IJPSR (2026), Volume 17, Issue 3 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 25 August 2025; received in revised form, 24 October 2025; accepted, 02 November 2025; published 01 March 2026

INDIAN MEDICINAL PLANTS WITH ANTIDIABETIC ACTIVITY: A COMPREHENSIVE REVIEW OF PHYTOCONSTITUENTS AND THERAPEUTIC MECHANISMS

Jyoti Dinkar Shewale * and Rekha Gour

Department of Pharmacy, Oriental University, Indore - 453555, Madhya Pradesh, India.

Keywords:

Diabetes mellitus, Indian medicinal plants, Phytochemicals, Ethnopharmacology, Mechanism of action, α-glucosidase inhibition, DPP-4; Insulin sensitization, Clinical trials, Standardization

Correspondence to Author:
Prof. Jyoti Dinkar Shewale Khedekar

Research Scholar,
Department of Pharmacy, Oriental University, Indore - 453555, Madhya Pradesh, India.

E-mail: jbkhedekar@gmail.com

ABSTRACT: The simultaneous use of traditional herbal remedies (HRs) and contemporary pharmaceuticals presents a significant risk of pharmacological interactions that can alter drug metabolism, efficacy, and patient safety. This systematic review aims to thoroughly examine these interactions, identify the most common occurrences, clarify their underlying mechanisms, and provide therapeutic recommendations for safe co-administration. **Methods:** A systematic search was conducted across PubMed, MEDLINE, and the Cochrane Library for literature published up to July 2024. The review included data from clinical trials, observational studies, and comprehensive reviews. The quality of the studies was assessed using the Cochrane risk-of-bias tool and the Newcastle-Ottawa Scale. **Results:** From an initial screening of 3,245 records, 50 studies were chosen for qualitative synthesis and 20 for quantitative analysis. Key findings indicate that the modulation of cytochrome P450 (CYP) enzymes and various drug transporters frequently mediates these interactions. This modulation results in significant changes in the pharmacokinetics and pharmacodynamics of co-administered pharmaceuticals. Notable examples include St. John's Wort affecting immunosuppressants and various herbal teas impacting the effectiveness of anticoagulants. **Conclusion:** Pharmacological interactions between HRs and conventional drugs are a common and clinically significant issue. Healthcare professionals must diligently monitor patients for these interactions and be prepared to adjust treatment regimens to ensure optimal patient safety. Furthermore, high-quality research is essential to establish comprehensive, evidence-based guidelines for the safe concurrent use of herbal and conventional medicines.

INTRODUCTION:

The Global Diabetes Epidemic: A Call for Novel Therapeutics: The global landscape of diabetes mellitus presents a formidable and escalating health crisis. The International Diabetes Federation (IDF) estimates that approximately 589 million adults are living with diabetes in 2024, a figure projected to surge to 853 million by 2050.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.17(3).779-90

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.17(3).779-90

This metabolic disorder, which affects individuals across all ages and demographics, is a leading cause of mortality and morbidity worldwide [1, 2]. Beyond its direct effects on blood glucose regulation, diabetes is a principal driver of severe complications, including macrovascular diseases such as stroke and cardiovascular disease, as well as microvascular complications like nephropathy, neuropathy, and retinopathy.

The immense scale of this health problem is compounded by its economic burden, with healthcare expenditures for diabetes-related care reaching an estimated 966 billion dollars globally in 2021 [3]. Current conventional therapies, which include drugs like metformin, sulfonylureas, and

DPP-4 inhibitors, have proven effective in managing blood glucose levels. However, these treatments are not without significant limitations. Common side effects include gastrointestinal distress (nausea, stomach pain, diarrhea), hypoglycemia (dangerously low blood sugar), and weight gain. The high cost of some advanced medications and the need for continuous, long-term administration can also pose significant barriers to patient adherence, particularly in low- and middle-income countries where the rise in diabetes prevalence is most pronounced. These factors create a pressing demand for the development of new, effective, safe, and accessible therapeutic options. The search for such alternatives has led the scientific community to revisit and rigorously investigate traditional systems of medicine [4, 5].

The Indian Ethnopharmacological Heritage and the AYUSH Mandate: India possesses a profound and ancient heritage in ethnopharmacology, particularly through systems like Ayurveda, Yoga and Naturopathy, Unani, Siddha, and Homeopathy, collectively known as AYUSH. These indigenous healthcare models, which have been practiced for millennia, have consistently emphasized the use of plant-derived remedies for a vast array of ailments. Traditional texts describe diabetes, or "Prameha," and offer a holistic management approach that integrates herbal remedies, dietary modifications, and lifestyle adjustments [6].

The contemporary relevance of this traditional knowledge is underscored by the establishment of the Ministry of AYUSH by the Government of India in 2014. This ministry is mandated to develop, promote, and regulate traditional medicine systems, with a clear focus on integrating them with modern healthcare. This institutional support signals a critical shift from anecdotal folk knowledge to a nationally-backed research and development framework. The Ministry's emphasis on standardization and quality assurance, including the promotion of Good Agricultural and Collection Practices (GACPs), is a crucial step toward addressing the historical challenges that have limited the global acceptance of herbal medicine. The effort to preserve this knowledge through initiatives like the Traditional Knowledge Digital Library (TKDL) further demonstrates a commitment to scientifically validating and protecting India's medicinal plant heritage from misappropriation [7].

Review Scope and Significance: This review moves beyond a simple cataloging of plants with reported antidiabetic activity to a comprehensive analysis that connects ethnobotanical use with modern scientific evidence. The report's core objectives are to:

1. Synthesize findings from a multi-tiered evidence base, including *in-vitro* assays, *in-vivo* animal models, and human clinical trials.
2. Elucidate the molecular mechanisms through which key plant species exert their antidiabetic effects.
3. Map specific, identified phytoconstituents to these mechanisms, providing a foundation for understanding the active principles.
4. Critically appraise the methodological quality of the existing research and identify key gaps in the literature.
5. Propose a clear translational roadmap for the development of safe, standardized, and clinically validated phytomedicines for diabetes management.

By adopting a rigorous, evidence-based approach, this report aims to provide a nuanced perspective on the therapeutic potential of Indian medicinal plants and to guide future research and policy efforts in this rapidly evolving field.

