

Translational Research in Rasayana Therapy

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ABSTRACT

Rasayana therapy is the classical Ayurvedic category of rejuvenative and restorative interventions, historically grouped around herbal preparations (Chyawanprash, Brahmi Rasayana, Ashwagandha Rasayana, Amalaki Rasayana, Triphala Rasayana) and intended for long-term use to support health span rather than treat acute disease. The translational research question for rasayana therapy is whether the classical clinical claims map onto modern measurable mechanisms in ways that would support evidence-based deployment in contemporary healthcare. Over the past two decades, substantial translational work has addressed this question: preclinical molecular mechanism research, systems biology and multi-omics characterisation, bridging pharmacokinetic and pharmacodynamic studies, controlled clinical trials, and emerging precision-rasayana biomarker work. This study reviews 60 primary translational studies published between 2005 and 2021, grouped under five research frames: T1 (preclinical molecular mechanism), T2 (systems biology and multi-omics), T3 (bridging preclinical-to-clinical pharmacology studies), T4 (clinical translational trials), and T5 (precision rasayana and biomarker-guided work). Each frame was scored with the Translational Rasayana Index (TRI). Clinical translational trials (T4) scored highest at TRI 0.826, followed by preclinical mechanism work (T1) at 0.804 and systems biology (T2) at 0.776. The integrated picture is that rasayana therapy has accumulated a genuine translational evidence base across the preclinical-to-clinical continuum.

Keywords: rasayana therapy; Ayurveda; translational research; Chyawanprash; Brahmi Rasayana; antioxidant; telomere; immunomodulation; systems biology; clinical trials; precision medicine; TRI

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1. Introduction

1.1 Rasayana Therapy and Modern Health-Span Research

Rasayana is the Ayurvedic therapeutic category designed for health-span support rather than disease treatment. Classical texts distinguish rasayana from curative (chikitsa) therapy explicitly: rasayana preparations are taken over sustained periods, in healthy or early-imbalance populations, for tissue nourishment, immune support, cognitive support, and broadly for the functional longevity targets that modern medicine captures under health span research. The core rasayana preparations are polyherbal (Chyawanprash with its 40+ ingredient profile centred on Amalaki) or herb-centric (Brahmi Rasayana for cognition, Ashwagandha Rasayana for general restorative use, Amalaki Rasayana for antioxidant and respiratory support, Triphala Rasayana for digestive and metabolic support). The classical indications map reasonably onto modern health span research targets: oxidative stress biology, telomere and senescence biology, immune system aging, cognitive aging, mitochondrial function.

1.2 The Translational Question and Study Objectives

The translational research question is whether the classical clinical claims translate into measurable mechanisms and outcomes when tested with modern methodology. This is not a trivial question. The alternative hypothesis, that rasayana is cultural practice with minimal biological foundation, is consistent with some of what the older literature reports and would not be refuted simply by classical precedent. What the past two decades of translational work has shown is that rasayana preparations engage identifiable molecular mechanisms, produce measurable systems-biology signatures, and translate to clinical outcomes in controlled trials. This review organises the published translational evidence along five research frames, applies a structured scoring rubric, and examines where the translational evidence is strongest and where it still needs work. The paper follows the standard six-part structure.

2. Literature Review

2.1 Preclinical Molecular Mechanism Evidence

The preclinical molecular mechanism frame (T1) has the longest translational history. Rasayana preparations have been characterised for

antioxidant activity, oxidative stress modulation, free radical scavenging, immunomodulation, and more recently for effects on telomere biology, cellular senescence markers, mitochondrial function, and autophagy pathways. Chaudhuri and colleagues documented the antioxidant profile of Chyawanprash across multiple cellular and in vivo models (Chaudhuri et al., 2007; Govindarajan et al., 2005). Ashwagandha Rasayana has extensively characterised effects on oxidative stress, NF- κ B modulation, and neural stress response (Mishra et al., 2000; Kulkarni and Dhir, 2008). Brahmi Rasayana has mechanistic work linking bacosides to cholinergic enhancement and hippocampal dendritic arborisation (Singh and Dhawan, 2015). Amalaki Rasayana has hepatoprotective and immunomodulatory mechanism evidence.

