

ZEBRAFISH MODELS IN RASAYANA PHARMACOLOGY AND AYURGENOMICS: A SCOPING REVIEW OF TRANSLATIONAL EVIDENCE

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Abstract

Background: Ayurveda prioritises individualised healthcare through *Prakriti* (constitutional phenotype) assessment and rejuvenation through *Rasayana* therapy. The emerging discipline of Ayurgenomics aims to correlate these traditional concepts with molecular and genomic frameworks. Despite this, there is a scarcity of experimentally tractable models for validating these principles. Zebrafish (*Danio rerio*) have become prominent in translational research because of their genetic similarity to humans, optical transparency, rapid development, and compatibility with high-throughput and multi-omics methodologies.

Materials and Methods: The scoping review was conducted in accordance with the Arksey and O'Malley framework and PRISMA-ScR guidelines. Electronic searches of PubMed, Scopus, Web of Science, MEDLINE, ScienceDirect, and Google Scholar were conducted for literature published up to December 2025 using terms related to zebrafish/*Danio rerio*, Ayurveda, *Rasayana*, Ayurgenomics, and traditional herbal medicines. Two reviewers independently screened titles/abstracts and full texts using predefined eligibility criteria. Of 1,245 records identified, 150 studies met the inclusion criteria.

Results: The evidence indicates that zebrafish effectively model developmental toxicity, organ-specific and molecular responses, modulation of oxidative stress, neurobehavioral alterations, metabolic regulation, and tissue regeneration. High-throughput embryo assays and disease-specific models facilitate mechanistic validation of herbal interventions. Nevertheless, the integration of *Prakriti*-based stratification and constitution-specific frameworks is limited, as most studies focus on isolated compounds rather than polyherbal or personalised approaches.

Conclusion: Zebrafish constitute a robust yet underutilised translational platform for advancing evidence-based *Rasayana* research and Ayurgenomics. The integration of multi-omics tools, standardised protocols, and constitution-oriented experimental designs has the potential to enhance precision-based Ayurvedic therapeutics and facilitate the integration of traditional knowledge with contemporary biomedical science.

Keywords: Ayurveda, Ayurgenomics, *Rasayana*, Zebrafish, Translational research.

Key messages:

Zebrafish (*Danio rerio*) is emerging as a robust vertebrate model for evaluating Ayurvedic drugs, offering advantages such as genetic homology with humans, optical transparency, rapid development, and suitability for high-throughput screening.

Experimental studies indicate Ayurvedic *Rasayana* herbs exert diverse biological effects in zebrafish models, including regenerative, neuroprotective, metabolic, immunomodulatory, and antioxidant activities.

Integrating zebrafish research with Ayurgenomics concepts provides a potential experimental platform to explore *Prakriti*-based personalised medicine, while emphasising the need for standardised experimental protocols and deeper mechanistic investigations.

Introduction

Ayurveda stands as one of the world's most venerable holistic healthcare systems, rooted in an indigenous knowledge base that harmonizes physical, psychological, and environmental factors into a sophisticated personalized medical framework.¹ The codification of this tradition, primary examples being the *Charaka Samhita*, *Susrutha Samhitha*, and *Ashtanga Hridaya*, established a robust methodology for individualized care centered on the concept of *Prakriti*, a constitutional classification of human phenotypes.² This phenotypic framework serves as the definitive guide for diagnosis and the implementation of multi-modal, plant-based therapeutic interventions.³

In recent years, the global shift toward integrative medicine has catalysed efforts to bridge Ayurvedic wisdom with contemporary biological science. This synergy has birthed the field of Ayurgenomics, which seeks to map the molecular and genomic underpinnings of *Prakriti* to advance the frontiers of predictive and personalized medicine.⁴ Parallel to this is the growing scientific scrutiny of *Rasayana*, an Ayurvedic branch dedicated to longevity and systemic revitalization. Modern research increasingly identifies *Rasayana* formulations as potent candidates for anti-aging and neuroprotective therapies.⁵

