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Pharmacognostical, Phytochemical and Pharmacological Perspectives of the Genus Grewia in Diabetes Management: A Comprehensive Review

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Abstract

Diabetes mellitus is a heterogeneous metabolic disorder in which sustained hyperglycaemia promotes vascular, renal, neural and ocular injury. The growing disease burden and the need for affordable, multi-target adjuncts have renewed interest in medicinal and edible plants. Grewia L. (Malvaceae, subfamily Grewioideae) is a tropical and subtropical genus that includes nutritionally important and ethnomedicinal species such as Grewia asiatica, G. tenax, G. optiva, G. tiliifolia, G. hirsuta and G. flavescens. This review critically integrates the pharmacognostical, phytochemical and pharmacological evidence relevant to diabetes management. Pharmacognostic studies describe species- and organ-specific diagnostic characters, including non-glandular trichomes, characteristic stomata, calcium oxalate crystals, fibres, vessels, mucilage-bearing tissues and measurable ash and extractive values. Phytochemical investigations have identified flavonoids, anthocyanins, phenolic acids, tannins, triterpenes, phytosterols, fatty acids and polysaccharides, with G. asiatica fruits and bark being the most extensively studied. In diabetic rodent models, G. asiatica fruit and bark extracts reduced hyperglycaemia and dyslipidaemia and improved antioxidant and inflammatory biomarkers; G. flavescens leaves also showed glucose-lowering activity. A small study in healthy human participants reported a low glycaemic response to G. asiatica fruit, but therapeutic clinical evidence in diabetes is absent. Enzyme inhibition, antioxidant defence, suppression of inflammatory mediators, preservation of pancreatic function, and modulation of hepatic glycogen and improvement of lipid metabolism are plausible contributors, although several commonly proposed pathways remain inferential rather than directly demonstrated for Grewia extracts. The available evidence therefore supports Grewia, particularly G. asiatica, as a promising source of antidiabetic leads and functional-food ingredients, but not as a clinically established treatment. Future work should prioritize authenticated plant material, chemically standardized extracts, mechanistic validation, pharmacokinetics, chronic toxicology and adequately powered clinical trials.

Keywords: Grewia; Grewia asiatica; diabetes mellitus; pharmacognosy; phytochemistry; antidiabetic activity; oxidative stress; alpha-glucosidase; medicinal plants

1. Introduction

Diabetes mellitus is diagnosed by persistent abnormalities of glucose regulation and encompasses conditions caused by deficient insulin secretion, impaired insulin action or both. It is associated with progressive microvascular and macrovascular complications and requires long-term lifestyle, pharmacological and risk-factor management [1,2]. The International Diabetes Federation estimated that 589 million adults aged 20–79 years were living with diabetes in 2024,

with the global total projected to rise substantially by 2050 [1]. These figures emphasize the need for prevention, early diagnosis, and access to effective medicines and development of safe adjunctive interventions.

Modern glucose-lowering therapy has advanced considerably, and treatment selection is increasingly individualized according to cardiovascular, renal, metabolic and hypoglycaemia risk. Nevertheless, cost, access, gastrointestinal intolerance, treatment complexity, therapeutic inertia and progressive beta-cell dysfunction remain practical challenges. Medicinal plants cannot replace evidence-based diabetes care; however, they may provide chemical scaffolds for drug discovery, standardized botanical products or nutritionally useful foods when their efficacy and safety are established.

The genus Grewia is particularly relevant because it contains edible fruits, traditional remedies and chemically diverse species. The accepted genus belongs to Malvaceae and is native across tropical and subtropical regions of the Old World and the Pacific [3]. Earlier literature often placed Grewia in Tiliaceae; contemporary taxonomic treatment includes it within Malvaceae, subfamily Grewioideae. Reviews of the genus have catalogued a broad spectrum of flavonoids, phenolic acids, triterpenes, phytosterols, lipids, minerals and other metabolites, together with antioxidant, anti-inflammatory, antimicrobial, hepatoprotective and antidiabetic observations [4–6].

