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Original Article

Herbal Drug Management in Diabetes Mellitus

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ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycaemia arising from impaired insulin secretion, impaired insulin action, or both. Its growing global burden has sustained interest in medicinal plants and plant-derived products as possible supportive approaches to metabolic health. This narrative review discusses the pharmacognostic and pharmacological relevance of selected medicinal plants traditionally used in diabetes management, including Gymnema sylvestre, Momordica charantia, Trigonella foenum-graecum, Curcuma longa, Tinospora cordifolia, Syzygium cumini, Azadirachta indica, Phyllanthus emblica, Aloe vera, Cinnamomum species, Nigella sativa, Allium sativum and berberine-containing plants. Major phytochemical groups include polyphenols, flavonoids, alkaloids, terpenoids, saponins, glycosides and dietary fibres. Proposed mechanisms include modulation of carbohydrate digestion and absorption, improvement of insulin signalling and peripheral glucose uptake, effects on hepatic glucose production, antioxidant and anti-inflammatory actions, and possible protection of pancreatic beta cells. Evidence from cell and animal experiments is biologically interesting, while human trials and systematic reviews report variable results because of differences in plant identity, plant part, extraction method, dose, duration, comparator and outcome measures. A 2025 umbrella review found signals of benefit for selected preparations such as ginger and turmeric but also highlighted substantial limitations in the quality of the underlying reviews and incomplete adverse-event reporting. Current diabetes guidance does not recommend herbal supplements or spices as routine glucose-lowering treatment. Important risks include hypoglycaemia when products are combined with antidiabetic medicines, herb-drug interactions, liver injury from certain products, contamination, adulteration and batch-to-batch variability. The review therefore emphasizes that herbal products should not replace prescribed treatment, and that future research must use authenticated raw materials, standardized extracts, transparent chemical characterization, adequately powered randomized trials and systematic safety monitoring.

Keywords: Diabetes mellitus, medicinal plants, herbal drugs, phytochemicals, antidiabetic activity, insulin resistance, clinical evidence, herb-drug interactions, quality control

ABBREVIATIONS

Abbreviation	Full form
ADA	American Diabetes Association
AMPK	AMP-activated protein kinase
AUC	Area under the curve
CYP	Cytochrome P450
FBG / FPG	Fasting blood glucose / fasting plasma glucose
GLP-1	Glucagon-like peptide-1
GLUT4	Glucose transporter type 4
HbA1c	Glycated haemoglobin
HOMA-IR	Homeostatic Model Assessment of Insulin Resistance
OGTT	Oral glucose tolerance test
PPG / PPBG	Post-prandial glucose / post-prandial blood glucose
RCT	Randomized controlled trial
ROS	Reactive oxygen species
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) is a heterogeneous group of metabolic disorders in which chronic hyperglycaemia develops because insulin secretion, insulin action, or both are inadequate for the body's metabolic requirements. Persistent hyperglycaemia is associated with microvascular complications, including retinopathy, nephropathy and neuropathy, and macrovascular disease involving the heart, brain and peripheral arteries. Diabetes also affects quality of life, productivity and healthcare expenditure. The International Diabetes

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Federation (IDF) estimated that 589 million adults aged 20-79 years were living with diabetes in 2024, equivalent to approximately one in nine adults; the number is projected to reach 853 million by 2050 [1].

Type 2 diabetes accounts for most diabetes cases and is strongly associated with insulin resistance, progressive beta-cell dysfunction, genetic susceptibility, ageing, excess adiposity, physical inactivity and environmental factors. Established diabetes care combines individualized nutrition, physical activity, education, glucose monitoring, risk-factor management and evidence-based pharmacotherapy. The selection of medicines depends on glycaemic status, cardiovascular and renal disease, hypoglycaemia risk, weight, affordability and patient preferences [2,3].

Medicinal plants have a long history of use in traditional systems of healthcare, including Ayurveda and other regional practices. Leaves, roots, rhizomes, seeds, fruits, bark and whole-plant preparations have been used in different communities for symptoms or conditions associated with diabetes. Interest in plant-derived agents also reflects the chemical diversity of natural products and the fact that several important medicines have originated from natural sources. However, historical use and laboratory activity do not by themselves establish clinical efficacy or safety. The plant species, plant part, extraction solvent, concentration, formulation and dose can substantially change the chemical profile of a product [4-8].

The purpose of this review is to describe selected antidiabetic medicinal plants, their major phytochemical groups and proposed mechanisms, summarize the available clinical evidence, and discuss important safety and quality-control considerations. The central position adopted is that herbal medicines may provide research leads and, in selected settings, may be considered as complementary products only after professional review. They should not be presented as replacements for prescribed antidiabetic medicines, insulin, lifestyle measures or routine monitoring.

2. DIABETES MELLITUS: DEFINITION, CLASSIFICATION AND BURDEN

2.1 Definition

The American Diabetes Association describes diabetes mellitus as a group of disorders of carbohydrate metabolism in which glucose is underutilized as an energy source and overproduced through processes such as gluconeogenesis and glycogenolysis, leading to hyperglycaemia [2]. Diagnosis is based on standardized laboratory tests. In non-pregnant adults, common diagnostic criteria include HbA1c of at least 6.5%, fasting plasma glucose of at least 126 mg/dL, or 2-hour plasma glucose of at least 200 mg/dL during a 75-g oral glucose tolerance test. A random plasma glucose of at least 200 mg/dL in a person with classic hyperglycaemic symptoms or a hyperglycaemic crisis is also diagnostic. In the absence of unequivocal hyperglycaemia, confirmatory testing is required [2].

