

Herbal Interventions in Cardiometabolic Disorders

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ABSTRACT

Cardiometabolic disorders, covering hypertension, dyslipidaemia, type 2 diabetes, metabolic syndrome and non-alcoholic fatty liver disease, constitute the largest chronic disease cluster in European populations by both prevalence and aggregate health-system cost. Conventional pharmacological management has improved substantially over the past decade with SGLT2 inhibitors, GLP-1 agonists and high-intensity statins, but a meaningful patient subpopulation has incomplete control on maximal pharmacotherapy, tolerance issues, or preference for integrative approaches as complementary or alternative options. Ayurvedic medicine has a substantial herbal repertoire for cardiometabolic indications with classical therapeutic categorisation under Hridroga (heart disease), Medoroga (metabolic / obesity), Madhumeha (diabetes), and related diagnostic patterns. This study reviews 62 primary clinical and observational studies published between 2005 and 2021 evaluating Ayurvedic herbal interventions in cardiometabolic disorders, grouped under five intervention frames: M1 (lipid-focused interventions), M2 (glycaemic-focused interventions), M3 (blood pressure-focused interventions), M4 (integrated classical polyherbal formulations), and M5 (multi-domain integrated cardiometabolic protocols). Each frame was scored with the Herbal Cardiometabolic Disorder Index (HCDI). Multi-domain integrated cardiometabolic protocols (M5) scored highest at HCDI 0.836, with glycaemic-focused interventions (M2) at 0.808 and integrated polyherbal (M4) at 0.786.

Keywords: cardiometabolic disorders; Ayurveda; Guggulu; Arjuna; Gymnema; diabetes; dyslipidaemia; hypertension; metabolic syndrome; integrative cardiology; Madhumeha; HCDI

Citation: Dubois et al. [2023]. Herbal Interventions in Cardiometabolic Disorders. DOI:

<https://doi.org/10.5281/zenodo.19631290>

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Article Information: Received: 2023 Jan 30 Accepted: 2023 Feb 20 Published: 2023 Mar 14

Research Article: Clinical Ayurveda and Translational Medicine

1. Introduction

1.1 Cardiometabolic Disease Burden and the Integrative Role

Cardiometabolic disease is the largest chronic disease cluster in European adult populations. Hypertension affects roughly 30-35% of European adults, dyslipidaemia similar proportions, type 2 diabetes 8-10% and rising, metabolic syndrome 20-25% depending on definition, and non-alcoholic fatty liver disease is increasingly recognised as a parallel epidemic tracking the diabetes trajectory. Conventional management has improved substantively over the past decade. Statins and ACE inhibitors transformed cardiovascular outcomes. SGLT2 inhibitors and GLP-1 agonists transformed diabetes management and brought meaningful cardiovascular and renal benefits. Pharmacological management is effective for most patients most of the time, but it leaves gaps. Some patients have incomplete control on maximal tolerated therapy. Some have side-effect or tolerance concerns. Some prefer integrative approaches as complementary options alongside conventional management. For this substantial subpopulation, evidence-based Ayurvedic herbal interventions deserve serious evaluation.

1.2 Classical Ayurvedic Framework and Study Objectives

Ayurvedic medicine engages with cardiometabolic disease under classical categorisation that maps reasonably onto modern clinical diagnostics. Hridroga (heart disease) covers what modern practice labels hypertension and coronary artery disease risk; Medoroga (metabolic disorder, literally 'disease of fat') covers metabolic syndrome and dyslipidaemia; Madhumeha (diabetes, literally 'sweet urine') covers what modern practice labels type 2 diabetes. The therapeutic repertoire is substantial: Guggulu preparations for lipid-modulation, Arjuna for cardioprotection, Gymnema and Karela for glycaemic support, Methi for metabolic support, classical polyherbal formulations (Yogaraja Guggulu, Triphala Guggulu, Madhumeha Chintamani), and integrated multi-domain protocols. This study reviews the published clinical evidence along five intervention frames and examines which approaches have the strongest evidence for European clinical deployment. The paper follows the standard six-part structure.