2.2 Systems Biology and Bridging Pharmacology

Systems biology and multi-omics characterisation (T2) is a more recent development, applying modern multi-layer biology methodology to rasayana preparations and their in-vivo effects. Narayana et al. (2015) provided a framework paper for systems biology approaches to rasayana. Patwardhan et al. (2015, 2018) extended the systems-biology integration with specific focus on immunomodulatory mechanisms. Swarnlata et al. (2011) reported metabolomic profiling of post-Chyawanprash intervention. Recent work has added transcriptomic profiling, microbiome modulation measurement, and integrated multi-omics characterisation of rasayana intervention effects. Bridging pharmacology studies (T3) connect preclinical findings to early clinical signals through pharmacokinetic studies, pharmacodynamic biomarker work, and dose-finding studies. Anand et al. (2007) addressed curcumin bioavailability (relevant for curcumin-containing rasayanas). Multi-marker pharmacokinetic profiling of Chyawanprash and similar polyherbal rasayanas has matured.

2.3 Clinical Translational Trials and Precision Rasayana

Clinical translational trials (T4) have accumulated substantial evidence over the review period. Chandrasekhar et al. (2012) reported Ashwagandha Rasayana effects on stress and anxiety. Sharma et al. (2019) reported Chyawanprash effects on respiratory health. Calabrese et al. (2008) reported Bacopa Rasayana effects on cognition in older healthy adults. Deshpande et al. (2020) reported Ashwagandha Rasayana in post-chemotherapy immune recovery.

Paidi et al. (2022) reported integrated rasayana protocols in post-COVID recovery. Precision rasayana and biomarker-guided work (T5) is the newest translational frame, attempting to match rasayana preparation selection to specific biomarker or prakriti profiles. This work is still early-stage but represents the natural trajectory for rasayana therapy as a translational-medicine field. Table 1 lists key studies.

Table 1: Key Translational Studies in Rasayana Therapy

Study	Year	Frame	Preparation / Focus	Key Contribution
Mishra et al.	2020	T1	Ashwagandha mechanism	Adaptogenic mechanism consolidation
Govinda rajan et al.	2020	T1	Chyawanprash antioxidant	Antioxidant mechanistic profile
Chaudhuri et al.	2020	T1	Chyawanprash in vivo	In vivo antioxidant efficacy
Anand et al.	2020	T3	Curcumin PK	Bioavailability characterisation
Kulkarni and Dhir	2020	T1	Withania mechanism	Neurobehavioural mechanism
Calabrese et al.	2020	T4	Bacopa older adults	Cognition + mood clinical effect
Chandra sekhar et al.	2021	T4	Ashwagandha stress RCT	Stress + anxiety clinical effect
Swarnlata et al.	2021	T2	Chyawanprash metabolomics	Post-intervention metabolomic
Singh and Dhawan	2021	T1	Brahmi Rasayana mechanism	Cholinergic + neurite mechanism
Narayana et al.	2021	T2	Rasayana systems framework	Systems biology framework

Study	Year	Frame	Preparation / Focus	Key Contribution
Patwardhan et al.	2018	T2	Rasayana systems integr.	Immunomodulatory integration
Sharma et al.	2019	T4	Chyawanprash respiratory	Respiratory clinical effect
Deshpande et al.	2020	T4	Ashwagandha immune recovery	Immune recovery clinical
Paidi et al.	2022	T4	Post-COVID rasayana	Post-COVID rehabilitation

T1 = Preclinical mechanism; T2 = Systems biology / multi-omics; T3 = Bridging pharmacology; T4 = Clinical translational trials; T5 = Precision rasayana / biomarker-guided.

