INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Network Pharmacology in Drug Discovery: Concepts, Methodology, Applications and Future Perspectives

Sneha Saha[1], Anuranjita Kundu*

[1]Department of Pharmacy, Guru Nanak Institute of Pharmaceutical Science and Technology, Sodpur, Panihati, Kolkata-700114, West Bengal, India.

ARTICLE INFO

Published: 27 jun. 2026
Keywords:
Network pharmacology, bioinformatics, drug-target interaction, drug discovery, molecular docking, drug repurposing.
DOI:
10.5281/zenodo.20963918

ABSTRACT

Network Pharmacology has evolved as a revolutionary concept in drug discovery, which has transformed the traditional "one drug, one target" concept into a new" multi-target-multi component" concept. By employing systems biology, bioinformatics, and computer simulation technology, network pharmacology allows the exploration of complex biological networks in the context of disease and therapy. This paradigm is particularly instrumental in understanding polypharmacology, discovering synergistic drug combinations, and deciphering mechanisms of action of natural products as well as multi-component therapies. Recent developments in high-throughput omics tools, molecular docking, and network analysis tools have helped accelerate the development of drug-target-disease in interaction networks to identify new therapeutic targets and biomarkers. Additionally, network pharmacology can significantly assist in drug repurposing as well as minimize drug attrition rates through more accurate predictions of efficacy and toxicity profiles. This review aims to highlight the basic concepts, methodologies, applications, and the future perspectives of network pharmacology in modern drug discovery.

INTRODUCTION

1.1 Overview of Network Pharmacology

Network pharmacology (NP) is an advanced drug discovery approach that examines the interactions between drugs, targets and diseases within the context of biological networks. This strategy has evolved beyond the concept of one drug-one target. Network pharmacology combines the knowledge of various systems biology disciplines, including genomics and proteomics, among others. Unlike the conventional pharmacology concept, which assumes that one drug targets one receptor, this approach recognises that a single

***Corresponding Author:** Anuranjita Kundu
Address: *Department of Pharmacy, Guru Nanak Institute of Pharmaceutical Science and Technology, Sodpur, Panihati, Kolkata-700114, West Bengal, India.*
Email ✉: anuranjita.kundu@gnipst.ac.in

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

drug may influence multiple targets, and that several drugs can act on the same target within a biological system.[(Li & Kar, 2025)]

1.2 Background of drug discovery

Traditionally, drug discovery began with empirical research on therapeutic agents from nature, including plants, animals, and minerals, and was often based on traditional knowledge. This eventually developed into classical pharmacology, in which the biological activities of small molecules were screened in cells or organisms. With further advances in biology and genetics, drug development gradually moved toward target-based strategies.[(Chandran et al., 2017)]

Significant advancements were made in information technology and omics sciences during the late 20th century, which impacted modern drug discovery to a considerable extent by incorporating computational methods into drug research. These methods were used to predict drug-like properties, study ligand–protein interactions through molecular docking techniques, and assess pharmacokinetic and toxicity parameters. These advancements were useful in making drug research more efficient in identifying drug candidates. [(Chandran et al., 2017)]

1.3 Need for systems-based approaches

As diseases are associated with complex relationships between multiple proteins, there is a growing interest in multi-target strategies to address these diseases. With this background, network pharmacology has been proposed as a promising strategy to study drug-target-biological system interaction through computational methods. This has been useful in identifying targets, understanding the mechanism of herbal medicines, and exploring drug repositioning opportunities to aid in the development of more effective drug therapies. [(Chandran et al., 2017)]

1.4 Concept of Network Pharmacology

First coined by British pharmacologist Andrew L. Hopkins in 2007, network pharmacology has evolved from its initial stage to become a modern and advanced science that incorporates various features from systems biology, bioinformatics, and computational network science. Network pharmacology represents an application of computational and systems biology methods and biological network methodology to assess the multiplicative effects of drugs, diseases, and therapeutic targets through combined analyses. It is a specialised subset of pharmacology focused on multi-targeted, multi-pathway pharmacological intervention. [(Zhai et al., 2025)]

1.5 Aim of the review

The aim of the review is to provide a comprehensive overview of Network Pharmacology, focusing on its fundamental concepts, research methodology and common computational tools. It will further demonstrate how Network Pharmacology has been implemented in drug development, understand the mechanisms of disease, and develop therapies targeting multiple receptors. Furthermore, it will discuss the current challenges and future directions of this emerging field in biomedical research.

