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#### **Declarations**

No funding was received for this study. The authors declare no conflict of interest. The study received ethical approval. All participants provided informed consent.

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# Medicinal Plants and Their Active Phytoconstituents Used in the Management of Diabetes Mellitus: A Comprehensive Review

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#### **ABSTRACT**

**Background**: Diabetes mellitus (DM) is a rapidly escalating global health crisis, characterised by chronic hyperglycaemia and associated with severe complications such as cardiovascular disease, nephropathy, neuropathy, and retinopathy. Despite advances in pharmacological therapies, long, term disease control remains challenging due to cost, side effects, and limited accessibility. This has renewed scientific interest in medicinal plants and their phytoconstituents, which have been traditionally used in diabetes management and offer multi, targeted therapeutic potential. Objective: This comprehensive review aims to critically evaluate the pharmacological efficacy, molecular mechanisms, and clinical relevance of medicinal plants and their active phytochemicals used in the prevention and management of diabetes mellitus. Methods: A systematic literature search was conducted in Google Scholar, ScienceDirect, PubMed, and Scopus using combinations of keywords such as "medicinal plants," "phytochemicals," "antidiabetic activity," and "diabetes mellitus." Studies published between 2010 and 2025 were screened for relevance, quality, and completeness. Out of 40 initially identified articles, 10 met the inclusion criteria and were synthesised. Data were analysed and categorised based on primary mechanisms of action, including insulin modulation, glucose metabolism regulation, oxidative stress reduction, and enzyme inhibition. Results: Numerous plant species exhibited potent antidiabetic activity across in vitro and in vivo models. Extracts from Afzelia africana, Helicteres angustifolia, Urtica dioica, Aloe vera, and Symplocos cochinchinensis significantly lowered blood glucose, enhanced insulin secretion, improved receptor sensitivity, and reduced oxidative stress. Key phytochemicals such as quercetin, ferulic acid, ursolic acid, rutin, and resveratrol demonstrated multifaceted effects, including  $\alpha$ , glucosidase inhibition,  $\beta$ , cell regeneration, GLUT4 translocation, and modulation of NF,  $\kappa B$  and Nrf2 pathways. Despite robust preclinical evidence, clinical translation remains limited due to challenges in standardisation, bioavailability, and large, scale validation. Conclusion: Medicinal plants and their bioactive constituents offer a promising, multi, targeted approach to diabetes management. By modulating glucose homeostasis, insulin dynamics, oxidative stress, and inflammation, these phytotherapeutics provide significant potential as complementary or alternative therapies. Future research should prioritise standardised extract development, clinical validation, and mechanistic elucidation to facilitate integration into modern diabetes care.

# Keywords

Diabetes mellitus, medicinal plants, phytochemicals, insulin resistance, oxidative stress, a, glucosidase inhibition, complementary medicine

# INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from defects in insulin secretion, insulin action, or both (1). It remains one of the most significant global public health challenges of the 21st century due to its rising prevalence, substantial morbidity, and increasing economic burden. According to the 2025 International Diabetes Federation (IDF) Diabetes Atlas, an estimated 589 million adults aged 20–79 years worldwide were living with diabetes in 2024, with the figure projected to reach 853 million by 2050 (2). This dramatic increase reflects a nearly four, fold rise in global prevalence since 1980 and highlights the urgent need for more effective prevention and management strategies (3). The vast majority of diabetes cases — approximately 90–96% — are type 2 diabetes mellitus (T2DM), which is strongly associated with obesity, sedentary lifestyles, and population ageing (4,5). The latest Global Burden of Disease analysis identifies diabetes as one of the top ten causes of mortality and disability worldwide, with a global prevalence rate of 6.1% and substantial health system impacts (6,7). The pathophysiology of T2DM is multifactorial, involving both impaired insulin secretion from pancreatic  $\beta$ , cells and insulin resistance in

