Computational Pharmacology Meets Phytopharmacology: A Scoping Review of Network-Based, Structure-Based, and Omics-Driven Discovery Strategies

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ABSTRACT

Computational pharmacology is increasingly reshaping phytopharmacology by enabling structured interpretation of medicinal plants, phytochemicals, botanical mixtures, molecular targets, biological pathways, and mechanism-oriented evidence. This scoping review maps how network-based computational pharmacology, structure-based phytochemical screening, and omics-driven mechanistic discovery are being used to support natural-product and phytopharmacological research. The review uses a scoping logic rather than an effectiveness-synthesis design, emphasizing evidence mapping, methodological classification, data-source transparency, validation practices, integration patterns, and research gaps. Network-based approaches are examined for their use in compound–target mapping, target prediction, disease-module analysis, protein–protein interaction networks, pathway enrichment, polypharmacology, and synergy hypothesis generation. Structure-based strategies are assessed for their roles in virtual screening, molecular docking, binding-mode assessment, molecular dynamics, pharmacophore modeling, QSAR where relevant, and ADMET prioritization. Omics-driven approaches are considered in relation to transcriptomics, proteomics, metabolomics, multi-omics integration, response signatures, biomarker discovery, and mechanism-of-action inference. Across these domains, the review highlights that computational convergence can strengthen hypothesis prioritization but cannot independently establish pharmacological mechanism, therapeutic efficacy, safety, or clinical relevance. Major limitations include database dependency, target-prediction uncertainty, pathway redundancy, hub overinterpretation, structural-model assumptions, scoring-function limitations, omics confounding, incomplete validation, and weak reproducibility. The review contributes an integrated conceptual map for computational–experimental phytopharmacology and identifies future priorities centered on transparent workflows, uncertainty-aware inference, orthogonal validation, standardized botanical characterization, and translationally meaningful evidence integration.

Key Words: *Computational pharmacology, Phytopharmacology, Network pharmacology, Phytochemicals, Molecular docking, Multi-omics*

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INTRODUCTION

Natural products continue to occupy an important position in pharmacological discovery because they provide chemically diverse scaffolds, biologically active metabolites, and historically productive starting points for therapeutic development. Contemporary natural-product research increasingly relies on computational approaches

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to prioritize compounds, contextualize biological activity, and connect chemical diversity with target- and pathway-level hypotheses, while historical analyses continue to show the enduring contribution of natural-product-derived compounds to pharmacotherapy [1, 2].

Plant-derived natural products present distinctive discovery challenges because medicinal plants and botanical preparations often contain heterogeneous mixtures of structurally diverse compounds that may act through multiple targets, context-dependent mechanisms, and variable pharmacokinetic or pharmacodynamic profiles. This chemical and biological complexity makes unstructured screening inefficient and strengthens the rationale for computational prioritization strategies that can organize plant chemical diversity into testable pharmacological hypotheses [3].

Computational phytopharmacology is also shaped by dependence on curated chemical, target, disease, interaction, and pathway databases. These resources allow researchers to connect phytochemicals with predicted targets and biological functions, but they also introduce coverage bias, annotation inconsistency, and uncertainty propagation when database-derived associations are treated as mechanistic evidence rather than as preliminary signals [4].

Network-based, structure-based, and omics-driven approaches have therefore become central to the methodological landscape of computational pharmacology applied to phytopharmacology. Network pharmacology can support systems-level reasoning about compound–target–pathway relationships and disease modules, but its outputs should be interpreted as hypothesis-generating rather than confirmatory unless supported by orthogonal pharmacological evidence [5]. The aim of this scoping review is to map how these computational strategies are used, integrated, validated, and limited in phytopharmacological discovery.