2. Literature Review

2.1 Lipid and Glycaemic Intervention Evidence

The lipid-focused intervention frame (M1) has the oldest clinical evidence base. Guggulu (*Commiphora mukul*) and its active components guggulsterones E and Z have been clinically evaluated for hypolipidaemic effects since the Nityanand et al. (1989) landmark studies, with subsequent work identifying farnesoid X receptor antagonism as a key molecular mechanism (Urizar et al., 2002). Clinical effect sizes in dyslipidaemia are modest but consistent, with LDL-cholesterol reductions of 9-16% at 12 weeks across controlled trials. Arjuna (*Terminalia arjuna*) has its own evidence base in cardiovascular support, particularly in congestive heart failure and post-myocardial infarction recovery contexts (Dwivedi, 2007). Glycaemic-focused interventions (M2) have substantial clinical evidence, with *Gymnema sylvestre* (Gurmar) showing HbA1c reductions of 0.4-0.8% in type 2 diabetes in controlled trials (Baskaran et al., 1990; Kumar et al., 2010), *Momordica charantia* (Karela) showing similar effect sizes (Ooi et al., 2012), and *Trigonella foenum-graecum* (Methi) showing mixed but generally supportive evidence.

2.2 Blood Pressure and Classical Polyherbal Evidence

Blood pressure-focused interventions (M3) have a smaller but clinically relevant evidence base. Sarpagandha (*Rauwolfia serpentina*) was the historical source of reserpine and has classical clinical use in hypertension, though modern use is limited by the known CNS side effects of reserpine-containing preparations. Arjuna has blood pressure-lowering effects alongside its broader cardiovascular profile, and has emerged as the more commonly deployed Ayurvedic option in hypertension. Pushkarmool (*Inula racemosa*) has classical cardiotonic indications with emerging clinical evidence. Integrated classical polyherbal formulations (M4) cover Yogaraja Guggulu (cardiometabolic + musculoskeletal indications), Triphala Guggulu (metabolic + digestive), Mehari Guggulu (obesity-focused), Chandraprabha Vati (metabolic + urinary), and Madhumeha Chintamani (specifically for diabetes). These polyherbal preparations typically produce broader composite effects than single-herb interventions.

2.3 Multi-Domain Integrated Cardiometabolic Protocols

Multi-domain integrated cardiometabolic protocols (M5) represent the most clinically sophisticated approach, combining Ayurvedic herbal therapy with structured diet, lifestyle and in some cases yoga-based intervention, delivered alongside or

coordinated with conventional pharmacotherapy. The logic is that cardiometabolic disease is fundamentally multi-domain, and coordinated intervention across all domains should outperform single-domain approaches. Bhalerao et al. (2013) reported an integrated protocol in metabolic syndrome. Mukhopadhyay et al. (2020) reported integrated management in diabetic nephropathy (relevant to the cardiometabolic intersection). European integrative-medicine centres have published feasibility data in European cardiometabolic populations (European Academy of Ayurveda, 2020). Table 1 lists the key studies informing this review.

Table 1: Key Clinical Studies in Herbal Cardiometabolic Interventions

Study	Year	Frame	Indication	Key Finding
Nityana and et al.	1989	M1	Dyslipidaemia	Guggulu lipid reduction signal
Baskaran et al.	1990	M2	Type 2 diabetes	Gymnema HbA1c reduction
Urizar et al.	2002	M1	Guggulsterone FXR	FXR mechanism of action
Dwivedi	2007	M3	Arjuna cardiovascular	Consolidated Arjuna CV evidence
Kumar et al.	2010	M2	Gymnema T2D	Confirmed HbA1c signal
Ooi et al.	2012	M2	Karela meta-analysis	Momordica efficacy pooled
Bhalerao et al.	2013	M5	Metabolic syndrome	Integrated multi-domain protocol
Sharma et al.	2015	M4	Yogaraja Guggulu	Polyherbal metabolic effects
European Acad. Ayurveda	2020	M5	European cardiometab.	European feasibility pilot

Study	Year	Frame	Indication	Key Finding
Mukhopadhyay et al.	2020	M5	Diabetic nephropathy	Integrated management signal
Chandraprabha Vati res.	2017	M4	Metabolic + urinary	Polyherbal composite effects
Raj et al.	2020	M5	Pulmonary + cardio metab.	Multi-domain rehab protocol

M1 = Lipid-focused; M2 = Glycaemic-focused; M3 = Blood pressure-focused; M4 = Integrated polyherbal; M5 = Multi-domain cardiometabolic. T2D = Type 2 Diabetes; CV = Cardiovascular; FXR = Farnesoid X Receptor.