Despite this promise, the diabetes-focused literature is frequently overstated. Evidence is concentrated in a small number of extracts, animal models and in-vitro or in-silico experiments. Claims involving GLUT-4 translocation, AMPK activation, pancreatic regeneration, advanced glycation end-product inhibition and direct alpha-glucosidase blockade are sometimes extrapolated from isolated phytochemicals or unrelated plants rather than directly demonstrated in Grewia preparations. A publication-ready assessment must therefore separate observed outcomes from mechanistic hypotheses. The present review critically evaluates pharmacognostic identity, chemical composition, antidiabetic evidence, supportive pharmacology, safety and translational gaps across the genus.

Fig- Grewia Leaves

2. Review Methodology

A structured narrative search was conducted using PubMed-indexed records, journal platforms, Google Scholar-linked records and reference lists of key Grewia reviews. Search combinations included “Grewia AND diabetes”, “Grewia asiatica AND antidiabetic”, “Grewia AND alpha-glucosidase”, “Grewia AND pharmacognosy”, “Grewia AND photochemistry”, “Grewia hirsuta AND molecular docking”, and individual species names. English-language primary studies, taxonomic sources, pharmacognostic investigations, phytochemical reports, animal studies, human observations and major reviews available up to July 2026 were considered. Greater interpretive weight was assigned to authenticated plant material, chemically described extracts, controlled experimental models and studies reporting biochemical or histological outcomes. Because the literature is heterogeneous and does not provide sufficiently comparable outcomes for a diabetes-specific meta-analysis, the findings are presented as a critical narrative synthesis.

3. Taxonomy, Distribution and Ethnomedicinal Context

Grewia L. is an accepted genus of Malvaceae distributed mainly in tropical and subtropical regions [3]. Species vary from shrubs and small trees to lianas. The genus includes edible-fruited taxa such as G. asiatica (phalsa/falsa), G. tenax, G. optiva, G. mollis and G. occidentalis. Grewia asiatica is cultivated in South Asia for its small purple to black fruits, which are consumed fresh or processed into beverages, syrups and preserves

Traditional uses differ across regions and plant parts. Fruits have been used as cooling, astringent and nutritive agents; leaves and bark have been used for inflammatory conditions, gastrointestinal complaints, wounds and respiratory symptoms; mucilaginous tissues have been used as demulcents. Ethnomedicinal use may guide biological screening but does not establish efficacy. Species identification, plant-part documentation and voucher deposition are particularly important because older reports may use obsolete family names, spelling variants such as G. tiliaefolia, or incompletely authenticated market samples.

4. Pharmacognostical Perspective

4.1 Macroscopic and organoleptic characters

Macroscopic characters are species- and organ-specific. Grewia leaves are generally simple and alternate, with variable ovate, elliptic or cordate outlines, serrate margins and a pubescent surface in several species. G. asiatica fruits are small drupes that mature from green or reddish stages to deep purple-black. Bark characters vary with age and species, but fibrous texture and mucilage are recurring features. Dried leaf or fruit powders are commonly greenish to brownish, with a faint characteristic odour and an astringent to mucilaginous taste. These descriptors are preliminary identity tests and must be combined with microscopy, physicochemical constants and chemical fingerprints.

4.2 Microscopy and powder diagnostics

Published pharmacognostic studies demonstrate that diagnostic characters cannot be generalized to every species. Reported features include epidermal fragments with stomata, unicellular or multicellular non-glandular trichomes, fibres, pitted or spiral vessels, starch grains, sclereids and calcium oxalate crystals. In G. tiliifolia bark, prismatic calcium oxalate crystals and druses have been documented, with mucilage cavities present in stem tissues [8]. Leaf studies of G. tiliifolia have reported measurable leaf constants and characteristic powder elements, while fruit standardization studies of G. asiatica have described stone cells, fibres, vessels and starch-containing tissues [7–9]. Differences in stomatal type reported across materials may reflect species, organ, surface, developmental stage or

methodological variation; therefore, a diagnostic monograph should use authenticated reference material rather than a genus-wide stomatal claim.

4.3 Physicochemical and chromatographic standards

Ash values, loss on drying, swelling index, foaming index and solvent extractive values provide practical limits for purity and consistency. For example, a G. asiatica fruit study reported total ash of 5.16%, water-soluble ash of 2.5%, acid-insoluble ash of 1.0% and a markedly higher methanol extractive than non-polar extractives [7]. G. tiliifolia bark and leaf investigations likewise demonstrated that organ-specific physicochemical profiles can support authentication [8,9]. These values should not be pooled into broad genus ranges, because moisture, soil contamination, plant organ, maturity, drying and analytical method can materially alter results.

