RESEARCH PAPER

Study of Ayurgenomics: Mapping Dosha, Dhatu and Mala Across the Molecular Landscape

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ABSTRACT

Background: Traditional Ayurvedic physiology understands health through a dynamic equilibrium of Dosha (regulatory biological principles), Dhatu (structural and metabolic tissue matrices), and Mala (excretory end-products). Modern biomedicine evaluates complex human diseases using high-throughput multi-omics (genomics, transcriptomics, proteomics, metabolomics, and gut metagenomics). Ayur-omics bridges these paradigms by examining molecular patterns underlying Ayurvedic clinical phenotypes.

Objective: To systematically map the classical Ayurvedic triad (Dosha, Dhatu, Mala) across modern molecular and cellular networks, synthesize empirical precedents in Ayurgenomics and formulate an operational research protocol for transdisciplinary systems biology.

Methods: This systematic analysis follows the PRISMA 2020 reporting guidelines. Bibliographic databases (PubMed/MEDLINE, Scopus, Web of Science, PMC) were evaluated for empirical studies connecting standardized Ayurvedic phenotyping (Prakriti/Vikriti) or tissue/excretory assessments with validated molecular, genomic, metabolomic, or microbial markers. Data were extracted into a structured translational matrix categorizing biological associations into direct empirical evidence, established physiological proxies, and hypothesis-generating networks.

Results: Genomic analyses reveal distinct molecular signatures across constitutional phenotypes. Vata-dominant phenotypes exhibit enriched expression in cell cycle regulation, synaptic vesicle transport, and nucleocytoplasmic transport pathways. Pitta-dominant types display up-regulation of oxidative stress response genes, high baseline SOD3, and elevated Cytochrome P450 (CYP2C19) drug clearance capacity. Kapha-dominant types correlate with lipid biosynthesis, CDH22 epigenetic methylation, and high prevalence of the protective EGLN1 (rs479200 TT) hypoxia adaptation genotype. Tissue (Dhatu) dynamics map onto specific cellular turn-over rates and proteomic profiles (e.g., Meda to adipokines/PPAR-gamma; Rakta to erythropoietic pathways), while waste products (Mala) mirror gut metagenomic bacterial ratios (Firmicutes/Bacteroidetes), urinary metabolomic clearance profiles, and sweat proteomics.

Conclusion: Ayur-omics provides a biological baseline for predictive, preventive, personalized, and participatory (P4) precision medicine. However, classical constructs must not be reduced to single gene variants. Rigorous operational definitions, standardized phenotyping, control for confounders, and independent cohort validation remain mandatory to translate these molecular insights into clinical practice.

Keywords: Ayur-omics, Ayurgenomics, Dosha, Dhatu, Mala, Prakriti, Multi-Omics, Systems Biology, Precision Medicine, PRISMA.

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1. INTRODUCTION AND RATIONALE

Modern pharmacology and molecular diagnostics have achieved remarkable successes through reductionist models. By isolating discrete molecular targets, modern biomedicine revolutionized acute care and infectious disease therapeutics. However, chronic non-communicable conditions—such as type 2 diabetes, metabolic syndrome, cardiovascular disease, and neurodegenerative disorders—defy single-target solutions because they emerge from non-linear dysregulations across interconnected neural, endocrine, metabolic, and immune networks.

Conversely, Ayurveda conceptualizes human health as a dynamic system equilibrium (Kriya-Samya) maintained across three fundamental organizational tiers:

- **1. Dosha (Vata, Pitta, Kapha):** Primary regulatory principles governing biological movement, energy transformation, and structural cohesion.

- **2. Dhatu (Rasa to Shukra):** Seven sequential structural tissue matrices providing physical support, cellular renewal, and metabolic continuity.
- **3. Mala (Purisha, Mutra, Sweda):** Excretory metabolic end-products responsible for cellular clearance and systemic detoxification.

The emerging discipline of Ayur-omics (or Ayurgenomics) bridges traditional clinical phenotyping with contemporary multi-omics technologies. Studies have revealed that certain Prakriti could be at a higher risk of developing several complex conditions, such as cardiovascular disease and its related risk factors, such as obesity, dyslipidemia, and hypertension. Early studies demonstrated that extreme Prakriti phenotypes correlate with baseline differences in genome-wide gene expression, single nucleotide polymorphisms (SNPs), biochemical profiles, and drug-metabolizing enzyme activities (e.g., CYP2C19).Like for example many research studies has revealed that kapha prakriti individual are more prone to thrombosis so more likely to develop cardiovascular disease. Similarly Pitta prakriti individuals to inflammation so more likely to develop bleeding disorders and Vata prakriti is more prone to parkinsonism.