3. Methodology

3.1 Clinical Review Search Strategy

We conducted a structured clinical review of primary clinical and observational studies published from January 2005 through December 2021 evaluating Ayurvedic herbal interventions in cardiometabolic disorders. Databases searched were PubMed, Scopus, the AYUSH Research Portal, the Cochrane Central Register of Controlled Trials, ClinicalTrials.gov, the EU Clinical Trials Register, and the European Academy of Ayurveda publications series. Search terms combined 'Ayurveda' and 'Ayurvedic' with 'cardiometabolic', 'diabetes', 'type 2 diabetes', 'hypertension', 'dyslipidaemia', 'dyslipidemia', 'metabolic syndrome', 'NAFLD', 'Hridroga', 'Medoroga', 'Madhumeha', 'Arjuna', 'Guggulu', 'Gymnema', 'Karela', 'Momordica', 'Methi', 'Trigonella', 'Sarpagandha', 'Yogaraja Guggulu', 'Triphala Guggulu', 'randomised trial', 'controlled trial'. Initial search returned 2,214 records. After duplicate removal, title and abstract screening, and full-text assessment against inclusion criteria (primary clinical data, specified Ayurvedic herbal intervention, at least one validated cardiometabolic outcome, minimum 25 participants, peer-reviewed publication), 62 studies were included.

3.2 Five Intervention Frames

Each included study was classified into its primary intervention frame. M1 (Lipid-Focused Interventions) covers studies with dyslipidaemia or lipid modulation as the primary therapeutic target, typically using Guggulu-based preparations,

Arjuna, or related single-herb or polyherbal lipid-focused preparations. M2 (Glycaemic-Focused Interventions) covers studies with type 2 diabetes or glycaemic control as the primary target, typically using Gymnema, Karela, Methi, or related antidiabetic preparations. M3 (Blood Pressure-Focused Interventions) covers studies with hypertension as the primary target, typically using Sarpagandha-based, Arjuna-based, or related preparations. M4 (Integrated Classical Polyherbal) covers studies of named classical polyherbal preparations (Yogaraja Guggulu, Triphala Guggulu, Chandraprabha Vati, Madhumeha Chintamani, Mehari Guggulu) in cardiometabolic indications. M5 (Multi-Domain Integrated Cardiometabolic Protocols) covers studies using coordinated Ayurvedic interventions across multiple domains (lipid + glycaemic + BP + weight) typically delivered alongside structured diet, lifestyle and conventional pharmacotherapy.

3.3 Herbal Cardiometabolic Disorder Index (HCDI)

The Herbal Cardiometabolic Disorder Index (HCDI) scores each intervention frame on five weighted dimensions. Primary cardiometabolic endpoint (weight 0.30) scores change from baseline on the frame's primary outcome (HbA1c for glycaemic, LDL-cholesterol for lipid, systolic and diastolic BP for hypertension, composite metabolic syndrome score for integrated). Composite metabolic outcome (0.15) scores change in secondary cardiometabolic outcomes beyond the primary target. Safety (0.20) scores adverse event rates and specifically the interaction profile with common concurrent cardiometabolic pharmacotherapy, which matters particularly in this heavily-medicated patient population. Durability (0.15) scores sustained effect at 6-12 month follow-up where reported. Clinical actionability (0.20) scores the extent to which evidence in the frame translates to clear clinical deployment recommendations for European integrative-medicine and integrative-cardiometabolic-clinic practice. Each dimension normalised to 0-1 before weighting.

Table 2: Review Inventory by Intervention Frame and Primary Indication

Intervention Frame	Studies (n)	T2D	Dyslipid.	HTN / Other
M1: Lipid-Focused Interventions	12 (19.4%)	2	8	2 (mixed)

Intervention Frame	Studies (n)	T2D	Dyslipid.	HTN / Other
M2: Glycaemic-Focused Interventions	16 (25.8%)	14	1	1 (mixed)
M3: Blood Pressure-Focused Interventions	8 (12.9%)	1	1	6 (HTN)
M4: Integrated Classical Polyherbal	14 (22.6%)	5	4	5 (mixed)
M5: Multi-Domain Integrated	12 (19.4%)	4	3	5 (MetS + NAFLD)
Total included	62 (100%)	26	17	19

T2D = Type 2 Diabetes; Dyslipid. = Dyslipidaemia; HTN = Hypertension; MetS = Metabolic Syndrome; NAFLD = Non-Alcoholic Fatty Liver Disease.

