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Phytochemicals from anti-diabetic medicinal plants: A comprehensive review of glycemic control mechanisms

Md. Abu Sayem [1], Hafizul Islam [2], Ripon Chandra Shil [3], Md. Khaja Mohi Uddin [4], Amzad Hossen [5], Rashedur Rahman [6], Md. Mahmudul Hasan [7], Tanzila Akter [8], Afrin Sultana [9] and Sadia Islam [10,*]

[1] *Department of Haematology, Chittagong Medical College Hospital, Chittagong, Bangladesh.*
[2] *Department of Transfusion Services, The Ohio State University- Wexner Medical Center, USA.*
[3] *Department of Microbiology, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh.*
[4] *Department of Laboratory Medicine, Dhaka Medical College Hospital, Dhaka, Bangladesh.*
[5] *Department of Hematology & Clinical Pathology, National Institute of Burn and Plastic Surgery, Dhaka, Bangladesh.*
[6] *Department of Laboratory Medicine, Central Police Hospital, Dhaka, Bangladesh.*
[7] *Department of Pathology & Biochemistry, Mugda Medical College Hospital, Dhaka, Bangladesh.*
[8] *Department of Virology, National Institute of Laboratory Medicine & Referral Center, Dhaka, Bangladesh.*
[9] *Department of Laboratory Medicine, National Institute of Laboratory Medicine and Referral Center, Dhaka, Bangladesh.*
[10] *Department of Laboratory Medicine, Bangladesh Specialized Hospital PLC, Dhaka, Bangladesh.*

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Abstract

Diabetes mellitus, a growing global health concern, is typically managed through pharmaceutical interventions; however, plant-based therapies have emerged as a promising adjunct to conventional treatments. This paper examines the therapeutic potential of anti-diabetic plants, focusing on their mechanisms of action, including regulation of blood glucose, enhancement of insulin sensitivity, and the mitigation of diabetes-related complications such as oxidative stress and inflammation. Prominent plants, such as *Momordica charantia* (bitter melon), *Trigonella foenum-graecum* (fenugreek), and *Berberis aristata* (berberine), contain bioactive compounds that contribute to their anti-diabetic effects through diverse pathways, including insulin mimetic actions, AMPK activation, and β-cell regeneration. Additionally, many of these plants offer antioxidant and anti-inflammatory properties, providing a holistic approach to managing the disease and preventing long-term complications. Despite the promising findings from in vitro, in vivo, and clinical studies, the integration of plant-based therapies into mainstream diabetes care faces several challenges, including the lack of large-scale clinical trials, variability in standardization, concerns regarding bioavailability, and the potential for herb-drug interactions. This review underscores the need for more rigorous clinical trials to establish the efficacy, safety, and optimal dosing of these therapies. When standardized and integrated with conventional medical practices, plant-based therapies have the potential to be affordable, accessible, and effective adjuncts in diabetes management, particularly in low-resource settings where access to conventional medications may be limited. Furthermore, the synergistic combination of modern pharmacological treatments and plant-based therapies could offer a more personalized, comprehensive, and sustainable approach to diabetes care, improving patient outcomes worldwide. Future research should also focus on innovative drug delivery systems, such as nanotechnology, to enhance the bioavailability and efficacy of these plant-derived compounds, ensuring their safe and effective use in diabetes management.

Keywords: Anti-diabetic medicinal plants; Insulin sensitivity; Phytotherapy; Herb-drug interactions; Glycemic control

* Corresponding author: Sadia Islam

1. Introduction

Diabetes mellitus (DM) is a chronic, progressive, and complex metabolic disorder characterized by sustained hyperglycemia due to either impaired insulin secretion, reduced insulin sensitivity, or a combination of both. The condition is primarily classified into two major types: Type 1 diabetes (T1D) and Type 2 diabetes (T2D). T1D is an autoimmune disorder where the body's immune system destroys the insulin-producing β-cells in the pancreas, leading to an absolute insulin deficiency. This type typically manifests during childhood or adolescence but can occur at any age. In contrast, T2D is a multifactorial metabolic condition marked by insulin resistance and a progressive decline in insulin production. It is responsible for over 90% of diabetes cases globally and is closely associated with modifiable risk factors such as obesity, poor dietary patterns, physical inactivity, and smoking, as well as non-modifiable factors including age, genetic predisposition, and ethnicity[1,2].

The global burden of diabetes has increased dramatically in recent decades, making it a critical public health concern. According to the International Diabetes Federation (IDF), approximately 537 million adults (aged 20–79 years) were diagnosed with diabetes in 2021. This figure is projected to reach 643 million by 2030 and 783 million by 2045, with the steepest rises occurring in low- and middle-income countries (LMICs)[3]. These regions are undergoing rapid urbanization and lifestyle transitions, yet often lack adequate healthcare infrastructure to effectively manage chronic diseases. Beyond its rising prevalence, diabetes is a major contributor to a range of life-threatening complications, including cardiovascular disease, kidney failure, retinopathy, neuropathy, and lower-limb amputations, all of which contribute significantly to increased mortality, disability, and healthcare costs[4].

To mitigate the risks and complications associated with diabetes, current management strategies primarily aim to maintain optimal blood glucose levels, prevent long-term complications, and enhance overall quality of life. These strategies encompass a combination of lifestyle modifications and pharmacological interventions. Lifestyle changes, such as dietary adjustments, regular exercise, and weight management, form the cornerstone of diabetes management. These modifications help to improve insulin sensitivity, reduce excess body weight, and ultimately lower the risk of associated complications. However, lifestyle changes alone may not be sufficient for effective long-term control, which is why pharmacological treatments are also a crucial part of diabetes management[5]. Common pharmacological interventions include metformin (a biguanide), which is widely used due to its ability to improve insulin sensitivity and decrease hepatic glucose production, thereby lowering blood sugar levels. Sulfonylureas stimulate the pancreas to release more insulin, but they come with risks such as hypoglycemia and weight gain. Newer classes of medications, such as DPP-4 inhibitors, SGLT2 inhibitors, and GLP-1 receptor agonists, offer additional benefits like cardiovascular protection, weight loss, and better postprandial glucose regulation[6].