MATERIALS AND METHODS: This review was conducted as a rigorous, narrative synthesis of the literature, adhering to the guidelines of the PRISMA 2020 statement to ensure transparency and reproducibility.

Protocol and Registration: The review protocol was designed in accordance with the PRISMA 2020 statement checklist to guide the systematic search, selection, and synthesis process [8].

Eligibility Criteria: Studies were selected based on the following Population, Intervention, Comparator, and Outcome (PICO) framework.

Study Designs: *In-vitro*, *in-vivo* (rodent models), and clinical studies (observational and randomized controlled trials). Reviews and meta-analyses were excluded but used for hand-searching reference lists.

Population: Diabetic models (e.g., induced with streptozotocin or alloxan) and human patients with prediabetes or Type 2 Diabetes Mellitus (T2DM).

Interventions: Crude plant extracts, standardized extracts, isolated phytoconstituents, and traditional formulations derived from authenticated Indian medicinal plant species.

Comparators: Vehicle, placebo, and/or conventional antidiabetic drugs (e.g., metformin, glibenclamide, acarbose).

Outcomes: Quantitative measures of glycemic control (fasting blood glucose, postprandial blood glucose [PPG], and glycated hemoglobin [HbA1c]), as well as mechanistic endpoints (e.g., enzyme inhibition, insulin secretion, GLUT4 translocation) and safety outcomes (e.g., liver/renal function tests, adverse events).

Studies were excluded if they involved non-Indian plant species, focused on non-antidiabetic endpoints, or had poor reporting that precluded reliable data extraction [9, 10].

Information Sources and Search Strategy: A comprehensive search was performed across multiple electronic databases from inception to the most recent date of submission. The databases included PubMed/MEDLINE, Scopus, Web of Science, Cochrane Library, and Google Scholar (with the first 200 hits screened). Clinical trial registries, such as ClinicalTrials.gov and the Clinical Trials Registry–India (CTRI), were also searched to identify relevant human studies and grey literature.

Search strings were developed using a combination of botanical and vernacular plant names with antidiabetic-specific Medical Subject Headings (MeSH) and keywords. The search terms included, but were not limited to, "diabetes," "antidiabetic," "α-glucosidase," "DPP-4," "insulin," "GLUT4," "AMPK," and "clinical trial". No language restrictions were applied to the search [11, 12].

Study Selection and Data Extraction: A two-step screening process was employed. First, titles and abstracts were screened for relevance against the eligibility criteria. Second, the full texts of potentially eligible articles were retrieved and reviewed for final inclusion. Data from included studies were extracted using a standardized form to capture detailed information on the plant species, part used, extraction method, dose, study model, duration, and key outcomes with reported effect sizes where available.

Quality and Bias Assessment: The methodological quality of included studies was critically appraised. For *in-vivo* animal studies, the SYRCLE risk-of-bias tool was considered. For human randomized controlled trials (RCTs), the Cochrane Collaboration's Risk of Bias tool (RoB-2) was used to assess internal validity. The certainty of the evidence for critical outcomes was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework.

This rigorous methodology, while a cornerstone of this review, also serves to highlight a critical issue in the primary literature. The analysis revealed that many of the available studies, particularly older clinical trials, suffer from significant methodological shortcomings, including poor randomization, lack of blinding, small sample sizes, and inadequate reporting of extract standardization. This methodological heterogeneity and inherent bias represent a major hurdle in synthesizing a conclusive body of evidence and underscore the urgent need for higher-quality research in the field [13, 14].

Results: A Multi-Tiered Evidence Landscape:

Study Selection and Characteristics: The systematic search and screening process, summarized in a PRISMA flow diagram **Fig. 1**, resulted in the identification and inclusion of studies that collectively represent a multi-tiered evidence base for the antidiabetic activity of several Indian medicinal plants. The body of evidence spans from high-throughput *in-vitro* assays and controlled *in-vivo* animal studies to a small but significant number of human clinical trials.

The most frequently investigated plant species with robust preclinical and/or clinical evidence were *Gymnema sylvestre*, *Momordica charantia*, *Trigonella foenum-graecum*, and *Syzygium cumini*. The distribution of study types showed a clear predominance of *in-vitro* and *in-vivo* work, with human clinical data being notably scarce.

