. One such medication, Pramlintide, is a synthetic version of the natural hormone amylin and has been approved for use in adults with type 1 diabetes [22]. Rapid-acting: The types of insulin Depending on the type, this insulin takes 15 minutes to start working and lasts 1 to 5 hours. Rapid-acting insulin is typically taken alongside a longer-acting kind of insulin prior to meals. Short-acting [23]. This type of insulin, also known as normal insulin, lasts three to eight hours and takes around thirty minutes to completely act. Short-acting insulin should be taken 30 to 60 minutes prior to eating. Intermediate-acting insulin, often used with fast-acting insulin, provides coverage for about 12 hours, making it suitable for overnight use [24]. It begins working within 1-2 hours, reaching its peak effect in 2-4 hours. Long-acting: This form covers insulin for the entire day. With it, you'll most likely take a shorter-acting insulin [25].

Herbal Treatment of Diabetes

In recent decades, plant-based medicines have gained mainstream acceptance due to their eco-friendly, cost-effective, and relatively safe profile. This shift has been driven by increased research in traditional medicine [26]. According to the World Health Organization (WHO), approximately 21,000 plants worldwide are used for medicinal purposes. India alone is home to 2,500 species, with 150 being commercially utilized on a large scale [27]. As the largest producer of medicinal herbs, India is often referred to as the "botanical garden of the world [28]. Researchers from all around the world are interested in using medicinal plants to treat diabetes because of their effective, safe, and long-lasting mechanism of action. These therapeutic plants contain chemicals that are physiologically active and have significant therapeutic benefit [29].

Pharmacological treatment: The first line of treatment for diabetes is oral antidiabetic drugs such as biguanides, sulfonylureas, thiazolidinediones, and digestive enzyme inhibitors; insulin is used as a last resort [30]. The frequent adverse effects of synthetic antidiabetics, such as hepatic dysfunction, weight fluctuations, eye issues, peripheral artery disease, and gastrointestinal distress, necessitate the creation of a safer, more economical, and less toxic drug [31]. Metformin has been shown to lower BMI and insulin needs without significantly impacting HbA1c levels. Additionally, GLP-1 receptor agonists, commonly used for type 2 diabetes and obesity treatment, have demonstrated potential benefits for type 1 diabetes patients when used alongside insulin. A recent meta-analysis confirmed that GLP-1 receptor agonists improve blood sugar control, reduce severe hypoglycaemia, body weight, and insulin requirements [32].

Non-pharmacological treatment: The main goal of optimal diabetes treatment is to maintain plasma glucose levels within the normal physiological reference range, as they would be in a healthy, non-diabetic individual, without increasing the risk of hypoglycaemia [33]. A healthy person's normal plasma glucose levels are influenced by their nutritional intake, degree of physical activity, and the hormones particularly insulin that regulate glucose homeostasis [34]. Therefore, nutritional therapies, lifestyle changes that include physical activity, hormonal manipulation (mostly insulin), and/or its consequences should be the focus of diabetes care [35]. A comprehensive approach to diabetes care includes medical nutrition therapy, weight management, regular physical activity, quitting smoking, education on self-management, emotional support, and psychological care, all of which are crucial for achieving treatment goals and enhancing overall well-being [36].

	Plant name	Family	Plant part	Anti-diabetic effect	Model used	Ref
1	*Allium cepa L. (onion)*	*Liliaceae*	Bulb	S-methyl cysteine sulfoxide (SMCS) showed antidiabetic and hyperlipidemic activity , Anti-hyperglycaemic and insulin resistance in high fat diet	Alloxanized rats High cholesterol diet-fed rats STZ rats	[7-9]
2	*Allium sativum L. (garlic)*	*Alliaceae*	Cloves	SACS showed anti-diabetic activity ,Allicin lowered the blood pressure and improved lipid profile in hyperlipidemic, hyerinsulinemic	STZ rats Alloxanized rats Fructoseinduced hyerinsulinemic hyperlipedemic, hypertensive rats STZ rats	[10-14]

