Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 06 July 2026
Revised 03 Aug 2026
Accepted 16 Aug 2026

Natural Resources for Human Health 2026, Vol. 6 (18s): 1357–1363

Antidiabetic Medicinal Plants of Uzbekistan and Central Asia: Ethnopharmacology and Mechanisms of Action – A Narrative Review

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ABSTRACT: Type 2 diabetes mellitus (T2DM) continues to rise sharply across Central Asia, driven by rapid urbanisation, dietary transition, and an ageing population, and places a growing burden on national health systems in the region, including Uzbekistan, where the number of adults living with diabetes is estimated to have grown from roughly 813,000 in 2011 to approximately 1.5 million in 2024, with nearly three-quarters of cases believed to remain undiagnosed. Traditional Central Asian medicine has for centuries employed a range of locally available plants to manage "sugar disease", yet only a fraction of this ethnopharmacological knowledge has been subjected to rigorous mechanistic and clinical evaluation. This narrative review synthesises recent (2008–2024) evidence on five medicinal plant taxa native to or widely used in Uzbekistan and the broader Central Asian region – Berberis vulgaris (barberry), Trigonella foenum-graecum (fenugreek), Juglans regia (walnut), Urtica dioica (stinging nettle), and Glycyrrhiza glabra (licorice) – with respect to their antidiabetic activity and underlying mechanisms. We discuss berberine, the principal isoquinoline alkaloid of Berberis species, which activates AMP-activated protein kinase, enhances insulin receptor and GLUT4 expression, suppresses hepatic gluconeogenesis, and favourably modulates gut microbiota composition; fenugreek seed constituents (4-hydroxyisoleucine, trigonelline, and furostanolic saponins), which have demonstrated clinically meaningful reductions in fasting and postprandial glycaemia in randomised trials; walnut leaf polyphenols, for which mechanistic and single-arm clinical

Natural Resources for Human Health
eISSN: 2583-1194

data suggest a hypoglycaemic effect but a recent double-blind placebo-controlled trial found no significant effect on glycaemic indices, illustrating the importance of distinguishing preclinical promise from confirmed clinical benefit; stinging nettle leaf extracts, which inhibit intestinal disaccharidases and glucose transport in vitro; and licorice root constituents, particularly glabridin and glycyrrhetinic acid, which enhance cellular glucose uptake and inhibit intestinal α-amylase activity. We additionally compare the five plants by principal bioactive constituent, proposed mechanism, and strength of clinical evidence, and discuss safety and herb-drug interaction considerations relevant to their concomitant use with conventional antidiabetic therapy. We conclude that Central Asian medicinal flora offers several mechanistically plausible and, in the case of fenugreek and berberine, clinically supported adjuncts to standard antidiabetic therapy, but that rigorous, adequately powered clinical trials using standardised regional plant material remain the principal unmet need before any of these plants can be recommended as evidence-based adjuncts to pharmacotherapy.

KEYWORDS:
antidiabetic plants; Central Asia; Uzbekistan; Berberis vulgaris; Trigonella foenum-graecum; Juglans regia; Urtica dioica; Glycyrrhiza glabra; type 2 diabetes; ethnopharmacology

1. Introduction

Diabetes mellitus has become one of the fastest-growing non-communicable disease burdens worldwide, with the International Diabetes Federation estimating that more than 530 million adults were living with diabetes globally in the early 2020s and projecting continued growth over the following decades, particularly in low- and middle-income regions undergoing rapid nutritional and epidemiological transition [1,2]. Central Asia, including Uzbekistan, Kazakhstan, Kyrgyzstan, Tajikistan, and Turkmenistan, has not been spared this trend: increasing urbanisation, reduced physical activity, and a shift toward energy-dense diets have been accompanied by a rising prevalence of type 2 diabetes mellitus (T2DM) and its vascular complications across the region.

National data illustrate the scale of the problem in Uzbekistan specifically. According to International Diabetes Federation country estimates, the number of adults aged 20–79 years living with diabetes in Uzbekistan rose from approximately 812,900 in 2011, corresponding to an age-standardised prevalence of 6.4%, to approximately 1.5 million in 2024, corresponding to a prevalence of 7.5%, with projections suggesting continued growth toward 2.2 million by 2050 [2]. Perhaps more strikingly, an estimated 74.0% of people with diabetes in Uzbekistan – roughly 1.1 million individuals – are believed to remain undiagnosed, underscoring both the scale of the underlying epidemic and the importance of accessible, culturally embedded approaches to glycaemic management, including the rational use of traditional remedies alongside improved screening and diagnosis [2].

