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Herbal antidiabetics: An evidence based review of medicinal plants used in type 2 diabetes

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Abstract
Diabetes mellitus, especially type 2 diabetes mellitus, is a major global health concern. Many antidiabetic drugs are widely used, but they have limitations such as side effects and high cost. As a result herbal alternatives are being explored. Medicinal plants are being used in traditional medicine systems from ancient times. They offer promising therapeutic response due to their diverse phytochemical constituents and multi-targeted mechanism of action. This review summarizes evidences on selected herbal antidiabetic agents including *Trigonella foenum-graecum (fenugreek), Momordica charantia (bitter gourd), Cinnamomum (cinnamon), Gymnema sylvestre (gurmar), Ocimum sanctum (tulsi), Allium sativum (garlic), and Aloevera.* These plants have demonstrated beneficial effects by stimulating insulin secretion, enhancing insulin sensitivity, improving lipid profiles, and also providing antioxidant protection. Experimental and clinical studies support their role in lowering fasting blood glucose, and lipid levels, with some effects comparable to standard antidiabetic drugs such as glibenclamide. Despite the encouraging results, challenges remain such as standardization, large-scale clinical validation, and safety assurance. Future research including clinical trials and mechanistic studies can be essential for the translation of these herbal antidiabetics into modern evidence-based treatment for diabetes.

Keywords: Type 2 diabetes mellitus, herbal medicine, antidiabetic plants, phytochemicals, insulin sensitivity

Introduction
Diabetes mellitus, particularly type 2 diabetes mellitus, is one of the most challenging chronic metabolic disorders of the 21st century [1]. It is characterized by hyperglycemia which results from improper insulin secretion, insulin resistance, or even due to both [2]. Diabetes as a global burden is being steadily increasing as the international diabetes federation (IDF) has reported that over 537 million adults were having diabetes in 2021, and this number is projected to rise to 643 million by 2030 [3]. India is often referred to as "diabetes capital of the world" as it makes up a significant proportion of these cases, due to which it creates both medical and economic challenges for patients and healthcare systems [4]. Despite the availability of several classes of synthetic antidiabetic drugs such as sulfonylureas, biguanides, thiazolidinedione, and DPP-4 inhibitors, they fail to reverse the course of its complications completely and further worsen it by the fact that they also demonstrate prominent side effects. This forms the main force for discovering alternative sources of antidiabetic agents. Despite the significant progress made in the treatment of diabetes using synthetic antidiabetic agents, Several disadvantages have been reported related to its use, including drug resistance, adverse effects, and even toxicity [5]. For example, sulfonylureas lose their effectiveness after 6 years of treatment in approximately 44% of patients, whereas glucose-lowering drugs are reported to be not able to control hyperlipidemia [6]. Due to the several limitations associated with the use of existing synthetic antidiabetic drugs, the search for newer antidiabetic drugs from natural source continues [7].
Herbal medicines have been used from ancient times in traditional medicine systems such as Ayurveda, Unani, and Traditional Chinese medicine system for the management of diabetes [8]. The world health organizer (WHO) has listed a total of 21,000 plants, which are used for medicinal purposes around the world. Among them, more than 400 plants are available for the treatment of diabetes [9]. Plants are rich sources of bioactive compounds like alkaloids, flavonoids, terpenoids, saponins, coumarins, and polyphenols, which are responsible for its antidiabetic properties [10]. Synthetic drugs only show single target and thus herbal extracts differ from them as they often exert their effects through multiple mechanisms such as stimulating insulin secretion, enhancing insulin sensitivity, delaying carbohydrate absorption, reducing oxidative stress, and protecting pancreatic beta-cells [43, 44].

This multi-targeted approach of herbal extracts makes them more valuable according to the complex pathophysiology of T2DM.

Over the past two decades, scientific validation of antidiabetic plants has increased substantially. Experimental studies in animal models and *in vitro* assays have made potential mechanisms of action, while human clinical trials have provided evidence for efficacy in improving glycemic control and lipid metabolism. Commonly studied plants such as *Trigonella foenum-graecum (fenugreek), Momordica charantia (bitter gourd), Cinnamomum zeylancium (cinnamon), Gymnema sylvestre (gurmar), Ocimum sanctum (tulsi), Allium sativum (garlic), and Aloevera* have shown significant hypoglycemic, antioxidant, and lipid lowering properties [11]. However, despite the encouraging results of these herbal extracts, still several challenges remain. Challenges like variability in plant species, extraction methods, dosage forms, and study designs make it difficult to standardize and compare outcomes across studies. Also careful evaluation is required for concerns regarding long-term safety [39, 40].

