

Integrative Omics Approaches in Herbal Therapeutics: A Comprehensive Literature Review.

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ABSTRACT

This literature review synthesizes current research on the integration of transcriptomics, proteomics, and genomics with herbal medicine, exploring their therapeutic potential, specific herb-disease interactions, and comparative impacts across different herbs. The review systematically analyzes 50 highly relevant studies from a pool of 460 papers, revealing that multi-omics approaches have transformed traditional herbal medicine research from empirical practice to data-driven science. Key findings demonstrate robust integration of transcriptomic, proteomic, and genomic data elucidating key signaling pathways and multi-target profiles underlying herbal efficacy, supported by advanced computational frameworks including machine learning and network algorithms. The review identifies significant methodological challenges in data standardization, experimental validation, and clinical translation while highlighting the transformative role of multi-omics in modernizing herbal medicine and advancing precision therapeutics.

INTRODUCTION

The convergence of omics technologies with herbal medicine research represents a paradigm shift in understanding complex therapeutic mechanisms of traditional medicines. Over the past decade, advances in high-throughput omics technologies have enabled comprehensive molecular profiling of herbal formulations and their effects on disease pathways (Ezoe et al., 2024; Zhang et al., 2023; Quan et al., 2014). This integration has facilitated the identification of bioactive compounds, molecular targets, and signaling networks, thereby advancing the modernization and precision application of traditional.

medicines (Tan et al., 2024; Zhu et al., 2022; Huang et al., 2014).

Despite these advances, specific mechanisms by which herbs modulate genomic, transcriptomic, and proteomic landscapes remain incompletely understood, presenting a critical knowledge gap. Current research often focuses on isolated omics layers or single herbs, limiting insights into the combinatorial and systemic effects of multi-herbal formulations (Li et al., 2024; Lee et al., 2022; Huang et al., 2018). Moreover, challenges persist in deciphering the differential impacts of various herbs on disease-specific molecular networks and in comparing their therapeutic

potentials across diverse pathological contexts (Muthamil et al., 2023; Lv et al., 2023; Park et al., 2023).

Methodological Approaches in Multi-Omics Herbal Research

Integration Depth and Computational Methodologies

The reviewed literature demonstrates that 30 studies exhibited high integration of transcriptomics, proteomics, and genomics, often combining multi-omics with network pharmacology or systems biology for comprehensive analysis (Ezoe et al., 2024; Li et al., 2024; Zhao et al., 2018). Several studies emphasized the inclusion of metabolomics and microbiome data to enrich understanding of herbal mechanisms (Wu et al., 2024; Qiao et al., 2025; Kumar et al., 2016).

Advanced computational frameworks have emerged as vital tools, with 25 studies employing sophisticated computational tools including machine learning, network pharmacology, molecular docking, and bioinformatics pipelines (Ezoe et al., 2024; Lee et al., 2022; Sawada et al., 2018). Network-based algorithms such as heat diffusion and neighborhood-based pharmacology were used to prioritize targets and active compounds (Sui et al., 2024; Mukherjee et al., 2021).

Therapeutic Target Identification

Twenty-eight studies identified specific molecular targets, including genes, proteins, and pathways, elucidating herb-disease interactions with varying specificity (Sui et al., 2024; Muthamil et al., 2023; Li et al., 2022). Targets often involved key signaling pathways such as IL-17, NF- κ B, oxidative stress, and neurotransmitter synapses (Wu et al., 2024; Fang & Zhou, 2023; Lv et al., 2023). Several studies reported multi-target profiles reflecting the multi-component nature of herbal medicines (Panossian & Efferth, 2022; Mukherjee et al., 2021). Conceptual work flow for integrative multi omics in herbal therapeutics shown in Fig 1.