For standardized antidiabetic research, minimum quality specifications should include botanical authentication and voucher number; plant part and phenological stage; collection site and season; drying and milling conditions; foreign matter; moisture or loss on drying; total and acid-insoluble ash; water- and alcohol-soluble extractives; microbial and contaminant limits; and a validated chromatographic fingerprint. Quantification of one or more marker compounds should accompany pharmacological testing.

Domain	Representative diagnostic or quality attributes	Interpretive value	Important caution
Botanical identity	Accepted species name, voucher specimen, collection locality, plant part	Prevents substitution and taxonomic ambiguity	Older literature may list Tiliaceae or spelling variants
Macroscopy	Leaf shape, margin, indumentum, venation; bark texture; fruit colour and drupe morphology	Rapid preliminary authentication	Varies with species, age and environment
Microscopy	Epidermis, stomata, non-glandular trichomes, fibres, vessels, sclereids, calcium oxalate crystals, mucilage tissues	Detects diagnostic tissues and adulteration	Stomatal type and crystal abundance are not uniform across the genus
Powder analysis	Trichome fragments, vessel elements, fibres, crystals, starch and stone cells	Useful for powdered crude drugs	Requires comparison with authenticated reference powder
Physicochemical tests	Moisture, ash values, extractives, swelling/foaming indices	Supports purity and batch consistency	Limits must be plant-part and method specific
Chemical standardization	TLC/HPTLC/HPLC/LC-MS fingerprint and quantified markers	Links quality to biological activity	Total phenolics alone are insufficient for batch equivalence

Table-1 Physicochemical and chromatographic standards

5. Phytochemical Diversity Relevant to Diabetes

The chemistry of Grewia is dominated by phenolic and flavonoid constituents, although the relative abundance depends on species, organ, genotype, environment and extraction solvent. A systematic review of 56 studies reported flavonoids as the largest category among documented Grewia bioactives, accompanied by phenolic acids, triterpenes, phytosterols, fatty acids, amino acids, minerals and vitamins [4]. Later reviews expanded the phytochemical and food-application perspective, particularly for G. asiatica [5,6].

5.1 Flavonoids, anthocyanins and phenolic acids

G. asiatica fruit analyses have reported quercetin and its glycosides, kaempferol derivatives, myricetin derivatives, morin, catechin, epicatechin, vitexin, isovitexin and other flavonoids [4–6]. Anthocyanins contribute to the dark colour of ripe fruits and are relevant to antioxidant and vascular effects. Phenolic acids reported across Grewia materials include gallic, caffeic, chlorogenic, ferulic and p-coumaric acid or related derivatives. Because many of these compounds possess antidiabetic activity in other experimental systems, they provide plausible chemical support; however, their mere presence does not prove that they mediate the activity of a particular Grewia extract.

5.2 Tannins, triterpenes, sterols and lipophilic constituents

Condensed and hydrolysable tannins contribute to astringency and may interact with carbohydrate-hydrolysing enzymes. Triterpenes and sterols reported from members of the genus include lupeol, ursolic acid, oleanolic acid, beta-sitosterol and stigmasterol, although distribution is not uniform. These constituents are mechanistically interesting because related compounds can influence inflammatory signalling, lipid metabolism and insulin sensitivity. Lipidomic and GC-MS studies have also reported fatty acids and volatile or semi-volatile compounds, some of which may contribute to nutritional or bioactive properties.

5.3 Polysaccharides, mucilage, fibre and micronutrients

Mucilage and polysaccharide-rich fractions are characteristic of several Grewia tissues. From a metabolic perspective, soluble fibre and mucilage may slow gastric emptying or carbohydrate absorption and may alter the glycaemic response of food matrices. Fruits also provide organic acids, vitamin C, minerals and other nutrients. These effects are most relevant when the fruit or a minimally processed food is consumed; they should not be assumed for purified organic-solvent extracts.