Confirming these traditional statements requires rigorous preclinical evaluation in order to elucidate the safety profiles and biological mechanisms of Ayurvedic formulations. While *in vitro* assays provide foundational insights, they often fail to capture the systemic complexity of a living organism. Even though rodent models are the historical standard, they are frequently constrained by high costs and low-throughput capabilities.⁶ Consequently, the zebrafish (*Danio rerio*) has emerged as a transformative translational platform. Its optical transparency, rapid embryonic development, and roughly 70% genetic homology with humans offer a unique vantage point for observing the physiological and molecular impacts of *Rasayana* compounds in real-time.⁷

Despite this potential, the application of zebrafish within the Ayurgenomics framework remains an underdeveloped frontier. While the general pharmacology of isolated herbal compounds in zebrafish is well-documented, there is no comprehensive synthesis of how this model can be leveraged to validate specific Ayurvedic principles or the synergistic nature of polyherbal formulations. This scoping review, therefore, critically maps the existing literature on zebrafish as a translational vehicle for *Rasayana* and Ayurgenomics, identifying current knowledge gaps and proposing a roadmap for evidence-based Ayurvedic therapeutics.

Materials and Method

This scoping review was conducted following the framework proposed by Arksey and O'Malley (2005)⁸ and further refined by the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses – Scoping Review) guidelines. The methodology included five steps (i) identifying the research question, (ii) identifying relevant studies, (iii) selecting studies, (iv) charting the data, and (v) collating, summarizing, and reporting the results.

Identifying the research question: Whether zebrafish (*Danio rerio*) can be a translational model for Ayurvedic medicine, with particular emphasis on Ayurgenomics and *Rasayana* (rejuvenation) therapies, with the aim of identifying gaps in current knowledge and comprehensively mapping existing literature to guide future research directions in evidence-based Ayurvedic pharmacology and systems biology?

Study Identification: A comprehensive literature identification process was undertaken from November 2023 to December 2025 to find all relevant studies related to of zebrafish (*Danio rerio*) as a translational model in Ayurgenomics and *Rasayana* research. The initial search strategy was designed according to the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews). The search strategy combined terms related to zebrafish/*Danio rerio*, Ayurveda/Ayurvedic medicine, *Rasayana*, Ayurgenomics, *Prakriti*, and traditional herbal/medicinal interventions, using the Boolean operators (“AND”, “OR”).

Electronic resources: The research question and protocol were referenced in developing the electronic search strategy. The search was conducted using the databases including PubMed, Scopus, Web of Science, Medline, Science direct, and Google Scholar. Records identified through database search: n = 1,245

Data charting, collection and analysis: For data charting, structured data extraction forms in Airtable were used. Box Drive, Google Docs, and Microsoft Excel were utilised for document management and data organisation. Each eligible study had the following fields extracted: author (s), publication year,

country/region, study design, zebrafish developmental stage (embryo, larva, or adult), strain/line where reported, sample size where reported, Ayurvedic medicine/herb/formulation or other traditional herbal intervention, preparation or extract type where reported, dose/concentration, route or mode of exposure, treatment duration and/or assessment time points, experimental model or disease/toxicity induction when applicable, comparator/control, outcome domain, specific outcome measures/ endpoints and key findings. When reported, molecular or mechanistic endpoints were also charted. Duplicate removal and reference management were done using EndNote and Zotero. The retrieved data was then compiled and descriptively synthesised based on the principal outcome domains, zebrafish model, and type of intervention.

Citation management process: Duplicate records were immediately removed through Endnote before the review process. After all abstracts were reviewed and screened for inclusion.

Study selection

This scoping review aimed to map the existing literature on zebrafish (*Danio rerio*) as a translational platform for Ayurgenomics and *Rasayana* research. It enabled identification, synthesis, and critical analysis, including molecular, pharmacological, regenerative, and toxicological studies relevant to Ayurveda and traditional herbal medicine.

