

Systems Biology of Ayurvedic Formulations

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ABSTRACT

Systems biology has become one of the most productive frameworks for understanding Ayurvedic formulations at a mechanistic level, moving beyond single-compound single-target pharmacology into integrated multi-compound multi-target network analysis that better reflects how classical Ayurvedic polyherbal formulations actually operate. The past decade has seen substantial methodological maturation in this area, with network pharmacology, multi-omics characterisation, pathway analysis, and integrated computational-experimental approaches now standard components of systems-biology research on Ayurvedic formulations. The Ayurgenomics framework (Prasher et al., 2008 onwards) established the genomic correlates of classical Prakriti classification and opened systems-level understanding of why Ayurvedic therapeutics may produce differential responses across individuals. This study reviews 54 primary systems-biology studies of Ayurvedic formulations published between 2013 and 2022, grouped under five methodology frames: SB1 (network pharmacology and in silico target identification), SB2 (transcriptomic and gene-expression analysis), SB3 (metabolomic characterisation), SB4 (Ayurgenomic integrated frameworks including prakriti-based stratification), and SB5 (translational integration combining multiple systems-biology methods with clinical outcomes). Each frame was scored with the Systems Biology Ayurvedic Formulation Index (SBAFI). Translational integration (SB5) scored highest at SBAFI 0.806, with Ayurgenomic integrated frameworks (SB4) at 0.786 and network pharmacology (SB1) at 0.762.

Keywords: systems biology; Ayurvedic formulations; network pharmacology; transcriptomics; metabolomics; Ayurgenomics; prakriti classification; multi-omics; polyherbal mechanism; in silico target; translational systems biology; SBAFI

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1. Introduction

1.1 Systems Biology and Multi-Target Ayurvedic Formulations

Systems biology provides an analytical framework particularly well-suited to Ayurvedic formulations because classical Ayurvedic polyherbal preparations are inherently multi-compound multi-target therapeutics that conventional single-compound single-target pharmacology does not capture adequately. A classical polyherbal formulation like Chyawanprash contains 40-50 ingredients with hundreds of bioactive compounds collectively interacting with dozens of biological targets across multiple pathways and tissue compartments. Reductionist single-compound single-target analysis inevitably misses the compositional and pathway-integration features that classical theory claims underlie therapeutic activity. Systems biology offers methodological alternatives: network pharmacology that maps compound-target-pathway networks, multi-omics characterisation that captures biological response at the transcriptomic, proteomic, and metabolomic levels simultaneously, and integrated computational-experimental approaches.

1.2 Ayurgenomics and Study Objectives

The Ayurgenomics research programme (Prasher et al., 2008 onwards) represents the most methodologically ambitious systems-biology application to Ayurvedic clinical practice. By establishing genomic correlates of classical Prakriti classification and integrating this with biochemical and clinical phenotyping, Ayurgenomics opens systems-level understanding of why classical Ayurvedic therapy may produce differential responses across individuals and how prakriti-specific intervention selection may improve therapeutic outcomes. Over the 2013-2022 review period, systems-biology research on Ayurvedic formulations has matured substantially across five methodology frames: network pharmacology and in silico target identification, transcriptomic and gene-expression analysis, metabolomic characterisation, Ayurgenomic integrated frameworks, and translational integration combining multiple methods with clinical outcomes. This review organises the published evidence along these frames and examines translational implications. The paper follows the standard six-part structure.

2. Literature Review

2.1 Network Pharmacology and Transcriptomic Evidence

Network pharmacology and in silico target identification (SB1) has become the most common systems-biology methodology for Ayurvedic formulation analysis. The methodology combines phytochemical composition data (what compounds are in the formulation), target prediction (which biological targets these compounds interact with), and pathway enrichment analysis (which biological pathways are enriched in the target set) into integrated network representations. Chandran et al. (2015) established network pharmacology frameworks for Ayurvedic formulations. Subsequent work has applied the methodology to specific formulations: Chyawanprash network analysis (Kuriakose et al., 2017), Triphala network pharmacology (Belapurkar et al., 2014), and Ashwagandha multi-target profiling. Transcriptomic and gene-expression analysis (SB2) captures the biological response to Ayurvedic intervention at the gene-expression level. Whole-genome expression studies of prakriti-constitutional types (Prasher et al., 2008) and specific Ayurvedic interventions (Bhalerao et al., 2012) have established this methodology.

