ISSN: 2231-3656

International Journal of Pharmacy and Industrial Research (IJPIR)

IJPIR |Vol. 16 | Issue 3 | Jul – Sep 2026

www.ijpir.com

DOI:https://doi.org/10.61096/ijpir.v16.iss3.2026.923.934

4DM+: A Scientifically Grounded Botanical Formulation for Metabolic Support and Healthy Glucose Balance — a Narrative Review of Gymnema Sylvestre and Pterocarpus Marsupium

Dr Leroy Rebello[1], Dr Sreesudha Chepyala[2] and Sahithi Polineni[3]

Department of Research and Development,
Biotex Life Solutions Pvt. Ltd., Secunderabad, Telangana, India

*Corresponding author**: Polineni Sahithi;**
E-mail: sahithi.biotexlife@gmail.com

Published on:

27.07.2026
Published by: Futuristic Publications

Abstract: 4DM+ is a proprietary botanical formulation from Biotex Life Solutions Pvt. Ltd. combining two phytochemical-rich, pharmacologically characterised herbs—Gymnema sylvestre R.Br. (Gurmar) and Pterocarpus marsupium Roxb. (Vijayasar)—for metabolic wellness and healthy glucose balance. This narrative review collates the botany, phytochemistry and pharmacology of each herb and evaluates the scientific rationale for their combined use as a foundation for future controlled clinical studies. Gymnema sylvestre leaf extract, rich in gymnemic acids, has been shown in vitro, preclinically and clinically to enhance endogenous insulin secretion, modulate beta-cell function, inhibit intestinal SGLT1-mediated glucose absorption, and improve glycaemic and biochemical parameters in human studies. Pterocarpus marsupium heartwood, a source of phenolics, flavonoids, epicatechin, pterostilbene, marsupsin and pterosupin, has shown antihyperglycaemic activity in newly diagnosed non-insulin-dependent diabetics, with GLUT4 upregulation, PPAR-γ activation and insulinotropic and antioxidant mechanisms. The two herbs act through complementary, partly non-overlapping mechanisms, providing a rationale for their combination in 4DM+. Both botanicals show favourable documented safety profiles, though robust clinical evidence for the combined formulation remains limited. The review concludes the combination is mechanistically justified as metabolic support rather than a diabetes treatment, and identifies priorities for standardisation and clinical evaluation.

Keywords: Gymnema sylvestre; Pterocarpus marsupium; gymnemic acids; glucose balance; metabolic support

1. Introduction

1.1 Global Burden of Metabolic Dysregulation

Metabolic dysregulation is a collective term for impaired fasting glucose, postprandial glucose, insulin resistance, dyslipidemia, and low-grade systemic inflammation, among other related abnormalities. This syndrome has become one of the most pressing public health priorities due to its complex pathophysiology and the significant morbidity and mortality associated with its progression. According to the International Diabetes Federation (IDF), 537 million adults were living with diabetes in 2021, with a forecast of 783 million by 2045[1]. Of these cases, the vast majority are caused by type 2 diabetes mellitus (T2DM) triggered by environmental factors superimposed on genetic susceptibility. Notably, there is a significantly larger population of prediabetic individuals who are at a higher risk of developing T2DM [2].

Currently, the pharmacological treatment of T2DM is limited by the presence of undesirable effects, contraindications, and other factors such as cost and adherence to treatment. These shortcomings have

stimulated a surge of scientific and commercial interest in botanical preparations that could help regulate blood glucose levels and support metabolic wellness in diabetic patients[3]. Medicinal plants with documented pharmacological activity in glucose metabolism regulation have been subject to extensive scientific investigations to identify their potential botanical nutraceuticals for managing or preventing diabetes.

1.2 Rationale for 4DM+

4DM+ is a botanical wellness product containing standardised extracts of two Ayurvedic medicinal plants, Gymnema sylvestre R.Br. (family Apocynaceae) and Pterocarpus marsupium Roxb. (family Fabaceae). These plants were selected for their documented ability to support glucose metabolism and provide a synergistic effect when combined. Gymnema sylvestre predominantly acts on the gastrointestinal tract and pancreas, while Pterocarpus marsupium mainly targets peripheral tissues and the liver[4]. This narrative review aims to provide a comprehensive evidence base for the ingredients used in the 4DM+ formulation. Specifically, this review will discuss the scientific rationale for using these botanicals, summarise the evidence from clinical and preclinical studies, and explore the pharmacokinetic and safety properties relevant to their use in the proposed formulation. It is important to note that this review aims to provide a scientific foundation for the proposed formulation and does not constitute medical advice or a claim of therapeutic efficacy.

1.3 Objectives of This Review

Examine the phytochemical composition of Gymnema sylvestre and Pterocarpus marsupium relevant to glucose metabolism support.

Elucidate the molecular mechanisms and cellular pathways of action for both botanicals.

Summarise the in vitro, preclinical, and clinical evidence for each botanical.

Explore the scientific rationale for combining Gymnema sylvestre and Pterocarpus marsupium in the 4DM+ formulation.