The methodological process was guided by the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) checklist to ensure transparency, reproducibility, and comprehensiveness. The selection of studies adhered to the inclusion and exclusion criteria established within the review protocol.

Eligibility Criteria

Inclusion Criteria: Sources of evidence were considered eligible for inclusion if they met the following criteria:

- Studies employing zebrafish (*Danio rerio*) as the experimental model, including embryonic, larval, and adult stages.
- Research evaluating Ayurvedic medicines, including *Rasayana* formulations, traditional/medicinal interventions relevant to Ayurvedic pharmacology. Studies reporting outcomes related to regeneration, anti-ageing, immunomodulation, neuroprotection, metabolic, toxicological, behavioural, physiological or molecular outcomes.
- Experimental and translational research published in peer-reviewed scientific journals.

Exclusion Criteria: Sources of evidence were excluded based on the following criteria:

- Publications not reporting primary empirical data, including editorials, commentaries, opinion articles, narrative reviews, and conference abstracts without accessible full texts.
- Studies published in languages other than English.
- Zebrafish studies not involving Ayurvedic medicines, *Rasayana* formulations, or traditional herbal/medicinal interventions within the scope of the review.

Results

Search Results: The database searches yielded 1,245 papers (presented in Fig. 1). PubMed (n = 320); Scopus (n = 280); Web of Science (n = 210); Medline (n = 150); science direct (n = 120); Google Scholar (n = 120); research gate (n = 45). No additional articles were obtained from grey literature searches.

Following the removal of duplicate records, the titles and abstracts of 1,050 articles were screened to assess their eligibility for inclusion, which resulted in the exclusion of 780 articles that did not meet the inclusion criteria. Consequently, the full texts of 270 articles were assessed for eligibility. At this stage, 120 articles were excluded for various reasons (see Figure 1), while 150 studies qualified for inclusion in the review. Two reviewers independently screened the titles/abstracts and full-text articles according to the predefined eligibility criteria. Disagreements were resolved through discussion between the two reviewers.

Trend analysis (Figure 2) demonstrates a pronounced increase in zebrafish-based experimental and review publications over recent years, reflecting their expanding application in biomedical and phytopharmacological research. In parallel, Ayurgenomics has emerged as a rapidly advancing field supported by accumulating evidence-based data. Despite these developments, the integration of zebrafish

models within Ayurgenomics research remains largely unexplored, revealing a critical research gap and defining the translational relevance of the present scoping review.

Outcome measures: The charted data were descriptively synthesized using zebrafish developmental stage, intervention characteristics, experimental model, comparator, and reported outcome domains. The included studies reported a wide range of developmental, physiological, behavioural, metabolic, regenerative, toxicological, and molecular outcomes. Specific endpoints included embryo survival and developmental abnormalities, organ-specific and physiological responses, oxidative stress markers, behavioural and neurocognitive measures, metabolic changes, tissue regeneration, and molecular or pathway-related responses. These results offer a more comprehensive body of evidence for investigating the possible applicability of zebrafish models to Ayurvedic pharmacology and, when relevant, to biological effects associated with *Rasayana*.

Among the 150 studies that satisfied the predefined eligibility criteria and were included in this scoping review, 20 representative studies were selected for **Table 1** to show the diversity of experimental approaches, interventions, zebrafish models, and major outcome domains identified across the evidence base. The selected studies encompass developmental and embryo toxicity, systemic and organ-specific effects, cardiac and oxidative stress responses, metabolic regulation, tissue regeneration, behavioural and neurocognitive outcomes, and neuroprotection.

Table 1 provide an illustrative representation of the mapped evidence base identified in this scoping review, including medicinal plant extracts and Ayurvedic formulations, to illustrate the range of zebrafish-based experimental approaches and major pharmacological and toxicological outcome domains. While some studies specifically evaluated Ayurvedic formulations, other studies investigated medicinal plants or plant-derived interventions relevant to Ayurvedic pharmacological concepts. These studies were deemed pertinent to the larger body of pharmacological evidence to assess the translational potential of *Rasayana*-related interventions. Accordingly, the presence of a study in the evidence map should not be interpreted as demonstrating a classical *Rasayana* effect unless such an effect was specifically investigated or supported by the study.

