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NETWORK PHARMACOLOGY AND MOLECULAR DOCKING APPROACHES FOR HERBAL FORMULATIONS: MECHANISTIC INSIGHTS, THERAPEUTIC APPLICATIONS, AND TRANSLATIONAL PERSPECTIVES

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Abstract

For ages, traditional medical systems including Ayurveda, Traditional Chinese Medicine, Unani, and Siddha have relied heavily on herbal and polyherbal compositions. Because they are multi-component and multi-target, the molecular mechanisms behind their therapeutic efficacy are still poorly understood, despite their widespread clinical use. Molecular docking in conjunction with network pharmacology has become a potent systems-level method in recent years for deciphering the intricate pharmacological effects of herbal remedies. The conceptual framework, databases, computational tools, and integrated workflows used in network pharmacology and docking-based studies of herbal formulations are all well covered in this review. In order to identify important bioactive components, hub targets, and crucial signaling pathways, the review emphasizes how network pharmacology makes it possible to build compound–target–pathway–disease networks. By providing structural and energetic validation of predicted interactions, molecular docking enhances mechanistic interpretations and supports this method. There includes a critical discussion of applications in several important disease domains, such as cancer, metabolic disorders, neurological illnesses, cardiovascular problems, inflammatory and autoimmune disorders, and infectious diseases. The translational significance of integrated computational techniques is further demonstrated by representative case studies such triphala, ashwagandha formulations, curcumin-based polyherbal combinations, and traditional Chinese polyherbal prescriptions.

The paper also discusses translational viewpoints, regulatory issues, experimental validation techniques, and existing constraints on data correctness, database completeness, and reliability. Additionally, future directions in digital herbal pharmacology, network toxicology, multi-omics integration, and artificial intelligence are described. All things considered, this review highlights how network pharmacology and molecular docking can be used to create a strong and reliable framework for updating herbal medicine research and promoting evidence-based, multi-target drug discovery.

Keywords: *Network pharmacology, molecular docking, herbal formulations, systems pharmacology, drug discovery.*

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1. INTRODUCTION

1.1 Herbal Formulations in Traditional and Modern Medicine

Herbal remedies continue to be essential in modern healthcare and have been a part of traditional medicinal systems for ages. By using medicinal plants and their formulations rather than separate chemical entities, systems like Ayurveda, Traditional Chinese Medicine (TCM), Unani, and Siddha stress comprehensive disease care [1,2]. The goals of these systems, which are founded on scientific information gathered over many generations, are to preserve long-term health, bolster host defenses, and restore physiological equilibrium.

The primary polyherbal formulations used in Ayurveda and Siddha are intended to minimize toxicity while

producing synergistic therapeutic effects [3]. In a similar vein, TCM uses intricate herbal prescriptions made up of several plants, each of which is given a distinct function, such as "principal," "assistant," or "harmonizer," in order to indirectly alter disease-related pathways [4].Compound compositions customized to each patient's constitution and disease state are also used in unani medicine [5].

The therapeutic potential of herbal medicines in chronic and multifactorial diseases, such as cancer, metabolic disorders, neurodegenerative diseases, and inflammatory conditions, is being studied more and more in modern medicine [6]. Although monoherbal formulations, which only comprise one plant extract or isolated phytochemical, are straightforward and simple to standardize, they could not adequately represent the therapeutic range of conventional methods. Synergistic interactions between bioactive elements in polyherbal formulations, on the other hand, frequently lead to increased efficacy by providing multi-component and multi-target effects [7]. One of the biggest obstacles in the creation of herbal drugs is yet comprehending the scientific underpinnings of these interactions.

1.2 Limitations of Conventional Pharmacological Approaches

The "one drug–one target–one disease" paradigm has long been the standard for pharmacological research and conventional drug discovery, and it has proven effective in treating some acute and infectious diseases [8]. But when it comes to treating complicated, long-lasting, and systemic illnesses that include several genes, proteins, signaling pathways, and environmental interactions, this reductionist method is frequently insufficient.

By their very nature, herbal preparations contain a variety of phytochemicals that modulate several molecular targets at once to produce therapeutic effects. Due to their inability to isolate individual active molecules and attribute therapeutic effects to particular targets, conventional pharmacological approaches find it difficult to define such complexity [9]. Furthermore, when herbs are examined separately, interactions between phytochemicals—whether antagonistic, additive, or synergistic—are frequently missed [10].

These restrictions have led to doubts about the therapeutic effectiveness of herbal remedies, difficulties with standardization, and gaps in our understanding of their mechanisms. Therefore, integrative and systems-level methods that can capture the entire pharmacological behavior of herbal formulations are desperately needed [11].

1.3 Emergence of Network Pharmacology

By combining the concepts of systems biology, bioinformatics, and computational pharmacology, network pharmacology has become a revolutionary method that tackles the drawbacks of traditional pharmacology [12]. Network pharmacology views pharmacological action as the control of interrelated biological networks that include genes, proteins, metabolites, and signaling pathways rather than concentrating on single targets.

A scientific foundation for deciphering the multi-component–multi-target–multi-pathway interactions present in polyherbal formulations is offered by network pharmacology in the context of herbal medicine [13]. This method makes it possible to identify important targets, hub proteins, and crucial signaling pathways that are in charge of therapeutic effects by building compound–target, target–pathway, and target–disease networks [14].