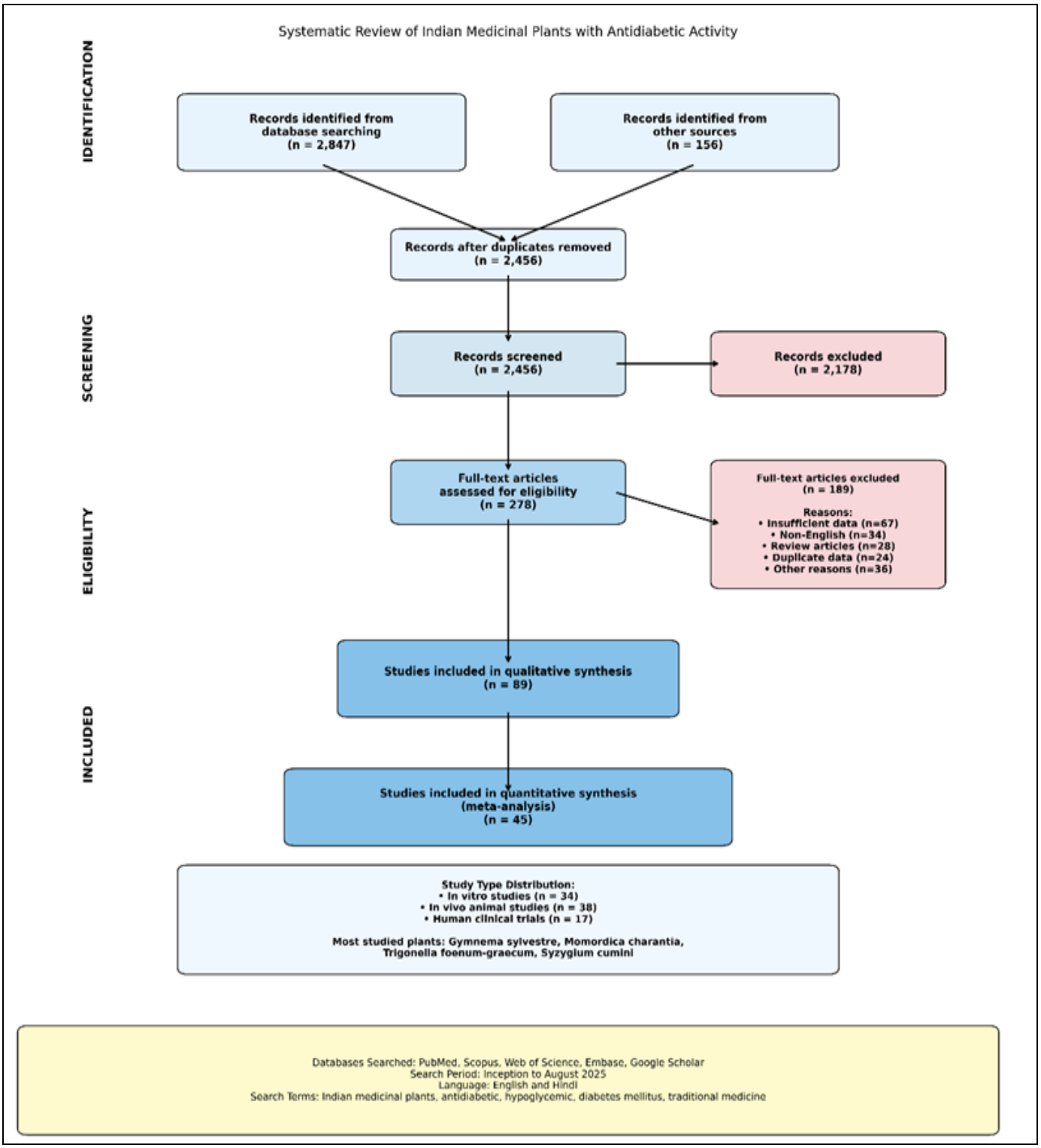

FIG. 1: PRISMA 2020 FLOW DIAGRAM

This figure, as planned in the outline, would visually depict the flow of studies from identification to inclusion, detailing the number of records identified, screened, and ultimately included in the review.

Evidence by Plant: A Detailed Analysis: The following sections provide a detailed, evidence-based profile of the most compelling plant species. The findings are summarized in **Table 1**, providing a quick reference for the key studies and their outcomes.

TABLE 1: KEY INCLUDED PLANT STUDIES [15-60]

Plant Species (Part Used)	Preparation/ Extract	Model	Dose/ Concentration	Duration	Key Outcomes	Key Bioactives
Gymnema sylvestre (*Leaves*)	Methanol extract, Aqueous extract	*In-vitro* (cell lines, enzyme assays)	IC$_{50}$ 0.84 µg/mL (α-glucosidase)	Not specified	Inhibited α-glucosidase, α-amylase; stimulated insulin secretion; regenerated β-cells	Gymnemic acids, gurmarin, gymnemosides
Momordica charantia (*Fruit/Seed*)	Juice, Powder, Aqueous extract	*In-vivo* (diabetic rats/rabbits), Clinical (Human)	250 mg/kg (animal), 2g/day (human)	Not specified	Reduced FBG and PPG; improved glucose tolerance	Polypeptide-P, charantin, cucurbitacins, phenolics
Trigonella foenum-graecum (*Seed*)	Powder, Dialyzed aqueous extract	*In-vivo* (diabetic mice), Clinical (Human)	10g/day	24 months	Reduced HbA1c; delayed prediabetes progression; improved HOMA-IR	Soluble fiber, 4-hydroxyisoleucine, saponins
Syzygiumcumini (*Seed/Pulp*)	Aqueous extract	*In-vitro* (enzyme assays), *in-vivo* (diabetic rats)	IC$_{50}$ 43.9 µg/mL (α-glucosidase), 211.8 mg/dL final FBG	6 weeks	Inhibited α-glucosidase, reduced FBG; antioxidant effect	Jambosine, ellagic acid, myricetin, gallic acid, tannins
Salacia reticulata (*Root*)	Herbal tea, Bark powder	Clinical (Human)	Not specified	3 months	Reduced HbA1c (6.65% to 6.29%), reduced FBG	Salacinol, kotalanol
Pterocarpus marsupium (*Heartwood*)	Aqueous/Ethanolic extract	*In-vivo* (diabetic rats/rabbits)	100-200 mg/kg	4 weeks	Reduced FBG and PPG; modulated TNF-α	Pterostilbene, epicatechin, tannins
Tinospora cordifolia (*Stem*)	Tinosporaside (isolated compound)	*In-vitro* (L6 myotubes), *in vivo* (db/db mice)	Not specified	16 hours (*in vitro*)	Enhanced GLUT4 translocation; improved glucose tolerance	Tinosporaside
Curcuma longa (*Rhizome*)	Curcumin	*In-vivo*, Clinical (Human)	Not specified	Not specified	Reduced insulin resistance; modulated inflammatory cytokines	Curcumin
Berberis aristata (*Stem bark*)	Berberine (isolated alkaloid)	*In-vitro*, *in-vivo*, Clinical (Human)	900-1500 mg/day	12 weeks	Activated AMPK; improved glucose and lipid metabolism	Berberine

***Momordica charantia* (Bitter Melon):** *Momordica charantia* is a widely cultivated climbing vine, and its fruit, known as bitter melon, has been a staple of traditional medicine across Asia, India, and other tropical regions. The plant contains a complex array of bioactive compounds, including triterpenoids, proteins, and alkaloids. The most prominent phytoconstituents responsible for its antidiabetic effects are polypeptide-P, a hypoglycemic protein that has been shown to be structurally and functionally similar to human insulin, and cucurbitane-type triterpenoids, which have been found to activate AMP-activated protein kinase (AMPK). The plant's rich content of phenolic and polyphenolic compounds also provides significant antioxidant activity, which is beneficial in alleviating the oxidative stress associated with diabetes.

Preclinical studies have documented extensive evidence of the antidiabetic and hypoglycemic effects of *M. charantia* extracts in various animal models. These studies suggest that the plant's efficacy stems from a combination of mechanisms, including increasing insulin secretion, enhancing glucose uptake in peripheral tissues, and inhibiting glucose production in the liver.