Developmental and Embryo toxicity Assessment: The reviewed studies reported developmental and embryo toxicity outcomes of Ayurvedic and herbal interventions using zebrafish embryo assays. The assessed outcomes included embryo survival, hatching delay, spinal curvature, yolk sac edema, and pericardial edema. Developmental alterations were reported following exposure to extracts of *Momordica charantia*, *Tinospora cordifolia*, *Curcuma longa*, *Dodonaea viscosa*, *Cinnamomum zeylanicum*, *Andrographis paniculata*, and *Orthosiphon stamineus* (Table 1). In addition, *Punica granatum* peel extract exhibited notable toxicity, with an LC_{50} of approximately 196 mg/mL, producing distinct developmental abnormalities. These findings demonstrate the utility of zebrafish embryo assays in evaluating the developmental toxicity of Ayurvedic and herbal interventions.

Systemic, Organ-specific, and Molecular Outcome Assessment: Numerous studies reported organ-specific and molecular responses in zebrafish following exposure to Ayurvedic and herbal interventions, particularly in relation to cardiac, neural, and redox-related pathways. Cardiac outcomes included heart rate alterations and hypertrophic changes after exposure to *Strychnos nux-vomica*, while *Yogendra Ras* was found to attenuate erythromycin-induced cardiac hypertrophy (Table 1). At the molecular level, studies assessing oxidative stress reported reduced reactive oxygen species (ROS) levels following treatment with *Aloe vera* polysaccharides and *Ocimum sanctum*. Collectively, these findings reflect the range of systemic and molecular endpoints evaluated in zebrafish-based Ayurvedic and phytopharmacological studies.

Behavioural, Neurocognitive, and Stress-related Assessment: Behavioural, neurocognitive, and stress-related outcomes were assessed in zebrafish exposed to Ayurvedic and herbal interventions. Assessed endpoints included anxiety-like behaviour, locomotor activity, exploratory behaviour, and stress responses following treatment with *Azadirachta indica*, *Coriandrum sativum* and *Withania somnifera* (Table 1). Memory-related and synaptic plasticity-associated outcomes were reported for *Rosmarinus officinalis* and *Ocimum sanctum*. Antidepressant-like behavioural responses were also documented in zebrafish treated with *Clitoria ternatea* root extracts. These observations summarise the behavioural and neurocognitive endpoints evaluated across the reviewed evidence.

Table 1. Representative studies illustrating major outcome domains in zebrafish-based research on Ayurvedic medicinal plants, plant-derived interventions and Ayurvedic formulations

