

Antidiabetic Potential of Eastern Himalayan Plants: A Gut Microbiome-Centered Pharmacological Perspective

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ABSTRACT

Type 2 diabetes mellitus (T2DM) is a multifactorial metabolic disorder characterized by insulin resistance, chronic inflammation, and gut microbiota dysbiosis. Recent studies have highlighted the role of the gut microbiome as a critical mediator of glucose homeostasis and metabolic regulation. Concurrently, several medicinal plants traditionally used in the Eastern Himalayas exhibit antidiabetic effects, potentially through microbiota-mediated pathways. This review provides a comprehensive analysis of five such plants—*Berberis aristata*, *Swertia chirayita*, *Zanthoxylum armatum*, *Paris polyphylla*, and *Nardostachys jatamansi*—focusing on their ethnomedical relevance, phytochemical composition, antihyperglycemic mechanisms, and gut microbiota-modulating potential. Key bioactive compounds such as berberine, mangiferin, and polyphyllin are discussed in relation to their ability to influence microbial diversity, short-chain fatty acid (SCFA) production, intestinal barrier function, and systemic metabolic parameters. By integrating traditional pharmacological knowledge with microbiome science, this review elucidates the mechanistic underpinnings and therapeutic prospects of these botanicals as microbiota-targeted agents for future antidiabetic therapies. **Keywords** Type 2 Diabetes Mellitus; Gut Microbiota; Eastern Himalayas; Medicinal Plants; Phytochemicals; *Berberis aristata*; Microbiota Modulation

INTRODUCTION

Type 2 Diabetes and the Gut Microbiota: A Pathophysiological Nexus

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder marked by insulin resistance, hyperglycaemia, and systemic inflammation. Traditionally associated with sedentary lifestyles and poor dietary habits, T2DM has increasingly been linked to alterations in the gut microbiota. The human gut harbours trillions of microbes that influence host metabolism, immunity, and endocrine function. In recent years, mounting evidence has highlighted the significant role of gut dysbiosis in the pathogenesis of T2DM[1,2]. Diabetic individuals often exhibit reduced microbial diversity, a higher Firmicutes-to-Bacteroidetes ratio, and decreased abundance of beneficial genera such as *Akkermansia*, *Bifidobacterium*, and *Faecalibacterium*. These alterations lead to impaired production of short-chain fatty acids (SCFAs), increased intestinal permeability, endotoxemia via lipopolysaccharide (LPS) translocation, and low-grade inflammation — all of which contribute to insulin resistance and β -cell dysfunction. Thus, modulation of the gut microbiota has emerged as a promising strategy for the prevention and management of T2DM. To our knowledge, this is the first integrative review of Eastern Himalayan antidiabetic plants through a gut microbiota lens[3,4].

Methodology

This review was conducted using a structured literature search across major scientific databases, including PubMed, Scopus, Web of Science, and Google Scholar. Keywords included combinations of “Type 2 diabetes,” “gut microbiota,” “Eastern Himalayan medicinal plants,” and specific plant names such as *Berberis aristata*, *Swertia chirayita*, *Zanthoxylum armatum*, *Paris polyphylla*, and *Nardostachys jatamansi*.

Articles published between 2000 and 2025 were reviewed, focusing on ethnobotanical relevance, phytochemical composition, gut microbiota interactions, and antidiabetic mechanisms. A total of 22 studies were included in this review, with the majority published between 2020 and 2025. These were selected based on their relevance to antidiabetic effects, gut microbiota modulation, and phytochemical profiles of Eastern Himalayan medicinal plants.

Inclusion criteria comprised peer-reviewed research articles, reviews, and ethnobotanical reports that provided data on the antidiabetic potential and/or microbiota-related effects of the selected plants. Studies published in English between 2000 and 2025 were considered.

Exclusion criteria involved non-peer-reviewed literature, articles without full-text access, studies unrelated to diabetes or gut microbiota, and those lacking specific reference to any of the five target plants.