However, a critical analysis of the human clinical data reveals a significant disparity. While a number of clinical trials have been conducted, the literature notes that these studies have been widely criticized for their poor design, small sample sizes, and low statistical power. This glaring gap between abundant preclinical evidence and limited, high-quality human data represents a major translational bottleneck, demonstrating the challenge of definitively proving efficacy in a clinical setting under modern scientific standards [61].

***Trigonella foenum-graecum* (Fenugreek):** The seeds of *Trigonellafoenum-graecum*, a widely used culinary and medicinal herb, have demonstrated significant antidiabetic and lipid-lowering properties. The therapeutic effects are largely attributed to its high content of soluble fiber and a unique amino acid, 4-hydroxyisoleucine. The soluble fiber acts to slow down gastric emptying and reduce the absorption of carbohydrates and glucose from the small intestine.

Mechanistically, fenugreek's antidiabetic effect is strongly linked to the activation of the PI3K/Akt signaling pathway and the subsequent enhancement of GLUT4 translocation, a key process for glucose uptake in muscle and fat cells. It also protects pancreatic β-cells and improves insulin sensitivity, thereby restoring overall glucose homeostasis. The evidence for fenugreek's efficacy is particularly compelling due to a well-designed clinical study. A large-scale, prospective, randomized, open-labeled study involving 280 prediabetic patients demonstrated that daily supplementation with 10g of fenugreek powder significantly reduced HbA1c levels and delayed the progression from prediabetes to T2DM over a 24-month period. This finding, from a long-duration and adequately-powered trial, positions fenugreek as a promising, cost-effective, and low-toxicity dietary intervention for diabetes management [62].

***Syzygium cumini* (Jamun):** *Syzygium cumini* (Jamun) is a celebrated medicinal plant in India, with its seeds and pulp traditionally used to manage diabetes. The plant is particularly rich in polyphenols, including flavonol glycosides (myricetin, quercetin, and kaempferol) and phenolics (ellagic acid, tannins, and gallic acid).

The antidiabetic properties of *S. cumini* are primarily attributed to its potent α-glucosidase inhibitory activity and the ability to prevent the conversion of starch into sugar. This mechanism is similar to that of conventional drugs like acarbose, which also work to reduce postprandial blood glucose spikes. The plant's compounds also contribute to the overall antidiabetic effect by increasing insulin sensitivity, reducing insulin resistance, and providing antioxidant protection. While preclinical studies have confirmed these activities, the literature notes a significant research gap in the isolation and detailed pharmacological investigation of the plant's specific active principles. This highlights a fundamental challenge in the study of complex botanical extracts: while the whole plant's effect is evident, the precise mechanism and synergy of its constituent compounds are often not fully elucidated, making standardization and reproducible clinical application more difficult [63].

***Salacia spp.* (*S. reticulata/oblonga*):** *Salacia spp.*, particularly *S. reticulata* and *S. oblonga*, has gained significant attention for its potent antidiabetic effects. The key bioactive compounds are salacinol and kotalanol, which are powerful inhibitors of α-glucosidase. By blocking this enzyme in the intestinal brush border, these compounds effectively slow the digestion and absorption of carbohydrates, thereby reducing postprandial hyperglycemia. The therapeutic potential of *Salacia* is supported by high-quality human clinical trials. A double-blind, randomized, placebo-controlled crossover study on 51 T2DM patients found that a herbal tea preparation containing *S. reticulata* led to a statistically significant reduction in HbA1c levels, from 6.65% to 6.29% (P=0.008), after a three-month treatment period. Other trials confirm that administration of *S. reticulata* root bark powder also results in significant reductions in FBG, HbA1c, and lipid levels.

The trials also concluded that the preparation was safe and well-tolerated, and in some cases, the use of the herbal tea was associated with a reduction in the required dose of concomitant conventional drugs like glibenclamide. This robust, high-quality evidence base positions *Salacia* as a model for the successful clinical validation of a traditional botanical remedy [64].

***Tinospora cordifolia* (Giloy):** The stem of *Tinosporacordifolia*, a renowned herb in Ayurveda, has been traditionally used for blood sugar control. Scientific investigation has identified tinosporaside as a key bioactive compound that exerts its antidiabetic effect through a dual-mechanism pathway. Studies show that tinosporaside stimulates glucose uptake in skeletal muscle cells by activating both the phosphatidylinositol-3-kinase (PI3K)-mediated pathway and the 5′-AMP-activated protein kinase (AMPK)-mediated pathway. These pathways are crucial for regulating glucose homeostasis and stimulating the translocation of GLUT4 to the cell membrane, thereby increasing glucose utilization. The plant is also known for its immunomodulatory properties, which is both a therapeutic benefit and a potential safety concern. The available data indicates that *Tinospora cordifolia* might increase immune system activity, which could worsen symptoms of autoimmune diseases like lupus or rheumatoid arthritis, and may interfere with immunosuppressant medications. Furthermore, due to its blood sugar-lowering effects, co-consumption with conventional antidiabetic drugs could lead to severe hypoglycemia. This highlights the importance of a nuanced understanding of herbal remedies, acknowledging that while they can be powerful therapeutic agents, their complex pharmacological profiles necessitate careful safety monitoring and may be contraindicated for certain patients [64].

Other Notable Plants: Several other Indian medicinal plants also show compelling antidiabetic promise. *Pterocarpusm arsupium* heartwood extracts have demonstrated a significant ability to decrease both fasting and postprandial blood glucose in diabetic animal models. A key finding is its ability to modulate the inflammatory cytokine TNF-α, which is implicated in insulin resistance and the pathogenesis of diabetes.

The extract has also been shown to protect against diabetic complications like cataracts. *Curcuma longa* (turmeric), and its primary active compound curcumin, is a powerful antioxidant and anti-inflammatory agent that acts on multiple targets. It modulates glucose transporters, activates AMPK, and inhibits inflammatory cytokines, thereby reducing insulin resistance and preventing diabetes-related complications. The alkaloid berberine, isolated from plants like *Berberis aristata*, has been extensively studied for its antidiabetic effects. Berberine is a potent activator of AMPK, a central energy-sensing enzyme that regulates glucose and lipid metabolism. Clinical trials using berberine have shown significant reductions in FBG and HbA1c in T2DM patients [65].