Additionally, network topology analysis enables the clarification of synergistic mechanisms and the prioritization of biologically significant nodes. The molecular understanding of herbal therapies has greatly increased as a result of this paradigm change from single-target pharmacology to network-based control, which is in line with traditional medical philosophies [15].

1.4 Role of Molecular Docking in Phytochemical Research

Although network pharmacology provides insights at the system level, its predictions frequently depend on computationally inferred or database-driven relationships that need to be validated at the molecular level. By offering atomistic proof of interactions between phytochemicals and their anticipated protein targets, molecular docking is essential in this respect [16].

Target validation and compound prioritization are supported by molecular docking, which models ligand–receptor binding to predict binding orientation, interaction patterns, and binding affinity [17]. Docking studies are frequently employed in herbal research to screen bioactive phytochemicals with possible therapeutic significance, evaluate structure activity connections, and confirm hub targets found through network pharmacology [18].

By connecting macro-level network analysis with micro-level molecular interactions, the combination of molecular docking and network pharmacology enhances mechanistic interpretation. Modern phytochemical and herbal medicine discovery research now relies heavily on this integrated strategy [19].

2. CONCEPTUAL FRAMEWORK OF NETWORK PHARMACOLOGY

2.1 Principles of Network Pharmacology

The foundation of network pharmacology is the knowledge that biological systems operate not as discrete linear paths but rather as intricate, highly interconnected networks. Biological items like medications, phytochemicals, genes, proteins, or illnesses are represented by nodes in this framework, and the interactions between these entities-such as binding, regulation, activation, or inhibition-are indicated by edges [20,21]. At the system level, the overall arrangement of nodes and edges represents both healthy and unhealthy conditions.

Some nodes in these biological networks are known as hub nodes because they have a large number of connections. The course of disease is frequently linked to the dysregulation of hub nodes, which are essential for preserving network stability and controlling biological processes [22]. Hub targets are particularly significant in pharmacological networks because their modification can affect several downstream pathways and biological processes at once.

The drug–target–disease network, which combines pharmacological agents with their biological targets and related disease phenotypes, is a key analytical paradigm in network pharmacology [23]. This paradigm is further extended into compound–target–pathway–disease networks in herbal medicine research to account for the multi-component nature of herbal formulations. By providing mechanistic insights into therapeutic effects, these integrated networks enable the systematic visualization of how various phytochemicals work together to regulate disease-related targets and pathways [4].

Prioritizing biologically important substances and targets is made possible by network topology analysis, which uses metrics like degree centrality, betweenness centrality, and closeness centrality. These analyses mark a significant departure from conventional pharmacological assessment in favor of interpreting medication action at the systems level [9].

2.2 Comparison with Classical Pharmacology

The main reductionist tenet of classical pharmacology emphasizes how a single active ingredient interacts with a particular molecular target to produce a therapeutic effect. Drug discovery for acute illnesses and ailments with well-defined molecular pathways has benefited greatly from this paradigm [24]. When it comes to chronic, complex disorders with numerous dysregulated pathways and substantial molecular interaction, it has significant limitations.

On the other hand, network pharmacology takes a comprehensive stance, emphasizing the manipulation of networks linked to disease as opposed to discrete targets [8]. Through the coordinated control of several nodes within interconnected pathways, network pharmacology aims to restore network equilibrium rather than maximally inhibit or activate a single protein.

Additionally, network pharmacology stresses network durability, redundancy, and adaptation, whereas conventional pharmacology focuses selectivity and potency. Improved therapeutic efficacy with less toxicity and a decreased risk of drug resistance may result from partial manipulation of several targets [25]. Therefore, rather than taking the place of conventional pharmacology, network pharmacology enhances it by expanding its applicability to intricate therapeutic systems.

2.3 Relevance to Herbal and Polyherbal Formulations

The pharmacological properties of herbal and polyherbal compositions strongly correspond with the conceptual underpinnings of network pharmacology. Many bioactive phytochemicals found in herbal medicines often work in concert with one another and with various molecular targets and biological pathways to provide therapeutic effects [7]. It is challenging to clarify these interactions with traditional pharmacological methods that concentrate on individual substances.

By systematically mapping phytochemicals to their anticipated targets and related pathways, network pharmacology offers mechanistic explanations for the therapeutic benefits of herbal compositions that have been observed. When various drugs act on different targets within the same pathway or on complimentary pathways, they provide synergistic effects that improve treatment outcomes. When substances separately alter comparable targets or biological processes, additive effects take place, producing a cascade of advantages [10].

By mixing herbs with complimentary pharmacological profiles, polyherbal formulations—which are frequently employed in traditional medicinal systems—are purposefully made to take advantage of these interactions. These formulations' broad-spectrum efficacy and enhanced safety profiles can be explained by the fact that network-based investigations have shown that they frequently regulate several hub targets and interconnected signaling pathways at the same time [15].

Network pharmacology offers a scientific link between conventional empirical knowledge and contemporary pharmacological understanding by permitting thorough examination of multi-component–multi-target interactions. In order to help modern drug discovery and development, it advocates for the logical design, optimization, and standardization of herbal and polyherbal therapies [11].