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peripheral tissues. Insulin is a peptide ligand that binds to the insulin receptor — a transmembrane tyrosine kinase — initiating autophosphorylation and downstream signalling through insulin receptor substrates (IRS) and phosphoinositide, 3, kinase (PI3K)—Akt pathways to promote glucose uptake, glycogen synthesis, and lipid metabolism (8). In T2DM, chronic nutrient excess, mitochondrial dysfunction, lipotoxicity, and endoplasmic reticulum (ER) stress impair these signalling cascades, resulting in reduced glucose transport and increased hepatic glucose output (9,10). Activation of pro, inflammatory cytokines, oxidative stress, and protein kinase C (PKC) pathways further exacerbate insulin resistance, contributing to endothelial dysfunction and accelerating vascular complications (11,12). Oxidative stress, in particular, plays a dual role — not only driving insulin resistance and  $\beta$ , cell apoptosis but also perpetuating inflammation, creating a vicious cycle that worsens glycaemic control (13).

Although synthetic antidiabetic agents and exogenous insulin remain the cornerstones of diabetes management, they are not without limitations. Issues such as high cost, limited accessibility in low, and middle, income countries, adverse effects (e.g., hypoglycaemia, gastrointestinal disturbances, weight gain), and declining patient adherence have prompted growing interest in complementary therapeutic approaches (14,15). In this context, medicinal plants and their bioactive phytochemicals have emerged as promising adjuncts or alternatives to conventional treatments. Globally, more than 28,000 plant species are documented to have medicinal use (16). Many of these plants — including Gymnema sylvestre, Momordica charantia, Trigonella foenum, graecum, and Phyllanthus spp. — have demonstrated hypoglycaemic, antioxidant, and anti, inflammatory activities in preclinical models (17–19). Their mechanisms include inhibition of carbohydrate, digesting enzymes ( $\alpha$ , amylase and  $\alpha$ , glucosidase), enhancement of insulin secretion and sensitivity, modulation of glucose transporters (e.g., GLUT4), attenuation of oxidative stress, and protection of  $\beta$ , cell function (20–22).

Recent advances in phytochemistry and molecular pharmacology have also deepened understanding of how specific plant, derived compounds — such as polyphenols, terpenoids, alkaloids, saponins, and stilbenes — target key molecular pathways implicated in T2DM pathogenesis (23,24). These compounds can modulate PKC signalling, inhibit pro, oxidant enzymes, and regulate transcription factors like NF, κB and Nrf2, thereby reducing inflammation, oxidative damage, and insulin resistance (25,26). Moreover, emerging evidence suggests that phytochemicals may exert beneficial epigenetic and gut microbiome, modulating effects, expanding their potential beyond glycaemic control alone (27).

Given the global rise in diabetes prevalence, the limitations of current therapies, and the mechanistic diversity of plant, derived interventions, a systematic appraisal of medicinal plants and their bioactive constituents is both timely and necessary. This review aims to comprehensively examine the therapeutic potential of medicinal plants in diabetes management, highlight their molecular targets and mechanisms of action, and identify key translational gaps that must be addressed to advance their clinical utility.

# MATERIALS AND METHODS

This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta, Analyses (PRISMA) guidelines to ensure transparency, reproducibility, and methodological rigour (1). A comprehensive literature search was performed across multiple electronic databases including PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar to identify relevant studies published between January 2010 and September 2025. The search was last updated on September 15, 2025.

# Search Strategy

The search strategy combined controlled vocabulary terms (MeSH) and free, text keywords related to diabetes mellitus, medicinal plants, and phytochemicals. Boolean operators (AND/OR) were used to enhance the search sensitivity and specificity. The primary search terms included:

("diabetes mellitus" OR "type 2 diabetes" OR "hyperglycemia") AND

("medicinal plants" OR "herbal medicine" OR "phytotherapy" OR "natural products" OR "phytochemicals") AND

("antidiabetic activity" OR "glucose metabolism" OR "insulin resistance" OR "oxidative stress")

Search filters were applied to include only peer, reviewed original articles, systematic reviews, meta, analyses, and clinical or preclinical studies published in English. Reference lists of included studies and relevant review articles were also screened manually to identify additional studies.

# Inclusion and Exclusion Criteria

- Studies were included if they met the following criteria:
- Investigated medicinal plants, plant extracts, or isolated phytochemicals for the management, prevention, or treatment of diabetes mellitus.
- Reported in vitro, in vivo (animal), or human clinical evidence of antidiabetic effects.
- Published between 2010 and 2025 in peer, reviewed journals.