The included studies were thematically categorized into five key areas:

- (1) antidiabetic effects of Eastern Himalayan plants;
- (2) modulation of gut microbiota by plant-derived compounds;
- (3) phytochemical characterization and pharmacological activity;
- (4) ethnomedicinal uses in metabolic disorders; and
- (5) microbiota-mediated mechanisms such as SCFA production, gut barrier restoration, and inflammation modulation.

Antidiabetic Eastern Himalayan Medicinal Plants: Ethnobotany and Emerging Pharmacological Insights

The Eastern Himalayan region is a biodiversity hotspot, harbouring a wealth of medicinal plants used traditionally to treat metabolic and gastrointestinal disorders. Several of these plants have demonstrated antidiabetic potential, with emerging interest in their ability to influence gut microbial composition and function. This section presents an overview of five key medicinal plants from this region with promising antidiabetic activity[4].

Berberis aristata: Known locally as "Daruharidra," *Berberis aristata* is rich in isoquinoline alkaloids, primarily berberine. Berberine exerts hypoglycaemic effects by enhancing insulin sensitivity, promoting glucose uptake, and modulating AMPK signalling. Notably, berberine has been shown to reshape gut microbial communities by increasing the abundance of *Akkermansia muciniphila* and SCFA-producing bacteria, thereby improving gut barrier function and reducing systemic inflammation[5].

Swertia chirayita: Traditionally used for treating fever and liver disorders, *Swertia chirayita* contains bitter secoiridoid glycosides such as swertiamarin and amarogentin. Preclinical studies suggest that these compounds enhance insulin secretion and possess antioxidant properties. While direct evidence of microbiota modulation is limited, its bitter compounds may influence bile acid metabolism, indirectly affecting gut microbial populations[6].

Zanthoxylum armatum: Commonly known as "Tejphal" or "Timur," *Zanthoxylum armatum* is used for gastrointestinal ailments and metabolic disorders. Its essential oils and alkaloids possess antimicrobial, carminative, and anti-inflammatory properties. While specific studies on its gut microbiota modulation are lacking, its traditional use for gut health supports the hypothesis of indirect microbiome-mediated effects[7].

Paris polyphylla: This plant, valued in traditional medicine for its adaptogenic and anti-inflammatory properties, contains steroidal saponins. These compounds exhibit hypoglycaemic and cytoprotective effects. Although its influence on gut microbiota remains unexplored, steroidal saponins in other plants have demonstrated prebiotic-like effects, suggesting potential microbiome modulation[8].

Nardostachys jatamansi: An aromatic rhizomatous herb, *Nardostachys jatamansi* is known for its neuroprotective and adaptogenic effects. Its constituents, such as jatamansone, confer antidiabetic and anti-inflammatory properties. Given the emerging recognition of the gut-brain axis in metabolic health, *N. jatamansi* may exert systemic benefits through neuromodulatory pathways involving the gut microbiota[9].

Modulation of Gut Microbiota in Type 2 Diabetes: Role of Eastern Himalayan Medicinal Plants

The human gut harbours trillions of microorganisms that play critical roles in host metabolism, immune function, and endocrine signaling. Increasing evidence has established a strong link between gut microbiota dysbiosis and the onset of Type 2 Diabetes Mellitus (T2DM). Alterations in microbial diversity and abundance can impair short-chain fatty acid (SCFA) production, increase intestinal permeability, elevate systemic endotoxemia (via lipopolysaccharide translocation), and disrupt bile acid metabolism—all of which contribute to insulin resistance and chronic low-grade inflammation[10,11].

Consequently, targeting the gut microbiome has emerged as a promising adjunct strategy for metabolic diseases. Medicinal plants, especially those rich in polyphenols, flavonoids, alkaloids, and saponins, are increasingly recognized for their ability to reshape gut microbial composition and function. These phytochemicals can act as substrates (prebiotics) for beneficial microbes, inhibit pathogenic bacteria, and influence microbial-derived metabolites with downstream metabolic effects[12].