Assess the safety, pharmacokinetic, and herb-drug interaction profiles of the ingredients.

Develop a framework for future clinical studies of 4DM+.

2. Methodology

This narrative review follows a predefined search strategy that aimed to identify published scientific literature on the pharmacology of Gymnema sylvestre and Pterocarpus marsupium. The databases searched include PubMed/MEDLINE, Scopus, Web of Science, Google Scholar, and the Cochrane Central Register of Controlled Trials (CENTRAL). The search terms include Gymnema sylvestre, Gurmar, gymnemic acids, GS4, Pterocarpus marsupium, Vijayasar, Malabar Kino, pterostilbene, marsupsin, epicatechin, glucose transporter, GLUT4, PPAR-γ, SGLT1, DPP-4, insulin secretion, beta-cell function, metabolic syndrome, blood glucose, glycemic control, and others. The search period spans back to the earliest records in the databases and up to June 2026. The studies included in this review were published in peer-reviewed journals and written in any language. Articles published in a language other than English were included in the review after translation.

The inclusion criteria comprised studies with original empirical data on the pharmacology of the two botanicals, including preclinical and clinical studies, as well as reviews. Additionally, the review includes pharmacokinetic and safety studies, as well as clinical studies published in peer-reviewed journals. Excluded studies include abstracts without full-text articles, conference proceedings, and reports that do not provide empirical evidence on the pharmacology of the two botanicals. The review uses a narrative synthesis approach that focuses on combining the findings of different studies. The level of evidence was evaluated based on the study design, sample size, characterisation of the extract, dosage, and outcome measures.

3. Product Profile: 4DM+ by BiotexLife Solutions

3.1 Product Concept and Positioning

4DM+ is a botanical wellness product developed and marketed by BiotexLife Solutions Private Limited. It is a nutraceutical formulation that supports metabolic function and promotes healthy glucose balance in diabetic patients. The product is not intended to replace or substitute pharmaceutical treatment for diabetes

but rather to complement a healthy lifestyle and ensure optimal glucose regulation. Table 1 below provides a summary of the product.

Table 1: 4DM+ Product Summary

Parameter	Details
Product Name	4DM+
Manufacturer	BiotexLife Solutions Private Limited
Product Category	Botanical Nutraceutical / Dietary Supplement
Active Ingredient 1	Gymnema sylvestre R.Br. – Leaf extract
Active Ingredient 2	Pterocarpus marsupium Roxb – Heartwood extract
Primary Claim	Supports metabolic function and healthy glucose balance
Target Population	Health-conscious adults
Regulatory Category	Nutraceutical / Botanical Dietary Supplement
Positioning Statement	Evidence-based botanical support; adjunct to diet and lifestyle

4. Phytochemical Characterisation

4.1 Gymnema sylvestre - Phytochemistry

Gymnema sylvestre R.Br. (family Apocynaceae) is a climbing plant native to India, Africa, and Australia. It has been used in traditional medicine for centuries, but most of the pharmacological literature originates from Indian ethnobotanical sources. The leaves of the plant have been reported to contain over 30 triterpenoid saponins, including gymnemic acids (GA) I-VII and their esters[5]. The major gymnemic acids are oleanane-type triterpenoid glycosides that possess tigloyl, methylbutyroyl, or acetyl ester moieties linked to the sugar chain.[6]

The plant also contains gymnemasaponins, which are triterpenoid saponins, and gurmarin, a polypeptide that inhibits sweet taste receptors in rodents. Other phytochemical constituents of Gymnema sylvestre include gymnestrogenin (a pentahydroxytriterpene), conduritol A, quercetin, luteolin, kaempferol and its glycosides, chlorogenic and protocatechuic acids, and alkaloids such as betaine, choline, and trimethylamine[7,8]. The commercial extract of Gymnema sylvestre used in most clinical studies is GS4, a standardised extract that contains a minimum of 25% gymnemic acids.

Fig 1: Taxonomic classification, botanical features, traditional names, and selected synonyms of Gymnema sylvestre (Retz.) R.Br. ex Sm.

4.2 Pterocarpus marsupium - Phytochemistry

Pterocarpus marsupium Roxb. (family Fabaceae) is a large deciduous tree native to India, Sri Lanka, and Nepal. It is known as Vijayasar or Beejaka in Ayurveda and has been used in traditional medicine to manage diabetes and support cardiovascular health. The bark, heartwood, and leaves of the tree have been investigated for their pharmacological properties. However, the heartwood is the most commonly used part in the preparation of extracts with therapeutic claims. The major phytochemical constituents of Pterocarpus marsupium heartwood include epicatechin ((-)-epicatechin), pterostilbene (3, 5-dimethoxy-4′-hydroxystilbene), marsupsin, pterosupin, liquiritigenin, isoliquiritigenin, and propterol [9, 10]. [11]

The heartwood of Pterocarpus marsupium is rich in flavonoids and phenolic compounds with antioxidant activity. The plant contains various flavonoid subclasses, including flavan-3-ols, chalcones, and C-glycosylflavones. The ethanolic extract of the heartwood is commonly used to prepare the Vijayasar tumbler, a traditional Ayurvedic preparation. The tumbler is made by boiling water in the heartwood vessel and then using the water for consumption. Clinical studies have used both the Vijayasar tumbler and standardised aqueous/alcoholic extracts to demonstrate the efficacy of Pterocarpus marsupium in managing diabetes and supporting metabolic health.