# Exclusion criteria included:

- Studies lacking sufficient methodological details or mechanistic data.
- Reports focusing on synthetic compounds or non, plant, based therapies.
- Non, English publications, conference abstracts, editorials, and commentaries.

# **Study Selection**

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All identified records were imported into EndNote (v20) for reference management. Two independent reviewers (AH and AA) screened titles and abstracts for relevance. Full texts of potentially eligible articles were then assessed against the inclusion criteria. Disagreements were resolved through discussion with a third reviewer (MQ). A PRISMA flow diagram was generated to illustrate the study selection process.

#### Data Extraction and Synthesis

From each eligible study, data was extracted using a standardized form capturing:

- Plant species and family
- Part used and extraction method
- Identified phytoconstituents
- Study model (in vitro, in vivo, or clinical)
- Mechanisms of action (e.g., insulin secretion, glucose uptake, oxidative stress modulation)
- Primary outcomes (e.g., fasting blood glucose, HbA1c, insulin sensitivity markers)

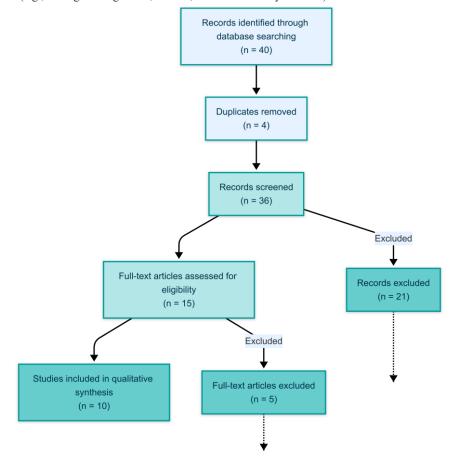


Figure 1 Review Flowchart

Extracted data were synthesized qualitatively due to heterogeneity in study designs, plant preparations, doses, and outcome measures. Where available, mechanistic insights were integrated to provide a molecular framework for understanding the antidiabetic effects of phytochemicals. The quality of included studies was appraised using the Joanna Briggs Institute (JBI) Critical Appraisal Tools for preclinical and clinical research (2).

# RESULTS

Following a systematic search strategy, 10 primary studies and several high, quality secondary sources published between 2010 and 2025 were included. These studies collectively investigated the antidiabetic activity of medicinal plants and their phytoconstituents through in vitro, in vivo, and limited clinical models. The PRISMA flow diagram summarising the screening and selection process is presented in Figure 1.

Across the included studies, plant, derived extracts demonstrated substantial hypoglycaemic effects, often comparable to or synergistic with conventional antidiabetic agents. These effects are typically mediated by stimulating insulin secretion, enhancing glucose uptake, regenerating pancreatic  $\beta$ , cells, or suppressing hepatic gluconeogenesis.

For instance, aqueous root bark extract of Afzelia africana significantly decreased fasting blood glucose (FBG) and prevented diabetes, related complications when administered at 100-200 mg/kg for 10 days in streptozotocin (STZ), induced diabetic rats (p < 0.05) (6). Similarly, ethanolic root extract of Helicteres angustifolia enhanced hepatic glucose uptake and reduced insulin resistance at 200-400 mg/kg over 28 days (7). Aqueous extract of Urtica dioica leaves exhibited rapid onset of hypoglycaemic action within 30 minutes post, administration, with effects lasting up to 3 hours (8). Other studies reported hepatoprotective effects, such as the reduction of AST and ALT following treatment with Chloroxylon swietenia extracts (9), and regeneration of pancreatic  $\beta$ , cells with Aloe vera extract (10).