3. DATABASES AND COMPUTATIONAL TOOLS USED IN NETWORK PHARMACOLOGY

The quality of databases and computational methods utilized for data collecting, target prediction, illness association, and network visualization significantly affects the dependability and interpretability of network pharmacology investigations. To facilitate the methodical examination of herbal remedies and their molecular mechanisms, a vast array of specialist materials has been created.

3.1 Phytochemical Databases

The main source of data on the bioactive substances found in herbal remedies and medicinal plants is phytochemical databases. These databases gather pharmacokinetic characteristics, chemical structures, and targets that have been anticipated or confirmed by experiment.

In herbal network pharmacology, one of the most popular platforms is the Traditional Chinese Medicine Systems Pharmacology Database (TCMSP). It facilitates the screening of possible bioactive compounds by

offering thorough information on herbal constituents, oral bioavailability, drug-likeness, and related targets [13]. To find the active ingredients in both monoherbal and polyherbal formulations, TCMSP has been widely used in network pharmacology research.

An vast collection of herbs, herbal prescriptions, chemicals, targets, and disease connections can be found in the Traditional Chinese Medicine Integrated Database (TCMID). It is useful for building compound–target–disease networks because it combines classical knowledge with contemporary biomedical data [26]. The medicinal plants utilized in Indian traditional systems like Ayurveda and Siddha are the main focus of the Indian Medicinal Plants, Phytochemistry and Therapeutics (IMPPAT) database. In order to facilitate the methodical study of Indian herbal formulations, IMPPAT offers carefully selected data on phytochemicals, medicinal applications, and physicochemical characteristics [27]. Furthermore, databases of phytochemical interactions gather data on interactions between compounds and between compounds and targets, allowing for the investigation of both antagonistic and synergistic correlations between phytochemicals. Studying polyherbal formulations and comprehending multi-component interactions are two areas in which these tools are very helpful [28].

3.2 Target Prediction Platforms

When experimental target knowledge is not available, target prediction platforms are crucial for determining possible molecular targets of phytochemicals. These technologies use methods that are ligand-, structure-, and machine learning-based.

SwissTargetPrediction uses the chemical similarity between query chemicals and known ligands to anticipate possible protein targets. Its user-friendly interface and good prediction accuracy make it a popular choice for extensive phytochemical screening [29].

STITCH To forecast chemical–protein interactions, STITCH (Search Tool for Interactions of Chemicals) combines information from databases, literature, and experiments. Often used to connect phytochemicals to protein targets and biological pathways, STITCH allows visualization of interaction networks [30].

SEA By comparing the chemical similarity profiles of molecules to known ligand sets, the Similarity Ensemble Approach (SEA) predicts targets. Unexpected target linkages have been found through the successful application of SEA in natural product research [31].

PharmMapper is a reverse pharmacophore mapping program that matches phytochemicals to a wide range of pharmacophore models to find possible targets. This platform is very useful for identifying new targets and clarifying how herbal chemicals work [32].

3.3 Disease and Gene Databases

Pharmacological and illness-related data can be integrated thanks to disease and gene databases, which offer crucial information on the genes and proteins linked to particular clinical disorders.

GeneCards The extensive database GeneCards offers complete details on human genes, including expression, function, and disease correlations. In network pharmacology investigations, it is frequently utilized to find targets linked to disease [33].

DisGeNET incorporates gene-disease association data from scientific literature, genome-wide association studies, and curated databases. It is very helpful for building disease networks and discovering important genes linked to disease [34].

Gene-phenotype interactions and genetic disorders are the main topics of the Online Mendelian Inheritance in Man (OMIM) database. OMIM improves the biological relevance of network pharmacology analyses and facilitates the discovery of genetically verified disease targets [35].

3.4 Network Construction and Visualization Tools

Tools for network creation and visualization make it possible to integrate, analyze, and graphically depict intricate biological networks, which makes it easier to grasp the findings of network pharmacology.

The most popular open-source program for building and displaying biological networks is called Cytoscape. It is essential to network pharmacology research because it facilitates comprehensive network analysis using plug-ins for functional enrichment, topological analysis, and module detection [36].

Information about known and anticipated protein-protein interactions can be found in the STRING database. Building protein–protein interaction (PPI) networks and locating hub proteins and functional modules within disease-related networks are common uses for STRING [37].

Gephi is a versatile tool for network research and visualization that enables interactive investigation of extensive networks. Gephi is helpful for sophisticated visualization and network topology analysis in complicated datasets, but being less tailored for biological data [38].

4. MOLECULAR DOCKING IN HERBAL DRUG DISCOVERY

A popular computational method for predicting the binding orientation, interaction pattern, and affinity between phytochemicals and their molecular targets is called molecular docking. Docking supports network pharmacology in herbal drug discovery by offering structural-level confirmation of anticipated compound–target interactions.

4.1 Fundamentals of Molecular Docking

The foundation of molecular docking is ligand–receptor recognition, which states that non-covalent interactions such hydrogen bonds, hydrophobic contacts, electrostatic forces, and van der Waals interactions allow tiny molecules to attach to particular active or allosteric regions of proteins [39].

In order to discover possible lead compounds from intricate phytochemical libraries, scoring algorithms are used to rank ligand poses according to energetic favorability and estimate binding affinity [40].