Fig 2: Taxonomic classification, botanical characteristics, traditional names, and selected synonyms of Pterocarpus marsupium (Roxb.) Willd.

5. Mechanisms of Action

5.1 Gymnema sylvestre - Mechanisms

5.1.1 Intestinal Glucose Absorption Modulation

The gymnemic acids in G. sylvestre possess structural similarity to glucose and have been shown to competitively inhibit sodium-dependent glucose transporter 1 (SGLT1) at the intestinal brush-border epithelium, reducing the rate and extent of glucose absorption from the diet [13, 14]. This intestinal mechanism of action may explain the clinical observations of reduced postprandial glucose excursions in humans without causing hypoglycemia under fasting conditions.

5.1.2 Pancreatic Beta-Cell Insulinotropic Activity

Shanmugasundaram et al. (1990) demonstrated that GS4 extract of G. sylvestre significantly increased insulin secretion in both mouse beta-cell cultures and human islet preparations. Subsequent

histopathological evaluations revealed increased beta-cell mass and islet number in G. sylvestre-treated animals compared to diabetic controls. The mechanism may involve gymnemic acid-induced alterations in beta-cell membrane permeability and calcium influx, resulting in glucose-dependent insulin secretion (GSIS). Notably, this effect was observed in the presence - but not absence - of stimulatory glucose concentrations, suggesting a glucose-dependent (non-hypoglycemic) mechanism. [15]

5.1.3 Sweet-Taste Receptor Modulation and Appetite Effects

Gurmarin and gymnemic acids reversibly inhibit sweet-taste receptors (T1R2/T1R3 heterodimer), reducing sweet taste perception and potentially attenuating cephalic-phase insulin responses to sweet stimuli. This effect has been demonstrated in rodent models and human taste perception studies and may contribute to decreased caloric intake from sweet foods when the product is consumed before meals.

5.2 Pterocarpus marsupium - Mechanisms

5.2.1 GLUT4 Upregulation and PPAR-γ Activation

Anandharajan et al. (2005) demonstrated that the isoflavone fraction of P. marsupium heartwood significantly upregulated GLUT4 protein expression and activated PPAR-γ transcription in L6 rat skeletal myotubes. This provides mechanistic evidence for the insulin-sensitising effects of P. marsupium at the peripheral tissue level. Activation of PPAR-γ is a recognised mechanism by which thiazolidinedione antidiabetic drugs improve insulin sensitivity and glucose utilisation.[17]

5.2.2 Insulinotropic and Insulin-Like Activity

Aqueous extracts of P. marsupium heartwood have demonstrated direct insulinotropic activity in isolated rat islets of Langerhans and insulin-like peripheral activity in cellular assays. Mohankumar et al. (2012) identified a high molecular weight fraction of the aqueous extract that demonstrated both direct stimulation of insulin secretion from pancreatic beta-cells and peripheral insulin-like glucose-uptake stimulation, suggesting multiple mechanisms of action in a single botanical extract.[18,19,20]

5.2.3 Antioxidant and Hepatoprotective Mechanisms

The phenolic and flavonoid constituents of P. marsupium heartwood have demonstrated antioxidant activity through multiple mechanisms, including free radical scavenging, metal chelation, and upregulation of endogenous antioxidant enzymes. Dar et al. (2022) demonstrated that heartwood extract protected HepG2 cells from oxyradical damage while also increasing glucose uptake in these cells. These findings suggest potential hepatoprotective and glucose utilisation-enhancing effects that may contribute to the metabolic benefits of P. marsupium.

5.2.4 Anti-inflammatory Activity via TNF-α Regulation

Halagappa et al. (2010) investigated the effect of an aqueous extract of P. marsupium on TNF-α in streptozotocin-induced diabetic rats and found that it significantly reduced TNF-α levels compared to control animals. This anti-inflammatory activity may contribute to the overall metabolic benefits of P. marsupium by modulating the inflammatory response associated with insulin resistance.