Sl. No.	Author(s)	Intervention/ Plant / Drug	Zebra fish Model / Effect Studied	Key Result / Outcome
1.	Thiagarajan et al., (2019) ⁹	<i>Momordica charantia</i> extract	Embryo toxicity, developmental toxicity	High doses reduced embryo survival, delayed hatching, spinal curvature, yolk sac edema.
2.	Romagosa et al., (2016) ¹⁰	<i>Tinospora cordifolia</i> extract	Embryo toxicity, teratogenicity	Dose- & plant-part-dependent teratogenicity; 5–10% caused maximum embryo fatality.
3.	Alatiayo et al., (2019) ¹¹	<i>Curcuma longa</i> extract	Embryo toxicity	Dose-dependent toxicity, bent trunks, enlarged yolk sacs.
4.	Wibowo et al., (2018) ¹²	<i>Punica granatum</i> peel ethanol extract	LC50 toxicity assessment	LC50 ~196 mg/ml (96h); Brevifolin = least toxic compound.
5.	Khan et al., (2021) ¹³	<i>Dodonaea viscosa</i> extracts	Embryo toxicity	Mortality at ≥ 0.7 $\mu\text{g/ml}$; severe teratogenicity & delayed hatching, cardiac oedema and delayed development.
6.	Biswas et al., (2021) ^{14,15}	Kajjali & Rasasindura (Ayurvedic Rasa drugs)	ROS & morphological toxicity	No significant toxicity in larvae; safe up to tested doses.
7.	Zhao et al., (2016) ¹⁶	<i>Strychnos nux-vomica</i> extract	Cardiotoxicity	Induced heart rate changes & morphological cardiac abnormalities.
8.	Xiaoqi et al., (2024) ¹⁷	<i>Aconitum carmichaeli</i> decoction	Neurotoxicity	Reduced larval movement $\rightarrow$ suggests neurotoxic effect.
9.	Balakrishna et al., (2020) ¹⁸	<i>Yogendra Ras</i> (Ayurvedic formulation)	Oxidative stress & cardiac hypertrophy model	Suppressed oxidative stress and reversed erythromycin-induced cardiac hypertrophy (similar to verapamil).
10.	Faal et al., (2022) ¹⁹	Resveratrol (<i>Vitis vinifera</i>)	Diabetic zebrafish model	$\downarrow$ blood sugar, $\uparrow$ intestinal absorption, $\downarrow$ inflammatory markers.
11.	Ran et al., (2017) ²⁰	Resveratrol	Lipid metabolism	Regulates lipid metabolism via specific molecular pathways.
12.	Zainol et al., (2020) ²¹	<i>Piper sarmentosum</i> extract	Regeneration assay	Accelerated tissue regeneration
13.	Gence et al., (2022) ²²	<i>Hypericum lanceolatum</i>	Tail regeneration & neurogenesis	Pro-regenerative, pro-neurogenic, anti-lipid, and antioxidant effects.

14.	Bernardi et al., (2013) ²³	<i>Azadirachta indica</i>	Behaviour assays	↓ activity & ↑ anxiety-like behaviour; no memory deficits.
15.	Zenki et al., (2020) ²⁴	<i>Coriandrum sativum</i>	Anxiety & locomotor behaviour	Anxiolytic effects comparable to clonazepam.
16.	Capatina et al., (2020) ²⁵	<i>Rosmarinus officinalis</i> essential oil	Cognitive impairment (scopolamine model)	Reversed scopolamine-induced memory loss; antioxidant, antidepressant-like effect.
17.	Kang et al., (2014) ²⁶	<i>Aloe vera</i> polysaccharide	Oxidative stress model	Showed significant antioxidant and protective effects in vivo.
18.	Khotimah et al., (2011) ²⁷	<i>Centella asiatica</i> methanolic extract	Neuroprotection (rotenone model)	↑ BDNF; protected dopaminergic neurons.
19.	Maddula et al., (2022) ²⁸	<i>Ocimum sanctum</i> leaf extract	Memory impairment (scopolamine)	Improved memory & reduced scopolamine-induced deficits.
20.	Ngadni et al., (2022) ²⁹	<i>Clitoria ternatea</i> root	Reserpine-induced stress	Anti-anxiety, anti-stress, antidepressant effects.

Discussion

This scoping review highlights the emerging application of structured zebrafish methodologies in the investigation of Ayurvedic medicinal plants, plant-derived interventions, and selected Ayurvedic formulations, including *Rasayana* drugs, providing preliminary mechanistic insights into their efficacy and safety.^{30,31} Although some studies directly investigate formulations or biological effects relevant to *Rasayana* pharmacology, a substantial proportion of the available evidence concerns individual medicinal plants and broader phytopharmacological outcomes. Therefore, the identified evidence should be interpreted as a broader preclinical foundation for Ayurvedic pharmacology, with only a subset providing direct evidence relevant to classical *Rasayana* concepts.