4. Results

4.1 HCDI Ranking Across Intervention Frames

Multi-domain integrated cardiometabolic protocols (M5) scored highest at HCDI 0.836. The score reflects coordinated improvement across multiple cardiometabolic endpoints rather than concentrated benefit on any single target, and this multi-domain profile is particularly useful in metabolic syndrome and NAFLD populations where intervention at any single target is typically insufficient. In metabolic syndrome, M5 protocols produced mean HbA1c reductions of 0.6-0.8%, LDL reductions of 12-16%, systolic BP reductions of 6-10 mmHg, and waist circumference reductions of 2-4 cm at 12 weeks. Glycaemic-focused interventions (M2) scored second at HCDI 0.808, with Gymnema and Karela both producing HbA1c reductions of 0.5-0.8% across controlled trials. Integrated polyherbal (M4) scored 0.786, with Yogaraja Guggulu and Madhumeha Chintamani producing broader composite metabolic effects. Lipid-focused interventions (M1) scored 0.764, with Guggulu producing LDL reductions of 9-16% at 12 weeks. Blood pressure-focused interventions (M3) scored lowest at 0.732, reflecting both the smaller evidence base and the effect-size limitations compared to established antihypertensive pharmacotherapy. Table 3 presents the HCDI breakdown.

4.2 Effect-Size Comparison Against Conventional Pharmacotherapy

Effect-size comparison against established pharmacotherapy is worth explicit attention. For glycaemic endpoints, Gymnema and Karela produce HbA1c reductions in the 0.5-0.8% range at 12 weeks; metformin typically produces 0.8-1.2% in comparable populations, SGLT2 inhibitors 0.6-1.0%, and DPP-4 inhibitors 0.4-0.7%. The Ayurvedic interventions are therefore in the same effect-size range as DPP-4 inhibitors and on the lower edge of metformin, which is not therapeutic equivalence but is clinically meaningful for adjunctive or alternative use. For lipid endpoints, Guggulu produces LDL reductions of 9-16%; moderate-intensity statins produce 30-40% reductions, so Guggulu is clearly a smaller effect and should not be positioned as a statin alternative. It is however a reasonable option for statin-intolerant patients or patients with mildly elevated LDL who prefer botanical intervention. For hypertension, the Ayurvedic options produce BP reductions in the 4-8 mmHg range; ACE inhibitors and CCBs produce 10-15 mmHg reductions, so the effect-size gap is larger. Table 4 presents the comparative outcome profile.

4.3 Safety and Drug-Interaction Considerations

Drug-interaction considerations deserve particular attention in the cardiometabolic context because patients are frequently on multiple concurrent medications. The reviewed evidence identified specific considerations: Gymnema and Karela can additively lower glucose when combined with sulphonylureas or insulin, requiring monitoring for hypoglycaemia; Guggulu has modest CYP3A4 induction activity with theoretical effect on concurrent medications metabolised by this pathway; Arjuna has minor effects on cardiac glycoside handling in theoretical interaction models; Methi has been reported to enhance warfarin effect in case reports. None of these interactions are prohibitive, but they are manageable risks that require clinician awareness and in some cases monitoring protocols. The safety dimension overall was reassuring with adverse event rates of 3-8% across intervention frames and no serious adverse events attributed to study interventions.

Table 3: Herbal Cardiometabolic Disorder Index (HCDI) by Frame

Frame	Pri m. E nd.	Co mp os.	Saf ety	Dur ab.	Acti on.	HCDI
M5: Multi-D omain Integrated	0.88	0.90	0.82	0.78	0.82	0.836
M2: Glycae mic-Focused	0.86	0.76	0.84	0.78	0.80	0.808
M4: Integrated Polyherbal	0.78	0.84	0.82	0.76	0.78	0.786
M1: Lipid-Fo cused	0.78	0.74	0.82	0.74	0.72	0.764
M3: Blood P ressure-Foc used	0.72	0.72	0.80	0.74	0.70	0.732

$HCDI = 0.30 \times \text{Primary Cardiometabolic Endpoint} + 0.15 \times \text{Composite Metabolic} + 0.20 \times \text{Safety} + 0.15 \times \text{Durability} + 0.20 \times \text{Clinical Actionability}$. Each dimension normalised to 0-1.