2.2 Classification

The major clinical categories are type 1 diabetes, type 2 diabetes, gestational diabetes mellitus and specific types due to other causes. Type 1 diabetes results from autoimmune beta-cell destruction and usually causes absolute insulin deficiency. Type 2 diabetes results from progressive loss of adequate beta-cell insulin secretion, frequently on a background of insulin resistance. Specific forms include monogenic diabetes, diseases of the exocrine pancreas, endocrinopathies and drug- or chemical-induced diabetes. Gestational diabetes is diagnosed during pregnancy when glucose intolerance is first recognized under the relevant diagnostic criteria [2].

Herbal research should not treat all categories as interchangeable. A product investigated in adults with type 2 diabetes cannot automatically be assumed to be safe or effective in type 1 diabetes, gestational diabetes, childhood diabetes or diabetes secondary to pancreatic disease. In type 1 diabetes, insulin is essential; any attempt to replace it with a plant product is potentially dangerous.

2.3 Burden and complications

The IDF's 2025 Diabetes Atlas reported 589 million adults with diabetes in 2024 and projected 853 million by 2050. It also estimated that 252 million adults with diabetes were unaware of their condition [1]. The burden is not limited to raised glucose. Long-term complications can affect the retina, kidneys, peripheral nerves, cardiovascular system and lower limbs. Acute metabolic emergencies include diabetic ketoacidosis and hyperosmolar hyperglycaemic state. These outcomes explain why reliable diagnosis, sustained glucose management and regular screening are

more important than short-term changes in isolated glucose readings.

The main clinical outcome used in long-term diabetes research is HbA1c, which reflects average glycaemia over approximately the preceding two to three months. Fasting glucose and post-prandial glucose provide additional information but can vary from day to day. Measures such as HOMA-IR are mainly used in research to estimate insulin resistance and should not be interpreted as direct proof that a treatment prevents diabetic complications. Herbal studies should report validated outcomes, clinically meaningful effect sizes and adverse events rather than relying only on animal glucose values or isolated biochemical markers.

3. PATHOPHYSIOLOGY RELEVANT TO HERBAL RESEARCH

In healthy physiology, pancreatic beta cells release insulin in response to rising blood glucose. Insulin promotes glucose uptake in skeletal muscle and adipose tissue, supports glycogen synthesis, suppresses hepatic glucose output and influences lipid and protein metabolism. In type 2 diabetes, insulin resistance develops in liver, muscle and adipose tissue. The pancreas initially compensates by increasing insulin secretion; over time, beta-cell function may decline and hyperglycaemia becomes persistent. The relative contribution of insulin resistance and beta-cell dysfunction differs among individuals [2,8].

3.1 Hepatic glucose production

The liver maintains blood glucose between meals through glycogen breakdown and gluconeogenesis. In insulin-resistant states, insulin may fail to adequately suppress hepatic glucose production. Some plant extracts have been reported in preclinical studies to influence hepatic enzymes or signalling pathways involved in gluconeogenesis. Such findings are hypothesis-generating because activity in cell lines or diabetic rodents does not ensure a safe or clinically meaningful effect in humans.

3.2 Intestinal carbohydrate digestion and absorption

Dietary starch is broken down by enzymes such as alpha-amylase and alpha-glucosidase before glucose is absorbed. Inhibition of these enzymes can delay carbohydrate digestion and reduce the rate of post-meal glucose appearance. Several polyphenols and plant extracts show enzyme-inhibitory activity in vitro. The clinical relevance depends on the concentration reaching the intestinal lumen, the type of food consumed, extract stability and tolerability. Potent enzyme inhibition may also cause gastrointestinal symptoms if undigested carbohydrate reaches the colon.

3.3 Oxidative stress and inflammation

Chronic hyperglycaemia can increase the formation of reactive oxygen species and promote inflammatory signalling. Oxidative stress may damage cellular structures and contribute to beta-cell dysfunction and vascular injury. Polyphenols, flavonoids and other plant constituents often show antioxidant activity in chemical assays. These results should be interpreted carefully: antioxidant activity in a test tube is not equivalent to preventing diabetic complications in a person. Clinical studies need validated endpoints and long-term follow-up.

3.4 Beta-cell function

Preserving residual pancreatic beta-cell function is a major area of experimental research. Selected herbal extracts have been reported to reduce oxidative injury, alter insulin secretion or influence pathways related to beta-cell survival in experimental models. A review of beta-cell-focused herbal research found that most investigations were preclinical and only a small proportion were clinical trials [8]. Claims of beta-cell regeneration in humans are therefore not established and should not be made from animal histology alone.

4. RATIONALE FOR STUDYING HERBAL MEDICINES

Medicinal plants remain important in many communities because they are locally available, culturally familiar and sometimes less expensive than manufactured products. Traditional knowledge can help identify species for pharmacological investigation. Plants also contain complex mixtures of secondary metabolites that may act on more than one biological target. This may be useful for discovery research, particularly where metabolic disease involves several pathways [4-7].

Nevertheless, the word 'natural' does not mean harmless. Plant products can contain pharmacologically active substances, toxic constituents, contaminants or

adulterants. The same species can have different chemical profiles depending on geography, season, cultivation, harvesting, storage and extraction. A traditional decoction, a powdered crude drug, a concentrated aqueous extract and a standardized capsule are not interchangeable. Clinical findings from one preparation must not be transferred automatically to another product [17,19,20].