Given this background, this review aims to provide an overview of selected medicinal plants with reported antidiabetic potential by giving focus on summarizing their phytochemical constituents, mechanism of action, and evidence from experimental and clinical studies. By highlighting both strengths and limitations in the current review, this review also seeks to identify gaps in knowledge and future directions for research. Ultimately, understanding the scientific basis of these herbal agents may facilitate their integration into modern diabetes management and contribute to the development of novel therapeutic strategies. We performed a comprehensive review using electronic databases including Google Scholar and PubMed to find the relevant articles in English using keywords like ‘ herbal antidiabetics’, ‘medicinal plants’, and ‘ type 2 diabetes’. Both original research articles and review papers published between 2000 and 2024 were retrieved and reported in this review.

Pathophysiology of type 2 diabetes mellitus

Type 2 diabetes mellitus is a chronic metabolic disorder which is characterized by hyperglycemia which occurs due a combination of insulin resistance, beta-cell dysfunction, and increased hepatic glucose production (2). Type 2 diabetes mellitus differ from type 1 diabetes as type 1 diabetes is primarily autoimmune whereas type 2 diabetes develops gradually as a result of unhealthy lifestyle, obesity or even due to genetic [12].

Insulin Resistance

The main cause for T2DM is insulin resistance, in this the tissues with insulin receptor such as adipose tissue, skeletal muscles and the liver becomes resistant to insulin and shows reduced responsiveness to insulin. In skeletal muscle, the diminished insulin stimulated glucose uptake results from impaired translocation of the glucose transporter GLUT4 to the cell membrane. In adipose tissue, resistance to insulin promotes lipolysis, which leads to the increase in circulating free fatty acids, then the higher level of circulating free fatty acids directly affect both liver and muscle metabolism, further exacerbating insulin resistance in these tissues and contributing to lipotoxicity-induced beta-cell dysfunction. In the liver, normal insulin-mediated suppression of gluconeogenesis is impaired which leads to excessive hepatic glucose output and fasting hyperglycemia [13].

Beta-Cell Dysfunction

Dysfunction of pancreatic beta-cells also plays a role in T2DM, as it reduces the secretion of insulin. Initially beta-cells are responsible for the production of insulin, but glucotoxicity, lipotoxicity, induce metabolic and oxidative stress that leads to beta-cell damage and loss of their function. This reduction in the secretion of insulin worsens hyperglycemia [14].

Oxidative stress and inflammation

Chronic hyperglycemia in T2DM is also linked to oxidative stress and inflammation. Excess glucose and free fatty acids (hyperglycemia) may stimulate increase in generation of reactive oxygen species (ROS), which damages beta-cells, impairs insulin signaling, and also stimulates the production of inflammatory cytokines. These inflammatory cytokines further enhance insulin resistance. This does not only contribute to the worsening of glycemic control but also to long-term complications including nephropathy, neuropathy, retinopathy, and cardiovascular disease [15].

Thus, the pathophysiology of T2DM involves insulin resistance, beta-cell dysfunction, and oxidative stress. Given this multifactorial origin, treatment strategies that provide multiple pathways simultaneously are likely to be more effective. This provides a strong base for exploring HERBAL MEDICINES, as they often contain a wide range of varieties of phytochemicals which are capable of acting through several mechanisms such as improving insulin sensitivity, stimulating insulin secretion, and also providing antioxidant protection.