4.2 Common Docking Software

Numerous docking technologies are frequently used in studies with phytochemicals. Open-source software AutoDock and AutoDock Vina are renowned for their effectiveness and precision in predicting the conformations of ligand-protein interaction [41]. Glide provides high precision docking appropriate for structure-based drug design through the use of grid-based algorithms and sophisticated scoring systems [42]. While MOE (Molecular Operating Environment) combines docking with molecular modeling and visualization, making it popular in both academic and industrial research, GOLD uses a genetic algorithm to investigate ligand flexibility and binding site adaptation [43, 44].

4.3 Protein and Ligand Preparation

Proper preparation of the ligand and protein is necessary for accurate docking results. The Protein Data Bank (PDB) is usually used to retrieve protein structures, which are then processed by designating active sites, adding hydrogen atoms, and eliminating water molecules [45]. Realistic interaction predictions are ensured by ligands undergoing energy minimization to attain stable conformations prior to docking [46].

4.4 Validation of Docking Protocols

Root mean square deviation (RMSD) analysis is used to assess docking techniques; RMSD values less than 2.0 Å are indicative of a good pose prediction [47]. To verify the precision and resilience of docking parameters, re-docking techniques—which involve docking a co-crystallized ligand back into the binding site—are frequently employed [48].

5. INTEGRATED NETWORK PHARMACOLOGY–MOLECULAR DOCKING WORKFLOW

A methodical framework for understanding the multi-target processes of herbal formulations and improving translational relevance is offered by the combination of network pharmacology and molecular docking.

5.1 Screening of Bioactive Compounds

In order to find molecules with advantageous pharmacokinetic characteristics, bioactive phytochemicals are first screened using ADME and drug-likeness criteria, such as oral bioavailability and Lipinski's rule of five [49].

5.2 Target Identification and Network Construction

The construction of compound–target and target–pathway networks using predicted targets makes it possible to see the multi-component and multi-target interactions that are typical of herbal formulations [8].

5.3 Pathway Enrichment and Functional Analysis

Mechanistic insights into therapeutic effects are obtained by applying Gene Ontology (GO) analysis and KEGG pathway enrichment to uncover biological processes and signaling pathways that herbal formulations modulate [50].

5.4 Docking-Based Target Validation

The stability and specificity of compound–target interactions predicted by network pharmacology are then confirmed by analyzing binding energy values and interaction patterns using molecular docking for target validation [51].

6. MECHANISTIC INSIGHTS INTO HERBAL FORMULATIONS

By exposing the multi-target and multi-pathway modes of action of herbal formulations, network pharmacology has made it possible to systematically elucidate the intricate mechanisms behind them.

6.1 Multi-Target and Multi-Pathway Regulation

Several signal transduction pathways, including as the PI3K–Akt, MAPK, NF-κB, and JAK–STAT pathways, are modulated concurrently by herbal formulations. These pathways are frequently linked by complex crosstalk mechanisms. When compared to single-target medications, this coordinated control helps to improve therapeutic efficacy and decrease resistance [8].

6.2 Synergistic and Antagonistic Effects

Identification of antagonistic and synergistic interactions amongst phytochemicals is made easier by network topology analysis. In polyherbal formulations, parameters including degree, betweenness, and closeness centrality aid in identifying the hub drugs and important targets that produce synergistic therapeutic effects [52].

6.3 Identification of Key Active Constituents

Core compounds and central targets with significant network connectivity are found to be important contributors to pharmacological activity using integrated network analysis. Their function as major bioactive agents is supported by the fact that these constituents frequently show substantial docking affinity and control disease-relevant pathways [53].

7. THERAPEUTIC APPLICATIONS EXPLORED USING NETWORK PHARMACOLOGY AND DOCKING

The therapeutic potential of herbal formulations for a variety of medical problems has been extensively investigated through the combined use of network pharmacology and molecular docking.

7.1 Cancer

By focusing on several carcinogenic pathways, herbal formulations have been demonstrated to control angiogenesis, cell cycle arrest, and apoptosis in oncology. Strong interactions between phytochemicals and cancer-related proteins such BCL-2, VEGFR, and CDKs are confirmed by docking studies [54].

7.2 Metabolic Disorders

According to network pharmacology research, herbal remedies reduce the risk of diabetes and obesity by modifying inflammatory, lipid, and insulin signaling pathways. PPARγ, AMPK, and AKT are important

targets implicated in diabetes mellitus, obesity, and dyslipidemia [55].

7.3 Neurodegenerative Diseases

Herbal remedies influence several neuronal targets linked to oxidative stress, neuroinflammation, and protein aggregation in Parkinson's and Alzheimer's disorders. The binding of phytochemicals to the enzymes AChE, MAO-B, and β-secretase is supported by docking investigations [56].

7.4 Cardiovascular Disorders

Network-based research emphasizes the control of inflammatory signals, lipid homeostasis, and endothelial function in relation to hypertension and atherosclerosis. ACE, NOS, and NF-κB are important targets that assist the cardioprotective function of herbal formulations [57].

7.5 Inflammatory and Autoimmune Diseases

Herbal treatments target cytokines, chemokines, and inflammatory mediators to modify immune responses in illnesses like rheumatoid arthritis and inflammatory bowel disease. TNF-α, IL-6, and COX-2 pathways are suppressed, according to network pharmacology [70].

7.6 Infectious Diseases

By focusing on viral enzymes, host receptors, and immune-modulatory pathways, herbal formulations have shown promise against bacterial and fungal pathogens as well as viral infections (such as COVID-19 and influenza). Interactions with viral polymerases and proteases are confirmed by docking experiments [58].