Discussion and Translational Outlook:

Synthesis of Key Findings:

The Multi-Target Therapeutic Profile: The analysis of evidence across multiple plant species reveals a unifying principle: the therapeutic efficacy of these botanicals is often a result of their multi-target pharmacological profile. Unlike many conventional drugs designed to act on a single molecular target, these plants possess a complex mixture of bioactive compounds that can modulate multiple, interconnected pathways simultaneously. This "network pharmacology" approach offers a potential advantage in managing a multifaceted disease like T2DM, which involves a cascade of metabolic dysfunctions.

The intricate connections between the identified phytoconstituents and their mechanisms of action are summarized in **Table 2.**

TABLE 2: PHYTOCONSTITUENT-MECHANISM CONCORDANCE

Phytoconstituent	Plant Source	Class	Proposed/Confirmed Mechanism(s) of Action
Gymnemic acids	*Gymnema sylvestre*	Triterpenoidsaponin	Blocks sugar absorption, inhibits α-glucosidase, stimulates insulin secretion, regenerates β-cells
Polypeptide-P, Charantin	*Momordica charantia*	Protein, Triterpenoid	Insulin-mimetic effect, activates AMPK, enhances glucose uptake
4-	*Trigonellafoenum-*	Amino acid	Stimulates insulin secretion, improves insulin

hydroxyisoleucine	*graecum*		sensitivity
Salacinol, Kotalanol	*Salacia reticulata*	Sulfonium compounds	Potent, specific α-glucosidase inhibition
Tinosporaside	*Tinospora cordifolia*	Terpenoid	Activates PI3K/Akt and AMPK pathways, enhances GLUT4 translocation
Berberine	*Berberis aristata*	Alkaloid	Activates AMPK, improves insulin resistance, inhibits gluconeogenesis, modulates gut microbiome
Curcumin	*Curcuma longa*	Polyphenol	Potent antioxidant/anti-inflammatory agent, activates AMPK and PPARγ
Pterostilbene	*Pterocarpus marsupium*	Stilbenoid	Protects β-cells, reduces inflammatory cytokines (TNF-α), inhibits aldose reductase

The evidence for plants like *Berberis aristata* and *Curcuma longa* demonstrates how their active compounds interact with central energy-sensing pathways (AMPK) and inflammatory markers (TNF-α, NF-${\kappa}$B), respectively. This ability to simultaneously address insulin resistance, hyperglycemia, and chronic inflammation all hallmarks of T2DM provides a powerful rationale for their therapeutic potential.

Standardization, Quality Control, and Formulation Science: the Path to Reproducibility: A recurring and critical limitation noted throughout the literature is the lack of standardization and quality control in herbal preparations. The phytochemical composition of a plant can vary significantly based on its geographic origin, cultivation practices, harvest season, and extraction method. This variability can lead to inconsistent and irreproducible clinical results, making it difficult to establish a reliable therapeutic dose or a consistent safety profile.

To bridge this gap, modern pharmaceutical science must be applied to traditional remedies. Quality control standards should be established using quantitative analytical techniques, such as High-Performance Liquid Chromatography (HPLC) and Thin-Layer Chromatography (TLC), to profile the phytochemical fingerprint and quantify key marker compounds. The adherence to Good Agricultural and Collection Practices (GACP) and Good Manufacturing Practice (GMP), as promoted by the Ministry of AYUSH, is essential to ensure a consistent and high-quality raw material supply chain. Furthermore, the bioavailability of many plant-derived compounds, such as curcumin and berberine, is often poor due to low solubility and extensive metabolism. This can lead to a reduced therapeutic effect. Advancements in formulation science offer a promising solution. Technologies such as nanoemulsions and alginate encapsulation can significantly enhance the solubility, stability, and absorption of these compounds. Nanoemulsions, which consist of drug-containing droplets in the nanometer range, have shown a significant ability to reduce blood glucose levels in preclinical studies. Similarly, alginate encapsulation provides a low-cost, biocompatible matrix that can protect the active compounds and enable their slow, targeted release, thereby improving their therapeutic effects.

Safety, Pharmacovigilance, and Regulatory Challenges: The belief that natural products are inherently safe is a widespread misconception that poses a significant public health risk. The use of herbal remedies, whether alone or in combination with conventional drugs, can lead to adverse events. Key safety concerns include the misidentification of a plant species, contamination with heavy metals, pesticides, or even synthetic drugs, and the potential for severe herb-drug interactions (HDIs). The co-consumption of a plant with hypoglycemic properties, such as

Tinospora cordifolia, alongside a conventional antidiabetic medication can lead to a synergistic effect that causes a dangerously low drop in blood sugar. Recognizing these risks, the Indian government, through the Ministry of AYUSH, has initiated the Ayush Suraksha program, a dedicated pharmacovigilance system for traditional medicine. This program is tasked with collecting and analyzing data on adverse drug reactions to establish a scientific evidence base for the clinical safety of AYUSH drugs. The regulatory landscape remains complex, with significant differences between how herbal products are regulated in India (as traditional medicines) versus in Western countries (where they may be classified as dietary

supplements or unapproved drugs), which can impede their global market access.

Translational Outlook and Future Directions: To fully realize the therapeutic potential of Indian medicinal plants for diabetes, a clear translational roadmap is necessary. The path forward is dependent on a concerted effort to:

Conduct Rigorous Clinical Trials: There is a pressing need for large-scale, multi-center, double-blind, randomized controlled trials that use standardized, high-quality extracts. These trials must be adequately powered and employ harmonized endpoints, such as HbA1c and FBG, to generate evidence that is robust and comparable across studies.

Explore Combination Therapies: Given their multi-target mechanisms, these plants show significant potential as adjuncts to conventional antidiabetic drugs. Future research should focus on a biomarker-guided approach to identify specific patient populations that would most benefit from such integrative care.

Harness Formulation Science: The development and clinical testing of advanced delivery systems like nanoemulsions and encapsulated formulations are crucial for improving bioavailability and ensuring consistent therapeutic outcomes.

Strengthen Regulatory and Pharmacovigilance Systems: A strict "safety-first" approach is paramount. This includes implementing and enforcing robust Good Manufacturing Practices, improving labeling transparency, and expanding pharmacovigilance programs to build trust and ensure patient safety.