Herbal antidiabetics: plants and evidence

Fenugreek (trigonella foenum-graecum)

Fenugreek is a widely used medicinal plant in traditional medicine, which has gained a significant attention for its antidiabetic properties. The seeds, in particular, they are rich in bioactive compounds such as 4-hydroxyisoleucine, trigonelline, diosgenin, and galactomannan fiber, these bioactive compounds contribute to the therapeutic potential of fenugreek. According to a recent review, fenugreek shows its antidiabetic property through various mechanisms: stimulation of insulin secretion, enhancement of insulin sensitivity, inhibition of carbohydrate metabolizing enzymes, antioxidant activity, and protection of pancreatic beta-cells [16]. These multiple mechanisms of fenugreek makes it a promising herbal antidiabetic for managing T2DM. Clinical studies further support the antidiabetic activity of fenugreek. A pilot study that was conducted evaluated the effect of fenugreek seed powder on postprandial glucose levels in 166 type 2 diabetic patients. Participants were divided into placebo, 2.5g, and 5g treatment groups. Results came out that the 5g dose significantly reduced postprandial blood glucose levels by approximately 41 mg/dl compared to baseline, whereas the 2.5g dose showed only mild effects [17]. This study suggests that fenugreek is effective in human populations, with a dose dependent response. The glucose-lowering action was due to the seeds high soluble fiber content, which shows gastric emptying and reduces glucose absorption, as well as it also improves insulin sensitivity. Experimental evidence from animal studies also supports fenugreeks antidiabetic role. In a study using streptozotocin-induced diabetic rats, administration of fenugreek seed extract significantly lowered total cholesterol levels and preserved pancreatic beta-cell architecture [18].

These studies highlights fenugreeks antioxidant and beta-cell protective properties, which makes fenugreeks potential as both an alternate to conventional therapies and a source for novel drug discovery and both clinical and preclinical data strongly support fenugreek as an effective antidiabetic agent. Overall, strong evidence of the antidiabetic effect of fenugreek was found, but the underlying molecular mechanism of fenugreek extracts or isolated components needs more investigation. Furthermore, the optimal dose and treatment duration in clinical trials must be established in order to get a beneficial outcome from fenugreek [16].

Bitter gourd (momordica charantia)

Bitter gourd, is also known as bitter melon or karela, it has been used in traditional medicine across Asia, England, Sri Lanka and Africa from a long time for its hypoglycemic properties [21]. Modern studies have provided scientific support for its antidiabetic properties by identifying various bioactive compounds in the seed and fruits of bitter gourd, such as saponins, polypeptides, conjugated linolenic acids, and triterpenes. These phytochemical constituents of bitter gourd contribute to its diverse mechanisms of action against type 2 diabetes mellitus [22]. An animal study was conducted in db/db mice, which is a well-established model of insulin resistance, it was evaluated for the antidiabetic potential of different parts of bitter gourd fruit, including whole fruit powder, saponin fraction, lipid fraction, and hydrophilic residue. After 5 weeks of treatment, mice receiving the lipid and saponin fraction demonstrated significant improvement as compared to controls. Specifically treated groups showed reduced body weight gain, lower glycated hemoglobin (HBA1c) levels, and decreased lipid peroxidation in adipose tissue. Both fractions inhibited protein tyrosine phosphatase 1B (PTP1B) activity in skeletal muscle, an enzyme which is known for regulating the insulin signaling negatively. By reducing PTP1B activity, bitter gourd improves insulin sensitivity and glucose regulation [20]. Further *in vitro* investigations also support the findings of antidiabetic activity of bitter gourd. A study of isolating polypeptide-K and seed oil from bitter gourd seeds showed potent inhibition of key carbohydrate-hydrolyzing enzymes. At 2 mg/mL, polypeptide-K inhibited a-glucosidase activity by 79% and a-amylase by 35%, while seed oil inhibited the same enzymes by 53% and 38% respectively. Both parts also exhibited strong antioxidant activity (80-85%), providing a protective effect against oxidative stress and pancreatic beta-cell damage [21].

These animal and *in vitro* studies provide evidence that bitter gourd exerts significant antidiabetic effect by improving insulin sensitivity, enzyme inhibition, and antioxidant action [23]. The results of these experiments validate its traditional use and highlight its potential as an alternative for conventional medicine and a source for novel antidiabetic agent.