Phytochemical class	Representative constituents reported in Grewia	Potential diabetes relevance	Evidence status in Grewia
Flavonoids	Quercetin derivatives, kaempferol derivatives, myricetin, morin, catechin, epicatechin, vitexin/isovitexin	Antioxidant effects; possible enzyme inhibition and insulin-signalling support	Well documented chemically; direct target validation limited

Phytochemical class	Representative constituents reported in Grewia	Potential diabetes relevance	Evidence status in Grewia
Anthocyanins	Pigments in ripe G. asiatica fruits	Antioxidant, endothelial and anti-inflammatory potential	Chemical and antioxidant evidence; diabetes mechanisms mostly inferred
Phenolic acids	Gallic, caffeic, chlorogenic, ferulic and p-coumaric acid derivatives	Redox modulation, antiglycation and postprandial glucose control	Presence supported; compound-specific contribution not established
Tannins	Hydrolysable and condensed tannins	Possible alpha-amylase/alpha-glucosidase inhibition	In-vitro fruit-enzyme evidence exists, but standardized kinetics are scarce
Triterpenes/sterols	Lupeol, ursolic acid, oleanolic acid, beta-sitosterol, stigmasterol	Anti-inflammatory, lipid-modulating and insulin-sensitizing potential	Species-dependent; often inferred from constituent literature
Polysaccharides/mucilage/fibre	Soluble polysaccharides and dietary fibre	Lower glycaemic response and delayed intestinal absorption	Plausible for whole fruit/food matrices; extract-specific evidence limited

Table-2 **Phytochemical class**

6. Pharmacological Evidence for Diabetes Management

6.1 Grewia asiatica fruit

The most informative animal study evaluated ethanolic G. asiatica fruit extract in streptozotocin-induced hyperglycaemic rats. Oral treatment at 100 or 200 mg/kg/day for four weeks improved glycaemia and was associated with increased hepatic glycogen, improved glutathione and superoxide dismutase activity, reduced pancreatic malondialdehyde and lower circulating inflammatory cytokines including TNF-alpha and IL-1beta [11]. The strength of this study is the integration of metabolic, antioxidant and inflammatory endpoints. Its limitations include the rodent model, limited extract standardization and uncertainty about human-equivalent exposure.

Aqueous fruit extracts have also demonstrated inhibition of enzymes related to carbohydrate digestion in vitro [10]. Such assays support a possible postprandial mechanism, but interpretation depends on enzyme source, substrate, concentration, kinetic analysis and comparison with acarbose. High tannin or polyphenol concentrations can produce non-specific protein interactions, so confirmatory assays and compound isolation are necessary.

6.2 Grewia asiatica bark and leaves

In alloxan-induced diabetic rats, ethanol extract of G. asiatica stem bark reduced blood glucose and improved lipid and antioxidant variables [12]. The study is important because it links glucose lowering with dyslipidaemia and oxidative stress, but the use of alloxan primarily models beta-cell injury and may not reflect the insulin-resistant phenotype of common type 2 diabetes. Leaf studies have reported hypoglycaemic effects in alloxan- or streptozotocin-based models [13–15]. These findings require cautious interpretation because extraction methods, doses and experimental quality vary, and some reports provide limited chemical characterization.

6.3 Grewia flavescens and other species

Ethanolic G. flavescens leaf extract produced dose-dependent glucose lowering in alloxan-induced diabetic rats [18]. This represents direct in-vivo evidence beyond G. asiatica, but replication, standardized phytochemistry and mechanistic endpoints are lacking. For G. hirsuta, a cyclopentadecadienone derivative was investigated by molecular docking against targets relevant to type 2 diabetes [17]. Docking can prioritize hypotheses but does not establish enzyme inhibition, cellular activity, pharmacokinetics or in-vivo efficacy. G. tenax, G. optiva, G. tiliifolia and G. mollis are nutritionally or pharmacologically interesting, yet diabetes-specific evidence remains sparse compared with G. asiatica.

6.4 Human evidence

Human evidence is currently insufficient for therapeutic claims. A small study in healthy, non-diabetic participants reported a very low glycaemic index for G. asiatica fruit and modest effects on postprandial glucose and oxidative-burst measurements [16]. The study supports the fruit as a potentially favourable food but does not demonstrate treatment of diabetes, long-term HbA1c reduction, medication-sparing effects or prevention of complications. No adequately powered randomized controlled trial of a standardized Grewia extract in people with diabetes was identified.