Long before the pharmacological classes of biguanides, sulfonylureas, and incretin-based therapies became available, Central Asian traditional medicine had already developed an extensive body of empirical practice directed at "sugar disease", drawing on the region's exceptionally rich and still only partly catalogued medicinal flora [1]. Plants such as barberry, fenugreek, walnut, stinging nettle, and licorice are used in Uzbek and broader Central Asian folk medicine either as decoctions, infusions, or dietary additions for patients with elevated blood sugar, frequently alongside, rather than instead of, conventional treatment. Over the past two decades, a substantial international literature has begun to test these traditional uses against modern pharmacological and clinical standards, identifying specific bioactive constituents and plausible molecular mechanisms, while at the same time revealing that not every traditionally used plant yields a clinically demonstrable glucose-lowering effect when tested rigorously.

Purpose of this review – to synthesise the currently available mechanistic, preclinical, and clinical evidence on the antidiabetic activity of five medicinal plant taxa prominent in Uzbek and Central Asian traditional medicine – Berberis vulgaris, Trigonella foenum-graecum, Juglans regia, Urtica dioica, and Glycyrrhiza glabra – and to critically assess the strength of evidence supporting their use, together with relevant safety considerations, as adjuncts in the management of type 2 diabetes mellitus.

2. Methods

This narrative review draws on peer-reviewed mechanistic studies, preclinical pharmacological studies, and randomised or controlled clinical trials concerning the antidiabetic activity of the five plant taxa discussed below, identified through searches of PubMed, Scopus, and Google Scholar using combinations of the terms "antidiabetic", "type 2 diabetes", "hypoglycaemic", "glycaemic control", together with genus-specific terms ("Berberis"/"berberine", "Trigonella foenum-graecum"/"fenugreek", "Juglans regia"/"walnut leaf", "Urtica dioica"/"stinging nettle", "Glycyrrhiza glabra"/"licorice"/"glabridin") and the terms "Central Asia" and "Uzbekistan" where applicable. Given the comparative scarcity of region-specific clinical literature identified for most of the genera discussed, studies conducted on plant material sourced from other regions (chiefly Iran, China, India,

and the broader Middle East, where the same species are native or cultivated) are also discussed, with the geographic origin of study material noted explicitly throughout, since the species themselves are the same as those found in Uzbek and Central Asian flora. Studies were prioritised for inclusion when they reported a defined extract or isolated constituent, a stated mechanism or clinical endpoint, and, where available, a comparison against placebo or an active comparator.

3. Berberis vulgaris (Barberry)

Berberis vulgaris and related Berberis species are widely distributed across Central Asia and have long been cultivated and gathered in Uzbekistan for both culinary and medicinal use, with the berries traditionally used in cooking, preserves, and sour seasonings, and the roots and bark employed in folk preparations for liver and metabolic complaints, including elevated blood sugar. The principal bioactive constituent of the genus is berberine, an isoquinoline alkaloid present in the roots, rhizomes, and stem bark, which has become one of the most extensively investigated plant-derived antidiabetic compounds worldwide.

A frequently cited early randomised clinical trial administered berberine (1.0 g/day) to adults with newly diagnosed type 2 diabetes mellitus over three months and reported significant reductions in fasting plasma glucose, postprandial glucose, and glycated haemoglobin, with an efficacy comparable to that of metformin in the same study, alongside favourable reductions in triglycerides and total cholesterol [3].

Subsequent mechanistic work has clarified how berberine achieves these effects. Berberine activates AMP-activated protein kinase (AMPK) in hepatocytes, adipocytes, and skeletal myocytes, a key cellular energy sensor that promotes glucose uptake and curtails lipogenesis; it increases phosphorylation of the insulin receptor, insulin receptor substrate-1, and Akt, while suppressing protein tyrosine phosphatase 1B, a negative regulator of insulin signalling; it upregulates glucose transporter type 4 (GLUT4) translocation to the plasma membrane in muscle and adipose tissue; it suppresses hepatic gluconeogenic enzyme expression and activates the TORC2/AMPK axis in the liver; and it favourably reshapes gut microbiota composition, increasing beneficial taxa such as Akkermansia muciniphila and Bacteroidetes while reducing circulating lipopolysaccharide-driven inflammatory signalling that otherwise contributes to insulin resistance [4].