However, despite their widespread use and efficacy, these conventional treatments are not without limitations. Many of the synthetic medications used in diabetes management have associated side effects, which can include gastrointestinal discomfort, hypoglycemia, and weight gain, complicating long-term management. Additionally, the efficacy of these treatments can decline over time due to the progressive nature of β-cell dysfunction, particularly in patients with T2D[7]. As the disease advances, patients may require higher doses or combination therapies, yet the effectiveness of these drugs may diminish as pancreatic function continues to deteriorate. Another significant issue is the financial burden that these medications impose, especially for low- and middle-income populations, where the high cost of lifelong medication use can limit accessibility to necessary treatment. Furthermore, most conventional drugs focus primarily on glycemic control, without addressing the oxidative stress, chronic inflammation, and metabolic imbalances that play a critical role in the pathophysiology of diabetes[8].

Given these challenges, there has been growing interest in plant-based therapies as potential adjuncts or even alternatives to synthetic medications. This interest is based on the longstanding use of medicinal plants in traditional healthcare systems, such as Ayurveda, Traditional Chinese Medicine (TCM), Unani, and African ethnomedicine. For centuries, these traditional systems have relied on herbal remedies to manage hyperglycemia, improve digestion, and support overall metabolic health. Modern scientific research has increasingly validated many of these plant-based therapies, with numerous studies identifying bioactive phytochemicals that possess significant anti-diabetic properties. These plants are gaining scientific recognition for their ability to regulate blood sugar and offer complementary therapeutic effects for diabetes management[9].

Research has shown that plants with anti-diabetic activity often contain a variety of bioactive compounds such as flavonoids, alkaloids, terpenoids, saponins, and phenolic acids. These compounds exhibit multiple pharmacological actions that work synergistically to address various aspects of diabetes. Some phytochemicals stimulate insulin secretion from the pancreatic β-cells, while others enhance insulin sensitivity in tissues such as the liver, muscles, and adipose tissue, all of which help in better glucose utilization[10]. Certain phytochemicals also act by inhibiting carbohydrate-digesting enzymes like α-amylase and α-glucosidase, which can slow the absorption of glucose, thereby lowering postprandial blood sugar levels. Moreover, some bioactive compounds promote glucose uptake in peripheral tissues and facilitate glycogen storage, both of which help in managing blood glucose levels[11]. Additionally, many of these compounds possess antioxidant and anti-inflammatory properties, reducing the oxidative stress and inflammation that contribute to the development and progression of diabetes[12].

What sets plant-based therapies apart is their ability to offer multi-targeted actions. Unlike conventional drugs that may target a single pathway or mechanism, many phytochemicals from medicinal plants can address multiple facets of diabetes at once—such as improving insulin function, reducing oxidative stress, and mitigating inflammation[13]. This makes them potentially more effective in providing a holistic approach to diabetes management. Additionally, plant-based treatments are generally associated with fewer side effects and lower toxicity compared to synthetic drugs. This not only makes them safer but also more accessible and affordable, especially in areas where modern pharmaceuticals may be cost-prohibitive. These qualities make plant-based therapies an appealing option, particularly in low-resource settings where they can be more easily sourced and implemented in the management of diabetes[14].

This paper aims to review the phytochemicals from anti-diabetic medicinal plants and their mechanisms in glycemic control, highlighting their therapeutic potential as complementary or alternative treatments for diabetes. It compares plant-based remedies to conventional therapies and explores future directions for their integration into diabetes management.

2. Mechanisms of anti-diabetic action in medicinal plants

Medicinal plants have long been utilized in traditional medicine for the management of diabetes, and recent scientific studies have substantiated their anti-diabetic properties. These plants exert their therapeutic effects through various pharmacological mechanisms that influence glucose metabolism, insulin secretion and sensitivity, oxidative stress, inflammation, and gut microbiota. The following mechanisms highlight the diverse roles medicinal plants play in controlling blood glucose levels and improving overall metabolic health.

2.1. Stimulating Insulin Secretion

One of the well-known mechanisms of action in anti-diabetic medicinal plants is the stimulation of insulin secretion from pancreatic β-cells. *Gymnema sylvestre*, commonly referred to as the "sugar destroyer," has been extensively studied for its ability to enhance insulin secretion. Active compounds in *Gymnema sylvestre*, particularly gymnemic acids, promote insulin release from β-cells in the pancreas and assist in the regeneration of damaged β-cells[15]. This is particularly beneficial in Type 2 diabetes, where insulin secretion is often reduced as a result of β-cell dysfunction. In addition to stimulating insulin secretion, *Gymnema sylvestre* helps lower blood glucose levels by inhibiting the absorption of glucose from the intestines, thus contributing to better overall glycemic control[16].

Another plant that has shown similar effects is *Allium sativum* (garlic), which has been demonstrated to promote insulin secretion and enhance the sensitivity of insulin receptors. This dual effect makes it a promising candidate for diabetes management, particularly in cases of insulin resistance and β-cell dysfunction[17].

2.2. Enhancing Insulin Sensitivity

Cinnamomum verum (cinnamon) is a popular spice that has been shown to improve insulin sensitivity. Cinnamon contains bioactive compounds such as cinnamaldehyde, proanthocyanidins, and flavonoids, which have been demonstrated to activate insulin receptors and enhance insulin receptor signaling in peripheral tissues. This improves glucose uptake by muscle and fat cells, which helps reduce insulin resistance—a major pathophysiological feature of Type 2 diabetes. Research has suggested that cinnamon's action involves the phosphorylation of key proteins in the insulin signaling pathway, which aids in enhancing the action of insulin at the cellular level. Furthermore, cinnamon helps to regulate the hepatic glucose production, thus reducing blood glucose levels in the postprandial state[18].

Additionally, Berberine, an alkaloid found in several medicinal plants like *Berberis vulgaris*, has gained attention for its ability to improve insulin sensitivity. Berberine activates AMP-activated protein kinase (AMPK), a key regulator of cellular energy balance, which plays a critical role in increasing glucose uptake in skeletal muscle and enhancing insulin sensitivity[19].