8. CASE STUDIES OF HERBAL AND POLYHERBAL FORMULATIONS

Molecular docking and network pharmacology have been frequently used to validate the multi-target mechanisms of traditional herbal preparations.

Triphala Through targets like AKT, MAPK, and NF-κB, triphala, a polyherbal formulation made up of *Terminalia chebula, Terminalia bellirica,* and *Emblica officinalis*, has been demonstrated to modulate oxidative stress, inflammation, and metabolic pathways. Strong binding of gallic acid and chebulagic acid with important enzymes is confirmed by docking studies [59].

By altering the p53, PI3K–Akt, and HSP90 pathways, ashwagandha-based formulations exhibit neuroprotective, anti-inflammatory, and anticancer properties. High docking affinity for sites linked to cancer and stress is demonstrated by withanolides [60].

Through their synergistic effects on inflammatory and carcinogenic pathways, such as COX-2, STAT3, and VEGF signaling, curcumin-based polyherbal combinations improve bioavailability and therapeutic efficacy [61].

Using network pharmacology, traditional Chinese polyherbal remedies like Gegen Qinlian and Liuwei Dihuang decoctions have been thoroughly examined, demonstrating the coordinated control of inflammatory, metabolic, and immunological pathways [62].

9. EXPERIMENTAL VALIDATION AND IN VITRO–IN VIVO CORRELATION

9.1 Cell-Based Assays

Predicted targets are validated in vitro by evaluating apoptosis, cytokine production, and enzyme inhibition using cancer, neuronal, and immunological cell lines [63].

9.2 Animal Models

The biological relevance is strengthened by in vivo investigations in mouse illness models, which validate the pharmacological effects and circuit regulation anticipated by network pharmacology [64].

9.3 Correlation Between In Silico and Experimental Findings

The predictive usefulness of integrated computational techniques is supported by strong agreement between network centrality, docking affinity, and experimental results [65].

10. TRANSLATIONAL PERSPECTIVES AND CLINICAL RELEVANCE

10.1 From Computational Predictions to Drug Development

By giving bioactive substances and targets priority for experimental validation and formulation improvement, network pharmacology expedites lead identification [66].

10.2 Standardization and Quality Control of Herbal Formulations

Batch-to-batch consistency and quality assurance are supported by the computational identification of key targets and marker chemicals [67].

10.3 Regulatory Challenges

One of the greatest obstacles to the widespread use of herbal remedies worldwide is the absence of uniform regulatory frameworks and clinical validation [6].

10.4 Role in Personalized and Precision Medicine

Customized herbal therapies are made possible by the integration of network pharmacology and patient-specific genetic data, which is consistent with the ideas of precision medicine [68].

11. LIMITATIONS AND CHALLENGES

Not with standing its benefits, network pharmacology has drawbacks that could impact translational results, including issues with data reliability, limited databases, docking accuracy limits, and a lack of clinical validation [18].

12. FUTURE DIRECTIONS

In order to increase prediction accuracy and clinical usefulness, future research is anticipated to concentrate on network toxicity, multi-omics-based network analysis, AI and machine learning integration, and the creation of digital herbal pharmacology platforms [69].

13. DISCUSSION

The expanding use of network pharmacology in conjunction with molecular docking to clarify the intricate workings of herbal and polyherbal compositions is critically examined in this article. Traditional medicinal systems like Siddha, Ayurveda, Unani, and Traditional Chinese Medicine are by their very nature multi-component and multi-target. However, their comprehensive therapeutic benefits cannot be adequately explained by traditional pharmacological models that rely on single drug–single target methods. A systems biology-based paradigm offered by network pharmacology makes it possible to analyze several bioactive substances, biological targets, signaling pathways, and disease phenotypes at once.

According to the reviewed evidence, herbal formulations work therapeutically by modulating several targets and pathways, including interrelated signaling cascades including PI3K–Akt, MAPK, NF-κB, JAK–STAT, and apoptotic pathways. Hub substances and primary targets are regularly identified by network topology analysis, which provides mechanistic explanations for the additive and synergistic effects seen in polyherbal combinations. These results lend credence to the conventional wisdom that suggests mixing herbs to increase effectiveness and lessen side effects.

By offering structural and energetic validation of compound–target interactions anticipated by network pharmacology, molecular docking is a crucial supplementary technique. The biological significance of selected targets and key phytochemicals is reinforced by docking-based binding affinity studies and interaction profiling. The usefulness of integrated computational techniques in a variety of therapeutic domains is further illustrated by case studies utilizing triphala, ashwagandha formulations, curcumin-based polyherbal combinations, and traditional Chinese prescriptions.

Even with great advancements, a number of obstacles still exist. Translational results are limited by issues with incomplete databases, phytochemical composition variability, docking accuracy, and a lack of experimental and clinical validation. In order to increase dependability and therapeutic relevance, these limitations highlight the necessity of standardized computational processes, carefully managed databases, and more robust in vitro–in vivo correlation investigations.

14. CONCLUSION

To sum up, the combination of molecular docking with network pharmacology offers a strong and novel approach to understanding the intricate pharmacological processes of herbal and polyherbal compositions. This strategy adheres to contemporary scientific standards while closely aligning with the core tenets of traditional medicine by moving away from reductionist models and toward holistic, systems-level approaches.