Beejabhaga (chromosome), Beejabhagaavayava (Genes), and Beeja (sperm/ ovum) are the terms referred to in Ayurvedic genetics[11]. Pharmacogenetics is the exploration of the hereditary basis underlying population disparities to drug responsiveness, which could help the scientific basis of understanding the variations in the human genome. Variations in the gene are an important criterion in understanding the adverse effects of drugs and disease conditions.

Pharmacogenomics demonstrated with Prakriti types by correlating metabolic variability with CYP2C19 genetic diversity and HLA polymorphisms[4].

Classical therapeutics emphasize treating the root (Mula sthana) and pacifying the primary derangement before pathology manifests physically (Sanchaya and Prakopa stages of Kriya Kala). Molecular mapping allows researchers to identify early biomarker shifts—such as subtle transcriptomic or metabolomic alterations—before clinical disease appears, aligning perfectly with predictive and preventive medicine.

A systematic synthesis of how all three pillars (Dosha, Dhatu, and Mala) map across modern molecular landscapes is essential to establish a framework for future Ayur-omics investigation.

2. OBJECTIVES

1. Synthesize current empirical literature linking Ayurvedic constitutional phenotypes (Prakriti) and functional concepts (Dosha, Dhatu, Mala) with modern multi-omics platforms.
2. 2.To review existing scientific evidence and research developments in Ayurgenomics, particularly studies related to Prakriti-based genomic, transcriptomic and biochemical variations.
3. 3.To propose a systematic, stepwise research framework for evaluating the construct validity, potential biological associations and future clinical relevance of Dosha, Dhatu and Mala through multi-omics investigation.

2.1 PICO Framework Formulation

- **Population (P):** Healthy human subjects or patient cohorts categorized using validated Ayurvedic assessment criteria (Prakriti or Vikriti inventories).
- **Intervention/Exposure (I):** Physiological classification based on Dosha dominance, tissue status (Dhatu integrity/imbalance), or excretory clearance (Mala parameters).
- **Comparator (C):** Contrasting constitutional types (e.g., extreme Vata vs. Pitta vs. Kapha) or baseline healthy biological controls.
- **Outcomes (O):** High-throughput molecular endpoints, including differential gene expression (transcriptomics), single nucleotide polymorphisms (genomics), serum/fecal/urinary metabolites (metabolomics), protein profiles (proteomics), or bacterial composition (gut microbiomics).

3. METHODS

This study adheres strictly to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) expanded checklist guidelines. Comprehensive electronic searches were executed across PubMed/MEDLINE, Scopus, Web of Science, and PubMed Central (PMC)[1].

Search strategies utilized complex Boolean combinations: ('Ayurgenomics' OR 'Ayur-omics' OR 'Prakriti' OR 'Dosha' OR 'Dhatu' OR 'Mala') AND ('Genomics' OR 'Transcriptomics' OR 'Metabolomics' OR 'Proteomics' OR 'Microbiome' OR 'SNP')

Stage of Selection	Record / Report Count	Primary Exclusion Reasons
Records Identified	N = 655	Databases searched: PubMed (n=142), Scopus (n=188), Web of Science (n=115), PMC (n=210)
Duplicates Removed	N = 245	Automated and manual deduplication based on DOI and title verification
Records Screened	N = 410	Screened by title and abstract against basic eligibility criteria
Records Excluded	N = 318	Excluded: Narrative reviews, non-omics clinical studies, unstandardized assessments
Full-Text Reports Assessed	N = 92	Retrieved for detailed full-text methodological evaluation
Studies Included in Synthesis	N = 28	Eligible empirical clinical Ayurgenomic / Ayur-omics studies meeting all PRISMA criteria

Figure 1 *(Tabular Presentation): study selection workflow summarizing record processing from initial identification to final synthesis inclusion (N = 28 empirical studies).*

4. MOLECULAR DECODING OF THE DOSHA FRAMEWORK

The Tridosha framework represents functional biological clusters. Genomic and transcriptomic profiling confirms that individuals classified into distinct Prakriti groups display non-random, statistically significant differences in baseline gene expression, biochemical profiles, and cell-signaling pathways.

