

Original Article

MULTI-OMICS-DRIVEN HERBAL RESEARCH: INTEGRATING METABOLOMICS, GENOMICS, AND SYSTEMS BIOLOGY TO DECODE THERAPEUTIC MECHANISMS

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ABSTRACT

Herbal medicines from traditional medical systems function as valuable resources which contain diverse medicinal compounds that can treat multiple medical conditions. The complex multi-component system of these products hinders their ability to meet conventional drug testing standards which focus on single drug and single target methods thus delaying their acceptance as modern clinical treatment methods. Multi-omics technologies which include genomics and transcriptomics and proteomics and metabolomics and systems biology have created a new scientific approach in phytomedicine research. This review examines how multi-omics research methods reveal the complex medicinal functions which herbal bioactive compounds possess. The research shows that genomic and transcriptomic analysis methods enable scientists to understand how phytochemicals control blood sugar levels through their impact on host gene networks and biological processes. The research investigates how the plant metabolomic profile which identifies all its phytochemicals interacts with herbal treatment to show metabolic changes in the host organism. This article demonstrates how systems biology and network pharmacology combine different high-throughput datasets into a unified system. Research scientists create detailed compound-target-disease networks which enable them to visualize how botanical extracts produce combined effects through multiple biological pathways. The development of standardized bioinformatic pipelines and data integration algorithms and the establishment of valid methods to measure the natural biological variability of herbal preparations continue to present major difficulties. The path from multi-omics data collection to the development of practical drug discovery solutions stands as the most important challenge which must be overcome to update herbal medicine practices while creating new network-based treatment methods.

Keywords: Multi-Omics, Network Pharmacology, Systems Biology, Metabolomics, Transcriptomics, Herbal Medicine, Phytochemicals

INTRODUCTION

Human beings have historically depended on natural products and herbal medicines as their primary source of medical knowledge. The research shows that these treatments can effectively treat chronic and complex medical conditions yet scientists find it challenging to determine precisely how these treatments work. The composition of herbal extracts contains more than 100

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secondary metabolites which include alkaloids and flavonoids and terpenoids and saponins that produce combined effects on multiple biological systems.

Pharmacological research used a reductionist framework for several decades which sought to identify one active ingredient that scientists could use to study one biological target. The method succeeded in producing essential medications such as artemisinin and paclitaxel but it failed to create a complete picture of how the entire herbal extract worked together to produce its effects. The research community has started using a comprehensive top-down method that combines high-throughput multi-omics with systems biology to solve this research limitation. This review shows how scientists use genomics transcriptomics and metabolomics to understand polypharmacological networks present in herbal medicines.

THE LIMITATIONS OF THE REDUCTIONIST PARADIGM

The standard process for discovering new drugs has maintained its focus on developing treatments which follow the "one drug, one target, one disease" approach. The method develops highly effective special ligands which bind to distinct proteins through its basis in the traditional lock-and-key system that governs receptor pharmacology. The method demonstrates success in treating urgent medical conditions and single-gene diseases but its effectiveness has started to decline when used for treating complex age-related chronic conditions and metabolic disorders and neurodegenerative diseases and heart disease.

The disease networks which exist in chronic conditions show strong structural resilience because their design includes multiple pathways and nodes; thus, blocking any pathway will cause compensatory effects which make single-target medications lose their effectiveness or produce dangerous side effects. The process of researchers trying to extract one active phytochemical from a known botanical medicine leads to the discovery that the extracted substance shows much less effective clinical results and higher toxicity than the complete plant extract which proves the shortcomings of reductionist bioassay-guided fractionation.

THE COMPLEXITY OF THE HERBAL MATRIX AND THE CONCEPT OF SYNERGY

The therapeutic effectiveness of whole herbal extracts surpasses that of their individual components because different plant parts interact with each other. Plant secondary metabolites have developed together to operate as a unified system instead of existing as separate compounds. The combination of different elements functioning together creates two different methods of drug action.

- **Pharmacodynamic Synergy:** The extract contains multiple phytochemicals that interact with different molecular targets which include receptors and enzymes and ion channels that exist throughout a common disease network. The herbal matrix produces an intensified therapeutic impact through its ability to control various disease pathway elements which surpasses the effects of treating a single pathway element.
- **Pharmacokinetic Synergy:** Certain constituents within an herbal extract may lack direct therapeutic activity but play a crucial supporting role by modifying the bioavailability of the primary active compounds. Supporting phytochemicals have the ability to block intestinal efflux pumps which include P-glycoprotein and they can also inhibit the hepatic metabolizing enzymes which include Cytochrome P450. This action prevents the active therapeutic agents from degrading too early and it improves their absorption throughout the body.