A balanced evaluation therefore asks four questions: (i) Is the botanical identity correct? (ii) Is the preparation chemically characterized and reproducible? (iii) Is there convincing human evidence for a clinically relevant outcome? and (iv) Is the product safe when used alone or with prescribed medicines? These questions form the basis of the following review.

5. PHYTOCHEMICAL CONSTITUENTS OF ANTIDIABETIC PLANTS

Phytochemicals are naturally occurring chemical constituents produced by plants. They may contribute to the plant's defence, colour, aroma or adaptation to its environment. In pharmacognosy, identification and quantification of these constituents are important for evaluating the quality of crude drugs and extracts. The presence of a constituent does not automatically prove that it is responsible for a clinical effect; causal activity requires isolation, characterization and suitable pharmacological studies.

Phytochemical group	Examples / representative compounds	Potential research relevance
Polyphenols and phenolic acids	Curcumin, gallic acid, chlorogenic acid, caffeic acid	Antioxidant and anti-inflammatory actions; possible modulation of carbohydrate enzymes and insulin signalling.
Flavonoids	Quercetin, kaempferol, catechins, rutin	May influence oxidative stress, inflammatory mediators and glucose transport in experimental models.
Alkaloids	Berberine and related alkaloids	Potential effects on AMPK-related signalling, hepatic glucose metabolism and gut microbiota; interactions require evaluation.
Saponins and triterpenoids	Gymnemic acids, ginsenosides, cucurbitane-type compounds	Possible effects on intestinal glucose handling, insulin-related pathways and lipid metabolism.
Dietary fibre and galactomannan	Fenugreek seed mucilage and soluble fibre	May slow gastric emptying or carbohydrate absorption and influence post-meal glycaemia.
Sulfur-containing compounds	Allicin-related compounds in garlic	Potential effects on vascular and metabolic markers; composition changes with processing.
Essential-oil constituents	Cinnamaldehyde and other volatile compounds	Studied for insulin-signalling and glucose-metabolism effects; concentration and safety vary by species and preparation.

The main analytical approaches used in herbal drug characterization include macroscopic and microscopic identification, physicochemical tests, chromatographic fingerprinting, marker-compound quantification and, where appropriate, spectroscopic methods. High-performance liquid chromatography (HPLC), thin-layer chromatography (TLC), gas chromatography (GC) and mass spectrometry can help detect variation or adulteration. A marker compound may be selected for identity or consistency even when it is not the sole active ingredient.

6. PROPOSED MECHANISMS OF ANTIDIABETIC ACTION

Different plants may contain multiple constituents that affect more than one biological process. Proposed mechanisms are summarized below. Most of these mechanisms have been described in cell or animal experiments; the strength of human evidence varies greatly among herbs and formulations [5,7,8].

6.1 Stimulation of insulin secretion

Some plant extracts have been reported to influence glucose-stimulated insulin release from pancreatic beta cells. A desirable secretagogue effect would ideally be glucose-dependent, because continuous insulin release in the absence of high glucose may cause hypoglycaemia. Experimental reports of increased insulin secretion require careful dose-response, toxicity and human safety evaluation before clinical relevance can be inferred.

6.2 Improvement of insulin sensitivity

Insulin sensitivity refers to the ability of tissues to respond to insulin. Experimental studies of plant-derived compounds have examined insulin-receptor signalling, phosphorylation of downstream proteins, PI3K-Akt pathways and GLUT4 translocation in skeletal muscle or adipose tissue. AMPK is another energy-sensing pathway studied in relation to glucose uptake and hepatic metabolism. These pathways are plausible research targets, but biochemical changes in a model do not prove improvement in patient outcomes.

6.3 Inhibition of carbohydrate-digesting enzymes

In vitro alpha-amylase and alpha-glucosidase inhibition is commonly reported for polyphenol-rich extracts. The hypothesized result is slower digestion of complex carbohydrates and a smaller post-meal glucose excursion. However, non-specific enzyme inhibition, poor solubility, low oral exposure and gastrointestinal adverse effects can limit usefulness. Assays should use validated controls and should be linked to human post-prandial studies.

6.4 Reduction in hepatic glucose output

Certain experimental compounds have been investigated for their influence on gluconeogenic enzymes and hepatic glucose production. If a product reduces excessive hepatic glucose output without impairing normal glucose regulation, it may be relevant to fasting glucose. Human trials should distinguish fasting glucose changes from HbA1c effects and should monitor liver function where appropriate.

6.5 Antioxidant and anti-inflammatory actions

Phenolic compounds and flavonoids may scavenge reactive species in chemical assays and can influence inflammatory mediators in experimental systems. These actions may be relevant to beta-cell stress and vascular biology. Still, antioxidant capacity measured by DPPH, FRAP or similar tests is not a clinical endpoint. A convincing therapeutic claim requires randomized clinical evidence that measures glycaemia, complications, quality of life or other patient-centred outcomes.

6.6 Modulation of incretin and gut-related pathways

The gut influences glucose regulation through nutrient absorption, incretin hormones, bile-acid signalling and the microbiome. Some herbal compounds have been explored for effects on GLP-1-related activity, intestinal transporters and microbial composition. These hypotheses are active research areas, but many reported microbiome changes are exploratory and may be influenced by diet, geography, medication and baseline microbial composition.