Microbiota-Mediated Antidiabetic Activity of Selected Plants

Berberis aristata

Berberis aristata is one of the most well-studied Himalayan plants for metabolic disorders. Its major alkaloid, berberine, exerts limited systemic absorption but robust local effects in the gut. Berberine modulates the microbiota by:

- Increasing the abundance of SCFA-producing bacteria such as *Blautia*, *Butyricicoccus*, and *Roseburia*.
- Decreasing endotoxin-producing bacteria like *Proteobacteria* and *Desulfovibrio*.
- Enhancing the expression of tight junction proteins, thereby restoring gut barrier integrity.
- Influencing GLP-1 secretion via microbial metabolites, contributing to improved insulin sensitivity and glycaemic control.

Several studies have shown that berberine's antidiabetic effects are significantly diminished in antibiotic-treated or germ-free animals, further confirming its microbiota-dependent pharmacology[13].

Swertia chirayita

Although direct studies on *S. chirayita* and the microbiome are limited, its rich profile of secoiridoid (like swertiamarin) and xanthenes may support gut health indirectly. Polyphenols from plants such as *Swertia chirayita* can:

- Inhibit microbial β -glucuronidase and other pro-inflammatory enzymes.
- Act as fermentable substrates, promoting the growth of *Lactobacillus* and *Bifidobacterium* spp.
- Reduce microbial-driven oxidative stress and improve gut redox balance.

Given its traditional use in digestive and hepatic disorders, *S. chirayita* may possess unrecognized benefits in microbial modulation that warrant focused studies[14].

Zanthoxylum armatum

This aromatic shrub contains monoterpenes (e.g., limonene, linalool) and polyphenols with antimicrobial and digestive properties. While direct gut microbiota studies are lacking, potential mechanisms include:

- Reduction of gut inflammation through inhibition of pro-inflammatory cytokines.
- Alteration of microbial niche conditions (e.g., pH, mucosal environment), favouring beneficial commensals.
- Possible modulation of microbial enzyme systems involved in bile acid and carbohydrate metabolism.

These activities suggest that *Z. armatum* may play a regulatory role in gut microbial dynamics and metabolic signaling[7].

Paris polyphylla

Known for its steroidal saponins, *P. polyphylla* offers unique potential for gut microbiota interaction. Saponins can:

- Bind and detoxify lipopolysaccharides (LPS), reducing systemic inflammation.
- Increase mucin secretion, strengthening the gut's protective mucus layer.
- Interact with gut microbes to produce bioactive saponin derivatives, which may influence glucose metabolism, lipid homeostasis, and even microbial population structure.

Though direct data is scarce, the structural similarity of *Paris* saponins to known microbiota-active compounds highlights its potential in microbiome-mediated glycaemic regulation[8].

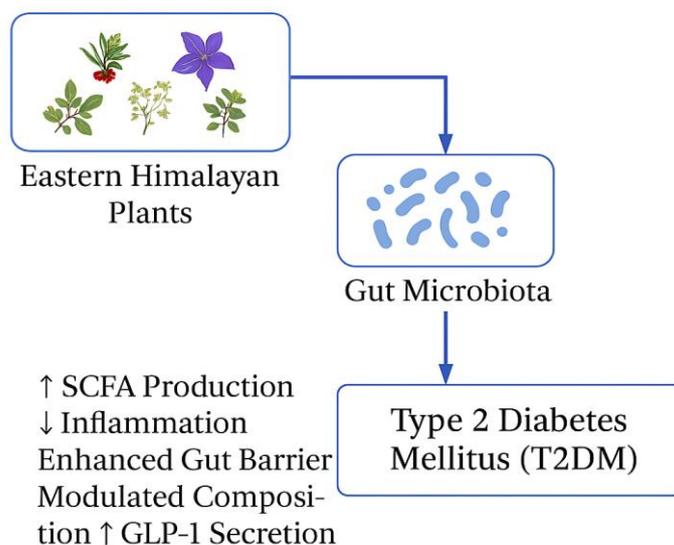
Nardostachys jatamansi

Traditionally used as a nervine tonic and adaptogen, *N. jatamansi* contains sesquiterpenes, neolignans, and valepotriates. While most research focuses on its neuroprotective and hepatoprotective properties, indirect gut microbiota modulation may be inferred via:

- Anti-inflammatory effects that reduce gut-derived systemic inflammation.
- Restoration of gut-brain axis balance, which is increasingly recognized in metabolic diseases.
- Possible influence on microbial oxidative stress via antioxidant compounds.