Table 1. Selected medicinal plants with glucose, lowering activity |

Plant species (family)	Part used	Extract type	Dose & Duration	Major Outcomes
Afzelia africana (Fabaceae)	Root bark	Aqueous	100-200 mg/kg, 10 days	↓ FBG, ↓ diabetic complications
Helicteres angustifolia (Sterculiaceae)	Root	Ethanol	200-400 mg/kg, 28 days	↑ Hepatic glucose uptake, ↓ insulin resistance
Urtica dioica (Urticaceae)	Leaves	Aqueous	200 mg/kg, single dose	Rapid hypoglycaemia (30 min), effect > 3 h
Chloroxylon swietenia (Rutaceae)	Root bark	Aqueous	200-400 mg/kg, 14 days	↓ FBG, ↓ AST/ALT
Aloe vera (Liliaceae)	Whole plant	Ethanol	300 mg/kg	$\uparrow \beta$ , cell regeneration, $\uparrow$ insulin

Modulation of Insulin Secretion and Sensitivity

Improving insulin dynamics is a major therapeutic goal in type 2 diabetes mellitus (T2DM). Several plant, derived agents demonstrated insulinotropic or insulin, sensitizing effects. Ethanolic extract of Anacardium occidentale significantly reduced fasting glucose and plasma insulin levels, indicating improved receptor sensitivity (11). Extracts of Allium sativum promoted glycogenesis and upregulated GLUT4 expression in skeletal muscle, contributing to improved glucose disposal (12). Moreover, Symplocos cochinchinensis extracts enhanced insulin sensitivity while reducing circulating insulin levels in diet, induced insulin, resistant models (13). Resveratrol, a polyphenol from Vitis vinifera, increased glucose uptake independently of insulin and augmented insulin receptor sensitivity (14).

Table 2. Plant extracts and compounds targeting insulin secretion and sensitivity |

Plant / Compound	Mechanism	Dose & Model	Major Outcomes
Anacardium occidentale	↑ Insulin sensitivity	100 mg/kg, neonatal rats	↓ FBG, ↓ plasma insulin
Allium sativum	↑ GLUT4, ↑ glycogenesis	STZ rats	↓ Blood glucose, ↑ muscle glucose uptake
Symplocos cochinchinensis	↓ Insulin resistance	250-500 mg/kg/day, diet, induced IR rats	↓ Plasma insulin, ↑ receptor sensitivity
Resveratrol (Vitis vinifera)	Insulin, mimetic activity	10–50 mg/kg	↑ Glucose uptake, ↑ insulin receptor sensitivity

Beyond direct insulin modulation, certain plants act by regulating carbohydrate digestion and absorption. Phyllanthus urinaria demonstrated significant  $\alpha$ , amylase and  $\alpha$ , glucosidase inhibition through compounds such as macatannin B, gallic acid, and corilagin (15). Ocimum basilicum extract enhanced hepatic glycogenesis and reduced glucose output in alloxan, induced diabetic rats (16). Corchorus olitorius seed extract, rich in anthraquinones and flavonoids, significantly decreased FBG levels and oxidative stress (17).



Figure 2 -Representative medicinal plants and natural sources with documented antidiabetic activity. (A) Afzelia africana (Fabaceae), (B) Helicteres angustifolia (Sterculiaceae), (C) Urtica dioica (Urticaceae), (D) Chloroxylon swietenia (Rutaceae), (F) Aloe vera (Liliaceae), (G) Anacardium occidentale (Anacardiaceae), (H) Allium sativum (Alliaceae), (I) Symplocos cochinchinensis (Symplocaceae), (J) Vitis vinifera (Vitaceae; resveratrol source), (K) Phyllanthus urinaria (Euphorbiaceae), (L) Ocimum basilicum (Lamiaceae), and (M) Corchorus olitorius (Tiliaceae). These plants and their phytoconstituents exhibit glucose, lowering, insulin, sensitizing, enzyme, inhibitory, and antioxidant effects, underscoring their potential as complementary therapeutic agents in diabetes management.