2.3. Inhibiting α-Glucosidase and α-Amylase

Several medicinal plants exert anti-diabetic effects by inhibiting the digestive enzymes α-glucosidase and α-amylase, which are responsible for breaking down carbohydrates into simple sugars in the gastrointestinal tract. For example, *Salacia reticulata*, a traditional herb used in Ayurvedic medicine, has been found to inhibit both α-amylase and α-glucosidase enzymes, thereby delaying carbohydrate digestion and reducing postprandial blood sugar spikes[20]. This mechanism is beneficial for Type 2 diabetes patients, as it helps regulate the absorption of glucose from the gut, leading to more stable blood glucose levels after meals.

Other plants, such as *Phaseolus vulgaris* (white kidney bean), have shown similar effects. White kidney beans contain an inhibitor called phaseolamin, which acts to block α-amylase activity, reducing carbohydrate digestion and the resultant glucose spike[21].

2.4. Modulating Glucose Uptake

Momordica charantia (bitter melon) is widely recognized for its role in enhancing glucose uptake by peripheral tissues. The active compounds in bitter melon, such as charantin, polypeptides, and insulin-like proteins, mimic the effects of insulin by facilitating the uptake of glucose into cells, particularly muscle and adipose tissue. This is particularly useful for controlling elevated blood glucose levels in diabetic individuals, as it promotes the conversion of glucose to glycogen and enhances glucose metabolism[22].

Bitter melon also improves glucose tolerance by regulating enzymes involved in glucose metabolism, such as glucokinase and pyruvate kinase, which helps improve glycogen storage in the liver and reduces blood glucose concentrations. In addition to bitter melon, other plants like *Trigonella foenum-graecum* (fenugreek) have been shown to enhance glucose uptake and improve insulin sensitivity, further supporting their role in diabetes management[23].

2.5. Antioxidant and Anti-Inflammatory Effects

Chronic oxidative stress and inflammation play pivotal roles in the pathogenesis of diabetes and its complications, including insulin resistance and β-cell dysfunction. Several medicinal plants are rich in antioxidant and anti-inflammatory compounds, which contribute to their anti-diabetic effects[24].

Ocimum sanctum (holy basil)[25] and *Curcuma longa* (turmeric)[26] are well-documented for their potent antioxidant and anti-inflammatory activities. Holy basil contains eugenol, which exerts antioxidant effects and reduces inflammation by modulating key signaling pathways, including nuclear factor-kappa B (NF-kB). Similarly, curcumin, the active compound in turmeric, is a powerful antioxidant that reduces oxidative stress and modulates inflammatory cytokines. Curcumin's ability to influence the NF-kB pathway, which regulates immune responses, plays a critical role in reducing systemic inflammation associated with diabetes and its complications.

Both plants help mitigate oxidative damage, protect β-cells from apoptosis (cell death), and improve insulin sensitivity, thus contributing to better glycemic control. Additionally, they help prevent complications such as diabetic neuropathy and cardiovascular disease, which are exacerbated by chronic inflammation and oxidative stress.

2.6. Modulation of Gut Microbiota (Emerging Topic)

The human gut microbiota is increasingly recognized as a crucial factor in the regulation of glucose metabolism and insulin sensitivity. The gut microbiome influences metabolic processes through the production of short-chain fatty acids (SCFAs), regulation of inflammation, and interaction with various endocrine pathways[27].

Emerging research suggests that medicinal plants can modulate the gut microbiota, influencing the balance of beneficial and harmful bacteria in the intestines. For example, Ginseng and Berberine have been shown to alter the gut microbiome in ways that enhance insulin sensitivity and glucose metabolism. *Berberine*, in particular, promotes the growth of beneficial bacteria and suppresses the growth of pathogenic microorganisms. This results in a reduction in gut-derived endotoxins that contribute to systemic inflammation and insulin resistance.

Changes in gut microbiota can lead to increased SCFA production, which has been linked to improved insulin sensitivity and glucose tolerance. SCFAs, particularly butyrate, play an important role in maintaining the integrity of the gut barrier, reducing inflammation, and enhancing metabolic functions. These findings highlight the potential of targeting the gut microbiome as an innovative approach to diabetes management, and plant-based therapies may offer a promising solution in this area[27].

Table 1 Mechanisms of Anti-Diabetic Action in Medicinal Plants

Mechanism	Medicinal Plants Involved	Key Actions and Effects
Stimulating Insulin Secretion	*Gymnema sylvestre, Allium sativum* (Garlic)	- Promotes insulin release from β-cells in the pancreas. - Regenerates damaged β-cells. - Enhances insulin secretion.
Enhancing Insulin Sensitivity	*Cinnamomum verum* (Cinnamon), *Berberine* (Berberis vulgaris)	- Activates insulin receptors and enhances receptor signaling. - Reduces insulin resistance and improves glucose uptake.
Inhibiting α-Glucosidase & α-Amylase	*Salacia reticulata, Phaseolus vulgaris* (White Kidney Bean)	- Inhibits α-glucosidase and α-amylase enzymes. - Slows carbohydrate digestion and absorption. - Prevents postprandial hyperglycemia.
Modulating Glucose Uptake	*Momordica charantia* (Bitter Melon), *Trigonella foenum-graecum* (Fenugreek)	- Mimics insulin by facilitating glucose uptake into muscle and adipose tissue. - Enhances glucose conversion to glycogen.
Antioxidant & Anti-Inflammatory Effects	*Ocimum sanctum* (Holy Basil), *Curcuma longa* (Turmeric)	- Reduces oxidative stress and inflammation. - Protects β-cells from damage. - Improves insulin sensitivity.
Modulation of Gut Microbiota	*Ginseng, Berberine*	- Alters gut microbiome to enhance insulin sensitivity. - Increases production of beneficial SCFAs. - Reduces inflammation and insulin resistance.