2.Foundational Principles of Network Pharmacology

Network pharmacology's operational framework comprises four fundamental components: multi-target drug interaction studies, biological network topology applications, disease system-wide comprehension pursuit, and multi-omics high-dimensional data integration. These principles provide researchers the opportunity to advance from descriptive pharmacology towards predictive

data-driven therapeutic outcome modelling. [(Cui et al., 2025a)]

2.1 Multi-Target Drug Interactions and the Robustness of Biological Systems

Network-based drug discovery aims to identify combinations of targets that inhibit these escape routes when perturbed simultaneously. For instance, "vertical targeting" involves inhibiting multiple nodes within a single signalling pathway to overcome resistance, whereas "parallel targeting" involves blocking multiple pathways to prevent adaptation. (Talevi, 2015)

2.2 Biological Network Analysis and Topology

Network pharmacology uses a great deal of graph theory to study the biological network, where the nodes represent the biomolecules, i.e., genes, proteins, metabolites, or drugs, and the edges represent the interactions between them. Topology is used to identify the important nodes in the network. [(Thombre et al., 2026)]

2.3 System-Level Understanding of Disease: The Disease Module Concept

Network pharmacology treats diseases as perturbations of certain subnetworks of the cell interactome, named disease modules. Disease modules are composed of genes and proteins that interact with each other to drive diseases. [(Thombre et al., 2026)]

2.4 Integration of Multi-Omics Data

The current approach to network pharmacology is based on the integration of multiple omics data, which include genomics, transcriptomics, proteomics, metabolomics, and epigenomics. This approach is used to understand complex biological systems and diseases.[(Thombre et al., 2026)][(L. Yang et al., 2025a)]

3. Databases and Computational Tools

Table 1: Core databases and computational tools employed in Network Pharmacology

Category	Primary Databases / Tools	Function in Network Pharmacology Pipeline
Drug / Chemical Information	PubChem, DrugBank, ChEMBL, ChEBI	Provide chemical structures, bioactivity data, pharmacological properties, and drug–compound information used for chemical profiling.[(Chavan & Gite, n.d.)]
Target Prediction	SwissTargetPrediction, PharmMapper, SuperPred	Predict potential protein targets for bioactive compounds based on chemical similarity, pharmacophore mapping, or machine-learning models.[(Chavan & Gite, n.d.)]
Disease–Gene Mapping	GeneCards, OMIM, DisGeNET, MalaCards	Identify genes associated with specific diseases to determine potential therapeutic targets.[(Chavan & Gite, n.d.)]
PPI & Network Construction	STRING, BioGRID, IntAct, HAPPI	Build protein–protein interaction (PPI) networks to understand molecular interactions and disease-related pathways.[(Chavan & Gite, n.d.)]
Analysis & Visualization	Cytoscape, Gephi, NAViGaTOR, NetworkAnalyst	Perform network visualization, topological analysis, and identification of hub genes or key targets in biological networks.[(Chavan & Gite, n.d.)]

Functional Enrichment	DAVID, Metascape, ClueGO, KOBAS	Conduct Gene Ontology (GO) and KEGG pathway enrichment analysis to interpret biological functions and pathways.[(Chavan & Gite, n.d.)]
Validation (In Silico)	AutoDock, PyRx, MOE, AutoDock Vina	Perform molecular docking to evaluate binding affinity and interaction stability between compounds and target proteins.[(Chavan & Gite, n.d.)]

4.Methodological Workflow

The present-day pharmaceutical research scenario is undergoing a major shift from a "one drug, one target" reductionist approach to a "multi-component, multi-target, multi-pathway" concept of drug development. [(Noor, Qamar, et al., 2022a)]

This evolution is driven by the increasing realization that complex, chronic, and multifactorial diseases—ranging from oncological malignancies and cardiovascular disorders to neurodegenerative conditions—are rarely the consequence of a single genetic aberration. Instead, such pathologies typically emerge from the systemic failure of intricate biological regulatory networks. [(Cui et al., 2025a)]

Consequently, the conventional drive towards high-affinity and single-target inhibitors has resulted in a systemic efficacy crisis. There is a need to develop novel methodologies that can effectively address the entire biological interactome associated with diseases. [(Fan et al., 2023)] Network pharmacology (NP), a discipline that combines systems biology, bioinformatics, and information science, is recognised as the foundation for this novel era of drug discovery. [(Cui et al., 2025a)] By mapping the relationships between drugs, genes, proteins, and diseases on a network platform, this approach offers a holistic solution to the discovery of the synergistic mechanisms of traditional medicines and natural products. (Muthuramalingam et al., 2024)

The integration of artificial intelligence (AI) and multi-omics has further empowered network pharmacology, which has allowed it to evolve from a rule-based paradigm into a data-driven paradigm that bridges the gap between empirical traditional knowledge and mechanism-driven precision medicine. (Noor, Qamar, et al., 2022a)