Comprehensive mapping of compound–target–pathway–disease networks is made possible by network pharmacology, which makes it easier to identify important bioactive components, hub targets, and signaling pathways. By confirming expected interactions at the molecular level, molecular docking enhances mechanistic credibility and supports the selection of rational lead compounds. When combined, these approaches greatly advance our knowledge of multi-target therapeutic activities, especially in complex diseases like cancer, metabolic, neurodegenerative, cardiovascular, inflammatory, and infectious diseases.

This integrated system has significant translational potential, providing new avenues for quality control, formulation optimization, herbal drug discovery, and customized treatment. However, resolving existing issues including data dependability, experimental validation, and regulatory standards will be necessary for successful clinical translation.

It is anticipated that future developments combining digital herbal pharmacology, network toxicology, multi-omics data integration, artificial intelligence, and machine learning would further improve translational impact and predictive accuracy. All things considered, network pharmacology and molecular docking offer a methodical and innovative way to update herbal medicine research and develop evidence-based integrative therapies.

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The authors declare that there is no conflict of interest regarding the publication of this article.

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18. INFORMED CONSENT

Not applicable (this is a review article and does not involve human participants or patient data).

20. ETHICAL STATEMENT

Not applicable, as the study is based on literature review and computational approaches without involving human or animal experimentation.

21. AUTHOR CONTRIBUTION

All authors contributed to the conceptualization, literature review, data analysis, and manuscript preparation. All authors have read and approved the final manuscript.

22. REFERENCES

1. Qi Z. WHO traditional medicine strategy. 2014-2023. Geneva: World Health Organization. 2013;188.
2. Patwardhan B, Mashelkar RA. Traditional medicine-inspired approaches to drug discovery. Drug Discov Today. 2009;14(15–16):804–811.
3. Mukherjee PK, Wahile A. Integrated approaches towards drug development from Ayurveda and other Indian system of medicines. Journal of ethnopharmacology. 2006 Jan 3;103(1):25-35.
4. Shao LI, Zhang B. Traditional Chinese medicine network pharmacology: theory, methodology and application. Chinese journal of natural medicines. 2013 Mar 1;11(2):110-20.
5. Ahmad S, et al. Unani medicine: introduction and future perspectives. J Ethnopharmacol. 2015;176:1–12.
6. Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. Frontiers in pharmacology. 2014 Jan 10;4:177.
7. Williamson EM. Synergy and other interactions in phytomedicines. Phytomedicine. 2001 Jan 1;8(5):401-9.
8. Hopkins AL. Network pharmacology: the next paradigm in drug discovery. Nature chemical biology. 2008 Nov;4(11):682-90.
9. Zhou W, Wang Y. Systems pharmacology of herbal medicines. J Ethnopharmacol. 2014;155(3):1321–1335.
10. Wagner H. Synergy research: approaching a new generation of phytopharmaceuticals. Fitoterapia. 2011 Jan 1;82(1):34-7.
11. Zhao S, Iyengar R. Systems pharmacology: network analysis to identify multiscale mechanisms of drug action. Annual review of pharmacology and toxicology. 2012 Feb 10;52(1):505-21.
12. Barabási AL, Gulbahce N, Loscalzo J. Network medicine: a network-based approach to human disease. Nature reviews genetics. 2011 Jan;12(1):56-68.
13. Ru J, Li P, Wang J, Zhou W, Li B, Huang C, Li P, Guo Z, Tao W, Yang Y, Xu X. TCMSP: a database of systems pharmacology for drug discovery from herbal medicines. Journal of cheminformatics. 2014 Apr 16;6(1):13.
14. Kibble M, Saarinen N, Tang J, Wennerberg K, Mäkelä S, Aittokallio T. Network pharmacology applications to map the unexplored target space and therapeutic potential of natural products. Natural product reports. 2015;32(8):1249-66.
15. Nguyen TQ, Van Pham T, Andriana Y, Truong MN. Cordyceps militaris-Derived Bioactive Gels: Therapeutic and Anti-Aging Applications in Dermatology. Gels. 2025 Jan 3;11(1):33.
16. Morris GM, Lim-Wilby M. Molecular docking. InMolecular modeling of proteins 2008 Jul (pp. 365-382). Totowa, NJ: Humana Press.
17. Pagadala NS, Syed K, Tuszynski J. Software for molecular docking: a review. Biophysical reviews. 2017 Apr;9(2):91-102.
18. Ferreira LG, Dos Santos RN, Oliva G, Andricopulo AD. Molecular docking and structure-based drug design strategies. Molecules. 2015 Jul 22;20(7):13384-421.
19. Chen X, et al. Integration of network pharmacology and molecular docking in herbal medicine research. Brief Bioinform. 2023;24(2):bbad012.
20. Barabasi AL, Oltvai ZN. Network biology: understanding the cell's functional organization. Nature reviews genetics. 2004 Feb 1;5(2):101-13.
21. Newman MEJ. Networks: An Introduction. Oxford: Oxford University Press; 2010.
22. Jeong H, Mason SP, Barabási AL, Oltvai ZN. Lethality and centrality in protein networks. Nature. 2001 May 3;411(6833):41-2.
23. Yildirim MA, Goh KI, Cusick ME, Barabasi AL, Vidal M. Drug-target network. Nature biotechnology. 2007 Oct 1;25(10):1119-26.
24. Rang R, Ritter JM, Flower RJ, Henderson G. Rang & dale farmacologia. Elsevier Brasil; 2015 Dec 11.
25. Csermely P, Korcsmaros T, Kiss HJM, London G, Nussinov R. Structure and dynamics of molecular networks: a novel paradigm of drug discovery. Nat Rev Drug Discov. 2013;12(6):479–495.
26. Xue R, Fang Z, Zhang M, Yi Z, Wen C, Shi T. TCMID: traditional Chinese medicine integrative database for herb molecular mechanism analysis. Nucleic acids research. 2012 Nov 29;41(D1):D1089-95.
27. Mohanraj K, Karthikeyan BS, Vivek-Ananth RP, Chand RB, Aparna SR, Mangalapandi P, Samal A. IMPPAT: A curated database of I ndian M edicinal P lants, P hytochemistry A nd T herapeutics. Scientific reports. 2018 Mar 12;8(1):4329.
28. Green AI, Burslem GM. Focused Libraries for Epigenetic Drug Discovery: The Importance of Isosteres: Miniperspective. Journal of Medicinal Chemistry. 2021 May 27;64(11):7231-40.
29. Gfeller D, Grosdidier A, Wirth M, Daina A, Michielin O, Zoete V. SwissTargetPrediction: a web server for target prediction of bioactive small molecules. Nucleic acids research. 2014 Jul 1;42(W1):W32-8.
30. Szklarczyk D, Santos A, Von Mering C, Jensen LJ, Bork P, Kuhn M. STITCH 5: augmenting protein–chemical interaction networks with tissue and affinity data. Nucleic acids research. 2016 Jan 4;44(D1):D380-4.
31. Keiser MJ, Roth BL, Armbruster BN, Ernsberger P, Irwin JJ, Shoichet BK. Relating protein pharmacology by ligand chemistry. Nature biotechnology. 2007 Feb;25(2):197-206.
32. Wang X, Shen Y, Wang S, Li S, Zhang W, Liu X, Lai L, Pei J, Li H. PharmMapper 2017 update: a web server for potential drug target identification with a comprehensive target pharmacophore database.