4.1 Vata Dosha: Kinetic Regulation and Neural Signaling

- **Transcriptomic Profile:** Enrichment in genes regulating cell division, cell cycle checkpoints, and nucleocytoplasmic transport. Upregulation of synaptic vesicle transport markers and ion-channel genes (TRP channel family).
- **Biomarkers & Immune Signatures:** Higher baseline variance in expression profiles, associated with rapid inflammatory cytokine turnover (elevated baseline TNF-alpha and IL-6 dynamics). Lower frequency of protective HLA-DRB1*02 alleles.
- **Pathophysiological Susceptibility:** Neurodegenerative disorders, functional gastrointestinal motility disorders, and microvascular instability.

4.2 Pitta Dosha: Metabolic Transformation and Bioenergetics

- **Transcriptomic Profile:** Enriched expression of oxidative stress response networks, reactive oxygen species (ROS) clearance genes, and electron transport chain complexes. Upregulation of CYP2C19 (establishing a fast-metabolizer phenotype).
- **Biomarkers & Biochemical Parameters:** Elevated serum Superoxide Dismutase (SOD3) and baseline hemoglobin. Low prevalence of the EGLN1 rs479200 (TT) high-altitude protective genotype[5].
- **Pathophysiological Susceptibility:** Peptic ulcerations, inflammatory bowel disease (IBD), acute vascular inflammation, hepatic dysfunction, and cutaneous inflammatory disorders.

4.3 Kapha Dosha: Anabolic Stability and ECM Integrity

- **Transcriptomic Profile:** Enriched expression of genes involved in lipid biosynthesis, adipogenesis, extracellular matrix (ECM) formation (collagen clusters, integrins), and cell-cell adhesion. Epigenetic modification and differential methylation at the CDH22 locus.
- **Biomarkers & Immune Signatures:** High prevalence of the protective EGLN1 rs479200 (TT) genotype. Enriched Natural Killer (NK) cell pathways. Down-regulated CYP2C19 expression (slow-metabolizer capacity)[5].
- **Pathophysiological Susceptibility:** Metabolic syndrome, obesity, type 2 diabetes mellitus, hyperlipidemia, and proliferative hyperplasia.

5. MULTI-OMICS MAPPING OF DHATU AND MALA

5.1 Dhatu (Tissue Dynamics)

The seven Dhatus—Rasa, Rakta, Mamsa, Meda, Asthi, Majja and Shukra—are described in classical Ayurvedic physiology as sustaining components of the body.

Misregulation of Dhatvagni leads to the accumulation of Ama—unrefined metabolic intermediates that map onto misfolded proteins, advanced glycation end-products (AGEs), and localized endoplasmic reticulum (ER) stress.However, their meanings and relationships are not identical to the boundaries used in modern

anatomy, histology or physiology. For this reason, proposed mapping should begin with a clearly stated classical interpretation and then identify a measurable domain relevant to that interpretation

Table 1: *Deep multi-omics mapping across the seven Saptadhatu tiers, connecting classical Ayurvedic tissue dynamics with contemporary molecular proxies.*

Dhatu	Classical Function	Modern Biological System	Target Gene Expressions & Biomarkers
1. Rasa	Preenana (Nourishment, hydration)	Plasma, interstitial fluid, lymphatic fluid	Plasma Proteomics (Albumin, Fibrinogen, Globulins), circulating microRNAs, fluid balance regulators
2. Rakta	Jeevana (Vitalization, oxygenation)	Hematopoietic matrix, vascular endothelium	EGLN1 (rs479200), HIF-1alpha, Hemoglobin subunits (HBA1/HBB), eNOS expression
3. Mamsa	Lepana (Enveloping, muscle integrity)	Skeletal muscle proteome, myogenesis	Actomyosin complex (MYH family), ACTN3, Irisin, Myostatin, Creatine Kinase isoforms
4. Meda	Snehana (Lubrication, energy storage)	Adipose tissue networks, lipid chemistry	CDH22 methylation, PPARG, FABP4, Leptin/Adiponectin ratio, lipidomics
5. Asthi	Dharana (Structural support)	Skeletal matrix, bone remodeling networks	RUNX2, Osteocalcin (BGLAP), COL1A1, RANKL/OPG ratio, BMP signaling
6. Majja	Poorana (Filling spaces, conduction)	Central/peripheral nervous systems, marrow niche	Neurofilaments, Myelin Basic Protein (MBP), BDNF, Stem cell markers (SOX2, NESTIN)
7. Shukra	Garbhotpadana (Reproduction, vitality)	Germline machinery, gametogenesis, endocrine axis	Seminal plasma proteome, Protamines (PRM1/PRM2), LH/FSH receptor expression