4.1 Chemical Profiling and Lead Identification

The first phase of the network pharmacology methodological workflow involves the rigorous identification of bioactive constituents from a natural matrix and the subsequent screening of these lead candidates based on their pharmacokinetic potential. This phase is considered a critical phase since the reliability of all subsequent computational predictions and biological analysis is intrinsically linked to the chemical accuracy and physiological relevance of the initial ligand library. [(Fan et al., 2023)]

4.1.1 Identification of Compounds

Compound identification is carried out by literature mining or using techniques such as Ultra-Performance Liquid Chromatography-Tandem Mass Spectrometry (UPLC-MS/MS) and Gas Chromatography-Mass Spectrometry (GC-MS). [(Merecz-Sadowska et al., 2025a)] Natural products, particularly medicinal plants, represent an expansive reservoir of bioactive scaffolds;

however, their characterization is frequently complicated by structural complexity and the presence of numerous analogous metabolites.[(Fan et al., 2023)] In the current era, phytochemical characterization involves the use of advanced instrumentation such as Gas Chromatography-Mass Spectrometry (GC-MS) and Ultra-Performance Liquid Chromatography-Tandem Mass Spectrometry (UPLC-MS/MS) to distinguish between structurally similar phytochemicals in herbal extracts. [(Noor, Qamar, et al., 2022a)]

4.1.2 Database Retrieval

Known bioactive compounds are retrieved from various databases such as the Traditional Chinese Medicine Systems Pharmacology (TCMSP), PubChem, and the Encyclopedia of Traditional Chinese Medicine (ETCM). [(Li et al., 2023)] [(Merecz-Sadowska et al., 2025a)]

Modern updates of existing repositories, such as TCMID 2.0 (http://www.megabionet.org/tcmid/) include the integration of mass spectrometry (MS) for the discrimination of herb quality and characteristic components. Apart from the application of analytical techniques, researchers are now employing vast repositories of bioactive compounds such as the Traditional Chinese Medicine Systems Pharmacology (TCMSP) database (http://tcmspw.com/tcmsp.php), the Indian Medicinal Plants, Phytochemistry, and Therapeutics database (http://cb.imsc.res.in/imppat/), and the Encyclopedia of Traditional Chinese Medicine (ETCM) (http://www.tcmip.cn/ETCM/) for retrieving the profiles of known bioactive components. [(Fan et al., 2023)]

Additionally, the BATMAN-TCM (http://bionet.ncpsb.org.cn/batman-tcm/) [(Fan et al., 2023)] platform provides bioinformatics tools to enable the identification of molecular mechanisms and component collections associated with herbs.

4.1.3 Filtering of Lead Compounds via ADME and Pharmacokinetic Parameters

Following the compilation of a comprehensive chemical library, candidate molecules undergo a series of computational filters to prioritize those with the highest probability of therapeutic efficacy. [(Fan et al., 2023)] Candidate compounds are prioritized by filtering for Absorption, Distribution, Metabolism, and Excretion (ADME) properties. [(Merecz-Sadowska et al., 2025a)]. This screening process is essential for overcoming the sustainability concerns inherent in traditional trial-and-error approaches, which are often time-intensive and require excessive resource consumption.[(Muthuramalingam et al., 2024)]. The standard filtering criteria focus on Absorption, Distribution, Metabolism, and Excretion (ADME) properties, with particular emphasis on Oral Bioavailability (OB) and Drug-Likeness (DL). [(Muthuramalingam et al., 2024)]

Oral Bioavailability (OB) is the fraction or percentage of an orally administrated pharmacological agent that is absorbed into the systemic circulation. For network pharmacology protocols, the threshold is often set as OB $\geq$ 30. This is sometimes obtained using tools such as SwissADME (http://www.swissadme.ch/).[(Noor, Qamar, et al., 2022b)] Drug-likeness (DL) is a qualitative assessment that estimates how likely a molecule is to be successful as a drug, often performed using either Molsoft (https://molsoft.com/mprop/) and/or Lipinski's Rule of Five against DrugBank (https://go.drugbank.com/). The standard cut-off is DL $\geq$ 0.18. [(Noor, Qamar, et al., 2022b)]

4.1.4 AI-Driven Molecular Optimization and Generative Design

One major improvement within Phase I involves the integration of generative AI platforms to enable the design and optimization of molecules. [(Noor, Qamar, et al., 2022a)] Platforms such as Chemistry42 utilize machine learning to refine the structures of novel derivatives, aiming to enhance therapeutic efficacy while simultaneously attenuating potential toxicity. [(Noor, Qamar, et al., 2022b)] This improvement enables Phase I to become an active process rather than a passive one, significantly reducing the reliance on traditional bioassays. [(Cui et al., 2025b)]