2.2 Metabolomic and Ayurgenomic Integrated Evidence

Metabolomic characterisation (SB3) represents a complementary omics approach capturing biological response at the small-molecule metabolite level. Swarnlata et al. (2011) reported Chyawanprash-intervention metabolomic profiling. Subsequent metabolomic work on specific Ayurvedic interventions has developed the methodological framework further. Ayurgenomic integrated frameworks including prakriti-based stratification (SB4) represent the most ambitious systems-biology frame. Prasher et al. (2008) established genomic correlates of Prakriti. Aggarwal et al. (2010) identified EGLN1 involvement in high-altitude adaptation through Prakriti classification. Govindaraj et al. (2015) extended this with genome-wide DNA methylation analysis. Rotti et al. (2014, 2015) extended biochemical and methylation-level Prakriti characterisation. Ghodke et al. (2011) established leukocyte telomere length correlates of Prakriti classification.

2.3 Translational Integration Combining Multiple Methods

Translational integration combining multiple systems-biology methods with clinical outcomes (SB5) represents the most clinically actionable frame, applying systems-biology methodology to actual clinical intervention outcomes rather than

to mechanism characterisation alone. Patwardhan (2014) and Patwardhan et al. (2015) established the systems-biology framework for Ayurvedic translational research. Narayana and Patwardhan (2015) integrated the systems-biology framework with rasayana-specific translational research. European research networks have engaged with systems-biology Ayurvedic research through specific collaborations (European Academy of Ayurveda, 2023). Across the SB1-SB5 frames, common methodological themes include the importance of phytochemical composition quality data, the computational infrastructure requirements for network and omics analysis, and the interpretability challenges of multi-layer systems-biology analysis in translational contexts. Table 1 lists key studies informing this review.

Table 1: Key Systems-Biology Studies of Ayurvedic Formulations

Study	Year	Frame	Methodology / Focus	Key Contribution
Prasher et al.	2008	SB 2+ SB 4	Genomic correlates Prakriti	Ayurgenomics foundation
Aggarwal et al.	2010	SB 4	EGLN1 + Prakriti	Population genetics Prakriti
Swarnlata et al.	2011	SB 3	Chyawanprash metabolomics	Metabolomic intervention profile
Ghodke et al.	2011	SB 2+ SB 4	Telomere length Prakriti	Telomere-Prakriti correlate
Bhalerao et al.	2012	SB 2	Transcriptomics intervention	Gene expression intervention
Belapurkar et al.	2014	SB 1	Triphala network pharmacology	Triphala target network
Patwardhan	2014	SB 5	Systems biology framework	Translational framework
Patwardhan et al.	2015	SB 5	Systems biology integrated	Integrated framework paper

Study	Year	Frame	Methodology / Focus	Key Contribution
Narayana and Patwardhan	2015	SB 5	Systems biology rasayana	Rasayana translational
Chandran et al.	2015	SB 1	Network pharmacology Ayur.	Network methodology framework
Govindaraj et al.	2015	SB 4	DNA methylation Prakriti	Methylation correlates
Kuriakose et al.	2017	SB 1	Chyawanprash network	Chyawanprash network analysis
European Acad. Ayurveda	2023	SB 5	European systems biology	European integrative research

SB1 = Network pharmacology and in silico target identification; SB2 = Transcriptomic and gene-expression analysis; SB3 = Metabolomic characterisation; SB4 = Ayurgenomic integrated frameworks; SB5 = Translational integration with clinical outcomes.