Its microbiota-related effects remain underexplored, presenting a valuable avenue for future pharmacological and microbiomic investigations[9].

Gut Microbiota—Plant—T2DM Axis



- **Figure 1.** Gut Microbiota—Plant—T2DM Axis: A schematic illustrating how bioactive compounds from Eastern Himalayan plants modulate the gut microbiota and influence host metabolic outcomes in Type 2 Diabetes Mellitus[22].

DISCUSSION

Toward a Microbiota-Informed Phytotherapeutic Paradigm for T2DM

Type 2 diabetes mellitus (T2DM) has evolved from being viewed solely as a disorder of insulin resistance to one involving chronic low-grade inflammation, gut dysbiosis, and systemic metabolic disruption. A pivotal role of the gut microbiota in the pathogenesis and potential reversal of T2DM is now well established. This paradigm shift opens new avenues for the development of microbiota-centered therapies, where phytochemicals from traditional medicinal plants serve as prebiotic agents or modulators of gut microbial communities[16,19].

This review focuses on five Eastern Himalayan medicinal plants—*Berberis aristata*, *Swertia chirayita*, *Zanthoxylum armatum*, *Paris polyphylla*, and *Nardostachys jatamansi*—which possess notable antidiabetic activities and emerging potential to influence gut ecology. Their bioactive compounds, including alkaloids, secoiridoids, saponins, and sesquiterpenes, interact not only with host metabolic pathways but also with the gut microbiota, facilitating a bidirectional pharmacological effect[17,20].

Recent studies reinforce these findings. For example, Dubey et al. (2024) conducted a meta-analysis demonstrating the clinical efficacy of *Berberis aristata* in improving glycaemic control and insulin sensitivity, particularly when combined with *Silybum marianum*, via synergistic antioxidant and microbiota-modulating effects. Furthermore, Askari et al. (2024) highlighted berberine's anti-inflammatory action mediated by the activation of PPAR- γ and AMPK, as well as its impact on gut microbial composition[19,20].

Similarly, a 2024 in vitro study by Oli et al. reported strong α -amylase inhibition by *Swertia chirayita* extracts, validating its traditional use in diabetes management and suggesting possible microbiome-mediated mechanisms through bitter glycosides and xanthenes that may influence bile acid metabolism[15,21].

Other plants like *Zanthoxylum armatum* and *Nardostachys jatamansi*, though less studied, show promising indirect effects through the gut-brain axis and mucosal immune modulation. The presence of anti-inflammatory monoterpenes, polyphenols, and adaptogenic compounds indicates potential benefits in restoring microbial and systemic balance[18]. Collectively, these findings suggest that Eastern Himalayan plants represent multifaceted therapeutic tools, capable of modulating metabolic, microbial, immune, and neuroendocrine systems simultaneously. Their polypharmacology is an asset rather than a limitation in managing complex diseases like T2DM[20].

Yet, critical gaps remain. The majority of current data stems from preclinical models, and comprehensive clinical trials incorporating metagenomic and metabolomic profiling are rare. Moreover, the exact mechanisms of microbial modulation—especially phytochemical-microbiota co-metabolism—remain poorly elucidated[21].

Table 1. Comparative overview of key phytochemicals, gut microbiota modulation, and antidiabetic mechanisms of selected Eastern Himalayan medicinal plants.

Plant Name	Key Phytochemicals	Microbiota Modulation	Antidiabetic Mechanism
<i>Berberis aristata</i>	Berberine	↑ SCFA-producers (<i>Akkermansia</i> , <i>Roseburia</i>); ↓ endotoxins	Enhances insulin sensitivity, restores gut barrier
<i>Swertia chirayita</i>	Swertiamarin, Amarogentin	Supports <i>Bifidobacterium</i> , influences bile acids	Boosts insulin secretion, antioxidant effects
<i>Zanthoxylum armatum</i>	Limonene, Alkaloids	Indirect via anti-inflammatory and antimicrobial actions	Reduces gut inflammation, modulates bile/carbohydrate metabolism
<i>Paris polyphylla</i>	Steroidal Saponins (Polyphyllin)	↑ Mucin secretion; ↓ LPS; potential prebiotic activity	Cytoprotection, glucose & lipid regulation
<i>Nardostachys jatamansi</i>	Jatamansone, Sesquiterpenes	Improves gut-brain axis, ↓ oxidative stress	Neuroendocrine modulation, anti-inflammatory

Table 1. Summary of phytochemicals, gut microbiota interactions, and antidiabetic actions of Eastern Himalayan medicinal plants[22].