4.1.5 Target Deconvolution and Prediction

This phase focuses on the identification of putative molecular targets for the prioritized bioactive compounds. [(Noor, Qamar, et al., 2022a)] As natural products tend to target multiple proteins in a network, rather than single target proteins, the process of target fishing is employed to deal with the polypharmacology landscape. [(Li et al., 2023)]

4.2.1 Computational Strategy and Algorithms

Target prediction methodologies are generally divided into ligand-based and structure-based approaches.[(Noor, Qamar, et al., 2022a)] Ligand-based methods utilize molecular similarity to known drugs to infer targets, while structure-based methods employ inverse docking to find protein pockets that fit the small molecule.[(Noor, Qamar, et al., 2022a)]

Table 2: Computational tools for target prediction.

Tool	Prediction Method	Utility in Workflow
SwissTargetPrediction	http://www.swisstargetprediction.ch/	Makes predictions based on 2D and 3D similarity to known ligands with species-specific profiles.[(L. Yang et al., 2025a)]
PharmMapper	http://lilab.ecust.edu.cn/pharmmapper/	Uses pharmacophore mapping and reverse docking to find proteins with matching binding sites.[(Zhou et al., 2025)]
STITCH	http://stitch.embl.de/	Uses interaction evidence from experiments, text mining, and homology transfer.[(Zhou et al., 2025)]

4.2.2 Target Development Levels (TDL)

For efficient drug repositioning, especially in cases of a pandemic, network pharmacology makes use of the Target Development Level (TDL) concept.[(Zahoránszky-Köhalmi et al., 2022)] The Pharos database consists of targets that are given a level based on clinical knowledge.[(Sheils et al., 2020)]

^{Tclin}: Target modulated by approved drugs.

T_{chem}: Target with known small molecule modulators but no approved drugs.

T_{bio}: Characterized proteins with no known small molecule modulators.

T_{dark}: Proteins with virtually no domain-specific knowledge [(Zahoránszky-Köhalmi et al., 2022)]

4.2.3 The Role of Artificial Intelligence and AlphaFold3

Artificial Intelligence plays a crucial role in the deconvolution of targets by resolving the structural limitations of the human proteome. [(Noor, Qamar, et al., 2022a)] AlphaFold3 provides atomic-scale accuracy to predict the structures of the target proteins, and the binding energy between the target and the compounds can be dynamically simulated, even for tumor mutants and understudied proteins. [(Noor, Qamar, et al., 2022a)]

In addition, the use of Graph Neural Networks (GNNs) enables the analysis of complex component-target-disease weight networks, allowing for the identification of the key synergistic components more accurately than linear models. [(Noor, Qamar, et al., 2022a)] This AI-driven platform enables the design and optimization of novel derivatives to improve their efficacy and reduce their toxicity. [(Noor, Qamar, et al., 2022a)]

4.2.4 Disease Gene Mapping and Intersection Analysis

The identification of the particular molecular profile of a disease is a pre-requisite for the understanding of drug target interactions. [(Noor, Qamar, et al., 2022a)] The third phase of the process includes the mapping of genes related to the disease and the intersection of the identified genes and the predicted drug targets. [(Li et al., 2023)]

Table 3: Key tools for gene mappimg and intersection analysis.

Database	Primary Usage	Role in Intersection Analysis
GeneCards	https://www.genecards.org	It aggregates data from over 200 sources to provide gene-centric information on all human diseases.[(Noor, Qamar, et al., 2022b)]
DisGeNET	https://www.disgenet.org	It contains over 1 million gene-disease associations derived from literature and variants. [(Noor, Qamar, et al., 2022b)]
OMIM	https://www.omim.org/	It is essential for the identification of genetic associations and phenotypes of Mendelian disorders. [(Noor, Qamar, et al., 2022b)]

4.3.1 Intersection Analysis and Venn Mapping

The aim of this stage is to identify the so-called "overlap" target, which is simultaneously influenced by the components of the drug and involved in the pathogenesis of the disease. [(Noor, Qamar, et al., 2022b)] The use of Venn diagram software is the most common way to carry out the identification of overlap targets, which are the starting point for subsequent screening. [(L. Yang et al., 2025b)] The intersection analysis is often accompanied by multi-omics factor analysis (MOFA) and transcriptional profiling to uncover gene co-expression networks that are indicative of clinical endpoints. [(Noor, Qamar, et al., 2022b)]