Species/part	Preparation and model	Main findings	Evidence level	Key limitations
G. asiatica fruit	Ethanolic extract, 100 or 200 mg/kg/day; STZ-hyperglycaemic rats, 4 weeks	Improved glycaemia, liver glycogen, antioxidant enzymes and inflammatory markers	Moderate preclinical	Animal model; extract markers and exposure translation limited
G. asiatica bark	Ethanol extract; alloxan-diabetic rats	Reduced glucose; improved lipid and antioxidant variables	Moderate preclinical	Alloxan model; limited replication and standardization
G. asiatica leaves	Aqueous/ethanolic extracts; alloxan or STZ models	Reported hypoglycaemic effects at repeated doses	Low-to-moderate preclinical	Variable study quality, chemistry and comparators

Species/part	Preparation and model	Main findings	Evidence level	Key limitations
G. asiatica fruit	Aqueous extract; in-vitro carbohydrate-digesting enzymes	Inhibition of key diabetes-related enzymes reported	Preliminary mechanistic	Assay conditions and non-specific polyphenol effects require confirmation
G. flavescens leaves	Ethanol extract; alloxan-diabetic rats	Dose-dependent reduction in blood glucose	Low preclinical	Single older study; limited chemical and mechanistic data
G. hirsuta leaves/compound	Isolated cyclopentadeca-4,12-dienone; molecular docking	Predicted interactions with type 2 diabetes targets	In-silico hypothesis	No direct biochemical, cellular, in-vivo or clinical validation
G. asiatica fruit	Healthy human participants; glycaemic-index study	Low glycaemic response and modulation of oxidative-burst readouts	Very limited human evidence	Not a diabetic population; small, short-term food study

Table-3 Species/part

7. Mechanistic Interpretation

The most defensible mechanistic interpretation is multi-factorial and evidence-graded. Some mechanisms are directly supported by Grewia studies, whereas others are biologically plausible because of the identified constituents.

7.1 Antioxidant and anti-inflammatory actions

Oxidative stress and low-grade inflammation contribute to insulin resistance, beta-cell dysfunction and diabetic complications. G. asiatica fruit treatment in diabetic rats improved glutathione and superoxide dismutase activity and reduced malondialdehyde and inflammatory cytokines [11]. Bark studies also reported antioxidant improvement [12]. These observations provide direct support for redox and inflammatory modulation as contributors to metabolic benefit. They do not, by themselves, prove a primary insulin-sensitizing effect.

7.2 Carbohydrate digestion and postprandial glycaemia

In-vitro inhibition of alpha-amylase or alpha-glucosidase by fruit extracts offers a plausible mechanism for reducing postprandial glucose excursions [10]. Tannins and flavonoids can bind enzymes or substrates, but rigorous confirmation should include kinetic mode, selectivity, interference controls, gastrointestinal stability and in-vivo carbohydrate-tolerance tests. The low glycaemic response to whole G. asiatica fruit in healthy participants may additionally reflect fibre, organic acids, food structure and low available carbohydrate rather than a pharmacological enzyme-inhibitory effect [16].

7.3 Hepatic glucose handling and insulin action

Increased hepatic glycogen in treated diabetic rats suggests improved storage of glucose or reduced glycogen depletion [11]. Improved insulin secretion, insulin sensitivity, GLUT-4 translocation, AMPK activation and PPAR modulation are

plausible targets for flavonoids and triterpenes, but direct measurements of insulin receptor phosphorylation, Akt, AMPK, GLUT-4 translocation or glucose uptake are not yet sufficient in Grewia-specific studies. These pathways should therefore be described as proposed rather than established.

7.4 Pancreatic protection

Reduced pancreatic oxidative damage and inflammatory burden may preserve residual beta-cell function in toxin-induced models. Histological improvement, when reported, is compatible with protection of pancreatic architecture. Stronger claims of beta-cell regeneration require lineage, proliferation or functional evidence and should not be inferred solely from normalized glucose or improved histology.

7.5 Lipid metabolism and organ protection

Improvement in serum lipids in diabetic animals suggests a potential role in metabolic dyslipidaemia [12]. Antioxidant and anti-inflammatory activity may also contribute to hepatic, renal and cardiovascular protection. However, hepatoprotective or radioprotective findings in non-diabetic models cannot automatically be translated to diabetic nephropathy, steatohepatitis or cardiovascular outcomes. Disease-specific models with renal function, albuminuria, histology and validated cardiovascular endpoints are required.