Zebrafish are widely utilized in mainstream biomedical research for toxicity assessment, mechanism-of-action studies, metabolic modelling, and regenerative biology,^{32,33,34} but their integration into Ayurveda-focused research remains limited. Current studies predominantly examine individual herbs or select *Rasayana* formulations, with minimal exploration of personalized therapeutic paradigms rooted in Ayurvedic principles.³⁵ Nevertheless, the available evidence points toward a promising convergence between Ayurveda's systems-based perspective and modern molecular, genetic, and developmental biology, offering a potential pathway for integrative and translational research.

Ayurveda conceptualizes health as a dynamic equilibrium influenced by constitutional factors, environmental interactions, metabolic processes, and psychosomatic patterns.³⁶ In this context, zebrafish offer an experimentally tractable vertebrate system capable of integrating multi-organ, molecular, and phenotypic readouts. Zebrafish are widely adopted in biomedical research due to their affordability, high fecundity, rapid development, external fertilization, embryonic transparency, and amenability to genetic manipulation.³⁷ The optical transparency of embryos allows real-time visualization of organogenesis, neurodevelopment, and tissue morphogenesis, facilitating investigations of developmental pathways relevant to human physiology.³⁸ Advances in genetic tools have further positioned zebrafish as a core platform for functional genomics, and pathway level investigations.³⁹ These attributes collectively support their suitability for modelling Ayurvedic concepts of systemic balance, adaptability, and resilience.

Polyherbal and Multi-target Pharmacology: Therapeutic effects may result from the combined action of several ingredients rather than from a single isolated active compound, which is a significant factor in Ayurvedic pharmacology. Zebrafish provide a practical platform for investigating such multi-component interventions because entire extracts or standardized polyherbal formulations can be evaluated *in vivo* while

concurrently monitoring multiple phenotypic, physiological, behavioural, and molecular endpoints. Comparative experimental designs that incorporate the entire formulations, individual ingredients, and appropriate controls can help identify additive, synergistic, or antagonistic responses. High-throughput embryo assays, reporter-based approaches, organ-specific imaging, transcriptomic and metabolomic profiling, and pathway-level analyses can further be integrated to characterize convergent biological responses across multiple targets. However, the evidence mapped in the present review remains predominantly focused on individual medicinal plants or isolated compounds, with relatively limited experimental investigation of polyherbal synergy. Therefore, in order to differentiate formulation-level effects from those owing to specific ingredients, future zebrafish research should give priority to chemically standardised formulations and comparative whole-formulation strategies.

Regenerative Biology and Rasayana Research: Extensive regenerative abilities across various tissues and organs, such as the heart, spinal cord, brain, liver, kidney, caudal fin, and sensory hair cells, positions zebrafish as a primary model in regenerative biology.^{40,41} The application of genetic tools, including transgenesis and loss-of-function mutations, has facilitated detailed investigation of specific regenerative pathways.^{42,43,44} Additionally, the small size and optical transparency of zebrafish embryos and larvae facilitate non-invasive live imaging of morphogenetic and regenerative processes in injury models.^{45,46} Longitudinal visualization of internal organs during regeneration and homeostasis has enabled parallel screening of compounds that promote or inhibit tissue repair.^{47,48}

The regenerative capacity of zebrafish provide an experimentally tractable system for investigating biological processes that may be relevant to selected *Rasayana* concepts, particularly tissue maintenance, repair, and homeostasis⁴⁹. However, regenerative responses observed in zebrafish should not be interpreted as direct evidence of *Rasayana* activity unless they are demonstrated in the context of a defined *Rasayana* intervention and appropriate mechanistic endpoints. Integrating these approaches with Ayurgenomics frameworks enables the linkage of *Prakriti*-specific responses with measurable molecular, organ-level, and behavioural phenotypes, thereby establishing a preclinical platform for precision Ayurvedic medicine. This approach underscores the translational relevance of zebrafish in elucidating the mechanistic basis of *Rasayana* formulations and their personalized therapeutic applications.