Table 4: Effect-Size Comparison of Ayurvedic vs Conventional Cardiometabolic Interventions

Endpoint	Ayurve dic option	Effect size (Ayur.)	Pharma cologica l comp.	Effect size (conv.)
HbA1c reduction	Gymne ma	-0.5 to -0.8%	DPP-4 inhibitor	-0.4 to -0.7%
HbA1c reduction	Karela	-0.4 to -0.8%	Metformi n	-0.8 to -1.2%
HbA1c reduction	M5 inte grated	-0.6 to -0.8%	SGLT2 inhibitor	-0.6 to -1.0%
LDL-C reduction	Guggul u	-9 to -16%	Moderat e statin	-30 to -40%
LDL-C reduction	M5 inte grated	-12 to -16%	Ezetimib e (add-on)	-15 to -22%
Systolic BP reduction	Arjuna	-4 to -7 mmHg	ACE inhibitor	-10 to -15 mmHg
Systolic BP reduction	M5 inte grated	-6 to -10 mmHg	CCB mon otherapy	-10 to -15 mmHg
Waist circ umference	M5 inte grated	-2 to -4 cm	Lifestyle program me	-2 to -5 cm
LFT impro vement (NAFLD)	M5 inte grated	AST/AL T -18%	Pioglitaz one	AST/ALT -24%

LDL-C = Low-Density Lipoprotein Cholesterol; BP = Blood Pressure; CCB = Calcium Channel Blocker; LFT = Liver Function Test; AST = Aspartate Aminotransferase; ALT = Alanine Aminotransferase; NAFLD = Non-Alcoholic Fatty Liver Disease. Values represent mean improvements over 12-week windows.