Scoping review rationale

A scoping review is appropriate for this interdisciplinary field because the evidence base is methodologically heterogeneous, conceptually broad, and distributed across pharmacology, phytopharmacology, natural-product chemistry, bioinformatics, network science, structural modeling, omics, and systems biology. Scoping review guidance supports this design when the objective is to map concepts, clarify evidence types, define methodological boundaries, and identify knowledge gaps rather than to estimate intervention effects or conduct pooled quantitative synthesis [6-8].

The review boundary is therefore defined around computational strategies used to investigate medicinal plants, phytochemicals, natural-product-derived compounds, botanical mixtures, pharmacological targets, protein–ligand interactions, biological pathways, disease-associated networks, omics signatures, and validation practices. It does not evaluate clinical efficacy, compare interventions, or infer causal treatment effects, because those aims require different evidence structures and appraisal methods [6].

The scoping questions focus on how network-based computational pharmacology is used for compound–target and disease-pathway mapping; how structure-based methods support phytochemical screening and binding-hypothesis generation; how transcriptomics, proteomics, metabolomics, and multi-omics contribute to mechanism-oriented interpretation; and how these strategies converge into integrated computational–experimental workflows. These questions require data charting across study type, natural-product context, computational method, data source, validation approach, integration pattern, and reported limitation [8].

The review uses transparent reporting principles to separate evidence identification, eligibility screening, data charting, methodological classification, validation mapping, and scoping synthesis. Critical appraisal is not framed as a formal risk-of-bias assessment for intervention effects; instead, methodological quality is addressed narratively through attention to database provenance, target-prediction assumptions, network construction, structural-protocol transparency, omics reproducibility, validation status, and risk of overclaiming [7].

Mapping strategy and evidence sources

The evidence-mapping strategy was designed to identify peer-reviewed journal literature relevant to computational pharmacology, phytopharmacology, natural products, medicinal plants, phytochemicals, network pharmacology, target prediction, molecular modeling, virtual screening, omics-driven mechanism discovery, and computational–experimental integration. Drug and target resources such as DrugBank were treated as important mapping references because they illustrate how structured drug-target annotations can support compound–target interpretation while still requiring caution when transferred to phytochemical and botanical contexts [9].

Search concepts combined computational pharmacology terms with phytopharmacology, medicinal-plant, phytochemical, natural-product, network, structural-modeling, and omics terms. Target-prediction tools were mapped as predictive resources rather than confirmatory evidence; for example, similarity-based platforms can prioritize plausible protein targets for small molecules, but predicted targets remain computational hypotheses until supported by biochemical, cellular, organismal, or translational evidence [10].

Protein–protein interaction resources were mapped because network pharmacology frequently depends on interaction graphs to identify candidate modules, hub nodes, disease-associated subnetworks, and pathway-level relationships. Such resources can support systems interpretation, but confidence scores, organism coverage, literature bias, and database incompleteness influence the resulting network topology and therefore affect downstream biological interpretation [11].

Pathway knowledgebases were mapped as interpretive resources for functional enrichment and mechanism-oriented synthesis. Curated pathway databases help organize predicted or measured targets into biological processes, but pathway enrichment should not be equated with direct pathway modulation because enrichment reflects annotation overlap, statistical representation, and database structure rather than causal pharmacological regulation [12].

Table 1 summarises the scoping review mapping framework used to identify, screen, chart, classify, and synthesize evidence at the intersection of computational pharmacology and phytopharmacology.

Table 1. Scoping Review Mapping Framework for Computational Pharmacology and Phytopharmacology: Evidence Sources, Search Concepts, Eligibility Criteria, Screening Logic, Data-Charting Fields, Analytical Domains, Validation Categories, and Reporting Safeguards