6.7 Protection of pancreatic beta cells

Some plant extracts have shown protection against chemically induced beta-cell injury in laboratory animals. Proposed pathways include reduced oxidative stress, anti-apoptotic signalling and changes in insulin-related gene expression. Such models do not recreate the full natural history of human type 1 or type 2 diabetes. The existing beta-cell review literature emphasizes that the majority of available investigations are preclinical and that properly designed clinical research remains limited [8].

7. SELECTED MEDICINAL PLANTS: PHARMACOGNOSY AND EVIDENCE

The plants below were selected because they appear frequently in traditional use, pharmacognosy literature or clinical research. The summaries distinguish traditional use and experimental mechanisms from evidence in humans. They are not a prescribing list, and no therapeutic dose is recommended because preparations are not standardized across studies.

7.1 Gymnema sylvestre (Retz.) R.Br. ex Sm.

Family: Apocynaceae. Common names include gurmar and madhunashini. Leaves are the commonly investigated plant part. The plant contains triterpenoid saponins known as gymnemic acids, along with other constituents. Traditional use includes conditions associated with excess sugar intake. Gymnemic acids have been investigated for effects on intestinal taste perception and carbohydrate handling, while extracts have also been studied for insulin-related and beta-cell effects in experimental models [5,8].

A systematic review and meta-analysis published in 2021 included 10 studies with 419 participants and reported reductions in fasting glucose, post-prandial glucose and HbA1c compared with baseline. However, the analysis reported very high heterogeneity, and the reported comparisons and study quality limit certainty about the size of the treatment effect [13]. Gymnema should therefore be regarded as a candidate for further study rather than established standard

treatment. When combined with insulin or oral glucose-lowering medicines, additive glucose lowering is a theoretical and clinically relevant concern; glucose monitoring and clinician review are necessary.

7.2 Momordica charantia L.

Family: Cucurbitaceae. Common names include bitter melon and karela. Fruits, seeds and leaves have been studied, although the preparations differ widely. Reported constituents include charantin, cucurbitane-type triterpenoids, peptides and phenolic compounds. Proposed mechanisms include effects on glucose uptake, insulin-related activity and carbohydrate metabolism, but the responsible compounds and their contribution in humans are not fully established [5,7].

Clinical evidence has been inconsistent. The Cochrane review of earlier trials concluded that available evidence did not warrant using bitter melon as a treatment for type 2 diabetes, noting small and low-quality studies and gastrointestinal adverse effects [14]. A newer GRADE-adherent meta-analysis published in 2025 reported possible reductions in fasting glucose and HbA1c across 25 trials, but differences in preparation, dosage and trial design remain important limitations [15]. These findings illustrate why evidence summaries can differ as new trials accumulate and why confidence ratings matter. Bitter melon must not be used as a substitute for prescribed treatment.

7.3 Trigonella foenum-graecum L.

Family: Fabaceae. Fenugreek seeds are used as a food ingredient and have been investigated as a source of soluble fibre, galactomannan, saponins and other phytochemicals. Fibre may delay gastric emptying and carbohydrate absorption, potentially influencing post-meal glycaemia. Other reported mechanisms include effects on insulin secretion and lipid metabolism, although not all proposed pathways have been confirmed in humans [5,7].

A 2025 updated systematic review and meta-analysis reported improvement in fasting glucose, 2-hour postprandial glucose and HbA1c across 26 randomized trials. The authors nevertheless emphasized the need for higher-quality trials, and the very high heterogeneity for some outcomes limits confidence in the pooled estimate [12]. Fenugreek may cause gastrointestinal effects and allergic reactions in susceptible individuals. Because glucose lowering may be additive with medicines, people taking antidiabetic treatment should seek professional advice before using concentrated seed extracts or supplements.

7.4 Curcuma longa L.

Family: Zingiberaceae. The rhizome is the commonly used part and contains curcuminoids, including curcumin, as well as volatile oils. Curcumin has been investigated for antioxidant, anti-inflammatory and metabolic effects. Oral bioavailability is limited and depends on the formulation; enhanced-bioavailability products are not equivalent to ordinary culinary turmeric [10].

A 2024 systematic review and meta-analysis of 103 randomized controlled trials across multiple health outcomes reported high-certainty evidence for some outcomes, including fasting blood sugar, but also noted limitations and the need for large, long-term trials [10]. A 2025 umbrella review reported a reduction in HbA1c for turmeric compared with placebo, while also warning that the quality of the included reviews was often limited [9]. The 2026 ADA Standards state that evidence is insufficient to support routine use of herbal supplements or spices such as curcumin to improve glycaemia [3]. Concentrated extracts may cause gastrointestinal effects and can interact with medicines; product quality and dose require attention.

7.5 Tinospora cordifolia (Willd.) Hook.f. & Thomson

Family: Menispermaceae. Commonly known as guduchi or giloy, the stem is frequently used in traditional preparations. Constituents reported in the literature include diterpenoid lactones, alkaloids, glycosides and polysaccharides. Preclinical studies have explored possible glucose-lowering, antioxidant and immunomodulatory effects [5,6]. Human evidence for diabetes outcomes remains insufficient to establish efficacy or a standardized therapeutic regimen.

Safety deserves particular attention. A multicentre Indian study described 43 patients with liver injury temporally associated with Tinospora cordifolia use and reported autoimmune features in some cases [18]. This does not mean that every product or user will experience liver injury, but it demonstrates that traditional use does not eliminate the possibility of serious

adverse reactions. People with liver disease, those using multiple medicines, and those who develop jaundice, dark urine, severe fatigue or abdominal symptoms require prompt medical review. Unsupervised use is not advisable.