Taken together, the berberine literature illustrates a case in which a Central Asian medicinal plant genus has yielded a single, well-characterised bioactive constituent with a multi-target mechanism of action and reasonably strong supporting clinical-trial evidence, making Berberis vulgaris among the better-validated antidiabetic plants discussed in this review. Its principal limitation for regional application is that essentially all supporting clinical trials have used a standardised, purified alkaloid preparation rather than a crude Berberis root or bark decoction of the kind traditionally prepared in Uzbekistan, so the magnitude of effect achievable with traditional preparations of variable berberine content remains uncertain.

4. Trigonella foenum-graecum (Fenugreek)

Fenugreek is cultivated throughout Central Asia and Uzbekistan both as a spice and as a traditional remedy for diabetes and digestive complaints, typically taken as a powder of the ripe seeds mixed with water or food, or incorporated into bread and porridge. Its seeds are rich in soluble fibre (galactomannan), the unusual amino acid 4-hydroxyisoleucine, the alkaloid trigonelline, and furostanolic saponins, each of which has been proposed to contribute to the plant's antidiabetic activity through a distinct mechanism: soluble fibre delays gastric emptying and slows intestinal carbohydrate absorption, thereby blunting postprandial glucose excursions; 4-hydroxyisoleucine potentiates glucose-stimulated insulin secretion from pancreatic beta cells in an insulin-sensitivity-dependent manner, which is thought to explain why fenugreek rarely causes hypoglycaemia in normoglycaemic individuals; and trigonelline has been shown experimentally to improve insulin sensitivity and modulate hepatic glucose metabolism, with additional neuroprotective and lipid-lowering properties reported in preclinical models.

Clinical evidence for fenugreek is comparatively strong among the plants considered in this review. A randomised, double-blind, placebo-controlled trial of a standardised fenugreek seed extract rich in furostanolic saponins, given as an adjunct to standard antidiabetic medication in patients with type 2 diabetes over twelve weeks, reported significant reductions in both fasting and postprandial glucose and in glycated haemoglobin relative to placebo, with no serious adverse events and preserved hepatic and renal function markers [5]. These findings are broadly consistent with earlier systematic reviews and meta-analyses of fenugreek supplementation, which have generally reported modest but statistically significant improvements in fasting glucose and glycaemic control across pooled randomised trials, while noting considerable heterogeneity in preparation, dose, and duration between studies, ranging from simple defatted seed powder taken with meals to concentrated saponin-standardised extracts taken as capsules.

Given the combination of a plausible, multi-component mechanism and supportive randomised trial data, fenugreek represents one of the more promising candidates among Central Asian antidiabetic plants for further standardisation and clinical development, and has the practical advantage, relative to berberine, of already being a familiar dietary spice in the region rather than a preparation requiring pharmaceutical-grade extraction.

5. Juglans regia (Walnut)

The walnut tree is widespread in Uzbekistan and across Central Asia, and besides the nut itself, which is a dietary staple, the leaves have a long history of use in regional folk medicine as a decoction for diabetes, skin conditions, and as a general tonic. Walnut leaves are rich in phenolic compounds, including flavonoids (notably quercetin derivatives), tannins, and naphthoquinones such as juglone, which have demonstrated antioxidant and, in some experimental models, hypoglycaemic activity, generally attributed to a combination of free-radical scavenging in pancreatic beta cells and modest inhibition of carbohydrate-digesting enzymes.

An early open-label human trial of an aqueous extract of walnut leaves in patients with type 2 diabetes reported a reduction in fasting blood glucose during the treatment period, and the authors proposed that the extract's phenolic constituents might act in part through inhibition of intestinal carbohydrate-digesting enzymes and enhancement of peripheral glucose utilisation [6]. However, this encouraging single-arm finding has not been consistently replicated under more rigorous trial conditions: a subsequent double-blind, placebo-controlled trial of a standardised hydroalcoholic walnut leaf extract (200 mg/day) given for eight weeks to patients with type 2 diabetes found no statistically significant effect of the extract on fasting blood glucose or the HOMA-IR index of insulin resistance relative to placebo, although it did observe reductions in body weight, body mass index, and systolic blood pressure in the treated group [7].