5.2.5 DPP-4 Inhibitory Hypothesis

In silico molecular docking studies by Kosaraju et al. (2014) identified potential inhibitory interactions between phytoconstituents of P. marsupium - and to a lesser extent G. sylvestre - and the active site of dipeptidyl peptidase-4 (DPP-4), the enzyme responsible for incretin degradation. If confirmed by in vitro and in vivo studies, this mechanism of action would provide additional support for the glucose-lowering effects of P. marsupium, acting via a similar mechanism to sitagliptan and other DPP-4 inhibitors. [21]

6. Clinical Evidence

6.1 Clinical Evidence for Gymnema Sylvestre

The published clinical evidence for G. sylvestre consists of open-label trials, controlled clinical trials, and systematic reviews/meta-analyses, primarily in T2DM or prediabetic populations, using the standardised GS4 extract at doses of 400–800 mg/day. Shanmugasundaram et al. (1990) conducted the earliest open-label study in IDDM patients and T2DM patients receiving conventional therapy, demonstrating significant reductions in HbA1c, fasting blood glucose, serum insulin, and improvements in lipid profiles compared to conventional therapy alone. Baskaran et al. (1990) later demonstrated improvements in fasting blood

glucose, postprandial glucose, HbA1c, and glycosylated plasma proteins in T2DM patients treated with GS4 extract for 18–20 months.[22,23,24,25,26]

More recently, clinical evidence for G. sylvestre has been evaluated in systematic reviews and meta-analyses. Al-Romaiyan et al. (2010) performed a meta-analysis of published trials using G. sylvestre, reporting that the evidence supports a beneficial effect on selected glycemic parameters, although with significant variability between trials in terms of extract type, dose, duration, and control groups. A 2026 review by Saritas and Serin concluded that G. sylvestre may be considered a "multi-target antidiabetic agent" based on the cumulative evidence from preclinical and clinical studies.

6.2 Clinical Evidence for Pterocarpus marsupium

The most informative clinical trial for P. marsupium is the landmark flexible-dose open trial conducted by the Indian Council of Medical Research (ICMR) Collaborating Centres (1998) in 97 patients with newly diagnosed NIDDM. The 12-week treatment with Vijayasar tumbler water resulted in a significant proportion of patients achieving normoglycemia, with the investigators concluding that the product demonstrated clinically relevant glucose-lowering activity in early-phase T2DM.[27,28,29,30]

Patidar et al. (2015) conducted a randomised controlled trial evaluating the efficacy of P. marsupium extract in T2DM patients over a 12-week treatment period. The study reported significant reductions in fasting blood glucose, postprandial glucose, and HbA1c compared to placebo, with no serious adverse events observed. Mohankumar et al. (2012) provided mechanistic evidence for the insulinotropic and insulin-like activity of the aqueous extract of P. marsupium heartwood. The review by Basnayake and Gunatilake (2024) summarised the pharmacological evidence for P. marsupium across multiple preparation types.

7. Synergistic Rationale for the 4DM+ Combination

The complementary mechanisms of action of G. sylvestre and P. marsupium are the rationale for their combination in 4DM+. As shown in Table 2, the two botanicals act on different but related aspects of glucose homeostasis and insulin function. While G. sylvestre primarily acts on intestinal glucose absorption and pancreatic insulin secretion, P. marsupium enhances peripheral glucose uptake, improves hepatic glucose metabolism, and modulates inflammatory and antioxidant pathways. This multi-target approach may provide additive or synergistic benefits for metabolic health.

Table 2: Mechanistic Complementarity in 4DM+

Biological Target	Gymnema sylvestre	Pterocarpus marsupium
Intestinal glucose absorption (SGLT1)	Primary mechanism - gymnemic acid inhibition	Not primary mechanism
Pancreatic insulin secretion	Insulinotropic via beta-cell membrane modulation	Insulinotropic via epicatechin/aqueous extract
Peripheral glucose uptake (GLUT4)	Secondary/indirect via insulin increase	Primary mechanism - GLUT4 upregulation
Insulin sensitisation (PPAR-γ)	Limited direct evidence	Primary mechanism - isoflavone-mediated PPAR-γ activation
Hepatic glucose metabolism	Indirect via systemic effects	Hepatoprotective, HepG2 glucose uptake improvement
Antioxidant defense	Moderate (quercetin, luteolin, chlorogenic acid)	Strong (epicatechin, pterostilbene, DPPH inhibition)
Anti-inflammatory (TNF-α)	Limited direct evidence	Demonstrated TNF-α reduction in diabetic rats
DPP-4 inhibition (hypothesis)	Molecular docking evidence	Molecular docking evidence

Islam et al. (2019) conducted a focused narrative review addressing the combination of G. sylvestre and P. marsupium as implemented in the 4DM formulation. The review concluded that the complementary

mechanisms of action of the two botanicals provide a rationale for their combination and recommended further combination pharmacology studies to explore potential interactions. No pharmacologically antagonistic interactions between the two botanicals have been reported in the literature.

8. Pharmacokinetics and Bioavailability Considerations

8.1 Gymnema sylvestre Pharmacokinetics

Pharmacokinetic data on gymnemic acids in humans are limited, with most studies being conducted in vitro or in animal models. Following oral administration, gymnemic acids are partially absorbed in the intestine, with peak plasma concentrations reached within 1–2 hours after dosing. The aglycone forms generated by intestinal and colonic hydrolysis of gymnemic acid glycosides may contribute to systemic activity. Hepatic metabolism, including glucuronidation and sulfation, is likely to occur, with renal excretion being the primary route of elimination. The food matrix is expected to significantly impact gymnemic acid bioavailability, with co-administration with a meal being necessary for optimal intestinal interaction.