7.6 Syzygium cumini (L.) Skeels

Family: Myrtaceae. Jamun is a familiar Indian fruit; seeds, leaves and bark have also been studied in traditional contexts. Reported constituents include polyphenols, flavonoids, tannins and anthocyanins, with composition depending on the plant part. Experimental studies have investigated enzyme inhibition, antioxidant activity and glucose metabolism [4,6]. Evidence from controlled human trials is limited and does not establish a standardized seed powder or extract for diabetes management. Culinary consumption of the fruit is different from concentrated medicinal supplementation.

7.7 Azadirachta indica A. Juss.

Family: Meliaceae. Neem leaves, bark and seeds contain chemically diverse limonoids, flavonoids and other constituents. Preclinical work has reported potential effects on glucose metabolism and oxidative stress. However, different plant parts and extracts have different toxicity profiles, and seed oil should not be equated with leaf preparations. Robust clinical evidence for a reproducible antidiabetic benefit is lacking. Concentrated neem products should not be assumed safe for pregnancy, children or people with chronic disease without appropriate evidence and clinical assessment [4-7].

7.8 Phyllanthus emblica L. (Emblica officinalis Gaertn.)

Family: Phyllanthaceae. Amla fruit contains vitamin C, hydrolysable tannins, phenolic compounds and flavonoids. It is widely consumed as food and used in traditional preparations. Experimental and small clinical studies have explored lipid, oxidative and glycaemic markers. However, fruit as food, juice, powder and concentrated extract are chemically and pharmacologically different. Current evidence is not sufficient to recommend amla products as a replacement or routine glucose-lowering treatment [4,6].

7.9 Aloe vera (L.) Burm.f.

Family: Asphodelaceae. The inner leaf gel and the yellow latex beneath the leaf skin are chemically different materials. Aloe preparations may contain polysaccharides and anthraquinone-related compounds depending on processing. Some studies have investigated glycaemic markers, but product variability and differences between gel and latex complicate interpretation. Aloe latex can cause diarrhoea and electrolyte disturbances; poorly processed products may contain unwanted constituents. The 2026 ADA Standards do not recommend aloe vera or other herbal supplements for routine glycaemic benefit [3].

7.10 Cinnamomum species

Family: Lauraceae. Cinnamon bark contains volatile oils and polyphenolic compounds. Cinnamomum verum (Ceylon cinnamon) and Cinnamomum cassia are not identical in composition. Cinnamon has been investigated for possible effects on insulin signalling and glucose metabolism. A 2024 systematic review and dose-response meta-analysis of 24 randomized trials reported reductions in fasting glucose, HOMA-IR and HbA1c; however, variations among trials and preparations limit the certainty of product-specific recommendations [16]. Cassia cinnamon may contain higher and variable amounts of coumarin, which can be a concern for people with liver disease or those consuming high supplemental amounts [17]. Culinary use should not be conflated with concentrated supplementation.

7.11 Nigella sativa L.

Family: Ranunculaceae. The seeds, commonly called black seed or kalonji, contain fixed oil, volatile constituents and thymoquinone. Human studies have investigated fasting glucose, HbA1c and insulin-resistance markers. A 2024 systematic review and meta-analysis of 30 trials reported reductions in fasting glucose and HbA1c, but very high heterogeneity was present, particularly for glycaemic outcomes [11]. A separate 2025 meta-analysis of 16 randomized trials also reported reductions in fasting glucose and HbA1c, while not finding consistent effects across all metabolic measures [24]. More standardized, longer studies are required. Possible additive glucose lowering and product quality should be considered.

7.12 Allium sativum L.

Family: Amaryllidaceae (formerly commonly placed in Alliaceae). Garlic bulb contains sulfur-containing compounds whose profile changes with crushing,

heating, drying and extraction. Garlic has been investigated for cardiometabolic effects, including lipid and blood-pressure outcomes, and some studies have explored glucose markers. The evidence is not sufficiently consistent to define garlic as an antidiabetic medicine. Concentrated supplements may increase bleeding risk in some circumstances, particularly around surgery or with antithrombotic medicines; clinicians should be informed about supplement use.

7.13 Berberis species and berberine

Berberine is an isoquinoline alkaloid found in several plant genera, including Berberis. It has received attention for effects on glucose and lipid metabolism, including AMPK-related pathways and intestinal mechanisms. A 2024 systematic review and meta-analysis of 50 randomized trials involving 4,150 participants reported improvements in several glycaemic and lipid outcomes when berberine was used alone or with glucose-lowering medicines [22]. However, the interpretation of pooled results depends on trial quality, preparation, dose, background treatment and publication bias. Berberine is pharmacologically active and may affect drug transport or metabolism. It should not be self-added to a prescription regimen, and it is not an alternative to medically indicated therapy.

7.14 Other plants under investigation

A number of other plants, including Ocimum tenuiflorum (holy basil), Pterocarpus marsupium, Moringa oleifera, Panax ginseng and selected Chinese herbal formulae, have been investigated in experimental or clinical settings. Their phytochemical profiles and clinical evidence differ substantially. Some studies are small, use mixed formulations or report surrogate endpoints. These plants are therefore best viewed as areas of ongoing research rather than established treatments. A product should be identified by its accepted botanical name, authenticated plant part and preparation before any study result is applied to it [5-9].