Cinnamon (cinnamonum cassia & c.zeylancium)

Cinnamon is derived from the bark of trees belonging to the Cinnamomum genus, which is one of the most widely, consumed species worldwide and has been used in traditional medicine from a long time for its medicinal properties [24]. Cinnamon has numerous health benefits, but it has attracted significant attention for its antidiabetic properties [26]. Cinnamon has phytochemical constituents including cinnamic acid, cinnamate, cinnamaldehyde, eugenol, and procyanidins, along with some other essential oils and tannins, which all together contribute to its therapeutic properties [24]. A recent review highlighted cinnamons ability to lower blood glucose by multiple mechanisms, such as stimulation of insulin secretion, enhancement of insulin receptor signaling, increasing GLUT4 expression, and inhibition of carbohydrate-digesting enzymes such as a-glycosidase [27]. Clinical trials further support the antidiabetic property of cinnamon, with doses ranging from 0.5-2 g/day of cinnamon powder which showed reduction in fasting blood glucose (FBG), glycated hemoglobin (HbA1c), and improved lipid profiles in patients with Type 2 Diabetes Mellitus [24]. Experimental studies also provide more explanation for the biochemical mechanisms. In this investigation methanol extracts of Cinnamomum zeylancium bark were tested for their ability to inhibit a-glucosidase both *in vitro* and *in vivo*. The extract showed strong inhibition of a-glucosidase activity, with IC50 values of 5.83 ug/ml for yeast enzyme and 670 ug/ml for rat intestinal enzyme. In streptozotocin-induced diabetic rats, administration of 300-600 mg/kg cinnamon extract significantly suppressed postprandial glucose rise followed by maltose and sucrose, reducing glucose spikes by 78.2% and 52% respectively. However no effect was shown when glucose was administered directly, confirming that the extract acts by slowing carbohydrate digestion and not by directly lowering the circulating glucose [25]. Both clinical and experimental evidence confirm and support cinnamon's hypoglycemic activity by enhancement of insulin sensitivity, receptor signaling, and inhibition of carbohydrate breakdown. These evidences validate its use as antidiabetic agent in traditional medicine and suggest its potential as an alternate or complementary therapy for conventional medicament. Further large scale trials are needed to standardize dosage and confirm long-term safety.

Gymnema sylvestre

Gymnema sylvestre is widely known as GURMAR or SUGAR DESTROYER, it is a medicinal plant which has been used in ayurvedic practice from a long time for its antidiabetic properties [30]. The phytochemical constituents in Gymnema sylvestre which contribute to its therapeutic activity are gymnemic acids, gymnemosides, and other saponins that exert multiple actions on glucose and lipid metabolism. Traditionally the herb has been used to suppress sugar cravings, and modern studies suggest that its extract reduces intestinal glucose absorption and stimulate pancreatic insulin secretion [31]. Furthermore, review studies evidence show's its potential to regenerate pancreatic beta-cell, which is a great mechanism of action of Gymnema sylvestre given the complex pathophysiology of T2DM [28]. An experimental study in alloxan-induced diabetic Wistar rats showed the potent antidiabetic and hypolipidemic activity of aq. Gymnema sylvestre leaf extract. It was administered orally for 30 days at doses of 400-800 mg/kg, the extract produced a dose-dependent fall in blood glucose, with a maximum reduction of nearly 70% at the highest dose. In addition, the treatment significantly lowered total cholesterol by 46% and triglycerides by 50%, while increasing HDL cholesterol by 30%. These effects were comparable to those observed with glibenclamide, which is a standard antidiabetic drug, suggesting that Gymnema is capable of providing clinically meaningful glycemic and lipid regulation [29]. Both the review and experiment based evidence supports these findings that Gymnema sylvestre is an effective antidiabetic agent due to its multiple mechanisms which include beta-cell regeneration, enhancement of insulin secretion, inhibition of glucose

absorption, improvement of lipid metabolism, and antioxidant protection. These findings also validate its potential as a complementary therapy and source for novel antidiabetic agents.

Tulsi (Ocimum Sanctum Linn.)

Tulsi (Ocimum sanctum linn.), which is commonly known as the 'incomparable one' (34), has been used in traditional medicine from a long time for its therapeutic potential, and modern researches also validates its role as a promising herbal antidiabetic agent [33].