8.2 Pterocarpus marsupium Pharmacokinetics

Pterostilbene, one of the major bioactive constituents of P. marsupium, has been studied more extensively than the complex mixture of constituents in the heartwood extract. Due to the methoxy groups on its phenolic rings, pterostilbene has greater lipophilicity and oral bioavailability compared to its parent compound resveratrol. In rodents, oral bioavailability of pterostilbene has been estimated to be around 80%, with extensive tissue distribution, including accumulation in the brain. Epicatechin has moderate oral bioavailability, undergoes extensive phase II metabolism (methylation, glucuronidation, sulfation), and is eliminated primarily via the kidneys and bile, with intestinal microbiota playing a role in its biotransformation.

9. Evidence Synthesis

Table 3: Summary of Key Clinical Studies - Gymnema sylvestre

Study (Year)	Design	Population	Intervention	Primary Outcomes	Evidence Level
Shanmugasundaram et al. (1990)	Open-label controlled	T2DM on conventional therapy	GS4 400 mg/day + conventional vs. conventional alone; 18–20 months	↓ FBG, ↓ HbA1c, ↓ insulin dose requirement	Level IIb
Baskaran et al. (1990)	Open-label	T2DM	GS4 400 mg/day; 18–20 months	↓ FBG, ↓ HbA1c, ↓ glycosylated plasma proteins	Level IIb
Al-Romaiyan et al. (2010)	Meta-analysis	T2DM and T1DM	Multiple GS preparations	Pooled glycemic improvement across trials	Level Ia
Saritas & Serin (2026)	Systematic review	Multiple populations	Multiple GS preparations	Multi-target antidiabetic mechanisms confirmed	Level Ia

Table 4: Summary of Key Clinical Studies - Pterocarpus marsupium

Study (Year)	Design	Population	Intervention	Primary Outcomes	Evidence Level
ICMR Collaborating Centres (1998)	Flexible-dose open trial, multicenter	97 newly diagnosed NIDDM	Vijayasar tumbler water; 12 weeks	Significant proportion achieved blood glucose normalisation	Level IIb
Patidar et al. (2015)	Randomised controlled trial	T2DM patients	P. marsupium extract vs.	↓ FBG, ↓ PPBG, ↓	Level Ib

			placebo; 12 weeks	HbA1c	
Anandharajan et al. (2005)	In vitro (L6 myotubes)	Cell culture	Isoflavone fraction	↑ GLUT4 protein, ↑ PPAR-γ activation	Level IV
Dar et al. (2022)	In vitro (HepG2 cells)	Hepatocellular culture	Heartwood extract	Oxyradical protection, ↑ glucose uptake	Level IV

10. Safety Profile and Regulatory Considerations

10.1 Safety of Gymnema sylvestre

G. sylvestre has a generally good safety profile, with no serious adverse events reported in clinical trials at the doses of 400–800 mg/day of standardised extract. The most concerning potential interaction is with pharmaceutical antidiabetic agents, as G. sylvestre may potentiate their hypoglycemic effects. Mild gastrointestinal side effects such as nausea and diarrhoea have been reported at higher doses. Long-term use of G. sylvestre has not been associated with significant adverse effects in clinical trials.

10.2 Safety of Pterocarpus marsupium

P. marsupium in the form of Vijayasar tumbler water or extract has been used traditionally for centuries without reports of hepatotoxicity or nephrotoxicity. Published preclinical toxicology studies have not demonstrated mutagenic or genotoxic effects of P. marsupium. Caution should be exercised when using P. marsupium in combination with pharmaceutical antidiabetic agents due to the potential for additive hypoglycemic effects. Epicatechin, a major constituent of P. marsupium, is found in various food items and has a well-established safety profile.

10.3 Regulatory Positioning of 4DM+

4DM+ must be positioned and marketed as a botanical nutraceutical/dietary supplement and not as a pharmaceutical agent. The product labelling, marketing materials, and scientific literature should comply with applicable nutraceutical regulations, which typically do not allow disease treatment or cure claims. In India, 4DM+ would fall under the jurisdiction of the Food Safety and Standards Authority of India (FSSAI). The scientific literature should support structure/function claims rather than disease-treatment claims.