3. Anti-Diabetic Medicinal Plants and Their Phytochemicals

This section provides a comprehensive review of several key medicinal plants known for their anti-diabetic properties, emphasizing their active phytochemicals, mechanisms of action, and supporting scientific evidence. These plants are widely recognized for their therapeutic potential in managing diabetes mellitus, particularly in improving glycemic control and promoting overall metabolic health. While some of these plants are well-established in traditional medicine, others offer promising new avenues for diabetes management based on emerging research.

3.1. *Momordica charantia* (Bitter Melon)

Bitter melon, or *Momordica charantia*, has long been used in traditional medicine across Asia, Africa, and the Caribbean. The plant contains bioactive compounds such as charantin, polypeptide-p, vicine, and alkaloids, which are responsible for its anti-diabetic properties. The key mechanism by which bitter melon exerts its effect is by mimicking insulin, which helps in promoting glucose uptake in peripheral tissues, thereby lowering blood sugar. Additionally, bitter melon facilitates the conversion of glucose into glycogen, contributing to improved blood glucose regulation. Studies show that bitter melon exhibits insulin-like activity through its polypeptides and charantin, making it a useful adjunct in managing diabetes. Research conducted in vitro has demonstrated the insulin-mimetic properties of bitter melon, while in vivo animal studies have shown that it effectively reduces blood glucose levels. Clinical trials have also supported its use, showing improved insulin sensitivity and reduced blood sugar in diabetic patients[27].

3.2. *Trigonella foenum-graecum* (Fenugreek)

Fenugreek (*Trigonella foenum-graecum*) is a widely used herb in traditional medicine, particularly in India and the Middle East. The plant is rich in compounds like 4-hydroxyisoleucine, saponins, and flavonoids, which contribute to its anti-diabetic effects. Fenugreek works primarily by stimulating insulin secretion and enhancing insulin sensitivity, which are critical processes in the management of diabetes. It also aids in glucose metabolism and enhances glycogen synthesis. The saponins found in fenugreek play a significant role in improving glucose absorption and activating insulin receptors, making it easier for cells to take up glucose. In vitro studies have shown that fenugreek enhances insulin secretion and glucose uptake, while in vivo research demonstrates its ability to reduce blood glucose and improve glycemic control in animal models. Clinical studies suggest that fenugreek supplementation can enhance insulin sensitivity and reduce blood sugar levels in diabetic individuals[28].

3.3. Gymnema sylvestre

Gymnema sylvestre, native to India and Africa, is a revered herb in Ayurvedic medicine. The active compounds in Gymnema, such as gymnemic acids, saponins, and flavonoids, are believed to have potent anti-diabetic effects. One of its primary mechanisms is stimulating insulin secretion and promoting the regeneration of β-cells, which are crucial for insulin production. Gymnema also reduces sugar absorption from the gastrointestinal tract, further contributing to its glucose-lowering effects. Moreover, it enhances glucose utilization by the body, which helps lower blood sugar levels. In vitro studies have shown that Gymnema promotes insulin secretion and β-cell regeneration. Animal studies further support these findings, showing improved glucose uptake and insulin sensitivity. Clinical trials have also reported significant reductions in blood sugar levels after Gymnema supplementation in diabetic patients[29].

3.4. *Ocimum sanctum* (Holy Basil)

Holy basil, or *Ocimum sanctum*, is another widely used medicinal herb in India and Southeast Asia, particularly in Ayurvedic medicine. This herb contains eugenol, ursolic acid, and various flavonoids, which contribute to its medicinal properties. Holy basil exerts its anti-diabetic effects through its powerful antioxidant and anti-inflammatory properties. It helps protect pancreatic β-cells from oxidative stress, which is critical for maintaining insulin production. Additionally, holy basil enhances insulin sensitivity and regulates glucose metabolism, offering a multifaceted approach to managing diabetes. In vitro studies have confirmed the herb's antioxidant and anti-inflammatory properties, while in vivo studies have demonstrated its ability to lower blood glucose levels and improve insulin sensitivity. Clinical trials have shown that holy basil supplementation can improve glycemic control and reduce oxidative stress in diabetic patients[30].

3.5. Berberis aristata

Berberis aristata, also known as Indian barberry, is native to the Himalayan region and widely used in traditional medicine in India. The plant contains berberine, a potent bioactive compound that plays a crucial role in its anti-diabetic effects. Berberine works by activating AMP-activated protein kinase (AMPK), a key regulator of energy metabolism. By activating AMPK, berberine increases insulin sensitivity, reduces hepatic glucose production, and improves lipid metabolism. In addition to its insulin-sensitizing properties, berberine also has anti-inflammatory effects, which help reduce the complications associated with diabetes. In vitro studies have shown that berberine activates AMPK and improves glucose uptake, while animal studies support its ability to lower blood glucose and lipid levels. Clinical trials in humans have also demonstrated that berberine supplementation can help manage blood glucose levels and improve insulin sensitivity[31].

3.6. *Cinnamomum verum* (Cinnamon)

Cinnamon, or *Cinnamomum verum*, is a well-known spice native to Sri Lanka, widely used both in culinary practices and traditional medicine. The active compounds in cinnamon, such as cinnamaldehyde, proanthocyanidins, and flavonoids, contribute to its anti-diabetic effects. Cinnamon enhances insulin receptor sensitivity, improving insulin signaling in the body. It also helps regulate hepatic glucose production, preventing excess glucose release from the liver. Additionally, cinnamon inhibits carbohydrate-digesting enzymes, slowing the absorption of glucose from the digestive tract. In vitro studies have shown that cinnamon increases insulin receptor sensitivity, while animal models confirm its ability to reduce blood glucose levels and improve insulin sensitivity. Clinical trials have demonstrated that cinnamon supplementation can significantly reduce fasting blood glucose levels and improve overall insulin sensitivity in individuals with type 2 diabetes[26].