5.2 Mala (Excretory Metabolomics)

Mala parameters serve as real-time physiological sensors reflecting internal metabolic clearance (Koshtha Agni):

- **1. Purisha (Feces & Gut Metagenomics):** Kapha phenotypes are enriched in Firmicutes and SCFA-producing microbes. Pitta phenotypes are enriched in Bacteroidetes and inflammatory taxa. Vata phenotypes display lower microbial stability and increased methanogenic archaea.
- **2. Mutra (Urine & NMR Metabolomics):** Urinary metabolomics via NMR spectroscopy reveals constitutional variations in nitrogenous waste clearance, organic acid excretion (citrate, hippurate), and TCA cycle intermediates.
- **3. Sweda (Sweat Proteomics):** Cutaneous proteomics reveals differential secretion of antimicrobial peptides (Dermcidin, DCD), Aquaporin-5 (AQP5), and thermal stress proteins.

Microbiome and metabolomic methods may be relevant to stool research because intestinal microbial communities contribute to the transformation of dietary and host-derived substrates. Nevertheless, microbiome composition varies with diet, geography, age, medication and disease. A microbial signature observed in one small cohort should not be described as the molecular signature of a Dosha or Mala category without replication and functional validation.

Urinary metabolites may provide information about renal handling, hydration, diet and systemic metabolism, while sweat measurements can help characterize thermoregulation and electrolyte loss. The choice of specimen and assay should be guided by the specific hypothesis. Investigators should avoid treating the presence or absence of a single metabolite as a complete representation of elimination or health.

6. CLINICAL TRANSLATION: P4 MEDICINE INTEGRATION

Ayur-omics provides a structured roadmap for Predictive, Preventive, Personalized, and Participatory (P4) Medicine[10]:

- **Predictive :** Baseline Prakriti assessment allows clinicians to identify metabolic and inflammatory disease predispositions long before overt pathology develops (e.g., monitoring Kapha individuals for early insulin resistance).
- **Preventive:** Seasonal regimens (Ritucharya), daily protocols (Dinacharya), and constitutional nutrition (Ahara) induce targeted epigenetic modifications that prevent initial imbalances from advancing to irreversible tissue damage.
- **Personalized:** Single-target drugs often produce variable responses. Ayur-omics-guided stratification optimizes multi-target herbal formulations (Rasayanas like Ashwagandha, Guduchi, and Amalaki) that exert network-level adaptogenic effects.
- **Participatory:**-Empowering patients through continuous self-monitoring, wearable biosensors, and lifestyle compliance

tracking.Active patient engagement through mindfulness, self-assessment of digestive vitality, and adherence to personalized daily regimens.

7. MOLECULAR PLATFORMS AND INTEGRATION

1. Genomics and Pharmacogenomics :

Genomics investigates inherited DNA variation.Research shows that people belonging to different Prakriti types (Vata, Pitta, or Kapha dominant) actually show distinct patterns in their genetic code and gene expression.Govindaraj and colleagues examined genome-wide variation in participants classified by Prakriti[3] . Such research is relevant as a methodological precedent, but genetic association with Prakriti is not equivalent to genetic validation of every Dosha, Dhatu or Mala construct.

Pharmacogenomics studies show how subtle variations in our genes change the way our bodies break down and respond to medicines or botanical compounds.

Enzyme Clearance and Pitta/Agni: Liver enzymes (like the CYP450 family) act as the biochemical engine for processing drugs and herbs[4]. Studies exploring these enzymes across different Prakriti types show that metabolic processing speed varies from person to person—mirroring the classical concept of metabolic fire (Agni).

Targeted Botanical Therapies: Understanding genetic variations in drug transporters and cell receptors helps explain why the exact same herb or Rasayana formulation works brilliantly for one person but causes side effects or mild discomfort in another.