11. Proposed Clinical Framework for Combined Herbal Metabolic-Support Products

Due to the lack of published clinical trials for finished combined herbal metabolic-support formulations, the following framework is proposed for future clinical investigations of such products. Particular attention should be paid to designs that: (a) evaluate the combined formulation as an entity, rather than its individual ingredients, (b) utilise standardised, authenticated botanical ingredients with documented marker compound content, (c) are relevant to the intended use as a nutraceutical, and (d) follow CONSORT 2010 reporting standards and ICH E6(R3) Good Clinical Practice guidelines.[31,32]

Table 5: Proposed Clinical Research Framework for a Combined Herbal Metabolic-Support Formulation

Study Phase	Design	Population	Duration	Primary Endpoints	Secondary Endpoints
Pilot / Phase I	Open-label safety & PK	Healthy adult volunteers (n=20–30)	4 weeks	Safety, tolerability, pharmacokinetic profiling of marker compounds	Fasting glucose, insulin, lipid panel, liver function
Phase II-A	Randomised, double-blind, placebo-controlled	Adults with borderline fasting glucose or metabolic wellness concern (n=60–	12 weeks	Change in fasting blood glucose and postprandial glucose AUC	HbA1c, HOMA-IR, lipid profile, body composition, QoL

		100)			
Phase II-B / Confirmatory	Randomised, double-blind, placebo-controlled, multi-centre	Adults with metabolic wellness concerns (n=150–200)	24 weeks	Fasting glucose, HbA1c, HOMA-IR	Lipid panel, inflammatory markers (CRP, TNF-α), safety, adherence

12. Discussion

The scientific literature reviewed in this manuscript provides a rationale for the combined use of G. sylvestre and P. marsupium for metabolic support based on the cumulative evidence from preclinical and clinical studies. While the evidence base is heterogeneous in terms of study design and methodology, it consistently demonstrates that both botanicals have mechanisms of action that are relevant to glucose metabolism and metabolic function.

The most compelling aspect of the 4DM+ formulation rationale is the complementarity of the mechanisms of action of its two ingredients. G. sylvestre primarily acts on intestinal glucose absorption and pancreatic insulin secretion, while P. marsupium enhances peripheral glucose uptake, improves hepatic glucose metabolism, and modulates inflammatory and antioxidant pathways. This multi-target approach may provide additive or synergistic benefits for metabolic health.

The 4DM+ formulation fits into the metabolic wellness space by providing a scientifically substantiated botanical option for those seeking metabolic support. It is not intended to be a pharmaceutical antidiabetic agent but rather a nutraceutical supplement that may support healthy glucose metabolism as part of a comprehensive wellness approach that includes diet, exercise, and medical supervision.

13. Future Research Directions

Botanical authentication and standardisation: Development and validation of HPLC-based marker-compound assays for gymnemic acids (≥25% by HPLC) and key P. marsupium constituents (epicatechin, pterostilbene, marsupsin) in the final 4DM+ formulation to ensure batch-to-batch consistency and enable dose-response characterisation.

Product-specific pharmacokinetic study: Characterisation of marker-compound pharmacokinetics (Cmax, Tmax, AUC, half-life, tissue distribution) following single and multiple doses of the final 4DM+ formulation in healthy human volunteers, to establish appropriate dosing intervals and confirm bioavailability.

Herb-drug interaction studies: Formal in vitro cytochrome P450 (CYP2C9, CYP3A4) and drug transporter interaction studies for gymnemic acids and pterostilbene to characterise the potential for pharmacokinetic interactions with commonly co-administered pharmaceutical agents (metformin, sulfonylureas, statins).

Randomised controlled trial (Phase II-A): A rigorous, double-blind, placebo-controlled trial of the final 4DM+ formulation in 60–100 adults with borderline fasting glucose or metabolic wellness concerns, measuring postprandial glucose AUC, fasting blood glucose, and HOMA-IR as primary endpoints over 12 weeks.

Mechanistic clinical substudies: Integration of surrogate mechanistic biomarkers (GLP-1, insulin secretion indices, HOMA-β, inflammatory markers) into the Phase II-A protocol to provide translational evidence linking the botanical mechanisms to clinical outcomes.

Long-term safety surveillance: Structured post-marketing surveillance of 4DM+ users over 12–24 months to characterise the long-term safety profile and identify any rare adverse events not captured in shorter trials.

DPP-4 inhibition validation: In vitro enzymatic assay confirmation of DPP-4 inhibitory activity for constituent phytochemicals, with correlation to incretin biology in appropriate in vivo models.

14. Limitations

The review acknowledges several limitations inherent in the evidence base. First, the clinical evidence for both botanicals is heterogeneous in terms of study design, extract type, dose, duration, population, and outcome measures. Second, most clinical studies utilised open-label designs without placebo controls. Third, the majority of trials were conducted in T2DM populations, while the intended application of 4DM+ is for metabolic wellness. Fourth, no clinical trial has been conducted on the final 4DM+ formulation - the combination, dose, and preparation form as manufactured by BiotexLife Solutions. The evidence presented

in this review represents the foundation for the scientific rationale, but not proof of efficacy for the specific product formulation. Fifth, pharmacokinetic profiling of the combined formulation is lacking, and potential pharmacokinetic/pharmacodynamic interactions between the two botanicals are unknown. Sixth, the authentication and marker-compound standardisation of the specific raw materials used in 4DM+ manufacturing have not been reported in the open literature.

15. Conclusion

4DM+ by BiotexLife Solutions Private Limited is a scientifically substantiated formulation offering a botanical option for metabolic and glucose regulation based on a plausible mechanistic connection between two botanical ingredients. The pharmacological and clinical evidence supporting the use of each of the two botanical ingredients has been considered extensive enough for combined use to address multiple mechanisms in the context of the pathophysiology of glucose regulation.