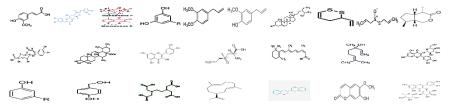


Figure 3 -Representative bioactive phytoconstituents isolated from antidiabetic medicinal plants. From left to right: Ferulic acid – a phenolic compound with antioxidant and glucose, lowering activity; Mansonone E and F – sesquiterpenoid derivatives with  $\beta$ , cell protective properties; Quercetin – a flavonoid known to enhance GLUT4 translocation and improve insulin sensitivity; Rutin – a glycosylated flavonoid exhibiting  $\alpha$ , glucosidase inhibitory activity;  $\beta$ , Sitosterol – a plant sterol with insulin, sensitizing effects; Ursolic acid – a pentacyclic triterpenoid modulating insulin signaling and oxidative stress; Allicin and ajoene – sulfur, containing compounds from Allium sativum with hypoglycaemic and lipid, lowering actions; Vinyldithiins – organosulfur derivatives that promote glycogenesis; Eugenol and methyl eugenol – phenylpropanoids that exert anti, inflammatory and insulin, sensitizing effects; Resveratrol – a stilbene polyphenol that enhances glucose uptake and insulin receptor signaling; Scopoletin – a coumarin derivative that improves glucose homeostasis; and Corilagin – a hydrolysable tannin demonstrating strong  $\alpha$ , amylase and  $\alpha$ , glucosidase inhibition. These diverse compounds act via multiple mechanisms including oxidative stress attenuation, modulation of insulin signaling, carbohydrate enzyme inhibition, and enhancement of peripheral glucose utilization.

8 Numerous phytochemicals have been isolated from antidiabetic plants, each exerting unique effects on glucose homeostasis and metabolic regulation. Phenolic compounds such as ferulic acid and quercetin scavenge reactive oxygen species and enhance insulin signaling. Flavonoids like rutin inhibit carbohydrate, digesting enzymes, while ursolic acid and  $\beta$ , sitosterol improve insulin sensitivity and lipid metabolism. Sulfur, containing compounds such as allicin and ajoene enhance glycogenesis and reduce oxidative stress, whereas resveratrol and scopoletin modulate cellular signaling cascades involved in glucose uptake and inflammation (20–22).

These phytochemicals target multiple pathways simultaneously — including  $\beta$ , cell regeneration, GLUT4 translocation, inhibition of  $\alpha$ , glucosidase and  $\alpha$ , amylase, modulation of inflammatory signaling (e.g., NF,  $\kappa$ B), and upregulation of antioxidant defenses (e.g., Nrf2). Their pleiotropic nature

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positions them as promising lead compounds for multi, target antidiabetic drug development. Morphological Diversity of Antidiabetic Plants The plants from which these bioactive molecules are derived exhibit significant morphological and taxonomic diversity, spanning multiple families including Fabaceae, Sterculiaceae, Lamiaceae, Euphorbiaceae, and Vitaceae. Their distribution across phylogenetically distinct groups underscores the evolutionary convergence of metabolic regulatory mechanisms in nature. This diversity also highlights a key translational opportunity: phytochemicals from unrelated species often share structural motifs and bioactivities, allowing for synergistic effects when used in poly, herbal formulations.

# DISCUSSION

Diabetes mellitus represents one of the most complex and burdensome metabolic disorders of the 21st century, with profound clinical, social, and economic implications. Characterised by chronic hyperglycaemia resulting from defects in insulin secretion, insulin action, or both, diabetes affects virtually every organ system, leading to complications including nephropathy, neuropathy, retinopathy, and cardiovascular disease (1,2). Despite significant advances in pharmacotherapy, current treatment regimens often face challenges such as drug resistance, adverse effects, cost constraints, and limited accessibility, particularly in low, and middle, income countries. Against this backdrop, the therapeutic potential of medicinal plants and their bioactive constituents has attracted increasing attention as a complementary or alternative strategy for diabetes management (3,4). Mechanistic Diversity of Plant, Derived Antidiabetic Agents

One of the most compelling features of phytotherapeutics is their ability to target multiple pathophysiological pathways simultaneously. Unlike many synthetic drugs designed to act on single molecular targets, plant, derived compounds exhibit polypharmacological actions that reflect the multifactorial nature of diabetes. The present review highlights four major mechanistic domains where medicinal plants exert their effects: (i) stimulation of insulin secretion, (ii) enhancement of insulin sensitivity, (iii) modulation of carbohydrate digestion and glucose absorption, and (iv) attenuation of oxidative stress and inflammation.