TABLE 3: SUMMARY OF HUMAN CLINICAL TRIALS

Plant Species	Study Design	Sample Size (N)	Intervention & Dose	Duration	Key Outcomes	Key Findings
Salacia reticulata	Double-blind, randomized, placebo-controlled crossover trial	51 T2DM subjects	Herbal tea preparation	3 months	HbA1c, FBG, lipid profile, Glibenclamide dose	Significant reduction in HbA1c (0.36%), no significant change in metformin dose, safe and well-tolerated
Trigonellafoenum-graecum	Prospective, randomized, parallel open-labeled study	280 prediabetic subjects	10g fenugreek powder daily	24 months	HbA1c, serum insulin, HOMA-IR	Significant reduction in HbA1c and HOMA-IR, delayed progression to T2DM, good compliance
Berberis aristata (Berberine)	Randomized clinical trial	Not specified	1200 mg berberine + 600 mg cinnamon daily	12 weeks	FBG, HbA1c	Significant reduction in FBG and HbA1c compared to placebo
Momordica charantia	Various (e.g., RCTs, studies on potency with OHA)	Varied; often low N	Capsule prep, powder, extract	Varied; often short	FBG, PPG, glucose tolerance	Evidence limited by poor design; needs further investigation for definitive conclusion

CONCLUSION: The scientific evidence reviewed in this report confirms that a select group of Indian medicinal plants with a long history of traditional use possess potent and mechanistically plausible antidiabetic properties. The multi-target nature of their bioactive compounds, which collectively modulate multiple pathways involved in diabetes pathogenesis, offers a compelling alternative to single-target conventional drugs. The evidence is particularly strong for *Salacia reticulata* and *Trigonellafoenum-graecum,* which have been supported by a growing body of rigorous, peer-reviewed clinical data showing significant reductions in key markers of glycemic control, such as HbA1c. The pathway to translating this traditional knowledge into globally accepted, evidence-based therapies is not without its challenges. The primary hurdles are the inconsistent quality of crude herbal materials and the lack of standardization, which have historically led to variable clinical outcomes. Addressing these issues will require a sustained commitment to applying modern analytical and formulation science to traditional remedies. In the end, the full

potential of these botanical interventions can only be realized through a collaborative effort involving academia, industry, and government. This effort must prioritize the conduct of well-designed, adequately powered randomized controlled trials using standardized extracts, combined with a robust safety monitoring system. By bridging the gap between traditional wisdom and modern scientific rigor, these plants could provide a significant and accessible new front in the global fight against diabetes.

ACKNOWLEDGEMENT: We express our gratitude and appreciation for the help and support received in the process of this review article finalization. I also extend my heartfelt thanks to my family for their understanding, encouragement, and unwavering support.

CONFLICT OF INTEREST: The authors have no conflicts of interest.

REFERENCES:

1. Przeor M: Some common medicinal plants with antidiabetic activity, known and available in Europe (A Mini-Review). Pharmaceuticals 2022; 15(1): 65.
2. Coman C, Rugina OD and Socaciu C: Plants and natural compounds with antidiabetic action. Notulae Botanicae Horti Agrobotanici Cluj-Napoca 2012; 40(1): 314-25.
3. Kamran SH, Ahmad M, Ishtiaq S, Ajaib M, Razashah SH and Shahwar DE: Metabolite profiling and biochemical investigation of the antidiabetic potential of *Loranthus pulverulentus* Wall n-butanol fraction in diabetic animal models. Journal of Ethnopharmacology 2024; 318: 116963.
4. Ferreres F, Andrade C, Gomes NG, Andrade PB, Gil-Izquierdo A, Pereira DM, Suksungworn R, Duangsrisai S, Videira RA and Valentão P: Valorisation of kitul, an overlooked food plant: Phenolic profiling of fruits and inflorescences and assessment of their effects on diabetes-related targets. Food Chemistry 2021; 342: 128323.
5. Fernández-Fernández AM, Dellacassa E, Medrano-Fernandez A and Del Castillo MD: Citrus waste recovery for sustainable nutrition and health. Food Wastes and By-products: Nutraceutical and Health Potential 2020; 193-222.
6. Fernández-Fernández AM, Iriondo-DeHond A, Nardin T, Larcher R, Dellacassa E, Medrano-Fernandez A and Castillo MD: *In-vitro* bioaccessibility of extractable compounds from tannat grape skin possessing health promoting properties with potential to reduce the risk of diabetes. Foods 2020; 9(11): 1575.
7. Timotius KH and Rahayu I: Overview of herbal therapy with leave of *Gynura procumbens* (Lour.) Merr. Journal of Young Pharmacists 2020; 12(3): 201.
8. Huang YS, Chen HH, Shyu YT and Wu SJ: Metabolic Regulation Mechanisms of the Hypoglycemic and Anti-Obesity Effects of *Ficus pumila* L. Var. awkeotsang Achene extracts in 3T3-L1 Cells. Food Science & Nutrition 2025; 13(4): 70176.
9. Muliasari H, Yeshi K, Oelgemöller M, Loukas A, Crayn D and Wangchuk P: Australian tropical medicinal plants and their phytochemicals with wound healing and antidiabetic properties. Phytochemistry Reviews 2025; 1-43.
10. Vargas J, García L and Baena Y: Nanotechnology and herbal products: Advances and perspectives in the treatment of diabetes and some of its complications. Journal of Applied Pharmaceutical Science 2023; 13(12): 001-14.
11. Makhoba XH: The role of pyridine derivatives on the treatment of some complex diseases: A review. Recent Developments in the Synthesis and Applications of Pyridines 2023; 143-58.
12. Singh B: Ethnopharmacological Properties, Biological Activity and Phytochemical Attributes of Medicinal Plants, Volume 1. CRC Press 2023.
13. Gaol AY, Ilyas S, Hutahaean S and Sipahutar H: Antidiabetic activity and immunostimulant potential of bosibosi (*Timonius flavescens* (Jacq) Baker) leaves ethanol extract in alloxan-induced diabetic rats. In Journal of Physics: conference series 2021; 1819(1): 012071). IOP Publishing.
14. Rajesham VV, Varsha D, Swathi E, Renu J and Rao TR: A review on phenolic compounds and their role in treatment and management of diabetes, including vanilic acid. World Journal of Biology Pharmacy and Health Sciences 2025; 22(3): 492-9.
15. Rajesham VV, Varsha D, Swathi E, Renu J and Rao TR: A review on phenolic compounds and their role in treatment and management of diabetes, including vanilic acid. World Journal of Biology Pharmacy and Health Sciences 2025; 22(3): 492-9.
16. Kırcı D and Gümüşok S: *Cistus laurifolius* L. InNovel Drug Targets With Traditional Herbal Medicines: Scientific and Clinical Evidence 2022; 141-150. Cham: Springer International Publishing.
17. Babu M, Ashok K, Jula V and Mullai NK: A review on traditional medicinal plants with anti-diabetic properties. Linguist Cult Rev 2021; 5(1): 1244-51.
18. Rathod S, Katolkar U, Agnihotri V, Potdar M and Goyal Y: Novel strategies of antioxidants in chronic inflammatory diseases. In Antioxidants as Nutraceuticals 2025; 157-193. Apple Academic Press.
19. Rathod S, Katolkar U, Agnihotri V, Potdar M and Goyal Y: Novel strategies of antioxidants in chronic inflammatory diseases. In Antioxidants as Nutraceuticals 2025; 157-193. Apple Academic Press.
20. Ukpabi-Ugo JC, Uhuo EN, Alaebo PO and Ekwere AE: Effects of methanol leaves extract of *Justicia carnea* on blood glucose level and lipid profile in alloxan-induced diabetic albino rats. Journal of Pharmaceutical & Allied Sciences 2020; 17(2).
21. Zafar A, Alruwaili NK, Panda DS, Imam SS, Alharbi KS, Afzal M, Shalaby K, Kazmi I and Alshehri S: Potential of natural bioactive compounds in management of diabetes: Review of preclinical and clinical evidence. Current Pharmacology Reports 2021; 7(3): 107-22.
22. Kumar A, Gangwar R, Ahmad Zargar A, Kumar R and Sharma A: Prevalence of diabetes in India: A review of IDF diabetes atlas 10th edition. Current Diabetes Reviews 2024; 20(1): 105-14.
23. Sharma K, Akre S, Chakole S, Wanjari MB and Wanjari M: Stress-induced diabetes: a review. Cureus 2022; 14(9).
24. Malaza N, Masete M, Adam S, Dias S, Nyawo T and Pheiffer C: A systematic review to compare adverse pregnancy outcomes in women with pregestational diabetes and gestational diabetes. International Journal of