The overall supportive evidence base for 4DM+ as a botanical dietary supplement is therefore credible, although not conclusive due to the lack of a clinical trial specifically addressing the final formulation. The next important steps in this regard, as outlined in this paper, include the need for botanical standardisation, assessment of pharmacokinetics, evaluation of potential drug-herb interactions, and large interventional studies with a placebo control. As a wellness product intended for general use but requiring professional counselling for correct application, 4DM+ appears to be a reasonable option addressing the diverse aspects of glucose regulation in a scientifically plausible manner.

Declarations

Funding

This manuscript was written in the absence of any external funding. The present review was prepared as documentation supporting the work of BiotexLife Solutions Private Limited on the 4DM+ botanical formulation. BiotexLife Solutions Private Limited supplied the information used for this review.

Conflicts of Interest

The authors declare that this manuscript was written and had not received any specific grants. However, the authors disclose a potential conflict of interest as current employees of Biotex Life Solutions. The views expressed in this article are solely those of the authors.

Data Availability

The data used for this review are publicly available in the scientific literature as cited in this paper. No additional data were generated for this study. The reference list can be provided upon request.

Ethical Statement

This study does not raise any ethical concerns. This is a narrative review with no studies performed on human or animal subjects. Therefore, no ethical approval was necessary.

Declaration of AI use

The authors utilised generative AI tools to a small extent, specifically for grammar correction and language support while preparing the manuscript. All scientific content, analyses, and conclusions originate from the authors themselves; they reviewed and revised the generated output and accept full responsibility for the completed manuscript.

References

1. International Diabetes Federation. IDF Diabetes Atlas, 10th edition. Brussels: IDF; 2021. Available at: https://www.diabetesatlas.org.
2. Tabák AG, Herder C, Rathmann W, Brunner EJ, Kivimäki M. Prediabetes: a high-risk state for diabetes development. Lancet. 2012;379(9833):2279-2290. doi:10.1016/S0140-6736(12)60283-9.
3. Govindaraghavan S, Sucher NJ. Quality assessment of medicinal herbs and their extracts: criteria and prerequisites for consistent safety and efficacy of herbal medicines. Epilepsy Behav. 2015;52(Pt B):363-371. doi:10.1016/j.yebeh.2015.03.004.

4. Islam A, Rebello L, Chepyala S. A review of anti-diabetic activity of Gymnema sylvestre and Pterocarpus marsupium: special emphasis on its combination in 4DM. Int J Nat Life Sci. 2019;3(2):40-51.
5. Kanetkar P, Singhal R, Kamat M. Gymnema sylvestre: a memoir. J Clin Biochem Nutr. 2007; 41(2):77-81. doi:10.3164/jcbn.2007010.
6. Tiwari P, Mishra BN, Sangwan NS. Phytochemical and pharmacological properties of Gymnema sylvestre: an important medicinal plant. BioMed Res Int. 2014; 2014:830285. doi:10.1155/2014/830285.
7. Pothuraju R, Sharma RK, Chagalamarri J, Jangra S, Kumar Kavadi P. A systematic review of Gymnema sylvestre in obesity and diabetes management. J Sci Food Agric. 2014; 94(5):834-840. doi:10.1002/jsfa.6458.
8. Yadav M, Lavania A, Tomar R, Prasad GBKS, Jain S, Yadav H. Complementary and comparative study on hypoglycemic and antihyperglycemic activity of various extracts of Eugenia jambolana seed, Momordica charantia fruits, Gymnema sylvestre, and Trigonella foenum graecum seeds in rats. Appl Biochem Biotechnol. 2010; 160(8):2388-2400. doi:10.1007/s12010-009-8799-1.
9. Basnayake PI, Gunatilake M. Pharmacological effects of Pterocarpus marsupium. BLDE Univ J Health Sci. 2024; 9(1):3-15. doi:10.4103/bjhs.bjhs_43_23.
10. Sharma S, Sharma M. Nutritional and medicinal insights into Pterocarpus marsupium: a review study. J Nat Remedies. 2026; 26(1):57-66. doi:10.18311/jnr/2026/49052.
11. Dar MI, Gul MZ, Koul S, et al. Heartwood extract of Pterocarpus marsupium Roxb. Offers defense against oxyradicals and improves glucose uptake in HepG2 cells. Metabolites. 2022; 12(10):947.
12. Saritas S, Serin I. Gymnema sylvestre as a multi-target antidiabetic agent: mechanistic insights and metabolic regulation. Int J Mol Sci. 2026; 27(12):5609. doi: 10.3390/ijms27125609.
13. Shimizu K, Iino A, Nakajima J, et al. Suppression of glucose absorption by some fractions extracted from Gymnema sylvestre leaves. J Vet Med Sci. 1997; 59(4):245-251. doi:10.1292/jvms.59.245.
14. Wang LF, Luo H, Miyoshi M, Imoto T, Hiji Y, Sasaki T. Inhibitory effect of gymnemic acid on intestinal absorption of oleic acid in rats. Can J Physiol Pharmacol. 1998; 76(10-11):1017-1023. doi: 10.1139/y98-123.
15. Al-Romaiyan A, Liu B, Asare-Anane H, et al. A novel Gymnema sylvestre extract stimulates insulin secretion from human islets in vivo and in vitro. Phytother Res. 2010; 24(9):1370-1376. doi:10.1002/ptr.3125.
16. Mishra A, Srivastava R, Srivastava SP, et al. Antidiabetic activity of heart wood of Pterocarpus marsupium Roxb. and analysis of phytoconstituents. Indian J Exp Biol. 2013; 51(5):363-374.
17. Anandharajan R, Pathmanathan K, Shankernarayanan NP, Vishwakarma RA, Balakrishnan A. Upregulation of GLUT4 and PPAR gamma by an isoflavone from Pterocarpus marsupium on L6 myotubes: a possible mechanism of action. J Ethnopharmacol. 2005; 97(2):253-260. doi:10.1016/j.jep.2004.11.023.
18. Grover JK, Vats V, Yadav S. Pterocarpus marsupium extract prevented alteration in metabolic patterns induced by fructose diet. Diabetes Obes Metab. 2005; 7(4):414-420.
19. Halagappa K, Girish HN, Srinivasan BP. The study of aqueous extract of Pterocarpus marsupium Roxb. on cytokine TNF-alpha in type 2 diabetic rats. Indian J Pharmacol. 2010; 42(6):392-396. doi:10.4103/0253-7613.71922.
20. Mohankumar SK, O'Shea T, McFarlane JR. Insulinotrophic and insulin-like effects of a high molecular weight aqueous extract of Pterocarpus marsupium Roxb. hardwood. J Ethnopharmacol. 2012; 141(1):72-79.
21. Kosaraju J, Dubala A, Chinni S, et al. A molecular connection of Pterocarpus marsupium, Eugenia jambolana and Gymnema sylvestre with dipeptidyl peptidase-4 in the treatment of diabetes. Pharm Biol. 2014; 52(3):268-271. doi:10.3109/13880209.2013.823550.
22. Shanmugasundaram ER, Rajeswari G, Baskaran K, Kumar BR, Shanmugasundaram KR, Ahmath BK. Use of Gymnema sylvestre leaf extract in the control of blood glucose in insulin-dependent diabetes mellitus. J Ethnopharmacol. 1990; 30(3):281-294. doi: 10.1016/0378-8741(90)90107-5.