Several phytochemicals, including flavonoids (e.g., quercetin, rutin), triterpenoids (e.g., ursolic acid), and phenolics (e.g., ferulic acid), have demonstrated the ability to stimulate pancreatic  $\beta$ , cell regeneration or enhance insulin biosynthesis (5–7). This is particularly relevant in the early stages of type 2 diabetes mellitus (T2DM), where residual  $\beta$ , cell function can still be harnessed to improve endogenous insulin output. Similarly, plant sterols such as  $\beta$ , sitosterol and polyphenols like resveratrol have been shown to enhance insulin receptor signalling and downstream glucose transporter (GLUT4) translocation, thereby improving peripheral glucose uptake (8,9). Such mechanisms are crucial for overcoming insulin resistance, a defining feature of T2DM and a primary driver of disease progression.

Equally important is the role of phytochemicals in modulating carbohydrate metabolism. Compounds such as corilagin and macatannin B exhibit inhibitory activity against  $\alpha$ , amylase and  $\alpha$ , glucosidase, two key digestive enzymes responsible for carbohydrate breakdown and glucose absorption (10). By slowing the postprandial rise in blood glucose, these natural enzyme inhibitors mimic the mechanism of clinically used drugs like acarbose but often with fewer gastrointestinal side effects. Moreover, the capacity of plant extracts to enhance glycogenesis and suppress hepatic gluconeogenesis — as demonstrated by Ocimum basilicum and Phyllanthus urinaria — represents an additional layer of metabolic regulation (11,12).

Chronic oxidative stress and low, grade inflammation are now recognised as central contributors to the onset and progression of diabetes and its complications. Hyperglycaemia, induced overproduction of reactive oxygen species (ROS) activates inflammatory signalling pathways such as NF,  $\kappa B$  and JNK, exacerbating insulin resistance, endothelial dysfunction, and  $\beta$ , cell apoptosis (13). Phytochemicals with strong antioxidant activity — including quercetin, scopoletin, and resveratrol — mitigate these effects by neutralising ROS and upregulating endogenous antioxidant enzymes like superoxide dismutase (SOD) and catalase (14). In addition, some compounds modulate key transcription factors such as Nrf2, enhancing cellular defence mechanisms and reducing inflammation, mediated tissue damage (15).

The anti, inflammatory properties of many plant, derived metabolites further extend their therapeutic potential beyond glycaemic control. For example, eugenol and methyl eugenol suppress pro, inflammatory cytokines such as TNF,  $\alpha$  and IL, 6, which are closely linked to insulin resistance and endothelial dysfunction (16). By addressing oxidative stress and inflammation concurrently, these agents not only improve metabolic outcomes but also contribute to the prevention of diabetic complications — a dimension often overlooked in conventional pharmacotherapy.

While preclinical studies have provided compelling evidence for the efficacy of medicinal plants in glucose regulation, their translation into clinical practice remains limited. Nevertheless, several clinical trials have demonstrated encouraging results. Extracts of Allium sativum have been shown to reduce fasting blood glucose and improve lipid profiles in patients with T2DM, while resveratrol supplementation has been associated with improved insulin sensitivity and reduced oxidative stress markers in humans (17,18). Such findings underscore the translational promise of phytotherapeutics, particularly as adjuncts to standard care. An important advantage of plant, based therapies lies in their accessibility and cost, effectiveness. In many regions, especially in low, resource settings, herbal preparations represent the primary or sole option for diabetes management. Furthermore, the lower incidence of adverse effects compared with synthetic drugs enhances patient adherence and long, term tolerability (19). The potential for synergistic interactions among phytochemicals — either within a single plant or in polyherbal formulations — also opens avenues for more effective, multi, targeted interventions (20).

Despite these advantages, several challenges must be addressed before medicinal plants can be fully integrated into mainstream diabetes care. One major limitation is the variability in phytochemical composition due to factors such as plant species, geographical origin, harvesting time, and extraction methods (21). Such variability complicates standardisation, dosage determination, and reproducibility of clinical outcomes. Furthermore, the pharmacokinetics and bioavailability of many phytochemicals remain poorly understood, limiting their efficacy when administered orally.

Another critical gap is the lack of large, scale, randomised controlled trials (RCTs) evaluating the safety and efficacy of these agents in human populations. Most available studies are preclinical or involve small sample sizes, limiting the generalisability of findings (22). Additionally, herbdrug interactions are an underexplored area of research. Since many patients use herbal preparations alongside conventional antidiabetic drugs, understanding potential synergistic or antagonistic effects is essential for clinical safety (23).