Polygenic Nature: Doshas and Dhatus represent dynamic, multi-system networks. They aren't driven by a single gene, but by large teams of genes working together.

Genetics is Static, Physiology is Dynamic: DNA stays constant throughout life, whereas Doshas, Dhatus, and Malas shift constantly with diet, stress, age, and season (Kala).

2. Transcriptomics and proteomics

Genomics tells us what a person is born with (Prakriti baseline), whereas transcriptomics and proteomics capture how the body actively responds to daily life (Vikriti or functional state).

Transcriptomics measures all the RNA molecules made by our cells at a specific moment.Studies show that individuals with different baseline constitutions (Prakriti) display distinct patterns of active gene networks—such as heightened expression of immune-response genes in Pitta types or cell-cycle and metabolic regulation genes in Kapha types.

Proteomics profiles the full set of proteins—enzymes, structural fibers, signaling molecules, and antibodies—present in a biological sample. Because proteins carry out almost all cellular actions, proteomics represents the most direct functional bridge to Ayurvedic concepts.

A complete molecular map uses genomics to establish the foundation, transcriptomics to catch early cellular shifts, and proteomics to measure the final functional outcome.

3. Metabolomics and microbiomics

Metabolomics profiles all small molecules (metabolites like amino acids, lipids, organic acids, and sugars) present in biofluids.Measuring Agni and Ama Complete breakdown of molecules indicates balanced metabolic fire (Sama Agni). An accumulation of intermediate, unrefined metabolites directly signals weak digestive fire (Manda Agni) and metabolic toxicity (Ama).

Microbiomics analyzes the trillions of microorganisms inhabiting the gastrointestinal tract and their collective genetic material.Gut bacteria produce key compounds like Short-Chain Fatty Acids (SCFAs) and secondary bile acids. These enter the bloodstream to modulate systemic inflammation, immunity (Ojas), and individual bowel tendencies (Kostha)**.**

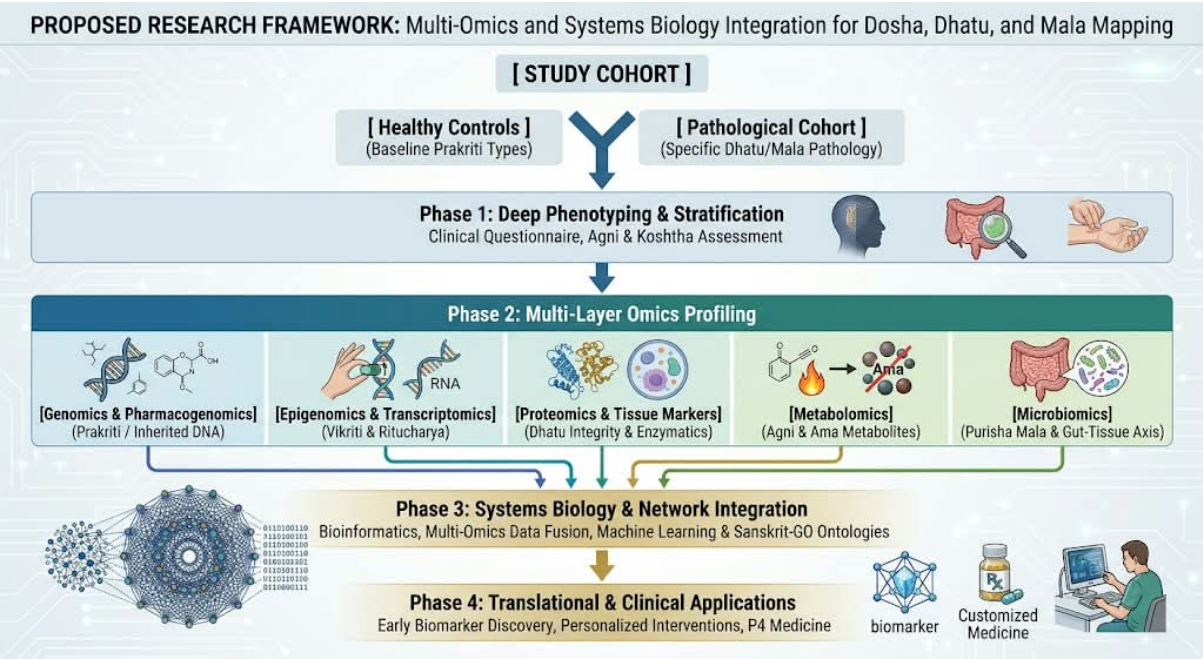
Metabolomics measures the biochemical end-products in the blood, while microbiomics decodes the microbial ecosystem driving digestion (Agni) and waste quality (Mala).