23. Baskaran K, Ahamath BK, Shanmugasundaram KR, Shanmugasundaram ER. Antidiabetic effect of a leaf extract from Gymnema sylvestre in non-insulin-dependent diabetes mellitus patients. J Ethnopharmacol. 1990; 30(3):295-305. doi:10.1016/0378-8741(90)90108-6.
24. Yeh GY, Eisenberg DM, Kaptchuk TJ, Phillips RS. Systematic review of herbs and dietary supplements for glycemic control in diabetes. Diabetes Care. 2003; 26(4):1277-1294. doi:10.2337/diacare.26.4.1277.
25. Devangan S, Varghese B, Johny E, et al. The effect of Gymnema sylvestre supplementation on glycemic control in type 2 diabetes: a systematic review and meta-analysis. Phytother Res. 2021; 35(12):6802-6812. doi:10.1002/ptr.7265.
26. Indian Council of Medical Research Collaborating Centres. Flexible dose open trial of Vijayasar in cases of newly diagnosed non-insulin-dependent diabetes mellitus. Indian J Med Res. 1998; 108:24-29.
27. Vats V, Grover JK, Rathi SS. Evaluation of anti-hyperglycemic and hypoglycemic effect of Trigonella foenum-graecum Linn, Ocimum sanctum Linn and Pterocarpus marsupium Linn in normal and alloxanized diabetic rats. J Ethnopharmacol. 2002; 79(1):95-100. doi:10.1016/S0378-8741(01)00374-9.
28. Mukhtar HM, Ansari SH, Ali M, Naved T, Bhat ZA. Effect of aqueous extract of Pterocarpus marsupium wood on alloxan-induced diabetic rats. Pharmazie. 2005; 60(6):478-479.
29. Dhanabal SP, Kokate CK, Ramanathan M, Kumar EP, Suresh B. Hypoglycaemic activity of Pterocarpus marsupium Roxb. Phytother Res. 2006; 20(1):4-8. doi:10.1002/ptr.1819.
30. Patidar A, Tonpay SD, Agrawal N. Hypoglycemic activity of Pterocarpus marsupium in patients with type 2 diabetes mellitus. Int J Basic Clin Pharmacol. 2015; 4(6):1189-1193. doi:10.18203/2319-2003.ijbcp20151356.
31. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ. 2010; 340:c332. doi:10.1136/bmj.c332.
32. International Council for Harmonisation. ICH E6 (R3) Guideline for Good Clinical Practice. International Council for Harmonisation; 2025.