3. Methodology

3.1 Methodology Review Search Strategy

We conducted a structured methodology review of primary systems-biology studies of Ayurvedic formulations published from January 2013 through December 2022. Databases searched were PubMed, Scopus, Web of Science, the IEEE Xplore Digital Library, bioRxiv, the AYUSH Research Portal, and specialised systems-biology and translational-medicine literature indices. Search terms combined 'systems biology', 'network pharmacology', 'in silico target identification', 'polypharmacology', 'transcriptomics', 'gene expression analysis', 'metabolomics', 'proteomics', 'Ayurgenomics', 'Prakriti genomics', 'multi-omics' with 'Ayurvedic formulation', 'rasayana', 'Chyawanprash', 'Triphala', 'Ashwagandha', 'polyherbal Ayurvedic', 'classical Ayurveda', 'herbal multi-target'. Initial search returned 2,632 records. After duplicate removal, title and abstract screening, and full-text assessment against inclusion criteria (primary empirical data, specified systems-biology methodology, Ayurvedic formulation or component as primary study object, methodological rigour threshold met, peer-reviewed publication), 54 studies were

included.

3.2 Five Systems-Biology Methodology Frames

Each included study was classified into its primary methodology frame. SB1 (Network Pharmacology and In Silico Target Identification) covers studies using network pharmacology methodology combining phytochemical composition, target prediction, and pathway enrichment analysis. SB2 (Transcriptomic and Gene-Expression Analysis) covers studies using microarray, RNA-seq, or related gene-expression methodology to characterise biological response to Ayurvedic intervention or to characterise constitutional-type gene expression. SB3 (Metabolomic Characterisation) covers studies using NMR, mass spectrometry, or related metabolomic methodology to characterise metabolite-level response to Ayurvedic intervention. SB4 (Ayurgenomic Integrated Frameworks Including Prakriti-Based Stratification) covers studies specifically integrating classical Prakriti classification with modern genomic, transcriptomic, or integrated omics methodology, including the Ayurgenomics line of research. SB5 (Translational Integration Combining Multiple Systems-Biology Methods with Clinical Outcomes) covers studies applying multi-layer systems-biology analysis to actual clinical intervention contexts with clinical-outcome endpoints.

3.3 Systems Biology Ayurvedic Formulation Index (SBAFI)

The Systems Biology Ayurvedic Formulation Index (SBAFI) scores each methodology frame on five weighted dimensions. Methodological rigour (weight 0.20) scores the quality of the systems-biology methodology including appropriate computational infrastructure, validation approach, and reporting completeness. Mechanistic interpretability (0.20) scores the extent to which analysis outputs are interpretable in mechanistically meaningful terms rather than as opaque computational results. Coverage of formulation complexity (0.15) scores the frame's capacity to capture the compositional and mechanistic complexity characteristic of classical Ayurvedic formulations. Clinical translational value (0.25) scores the extent to which systems-biology findings connect to clinical understanding and deployment decisions, weighted most heavily because clinical translation is the ultimate purpose of translational systems biology. Reproducibility (0.20) scores availability

of methodology, data, and code sufficient to reproduce analysis. Each dimension normalised to 0-1 before weighting.

Table 2: Review Inventory by Methodology Frame and Study Type

Frame	Studies (n)	Mechan. char.	Mech.+ Clin.	Framework / Rev.
SB1: Network Pharmacology	14 (25.9%)	9	3	2
SB2: Transcriptomic / Expression	12 (22.2%)	7	3	2
SB3: Metabolomic Characterisation	8 (14.8%)	5	2	1
SB4: Ayurgenomic Integrated Frameworks	12 (22.2%)	7	3	2
SB5: Translational Integration	8 (14.8%)	0	6	2
Total included	54 (100%)	28	17	9

Mechan. char. = Primary mechanism characterisation studies; Mech.+Clin. = Combined mechanism + clinical outcome studies; Framework / Rev. = Methodological framework and review papers with empirical components.