Mapping component	Operational definition	Implementation rule	Evidence field required	Classification dimension	Quality-control action	Potential limitation	Reporting requirement
Evidence-source identification	Locating journal literature relevant to computational phytopharmacology	Search multidisciplinary scholarly databases and publisher platforms using combined pharmacology, natural-product, network, structure, and omics terms	Database or source type	Evidence origin	Remove duplicate records by DOI, title, year, and journal	Exact database counts are not reported when not count-auditable	Do not invent search or screening numbers
Search concepts	Conceptual blocks used to retrieve relevant evidence	Combine computational pharmacology, phytopharmacology, medicinal plants, natural products, target prediction, docking, virtual screening, and omics terms	Search concept category	Topic domain	Check whether retrieved studies match at least one review question	Search sensitivity may vary across platforms	Report search logic without overstating completeness
Eligibility criteria	Rules determining whether evidence is relevant	Include peer-reviewed journal articles with DOI information and direct methodological relevance	Study type, DOI, domain fit	Inclusion/exclusion status	Exclude non-peer-reviewed and weak-fit sources	Some relevant methods may be underrepresented if poorly indexed	State eligibility boundaries clearly
Screening logic	Sequential review of relevance and methodological fit	Screen title, abstract, and available full text or metadata	Reason for inclusion or exclusion	Screening stage	Apply domain relevance and methodological-detail checks	Full reproducibility is limited without exported record logs	Avoid PRISMA-style counts unless verified
Data charting	Structured extraction of evidence fields	Extract method type, natural-product context, computational strategy, data source, validation	Charting field completion	Evidence attribute	Mark absent information as not clearly reported	Reporting quality varies by article	Do not infer unreported data

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		approach, and limitation					
Analytical-domain classification	Assignment to network-based, structure-based, omics-driven, or integrative domains	Classify each source by primary and secondary computational role	Primary strategy and secondary strategy	Discovery domain	Check that classification matches manuscript claim	Some studies span multiple domains unevenly	Avoid forcing a single-domain interpretation
Validation mapping	Identification of how computational claims are tested or supported	Distinguish computational consistency, experimental validation, in vivo evidence, and translational relevance	Validation type	Evidence strength	Separate prediction from validation	Validation may be partial or indirect	State validation level cautiously
Reporting safeguards	Controls against overclaiming and unsupported synthesis	Use cautious language for predicted targets, docking poses, pathway enrichment, and omics associations	Overclaiming risk	Interpretation category	Reject claims unsupported by charted evidence	Computational convergence may be mistaken for proof	Distinguish hypothesis generation from pharmacological validation

Network-based computational pharmacology

Network-based computational pharmacology provides a systems-oriented framework for organizing relationships among phytochemicals, predicted targets, biological pathways, disease-associated genes, and multi-component botanical preparations. In phytopharmacology, this approach is frequently used to convert complex medicinal-plant information into compound–target networks, target–pathway maps, and disease-relevant interaction structures that can support mechanistic hypothesis generation [13].

Systems pharmacology has particular relevance for botanical and traditional medicine research because multi-component preparations may contain compounds with overlapping, complementary, or context-dependent target profiles. However, the value of a network workflow increases when computational predictions are connected to experimental or clinical evidence streams rather than being presented as standalone confirmation of pharmacological mechanism [14].

Formula-focused and botanical network pharmacology commonly uses target prediction, disease-gene retrieval, protein–protein interaction mapping, functional enrichment, and mechanism-oriented visualization to infer candidate pathways. These steps can help prioritize research directions, but the resulting mechanisms are sensitive to compound selection, database coverage, disease-term definition, target-prediction thresholds, and pathway redundancy [15].

A major limitation of network-based phytopharmacology is that database choices and network-construction rules can alter the inferred mechanism. Predicted targets may be false positives, high-degree nodes may reflect literature or database bias, and pathway enrichment may reflect annotation density rather than true biological modulation; therefore, hub status or centrality should not automatically be interpreted as causal pharmacological importance [16].

Contemporary network pharmacology workflows increasingly combine compound–target mapping, disease-network construction, PPI analysis, enrichment interpretation, and visualization, but these outputs require careful biological framing and validation planning [17]. Integrated examples that combine network pharmacology with docking and experimental checking illustrate how computational analysis can guide follow-up research, provided that predicted interactions, docking poses, and pathway hypotheses remain distinct from validated pharmacological mechanisms [18].