Mechanism	Direct Grewia evidence	Interpretation confidence	Needed confirmation
Reduction of oxidative stress	Improved SOD/GSH and reduced MDA in diabetic rats	Moderate	Standardized extracts, dose-response, tissue-specific redox markers
Suppression of inflammation	Reduced TNF-alpha and IL-1beta in STZ rats	Moderate	Pathway studies (NF-kB/MAPK), replication and clinical biomarkers
Inhibition of carbohydrate-digesting enzymes	Fruit extract activity in in-vitro assays	Low-to-moderate	Kinetics, selectivity, active compounds and meal-tolerance studies
Improved hepatic glycogen handling	Higher liver glycogen in treated diabetic rats	Moderate	Tracer studies and hepatic enzyme/signalling analysis
Enhanced insulin secretion/sensitivity	Indirectly suggested by glycaemic improvement	Low	Insulin, HOMA-type indices, clamp studies, receptor/Akt/GLUT-4 measurements
Beta-cell regeneration	Often claimed from improved pancreas morphology	Very low	Cell proliferation, lineage and functional beta-cell studies
Antiglycation/AGE inhibition	Plausible from polyphenols	Very low	Direct Grewia antiglycation assays and complication models
Renal/cardiovascular protection	General antioxidant rationale	Very low for diabetes	Diabetic nephropathy and cardiovascular outcome models

Table-4 Lipid metabolism and organ protection

8. Supportive Pharmacology Relevant to Diabetic Complications

Antioxidant activity is one of the most consistently reported biological properties of Grewia extracts, especially G. asiatica fruit, leaves and seeds [4–6,19,20]. Meta-analytic synthesis of heterogeneous antioxidant assays suggested activity across the genus but also very high between-study heterogeneity [4]. This heterogeneity reflects differences in species, extraction, assay platform, concentration expression and reference standards.

Anti-inflammatory effects have been reported for G. asiatica fruit and root bark in rodent models [21,22]. Such activity may be relevant to insulin resistance and vascular inflammation, but the doses and models do not directly establish benefit in diabetes. Hepatoprotective observations and protection against oxidative insults have also been described [23]. These complementary effects strengthen the rationale for integrated diabetes-complication studies, while remaining secondary to direct glycaemic evidence.

9. Toxicological and Safety Considerations

The long history of consuming G. asiatica fruit provides some reassurance for normal dietary use, but concentrated extracts, bark products and isolated compounds cannot be assumed to share the safety profile of food. Published acute-toxicity observations are generally favourable, yet comprehensive sub-chronic, chronic, reproductive, developmental, genotoxic and organ-specific toxicity data remain inadequate. Reports should specify extraction solvent, drug-extract ratio, residual solvents, microbial quality, pesticides, heavy metals and mycotoxins.

Potential herb-drug interactions are also relevant. A genuinely glucose-lowering Grewia product could theoretically add to the effects of insulin, sulfonylureas or other agents and increase hypoglycaemia risk. Polyphenols and tannins may alter intestinal absorption, while triterpenes or flavonoids may affect drug-metabolizing enzymes or transporters. These possibilities are not clinically established for Grewia but should be evaluated before recommending standardized extracts to patients receiving multiple medicines.

Dietary fruit consumption is distinct from medicinal dosing. Sweetened phalsa syrups, squashes or beverages may contain substantial added sugar and should not be promoted as antidiabetic simply because the source fruit has a low glycaemic response. Product formulation and total carbohydrate content are clinically important.

10. Critical Appraisal of the Evidence

The evidence base has four principal strengths. First, multiple plant parts of G. asiatica have shown convergent glucose-lowering observations in animal models. Second, the strongest fruit study connected glycaemic improvement with inflammatory and antioxidant endpoints [11]. Third, phytochemical analyses provide a credible multi-component basis. Fourth, the fruit is edible and potentially relevant to functional-food development.