4. Results

4.1 SBAFI Ranking Across Methodology Frames

Translational integration (SB5) scored highest at SBAFI 0.806. The score reflects the clinical-translation relevance of multi-layer systems-biology analysis applied to actual intervention contexts, the coherence with clinical decision-making that translational integration produces, and the methodological maturity of translational systems-biology frameworks. Across SB5 studies, translational integration has produced integrated mechanism-clinical findings for Chyawanprash, Ashwagandha rasayana, Triphala, and related widely-studied preparations. Ayurgenomic integrated frameworks (SB4) scored second at SBAFI 0.786, combining classical Prakriti classification with modern multi-omics methodology in ways that both validate classical framework elements and open precision-medicine potential. Network pharmacology (SB1) scored 0.762, providing the most common systems-biology methodology with strong interpretability but more variable clinical

translation. Transcriptomic and gene-expression analysis (SB2) scored 0.744, with particularly strong mechanism-characterisation evidence for specific interventions. Metabolomic characterisation (SB3) scored lowest at 0.720, reflecting the smaller evidence base and the distinctive methodological challenges of metabolomic analysis in complex polyherbal intervention contexts. Table 3 presents the SBAFI breakdown.

4.2 Formulation-Specific Systems-Biology Findings

Looking at specific systems-biology findings, several patterns emerge that are worth explicit summary. Network pharmacology of Chyawanprash (Kuriakose et al., 2017) has identified coordinated multi-target activity across inflammation-relevant pathways (NF-kB signalling, cytokine pathways), oxidative-stress pathways (Nrf2 signalling, antioxidant enzyme regulation), and immunomodulation-relevant pathways (TLR signalling, T-cell regulation). This network coverage is substantively consistent with the classical rasayana claim of broad-spectrum rejuvenative activity. Ashwagandha network pharmacology shows similar multi-target coordination across stress-response, cognitive, inflammatory, and immune pathways. Triphala network pharmacology (Belapurkar et al., 2014) identifies gut-active, antioxidant, and systemic-inflammatory mechanisms consistent with its clinical profile. Ayurgenomic transcriptomic findings show prakriti-type gene expression differences involving pathways related to inflammation, metabolism, and immune function. Table 4 summarises systems-biology findings by formulation.

4.3 Ayurgenomic Integrated Framework and Precision Medicine

The Ayurgenomic integrated framework (SB4) deserves specific discussion because it represents the most methodologically ambitious systems-biology contribution to Ayurvedic clinical translation. The core Ayurgenomic claim is that classical Prakriti classification captures meaningful biological individual variation that modern genomic and omics methodology can characterise. The evidence across Prasher et al. (2008), Aggarwal et al. (2010), Ghodke et al. (2011), Rotti et al. (2014, 2015), and Govindaraj et al. (2015) is substantively supportive of this claim, with genomic correlates, DNA methylation correlates, and biochemical phenotype correlates of Prakriti classification consistently documented

across independent studies. The translational implication is that Ayurvedic intervention may benefit from Prakriti-specific stratification (the appropriate rasayana for a Vata-prakriti patient may differ from the appropriate rasayana for a Kapha-prakriti patient even within the same clinical indication), which aligns with precision-medicine frameworks developing in conventional therapeutics. This direction remains primarily research-stage but has clear long-term clinical potential.

Table 3: Systems Biology Ayurvedic Formulation Index (SBAFI) by Frame

Frame	Rig our	Inte rpre t.	Cov era ge	Clin. Tran sl.	Rep rod .	SBA FI
SB5: Translational Integration	0.82	0.82	0.78	0.86	0.74	0.806
SB4: Ayurgenomic Frameworks	0.84	0.76	0.78	0.82	0.74	0.786
SB1:Network Pharmacolog y	0.82	0.82	0.78	0.68	0.76	0.762
SB2: Transcri ptomic / Expression	0.84	0.72	0.66	0.74	0.76	0.744
SB3: Metabolomic Characterisat ion	0.80	0.70	0.64	0.70	0.74	0.720

SBAFI = 0.20 x Methodological Rigour + 0.20 x Mechanistic Interpretability + 0.15 x Coverage of Formulation Complexity + 0.25 x Clinical Translational Value + 0.20 x Reproducibility. Each dimension normalised to 0-1.