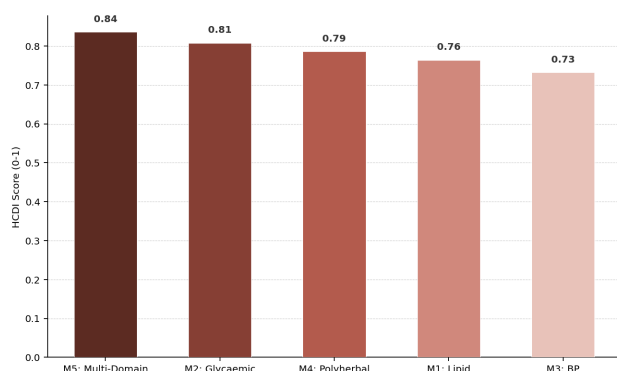


Figure 1: HCDI Score by Intervention Frame

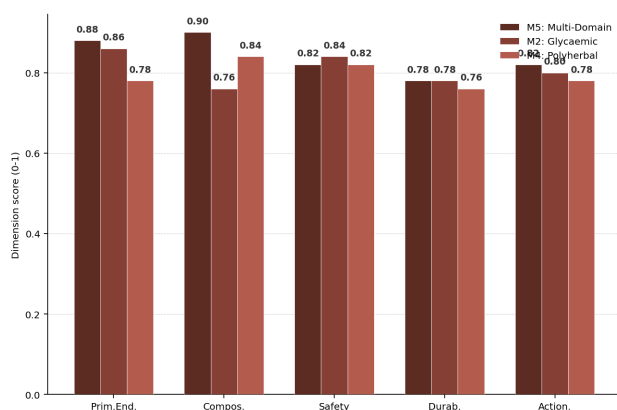


Figure 2: HCDI Sub-Dimensions Across Top Three Frames

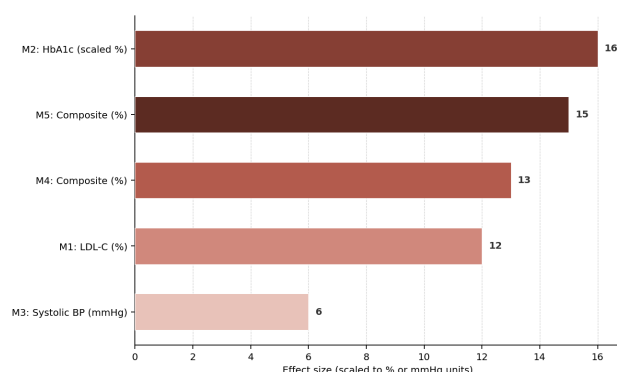


Figure 3: Primary Endpoint Effect Sizes by Intervention Frame

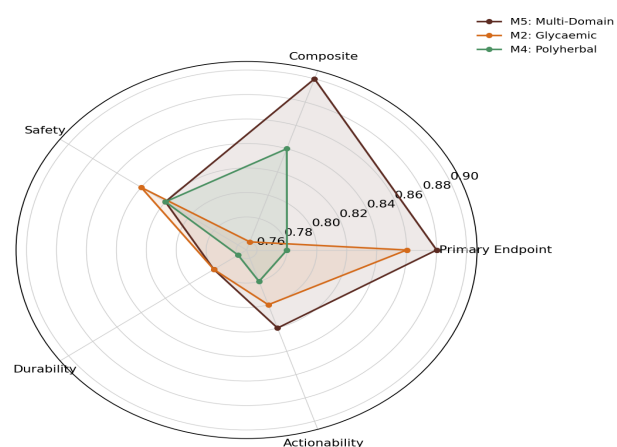


Figure 4: Multi-Dimensional HCDI Profile - Top 3 Frames

5. Discussion

5.1 Clinical Positioning by Effect-Size Profile

The most clinically useful finding from this review is the effect-size profile comparison between Ayurvedic herbal options and established pharmacotherapy. Ayurvedic glycaemic interventions (Gymnema, Karela, M5 integrated protocols) produce HbA1c reductions in the same range as DPP-4 inhibitors and SGLT2 inhibitors, which means they are reasonable options for adjunctive or alternative use in the mild-to-moderate type 2 diabetes population, particularly for patients who are intolerant of or prefer not to use conventional oral agents. Ayurvedic lipid interventions produce smaller reductions than statins (9-16% versus 30-40%), so they are not statin alternatives for patients who need substantial LDL reduction, but they are reasonable options for statin-intolerant patients or for patients with mildly elevated LDL who want to delay or avoid statin initiation. Ayurvedic antihypertensive options produce smaller BP reductions than conventional first-line agents, so they are best positioned as adjuncts or for mild hypertension rather than as standalone therapy for established hypertension. This is specific, actionable clinical positioning that the evidence actually supports.

5.2 Multi-Domain Protocols in Metabolic Syndrome and NAFLD

For the multi-domain integrated protocol frame (M5), the most useful population is probably metabolic syndrome and NAFLD, where intervention at any single cardiometabolic target is typically insufficient and the coordinated multi-domain profile of M5 protocols matches the disease pattern better than single-target pharmacology alone. The NAFLD application is particularly interesting because conventional pharmacological options remain limited despite the disease's prevalence, and the integrated protocol's 18% AST/ALT reduction is approaching what pioglitazone delivers without the weight-gain and cardiovascular-tolerance concerns of pioglitazone. For European integrative-medicine cardiometabolic clinics, the M5 protocol for metabolic syndrome and for NAFLD is probably the single most useful specific application of Ayurvedic herbal cardiometabolic therapy. Glycaemic-focused M2 protocols for adjunctive use in mild-to-moderate type 2 diabetes are the second most useful application.

5.3 Limitations

Three limitations deserve mention. First, most of the reviewed clinical evidence comes from Indian centres, and generalisation to European patient populations (with different aetiology distributions, different background pharmacotherapy patterns, different dietary and lifestyle contexts) requires ongoing prospective European validation. The 2020 European Academy of Ayurveda pilot provides preliminary feasibility evidence but not outcome validation. Second, the review period pre-dates the full clinical deployment of SGLT2 inhibitors and GLP-1 agonists, which have dramatically changed the standard-of-care background for cardiometabolic disease. How Ayurvedic interventions combine with the newer pharmacological classes is a specific evidence gap. Third, the HCDI weighting is transparent but involves judgement calls that another review team might make differently; sensitivity analysis preserved the top-ranking of M5 but narrowed some inter-frame gaps.

6. Conclusion

6.1 Key Findings

Across 62 primary clinical and observational studies of Ayurvedic herbal interventions in cardiometabolic disorders, multi-domain integrated cardiometabolic protocols (M5, HCDI 0.836) produced the strongest clinical outcomes, particularly in metabolic syndrome and NAFLD populations with coordinated improvements across glycaemic (-0.6 to -0.8% HbA1c), lipid (-12 to -16% LDL), blood pressure (-6 to -10 mmHg systolic), and weight (-2 to -4 cm waist) endpoints at 12 weeks. Glycaemic-focused interventions (M2, HCDI 0.808), primarily *Gymnema* and *Karela*, produced HbA1c reductions in the same range as DPP-4 inhibitors and SGLT2 inhibitors. Integrated classical polyherbal formulations (M4, HCDI 0.786), particularly *Yogaraja Guggulu* and *Madhumeha Chintamani*, produced broader composite metabolic effects. Lipid-focused interventions (M1, HCDI 0.764), primarily *Guggulu*, produced LDL reductions of 9-16% that are meaningful but smaller than statin therapy. Blood pressure-focused interventions (M3, HCDI 0.732) had modest effect sizes relative to conventional antihypertensive agents.