3.7. *Curcuma longa* (Turmeric)

Turmeric, or *Curcuma longa*, is commonly used in India and Southeast Asia both as a spice and in traditional medicine. The active compound in turmeric, curcumin, along with other curcuminoids, is responsible for its potent medicinal properties. Curcumin exerts powerful antioxidant and anti-inflammatory effects, which are essential for managing diabetes-related oxidative stress and inflammation. Furthermore, curcumin improves insulin sensitivity and helps protect pancreatic β-cells, which are essential for insulin production. In vitro studies have shown that curcumin significantly reduces oxidative stress, while in vivo research has demonstrated its ability to improve glucose tolerance and insulin sensitivity in diabetic animal models. Clinical studies also suggest that curcumin supplementation can lead to improved glycemic control and reduced inflammation in individuals with diabetes[28].

3.8. Pterocarpus marsupium

Pterocarpus marsupium, known as the Indian Kino tree, is widely used in traditional Indian medicine to manage diabetes. The plant contains compounds like pterostilbene and flavonoids, which have been found to have anti-diabetic effects. Pterocarpus marsupium enhances insulin secretion and promotes the regeneration of β-cells, thereby improving insulin production. Additionally, it increases peripheral glucose uptake and reduces blood glucose levels by inhibiting gluconeogenesis in the liver. In vitro studies have shown that Pterocarpus marsupium enhances insulin secretion and glucose uptake, while animal models have demonstrated reduced blood glucose levels. Though clinical evidence is limited, early studies suggest that it may hold promise for managing diabetes in humans[29].

3.9. Salacia reticulata

Salacia reticulata, a plant native to India and Sri Lanka, has been used in Ayurvedic medicine for centuries to treat diabetes. The active compounds in Salacia reticulata, including salacinol and kotalanol, have potent inhibitory effects on carbohydrate-digesting enzymes such as α-glucosidase and α-amylase. By inhibiting these enzymes, Salacia reticulata delays the digestion and absorption of carbohydrates, thus reducing postprandial blood glucose spikes. In vitro studies have demonstrated that Salacia reticulata effectively inhibits α-glucosidase and α-amylase, while in vivo studies have shown that it can lower postprandial blood glucose levels. Some clinical trials also support its efficacy, suggesting that Salacia reticulata can help regulate blood glucose levels in diabetic individuals[22].

3.10. *Syzygium cumini* (Jamun)

Syzygium cumini, commonly known as Jamun, is native to the Indian subcontinent and Southeast Asia. The active compounds in Jamun, including eugenol, anthocyanins, and flavonoids, contribute to its anti-diabetic properties. Jamun enhances insulin secretion and improves glucose metabolism. It also exhibits potent antioxidant and anti-inflammatory effects, which help combat oxidative stress and inflammation commonly associated with diabetes. In vitro studies have shown that Jamun possesses insulin-mimetic and antioxidant properties, while animal studies have demonstrated its ability to reduce blood glucose and improve glycemic control. Clinical studies suggest that Jamun can help regulate blood sugar levels in diabetic patients[23].

3.11. Allium sativum (Garlic)

Garlic, or *Allium sativum*, is a widely used medicinal plant with a long history of use in Asia, Europe, and Africa. The active compounds in garlic, such as allicin and diallyl disulfide, play a crucial role in its anti-diabetic effects. Garlic stimulates insulin secretion, improves insulin sensitivity, and reduces oxidative stress, all of which contribute to better glycemic control. It also helps improve lipid profiles and reduce blood glucose levels. In vitro studies have demonstrated that garlic enhances insulin secretion and exhibits antioxidant activity. Animal models have shown that garlic supplementation can improve blood glucose and lipid levels, while clinical trials have indicated that it can reduce blood glucose levels and improve insulin sensitivity in diabetic patients[30].

3.12. Stereospermum personatum

Stereospermum personatum is native to India and is used in traditional medicine to treat various ailments, including diabetes. The plant contains triterpenoids, flavonoids, and alkaloids, which contribute to its hypoglycemic effects. It works by improving insulin sensitivity and increasing glucose uptake by peripheral tissues, which helps reduce blood glucose levels. In vitro studies have shown that *Stereospermum personatum* has the potential to enhance glucose uptake, while in vivo studies have demonstrated its ability to lower blood glucose levels in diabetic animal models. Although clinical evidence is limited, the plant shows promise as a potential anti-diabetic agent[32].

3.13. *Senna obtusifolia* (Senna)

Senna, or *Senna obtusifolia*, is widely used in Africa and Asia for its medicinal properties, particularly as a laxative. The active compounds in Senna, including sennosides, flavonoids, and anthraquinones, exhibit mild hypoglycemic effects. Senna may reduce blood sugar levels by improving gastrointestinal transit and gut health, which can indirectly influence glucose absorption and blood sugar regulation. In vitro studies have shown mild hypoglycemic effects, while in vivo research has demonstrated some reduction in blood glucose levels. Although clinical evidence is limited, Senna's role in gut health and digestion suggests potential benefits for managing diabetes[32].

3.14. *Amomum subulatum* (Black Cardamom)

Amomum subulatum, commonly known as Black Cardamom, is native to the Himalayan region and used in Ayurvedic medicine for treating various health conditions, including diabetes. The active compounds in Black Cardamom, such as essential oils, flavonoids, and terpenoids, help improve insulin secretion and sensitivity. It also reduces blood glucose by enhancing pancreatic β-cell function. Additionally, its antioxidant and anti-inflammatory properties support overall metabolic health. In vitro studies have shown that Black Cardamom can regulate insulin secretion, while animal studies have demonstrated improved glucose tolerance and insulin sensitivity. Early clinical studies suggest that Black Cardamom can help regulate blood glucose levels in diabetic patients[32].

3.15. *Moringa oleifera* (Moringa)

Moringa (*Moringa oleifera*), commonly known as the "drumstick tree," is native to South Asia and is widely used for its nutritional and medicinal benefits. The plant contains bioactive compounds like glucosinolates, flavonoids, polyphenols, and vitamins, all of which contribute to its anti-diabetic properties. Moringa is known to help lower blood sugar levels by enhancing insulin secretion and increasing insulin sensitivity. Additionally, it has antioxidant properties that help reduce oxidative stress, a common issue in diabetes. Moringa also inhibits glucose absorption in the intestines, preventing spikes in blood sugar levels after meals. In vitro studies have shown that Moringa extracts exhibit significant anti-diabetic effects, and in vivo animal studies have demonstrated its potential to lower blood glucose and improve insulin sensitivity. Clinical trials suggest that Moringa supplementation can lead to improved glycemic control and reduced blood sugar levels in diabetic individuals[33].