Environmental Research and Public Health 2022; 19(17): 10846.
25. Kottaisamy CP, Raj DS, Prasanth Kumar V and Sankaran U: Experimental animal models for diabetes and its related complications—a review. Laboratory Animal Research 2021; 37(1): 23.
26. Modzelewski R, Stefanowicz-Rutkowska MM, Matuszewski W and Bandurska-Stankiewicz EM: Gestational diabetes mellitus recent literature review. Journal of Clinical Medicine 2022; 11(19): 5736.
27. Holt RI, Cockram CS, Ma RC and Luk AO: Diabetes and infection: review of the epidemiology, mechanisms and principles of treatment. Diabetologia 2024; 67(7): 1168-80.
28. Sweeting A, Hannah W, Backman H, Catalano P, Feghali M, Herman WH, Hivert MF, Immanuel J, Meek C, Oppermann ML and Nolan CJ: Epidemiology and management of gestational diabetes. The Lancet 2024; 404(10448): 175-92.
29. Liang J, He Y, Huang C, Ji F, Zhou X and Yin Y: The regulation of selenoproteins in diabetes: A new way to treat diabetes. Current Pharmaceutical Design 2024; 30(20): 1541-7.
30. Weinberg Sibony R, Segev O, Dor S and Raz I: Overview of oxidative stress and inflammation in diabetes. Journal of Diabetes 2024; 16(10): 70014.
31. Yameny AA: Diabetes mellitus overview 2024. Journal of Bioscience and Applied Research 2024; 10(3): 641-5.
32. Kour V, Swain J, Singh J, Singh H and Kour H: A review on diabetic retinopathy. Current Diabetes Reviews 2024; 20(6): 74-88.
33. Sheng B, Pushpanathan K, Guan Z, Lim QH, Lim ZW, Yew SM, Goh JH, Bee YM, Sabanayagam C, Sevdalis N and Lim CC: Artificial intelligence for diabetes care: current and future prospects. The Lancet Diabetes & Endocrinology 2024; 12(8): 569-95.
34. Kumar A, Gangwar R, Ahmad Zargar A, Kumar R and Sharma A: Prevalence of diabetes in India: A review of IDF diabetes atlas 10th edition. Current Diabetes Reviews 2024; 20(1): 105-14.
35. Gupta S, Sharma N, Arora S and Verma S: Diabetes: a review of its pathophysiology, and advanced methods of mitigation. Current Medical Research And Opinion 2024; 40(5): 773-80.
36. Xu Y, Lu J, Li M, Wang T, Wang K, Cao Q, Ding Y, Xiang Y, Wang S, Yang Q and Zhao X: Diabetes in China part 1: epidemiology and risk factors. The Lancet Public Health 2024.
37. Pishdad R, Auwaerter PG and Kalyani RR: Diabetes, SGLT-2 inhibitors, and urinary tract infection: a review. Current Diabetes Reports 2024; 24(5): 108-17.
38. Ray GW, Zeng Q, Kusi P, Zhang H, Shao T, Yang T, Wei Y, Li M, Che X and Guo R: Genetic and inflammatory factors underlying gestational diabetes mellitus: a review. Frontiers in Endocrinology 2024; 15: 1399694.
39. Lu X, Xie Q, Pan X, Zhang R, Zhang X, Peng G, Zhang Y, Shen S and Tong N: Type 2 diabetes mellitus in adults: pathogenesis, prevention and therapy. Signal Transduction and Targeted Therapy 2024; 9(1): 262.
40. Mackenzie Sc, Sainsbury CA and Wake DJ: Diabetes and artificial intelligence beyond the closed loop: a review of the landscape, promise and challenges. Diabetologia 2024; 67(2): 223-35.
41. Byndloss M, Devkota S, Duca F, Niess JH, Nieuwdorp M, Orho-Melander M, Sanz Y, Tremaroli V and Zhao L: The gut microbiota and diabetes: research, translation, and clinical applications 2023 Diabetes, Diabetes Care, and Diabetologia Expert Forum. Diabetes 2024; 73(9): 1391-410.
42. Mallik R, Kar P, Mulder H and Krook A: The future is here: an overview of technology in diabetes. Diabetologia 2024; 67(10): 2019-26.
43. Darwitz BP, Genito CJ and Thurlow LR: Triple threat: how diabetes results in worsened bacterial infections. Infection and Immunity 2024; 92(9): 00509-23.
44. Bielka W, Przezak A, Molęda P, Pius-Sadowska E and Machaliński B: Double diabetes when type 1 diabetes meets type 2 diabetes: definition, pathogenesis and recognition. Cardiovascular Diabetology 2024; 23(1): 62.
45. Alfaris N, Waldrop S, Johnson V, Boaventura B, Kendrick K and Stanford FC: GLP-1 single, dual, and triple receptor agonists for treating type 2 diabetes and obesity: a narrative review. E Clinical Medicine 2024; 75.
46. Drucker DJ: GLP-1-based therapies for diabetes, obesity and beyond. Nature Reviews Drug Discovery 2025; 1-20.
47. Templer S, Abdo S and Wong T: Preventing diabetes complications. Internal Medicine J 2024; 54(8): 1264-74.
48. Młynarska E, Czarnik W, Dzieża N, Jędraszak W, Majchrowicz G, Prusinowski F, Stabrawa M, Rysz J and Franczyk B: Type 2 diabetes mellitus: new pathogenetic mechanisms, treatment and the most important complications. Int Jo of Mole Scien 2025; 26(3): 1094.
49. Butt MD, Ong SC, Rafiq A, Kalam MN, Sajjad A, Abdullah M, Malik T, Yaseen F and Babar ZU: A systematic review of the economic burden of diabetes mellitus: contrasting perspectives from high and low middle-income countries. Journal of Pharmaceutical Policy and Practice 2024; 17(1): 2322107.
50. Yao H, Zhang A, Li D, Wu Y, Wang CZ, Wan JY and Yuan CS: Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis. BMJ 2024; 384.
51. Dailah HG: The influence of nurse-led interventions on diseases management in patients with diabetes mellitus: a narrative review. In Healthcare 2024; 12(3): 352. MDPI.
52. Dilixiati D, Waili A, Tuerxunmaimaiti A, Tao L, Zebibula A and Rexiati M: Risk factors for erectile dysfunction in diabetes mellitus: a systematic review and meta-analysis. Frontiers in Endocrinology 2024; 15: 1368079.
53. Avogaro A: Diabetes and obesity: the role of stress in the development of cancer. Endocrine 2024; 86(1): 48-57.
54. Jha R, Lopez-Trevino S, Kankanamalage HR and Jha JC: Diabetes and renal complications: an overview on pathophysiology, biomarkers and therapeutic interventions. Biomedicines 2024; 12(5): 1098.
55. Aryal D, Joshi S, Thapa NK, Chaudhary P, Basaula S, Joshi U, Bhandari D, Rogers HM, Bhattarai S, Sharma KR and Regmi BP: Dietary phenolic compounds as promising therapeutic agents for diabetes and its complications: A comprehensive review. Food Science & Nutrition 2024; 12(5): 3025-45.
56. Takele WW, Vesco KK, Josefson J, Redman LM, Hannah W, Bonham MP, Chen M, Chivers SC, Fawcett AJ, Grieger JA and Habibi N: Effective interventions in preventing gestational diabetes mellitus: A systematic review and meta-analysis. Communications Medicine 2024; 4(1): 75.
57. Liu P, Zhang Z, Cai Y, Li Z, Zhou Q and Chen Q: Ferroptosis: mechanisms and role in diabetes mellitus and its complications. Ageing Res Reviews 2024; 94: 102201.
58. Strati M, Moustaki M, Psaltopoulou T, Vryonidou A and Paschou SA: Early onset type 2 diabetes mellitus: an update. Endocrine 2024; 85(3): 965-78.