THE ADVENT OF SYSTEMS BIOLOGY AND MULTI-OMICS

Researchers need to change their fundamental ways of analyzing data because they need to study the complex web of interactions between multiple components and multiple targets. The new analytical framework which systems biology provides is needed for this particular research work. Systems biology studies organisms as complete networks which depend on their various biological parts to work together. Researchers now use high-throughput "omics" technologies to create maps of biological networks which they study. Genomics and transcriptomics reveal the genetic predispositions of the host and provide a comprehensive snapshot of how herbal compounds globally upregulate or downregulate gene expression. mRNA transcription changes do not produce direct relationships with changes in physiological functions. The herbal formulation produces specific metabolic changes which lead to particular physiological outcomes. Metabolomics functions as the primary method to measure these physiological outcomes and metabolic transformations which the herbal product causes.

RATIONALE AND SCOPE OF THE REVIEW

The combination of traditional ethnomedicine with modern bioinformatics establishes a foundation for the development of evidence-based phytotherapy research. The review presents a detailed investigation of how multi-omics platforms function in botanical research studies. The article demonstrates that current experimental research enables scientists to use metabolomics and genomics together with systems-level network pharmacology as an effective quantitative method to unlock the intricate treatment pathways and combined effects and total medicinal power of herbal remedies.

Figure 1

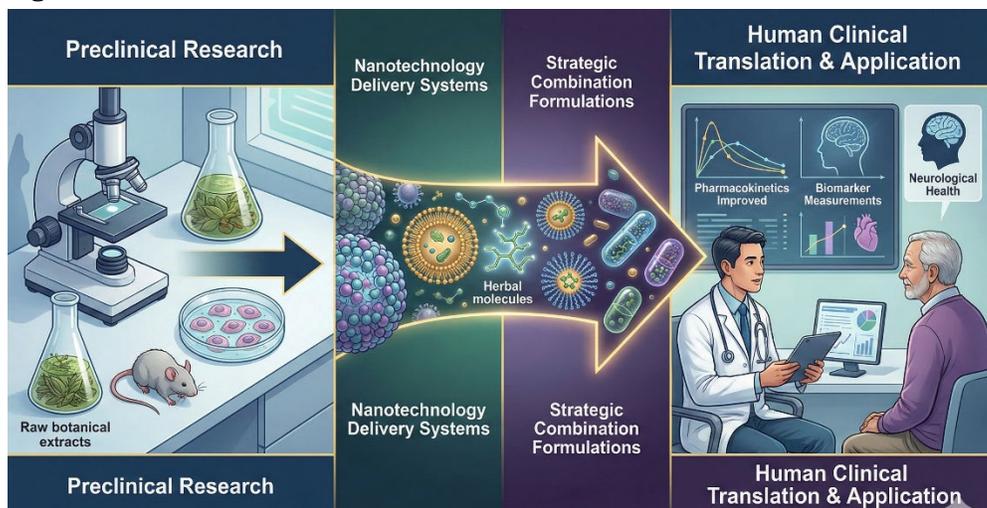


Figure 1 Bridging the Gap: From Lab Bench to Bedside

THE SHIFT FROM REDUCTIONISM TO SYSTEMS BIOLOGY

Systems biology analyzes biological systems through studying their molecular interactions instead of examining their single molecular components. The research shows that herbal remedies work because diseases develop through multiple genetic changes and protein defects which disrupt entire biological systems. Herbal medicines work as network therapeutics because they treat multiple parts of a disrupted disease network to bring back normal body functions. The researchers need to create complete data sets which show all genetic and protein and metabolic information about the organism to achieve their research goals through multi-omics platforms.