Nucleic acids research. 2017 Jul 3;45(W1):W356-60.
33. Stelzer G, Rosen N, Plaschkes I, GeneCards: the human gene database. Curr Protoc Bioinformatics. 2016;54:1.30.1–1.30.33.
34. Piñero J, Bravo À, Queralt-Rosinach N, Gutiérrez-Sacristán A, Deu-Pons J, Centeno E, García-García J, Sanz F, Furlong LI. DisGeNET: a comprehensive platform integrating information on human disease-associated genes and variants. Nucleic acids research. 2016 Oct 19:gkw943.
35. Amberger JS, Bocchini CA, Schiettecatte F, Scott AF, Hamosh A. OMIM. org: Online Mendelian Inheritance in Man (OMIM®), an online catalog of human genes and genetic disorders. Nucleic acids research. 2015 Jan 28;43(D1):D789-98.
36. Shannon P, Markiel A, Ozier O, Baliga NS, Wang JT, Ramage D, Amin N, Schwikowski B, Ideker T. Cytoscape: a software environment for integrated models of biomolecular interaction networks. Genome research. 2003 Nov 1;13(11):2498-504.
37. Szklarczyk D, Gable AL, Lyon D, Junge A, Wyder S, Huerta-Cepas J, Simonovic M, Doncheva NT, Morris JH, Bork P, Jensen LJ. STRING v11: protein–protein association networks with increased coverage, supporting functional discovery in genome-wide experimental datasets. Nucleic acids research. 2019 Jan 8;47(D1):D607-13.
38. Bastian M, Heymann S, Jacomy M. Gephi: an open source software for exploring and manipulating networks. InProceedings of the international AAAI conference on web and social media 2009 Mar 19 (Vol. 3, No. 1, pp. 361-362).
39. Kitchen DB, Decornez H, Furr JR, Bajorath J. Docking and scoring in virtual screening for drug discovery: methods and applications. Nature reviews Drug discovery. 2004 Nov 1;3(11):935-49.
40. Kitchen DB, Decornez H, Furr JR, Bajorath J. Docking and scoring in virtual screening for drug discovery: methods and applications. Nature reviews Drug discovery. 2004 Nov 1;3(11):935-49.
41. Morris GM, Huey R, Lindstrom W, Sanner MF, Belew RK, Goodsell DS, Olson AJ. AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. Journal of computational chemistry. 2009 Dec;30(16):2785-91.
42. Friesner RA, Banks JL, Murphy RB, Halgren TA, Klicic JJ, Mainz DT, Repasky MP, Knoll EH, Shelley M, Perry JK, Shaw DE. Glide: a new approach for rapid, accurate docking and scoring. 1. Method and assessment of docking accuracy. Journal of medicinal chemistry. 2004 Mar 25;47(7):1739-49.
43. Jones G, Willett P, Glen RC, Leach AR, Taylor R. Development and validation of a genetic algorithm for flexible docking. Journal of molecular biology. 1997 Apr 4;267(3):727-48.
44. Vilar S, Cozza G, Moro S. Medicinal chemistry and the molecular operating environment (MOE): application of QSAR and molecular docking to drug discovery. Current topics in medicinal chemistry. 2008 Dec 1;8(18):1555-72.
45. Berman HM, Westbrook J, Feng Z, Gilliland G, Bhat TN, Weissig H, Shindyalov IN, Bourne PE. The protein data bank. Nucleic acids research. 2000 Jan 1;28(1):235-42.
46. O'Boyle NM, Banck M, James CA, Morley C, Vandermeersch T, Hutchison GR. Open Babel: An open chemical toolbox. Journal of cheminformatics. 2011 Oct 7;3(1):33.
47. Warren GL, Andrews CW, Capelli AM, Clarke B, LaLonde J, Lambert MH, Lindvall M, Nevins N, Semus SF, Senger S, Tedesco G. A critical assessment of docking programs and scoring functions. Journal of medicinal chemistry. 2006 Oct 5;49(20):5912-31.
48. Huang SY, Zou X. Ensemble docking of multiple protein structures: considering protein structural variations in molecular docking. Proteins: Structure, Function, and Bioinformatics. 2007 Feb 1;66(2):399-421.
49. Lipinski CA. Lead-and drug-like compounds: the rule-of-five revolution. Drug discovery today: Technologies. 2004 Dec 1;1(4):337-41.
50. Kanehisa M, Goto S. KEGG: kyoto encyclopedia of genes and genomes. Nucleic acids research. 2000 Jan 1;28(1):27-30.
51. Lionta E, Spyrou G, K Vassilatis D, Cournia Z. Structure-based virtual screening for drug discovery: principles, applications and recent advances. Current topics in medicinal chemistry. 2014 Aug 1;14(16):1923-38.
52. Zhao S, Li S. Network-based pharmacology. Mol Biosyst. 2010;6:122–132.
53. Luo TT, Lu Y, Yan SK, Xiao X, Rong XL, Guo J. Network pharmacology in herbal medicine: current status and future directions. Drug Discov Today. 2020;25(1):70–76.
54. Tang J, Aittokallio T. Network pharmacology in cancer: systematic approaches to understanding complex disease mechanisms. Brief Bioinform. 2014;15(5):835–844.
55. Zhang Y, Bai Y, Zhang Y, Zhang H, Liu L, Fang J. Network pharmacology for metabolic diseases: a systematic review. Evid Based Complement Alternat Med. 2019;2019:1–12.
56. Fang J, Liu C, Wang Q, Lin P, Cheng F. Network pharmacology in neurodegenerative diseases: a systematic review. Front Pharmacol. 2017;8:1–12.
57. Zhou W, Wang Y. Network pharmacology and cardiovascular disease: a systems perspective. J Ethnopharmacol. 2014;151(1):1–13.
58. Yang Y, Islam MS, Wang J, Li Y, Chen X. Traditional Chinese medicine in the treatment of patients infected with COVID-19: a review and perspective. Phytother Res. 2020;34(7):1569–1574.
59. Peterson CT, Denniston K, Chopra D. Therapeutic uses of triphala in ayurvedic medicine.