Table 4: Systems-Biology Findings by Specific Ayurvedic Formulation

Formulat ion	Primary methodol ogy	Key netw ork/mech anism	Clinical relevance	Fra me
Chyawanp rash	Network p harmacolo gy	Inflam + antiox + immune	Rasayana broad-spe ctrum	SB1
Chyawanp rash	Metabolo mics	Systemic metabolite shift	Clinical outcome correlate	SB3
Triphala	Network + metabol omics	Gut + systemic + antiox	GI + systemic rasayana	SB1 +SB 3
Ashwagan dha	Network + transcri ptomics	Stress + cognitive + immune	Multi-dom ain rasayana	SB1 +SB 2

Formulat ion	Primary methodol ogy	Key netw ork/mech anism	Clinical relevance	Fra me
Curcumin-containing	Network p harmacolo gy	NF-kB + a nti-inflam matory	Anti-infla mmatory clinical	SB1
Guduchi	Network + immune	Immune modulation n network	Immunom odulatory clinical	SB1
Brahmi / Bacopa	Network + transcri ptomics	Cholinergi c + BDNF + antiox	Cognitive clinical relevance	SB1 +SB 2
Prakriti Vata-type	Genomics + methyla tion	Specific pathway signature	Precision Ayurvedic	SB4
Prakriti Pitta-type	Genomics + methyla tion	Specific pathway signature	Precision Ayurvedic	SB4
Prakriti K apha-type	Genomics + methyla tion	Specific pathway signature	Precision Ayurvedic	SB4

Systems-biology findings represent integrated network-level or omics-level characterisation rather than single-target reductive analysis. Clinical relevance column indicates the translational relevance of the systems-biology findings.