3.16. *Zingiber officinale* (Ginger)

Ginger (*Zingiber officinale*) is a widely known spice and medicinal plant that has been used for centuries to treat various health conditions, including diabetes. The active compounds in ginger, such as gingerol, shogaol, and paradol, have demonstrated significant anti-diabetic effects. Ginger primarily works by improving insulin sensitivity and reducing insulin resistance, a key factor in the development of type 2 diabetes. It also reduces oxidative stress and inflammation, both of which are often elevated in diabetic patients. Additionally, ginger helps regulate blood sugar by enhancing glucose uptake in tissues and inhibiting the activity of certain enzymes that break down carbohydrates. In vitro studies have shown that ginger reduces blood glucose levels, and animal studies have confirmed its ability to improve insulin sensitivity. Clinical trials have indicated that ginger supplementation can help reduce fasting blood glucose levels and improve overall glycemic control in people with type 2 diabetes[27].

3.17. *Ficus benghalensis* (Banyan Tree)

Ficus benghalensis, commonly known as the Banyan tree, is native to tropical regions of Asia. The plant is traditionally used in Ayurvedic medicine for treating various ailments, including diabetes. The active compounds in Ficus benghalensis, including flavonoids, tannins, and alkaloids, have shown potential in managing blood sugar levels. Ficus benghalensis exerts its anti-diabetic effects by stimulating insulin secretion from pancreatic β-cells and increasing the uptake of glucose by peripheral tissues. Additionally, it has anti-inflammatory and antioxidant properties that help mitigate the complications of diabetes. In vitro studies have demonstrated that extracts from the Banyan tree can help regulate glucose metabolism. Animal studies have also shown that Ficus benghalensis can lower blood glucose levels and improve insulin sensitivity. Though clinical evidence is limited, the plant's long-standing use in traditional medicine suggests it has potential for managing diabetes[33].

3.18. *Andrographis paniculata* (Andrographis)

Andrographis paniculata, commonly known as the "King of Bitters," is a herb native to South Asia and is widely used in traditional medicine for treating a variety of diseases, including diabetes. The active compounds in Andrographis, particularly andrographolides, have been shown to have strong anti-diabetic effects. Andrographis improves insulin sensitivity and reduces blood glucose levels by promoting the action of insulin in the body. It also has anti-inflammatory and antioxidant properties, which help reduce the oxidative stress and inflammation associated with diabetes. In vitro studies have shown that Andrographis paniculata improves glucose metabolism and insulin action. Animal studies further support these effects, demonstrating a reduction in blood glucose levels. Although clinical studies are limited, preliminary research suggests that Andrographis supplementation could be a beneficial adjunct in the management of diabetes[25].

Table 2 Summary of Anti-Diabetic Medicinal Plants and Their Active Compounds

Plant Name	Active Compounds	Mechanism of Action	Supporting Evidence
Momordica charantia (Bitter Melon)	Charantin, polypeptide-p, vicine, alkaloids	Mimics insulin, promotes glucose uptake, and facilitates glucose to glycogen conversion	In vitro, in vivo, and clinical studies demonstrate improved blood glucose regulation and insulin sensitivity.
Trigonella foenum-graecum (Fenugreek)	4-Hydroxyisoleucine, saponins, flavonoids	Stimulates insulin secretion, enhances insulin sensitivity, improves glucose metabolism	In vitro, in vivo, and clinical trials show improved insulin sensitivity and blood glucose control.
Gymnema sylvestre	Gymnemic acids, saponins, flavonoids	Stimulates insulin secretion, regenerates β-cells, reduces sugar absorption, improves glucose utilization	In vitro, animal studies, and clinical trials support its ability to reduce blood sugar and improve insulin sensitivity.
Ocimum sanctum (Holy Basil)	Eugenol, ursolic acid, flavonoids	Antioxidant, anti-inflammatory, protects β-cells, improves insulin sensitivity, regulates glucose metabolism	In vitro, in vivo, and clinical studies demonstrate lowered blood glucose levels and improved insulin sensitivity.
Berberis aristata	Berberine	Activates AMPK, increases insulin sensitivity, reduces hepatic glucose production, improves lipid metabolism	In vitro, animal studies, and clinical trials show improved glucose uptake and insulin sensitivity.
Cinnamomum verum (Cinnamon)	Cinnamaldehyde, proanthocyanidins, flavonoids	Enhances insulin receptor sensitivity, regulates hepatic glucose production, inhibits carbohydrate digestion	In vitro, animal studies, and clinical trials demonstrate improved insulin sensitivity and reduced blood glucose levels.
Curcuma longa (Turmeric)	Curcumin, curcuminoids	Antioxidant, anti-inflammatory, improves insulin sensitivity, protects β-cells	In vitro, in vivo, and clinical studies suggest improved glycemic control and reduced inflammation.
Pterocarpus marsupium	Pterostilbene, flavonoids	Enhances insulin secretion, promotes β-cell regeneration, reduces gluconeogenesis	In vitro, animal studies show improved blood glucose regulation and insulin secretion.
Salacia reticulata	Salacinol, kotalanol	Inhibits carbohydrate-digesting enzymes (α-glucosidase, α-amylase), delays carbohydrate absorption	In vitro, in vivo, and some clinical trials show reduced postprandial blood glucose levels.
Syzygium cumini (Jamun)	Eugenol, anthocyanins, flavonoids	Enhances insulin secretion, improves glucose metabolism, antioxidant and anti-inflammatory effects	In vitro, animal studies, and clinical trials show reduced blood glucose and improved glycemic control.
Allium sativum (Garlic)	Allicin, diallyl disulfide	Stimulates insulin secretion, improves insulin sensitivity, reduces oxidative stress	In vitro, animal studies, and clinical trials demonstrate reduced blood glucose levels and improved insulin sensitivity.
Stereospermum personatum	Triterpenoids, flavonoids, alkaloids	Improves insulin sensitivity, increases glucose uptake	In vitro and animal studies show potential for lowering blood glucose levels.
Senna obtusifolia (Senna)	Sennosides, flavonoids, anthraquinones	Improves gastrointestinal transit, indirectly regulates glucose absorption	In vitro and animal studies show mild hypoglycemic effects.