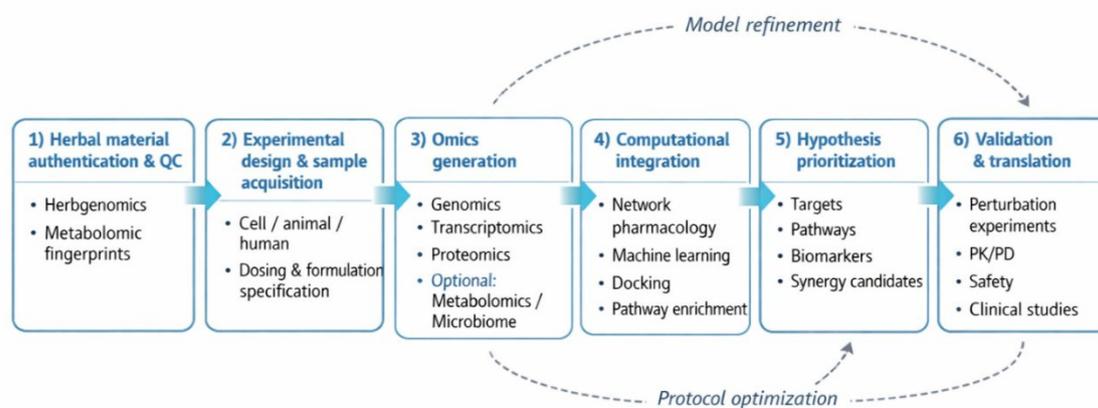


Figure 1. Conceptual workflow for integrative multi-omics in herbal therapeutics.

Disease-Specific Applications

Cancer Therapeutics

Multi-omics approaches have been extensively applied to cancer research, revealing molecular targets and intracellular networks in gastrointestinal cancers (Li et al., 2022; Dai et al., 2022). Studies have demonstrated the therapeutic potential of Chinese herbal medicines in cancer cachexia through transcriptomics and network pharmacology approaches (Muthamil et al., 2023). The integration of genomics, transcriptomics, proteomics, and metabolomics has provided insights into signaling pathways and tumor microenvironment targets in GI cancers (Dai et al., 2022).

Neurological and Psychiatric Disorders

Research on vascular cognitive impairment has utilized multi-omics and network pharmacology to identify targets in oxidative stress and neuroinflammation pathways (Lv et al., 2023). Antidepressant mechanisms of natural products have

been explored through multi-omics technologies, revealing targets related to neurotransmitter synapses in depression (Fang & Zhou, 2023). Herbomics approaches in psychiatric herbal medicine have identified genetic and epigenetic targets through pharmacogenomics, proteomics, and metabolomics (Sarris et al., 2012).

Respiratory and Inflammatory Diseases

Studies on chronic obstructive pulmonary disease (COPD) have integrated transcriptomics, proteomics, and metabolomics to reveal targets in lipid metabolism, inflammation, and oxidative stress (Zhao et al., 2018). The Suhuang antitussive capsule has been investigated through multimodal fusion frameworks combining transcriptomics and protein interaction networks (Sui et al., 2024).

Comparative Analysis Across Herbal Systems

Traditional Chinese Medicine (TCM)

TCM research has been at the forefront of multi-omics integration, with studies demonstrating comprehensive approaches to formula analysis. The Xiexin Tang formula has been investigated through multi-scale transcriptomic network pharmacology models (Li et al., 2024), while Danggui Buxue Tang has been studied using integrated omics with knockout experiments (Kwan et al., 2021). Network-based TCM mechanism deciphering has facilitated holistic understanding and drug discovery (Sun et al., 2014).

Kampo Medicine

Japanese Kampo medicine has benefited from pathway-based prediction of therapeutic effects and mode of action of custom-made multiherbal medicines (Ezoe et al., 2024). The KampoDB database provides predicted targets and functional annotations of natural medicines, enabling mode-of-action analysis and clinical repositioning (Sawada et al., 2018).