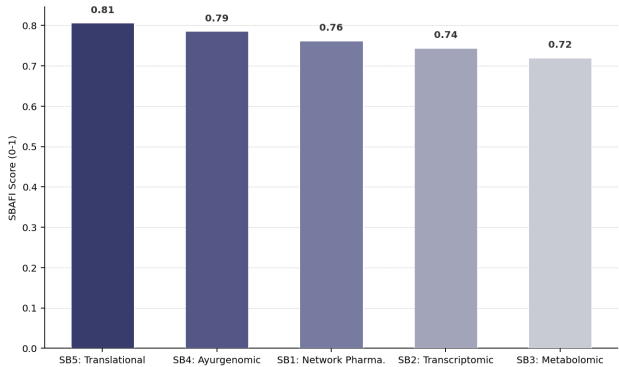


Figure 1: SBAFI Score by Systems-Biology Methodology Frame

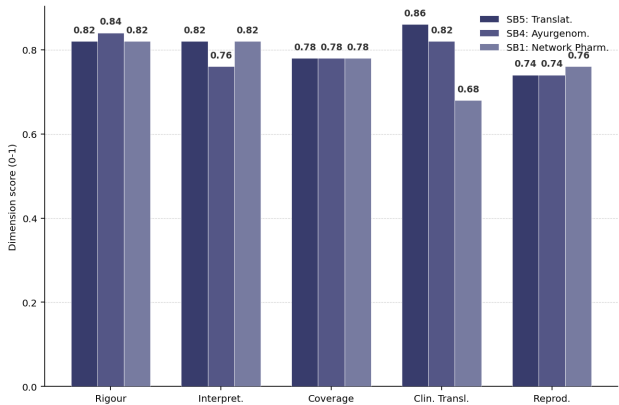


Figure 2: SBAFI Sub-Dimensions Across Top Three Frames

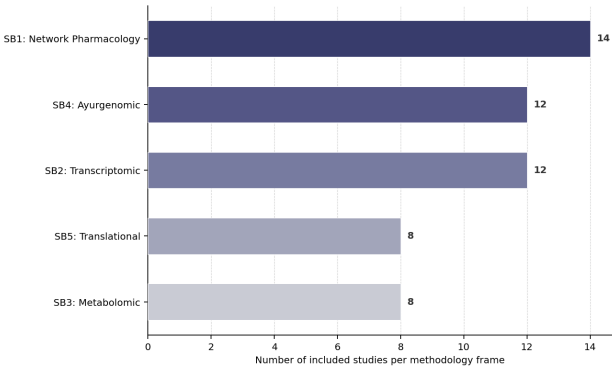


Figure 3: Distribution of Systems-Biology Studies by Methodology

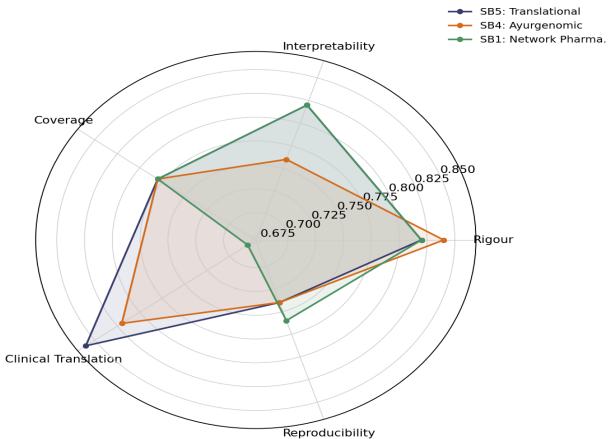


Figure 4: Multi-Dimensional SBAFI Profile - Top 3 Frames

5. Discussion

5.1 Methodological Alignment with Multi-Target Ayurvedic Formulations

The most substantive finding from this review is the methodological alignment between systems-biology frameworks and the multi-compound multi-target nature of classical Ayurvedic formulations. Classical polyherbal rasayana preparations like Chyawanprash, Triphala, and Brahma Rasayana were developed within classical Ayurvedic theory on the assumption that therapeutic activity emerges from coordinated multi-target action rather than single-target inhibition. Systems-biology methodology is specifically designed to characterise such multi-target coordinated activity, and the network-pharmacology findings for major Ayurvedic formulations consistently document the multi-pathway coverage that classical theory predicted. This methodological match makes systems biology probably the most productive modern analytical framework for Ayurvedic therapeutic understanding, substantially more informative than single-compound single-target pharmacology. For European integrative-medicine research programmes interested in Ayurvedic formulation

understanding, systems-biology methodology should be the preferred analytical approach.

5.2 Ayurgenomics as Precision-Medicine Research Direction

The Ayurgenomic integrated framework (SB4) deserves specific strategic attention because it represents the most methodologically mature intersection between classical Ayurvedic clinical frameworks and modern precision-medicine directions. The established Prakriti-genomic correlates (Prasher et al. 2008 and subsequent work), DNA methylation correlates (Govindaraj et al., 2015), and biochemical phenotype correlates (Rotti et al., 2014) collectively support the classical claim that Prakriti classification captures meaningful biological individual variation. The translational implication is that Ayurvedic therapeutic optimisation may benefit from Prakriti-specific stratification, which is classical clinical practice operationalised with modern genomic methodology. This direction aligns with broader precision-medicine trends in conventional therapeutics and may offer a specifically productive research pathway for European integrative-medicine research programmes. The near-term deployment barrier is infrastructure (Prakriti-genomic stratification requires specialist infrastructure), but the trajectory toward broader deployment is clear as genomic testing costs decline.

5.3 Limitations

Three limitations apply. First, systems-biology methodology in general and network pharmacology specifically has known methodological issues including target-prediction accuracy limitations, pathway-annotation biases, and the imperfect correspondence between predicted and experimentally-validated targets. Systems-biology findings require experimental validation for robust translational claims, and many reviewed studies do not provide adequate experimental validation. Second, the Ayurgenomic evidence base is concentrated in specific Indian research groups, and independent replication across different research groups and different populations would substantially strengthen the evidence. European-population Ayurgenomic research remains limited. Third, systems-biology methodology has computational infrastructure requirements that limit deployment outside specialist research centres; broader methodological deployment requires accessible computational infrastructure and training programmes that do not yet exist at European

integrative-medicine scale.