Expanding the Mechanistic Evidence Base for Rasayana Biology: The mechanistic basis underlying *Rasayana* interventions represents a significant gap in its scientific understanding.⁵⁰ Modern methodologies, such as CRISPR/Cas9 genome editing, fluorescent reporter systems, single-cell and bulk multi-omics, and lineage tracing, facilitate the identification of bioactive fractions, conserved molecular pathways, and cellular targets implicated in ageing modulation, immunoregulation, cytoprotection, and metabolic homeostasis.^{33,51,52,53} Zebrafish models enable longitudinal *in vivo* monitoring of therapeutic responses, supporting the assessment of temporal dynamics and adaptive changes resulting from *Rasayana* interventions.⁴⁹ Future research that integrates transcriptomic, epigenomic, and metabolomic profiling with Ayurgenomics stratification may clarify how classical formulations produce context-dependent effects in relation to constitutional variability.

High-Throughput Screening and Bioactivity Profiling: The integration of automated embryo handling systems and imaging-based phenotypic pipelines has significantly reduced manual intervention, facilitating scalable *in vivo* screening for organisms within the 0.5–2 mm size range.^{38,54} By merging biological complexity with throughput efficiency, zebrafish assays enable early-stage toxicity profiling, phenotypic discovery, and preliminary target identification for Ayurvedic formulations.^{55,56} These methodologies are particularly valuable for the systematic prioritization of *Rasayana* candidates before advancing to mammalian or clinical studies.

Efficacy and Mechanistic Validation: Zebrafish models facilitate molecular and genetic investigation of therapeutic mechanisms underlying herbal interventions. CRISPR/Cas9-generated mutants and reporter lines enable detailed analysis of gene expression dynamics, signaling cascades, and physiological responses following exposure to Ayurvedic formulations.⁵⁷ These methodologies have been applied to study mitochondrial function, neurodegeneration, metabolic regulation, cardiomyocyte physiology, immune cell behaviour, and RNA biology.^{58,59,60} Additionally, disease-specific zebrafish models of inflammation, metabolic disorders, cardiovascular dysfunction, and neurodegeneration support efficacy evaluation and mechanistic validation of herbal therapies within defined pathological contexts.⁶¹

Although interspecies differences exist, zebrafish possess conserved physiological and molecular pathways with humans.⁶² For example, zebrafish adipose tissue demonstrates structural and molecular similarities to mammalian white adipocytes, supporting translational research in lipid metabolism and metabolic disorders.⁶³ Live imaging with fluorescent lipophilic dyes enables real-time quantification of adipose tissue dynamics, facilitating pharmacological and genetic screening of metabolic modulators.⁶⁴

Neuroprotection and Neurodegenerative Models: Neurodegenerative disorders frequently progress without overt symptoms, which necessitates the use of sensitive models for early-stage intervention. The genetic, anatomical, and functional similarities to the human nervous system, makes zebrafish appropriate for neuroprotection research.^{65,66} Herbal extracts rich in polyphenols and flavonoids have shown neuroprotective effects in zebrafish by reducing oxidative stress, neuroinflammation, and neuronal damage.^{67,68} These results underscore the utility of zebrafish for evaluating *Medhya Rasayana* (nootropic and cognitive enhancers) formulations and neuroprotective strategies.

Limitations of the Evidence

The evidence mapped in this scoping review is predominantly descriptive, with relatively few hypothesis-driven studies that integrate Ayurgenomics, *Prakriti*-based stratification, or systems-level analyses. Considerable heterogeneity exists across experimental designs, dosing strategies, outcome measures, and reporting standards, which limits cross-study comparability and synthesis. Furthermore, direct experimental validation of *Prakriti*-informed therapeutic stratification and personalized Ayurvedic interventions in zebrafish remains limited and underexplored. These gaps point the need for more standardized, mechanism-oriented, and constitution-specific studies to strengthen the translational relevance of zebrafish models in Ayurveda research.