Future research should focus on overcoming these limitations through multidisciplinary approaches. Advanced techniques such as metabolomics, transcriptomics, and molecular docking can provide deeper insights into the mechanisms of action and molecular targets of phytochemicals. Standardisation of plant extracts and rigorous characterisation of active constituents are necessary to ensure consistency across studies. Moreover,

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formulation science — including nanoencapsulation and targeted delivery systems — offers promising solutions to improve the bioavailability and pharmacokinetics of plant, derived compounds (24).

Clinical research should prioritise well, designed RCTs that evaluate not only glycaemic outcomes but also broader metabolic, inflammatory, and cardiovascular endpoints. Integrating traditional knowledge with modern drug discovery pipelines can accelerate the identification of novel lead compounds. Lastly, regulatory frameworks must evolve to accommodate evidence, based phytomedicine, ensuring quality, safety, and efficacy without imposing prohibitive barriers to innovation.

# **CONCLUSION AND FUTURE PERSPECTIVES**

Diabetes mellitus remains a critical global health challenge, with its prevalence and associated complications continuing to rise despite advances in conventional therapy. The evidence presented in this review highlights the substantial therapeutic promise of medicinal plants and their phytoconstituents in addressing the multifactorial nature of this disease. Through diverse mechanisms — including stimulation of insulin secretion, enhancement of receptor sensitivity, modulation of glucose metabolism, inhibition of key digestive enzymes, and attenuation of oxidative stress and inflammation — plant, derived compounds target multiple pathological pathways simultaneously. This multimodal activity not only offers superior metabolic regulation but also holds potential to delay or prevent secondary complications associated with chronic hyperglycaemia.

Importantly, the accessibility, cost, effectiveness, and generally favourable safety profile of herbal medicines make them especially relevant in low, and middle, income countries, where access to advanced therapies remains limited. However, several barriers continue to impede their clinical translation. These include variability in phytochemical content, poor bioavailability, limited pharmacokinetic data, and a paucity of large, scale, well, designed clinical trials. Addressing these challenges will require rigorous standardisation protocols, innovative formulation strategies, and integration of modern omics, based approaches to elucidate precise molecular targets.

Future research should also explore synergistic effects between phytochemicals and existing antidiabetic agents, optimise dosing regimens, and investigate long, term safety outcomes. Establishing clear regulatory frameworks and evidence, based guidelines for herbal interventions will further accelerate their acceptance in mainstream diabetes care. Ultimately, the convergence of traditional knowledge with modern pharmacological science offers a powerful avenue for developing next, generation, plant, based therapeutics. By bridging these domains, medicinal plants may transition from complementary options to integral components of comprehensive, patient, centred diabetes management strategies.