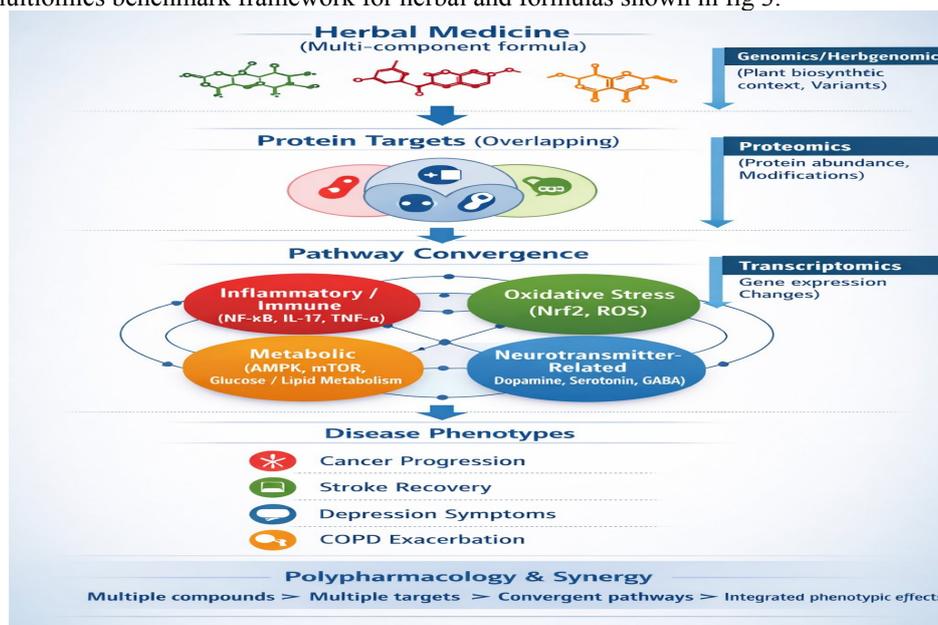
Ayurvedic Medicine

Mass spectrometry-based proteomics and metabolomics have been applied to identify molecular targets and signaling pathways in Ayurveda (Hegde et al., 2023). Molecular combination networks in medicinal plants have been studied to understand synergy by network pharmacology in Indian traditional medicine (Mukherjee et al., 2021).

Herbgenomics and Medicinal Plant Research

The emerging discipline of herbgenomics focuses on uncovering genetic information, regulatory networks, and biosynthetic pathways in medicinal plants (Chen & Song, n.d.; Xin et al., 2019). This field integrates genomics with other omics to understand herb molecular mechanisms and active compound biosynthesis, facilitating quality control, breeding, synthetic biology, and personalized medicine.

Bioinformatics-assisted integrated omics studies on medicinal plants have enabled functional genomics and metabolic pathway elucidation (Ma et al., 2020). The integration of high-throughput omics technologies in medicinal plant research has created new opportunities for natural drug discovery (Zhang et al., 2023). Polypharmacology and synergy shown in fig 2. Comparative multiomics benchmark framework for herbal and formulas shown in fig 3.