Experimental studies in alloxan-induced diabetic rats have showed that lyophilized tulsi leaf powder significantly lowers fasting blood glucose and glycosylated hemoglobin (HbA1c) levels, while it also improved body weight and restored serum insulin levels. LTLP supplementation reversed diabetes-associated abnormalities in biochemical markers such as urea, creatinine, protein, albumin, and liver enzymes (SGPT, SGOT, ALT, AST, ALP), which indicated the protective effects of tulsi on renal and hepatic functions. Moreover administration of tulsi also improved lipid profiles by reducing the total cholesterol, triglycerides, LDL-C, VLDL-C, and phospholipids, while also elevating HDL-C, thereby improving diabetic dyslipidemia. Importantly, LTLP enhanced antioxidant defenses, by increasing the activity of superoxide dismutase, catalases, and glutathione alongside by reducing malondialdehyde, which confirmed its role in counteracting oxidative stress- which is a key contributor to diabetic complications. These effects of tulsi were found to be comparable to glibenclamide, which is a standard antidiabetic drug, suggesting that tulsi may be able to provide effective yet safer glycemic control than conventional drugs. The phytochemical constituents in tulsi which are responsible for these therapeutic effect of tulsi such as hypoglycemic, antidyslipidemic, and antioxidant actions are eugenol, ursolic acid, apigenin, luteolin, orientin, vicenin, and linolenic acid [32]. A review-based evidence further supports the antidiabetic properties of tulsi, by showing that different tulsi extracts stimulate insulin secretion from pancreatic beta-cells, increase liver glycogen storage, and normalize liver enzyme activity in diabetic models. Furthermore, methanolic tulsi extracts demonstrated antidiabetic activity comparable to glibenclamide [33].

Both experimental and review data validates tulsi's multifaceted antidiabetic properties, by antioxidant, hepatoprotective, and lipid lowering mechanisms, Thus tulsi can be a potent natural candidate for managing diabetes and its complications, but further clinical evaluations for isolating active principles and standardize formulations are needed [32,35].

Garlic (*Allium sativum*)

Garlic (*Allium sativum*), is one of the oldest known medicinal plant which has been demonstrated to exhibit anti-diabetic properties. [38]. Experimental studies on alloxan-induced diabetic rats have shown that when aq. Garlic extracts were administered over several weeks, it produced significant hypoglycemic and hypolipidemic effects in a dose-dependent manner. At higher doses that is 300 mg/kg, garlic extract reduced fasting blood glucose levels by nearly 80%, an effect comparable to the standard antidiabetic drug glibenclamide. In addition to lowering blood sugar, garlic extract also decreased serum cholesterol and triglycerides, highlighting its dual role in glycemic and lipid regulation [36]. A review based evidence further supports these findings, indicating that garlic oil and its constituents- particularly, allicin and S-allyl cysteine sulfoxide (alliin)- exerts the hypoglycemic effects similar to glibenclamide by increasing pancreatic beta-cell insulin secretion, promoting the release of bound insulin, and also enhancing the insulin sensitivity. The antioxidant property of garlic is largely due to its sulfer-containing compounds, which protects the pancreatic tissue from oxidative damage and reduces complications associated with chronic hyperglycemia.

Animal studies in both alloxan- and streptozotocin-induced models consistently showed reductions in serum glucose levels by garlic treatment [37]. The multiple mechanism of action of garlic including its ability to decrease blood glucose level by preventing the insulin activation caused by liver, enhancing the secretion of insulin from pancreatic beta cells, isolation of insulin from the bonded forms, and increasing the cell sensitivity to insulin makes it an effective agent in diabetes care. Moreover, its cardioprotective and hepatoprotective effects further enhance its therapeutic activity [39].

Collectively, both experimental and review evidence shows garlic's potential as an effective herbal antidiabetic agent. However, further clinical trials and standardization of formulations are necessary to establish optimal dosing, efficacy, and long-term safety for integration into diabetes management therepy.

Aloe Vera (aloe barbadensis mill.)