Implications for Research, Practice, and Policy

The findings of this scoping review suggest that zebrafish-based Ayurvedic research should advance beyond descriptive screening studies toward integrative, hypothesis-driven experimental designs consistent with precision medicine paradigms. Incorporating Ayurgenomics, *Prakriti*-based stratification, multi-omics integration, network pharmacology, and computational modelling may facilitate identification of constitution-specific therapeutic signatures and deepen mechanistic understanding of Ayurvedic formulations. The development of standardized experimental protocols and reporting frameworks will be critical for improving reproducibility, comparability, and translational relevance.

Zebrafish models demonstrate strong potential as ethically favourable and experimentally efficient platforms for evaluating *Rasayana* formulations across multiple biological domains, including adaptogenic, immunomodulatory, metabolic, neuroprotective, cardioprotective, and regenerative effects.^{53,69} Their suitability for rapid *in vivo* screening supports rational formulation selection, dose optimization, and early identification of safety concerns, strengthening the preclinical evidence base for Ayurvedic therapeutics.

The evidence synthesized also highlights the relevance of zebrafish models for advancing personalized and integrative therapeutic strategies. Genetic tractability and phenotypic plasticity allow high-throughput assessment of inter-individual variability in drug metabolism, toxicity, and efficacy.⁷⁰ Findings from zebrafish xenograft models demonstrate feasibility for evaluating patient-specific therapeutic responses, particularly in oncology.⁷¹ These approaches may be extended to experimentally validate Ayurgenomics hypotheses and *Prakriti*-informed therapeutic stratification through differential pathway activation and pharmacokinetic profiling across genetically modified zebrafish lines.^{72,73}

Zebrafish assays further support the systematic evaluation of herb–drug interactions and combinatorial therapies, with evidence indicating modulation of cytochrome P450 enzymes by herbal bioactive compounds and consequent effects on pharmacokinetics.^{74,75,76} Such applications have direct implications for evidence-based integrative practice and safer therapeutic translation.

From a policy perspective, recognition of zebrafish as a valid and ethically acceptable vertebrate model for Ayurvedic research supports harmonization of ethical review processes and encourages broader institutional adoption. Policy-level emphasis on standardized guidelines, interdisciplinary training, and utilization of shared resources such as the Zebrafish Model Organism Database (ZFIN) may further strengthen methodological rigor, data transparency, and global acceptance of zebrafish-based Ayurveda research.

Conclusion

The current review demonstrates that zebrafish represent a substantial yet underutilized translational model for advancing Ayurgenomics and *Rasayana* research. Ayurvedic concepts that have historically lacked experimentally tractable platforms can be systematically investigated using zebrafish, owing to their genetic homology with humans, optical transparency, rapid development, and compatibility with high-throughput and multi-omics approaches. The synthesized evidence indicates that zebrafish provide a potentially valuable translational platform for investigating Ayurvedic medicinal plants, plant-derived interventions, and selected Ayurvedic formulations, including interventions relevant to *Rasayana* pharmacology. The available evidence provides preliminary support for investigating biological processes associated with regeneration, metabolic regulation, neuroprotection, oxidative stress, and systemic homeostasis. However, direct experimental validation of classical *Rasayana* concepts and *Prakriti*-informed responses remains limited. Future studies integrating standardized *Rasayana* formulations, mechanistic endpoints, multi-omics approaches, and Ayurgenomics-based stratification are required to establish more direct links between traditional Ayurvedic concepts and experimentally measurable biological effects. Despite persisting methodological challenges such as standardization of polyherbal formulations, dose translation, and modelling of higher-order Ayurvedic constructs, recent research establishes zebrafish as a scientifically robust bridge between traditional knowledge systems and contemporary biology. Strategic integration of zebrafish models through *Prakriti*-relevant phenotypic stratification, standardized *Rasayana* libraries, and multi-model experimental pipelines can support the evolution of Ayurveda toward a precision-oriented, evidence-based framework. Together, the convergence of zebrafish research with Ayurvedic science represents a critical step toward harmonizing traditional medicine with modern biomedical innovation, enabling novel avenues for drug discovery, personalized interventions, and integrative global healthcare.

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