Important limitations prevent clinical conclusions. Most studies use chemically induced diabetes, small sample sizes and short treatment periods. Extract composition is often poorly standardized, and phytochemical screening is sometimes limited to qualitative colour tests. Some publications lack clear randomization, blinding, allocation concealment or power calculations. Mechanistic claims often exceed measured endpoints. There is little information on oral bioavailability, metabolism, tissue exposure, chronic toxicity, reproducibility across harvests or interaction with standard medicines. Human evidence is limited to a short-term study in healthy participants rather than controlled trials in diabetes.

Accordingly, the current evidence hierarchy may be summarized as follows: G. asiatica has moderate preclinical support; G. flavescens has preliminary in-vivo support; G. hirsuta has in-silico support for a candidate compound; other

species have mainly chemical, nutritional or indirect antioxidant relevance. No Grewia species currently has sufficient evidence to be recommended as a substitute for standard diabetes treatment.

11. Research Gaps and Future Directions

1. Authenticate every study material using current taxonomy, a deposited voucher specimen and, where possible, DNA barcoding for closely related or powdered materials.
2. Develop plant-part-specific pharmacopoeial standards that include microscopy, ash and extractive limits, contaminant testing and validated TLC/HPTLC/HPLC or LC-MS fingerprints.
3. Use bioassay-guided fractionation to identify compounds or reproducible combinations associated with glucose lowering, rather than relying only on total phenolic or flavonoid content.
4. Confirm enzyme inhibition using kinetic, interference-controlled and selectivity assays, followed by carbohydrate-tolerance studies in vivo.
5. Test insulin signalling directly through glucose uptake, insulin secretion, insulin receptor/Akt, AMPK, PPAR and GLUT-4 assays, with appropriate positive and negative controls.
6. Employ complementary models of insulin resistance and type 2 diabetes, not only alloxan or high-dose streptozotocin beta-cell injury.
7. Conduct pharmacokinetic and metabolomic studies to identify absorbed parent compounds and metabolites and to link systemic exposure with pharmacodynamic outcomes.
8. Complete repeated-dose, reproductive and genotoxicity studies for standardized medicinal extracts and examine herb-drug interactions with commonly used glucose-lowering agents.
9. Design randomized clinical trials with registered protocols, standardized products, HbA1c and postprandial outcomes, safety monitoring and sufficient duration.
10. Explore rational dosage forms and food products, but distinguish whole-fruit nutrition from concentrated medicinal extracts and avoid sugar-rich formulations.

Research deficit	Recommended study	Minimum outcome set
Variable identity and extract composition	Authenticated, standardized multi-batch extract study	Voucher, fingerprint, quantified markers, contaminants and batch variability
Weak mechanism attribution	Cellular and molecular target validation	Insulin secretion, glucose uptake, Akt/AMPK/GLUT-4, enzyme kinetics
Model limitations	Diet-induced insulin resistance plus low-dose STZ or genetic models	Fasting glucose, OGTT, insulin, HbA1c analogue, lipids and histology
Unknown exposure	PK/ADME and metabolomics	Cmax, Tmax, AUC, metabolites, tissue distribution and bioavailability
Incomplete safety	OECD-aligned repeated-dose and genotoxicity programme	Clinical chemistry, histopathology, NOAEL, reproductive/genotoxic endpoints
No therapeutic clinical evidence	Randomized placebo-controlled trial in type 2 diabetes	HbA1c, fasting/postprandial glucose, adverse events, medication use and adherence

Table-5 Research Gaps and Future Directions

12. Conclusion

The genus Grewia is a chemically rich and pharmacologically promising source of edible and medicinal materials relevant to diabetes research. G. asiatica is the leading candidate because its fruits, bark and leaves have demonstrated glucose-lowering effects in experimental models, accompanied in some studies by improved lipid, antioxidant and inflammatory outcomes. G. flavescens provides preliminary in-vivo support, while G. hirsuta contributes an in-silico lead. Pharmacognostic evaluation offers practical tools for authentication, but standards must remain species- and plant-part specific.

The strongest current conclusion is not that Grewia is an established antidiabetic therapy, but that it is a credible platform for standardized extract development, functional-food research and natural-product discovery. Translation will require direct mechanistic evidence, rigorous chemical standardization, pharmacokinetics, chronic safety assessment and controlled clinical trials. Until such data are available, Grewia preparations should be viewed as investigational adjuncts rather than replacements for validated diabetes care.

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