CONCLUSION

Conclusion: Reimagining Diabetes Therapy through the Gut–Plant Alliance

The global diabetes epidemic demands innovative solutions that transcend glucose-centric paradigms and embrace the complexity of metabolic disease. This review illuminates the untapped therapeutic potential of Eastern Himalayan medicinal plants—not only as sources of hypoglycaemic agents but as modulators of the human gut microbiota, a dynamic metabolic ecosystem now recognized as central to the pathophysiology of type 2 diabetes mellitus (T2DM). Plants such as *Berberis aristata*, *Swertia chirayita*, *Zanthoxylum armatum*, *Paris polyphylla*, and *Nardostachys jatamansi* possess rich phytochemical profiles that interact with host and microbial systems in synergistic ways. From enhancing short-chain fatty acid production and mucosal barrier integrity to reducing endotoxemia and modulating bile acid pathways, these botanicals operate along the microbiota–immune–endocrine axis—offering a systems-level therapeutic approach that synthetic drugs often fail to achieve.

Recent studies from 2024 further validate their roles in modulating microbial composition, improving insulin sensitivity, and attenuating inflammatory pathways—marking a significant advancement in both ethnopharmacology and translational medicine. Importantly, these plants embody a polypharmacological advantage, addressing the multifactorial nature of T2DM by targeting interconnected metabolic, microbial, and neuroendocrine pathways. However, the journey from traditional use to clinical application is incomplete. The field must now move beyond descriptive ethnobotany and preclinical promise to mechanism-driven, microbiome-integrated clinical research. This includes rigorous trials with metagenomic, metabolomic, and transcriptomic profiling to decode plant–microbe–host interactions at a systems biology level.

In essence, Eastern Himalayan botanicals represent more than natural remedies—they are cultural blueprints for next-generation, personalized metabolic therapies. By harnessing their microbiota-mediated mechanisms, we can pave the way for accessible, sustainable, and biologically intelligent interventions that reflect both the wisdom of tradition and the rigor of modern science.

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LIMITATIONS

Despite presenting a comprehensive overview, this review has several limitations. First, the current evidence base on gut microbiota modulation by Eastern Himalayan plants is limited and largely preclinical. The paucity of direct human studies restricts the translational applicability of many findings. Additionally, the synergistic or antagonistic interactions between plant-derived bioactive and gut microbial taxa remain underexplored. Variability in phytochemical content due to geographical and environmental factors also complicates standardization and reproducibility. Finally, the lack of integrated omics data—such as metagenomics, metabolomics, and transcriptomics—limits mechanistic clarity.

Future Directions

To bridge the knowledge gaps, future research should prioritize:

- Clinical studies evaluating the antidiabetic efficacy of these botanicals with concurrent gut microbiota profiling.
- Metagenomic and metabolomic analyses to decode plant–microbe–host interactions at a systems level.
- Isolation and characterization of key microbiota-active phytochemicals with defined modes of action.
- Formulation of targeted phytobiotics or synbiotics incorporating Eastern Himalayan plant extracts with specific microbial strains.
- Long-term safety and efficacy trials to assess their role as adjunct therapies alongside conventional antidiabetic agents.

Harnessing the integrative power of ethnobotany, pharmacology, and microbiome science may pave the way for culturally rooted, precision-guided, and evidence-based interventions in metabolic health.

Authors' Contributions

Divya Pradhan conceptualized the study, led the literature review, and developed the primary manuscript draft. She also coordinated the integration of pharmacological and microbiome-related content and supervised the overall direction of the review. Nisha Limboo contributed to literature collection, assisted in data synthesis, and helped refine the manuscript with a focus on phytochemical and ethnobotanical aspects. Both authors critically reviewed and approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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