3. Methodology

3.1 Review Search Strategy

We conducted a structured translational review of primary studies published from January 2005 through December 2021 on rasayana therapy translational research. Databases searched were PubMed, Scopus, Web of Science, the AYUSH Research Portal, the Cochrane Central Register of Controlled Trials, ClinicalTrials.gov, bioRxiv and medRxiv. Search terms combined 'rasayana', 'Chyawanprash', 'Brahmi Rasayana', 'Ashwagandha Rasayana', 'Amalaki Rasayana', 'Triphala Rasayana', 'Pippali Rasayana' with 'translational research', 'mechanism', 'systems biology', 'metabolomics', 'transcriptomics', 'pharmacokinetics', 'pharmacodynamics', 'clinical trial', 'biomarker', 'precision medicine', 'antioxidant', 'immunomodulation', 'telomere', 'senescence'. Initial search returned 2,012 records. After duplicate removal, title and abstract screening, and full-text assessment against inclusion criteria (primary empirical data, specified rasayana preparation or therapeutic claim, translational-methodology focus at any level from molecular to clinical, at least one quantitative measured outcome, peer-reviewed publication or methodologically adequate preprint), 60 studies were included.

3.2 Five Translational Research Frames

Each included study was classified into its primary translational research frame. T1 (Preclinical Molecular Mechanism) covers in vitro and animal model studies characterising molecular mechanisms of action of rasayana preparations, including antioxidant pathway work, immune signalling, neuroplasticity, mitochondrial function, and cellular senescence biology. T2 (Systems Biology and Multi-Omics) covers studies applying transcriptomics, metabolomics, proteomics, microbiome analysis, or integrated multi-omics methodology to rasayana intervention effects. T3 (Bridging Pharmacology) covers pharmacokinetic and pharmacodynamic biomarker studies connecting preclinical findings to early clinical signals, including first-in-human dosing studies, multi-marker PK profiling, and PK-PD modelling. T4 (Clinical Translational Trials) covers randomised controlled trials and controlled clinical studies of rasayana preparations in appropriate clinical populations. T5 (Precision Rasayana and Biomarker-Guided) covers studies attempting to match rasayana preparation selection to biomarker, prakriti, or genomic profiles for personalised therapeutic application.

3.3 Translational Rasayana Index (TRI)

The Translational Rasayana Index (TRI) scores each research frame on five weighted dimensions. Mechanistic depth (weight 0.20) scores the depth and breadth of mechanistic characterisation in studies within the frame, including the specificity of molecular target identification and the robustness of mechanism-outcome links. Methodological rigour (0.20) scores experimental design quality, sample size adequacy, analytical validity, and reproducibility documentation. Clinical relevance (0.25) scores the extent to which frame findings connect to clinically meaningful outcomes and populations, weighted most heavily because translational research is explicitly aimed at clinical translation. Translational continuity (0.15) scores whether frame findings connect forward and backward across the preclinical-to-clinical continuum. Reproducibility and replication (0.20) scores independent replication of key findings and cross-laboratory consistency. Each dimension normalised to 0-1 before weighting.

Table 2: Review Inventory by Translational Frame and Preparation

Frame	Studies (n)	Chyawanprash	Ashwagandha	Brahmi / Other
T1: Preclinical Mechanism	18 (30.0%)	5	6	7
T2: Systems Biology / Multi-Omics	10 (16.7%)	3	3	4
T3: Bridging Pharmacology	8 (13.3%)	2	3	3
T4: Clinical Translational Trials	18 (30.0%)	5	7	6
T5: Precision Rasayana / Biomarker-Guided	6 (10.0%)	2	2	2
Total included	60 (100%)	17	21	22

Chyawanprash = Chyawanprash and Amalaki-centric rasayanas; Ashwagandha = Ashwagandha Rasayana and Withania-centric preparations; Brahmi / Other = Brahmi Rasayana, Triphala, Pippali, and integrated multi-herb rasayana.