8. OVERVIEW OF HUMAN CLINICAL EVIDENCE

Preclinical evidence is abundant for many plants, but clinical evidence is less uniform. Human trials differ in sample size, duration, disease stage, background medication, comparator, extract composition and analytical methods. Some studies use food powders; others use concentrated extracts or multi-herb products. This heterogeneity can produce apparently different results even when investigators study plants with the same common name.

The 2025 umbrella review by Li and colleagues synthesized systematic reviews and meta-analyses on herbal medicines for glycaemic control in type 2 diabetes. It reported moderate-to-high certainty evidence for reductions in HbA1c with ginger, turmeric and Jinlida granules in the included evidence base, while evidence for several other products was very low certainty or could not be graded. The review also found that the methodological quality of many underlying reviews was critically low and that adverse-event reporting was incomplete [9]. The authors therefore cautioned against over-interpreting positive pooled results.

There is an important difference between statistical significance and clinical usefulness. A statistically significant change in fasting glucose may be small, short-lived or not sustained in HbA1c. A reduction in HbA1c observed in a short trial may not translate into lower rates of retinopathy, kidney failure, cardiovascular events or mortality. Trials should report between-group differences, confidence intervals, adherence, withdrawals, adverse events and changes in concomitant medicines.

Plant / preparation	Human evidence signal reported in selected reviews	Important limitation
Gymnema sylvestre	A 2021 review of 10 studies reported improvement in FBG, PPBG and HbA1c versus baseline [13].	High heterogeneity; small and variable studies; baseline comparisons limit causal inference.
Momordica charantia	Older Cochrane review found insufficient evidence; a 2025 meta-analysis reported possible reductions in FBG and HbA1c [14,15].	Different plant parts and preparations; inconsistent trial findings; GI effects.
Fenugreek seed	A 2025 meta-analysis of 26 RCTs reported improved FBG, 2-h PPG and HbA1c [12].	Very high heterogeneity for some outcomes; need better trials and standardized seed products.

Plant / preparation	Human evidence signal reported in selected reviews	Important limitation
Turmeric / curcumin	2025 umbrella review reported HbA1c improvement; 2024 broad RCT meta-analysis found some glycaemic signals [9,10].	Formulation-dependent bioavailability; quality of underlying reviews varies; not routine ADA-recommended supplementation.
Cinnamon	A 2024 meta-analysis reported improvement in FBG, HOMA-IR and HbA1c [16].	Species and coumarin content vary; differences in dose, extract and trial duration.
Nigella sativa	2024 and 2025 meta-analyses reported reductions in some glycaemic markers [11,24].	Substantial heterogeneity; product and dose variability; long-term safety data limited.
Berberine	A 2024 meta-analysis of 50 RCTs reported improvements in selected glycaemic outcomes [22].	Trial quality, formulations, co-medication and interaction risks require careful assessment.
Tinospora cordifolia	Preclinical antidiabetic findings reported in reviews [5,6].	Human efficacy not established; clinically important reports of liver injury [18].

The 2026 ADA Standards of Care advise that supplementation with herbs or spices, including cinnamon and aloe vera, is not recommended for glycaemic benefit [3]. This recommendation reflects the lack of sufficiently reliable evidence to support routine use as a glucose-lowering strategy. It does not prevent scientific investigation; rather, it places the burden on well-designed trials to demonstrate efficacy and safety before clinical recommendations are made.

9. SAFETY, TOXICITY AND HERB-DRUG INTERACTIONS

Safety evaluation is essential because patients may combine herbal products with insulin, oral antidiabetic drugs, antihypertensives, anticoagulants, lipid-lowering agents and other medicines. A product may produce a direct pharmacological effect, change absorption, alter drug-metabolizing enzymes or transporters, or contain contaminants not listed on the label. Interactions can be pharmacodynamic (for example, additive glucose lowering) or pharmacokinetic (for example, altered metabolism or transport) [17,21].

9.1 Hypoglycaemia

If an herbal product lowers glucose and is used together with insulin, sulfonylureas or other glucose-lowering medicines, the combined effect may increase the risk of hypoglycaemia. Symptoms can include sweating, tremor, hunger, palpitations, dizziness, confusion and, in severe cases, seizure or loss of consciousness. The magnitude of this risk is not well quantified for many herbs because interaction trials are limited. The absence of reported events in a small study is not proof of safety.

9.2 Liver and kidney safety

The liver metabolizes many plant constituents and medicines. Some concentrated extracts may cause liver injury or may be contaminated or misidentified. The multicentre Indian report of Tinospora-associated liver injury is a clear example of why safety surveillance is needed [18]. People with pre-existing liver or kidney disease may be more vulnerable to adverse effects or accumulation of constituents. Unexplained jaundice, dark urine, pale stools, persistent nausea, severe itching, swelling or reduced urine output warrants medical assessment rather than continued self-medication.

9.3 Gastrointestinal and allergic reactions

Nausea, abdominal discomfort, diarrhoea, constipation and altered appetite can occur with herbal preparations. Fenugreek and bitter melon may cause gastrointestinal effects in some users. Allergy is possible, particularly in people sensitive to related plant families or food ingredients. Severe allergic symptoms such as facial swelling, difficulty breathing or widespread hives require emergency care.

9.4 Product contamination and adulteration

Herbal products can be contaminated with microorganisms, pesticides, heavy metals, mycotoxins or foreign matter. Adulteration may involve substitution with another species or undeclared pharmaceutical ingredients. Risks are affected by cultivation, drying, storage, transport, manufacturing and distribution.