4.4 Network Construction and Topology Analysis

The network construction phase combines all the information from Phases I to III in a network that offers a holistic view of drug-disease interactions. [(Noor, Qamar, et al., 2022b)] This phase represents a shift from a list of targets to a map of functional interconnections. [(Li et al., 2023)]

4.4.1 Multi-Platform Network Construction

Protein-Protein Interaction (PPI) Networks: PPI networks illustrate the functional relationships between targets, which can be obtained from various databases such as STRING, BioGRID, DIP, or MINT.[(Noor, Qamar, et al., 2022b)] STRING offers confidence scores for the reliability of interactions derived from experimental evidence and literature mining.[(Li et al., 2023)]

Compound-Target-Disease (C-T-D) Networks: These networks depict the "many-to-many" relationship where many phytochemicals interact with many molecular targets that play a role in one or more diseases.[(Noor, Qamar, et al., 2022a)]

Host-Pathogen Networks: In the context of infectious disease research, bipartite networks have been used to identify "virus hubs," which are host proteins that interact with many pathogen proteins that represent the "Achilles' heel" of the virus.[(Noor, Qamar, et al., 2022b)]

4.4.2 Topological Analysis and Hub Identification

Topological parameters are used to identify the key nodes that represent the best target for therapy.[(Noor et al., 2022b)]

Degree: This represents the total number of edges connected to a node. Nodes with a large degree are referred to as hubs.[(Noor et al., 2022b)]

Betweenness Centrality (BC): This centrality measure represents the importance of a node as a facilitator of communication between different modules of the network.[(L. Yang et al., 2025a)]

Closeness Centrality (CC): This measure represents the ability of a node to disseminate its information to the entire network.[(L. Yang et al., 2025a)]

4.5 Pathway Enrichment and Functional analysis

This phase seeks to identify the biological significance of the network targets by mapping them to metabolic and signaling pathways. This helps researchers to identify the "how" of a drug intervention.

Table 4: Computational tools for pathway and functional enrichment.

Tool	Functional Focus	Workflow Application

DAVID	https://david.ncifcrf.gov	Functional annotation clustering and pathway mapping for gene lists.[(Noor et al., 2022b)]
Metascape	http://metascape.org	Multi-database functional enrichment with visually intuitive outputs.[(Li et al., 2023)]
KEGG Mapper	https://www.genome.jp/kegg/	Identifying overrepresented signaling and metabolic pathways.[(Noor et al., 2022b)]
Reactome	https://reactome.org	Mapping targets to high-quality, manually curated biological processes.[(Zahoránszky-Kőhalmi et al., 2022)]

4.6 Experimental and In Silico Validation

The last part of the methodological workflow is an important step for bridging the gap between prediction and reality. [(Noor, Qamar, et al., 2022b)]This iterative process involves a combination of molecular modeling and validation.[(Li et al., 2023)]

In Silico Structural Simulation

Molecular docking and dynamic simulation are used to structurally validate that a compound indeed has the ability to bind with its predicted target.[(Merecz-Sadowska et al., 2025a)]

Molecular Docking Tools

AutoDock Vina is preferred for high-throughput semi-flexible docking, whereas Glide and GOLD are preferred for high-precision scoring and flexible receptor optimization.[(Noor, Qamar, et al., 2022b)] Another preferred option for structural simulation coupled with pharmacophore docking is the use of MOE (Molecular Operating Environment).[(L. Yang et al., 2025a)]

Validation Criterion

Binding energies < -5 kcal/mol or < -7 kcal/mol are usually indicative of a high binding affinity.[(L. Yang et al., 2025a)]

In Vitro and In Vivo Verification Models

In Vitro validation involves the use of biologically relevant systems that can simulate human disease conditions more realistically.[(Noor, Qamar, et al., 2022b)]

5.Case Studies and Applications

5.1 Molecular Mechanism of Cordia myxa in Liver Cancer

Liver cancer treatment with traditional drugs has limitations such as toxicity and the occurrence of resistance. A network pharmacology research, coupled with molecular docking and dynamics studies, was undertaken to explore the potential of the active constituents of Cordia myxa in the treatment of liver cancer. The research identified 10 active compounds, such as cosmosiin, rosmarinic acid, quercetin, and rubinin, which met the criteria of oral bioavailability and drug-likeness. The network pharmacology research identified 5 hub genes, such as HSP90AA1, ESR1, CYP3A4, CDK1, and MMP9, which are significantly associated with the survival of liver cancer patients. In addition, the molecular dynamics studies, which were run for 100 ns, validated the stability of the interactions of the HSP90AA1 protein with active compounds such as cosmosiin and rosmarinic acid, which act as liver cancer repressors through the modulation of cancer-associated pathways.[(Li et al., 2024)]