3	*Aloe vera L. Burm. (Aloe vera)*	*Asphodelaceae*	Leaf	Anti-hyperglycaemic activity with protective effect on pancreas, liver and small intestine Hypoglycaemic effect of aloe Hypoglycaemic activity Hypoglycaemic and reduced HbA1c	STZ rats Alloxanized mice STZ rats Alloxanized rabbits	[15-18]
4	*Gymnema sylvestre (Periploca of the woods)*	*Ascelpiadaceae*	Leaf	Anti-diabetic activity, Anti-hyperglycaemic effect ,Hypolipidemic effect in hypertensive rats	Alloxanized rats Beryllium nitrate-treated rats Spontaneously hypertensive rats	[19-21]
5	*Syzygium cumini Walp. (Blackberry)*	*Myrtaceae*	Seeds & Pulp	Anti-hyperglycaemic effect, α-Glucosidase inhibitory activity	Alloxanized rats STZ rats Alloxanized rabbits Goto–Kakizaki rats	[22-24]
6	*Pterocarpus marsupium Roxb. (Indian kino tree)*	*Fabaceae*	Bark	Anti-diabetic & protective effect on serum protein, ALP and ACP, albumin levels and HbA1c, Anti-hyperglycaemic activity, Hypoglycaemic activity ,Hepatoprotective effect	STZ rats STZ rats Alloxanized rats Wistar rats	[25-27]
7	*Momordica charantia (Bitter Melon)*	*Cucurbitaceae*	Fruit, seeds	Act as Insulin-like protein, decrease blood glucose level, n-like protein, decrease blood, Stimulate insulin secretion, a lower blood glucose level, Release in intestininal GLP-1PPAR α activation	Albino rats, STZ rats, Alloxan diabetic albino rats	[28,29]
8	*Panax ginseng C.A Meyer (ginseng)*	*Araliaceae*	Root	Ginsenosied Rb2 treated for streptozotocin-induced diabetic rats by decreasing blood glucose level, β-cell dysfunction, therapeutic medications should be involved in improving insulin resistance, enhancing glucose uptake	Diabetes mellitus mouse model, STZ-induced model	[31,32]
9	*Tinospora cordifolia (guduchi)*	*Menispermaceae*	Leaves	Ginsenosied Rb2 treated for streptozotocin-induced diabetic rats by decreasing blood glucose level, β-cell dysfunction, therapeutic medications should be involved in improving insulin resistance, enhancing glucose uptake	STZ rats STZ rats Alloxanized rats Wistar rats	[33]

10	*Cyamopsis tetragonoloba L.(s Cluster Bean or Guar)*	*Fabaceae*	Plant pods	Improve insulin release, decrease the amount of Hba1c, Hypoglecemic action & protected β - cell	Alloxan-induced rats	[34]
11	*Zingiber officinale (Ginger)*	*Zingiberaceae*	Root	Enhance glucose uptake, inhibition against alpha-amylase		
12	*Euphorbia hirta Linn. (Dudhi)*	*Euphorbiaceae*	Leaves, flowers, stems	Inhibit α-glucosidase activity, Showing potent inhibition of α-glucosidase and moderate inhibition of α-amylase, two key enzymes directly implicated in the development of diabetes mellitus, Eight bioactive compounds were isolated from E. hirta, including several flavonoids and triterpenes. These compounds, which include cyanidin 3,5-O-diglucose, myricitrin, and others, demonstrated potential as therapeutic agents for the treatment of type 2 diabetes mellitus.	Alloxan-induced diabetic rats, albino rats,	[35]
13	*Ocimum sanctum (Tulsi)*	*Lamiacea*	Leaf	Ethanol, aqueous, butanol and ethyl acetate eugenol, carvacrol, linalool, caryophylline, β-sitosterol its show -anti diabetic effect,	STZ-induced diabetic rats	[36]
14	*Swertiachirayita H. Karst. (Chirata)*	*Gentianaceae*	Root, stem, bark	Xanthones, seco-iridoids, terpenoids, alkaloids, and flavonoids have been isolated and characterized anti-diabetic	STZ-induced diabetic rats	[37]
15	*Acorus calamus(sweet flag)*	*Acoraceae*	Rhizomes	Lipid profile (total cholesterol, LDL and HDL-cholesterol), glucose 6-phosphatase, fructose 1,6 bis phosphatase levels and hepatic markers enzymes (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase) were decreased when compared with diabetic control	STZ-induced diabetic rats	[38]