This divergence between an earlier open-label, uncontrolled report and a later placebo-controlled trial is instructive: it underscores why claims of antidiabetic efficacy for traditionally used plants must be weighed according to study design, and it illustrates that walnut leaf extract, despite genuine antioxidant and metabolic activity, cannot currently be regarded as having a clinically confirmed glucose-lowering effect, even though its cardiometabolic and weight-related benefits may still be of interest for patients with diabetes who also present with overweight or mild hypertension, both common comorbidities in this population.

6. Urtica dioica (Stinging Nettle)

Stinging nettle grows abundantly as a wild plant throughout Central Asia, including Uzbekistan, and its aerial parts are traditionally prepared as an infusion for a wide range of complaints, including diabetes, urinary disorders, joint pain, and general debility, often collected in early spring when the leaves are most tender. Phytochemical analysis of nettle leaf extracts has identified a range of phenolic constituents, with rutin and caffeoylquinic acid derivatives typically predominating, alongside smaller amounts of other flavonoid glycosides and organic acids.

In vitro pharmacological work on a hydroethanolic extract of Urtica dioica leaves has demonstrated two complementary mechanisms relevant to postprandial glycaemic control: inhibition of intestinal disaccharidase enzymes, with maltase activity reduced by over half and sucrase activity reduced by nearly half at the concentration tested, and a nearly 1.5-fold reduction in glucose transport across a Caco-2 intestinal epithelial cell model, consistent with inhibition of intestinal glucose transporters such as GLUT2 [8]. These findings provide mechanistic support for the traditional use of nettle in glycaemic control through a predominantly intestinal, rather than systemic, mode of action, analogous in principle to the mechanism of pharmaceutical alpha-glucosidase inhibitors such as acarbose, although confirmatory clinical trials in patients with diabetes using standardised extracts remain to be conducted, and the available evidence for nettle in this review is accordingly the least clinically mature of the five plants discussed.

7. Glycyrrhiza glabra (Licorice)

Licorice root is another plant with deep roots in Central Asian and Uzbek traditional pharmacy, used historically both as a sweetening and flavouring agent and as a remedy for respiratory, gastrointestinal, and metabolic complaints; Glycyrrhiza glabra and related species grow wild across the region and have also been the subject of dedicated cultivation and breeding programmes in Uzbekistan given their commercial as well as medicinal importance. The root contains a complex mixture of triterpenoid saponins, chiefly glycyrrhizin and its aglycone glycyrrhetinic acid, together with flavonoids including glabridin and liquiritigenin, which together account for most of its documented pharmacological activity.

A comparative screening study of licorice extracts from eight different geographic origins found broadly consistent glucose-uptake-promoting activity across samples (92–101 arbitrary units relative to control) and substantial α-amylase inhibitory activity (57–70 units), approaching that of the pharmaceutical standard acarbose (78.4 units) in the same assay system, with glabridin identified as activating the AMPK pathway in cultured muscle cells in a manner mechanistically analogous to berberine, and glycyrrhetinic acid shown in earlier animal studies to ameliorate hyperglycaemia in streptozotocin-induced diabetic models [9]. Taken together, these data indicate that licorice acts through a combination of enhanced peripheral glucose uptake and inhibition of intestinal starch-digesting enzymes, placing it mechanistically at the intersection of the berberine/AMPK pathway and the nettle/enzyme-inhibition pathway described above.

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eISSN: 2583-1194

An important caveat specific to licorice, discussed further in Section 9 below, is that glycyrrhizin and its metabolites inhibit 11β-hydroxysteroid dehydrogenase type 2, an enzyme that normally inactivates cortisol in mineralocorticoid-sensitive tissues; sustained high-dose licorice consumption can therefore produce a pseudo-hyperaldosteronism syndrome with sodium retention, hypokalaemia, and hypertension, which would be expected to work against, rather than for, good metabolic control in patients with diabetes, so any recommendation regarding licorice must be qualified accordingly.

8. Comparative Overview

Figure 1 summarises, in schematic form, the principal site of action within the body for each of the five plants discussed above, and Table 1 below summarises the corresponding bioactive constituent, proposed mechanism, and strength of clinical evidence.