Table 2 maps major network-based computational pharmacology strategies according to input data, analytical objective, network representation, biological interpretation, validation requirement, and phytopharmacological relevance.

Table 2. Network-Based Computational Pharmacology Strategies in Phytopharmacology: Data Sources, Network Representations, Target-Prediction Approaches, Systems-Level Outputs, Validation Requirements, Methodological Limitations, and Discovery Relevance

Network-based strategy	Typical input data	Network representation	Primary analytical objective	Typical computational output	Biological interpretation	Validation requirement	Main methodological limitation	Phytopharmacological relevance
Compound–target network mapping	Phytochemical lists, predicted targets, curated target annotations	Bipartite compound–target graph	Identify candidate target space for phytochemicals	Predicted compound–target links	Suggests possible pharmacological interaction space	Biochemical or cellular target engagement testing	Target predictions may be incomplete or false positive	Useful for prioritizing phytochemicals and candidate mechanisms
Target fishing	Chemical structures, similarity data, pharmacophore or bioactivity annotations	Compound-to-protein prediction map	Infer possible protein targets for compounds with incomplete annotation	Ranked candidate targets	Generates target hypotheses	Orthogonal target validation and activity assays	Similarity-based inference depends on training data and known ligand space	Important for under-characterized phytochemicals
Protein–protein interaction analysis	Predicted targets, disease genes, PPI databases	Target–target or disease-module network	Identify interaction neighborhoods and candidate modules	PPI subnetworks, hub nodes, modules	Supports systems-level context for predicted targets	Perturbation experiments and disease-relevant model testing	Literature bias, confidence-score uncertainty, and hub overinterpretation	Helps connect phytochemical targets to disease biology
Disease-module mapping	Disease-associated genes, predicted targets, pathway annotations	Disease–target overlap or module graph	Relate phytochemical targets to disease-associated biological regions	Candidate disease modules	Suggests possible disease-relevant mechanisms	Disease-model validation and causal testing	Disease-gene lists vary by source and definition	Supports mechanism prioritization for botanical interventions
Pathway enrichment	Predicted or measured target sets, pathway databases	Target-to-pathway annotation network	Identify overrepresented biological functions	Enriched pathways or functional categories	Indicates pathway-level association	Functional assays and pathway-activity measurements	Enrichment does not prove pathway modulation	Useful for organizing multi-target phytochemical effects
Hub and centrality analysis	PPI or compound–target networks	Ranked network nodes	Identify structurally prominent nodes	Degree, betweenness, closeness, or related rankings	Suggests network prominence, not causality	Node-specific perturbation and rescue experiments	Centrality can reflect database bias or network topology artifacts	Helps prioritize but must not define “key targets” without validation
Polypharmacology mapping	Multiple compounds, multiple targets, pathway annotations	Multi-layer compound–target–pathway graph	Explore multi-target activity patterns	Overlapping target and pathway profiles	Suggests coordinated or distributed pharmacological hypotheses	Multi-target pharmacology and phenotypic validation	Interaction effects are often inferred rather than tested	Relevant to botanical mixtures and multi-component preparations
Synergy hypothesis mapping	Compound combinations, predicted targets,	Combination-target-pathway network	Generate hypotheses about complementa	Candidate synergistic target/pathway patterns	Suggests possible cooperative activity	Combination-index studies, dose-response	Network complementarity does not prove synergy	Useful for designing experiments on botanical mixtures

	pathway relations		ry mechanisms			assays, and mechanistic testing		
Network-docking integration	Predicted targets, selected compounds, protein structures	Network-prioritized structural workflow	Prioritize target–compound pairs for structural assessment	Candidate docked interactions	Adds structural plausibility to network hypotheses	Binding assays and functional validation	Docking may reinforce false-positive network targets	Bridges systems-level and structure-level prioritization

Structure-based phytochemical screening

Structure-based phytochemical screening provides a complementary perspective to network pharmacology by evaluating whether a phytochemical or natural-product-derived compound is structurally compatible with a candidate protein site. Molecular docking and virtual screening can support prioritization of compounds and targets, especially when natural-product libraries are large and experimental screening capacity is limited, but these approaches should be interpreted as structural hypothesis-generation methods rather than direct demonstrations of binding or efficacy [19-21].