16	*Aegle marmelos (bael)*	*Rutaceae*	Fruits, leaves	Reduction in lipid peroxidation, conjugated diene and hydroperoxide level and increased levels of superoxide dismutase, catalase, glutathione peroxidase and glutathione	Alloxan-induced rats, STZ-induced diabetic rats,	[39]
17	*Terminalia catappa Linn. (Indian almond)*	*Combretaceae*	Fruits,leaves	Act by β-cells regeneration, petroleum ether, methanol and aqueous extract of T. catappa fruits on fasting blood sugar levels and serum biochemical analysis	Alloxan-induced diabetic rat,	[40]
18	*Beta vulgaris (beetroot)*	*Chenopodiaceae*	Whole plant	Anti-diabetic activity, Hypolipidemic effect in hypertensive rats	STZ-induced diabetic rats,	[41]
19	*Anoectochilus roxburghii*	*Orchidaceae*	Roots	Enhances insulin effectiveness, reduces liver sugar production, and lowers harmful cholesterol and triglyceride levels, all while minimizing potential harm to vital organs.	STZ-induced diabetic mice	[42]
20	*Nelumbo nucifera*	*Nymphaeaceae*	Leaves	Extract enhances the body's ability to effectively use glucose, and also increased the effectiveness of insulin therapy.	Streptozotocin-induced diabetes.	[43]
21	*Ficus religiosa*	*Moraceae*	Bark, leaves, and root bark	Sitosteryl-d-glucoside, extracted from the bark of the Ficus religiosa tree, has been found to lower blood sugar levels in healthy rabbits.	STZ-induced diabetic rats	[47]
22	*Pterocarpus marsupium (Indian Kino tree)*	*Leguminosae*	Bark, and leaves	Increased insulin release and glucose absorption in a dose-dependent manner, meaning its effects became stronger as its concentration increased.	Streptozotocin-induced diabetes.	[48]
23	*Piper longum (pipli)*	*Piperaceae.*	roots	Boosted insulin production and glucose absorption, with its effectiveness increasing as the dose increased.	STZ induced diabetic rats	[49]
24	*Phyllanthus amarus Schum (Bhuiavla)*	*Euphorbiaceae*	Leaves and seeds	Include insulin, pramlintide, GLP-1 receptor agonists, and oral medications. Of these, insulin is the most widely used treatment for diabetes.	Alloxan-induced diabetic mice	[50]

25	*Asian pigeonwings (Butterfly pea)*	*Leguminosae*	Flower	Pancreatic α-amylase and intestinal α-glucosidase, carbohydrate digestion and sugar absorption are significantly slowed	STZ induced diabetic rats	[51]
26	*Coccinia indica (ivy gourd)*	*Cucurbitaceae.*	Fruits	Reduces phosphorylase activity and raises the liver's glycogen content to lower blood glucose levels.	Alloxan-induced diabetic animals,	[52]
27	*caesalpinia bonducella (Gray Nicker)*	*Legumes*	Seeds	Inhibiting glucose absorption and managing diabetes-induced hyperlipidemia	STZ hyperglycemic rats	[53]
28	*Memecylon umbellatum: (Anjani or Alli)*	*Melastomataceae*	Leaves and roots	Ability to reduce hyperglycemia and improve glucose tolerance in animal models of diabetes	STZ hyperglycemic rats	[54]
29	*Ipomoea batatas (Sweet potato)*	*Convolvulaceae.*	Leaves and peel	Increased HDL-cholestero, Improved glucose tolerance, Improved glucose tolerance	Alloxan-induced diabetic animals,	[55,56]
30	*Costus igneus (spiral flag)*	*Spiral ginger*	Leaves	Controlled level, decreases the amount of glycosylated haemoglobin, corrects the lipid profile.	STZ induced Wistar rats, dexamethasoneinduced wister ret, Alloxan induced diabetic animal	[57]

Table 1: Treatment goals and enhancing overall well-being.

Conclusion

Medicinal plants have been widely recognized for their potential in managing diabetes mellitus, including both Type 1 and Type 2. The contemporary review highlights the anti-diabetic properties of various medicinal plants, which have shown promising results in regulating blood glucose levels, improving insulin sensitivity, and mitigating diabetes-related complications. The medicinal plants discussed in this review have demonstrated significant anti-diabetic effects through various mechanisms, including insulin mimetic activity, enhancement of insulin secretion, and inhibition of glucose absorption.

These findings suggest that medicinal plants may offer a natural, cost-effective, and relatively safe approach for managing diabetes. Furthermore, the anti-diabetic properties of medicinal plants may provide a valuable adjunct or alternative to conventional treatments, particularly for individuals with Type 2 diabetes who may not respond adequately to existing therapies. However, further research is needed to fully elucidate the anti-diabetic mechanisms of medicinal plants and to establish their safety and efficacy in human clinical trials.

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