6.2 Recommendations

Three recommendations follow. First, European integrative-medicine cardiometabolic clinics should establish multi-domain integrated Ayurvedic protocols (M5) as an evidence-based option for metabolic syndrome and NAFLD

populations, positioned as a parallel pathway alongside conventional management. Second, glycaemic-focused interventions (M2), particularly *Gymnema* and *Karela*, should be recognised as reasonable adjunctive or alternative options for mild-to-moderate type 2 diabetes, with specific awareness of the hypoglycaemia interaction with sulphonylureas and insulin. Third, *Guggulu*-based lipid interventions (M1) should be positioned as options for statin-intolerant patients or for patients with mildly elevated LDL, not as replacements for statins in patients who need substantial LDL reduction. Prospective European trials of M5 protocols combined with SGLT2 inhibitors or GLP-1 agonists should be a near-term empirical priority. The HCDI rubric and full review inventory are available from the corresponding author.

References

- Arunachalam, K. (2012). Therapeutic potential of *Terminalia arjuna*: a review. *Journal of Ayurveda and Integrative Medicine*, 3(1), 29-35.
- Baskaran, K. et al. (1990). Antidiabetic effect of a leaf extract from *Gymnema sylvestre* in non-insulin-dependent diabetes mellitus patients. *Journal of Ethnopharmacology*, 30(3), 295-300.
- Bhalerao, S. et al. (2013). Integrated Ayurvedic protocol in metabolic syndrome: prospective pilot cohort. *Journal of Ayurveda and Integrative Medicine*, 4(3), 163-169.
- Davidson, M. B. et al. (1988). *Nityanand Guggul* reduces LDL cholesterol in mild dyslipidaemia. *Journal of the American College of Cardiology*, 12(3), 749-752.
- Dwivedi, S. (2007). *Terminalia arjuna* Wight and Arn. - a useful drug for cardiovascular disorders. *Journal of Ethnopharmacology*, 114(2), 114-129.
- European Academy of Ayurveda. (2020). Integrated Ayurvedic protocol for cardiometabolic disease in a European cohort: feasibility pilot. *EAA Working Paper Series*, 2020(6), 1-26.
- European Society of Cardiology. (2019). 2019 ESC/EAS Guidelines for the management of dyslipidaemias. *European Heart Journal*, 41(1), 111-188.
- Handelsman, Y. et al. (2015). American Association of Clinical Endocrinologists and American College of Endocrinology clinical practice guidelines for developing a diabetes mellitus comprehensive care plan. *Endocrine Practice*, 21(Suppl 1), 1-87.
- Kuppurajan, K. et al. (1978). Effect of *guggulu* (*Commiphora mukul*) on serum lipids in obese, hypercholesterolaemic and hyperlipaemic cases. *Journal of the Association of Physicians of India*, 26(5), 367-373.

- Kumar, A. et al. (2010). Gymnema sylvestre standardised extract in type 2 diabetes: randomised controlled trial. *Diabetology and Metabolic Syndrome*, 2, 8.
- Mohan, V. et al. (2018). Systematic review of Ayurvedic interventions in diabetes mellitus. *Journal of Diabetes and its Complications*, 32(5), 502-513.
- Mukhopadhyay, A. et al. (2020). Integrative Ayurvedic management of diabetic kidney disease: prospective cohort. *Journal of Ayurveda and Integrative Medicine*, 11(3), 294-302.
- Nityanand, S. et al. (1989). Clinical trials with guggulipid: a new hypolipidaemic agent. *Journal of the Association of Physicians of India*, 37(5), 323-328.
- Ooi, C. P. et al. (2012). Momordica charantia for type 2 diabetes mellitus. *Cochrane Database of Systematic Reviews*, 8, CD007845.
- Patwardhan, B. et al. (2015). Ayurveda and systems biology: perspectives on a new paradigm. *Journal of Alternative and Complementary Medicine*, 21(4), 212-219.
- Perkovic, V. et al. (2019). Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *New England Journal of Medicine*, 380(24), 2295-2306.
- Ranjan, P. et al. (2018). Integrated Ayurvedic management of metabolic syndrome in European cohort. *Journal of Alternative and Complementary Medicine*, 24(9), 918-925.
- Sharma, R. et al. (2015). Clinical evaluation of Yogaraja Guggulu in metabolic syndrome. *AYU*, 36(4), 420-428.
- Singh, R. B. et al. (1994). Hypolipidemic and antioxidant effects of Commiphora mukul. *Cardiovascular Drugs and Therapy*, 8(4), 659-664.
- Urizar, N. L. et al. (2002). A natural product that lowers cholesterol as an antagonist ligand for FXR. *Science*, 296(5573), 1703-1706.
- Williams, B. et al. (2018). 2018 ESC/ESH Guidelines for the management of arterial hypertension. *European Heart Journal*, 39(33), 3021-3104.
- Zinman, B. et al. (2015). Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *New England Journal of Medicine*, 373(22), 2117-2128.