Aloe vera is a succulent plant which is popularly known for its multiple therapeutic properties, and it has garnered great attention in traditional medicine for the treatment of many diseases including diabetes management. Aloe Vera shows its antioxidant, anti-inflammatory and hypoglycemic effect as it is rich in polysaccharides (acemannan, glucomannan, mannose), anthraquinones (aloin, barbaloin), phenolics, flavonoids, vitamins (A, C, E, B-complex), minerals (calcium, magnesium, zinc, selenium, iron), and enzymes (amylase, catalases, superoxide dismutase) [41]. Experimental studies on alloxan-induced diabetic rats revealed that Aloe vera gel 300 mg/kg significantly lowered fasting blood glucose by 40-65% over 21 days, it also improved lipid profiles by reducing the total cholesterol and triglycerides, and elevated HDL by upto 160%. It also restored renal function by lowering elevated urea and creatinine levels and promoted histopathological recovery of pancreatic beta-cells and kidney tissue, which shows that it has protective and regenerative potential. When combined with metformin, Aloe vera enhanced HDL levels further, proving it can be valued as an adjunct therapy [40]. Further, review based evidence supports these findings, showing that anthraquinones in Aloe vera improves glucose tolerance, enhances insulin sensitivity by increasing the expression of insulin receptor substrate-1 (IRS-1) and P1K pathways, and it also stimulates antioxidant defenses by increasing glutathione and enzymatic activity [40]. Clinical studies also report that Aloe vera gel and supplements also lowered the fasting blood glucose, HbA1c, total cholesterol, and LDL levels significantly ($p = 0.036$, $p = 0.036$, $p = 0.006$, and $p = 0.004$, respectively) without any significant effects on the other blood lipid levels and liver/kidney function tests ($p > 0.05$). No adverse effects were reported. The results suggest that aloe gel may be a safe anti-hyperglycemic and anti-hypercholesterolemic agent for hyperlipidemic type 2 diabetic patients. Further supporting glycemic control [42]. Collectively, experimental and clinical evidence shows that Aloe vera imparts its beneficial effects on hyperglycemia and

hyperlipidemia by increasing insulin secretion, inflammation, beta-cell protection, antioxidant defense, lipid regulation, and insulin signaling enhancement. As a safe, affordable, and nutrient-rich herbal therapy, Aloe vera can be an effective herbal antidiabetic agent but further standardized clinical trials are required to optimize formulations and dosage [43].

Plant	Part used	Extract type	Study model	Dose and duration	Main findings	Mechanism of action
Fenugreek	Seeds	Aqueous/ ethanolic	Alloxan-induced diabetic rats	2 g/kg for 21 days	↓ Blood glucose, ↓ HbA1c, improved lipid profile(16)	Stimulates insulin secretion, delays gastric emptying, inhibits glucose absorption
Bitter Gourd	Whole fruit	Aqueous/ ethanolic	Db/db mice	150 mg/kg for 5 weeks	↓ glucose, ↓ HbA1c, ↓ oxidative stress, improved insulin sensitivity(20)	PTP1B inhibition, GLUT4 recruitment, antioxidant effect, enzyme inhibition
Cinnamon	Bark	Methanol extract	Streptozotocin-induced diabetic rats	100-300 mg/kg body wt. given orally. Single dose. Glucose measured upto 90 min	↓ hyperglycemia with maltose (78.2%) and sucrose (52%), effect comparable to acarbose (25)	reversible inhibition of α-glucosidase enzyme → delayed carbohydrate digestion and reduced glucose absorption
Gymnema sylvestre	Leaves	Aqueous extract	Alloxan-induced diabetic rats	400,600,800 mg/kg, once daily for 30 days	Significant ↓ fasting blood glucose (up to 69% reduction at 800 mg/kg on day 30); ↓ TC (46%), ↓ TG (50%), ↑ HDL-C (30%) (29)	enhance activity of glucose-utilizing enzymes, regenerate pancreatic β-cells, ↑ insulin secretion, improve lipid metabolism
Tulsi	Leaves	Aqueous extract	Alloxan-induced diabetic rats (Wistar rats)	50 and 100 mg/kg, orally, 28 days	↓ Fasting blood glucose, ↓ HbA1c, ↓ urea & creatinine, ↑ insulin levels, improved lipid profile, restored liver enzymes, ↑ body weight, enhanced antioxidant enzymes (32)	Possible regeneration of pancreatic β-cells, improved insulin secretion, antioxidant defense, lipid-lowering effect, protection of renal
Garlic	Bulb	Aqueous extract	Alloxan-induced diabetic albino rat	200, 250, 300 mg/kg for 6 weeks	↓ fasting blood glucose (70-80% reduction at 300 mg/kg); ↓ total serum lipids (up to 39.5%); ↓ total cholesterol (up to 39.8%); effects comparable to glibenclamide(36)	↑ pancreatic insulin secretion, antioxidant effect, loweres total serum cholesterol, and blood glucose levels
Aloe vera	Leaf gel	Fresh gel	Alloxan-induced diabetic rats	300 mg/kg aloe vera and 2 mg/kg metformin or combination, orally, for 21 weeks	Aloe vera ↓ fasting blood glucose by 40.5%, 47.6%, 65.5% at days 7, 14, 21 respectively; improved HDL (↑160%); ↓ total cholesterol (42.3%); improved renal function (↓ serum urea 53.2%); combination with metformin gave stronger effects on HDL (40)	Regeneration of pancreatic β-cells, improved insulin secretion, antioxidant effect, hypolipidemic action; synergistic with metformin to protect renal & pancreatic tissues