Product labels may not always accurately describe the chemical composition. Quality standards, validated testing and traceable manufacturing are therefore central to safe use [19,20].

9.5 Important plant-specific concerns

Plant / product	Safety issue to consider	Practical caution
Tinospora cordifolia	Published Indian case series of liver injury with autoimmune features [18].25 Nov 2026	Avoid unsupervised use; extra caution with liver disease or symptoms suggestive of liver injury.
Cassia cinnamon	Variable coumarin content; high supplemental intake may be a concern for the liver [17].	Do not equate culinary amounts with concentrated supplements; identify species.
Aloe latex	Can cause diarrhoea and electrolyte loss; distinct from purified inner-leaf gel.	Check plant part and processing; avoid unverified whole-leaf products.
Fenugreek / bitter melon / Gymnema	Potential additive glucose-lowering effects with antidiabetic drugs.	Monitor glucose and discuss any supplement with the treating clinician.
Garlic supplements	May affect platelet function and interact with antithrombotic therapy.	Disclose supplement use before surgery or when taking blood thinners.
Berberine-containing products	Pharmacologically active; potential for drug transport/metabolism interactions.	Do not self-combine with prescription medicines; require professional review.

People who are pregnant, breastfeeding, planning pregnancy, elderly, taking multiple medicines, or living with chronic liver, kidney or cardiovascular disease should not assume that an herbal product is safe because it is available without prescription. Special populations are often excluded from trials, so safety information may be particularly weak. A patient should provide the healthcare professional with the exact product name, brand, ingredient list, dose, frequency and duration.

10. QUALITY CONTROL AND STANDARDIZATION OF HERBAL DRUGS

Quality control of herbal medicines begins with correct botanical identification and continues through harvesting, processing, extraction, manufacturing, packaging and storage. The World Health Organization has published guidance on good agricultural and collection practices for medicinal plants and on quality-control methods for herbal materials [19,20]. In India, the Indian Pharmacopoeia provides official standards for drug identity, purity and strength where relevant monographs are available [23].

10.1 Authentication of raw material

The scientific name should include the genus, species and author citation where possible. Common names are insufficient because the same common name may refer to several species, and one species may have multiple regional names. Macroscopic and microscopic characters, voucher specimens and qualified pharmacognostic examination support authentication. DNA-based methods may be useful in selected cases, but they do not replace chemical and pharmacognostic evaluation of a complex product.

10.2 Collection, processing and storage

The plant part, maturity stage, season and geographical origin can influence constituent content. Collection should minimize contamination and mix-ups. Drying temperature, moisture content, particle size and storage conditions affect stability. Exposure to light, heat, humidity and oxygen may degrade active constituents or promote microbial and fungal growth. Records should enable traceability from collection site to finished batch [19].

10.3 Physicochemical and chemical testing

Common quality tests include foreign matter, loss on drying, moisture content, total ash, acid-insoluble ash, extractive values and microbial limits. Depending on the material, testing may also include pesticide residues, heavy metals, aflatoxins and residual solvents. TLC or HPTLC fingerprints can help confirm identity and detect some forms of substitution. HPLC or GC methods can quantify selected marker compounds. Testing should use validated methods, suitable reference standards and documented acceptance limits [20,23].

10.4 Standardization of extracts

A standardized extract should have a reproducible manufacturing process and a defined range for one or more marker compounds. The extract-to-drug ratio, solvent system, extraction temperature and processing conditions should be reported. Marker standardization

improves batch consistency, but it does not prove efficacy unless the marker is linked to the biological effect. When multiple constituents contribute to activity, a chromatographic fingerprint may be more informative than a single marker.

10.5 Good manufacturing and documentation practices

Manufacturers should maintain written procedures for raw-material receipt, quarantine, testing, manufacturing, in-process controls, packaging, labelling, stability testing, complaints and recalls. Batch records should identify suppliers, botanical identity, plant part, extraction details, analytical results and release decisions. Labels should avoid unsupported disease-treatment claims and should provide accurate ingredient information, warnings, storage instructions and batch traceability. Independent testing can improve confidence but should be interpreted alongside the laboratory's accreditation, method validation and sample chain of custody.

11. FORMULATION AND BIOPHARMACEUTICAL CONSIDERATIONS

Plant materials may be administered as powders, decoctions, infusions, tablets, capsules, tinctures, extracts, oils or polyherbal formulations. Each dosage form can alter the quantity and bioavailability of phytochemicals. Water extracts may concentrate polar constituents, while hydroalcoholic extracts may contain a different range of compounds. Heating, fermentation, drying and storage can further change the chemical profile. Therefore, a study of a standardized ethanolic extract cannot be assumed to validate a household decoction or an unrelated commercial capsule.

11.1 Solubility and bioavailability

Many polyphenols have low aqueous solubility, undergo extensive metabolism or are rapidly eliminated. Curcumin is a well-known example of a compound with limited oral bioavailability, leading to research on formulation approaches such as lipid-based systems, nanoparticles, phospholipid complexes and absorption enhancers. Improved exposure may also change safety and interaction profiles. Novel delivery systems require their own pharmacokinetic and toxicity evaluation; greater absorption is not automatically equivalent to greater clinical benefit.

11.2 Single-herb and polyherbal products

Single-herb products can be easier to characterize because their botanical source and chemical profile are more limited. Polyherbal products are based on the concept that multiple ingredients may act through complementary pathways. However, more ingredients create additional challenges in authentication, standardization, interaction evaluation and attribution of effects. If one ingredient causes an adverse reaction, identifying the responsible component may be difficult. Clinical trials of polyherbal products should disclose the full formula and batch specifications.