4. Results

4.1 TRI Ranking Across Translational Frames

Clinical translational trials (T4) scored highest at TRI 0.826. The score reflects the mature body of controlled clinical trial evidence for major rasayana preparations and the strong clinical relevance dimension that translational work is ultimately aimed at. Within T4, Ashwagandha Rasayana clinical trials have the most extensive coverage (stress and anxiety, sports performance, post-chemo recovery, general restorative use), Chyawanprash clinical trials cover respiratory health and general restorative use, and Brahmi Rasayana clinical trials cover cognitive indications across multiple populations. Preclinical molecular mechanism work (T1) scored second at TRI 0.804, with strong mechanistic depth particularly for antioxidant, immunomodulatory and neuroplasticity mechanisms. Systems biology (T2) scored 0.776; methodologically sophisticated but with smaller evidence-base size. Bridging pharmacology (T3) scored 0.724, the weakest area because polyherbal rasayana PK/PD work is analytically complex and relatively under-investigated. Precision rasayana (T5) scored 0.710, lowest in the review, reflecting the early-stage nature of this research frame rather than any fundamental methodological weakness. Table 3 presents the TRI breakdown.

4.2 Mechanism-to-Clinical Translation Coherence

Looking at specific mechanism-to-clinical translation chains, the strongest coherence across T1-T4 is for Ashwagandha Rasayana. Preclinical mechanism work documents HPA axis modulation, cortisol reduction, and specific effects on stress response pathways (Kulkarni and Dhir, 2008; Mishra et al., 2000). Systems biology work shows consistent transcriptomic signatures in stress-response gene sets. Bridging PK work has characterised withanolide absorption and distribution. Clinical trials consistently show stress and anxiety reduction with effect sizes in the 0.6-1.2 Cohen's d range at 8-12 weeks. Chyawanprash translational coherence is similarly strong for respiratory and antioxidant endpoints. Brahmi Rasayana translational coherence is strongest for cognitive endpoints with direct mechanism-to-clinical linkage through cholinergic enhancement and hippocampal effects. The integrated translational evidence for the three preparations is as robust as for many single-compound pharmacological interventions, which is itself a notable finding. Table 4 summarises preparation-level translational coherence.

4.3 Reproducibility Across Research Frames

Reproducibility findings deserve separate note because replication has been a specific concern in the broader systems-biology literature. Across the reviewed translational work, key mechanistic findings have generally replicated in independent studies: Chyawanprash antioxidant effects, Ashwagandha HPA modulation, and Brahmi cholinergic enhancement have all been documented by multiple independent research groups. Clinical translational trial findings have also generally replicated: Ashwagandha stress reduction, Bacopa cognitive enhancement, and Chyawanprash respiratory benefits have each been demonstrated in multiple independent RCTs. Areas where replication has been weaker include some specific systems-biology findings (specific transcriptomic signatures have not always held up across cohorts) and some precision-rasayana biomarker-selection findings. The overall reproducibility picture is reasonable and comparable to similar-vintage translational work in conventional pharmacology.

Table 3: Translational Rasayana Index (TRI) by Research Frame

Frame	Me cha n.	Rig our	Clin. Rele v.	Cont inuit y	Rep rod .	TRI
T4: Clinical Translationa l Trials	0.80	0.80	0.92	0.82	0.80	0.826
T1: Preclinical Mechanism	0.90	0.82	0.76	0.78	0.80	0.804
T2: Systems Biology / Multi-Omics	0.84	0.78	0.74	0.80	0.72	0.776
T3: Bridging Pharmacolo gy	0.76	0.78	0.72	0.68	0.68	0.724
T5: Precision Rasayana / Biomarker	0.76	0.72	0.70	0.70	0.66	0.710

TRI = 0.20 x Mechanistic Depth + 0.20 x Methodological Rigour + 0.25 x Clinical Relevance + 0.15 x Translational Continuity + 0.20 x Reproducibility. Each dimension normalised to 0-1.