59. Eleftheriadou A, Spallone V, Tahrani AA and Alam U: Cardiovascular autonomic neuropathy in diabetes: an update with a focus on management. Diabetologia 2024; 67(12): 2611-25.
60. Grattoni A, Korbutt G, Tomei AA, García AJ, Pepper AR, Stabler C, Brehm M, Papas K, Citro A, Shirwan H and Millman JR: Harnessing cellular therapeutics for type 1 diabetes mellitus: progress, challenges, and the road ahead. Nature Reviews Endocrinology 2025; 21(1): 14-30.
61. Eleftheriadou A, Spallone V, Tahrani AA and Alam U: Cardiovascular autonomic neuropathy in diabetes: an update with a focus on management. Diabetologia 2024; 67(12): 2611-25.
62. Ansari P, Khan JT, Chowdhury S, Reberio AD, Kumar S, Seidel V, Abdel-Wahab YH and Flatt PR: Plant-based diets and phytochemicals in the management of diabetes mellitus and prevention of its complications: A review. Nutrients 2024; 16(21): 3709.
63. Espino-Gonzalez E, Dalbram E, Mounier R, Gondin J, Farup J, Jessen N and Treebak JT: Impaired skeletal muscle regeneration in diabetes: from cellular and molecular mechanisms to novel treatments. Cell Metabolism 2024; 36(6): 1204-36.
64. Jiao YR, Chen KX, Tang X, Tang YL, Yang HL, Yin YL and Li CJ: Exosomes derived from mesenchymal stem cells in diabetes and diabetic complications. Cell Death & Disease 2024; 15(4): 271.
65. Yu MG, Gordin D, Fu J, Park K, Li Q and King GL: Protective factors and the pathogenesis of complications in diabetes. Endocrine Reviews 2024; 45(2): 227-52.

How to cite this article:
Shewale JD and Gour R: "Indian medicinal plants with antidiabetic activity: a comprehensive review of phytoconstituents and therapeutic mechanisms". Int J Pharm Sci & Res 2026; 17(3): 779-90. doi: 10.13040/IJPSR.0975-8232.17(3).779-90.