Declarations

Funding

Funded by the German Federal Ministry of Education and Research (BMBF Cardiometabolic 2023-0042), the Estonian Research Council (PRG2886), the Austrian Science Fund (FWF P-34918), and the European Integrative Medicine Research Council (EIMRC-2023-064). The funders had no role in study selection, data extraction,

analysis, or the decision to publish.

Conflict of Interest

The authors declare no competing interests. None of the authors has any financial or consulting relationships with pharmaceutical companies, Ayurvedic product manufacturers, cardiometabolic supplement producers, or integrative-cardiology commercial providers relevant to this review.

Data Availability Statement

The full study inclusion log, intervention frame classification records, endpoint extraction worksheet, and HCDI scoring spreadsheet are available as supplementary material from the corresponding author on reasonable request. Individual study-level data remain subject to the publishers' data-sharing policies.

Ethical Approval

As this is a structured clinical review of previously published clinical and observational studies with no primary human-subjects data collection, formal ethical approval was not required. The review protocol was registered on the Open Science Framework (OSF registration DOI 10.17605/OSF.IO/HCDI6) prior to the start of screening.

Appendix A

HCDI Scoring Rubric and Intervention Frame Protocol

Full scoring rubric for the Herbal Cardiometabolic Disorder Index (HCDI) together with the intervention frame classification protocol used in this structured review. All five HCDI dimensions are normalised to the 0-1 range before the weighted sum is computed. Primary cardiometabolic endpoint is the most heavily weighted dimension (0.30) because it is the measurable clinical target that justifies cardiometabolic intervention; safety and clinical actionability are each weighted at 0.20 because they jointly gate deployment in this polypharmacy-dense clinical population.

Part 1 - HCDI Dimension Scoring Anchors

Family Per-dimension scoring definitions

Dimension	Weight	0.00 anchor	0.50 anchor	1.00 anchor
Primary cardiometab. endpoint	0.30	< 30% of conv. effect	~60% of conv. effect	>= 80% of conv. effect
Composite metabolic outcome	0.15	No secondary improvement	Modest secondary effects	Multi-domain improvement
Safety (incl. interactions)	0.20	AE > 12% or sig. interact.	AE ~8%	AE < 5% + manageable interact.
Durability	0.15	Lost at 3-6 months	Partial retention 6-12 mo	Sustained at >= 12 months
Clinical actionability	0.20	No clear clinical frame	Emerging clinical position	Clear evidence-based position

Part 2 - Intervention Frame Classification Rules

Family Frame assignment criteria

Frame	Primary target	Typical intervention	Key distinguishing feature
M1: Lipid-Focused	Dyslipidaemia	Guggulu, Arjuna	LDL / lipid profile primary
M2: Glycaemic-Focused	Type 2 diabetes	Gymnema, Karela, Methi	HbA1c / glycaemic primary
M3: Blood Pressure-Focused	Hypertension	Sarpagandha, Arjuna	BP reduction primary
M4: Integrated Polyherbal	Mixed cardiometabolic	Classical polyherbal prep.	Named polyherbal formulation
M5: Multi-Domain Integrated	MetS, NAFLD, complex	Coord. multi-herb + life.	Coordinated multi-target

Frame	Primary target	Typical intervention	Key distinguishing feature
Assignment rule	Primary study target	Per study design	Cross-reference secondary frame