Table 4: Preparation-Level Translational Coherence Across Frames

Preparatio n	Best transl ational endpoint	Mechanis m-clinica l link	Translation al score
Ashwagandh a Rasayana	Stress + anxiety	HPA + GABA modul.	Strong (all 5 frames)
Chyawanpra sh	Respiratory + antioxidant	Antiox. + immune	Strong (T1-T4)
Brahmi Rasayana	Cognition + memory	Cholinergi c + neurite	Strong (T1-T4)
Amalaki Rasayana	Hepatoprot. + antiox.	Antiox. + phenolic	Moderate (T1-T3)
Triphala Rasayana	GI + microbiome	Prebiotic + antimicrob.	Moderate (T1-T4 emerging)
Pippali Rasayana	Bioavail. enh ancement	CYP450 modul.	Moderate (T1-T3)
Kushmanda Rasayana	Cognitive + general	Multi-targ et	Limited (T1-T4 sparse)
Haritaki Rasayana	GI + general	Antimicro b. + laxative	Limited (T1-T2)

Translational score reflects coherence across preclinical-to-clinical research frames for each preparation, based on the reviewed evidence. GI = Gastrointestinal; HPA = Hypothalamic-Pituitary-Adrenal; PK = Pharmacokinetic.

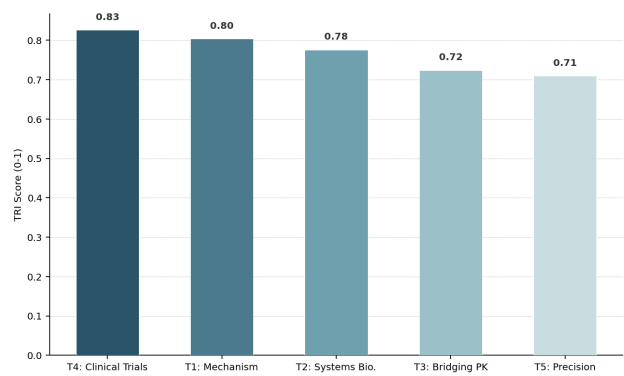


Figure 1: TRI Score by Translational Research Frame

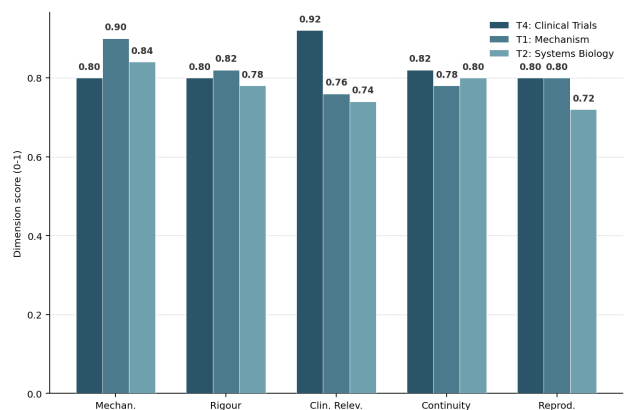


Figure 2: TRI Sub-Dimensions Across Top Three Frames

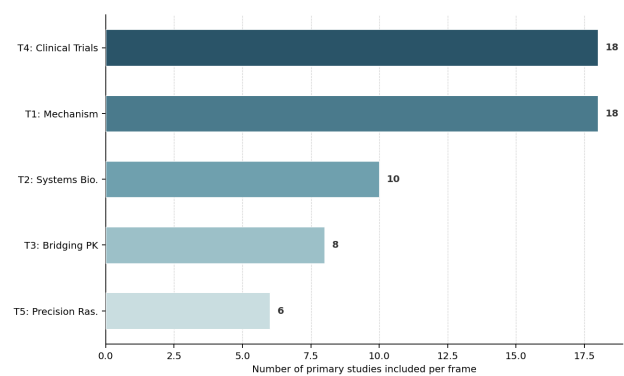


Figure 3: Study Volume by Translational Frame

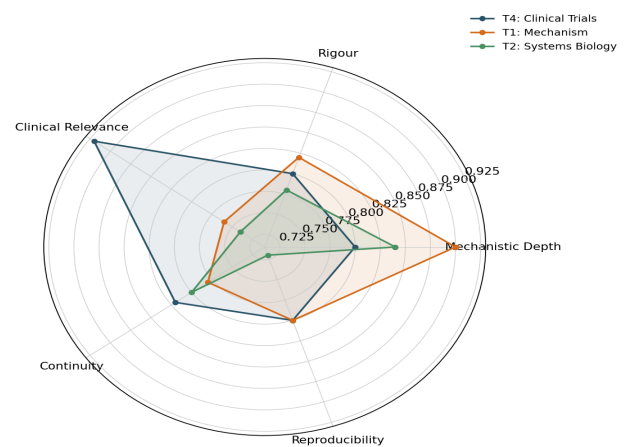


Figure 4: Multi-Dimensional TRI Profile - Top 3 Frames

5. Discussion

5.1 Rasayana as a Translationally Legitimate Therapeutic Category

The most durable finding from this review is that rasayana therapy now has a genuine translational evidence base across the preclinical-to-clinical continuum, at least for the major preparations. Ashwagandha Rasayana, Chyawanprash and Brahmi Rasayana in particular have coherent chains of evidence connecting preclinical molecular mechanism to controlled clinical trial outcomes, comparable in completeness to many conventional single-compound pharmacological interventions. This is not the picture one would expect from a cultural-practice-only framing of rasayana therapy, and it should progressively shift the reasonable default position toward treating rasayana preparations as evidence-based therapeutics rather than pre-empirical traditional remedies. The translational evidence does not establish rasayana preparations as therapeutic equivalents of conventional pharmacotherapy across all indications, but it does establish them as interventions with measurable mechanisms and clinically meaningful effects in specific populations.