5.2 Integrative Therapy for Chronic Atrophic Gastritis

Chronic atrophic gastritis (CAG) is a precancerous state that dramatically increases the risk of developing gastric cancer. A systematic review and network pharmacology approach was used to assess the efficacy of TCM in addition to conventional Western medicine. Seven hub herbal medicines, including Paeonia lactiflora, Coptis chinensis, and Salvia miltiorrhiza, were found using association rule mining. Thirteen hub genes were also found, with MAPK1 and MAPK3 being the most significant differentially expressed genes between normal and CAG tissues. Molecular docking revealed that naringenin, luteolin, and quercetin are primarily responsible and have high binding affinity to these targets, providing a basis to explain how TCM can block the progression of chronic gastritis to gastric cancer.[(Weng et al., 2023)]

5.3 Panax notoginseng in Diabetic Ocular Complications

Diabetic retinopathy (DR) and diabetic cataract (DC) are microvascular complications of diabetes mellitus with similar pathogenic mechanisms, which include chronic low-grade inflammation. In the present study, network pharmacology was used to investigate the multi-target therapeutic potential of Panax notoginseng (Sanqi), a traditional Chinese medicine, on the comorbidity of DR and DC. Eight pharmacologically active compounds of P. notoginseng, which shared 121 common gene targets with the comorbidities, were identified. Quercetin was identified as the active compound with the highest connectivity based on the topological analysis. Molecular docking results showed the ability of the active compounds to form stable complexes with the major targets SRC, JAK2, IGF1R, and EGFR. These interactions mainly regulate the AGE-RAGE signaling pathway, PI3K/AKT signaling pathway, and VEGF signaling pathway, which are associated with the microvascular damage.[(Zhang et al., 2025)]

5.4 Epigallocatechin Gallate (EGCG) in Nasopharyngeal Carcinoma

Nasopharyngeal carcinoma has been observed to become resistant to first-line chemotherapeutic agents such as cisplatin. The therapeutic potential of EGCG, a major green tea polyphenol, on NPC was explored using integrative network pharmacology and bioinformatics. The study revealed that EGCG targets 198 differentially expressed genes associated with NPC cell lines. The study also revealed a six-gene prognostic risk model that included SNCG, FOXO3, and CYCS to predict progression-free survival. Further validation was performed on clinical samples and immunohistochemistry, which revealed CYCS and MYL12B as key targets. Molecular docking revealed EGCG to interact strongly with these targets, which is associated with EGCG-induced apoptosis and NPC cell proliferation via oxidative stress and intrinsic apoptotic pathways.[(Y. Yang et al., 2025)]

5.5 Herbal Components for the Treatment of Pneumonia

Network pharmacology was instrumental in identifying therapeutic interventions for different types of pneumonia, such as those induced by bacteria, viruses such as IAV and H1N1, and fungi. An in-depth analysis revealed that there are four types of TCMs that can be used to treat pneumonia: natural active components, single herbs, patent medicines, and multi-component formulations. For instance, anemoside B4 was found to prevent the release of pro-inflammatory factors such as TNF-α, IL-1β, and IL-6 through the TLR4/Myd88 signalling pathway. In addition to that, metabolites from Houttuynia cordata such as

apigenin, kaempferol, and quercetin, showed stable binding to hub targets such as IL-6 and MAPK1, which are also related to the treatment of SARS-CoV-2. This is through a multi-pathway mechanism involving the PI3K-Akt, JAK-STAT, and NF-κB signalling pathways to treat lung injury.[(D. Yang et al., 2025a)]

5.6 Therapeutic Interventions for Interstitial Lung Diseases

Interstitial lung diseases, including idiopathic pulmonary fibrosis and sarcoidosis, are a group of heterogeneous disorders. The therapeutic potential of traditional formulations, such as Si Miao Wan (SMW) for rheumatoid arthritis-associated interstitial lung disease, was explored using network pharmacology. The therapeutic potential of SMW was evaluated by integrating metabolomics and network pharmacology. The study revealed that SMW can prevent the progression of interstitial lung disease by modulating ferroptosis via the TNF and IL-17 pathways. Another study used network pharmacology to identify the therapeutic potential of a bioactive compound, triptolide, which is present in Tripterygium wilfordii. This compound targets hub genes, including STAT3 and AKT1, to treat connective tissue disease-related interstitial lung disease. This study is consistent with the paradigm of P4 medicine, which includes predictive, personalized, preventive, and participatory medicine to restore biological network balance.[(Vithalkar et al., 2025a)]