THE LIMITATIONS OF THE TRADITIONAL REDUCTIONIST PARADIGM

The reductionist approach which defines modern pharmacological research and drug discovery through its "one-disease one-target one-drug" model has served as their primary research method for multiple decades. The "magic bullet" approach which targets specific diseases through precise treatment methods has shown success in treating acute and infectious diseases but encounters difficulties when facing complex chronic metabolic syndrome and neurodegenerative disorders and cardiovascular disease. Researchers use reductionism in herbal medicine to study plants by extracting their active components to examine their effects on specific biological receptors. The process removes all active chemical compounds found in the entire herbal plant. Researchers observe that when they test an isolated compound its therapeutic effects do not match those of the complete botanical extract while the compound shows unexpected harmful effects which the entire plant does not display. Systems biology establishes its approach to biological systems by studying all biological elements because it believes that all physiological networks connect and complete systems exceed their individual components.

NETWORK PHARMACOLOGY AND PHYTOCHEMICAL SYNERGY

The application of systems biology to botanical research begins with the current development of "network pharmacology" which represents its most dynamic research area. The discipline of bioinformatics together with its advanced computational modeling methods establishes a complete system that describes all the complicated interactions between multiple bioactive compounds in herbal treatments and their various human body molecular targets. Herbal medicines implement their "multi-component, multi-target" approach because synthetic pharmaceuticals design their products to achieve one specific target through strong binding power. The various phytochemicals which exist in an herb show only minor binding strength to particular cellular receptors. However, when delivered together, they exert a profound synergistic effect. The combined effects of this synergy enable better treatment results because it increases the absorption of essential active components while reducing negative reactions through its controlled impact on multiple linked biological systems.

MULTI-OMICS PLATFORMS: DECODING SYSTEM-WIDE RESPONSES

Researchers need to gather empirical evidence which should be collected across complete system networks to achieve successful mapping and validation of their network therapeutics. The complete integration of multi-omics technologies establishes itself as an essential requirement for contemporary herbal research. Scientists can create a complete multidimensional model which shows how a host responds to herbal treatment by integrating data from different biological levels:

- **Transcriptomics:** The complete analysis of RNA transcript data enables researchers to demonstrate how herbal extracts affect gene expression patterns which result in increased therapeutic pathways and decreased inflammatory pathways.
- **Proteomics:** Because proteins perform essential work to execute all cellular processes, scientists can study herb-related changes to cellular functions and signaling pathways and their results on cell structure by examining proteome transformations.
- **Metabolomics:** Metabolomics research tracks the chemical fingerprints which cells release during their biological activities. The system analyzes how human metabolism processes plant phytochemicals and how human metabolism returns to its normal state.

BRIDGING THE GAP WITH TRADITIONAL KNOWLEDGE SYSTEMS

The transition to systems biology functions as a crucial link that connects present-day scientific practices with traditional medical systems including Ayurveda and Traditional Chinese Medicine (TCM). Holistic principles have guided these historical frameworks for thousands of years because they view the human body as an interconnected biological system instead of separate unconnected body parts. Network pharmacology and multi-omics provide modern science with analytical tools that enable researchers to decode and quantify traditional herbal formulations through their complex systemic mechanisms.

GENOMICS AND TRANSCRIPTOMICS: UNVEILING GENE EXPRESSION SIGNATURES

Understanding how complex herbal extracts alter the cellular blueprint requires deep molecular profiling at the nucleic acid level.

TRANSCRIPTOMIC PROFILING (RNA-SEQ)

High-throughput RNA sequencing (RNA-Seq) has transformed our capability to assess the complete time-based changes in host gene expression that occur after herbal treatment. Researchers use the transcriptomic analysis of healthy tissues versus diseased tissues and herb-treated tissues to identify particular pathways that the treatment affects. The transcriptomic analysis of *Salvia miltiorrhiza* (Danshen) extracts shows that the complex formulas which compose the extract downregulate pro-inflammatory cytokine transcripts while they increase the levels of antioxidant defense genes in models of cardiovascular disease.

EPIGENOMICS AND PHARMACOGENOMICS

Emerging research demonstrates that phytochemicals function as epigenetic regulators. The compounds epigallocatechin gallate (EGCG) and curcumin demonstrate the ability to change DNA methylation patterns and histone acetylation, which results in the reactivation of silent tumor suppressor genes. The study of pharmacogenomics reveals how host genetic variations (polymorphisms) affect the effectiveness and harmful effects of herbal treatments, which enables the development of customized phytomedicine treatments.

METABOLOMICS: THE BRIDGE BETWEEN PHENOTYPE AND MECHANISM

The analysis of all small-molecule metabolites in a biological system shows the complete physiological state and physical appearance of an organism. Researchers study herbal medicine through this method which they use to investigate two different areas.