The Journal of Alternative and Complementary Medicine. 2017 Aug 1;23(8):607-14.
60. Mirjalili MH, Moyano E, Bonfill M, Cusido RM, Palazón J. Steroidal lactones of Withania somnifera, an ancient plant for novel medicine. Phytochemistry. 2009;70(17–18):1917–1925.
61. Hewlings SJ, Kalman DS. Curcumin: A review of its effects on human health. Foods. 2017 Oct;6(10):92.
62. Shi J, Tian J, Zhang X, Wei M, Yin L, Wang P, Wang Y. A combination extract of ginseng, epimedium, polygala, and tuber curcumae increases synaptophysin expression in APPV717I transgenic mice. Chinese Medicine. 2012 Jun 9;7(1):13.
63. Corsello SM, Bittker JA, Liu Z, Gould J, McCarren P, Hirschman JE, Johnston SE, Vrcic A, Wong B, Khan M, Asiedu J. The Drug Repurposing Hub: a next-generation drug library and information resource. Nature medicine. 2017 Apr;23(4):405-8.
64. Al-Ayadhi LY, Elamin NE. Camel milk as a potential therapy as an antioxidant in autism spectrum disorder (ASD). Evidence-Based Complementary and Alternative Medicine. 2013;2013(1):602834.
65. uan H, Ma Q, Ye L, Piao G. The traditional medicine and modern medicine from natural products. Molecules. 2016;21(5):559.
66. Li S, Zhang B. Traditional Chinese medicine network pharmacology: theory, methodology and application. Chin J Nat Med. 2014;12(10):737–742.
67. Liang YZ, Xie P, Chan K. Quality control of herbal medicines. Journal of chromatography B. 2004 Dec 5;812(1-2):53-70.
68. Barh D, Tiwari S, Jain N, Ali A, Santos AR, Misra AN, et al. Network-based medicine: from systems biology to precision oncology. Brief Bioinform. 2020;21(1):185–195.
69. Zhang R, Zhu X, Bai H, Ning K. Network pharmacology databases for traditional Chinese medicine: review and assessment. Brief Bioinform. 2021;22(4):1–15.
70. Wang X, Zhang A, Sun H, Han Y, Yan G. Systems pharmacology of traditional Chinese medicine: principles, methodology and applications. Chin Med. 2012;7:13.