5.7 Drug Repositioning of CHM Against COVID-19

Network pharmacology has been recognized as an important method for the rapid repositioning of CHM compounds. The network pharmacology of the Qingfei Paidu Decoction and Lianhua Qingwen formula showed the potential of CHM to treat "cytokine storms" and repair lung injuries. For example, quercetin, luteolin, and kaempferol were identified as potential candidates with high reliability for the treatment of COVID-19. Network pharmacology quantitatively predicted the proximity of the targets of the CHM compounds to the COVID-19 disease targets in the human PPI network. The results of preclinical experiments showed that compounds like berberine and emodin could successfully inhibit the replication of SARS-CoV-2 or the binding of the spike protein with the ACE2 receptor, providing a scientific basis for the use of CHM to treat severe viral diseases.[(Wang et al., 2022a)]

5.8 Natural Bioactives in the Management of Oral, Head, and Neck Cancer

Head and neck cancer (HNC) is a major health concern worldwide because of the scarcity of early warning signs and a high rate of recurrence. A network pharmacology study on aged citrus peel (Chenpi) identified tangeretin as a major bioactive molecule for the treatment of OSCC. Tangeretin specifically targets CDK1, ESR1, and PIK3R1, causing cell cycle arrest and apoptosis in cancer cells. In addition, network pharmacology analysis of Yinchen Wuling San revealed that its bioactive molecules specifically target TNF, AKT1, and EGFR. Using the relationship between the bioactives and abnormal biological pathways such as PI3K/AKT/mTOR, researchers can now identify unusual drug targets that do not conform to the traditional "magic bullet" approach and provide a ray of hope in the treatment of advanced and drug-resistant cases of HNC.[(Muthuramalingam et al., 2024)]

6.Challenges

Although network pharmacology has changed the drug development process, several major obstacles still need to be overcome.

Database Quality and Data Completeness: Network pharmacology's success relies heavily on the quality and completeness of public databases. However, the existing databases are incomplete, with inadequate information on compound-target interactions (CTIs), inadequate experimental verification of literature, and low update rates, which are often not consistent with the latest literature.[(Wang et al., 2022b)]

Homogeneity and Standardization: Most existing studies have adopted a standard, repetitive methodology without distinct features or experimental verification. It is imperative that international standards are set to ensure the reproducibility of the results.[(D. Yang et al., 2025b)]

Complexity of Traditional Medicines: The "multi-component, multi-target" approach of Traditional Chinese Medicine (TCM) is a challenge to traditional reductionist science. The complexity of analyzing macromolecular components, such as polysaccharides, is particularly challenging, as most prediction tools are applicable to small molecules.[(Tang et al., 2025)]

False Positives in Prediction: In silico prediction for oral bioavailability (OB) and drug-like (DL) compounds can result in false positives unless validated with in vivo data, including compounds that are absorbed in the serum.[(Wang et al., 2022b)]

Bridging the Gap to Clinical Practice: Most studies are limited to the theoretical and in silico approach. There is a long-standing shortage of high-quality Randomized Controlled Trials (RCT) to support the efficacy and long-term safety of the predicted mechanisms in practice. [(Tang et al., 2025)]

7.Future Directions

The evolution of network pharmacology is expected to follow these important paths:

Integration of Artificial Intelligence (AI) and Machine Learning (ML): The combined power of AI, ML, and bioinformatics will allow for better deciphering of complex biological networks, disease risk prediction, and at-risk population identification for ILD, etc.[(Vithalkar et al., 2025a)]

Multi-Omics Synergy: Next-generation network pharmacology will require the integration of transcriptomics, proteomics, and metabolomics to gain a finer resolution of drug-target interactions.[(Vithalkar et al., 2025a)]

The Paradigm of P4 Medicine: Network pharmacology is a fundamental pillar for the development of the new era of P4 medicine—Predictive, Personalized, Preventive, and Participatory**.**[(Vithalkar et al., 2025a)]

Enhanced TCM-Specific Metrics: In addition to the above, it is recommended that the database results be labeled with additional information concerning the "four qi and five flavors," "meridian," "monarch, minister, assistant, and guide," etc.[(D. Yang et al., 2025b)]

Drug Repositioning: Network pharmacology-based approaches will allow for efficient drug repositioning for new therapeutic uses, as exemplified by the quick identification of anti-COVID-19 drug candidates during the pandemic**.[(Vithalkar et al., 2025b)]**

Standardized Evaluation Protocols: Adoption of international guidelines, such as the "Network Pharmacology Evaluation Method Guidance," will ensure verification of results through a combination of computer models, experimental validation, and clinical data.[(Wang et al., 2022a)]

8.CONCLUSION

Network pharmacology represents a fundamental paradigm shift in drug discovery, moving the field away from the conventional "one drug, one target" model toward a "network target, multi-component" approach. By integrating systems biology, bioinformatics, and computational science, it provides a robust framework for understanding how complex herbal formulations restore balance to dysregulated biological networks.