PHYTOMETABOLOMICS (PLANT PROFILING)

The traditional practice of herbal medicine suffers from its inability to establish proper quality control methods and standardized procedures. The chemical composition of a plant changes when it experiences different environmental conditions and soil types and different times of harvesting. Researchers use ultra-high-performance liquid chromatography with mass spectrometry and Nuclear Magnetic Resonance spectroscopy to create precise chemical fingerprints of herbal extracts. The process guarantees consistency between product batches while detecting all possible bioactive ligands present in the product.

HOST PHARMACOMETABOLOMICS

The metabolic balance of the host changes through the administration of an herbal extract. Researchers can discover endogenous metabolic biomarkers which indicate treatment effectiveness by analyzing biofluids or tissues before and after treatment. The treatment responds to multiple herbal therapies which research shows produce broad effects on metabolic syndrome through their impact on lipid metabolism and amino acid biosynthesis and tricarboxylic acid (TCA) cycle functions.

NETWORK PHARMACOLOGY: DECODING MULTI-TARGET MECHANISMS

The enormous data output from multi-omics technologies requires advanced computer systems for proper understanding. Network pharmacology represents the field that connects systems biology with bioinformatics and polypharmacology research. The researchers use the TCMSP database and PubChem database to predict how hundreds of phytometabolites will interact with human protein targets through computational methods. The system integrates predictions with established disease-target networks to develop multipartite "Compound-Target-Disease" models. The topological analysis of these networks enables researchers to:

- **Identify Hub Genes:** Identify the most closely interacting proteins such as the targeted protein kinases responsible for the disease.
- **Predict Synergistic Pairs:** Which phytochemicals act synergistically to potentiate or diminish the toxic effects?
- **Reveal Off-Target Effects:** Consider conceivable adverse herb-drug interactions & explain these in terms of categories that are known.

CHALLENGES AND FUTURE DIRECTIONS

While the multi-omics paradigm offers unprecedented insights, several distinct challenges must be addressed:

- **Data Integration:** The process of combining different types of datasets (for example matching transcriptomic fold-changes with metabolomic flux) presents difficulties in terms of computational processing. The field needs advanced machine learning algorithms together with artificial intelligence (AI) technology to achieve effective integration of multi-omics data into unified biological stories.
- **False Positives in Network Pharmacology:** Many computational target predictions use structural homology and literature mining which creates a risk of generating incorrect results. The computational results require verification through in vitro and in vivo testing which includes CRISPR-Cas9 knockouts & surface plasmon resonance techniques.
- **Microbiome Interactions:** Future multi-omics studies must incorporate metagenomics to establish the metabolic pathways through which the gut microbiome transforms dietary phytochemicals into biologically active secondary compounds.

CONCLUSION

The field of herbal medicine research experiences fundamental change through the application of genomics together with transcriptomics and metabolomics and systems biology. The transition to this new approach represents a major shift away from outdated reductionist research methods which focused on developing drugs that target specific biological points. Scientists used analytical methods which removed native phytochemical components from botanical medicines, resulting in their complete therapeutic potential remaining undiscovered for several decades. The field of multi-omics-driven network pharmacology now offers an evidence-based framework which enables researchers to understand the complete synergistic functions of natural products. Scientists in the current research environment possess the ability to analyze and comprehend vast biological data which contains multiple types of biological information. The development of high-throughput sequencing technologies and advanced bioinformatics pipelines enables researchers to create detailed models which show how plant metabolites interact with various human bodily systems. The development of data integration algorithms together with artificial intelligence models will improve the speed and accuracy of predicting herbal product combinations and their possible toxic effects.

The comprehensive approach which examines entire systems will speed up the process of discovering new network-based drugs. The future of drug discovery research will focus on creating multi-component drugs which can restore normal body functions throughout all disrupted biological systems, instead of finding single active substances which function as "magic bullets." The present-day world sees this paradigm shift as a method to unite the two different knowledge systems which existed between traditional ethnomedical practices and contemporary clinical methods. Systems biology provides scientific evidence which proves the effectiveness of ancient holistic healing practices, thus transforming historical knowledge into validated scientific knowledge. The present-day convergence between past botanical knowledge and present-day research establishes a new medical field which

enables the safe and effective treatment of complex chronic diseases using natural products that combine multiple therapeutic methods.

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