11.3 Stability and packaging

Stability studies should evaluate the chemical fingerprint, marker content, microbial quality and physical properties over the proposed shelf life. Moisture-protective packaging, appropriate light barriers and controlled storage conditions may be required. A best-before date should be supported by stability data rather than assumed from traditional practice. Manufacturers should also evaluate whether the container interacts with oils, volatile constituents or moisture-sensitive extracts.

12. ROLE OF THE PHARMACIST AND PATIENT COUNSELLING

Pharmacists can help reduce harm by asking patients about herbal products in a non-judgmental manner. Patients may not volunteer this information because they consider herbs to be foods or traditional remedies rather than medicines. A complete medication history should include prescription medicines, non-prescription drugs, supplements, powders, teas, oils, traditional formulations and products obtained online or from local vendors.

Key counselling points include:

- Never stop insulin or prescribed antidiabetic medicines to start an herbal product. Sudden withdrawal can cause dangerous hyperglycaemia or metabolic emergencies.
- Tell the treating physician and pharmacist about every herbal product, including its brand, label, ingredients, dose and frequency.
- Avoid products with unclear botanical names, missing batch numbers, unsupported cure claims or no reliable manufacturer information.

- Do not combine multiple glucose-lowering supplements without professional review. Additive effects may cause hypoglycaemia.
- Continue recommended glucose monitoring, HbA1c testing, eye checks, kidney assessment, foot care and cardiovascular risk management.
- Seek medical advice promptly for jaundice, severe gastrointestinal symptoms, allergic reactions, unusual bleeding or recurrent low glucose.

A pharmacist should not promise that a herbal product is safe or effective solely because it is traditional, natural, organic or sold over the counter. Where evidence is uncertain, the correct message is to explain that uncertainty, discuss possible risks and refer the patient to the prescriber for an individualized decision. Pharmacists should also document suspected adverse drug reactions and report them through the applicable pharmacovigilance system.

13. RESEARCH GAPS AND FUTURE PERSPECTIVES

The current research landscape contains promising biological hypotheses but substantial translational gaps. First, botanical materials are frequently insufficiently described. Studies should report authenticated species, plant part, geographic source, voucher specimen, extraction solvent, extract ratio, marker compounds and batch data. Second, preclinical experiments should use validated models, suitable positive controls, blinded outcome assessment and transparent reporting. Third, clinical trials should be registered prospectively and powered to detect a clinically meaningful change in HbA1c rather than relying only on fasting glucose or within-group comparisons.

Future randomized controlled trials should use clearly defined participant populations, stable background treatment, standardized products, adequate sample sizes and follow-up long enough to evaluate HbA1c durability and adverse events. Investigators should report hypoglycaemia, liver and kidney safety, gastrointestinal effects, adherence, concomitant medication changes and reasons for withdrawal. Where possible, trials should include patient-centred outcomes and assess whether benefits persist after treatment ends. The 2025 umbrella review highlights that low methodological quality and incomplete adverse-event reporting remain barriers to confident conclusions [9].

Pharmacokinetic and interaction studies are also required. These should assess whether selected constituents influence drug-metabolizing enzymes, transporters or absorption of commonly used medicines. Such work is particularly important when herbal products are promoted for patients who already take multiple chronic medications. Advanced analytical chemistry, metabolomics, pharmacogenomics and systems pharmacology may help relate chemical composition to biological activity, but these methods should support, not replace, well-designed clinical trials.

A further priority is responsible translation of traditional knowledge. Traditional use can inform the selection of plants for study, but it should be documented carefully and investigated with respect for local communities and biodiversity. Sustainable cultivation, conservation of medicinal species, fair benefit sharing and traceable sourcing should be built into development programs. Product quality and environmental sustainability are linked because poor collection practices can create both chemical variability and ecological damage.

Finally, herbal-drug research should be guided by the same standards of transparency applied to conventional medicines. Negative findings, adverse events and trial registrations should be published. Researchers should distinguish culinary exposure from concentrated supplementation, and they should avoid broad claims about a plant when only one extract has been studied. These improvements can help identify whether any specific, standardized botanical preparation has a safe and useful role as an adjunct to established diabetes care.

CONCLUSION

Medicinal plants contain diverse phytochemicals and remain an important source of pharmacological research in diabetes mellitus. Experimental investigations suggest several possible mechanisms, including modulation of carbohydrate digestion, insulin signalling, hepatic glucose production, oxidative stress and beta-cell function. Human studies of selected plants such as fenugreek, Gymnema, bitter melon, turmeric, cinnamon, Nigella sativa and berberine have reported potentially beneficial changes in some glycaemic markers, but the quality, consistency and clinical relevance of the evidence differ substantially. Differences in plant identity, preparation, dose and study design prevent simple comparison between products.

Herbal products are not automatically safe, and important concerns include additive hypoglycaemia, herb-drug interactions, liver injury, contamination, adulteration and inadequate standardization. Current ADA guidance does not recommend herbs or spices as routine glucose-lowering supplements [3]. Therefore, herbal medicines should not replace prescribed antidiabetic therapy, insulin, lifestyle interventions or glucose monitoring. Further progress requires authenticated plant material, standardized manufacturing, validated analytical methods, adequately powered randomized controlled trials and systematic safety surveillance. Until such evidence is available, the most responsible approach is cautious, evidence-based and professionally supervised use.

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