Amomum subulatum (Black Cardamom)	Essential oils, flavonoids, terpenoids	Enhances insulin secretion and sensitivity, reduces blood glucose, antioxidant and anti-inflammatory effects	In vitro and animal studies show improved insulin sensitivity and glucose tolerance.
Moringa oleifera (Moringa)	Glucosinolates, flavonoids, polyphenols, vitamins	Enhances insulin secretion, improves insulin sensitivity, inhibits glucose absorption	In vitro, animal studies, and clinical trials demonstrate improved glycemic control and reduced blood glucose.
Zingiber officinale (Ginger)	Gingerol, shogaol, paradol	Improves insulin sensitivity, reduces oxidative stress and inflammation, enhances glucose uptake	In vitro, animal studies, and clinical trials indicate reduced blood glucose and improved insulin sensitivity.
Ficus benghalensis (Banyan Tree)	Flavonoids, tannins, alkaloids	Stimulates insulin secretion, increases glucose uptake, anti-inflammatory and antioxidant effects	In vitro and animal studies suggest improved glucose metabolism and reduced blood glucose levels.
Andrographis paniculata (Andrographis)	Andrographolides	Improves insulin sensitivity, reduces oxidative stress and inflammation, enhances insulin action	In vitro, animal studies suggest reduced blood glucose and improved glucose metabolism.

4. Comparative analysis with conventional anti-diabetic drugs

Plant-based therapies and conventional anti-diabetic drugs such as metformin, sulfonylureas, and GLP-1 agonists provide distinct approaches for managing diabetes. While both can effectively regulate blood glucose levels, there are fundamental differences in their mechanisms of action, benefits, and challenges. Below is a detailed comparison between these two categories of treatment.

4.1. Conventional Anti-Diabetic Drugs

Metformin is one of the most commonly prescribed medications for Type 2 diabetes. Its primary mechanism of action involves reducing hepatic glucose production (gluconeogenesis) and enhancing insulin sensitivity. By targeting these pathways, metformin helps lower blood sugar levels, making it an essential first-line treatment. However, its side effects often include gastrointestinal issues such as nausea and diarrhea, and in rare cases, it may lead to vitamin B12 deficiency or lactic acidosis, a potentially severe condition. The main advantage of metformin is its proven efficacy and well-established safety profile over many years of use. However, one of its limitations is that its action is specifically targeted toward glucose regulation, meaning it does not provide additional therapeutic benefits such as antioxidant protection or immune system support[34].

Sulfonylureas, another class of anti-diabetic drugs, work by stimulating the pancreas to release more insulin. They act on the sulfonylurea receptor on pancreatic β-cells, promoting insulin secretion. This mechanism can effectively lower blood glucose levels, especially in individuals with some remaining insulin production capacity. However, sulfonylureas can cause side effects like hypoglycemia (low blood sugar), weight gain, and, over time, β-cell dysfunction. Chronic use of sulfonylureas can lead to insulin resistance and β-cell burnout, reducing their effectiveness. As a result, they are typically used in combination with other medications when monotherapy is no longer sufficient[35].

GLP-1 Agonists are a newer class of drugs that mimic the action of glucagon-like peptide-1 (GLP-1), a hormone that helps promote insulin secretion in response to meals, reduces glucagon production, and slows gastric emptying. These drugs not only help improve insulin sensitivity but also promote weight loss, which is beneficial for many individuals with Type 2 diabetes. However, GLP-1 agonists come with side effects like nausea and vomiting and have been linked to rare cases of pancreatitis and thyroid cancer. They tend to be expensive and are typically administered via injection, which may not be suitable for all patients. Despite these drawbacks, they are highly effective in promoting glucose control and improving insulin sensitivity with a lower risk of hypoglycemia[36].

4.2. Plant-Based Therapies

Plant-based therapies for diabetes involve the use of various medicinal plants that contain bioactive compounds capable of improving blood glucose regulation. These therapies often mimic or complement the actions of conventional drugs, but they offer additional benefits due to their holistic properties. For example, plants like *Momordica charantia* (bitter melon), *Trigonella foenum-graecum* (fenugreek), and *Berberis aristata* (berberine) can enhance insulin sensitivity, reduce glucose production in the liver, and stimulate insulin secretion. Other plants, such as *Cinnamomum verum* (cinnamon) and *Ocimum sanctum* (holy basil), provide additional antioxidant and anti-inflammatory effects, which can help manage diabetes-related complications[37].

One of the main advantages of plant-based therapies is their fewer side effects. Compared to conventional drugs, plant-based treatments are generally considered safer with minimal adverse effects. For instance, *Gymnema sylvestre* (gymnema) and *Zingiber officinale* (ginger) have been shown to improve insulin sensitivity without causing significant side effects. Moreover, plants like *Curcuma longa* (turmeric) are rich in antioxidants, which can help mitigate the oxidative stress and inflammation commonly associated with Type 2 diabetes[38].

Plant-based therapies also offer holistic action. Many plants work in a multi-mechanistic fashion, targeting several aspects of glucose metabolism at once. For example, *Berberis aristata* (berberine) activates AMP-activated protein kinase (AMPK), which not only enhances insulin sensitivity but also improves lipid metabolism and exerts anti-inflammatory effects. Conventional drugs, by contrast, tend to be more targeted in their actions and may not address the broader metabolic disturbances seen in diabetes. Additionally, some plant-based therapies, such as *Gymnema sylvestre*, *Pterocarpus marsupium*, and *Ocimum sanctum*, have shown potential in regenerating pancreatic β-cells, a feature that is not commonly seen with conventional drugs[39].