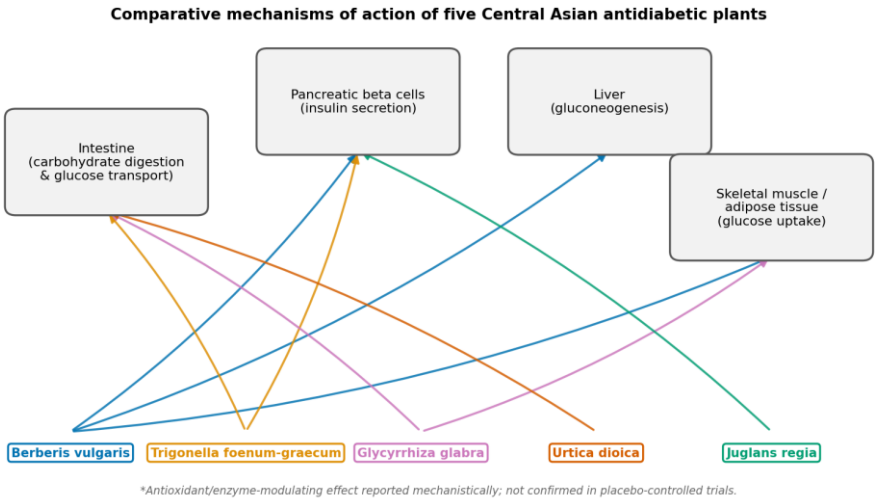


Figure 1. Comparative mechanisms of action of five Central Asian antidiabetic plants, by principal target organ or tissue (schematic, based on the mechanistic and clinical studies cited in Sections 3–7).

Plant (part used)	Principal constituent(s)	Proposed mechanism	Strength of clinical evidence
Berberis vulgaris (root/bark)	Berberine	AMPK activation; ↑insulin receptor/GLUT4; ↓hepatic gluconeogenesis; gut microbiota modulation	Moderate–strong (RCT vs. metformin-comparable effect)
Trigonella foenum-graecum (seed)	4-hydroxyisoleucine, trigonelline, furostanolic saponins	Delayed carbohydrate absorption; glucose-dependent insulin secretion; ↑insulin sensitivity	Strong (placebo-controlled RCT, consistent meta-analyses)
Juglans regia (leaf)	Flavonoids, tannins, juglone	Antioxidant protection of beta cells; mild enzyme inhibition (mechanism not confirmed clinically)	Weak–mixed (open-label positive; placebo-controlled RCT negative)
Urtica dioica (leaf)	Rutin, caffeoylquinic acids	Intestinal disaccharidase inhibition; ↓GLUT2-mediated glucose transport	Preclinical/in vitro only; no clinical trials identified
Glycyrrhiza glabra (root)	Glabridin, glycyrrhetinic acid, glycyrrhizin	AMPK activation (glabridin); α-amylase inhibition; peripheral glucose uptake	Preclinical/mechanistic; safety caveat limits clinical use

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eISSN: 2583-1194

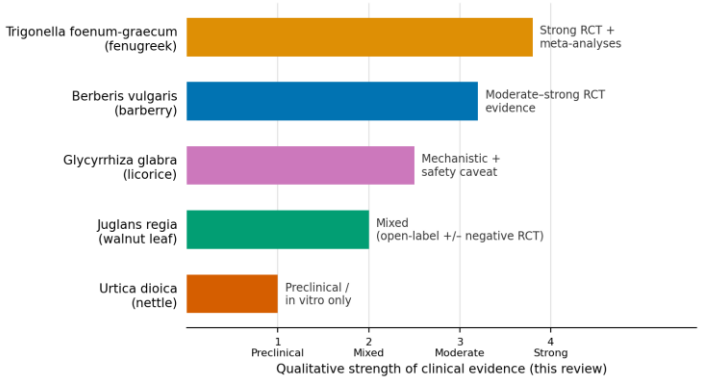


Figure 2. Qualitative strength of clinical evidence for each plant, scored on a 1 (preclinical/in vitro only) to 4 (strong, placebo-controlled randomised trials with supporting meta-analyses) scale, as assessed in this review.