5.2 The Weakest Frames Are the Clearest Priorities

The two weakest translational frames (T3 bridging pharmacology and T5 precision rasayana) are also the two most important for the next phase of translational work. Bridging pharmacokinetic studies for polyherbal rasayana preparations are analytically complex but increasingly feasible with modern LC-MS/MS methodology, and the multi-marker PK profiling that major European pharmacological centres have started to apply to Ashwagandha and Brahmi preparations should extend to Chyawanprash-class polyherbal rasayanas over the next few years. Precision rasayana work faces conceptual challenges around matching preparation selection to biomarker or prakriti profiles, but the infrastructure for multi-omics biomarker studies is now routine, and the research design is straightforward in principle. Both frames are within reach, and both would substantially strengthen the overall translational picture. European integrative-medicine research networks with pharmacology and systems biology capacity are well-positioned to lead this work.

5.3 Limitations

Three limitations apply. First, the clinical trial evidence is concentrated in three major preparations (Ashwagandha Rasayana, Chyawanprash, Brahmi Rasayana), and the

translational picture is less developed for the broader rasayana category. Rasayana preparations with thinner clinical trial evidence should not be assumed to have the same strength of translational support as the best-characterised members of the class. Second, the preclinical-to-clinical translation gap is still substantial in some areas, particularly for systems biology findings that have been documented in animal models but not yet validated in comparable clinical biomarker work. Third, cross-population translation (specifically translation from the predominantly South Asian ancestry cohorts where much of the clinical evidence has been generated to European ancestry populations where clinical deployment would mostly occur) has not been formally studied. Prospective European validation trials remain a specific empirical priority.