ADMET and drug-likeness prediction tools are frequently used after initial structural prioritization to identify compounds with more plausible pharmacokinetic or medicinal-chemistry profiles. These tools can help deprioritize compounds with unfavorable predicted absorption, distribution, metabolism, excretion, or toxicity characteristics, but predicted ADMET behavior does not demonstrate safety, exposure, tolerability, or therapeutic suitability in biological systems [22].

Integrated structure-based workflows may combine pharmacophore modeling, virtual screening, molecular docking, ADMET filtering, and molecular dynamics simulation to refine candidate compounds before experimental testing. Such workflows can improve prioritization by assessing complementary features such as interaction patterns, binding-site compatibility, predicted physicochemical behavior, and simulated complex stability; however, they remain dependent on protein-structure quality, ligand preparation, force-field assumptions, and the biological relevance of the selected target model [23].

QSAR-based virtual screening is relevant when phytochemical or natural-product datasets contain sufficient structural and activity information to support model development or compound ranking. Its value depends on transparent descriptor selection, applicability-domain assessment, appropriate validation, and avoidance of overextending predictions to chemical spaces not represented in the training data [24].

The principal interpretive challenge in structure-based phytochemical screening is the temptation to overstate computational outputs. A docking score is not equivalent to binding affinity, a predicted binding pose is not proof of target engagement, a stable simulated trajectory is not evidence of therapeutic efficacy, and predicted ADMET behavior is not demonstrated safety; each output should instead be treated as a prioritization signal requiring biochemical, biophysical, cellular, in vivo, or translational confirmation [19].

Omics-driven mechanistic discovery

Omics-driven mechanistic discovery expands computational phytopharmacology beyond predicted compound–target interactions by mapping biological responses associated with phytochemicals, medicinal plants, botanical mixtures, or natural-product-derived compounds. Metabolomics is especially relevant because it can profile plant chemical composition, characterize natural-product diversity, support metabolite annotation, and help connect chemical features with pharmacological or biosynthetic hypotheses [25].

Proteomics can contribute to phytopharmacological mechanism mapping by identifying changes in protein abundance, post-translational patterns, pathway-level protein responses, and cellular processes that may be affected by medicinal-plant extracts or bioactive natural compounds. These outputs can strengthen biological interpretation, but protein-level associations still require careful validation before being treated as evidence of causal pharmacological action [26].

Medicinal-plant metabolomics also highlights important reproducibility challenges, including variability in plant source, harvest conditions, extraction protocols, analytical platforms, ionization behavior, metabolite annotation confidence, and data-processing pipelines. These issues matter because poorly controlled metabolomics workflows can produce apparent chemical or mechanistic differences that reflect technical or biological variability rather than meaningful pharmacological effects [27].

Multi-omics approaches can integrate transcriptomics, proteomics, metabolomics, and related data layers to provide richer context for biosynthetic pathways, response signatures, bioactive potential, and mechanism-oriented hypotheses. However, multi-omics integration does not automatically resolve confounding, establish causal direction, or validate a target; it must be supported by

transparent integration logic, external confirmation, and biologically appropriate experimental models [28].

Artificial intelligence and multi-omics integration are increasingly discussed as ways to improve natural-product discovery by linking chemical information, biological signatures, and mechanism-oriented datasets. Their translational value will depend on data provenance, model interpretability, benchmark quality, uncertainty reporting, and prospective validation rather than on algorithmic complexity alone [29].