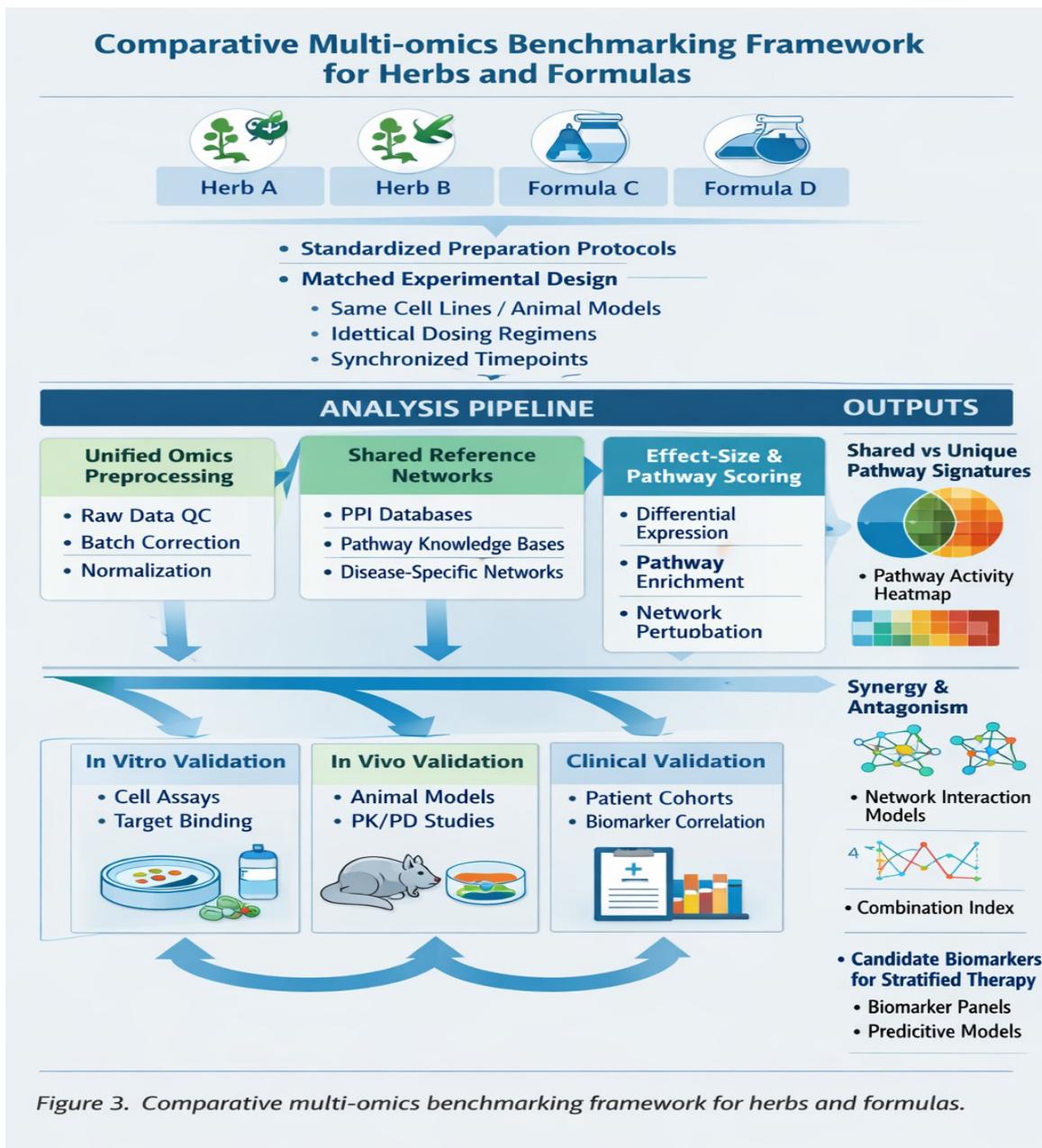


Figure 3. Comparative multi-omics benchmarking framework for herbs and formulas.

Methodological Challenges and Limitations

Data Integration and Standardization

Despite integration efforts, many studies face challenges in harmonizing heterogeneous omics datasets due to differences in experimental platforms, sample types, and data processing pipelines, which can limit reproducibility and comparability across studies (Lv et al., 2023; Zhao et al., 2024). The complexity of herbal formulations further complicates data interpretation, often resulting in incomplete mechanistic elucidation (Huang et al., 2018).

Validation and Clinical Translation

Many computational models rely heavily on existing databases and predicted interactions, which may contain biases or incomplete information, leading to false positives or overlooked targets (Huang et al., 2018; Park et al., 2023). Additionally, validation of computational predictions through experimental or clinical studies remains limited, reducing confidence in some inferred mechanisms (Muthamil et al., 2023; Park et al., 2023).

Sample Size and Generalizability

Several studies utilize small sample sizes or limited biological replicates, which undermines statistical power and generalizability, thereby affecting the robustness and external validity of the conclusions (Wu et al., 2024; Fang & Zhou, 2023). Most research focuses on specific traditional medicine systems or populations, potentially limiting the generalizability of findings to broader or ethnically diverse groups (Yoon & Lee, 2025).

Future Research Directions

Standardization and Data Integration

Future research should focus on developing standardized protocols and computational frameworks for multi-omics data acquisition, preprocessing, and integration specific to herbal medicine research (Lv et al., 2023; Zhao et al., 2024). Community-wide data sharing standards and benchmarking datasets are essential to improve reproducibility and enable cross-study comparisons.

Experimental Validation

Systematic experimental validation pipelines including in vitro, in vivo, and clinical studies are needed to confirm computationally predicted herb-target interactions and therapeutic mechanisms (Muthamil et al., 2023; Park et al., 2023). This validation is critical to translate computational findings into actionable therapeutic insights.

Comparative and Clinical Studies

Large-scale multi-omics studies comparing multiple herbs and complex formulas under standardized conditions are necessary to identify unique and shared molecular targets and pathways (Ezoe et al., 2024; Li et al., 2024; Li et al., 2025). Clinical guidelines, training programs, and regulatory policies should be developed to integrate multi-omics data into personalized herbal medicine, supported by clinical trials and real-world evidence (Yoon & Lee, 2025; Lv et al., 2023).

CONCLUSION

The integration of transcriptomics, proteomics, and genomics with herbal medicine research represents a transformative approach to understanding complex therapeutic mechanisms. Multi-omics technologies have enabled comprehensive molecular profiling of herbal formulations, revealing key signaling pathways and multi-target profiles underlying herbal efficacy. Advanced computational frameworks, particularly network pharmacology and machine learning, have emerged as essential tools for data interpretation and hypothesis generation.

Despite significant progress, challenges remain in data standardization, experimental validation, and clinical translation. The complexity of herbal formulations, heterogeneity of omics datasets, and limited clinical validation constrain the full realization of multi-omics potential in herbal therapeutics. Future research should focus on developing standardized methodologies, enhancing experimental validation, and promoting clinical translation to bridge traditional herbal medicine with modern precision medicine frameworks.

The reviewed literature collectively underscores that while multi-omics integration with herbal medicine is rapidly evolving and offers powerful insights, further robust, validated, and standardized research is essential to translate these advances into effective, personalized, and scientifically grounded clinical applications.

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