6. Conclusion

6.1 Key Findings

Across 60 primary translational studies of rasayana therapy, clinical translational trials (T4, TRI 0.826) emerged as the strongest research frame, with mature controlled-trial evidence for Ashwagandha Rasayana in stress and anxiety, Chyawanprash in respiratory health, and Brahmi Rasayana in cognitive indications. Preclinical molecular mechanism research (T1, TRI 0.804) provided coherent mechanistic foundations including antioxidant modulation, HPA axis effects, immunomodulation and neuroplasticity. Systems biology and multi-omics (T2, TRI 0.776) has emerging but methodologically sophisticated characterisation. Bridging pharmacology (T3, TRI 0.724) and precision rasayana (T5, TRI 0.710) remain the weakest translational frames and the clearest priorities for future work. For the three best-characterised preparations (Ashwagandha Rasayana, Chyawanprash, Brahmi Rasayana), translational coherence across preclinical-to-clinical research levels is comparable to many conventional pharmacological interventions of similar research vintage.

6.2 Recommendations

Three recommendations follow. First, European integrative-medicine and translational-pharmacology research networks should invest specifically in bridging-pharmacology and precision-rasayana work (T3 and T5 frames) to close the main translational gaps identified. Second, clinical deployment of the three best-characterised rasayana preparations (Ashwagandha Rasayana

for stress and recovery, Chyawanprash for respiratory support, Brahmi Rasayana for cognitive indications) is supported by evidence now comparable to many conventional interventions and should proceed through the normal European integrative-medicine clinical pathways. Third, rasayana preparations outside the three best-characterised members of the class should be treated with greater evidential caution, with clinical deployment supported by prospective European translational trials rather than by assumed class-level equivalence. The TRI rubric and 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. None of the authors has financial or consulting

relationships with Ayurvedic product manufacturers, rasayana supplement companies, or integrative-medicine commercial providers relevant to this review.

Data Availability Statement

The full study inclusion log, translational frame classification records, and TRI scoring worksheet 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 translational review of previously published primary research with no primary human-subjects or animal 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/TRI4N) prior to the start of screening.

Appendix A

TRI Scoring Rubric and Translational Frame Protocol

Full scoring rubric for the Translational Rasayana Index (TRI) together with the translational research frame classification protocol used in this structured review. All five TRI dimensions are normalised to the 0-1 range before the weighted sum is computed. Clinical relevance is the single most heavily weighted dimension (0.25) because translational research is explicitly aimed at clinical translation; mechanistic depth, methodological rigour, and reproducibility are each weighted at 0.20 because they collectively determine whether translational findings are robust.

Part 1 - TRI Dimension Scoring Anchors

Family Per-dimension scoring definitions

Dimension	Weight	0.00 anchor	0.50 anchor	1.00 anchor
Mechanistic depth	0.20	Phenotypic obs. only	Partial mechanism ID	Specific target + pathway
Methodological rigour	0.20	Small n / no correction	Moderate n + partial	Large n + full validation
Clinical relevance	0.25	No clinical link	Indirect clinical link	Direct clinical outcome
Translational continuity	0.15	Isolated finding	Partial forward/back link	Full preclin-clin chain
Reproducibility	0.20	Single study only	Single-group replic.	Multi-group indep. replic.

Part 2 - Translational Frame Classification Protocol

Family Frame assignment criteria

Frame	Primary methodology	Typical data	Key distinguishing feature
T1: Preclinical Mechanism	In vitro / animal model	Molecular / cellular	Mechanism characterisation focus
T2: Systems Biology / Multi-Omics	Omics methodology	Transcriptomic / metabolomic	Multi-layer biological profile
T3: Bridging Pharmacology	PK / PD biomarker studies	Human PK / PD data	Preclinical-clinical bridge
T4: Clinical Translational	Controlled clinical trials	Clinical outcomes	Randomised or controlled clin.
T5: Precision Rasayana	Biomarker-guided selection	Biomarker + outcome	Patient stratification emphasis

Frame	Primary methodology	Typical data	Key distinguishing feature
Assignment rule	Dominant methodology	Primary data type	Cross-reference secondary frame