Table 3 compares network-based, structure-based, and omics-driven discovery strategies by evidentiary role, analytical output, integration potential, validation requirement, and major failure risk.

Table 3. Comparative Mapping of Network-Based, Structure-Based, and Omics-Driven Discovery Strategies in Computational Phytopharmacology: Inputs, Analytical Outputs, Mechanistic Roles, Integration Opportunities, Validation Needs, Translational Relevance, and Failure Risks

Discovery strategy	Primary input	Core analytical method	Typical output	Mechanistic role	Integration opportunity	Validation requirement	Main strength	Major failure risk	Translational relevance
Network-based computational pharmacology	Phytochemical lists, predicted targets, disease genes, PPI networks, pathway databases	Compound–target mapping, target prediction, disease-module analysis, enrichment, network topology	Candidate targets, modules, pathways, hub nodes, polypharmacology hypotheses	Generates systems-level hypotheses about multi-target and pathway relationships	Can guide docking target selection and omics pathway interpretation	Target engagement, pathway perturbation, phenotypic testing, disease-model validation	Organizes complex botanical systems into interpretable biological maps	Database bias, false-positive targets, hub overinterpretation, pathway redundancy	Useful for prioritizing targets and mechanisms but insufficient alone for translation
Structure-based phytochemical screening	Chemical structures, protein structures, binding-site models, compound libraries	Virtual screening, molecular docking, pharmacophore modeling, molecular dynamics, QSAR, ADMET prediction	Ranked compounds, predicted binding poses, interaction patterns, simulated stability, predicted ADMET profiles	Assesses structural plausibility of compound–target hypotheses	Can test network-prioritized targets and refine candidate phytochemicals	Binding assays, enzymatic assays, cellular target engagement, pharmacokinetic and toxicity testing	Provides molecule-level prioritization and interaction hypotheses	Scoring-function error, protein-model uncertainty, ligand-preparation artifacts, overinterpretation of docking or MD	Useful for lead prioritization when followed by experimental confirmation
Omics-driven mechanistic discovery	Transcriptomic, proteomic, metabolomic, lipidomic, or multi-omics datasets	Differential profiling, pathway analysis, signature mapping, biomarker discovery, integration modeling	Response signatures, altered pathways, candidate biomarkers, mechanism hypotheses	Links phytochemical or botanical exposure to biological response patterns	Can support or challenge network and structural predictions through response-level evidence	Independent cohorts, orthogonal assays, time-course validation, causal perturbation testing	Captures biological response complexity across molecular layers	Batch effects, small samples, confounding, tissue specificity, correlation mistaken for causality	Useful for mechanism refinement and biomarker prioritization but requires external validation
Network–structure integration	Network-prioritized compounds and targets plus protein structures	Target selection followed by docking, pharmacophore modeling, or MD	Structurally prioritized target–compound pairs	Adds structural plausibility to network hypotheses	Connects systems-level mapping with molecule-level assessment	Binding and functional assays against prioritized targets	Reduces search space for structural screening	Docking may reinforce false-positive network predictions	Supports focused experimental planning

Structure–omics integration	Structurally prioritized compounds plus omics response data	Compare predicted interactions with expression, protein, or metabolite signatures	Concordant or discordant structure–response evidence	Tests whether predicted interactions align with biological response patterns	Links molecular compatibility with cellular or tissue-level signatures	Perturbation experiments and mechanistic rescue studies	Helps distinguish plausible binding hypotheses from biologically irrelevant predictions	Omics associations may be indirect or confounded	Supports mechanism refinement when response data are strong
Network–omics integration	Predicted targets, disease modules, pathway maps, omics signatures	Overlay of target networks with transcriptomic, proteomic, or metabolomic response profiles	Mechanism maps, enriched response modules, candidate biomarkers	Connects predicted targets with measured biological changes	Can identify pathway concordance or reveal conflicts	Orthogonal validation and causal testing	Strengthens systems-level interpretation	Shared pathway databases can amplify annotation bias	Useful for biomarker and pathway prioritization
Full network–structure–omics convergence	Phytochemical data, target predictions, structures, pathway data, and omics profiles	Evidence triangulation across systems, structural, and response layers	Prioritized compounds, targets, pathways, biomarkers, and validation agenda	Builds mechanistic plausibility across independent evidence layers	Supports staged computational–experimental workflows	Biochemical, cellular, in vivo, pharmacokinetic, toxicological, and translational validation	Provides the richest hypothesis-prioritization framework	Computational convergence may be mistaken for causal proof	Potentially valuable for translation only when experimentally anchored