9. Safety and Herb–Drug Interaction Considerations

Because most patients in Uzbekistan and the wider region who use these plants do so as an adjunct to, rather than a replacement for, prescribed antidiabetic medication, safety and interaction considerations are as clinically important as efficacy. Berberine has well-documented inhibitory effects on several cytochrome P450 isoenzymes (notably CYP2D6 and CYP3A4) and on P-glycoprotein-mediated drug transport, raising the potential for interactions with a range of commonly co-prescribed drugs, and its combination with metformin, while studied and generally well tolerated, can in principle increase the risk of gastrointestinal adverse effects and, theoretically, additive glucose-lowering effects requiring dose adjustment and closer glucose monitoring. Fenugreek, by virtue of its high soluble-fibre content, may reduce the absorption of concomitantly administered oral medications if taken at the same time, and its mild antiplatelet activity warrants caution in patients also taking anticoagulant or antiplatelet therapy. Licorice, as discussed in Section 7, carries a distinct and clinically significant risk of pseudo-hyperaldosteronism, hypokalaemia, and hypertension with sustained high-dose use, and should specifically be avoided or used only under medical supervision in patients with hypertension, chronic kidney disease, or heart failure, all of which are common comorbidities in older patients with long-standing type 2 diabetes. Walnut leaf and nettle preparations have not revealed major safety signals in the trials reviewed here, though the overall evidence base for both remains small. None of the five plants has been adequately studied for interaction with sodium–glucose cotransporter-2 inhibitors or glucagon-like peptide-1 receptor agonists, the newer antidiabetic drug classes now entering wider use in the region, which represents a further gap for future research.

10. Translational Priorities for the Region

From a translational standpoint, three priorities emerge for Uzbek and wider Central Asian antidiabetic phytotherapy research. First, standardisation: almost none of the clinical studies reviewed used plant material characterised to a defined marker-compound content, which severely limits reproducibility and cross-study comparison; future regional studies should quantify active constituents (for example berberine content in Berberis extracts, furostanolic saponin content in fenugreek extracts, or glabridin content in licorice extracts) using validated analytical methods such as HPLC. Second, adequately powered, placebo-controlled clinical trials conducted specifically in Central Asian populations and using regionally sourced plant material are needed, since the existing clinical evidence base for all five plants originates predominantly from Iran, China, India, and South Asia rather than from Uzbekistan or its immediate neighbours, and phytochemical content is known to vary with soil, climate, and harvesting practice. Third, safety and interaction data deserve more systematic attention, since most patients using these plants in Central Asia do so as an adjunct to, rather than a replacement for, prescribed antidiabetic medication, and the undiagnosed-diabetes gap noted in the Introduction means that a considerable number of people may also be using these plants outside any formal medical supervision at all.

11. Conclusion

Central Asian and Uzbek traditional medicine has long used Berberis vulgaris, Trigonella foenum-graecum, Juglans regia, Urtica dioica, and Glycyrrhiza glabra in the management of diabetes, and modern pharmacological research has, for each of these plants, identified at least plausible mechanisms of antidiabetic action. The strength of supporting evidence, however, differs considerably between them: berberine and fenugreek are supported by randomised clinical trials demonstrating clinically meaningful improvements in glycaemic indices, licorice and nettle are supported chiefly by mechanistic and in vitro work with licorice additionally carrying a clinically important safety caveat, and the clinical evidence for walnut leaf is mixed, with a placebo-controlled trial failing to confirm an isolated glucose-lowering effect. Given that Uzbekistan already carries a substantial and apparently still-growing diabetes burden, with a particularly high proportion of undiagnosed cases, we conclude that Central

Asian medicinal flora constitutes a genuine and only partly validated resource for antidiabetic phytotherapy, and that standardised extracts, rigorous regional clinical trials, and systematic safety and drug-interaction studies represent the principal steps required before any of these plants can be recommended on an evidence-based footing as adjuncts to conventional antidiabetic pharmacotherapy.

Acknowledgements

[To be completed by the author(s).]

Author Contributions

[To be completed by the author(s).]

Conflict of Interest

The authors declare that there is no conflict of interest.

Ethics Statement

This article is a narrative literature review and did not involve new data collection from human or animal subjects; ethical approval was therefore not required.

Data Availability Statement

No new data were generated in this review. All sources discussed are cited in the reference list and are publicly available through the indicated journals and databases.

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