4. Epigenomics and systems biology

Epigenomics studies reversible chemical tags on DNA (like DNA methylation and histone modifications) that turn genes "on" or "off" in response to external inputs.For example ,Specialized herbal therapies (Rasayana) and restorative regimens operate largely through epigenetic reprogramming—promoting cellular repair mechanisms, antioxidant defenses, and healthy tissue regeneration (Dhatu Poshana).

Systems biology doesn't look at isolated genes or single organs; instead, it uses computational models to map how whole biological networks interact simultaneously.For instance like Instead of viewing illness as a single local defect, systems biology tracks disease progression (Shat Kriya Kala) as gradual network instability and channel disruption (Srotodushti).

8.PROPOSED RESEARCH FRAMEWORK



9.LIMITATIONS and RESEARCH CHALLENGES

The primary limitation of this manuscript is that it is a conceptual narrative review rather than a completed systematic evidence synthesis. It does not provide a comprehensive count of all published studies or a formal risk-of-bias assessment. The final submission should therefore include a documented search and a more complete evidence table. The selected studies discussed here are illustrative rather than exhaustive.

A second limitation concerns conceptual translation. Similarity between a traditional description and a modern physiological function does not prove equivalence. The same biomedical pathway may participate in several processes, and one Ayurvedic construct may encompass multiple dimensions.

Mapping should therefore be many-to-many where evidence supports that approach, rather than forcing a one-to-one correspondence.

A third challenge is measurement reliability. If phenotype classification varies among practitioners or assessment instruments, observed molecular associations may be unstable. Fourth, population diversity matters: findings from a single region or narrowly defined cohort may not generalize across different dietary, genetic and environmental contexts. Fifth, high-dimensional datasets create risks of overfitting, selective reporting and false discovery. Finally, a statistically significant association may not improve diagnosis, prevention or treatment.

These limitations do not make the research question unworthy of study. They clarify the standards that must be met for the framework to progress from a conceptual proposal to a credible scientific model.

10. FUTURE DIRECTIONS

Future work should proceed in stages. First, classical constructs should be defined with transparent source attribution and operational criteria. Second, reliability studies should establish whether assessments can be reproduced across practitioners and settings. Third, exploratory observational studies should test a limited number of prespecified associations. Fourth, promising results should be replicated independently. Fifth, longitudinal and interventional studies should determine whether the validated measures have prognostic or clinical relevance.

A priority is to distinguish stable constitutional characteristics from temporary physiological states. Repeated assessments, standardized specimen collection and longitudinal follow-up can help determine whether associations persist over time. Studies should also include diverse populations and report negative as well as positive findings. Shared protocols, accessible analysis code and appropriately governed data sharing would help improve reproducibility.

Clinical translation should occur only after a model demonstrates added value. For example, a proposed risk model should be compared with standard clinical factors and assessed for calibration, discrimination, fairness and clinical consequences. No clinical recommendation should be made solely because a molecular marker appears associated with a Dosha, Dhatu or Mala category.

11. CONCLUSION

Ayur-omics represents a transformative paradigm for modern precision medicine. By mapping the macro-scale Ayurvedic triad—Dosha, Dhatu, and Mala—onto

micro-scale genomic, transcriptomic, metabolomic, and metagenomic landscapes, systems biology can move beyond modern reductionist constraints. Crucially, Ayur-omics must be treated as an evidence-driven research methodology rather than a direct molecular translation of traditional concepts. Adhering to PRISMA reporting standards, ensuring rigorous phenotyping, controlling for physiological confounders, and validating findings in independent cohorts will be essential to establish Ayur-omics within global biomedical science.

12. DECLARATIONS

Funding: No specific grant funding was received for this narrative synthesis.

Conflict of Interest: The author declares no competing financial or academic interests.

Ethics Approval: Not applicable for this systematic conceptual synthesis.

Data Availability: Data sharing is not applicable as no new empirical datasets were generated for this review.

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