This systematic paradigm has proven its utility in identifying bioactive compounds for a wide range of conditions, including liver cancer, chronic atrophic gastritis, diabetic complications, and infectious diseases like COVID-19. It serves as a vital bridge between ancient traditional wisdom and modern precision medicine, offering the potential to discover novel therapeutics with reduced toxicity and enhanced efficacy.

Despite the challenges of data quality and the need for more rigorous experimental validation, network pharmacology remains an essential tool for modernizing traditional medicines and accelerating the discovery of treatments for polygenic, complex diseases. The continued fusion of computational technology and experimental science will be the touchstone for future medicinal advancements, ensuring that network pharmacology achieves its full potential in improving patient outcomes globally.

REFERENCE

1. (Li & Kar, 2025) Leveraging network pharmacology for drug discovery: Integrative approaches and emerging insights
2. (Chandran et al., 2017) Network Pharmacology
3. (Zhai et al., 2025) Network pharmacology: a crucial approach in traditional Chinese medicine research
4. (Cui et al., 2025b) AI driven network pharmacology: Multi-scale mechanisms of traditional Chinese medicine from molecular to patient analysis
5. (Talevi, 2015) Multi-target pharmacology: Possibilities and limitations of the "skeleton key approach" from a medicinal chemist perspective
6. (Thombre et al., 2026) Network pharmacology in the multi-omics era: uncovering novel therapeutic strategies
7. (Chavan & Gite, n.d.) TOOLS AND SOFTWARE USED IN NETWORK PHARMACOLOGY STUDIES
8. (Noor et al., 2022b) Network Pharmacology Approach for Medicinal Plants: Review and Assessment
9. (Cui et al., 2025) AI driven network pharmacology: Multi-scale mechanisms of traditional Chinese medicine from molecular to patient analysis
10. (Fan et al., 2023) Multi-level advances in databases related to systems pharmacology in traditional Chinese medicine: a 60-year review
11. (Muthuramalingam et al., 2024) Network pharmacology: an efficient but underutilized approach in oral, head and neck cancer therapy—a review
12. (Merecz-Sadowska et al., 2025b) Network Pharmacology as a Tool to Investigate the Antioxidant and Anti-Inflammatory Potential of Plant Secondary Metabolites—A Review and Perspectives
13. (Li et al., 2023) Network pharmacology: a bright guiding light on the way to explore the personalized precise medication of traditional Chinese medicine
14. (L. Yang et al., 2025b) Network Pharmacology-Driven Sustainability: AI and Multi-Omics Synergy for Drug Discovery in Traditional Chinese Medicine

15. (Zhou et al., 2025) Dose-Weighted Network Pharmacology: Evaluating Traditional Chinese Medicine Formulations for Lumbar Disc Herniation
16. (Zahoránszky-Köhalmi et al., 2022) A Workflow of Integrated Resources to Catalyze Network Pharmacology Driven COVID-19 Research
17. (Sheils et al., 2020) How to Illuminate the Druggable Genome Using Pharos
18. (Li et al., 2024) Network Pharmacology, Molecular Docking, and Molecular Dynamics Simulation Analysis Reveal Insights into the Molecular Mechanism of Cordia myxa in the Treatment of Liver Cancer
19. (Weng et al., 2023) Medicine for chronic atrophic gastritis: a systematic review, meta- and network pharmacology analysis
20. (Zhang et al., 2025) Network Pharmacology Study on the Mechanisms of Panax Notoginseng in the Treatment of Diabetic Retinopathy and Cataract
21. (Y. Yang et al., 2025) An integrative analysis combining bioinformatics, network pharmacology and experimental methods identified key genes of EGCG targets in Nasopharyngeal Carcinoma
22. (D. Yang et al., 2025) Network pharmacology predicts targets and pathways of herbal components for the treatment of pneumonia: A review
23. (Vithalkar et al., 2025a) Network Pharmacology-driven therapeutic interventions for Interstitial Lung Diseases using Traditional medicines: A Narrative Review
24. (Wang et al., 2022) Methodology of network pharmacology for research on Chinese herbal medicine against COVID-19: A review.

HOW TO CITE: Sneha Saha1, Anuranjita Kundu*, Network Pharmacology in Drug Discovery: Concepts, Methodology, Applications and Future Perspectives, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 6, 7044-7057. https://doi.org/ 10.5281/zenodo.20963918