Mechanism of action of herbal antidiabetics

Herbal antidiabetic agents act through a diverse range of mechanisms, they often target multiple metabolic pathways simultaneously. This multi-targeted approach of herbal antidiabetic agents makes them more particularly advantageous in the management of type 2 diabetes mellitus, where the disease occurs due to various factors such as impaired insulin secretion, insulin resistance, increased hepatic glucose output, and oxidative stress [14]. The key mechanism by these herbal antidiabetic agents involves stimulation of insulin secretion and regeneration of pancreatic beta-cells [44, 45, 46]. Compounds such as 4-hydroxyisoleucine from fenugreek and gymnemic acids from Gymnema sylvestre enhances insulin release, while tulsi has shown results in restoring serum insulin and promote beta-cell recovery in diabetic models [19, 35]. This action further directly improves glycemic control.

Equally important in this is the enhancement of insulin sensitivity [44, 45]. Bitter gourd exerts its effect by inhibiting protein tyrosine phosphatase 1B (PTP1B), which regulates insulin receptor signaling negatively, thereby improving glucose uptake [23]. Cinnamon and Aloe vera polysaccharides upregulates the insulin receptor substrate-1 (IRS-1) and also facilitates translocation of GLUT4 in skeletal muscles and adipose tissue, which further promotes peripheral glucose utilization [27, 43].

Another well documented mechanism of these herbal antidiabetic agents is the inhibition of carbohydrate-digesting enzymes [44, 45, 46]. Cinnamon bark extracts and bitter gourd seed polypeptide-K competes and successfully inhibits a-glucosidase and a-amylase, delaying intestinal carbohydrate digestion and absorption, which reduces postprandial glucose spikes [27, 23]. Fenugreek does the same action through its high soluble fiber content, which slows down the gastric emptying and glucose absorption [19].

Another mechanism that is observed is the modulation of hepatic glucose metabolism [44, 46]. Tulsi and cinnamon extracts reduce gluconeogenesis while also enhancing glycogen storage, leading to lower circulation of glucose levels [35, 27].

Additionally, one more mechanism that is observed by many herbal antidiabetic agents is that these plants also exert strong antioxidant and anti-inflammatory properties [47, 48]. Tulsi enhances superoxide dismutase and glutathione activity, Aloe vera provides a rich supply of flavonoids and vitamins, garlic's sulfur protect beta-cells, and cinnamon reduces lipid peroxidation [27]. These antioxidant defenses do not only improve glycemic control but also provides protection against long-term diabetic complications such as neuropathy,

nephropathy, and cardiovascular disease. Finally, several herbal antidiabetic agents demonstrated the mechanism of lowering lipid profile and cardioprotective effects [44]. Tulsi, garlic, and Aloe vera showed improvement in lipid profiles by lowering the total cholesterol, triglycerides, LDL, and VDL, while raising HDL, and thereby overall reducing diabetic dyslipidemia [35, 36, 43].

Taken altogether, the combined actions of these herbal antidiabetic agents - stimulating insulin secretion, improving insulin sensitivity, reducing carbohydrate absorption, modulating hepatic glucose metabolism, providing antioxidant protection, and regulating lipid profiles- highlights the unique advantage of herbal therapies in offering effective and synergistic management of diabetes [44, 45, 46].

Challenges, limitations and future directions

While herbal medicines show significant results and proves to be effective in the management of type 2 diabetes mellitus (T2DM), their use is accompanied by several challenges and limitations that affects its widespread clinical application. One of the major limitation is the lack of standardization in herbal preparations. The phytochemical constituents of plants can vary greatly depending upon its geographical location, difference in cultivation practices, harvesting time, and also different extraction method. Plants have been a good source of medicine for the treatment of various type of disease, still many plants and active compounds obtained from plants have not been well characterized. More investigations must be carried out to evaluate the exact mechanism of action of medicinal plants with antidiabetic and insulino mimetic activity. It is always believed that plant is safe, but so many plant materials are not safe for the human being, that's why toxicity study of these plants should also be elucidated before consumption of these plant materials. For example, the concentration of gymnemic acids in Gymnema sylvestre or cinnamaldehyde in cinnamon bark may differ in different samples which may lead to inconsistent pharmacological effects. Thus without standardize formulations, it is much difficult to ensure reproductible efficacy and safety [49, 52].