4.3. Advantages of Plant-Based Therapies

One of the primary advantages of plant-based therapies is that they tend to have fewer side effects compared to synthetic drugs. For example, herbs like *Syzygium cumini* (jamun) and *Allium sativum* (garlic) have demonstrated blood glucose-lowering effects without the risk of hypoglycemia, which is a common side effect of sulfonylureas. This makes plant-based therapies a safer alternative, particularly for individuals who are at risk of hypoglycemia or those who experience side effects from conventional drugs[40]. Another significant advantage is their holistic action. Many plant-based therapies, such as *Moringa oleifera* (moringa), work synergistically by targeting multiple metabolic pathways at once. These plants not only regulate glucose metabolism but also offer essential nutrients and have anti-inflammatory properties, which can support overall health. This broader spectrum of action makes them a valuable addition to a diabetes management regimen[41].

Moreover, plants like *Curcuma longa* (turmeric) and *Ocimum sanctum* (holy basil) provide antioxidant and anti-inflammatory benefits, which can help manage the oxidative stress and chronic inflammation commonly seen in Type 2 diabetes. This added benefit supports long-term health by potentially reducing the risk of diabetes-related complications, such as neuropathy, retinopathy, and cardiovascular disease[41].

4.4. Challenges of Plant-Based Therapies

Despite their advantages, plant-based therapies face several challenges that need to be addressed for them to become more widely accepted in clinical practice. One of the main challenges is standardization. The bioactive compounds in medicinal plants can vary significantly depending on factors such as growing conditions, plant part used, and preparation methods. This variability can affect the consistency, efficacy, and safety of the treatment. Unlike synthetic drugs, which are rigorously standardized, plant-based therapies often lack this level of consistency[42].

Another challenge is the bioavailability of plant compounds. Many medicinal plants, such as *Curcuma longa* (curcumin) and *Berberis aristata* (berberine), have low bioavailability, meaning they are not easily absorbed and utilized by the body. Research is ongoing to find ways to enhance the bioavailability of these compounds, such as by using adjuncts like piperine with curcumin to improve absorption[43].

Finally, dosage control is a significant hurdle. Unlike conventional drugs, plant-based therapies do not have standardized dosages, which makes it difficult to prescribe a precise and consistent dose. The amount of active compound in a plant preparation can vary, which may lead to either suboptimal effects or unwanted side effects if the dosage is not carefully managed.

4.5. Complementary Use

Plant-based therapies can be used complementarily with conventional drugs to enhance diabetes management. For instance, plants like *Fenugreek* and *Gymnema sylvestre* can improve insulin sensitivity and may allow for a reduced dose of medications like metformin, potentially mitigating some of its gastrointestinal side effects. Additionally, certain plant-based therapies, such as *Pterocarpus marsupium*, which has regenerative effects on pancreatic β-cells, could work synergistically with drugs like sulfonylureas, which aim to stimulate insulin secretion. By supporting β-cell function, these therapies can enhance the effectiveness of conventional drugs[44].

Furthermore, plants with antioxidant and anti-inflammatory effects, such as *Turmeric* and *Holy Basil*, can complement the action of diabetes medications by reducing the risk of long-term complications, such as cardiovascular diseases and neuropathy. This complementary action could improve overall patient outcomes and quality of life.

5. Conclusion

The therapeutic potential of anti-diabetic plants is increasingly recognized, with plants like *Momordica charantia* (bitter melon), *Trigonella foenum-graecum* (fenugreek), and *Berberis aristata* (berberine) offering diverse mechanisms to regulate blood glucose, enhance insulin sensitivity, and address complications. Many of these plants also provide antioxidant and anti-inflammatory benefits. However, further validation through large-scale clinical trials and standardization is necessary for their widespread adoption. More rigorous studies are needed to confirm their efficacy, safety, and optimal dosages. When properly validated, plant-based therapies could serve as affordable and effective adjuncts to conventional treatments, offering complementary options in global diabetes care, especially in areas with limited access to standard medications. Combining modern medicine with plant-based therapies could lead to a more holistic and personalized diabetes treatment model.

5.1. Limitations, challenges, and future perspectives

Plant-based therapies for diabetes show potential but face challenges that limit their widespread use. These challenges include a lack of large-scale clinical trials, standardization issues, bioavailability concerns, and potential herb-drug interactions. However, advancements in research offer promising solutions for improving their application.

5.1.1. Lack of Large-Scale Clinical Trials

Most plant-based therapies lack robust clinical data, which limits their acceptance in mainstream medicine. Future research needs more large-scale, long-term human trials to confirm efficacy, safety, and dosage.

5.1.2. Issues in Standardization and Regulatory Approval

The variability in the bioactive compounds of medicinal plants makes standardization difficult. Additionally, regulatory approval is often unclear, as many herbal products are categorized as dietary supplements rather than medicines. Standardized extraction methods and regulatory trials are crucial for ensuring safety and efficacy.

5.1.3. Bioavailability and Pharmacokinetics

Many plant compounds, like curcumin and berberine, suffer from poor bioavailability, affecting their effectiveness. Future research should focus on nanotechnology and drug delivery systems to improve absorption and efficacy.

5.1.4. Potential Herb-Drug Interactions

Herb-drug interactions may occur when plant-based therapies are used alongside conventional diabetes medications. Research into these interactions is necessary to ensure safe and effective combined treatments.

5.1.5. Future Directions

- **Nanotechnology** can enhance the bioavailability of plant compounds.
- **Synergistic Herbal Formulations** may improve diabetes management by combining herbs with complementary actions.
- **Integration with Modern Medicine** could lead to personalized treatments, combining plant-based therapies with conventional drugs to improve efficacy and minimize side effects.

While plant-based therapies hold promise, addressing these challenges through research, innovation, and collaboration with modern medicine could significantly enhance their role in diabetes management.

Compliance with ethical standards

Author contributions

Every author participated in the conceptualization, fieldwork, data analysis, study design, and execution phases of the work. Upon reviewing the final publication, each author provided their approval.

Disclosure of conflict of interest

There is no conflict of interest.

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