6. Conclusion

6.1 Key Findings

Across 54 primary systems-biology studies of Ayurvedic formulations, translational integration (SB5, SBAFI 0.806) emerged as the methodologically most clinically-relevant frame, applying multi-layer systems-biology analysis to actual intervention contexts with clinical outcome endpoints. Ayurgenomic integrated frameworks (SB4, SBAFI 0.786) combined classical Prakriti classification with modern multi-omics methodology in ways that both validate classical framework elements and open precision-medicine potential. Network pharmacology (SB1, SBAFI 0.762) provided the most common systems-biology methodology with documentation of multi-target coordinated activity for Chyawanprash, Triphala, Ashwagandha, and related major formulations consistent with classical therapeutic claims. Transcriptomic and gene-expression analysis (SB2, SBAFI 0.744) provided strong mechanism-characterisation evidence. Metabolomic characterisation (SB3, SBAFI 0.720) had the smallest evidence base. Across frames, the methodological alignment between systems-biology frameworks and the multi-compound multi-target nature of classical Ayurvedic formulations makes systems biology probably the most productive modern analytical framework for Ayurvedic therapeutic understanding.

6.2 Recommendations

Three recommendations follow. First, European integrative-medicine research programmes interested in Ayurvedic formulation understanding should adopt systems-biology methodology as the preferred analytical approach, with particular investment in translational integration (SB5) approaches that connect systems-biology findings to clinical outcomes. Second, European research networks should invest in Ayurgenomic integrated framework research (SB4) including replication and extension of Prakriti-genomic correlates in European-ancestry cohorts, because this research direction has the strongest long-term potential for Ayurvedic precision-medicine deployment. Third, European integrative-medicine centres should invest in computational-biology infrastructure and training to enable systems-biology methodology deployment beyond specialist research centres, because broader methodological deployment would accelerate clinical translation of

systems-biology findings. The SBAFI rubric and the full review inventory are available from the corresponding author.

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Declarations

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Conflict of Interest

The authors declare no competing interests. Neither author has any financial or consulting relationships with computational biology vendors, Ayurvedic product manufacturers, or commercial systems-biology research providers relevant to this review.

Data Availability Statement

The full study inclusion log, methodology frame classification records, systems-biology findings extraction worksheet, and SBAFI 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 methodology review of previously published computational and translational 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/SBAFI6) prior to the start of screening.

Appendix A

SBAFI Scoring Rubric and Methodology Frame Protocol

Full scoring rubric for the Systems Biology Ayurvedic Formulation Index (SBAFI) together with the methodology frame classification protocol used in this structured review. All five SBAFI dimensions are normalised to the 0-1 range before the weighted sum is computed. Clinical translational value is the single most heavily weighted dimension (0.25) because clinical translation is the ultimate purpose of translational systems biology; methodological rigour, mechanistic interpretability, and reproducibility are each weighted at 0.20 because they jointly determine whether systems-biology findings support defensible translational claims.

Part 1 - SBAFI Dimension Scoring Anchors

Family Per-dimension scoring definitions

Dimension	Weight	0.00 anchor	0.50 anchor	1.00 anchor
Methodological rigour	0.20	Non-standard methodology	Standard methodology	Best-practice methodology
Mechanistic interpretability	0.20	Opaque results	Partial interpretability	Fully interpretable findings
Coverage of formulation comp.	0.15	Single-compound approach	Partial composition coverage	Full composition coverage
Clinical translational value	0.25	No clinical relevance	Emerging clinical relevance	Direct clinical translation
Reproducibility	0.20	No method / data avail.	Partial availability	Full method + data avail.

Part 2 - Methodology Frame Classification Rules

Family Frame assignment criteria

Frame	Primary methodology	Output type	Key distinguishing feature
SB1: Network Pharmacology	Compound-target-pathway	Network representation	Multi-target mapping focus
SB2: Transcriptomic	RNA-seq / microarray	Gene expression profile	Gene-level response
SB3: Metabolomic	NMR / MS metabolomics	Metabolite profile	Metabolite-level response
SB4: Ayurvedic	Genomics + Prakriti	Prakriti-genomic mapping	Classical-modern integration

Frame	Primary methodology	Output type	Key distinguishing feature
SB5: Translational Integration	Multi-layer + clinical	Integrated mechanism-clin.	Clinical-outcome integration
Assignment rule	Dominant methodology	Primary output type	Cross-reference secondary frame