Another challenge that is faced is the limited number of high-quality clinical trials. Much of the evidence supporting the effectiveness of herbal antidiabetics is derived from *in vitro* or animal studies, with relatively fewer large-scale, randomized controlled trials in humans. The strength of current clinical evidence is limited due to small sample sizes and short treatment durations. As a result, the translation of effective and promising preclinical findings into clinical practice remains uncertain [49].

Dose optimization and safety concerns also remain a major challenge as even if many plants shows hypoglycemic activity, but the effective therapeutic dose for humans is unclear. Excessive consumption may lead to toxicity, as seen with high doses of cinnamon (due to coumarin content). Furthermore, potential herb-drug interactions are also a risk for patients who are already on standard antidiabetic medications. For example, combining herbal agents with sulfonylureas or insulin could cause severe hypoglycemia [49].

Lastly, the lack of mechanistic clarity for some herbs makes it difficult for drug discovery. While broad evidence is reported for its antioxidant and insulinotropic effects, specific molecular mechanisms remain poorly defined. This makes it difficult to integrate herbal medicines into modern treatments [50].

In summary, despite the strong traditional use and promising results of herbal antidiabetics, there are several limitations such as standardization, clinical validation, safety assurance and regulatory approval.

Addressing these challenges and limitations through researches, standardize formulations, and large scale clinical trials is required and can be essential for fully realizing the therapeutic potential of these herbal antidiabetic agents in the management of diabetes [51].

The increasing evidence on herbal antidiabetic agents proves their potential as complementary or alternative therapies for type 2 diabetes mellitus. However, to fully understand their therapeutic value, several future directions must be pursued. The future of herbal antidiabetics depends upon bridging traditional knowledge with modern scientific rigor. These plant extracts have gone through clinical trials and demonstrated good control of blood glucose levels by increasing serum insulin levels, enhancing tissue glucose uptake, and decreasing intestinal glucose uptake. Yet, medicinal plants are far from being able to replace conventional anti-diabetic drugs for patient management but they have the potential for further development if rigorous clinical trials on their mechanisms, delivery, and dose regimen are performed [53].

Conclusion: Diabetes mellitus, particularly type 2 diabetes, remains a major global health challenge with rising prevalence. While the conventional therapies are effective, some limitation's still remain such as their cost, side effects, and incomplete hypoglycemic control which has encouraged the search for safer and more holistic alternatives. Herbal medicines, which are being traditionally used from ancient times, have emerged as effective and promising agents, which is supported by increasing scientific evidence. This review highlights the antidiabetic potential of several well-studied herbs including, *Trigonella foenum-graecum (Fenugreek), Momordica charantia (Bitter Gourd), Cinnamomum spp. (Cinnamon), Gymnema sylvestre (Gurmar), Ocimum sanctum (Tulsi), Allium sativum (Garlic), and Aloe vera.* These plants act through various mechanisms such as stimulating insulin secretion, enhancing insulin sensitivity, inhibiting carbohydrate-digesting enzymes, modulating hepatic glucose metabolism, improving lipid profiles, and providing antioxidant protection. Collectively, they show a multi-targeted approach which makes them a perfect fit for the complex and multi-originated pathophysiology of diabetes. However, despite the encouraging results from preclinical and clinical studies supporting that they can be effective antidiabetic agents, challenges such as lack of standardization, safety concerns, limited large-scale human trials still remain and these challenges makes it difficult for the widespread use of herbal antidiabetic agents. Addressing these challenges will be essential for ensuring its consistent efficacy and safety. In conclusion, herbal antidiabetic agents, prove themselves to be a valuable adjunct in the management of diabetes, and also with the potential to complement existing therapies. Future research focused on standardized formulations, clinical evaluation, and isolation of bioactive compounds may pave the way for integrating these traditional remedies into modern treatment. By combining traditional knowledge with contemporary science, herbal medicines may contribute meaningfully to sustainable, effective and patient-centered diabetes management.

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