## REFERENCES

- 1. Berg JM, Tymoczko JL, Stryer L. Biochemistry. 5th ed. New York: W.H. Freeman and Company; 2002.
- Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care. 2003;26(Suppl 1):S5–20.
- 3. World Health Organization. Global Diabetes Compact: Preventing and managing diabetes worldwide. Geneva: WHO; 2024. Available from: <a href="https://www.who.int/">https://www.who.int/</a>
- 4. Zahory D, Hopf M. Domestication of plants in the Old World. 3rd ed. Oxford: Oxford University Press; 2000.
- 5. Soumyanth A. Traditional Medicines for Modern Times: Antidiabetic Plants. Boca Raton: CRC Press; 2006.
- 6. Oyedemi SO, Adewusi EA, Aiyegoro OA, Akinpelu DA. Antidiabetic and haematological effect of aqueous extract of stem bark of Afzelia africana on streptozotocin–induced diabetic Wistar rats. Asian Pac J Trop Biomed. 2011;1(5):353–8.
- 7. Hu X, Cheng D, Zhang Z. Antidiabetic activity of Helicteres angustifolia root. Pharm Biol. 2016;54(6):938-44.
- 8. Shao GN, Kim H, Imran SM. Hypoglycaemic effects of Urtica dioica extract in diabetic rats. Process Biochem. 2016;51(8):1101–7.
- 9. Kadali SDRM, Das MC, Vijayaraghavan R, Kumar MV. Evaluation of antidiabetic activity of aqueous and ethanolic extracts of leaves of Chloroxylon swietenia in streptozotocin, induced diabetes in albino rats. Biomed Pharmacol J. 2017;10(3):1347–53.
- 10. Pothuraju R, Sharma RK, Onteru SK, Singh S, Hussain SA. Hypoglycaemic and hypolipidaemic effects of Aloe vera extract preparations: A review. Phytother Res. 2016;30(2):200–7.
- 11. Jaiswal YS, Tatke PA, Gabhe SY, Vaidya AB. Antidiabetic activity of extracts of Anacardium occidentale Linn. leaves on streptozotocin, induced diabetic rats. J Tradit Complement Med. 2017;7(4):421–7.
- 12. Liu CT, Hsu TW, Chen KM, Tan YP, Lii CK, Sheen LY. Antidiabetic effect of garlic oil is associated with ameliorated oxidative stress but not reduced pro, inflammatory cytokines in skeletal muscle of diabetic rats. J Tradit Complement Med. 2012;2(2):135–44.
- 13. Antu KA, Riya MP, Nair A, Mishra A, Srivastava AK, Raghu KG. Symplocos cochinchinensis enhances insulin sensitivity via downregulation of lipogenesis and insulin resistance in high, energy diet rat model. J Ethnopharmacol. 2016;193:500–9.
- 14. Palsamy P, Subramanian S. Resveratrol normalises hyperglycaemia in streptozotocin–nicotinamide induced experimental diabetic rats. Biomed Pharmacother. 2008;62(9):598–605.
- 15. Gunawan, Puteri MD, Kato E, Kawabata J. α, Amylase inhibitors from an Indonesian medicinal herb, Phyllanthus urinaria. J Sci Food Agric. 2012;92(3):606–9.
- 16. Ezeani C, Ezenyi I, Okoye T, Okoli C. Ocimum basilicum extract exhibits antidiabetic effects via inhibition of hepatic glucose mobilisation and carbohydrate metabolising enzymes. J Intercult Ethnopharmacol. 2017;6(1):22–7.
- 17. Egua MO, Etuk EU, Bello SO, Hassan SW. Anti, diabetic activity of ethanolic seed extract of Corchorus olitorius. Int J Sci Basic Appl Res. 2013;12(1):8–21.
- 18. Hussain AI, Anwar F, Sherazi STH, Przybylski R. Chemical composition, antioxidant and antimicrobial activities of basil (Ocimum basilicum) essential oils depend on seasonal variations. Food Chem. 2008;108(3):986–95.
- 19. El, Saber Batiha G, Beshbishy AM, Wasef LG, Elewa YH, Al, Sagan AA, El, Hack A, et al. Chemical constituents and pharmacological activities of garlic (Allium sativum L.): A review. Nutrients. 2020;12(3):872.
- 20. Martins N, Petropoulos S, Ferreira IC. Chemical composition and bioactive compounds of garlic (Allium sativum L.) as affected by pre, and post, harvest conditions: A review. Food Chem. 2016;211:41–50.
- 21. Zhang LZ, Guo YJ, Tu GZ, Guo WB, Miao F. Studies on chemical constituents of Phyllanthus urinaria L. Zhongguo Zhong Yao Za Zhi. 2000;25(10):615–7.

Hussain et al. https://doi.org/10.61919/ectdsm0

22. Khair, ul, Bariyah S, Ahmed D, Ikram M. Ocimum basilicum: A review on phytochemical and pharmacological studies. Pak J Chem. 2012;2(2):78–85.

- 23. Azuma K, Nakayama M, Koshioka M, Ippoushi K, Yamaguchi Y, Kohata K, et al. Phenolic antioxidants from the leaves of Corchorus olitorius L. J Agric Food Chem. 1999;47(10):3963–6.
- 24. Palsamy P, Subramanian S. Modulation of oxidative stress and inflammatory markers by plant, derived polyphenols in diabetes management. Acta Diabetol. 2022;59(6):729–41.
- 25. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation; 2025. Available from: https://diabetesatlas.org/
- 26. Our World in Data. Diabetes prevalence (2025 update). Oxford: Global Change Data Lab; 2025. Available from: https://ourworldindata.org/