Scoping synthesis

The mapped evidence indicates that network-based, structure-based, and omics-driven strategies occupy complementary positions in computational phytopharmacology. Network approaches organize phytochemical, target, disease, and pathway information into systems-level hypotheses; structure-based approaches test whether selected compound–target pairs are chemically and spatially plausible; and omics-driven approaches examine whether biological response signatures align with predicted mechanisms. Integrated network–docking workflows illustrate this convergence, but they also show why computational agreement should not be treated as experimental validation [30].

A useful convergence architecture begins with phytochemical or botanical information, proceeds through compound–target and disease-network mapping, refines candidate target–compound relationships through structural screening, and then uses omics data to assess whether predicted mechanisms correspond to measurable biological response patterns. Emerging platforms that integrate chemical profiles, target prediction, and biological signatures can support this type of mechanism exploration, provided that users preserve uncertainty and avoid treating platform output as proof of mechanism [31]. Knowledge-graph approaches further illustrate how heterogeneous natural-product evidence can be organized across compounds, targets, pathways, pharmacokinetic processes, drug interactions, and contextual biomedical knowledge. Such frameworks may support translational safety assessment and hypothesis prioritization, but their outputs remain dependent on ontology quality, evidence provenance, literature coverage, and the ability to distinguish asserted relationships from experimentally confirmed mechanisms [32].

Figure 1 illustrates the convergent discovery architecture linking network-based computational pharmacology, structure-based phytochemical screening, omics-driven mechanistic discovery, and experimental validation.

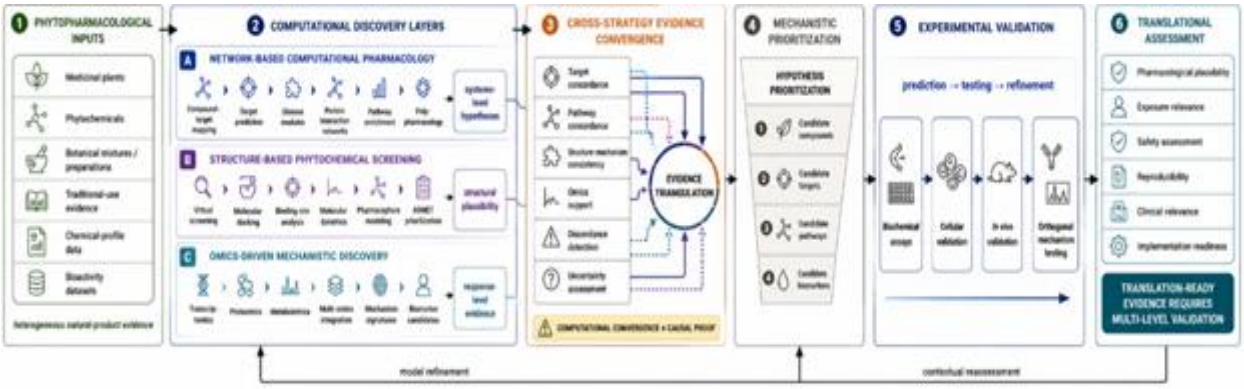

Figure 1. Integrated Computational–Experimental Convergence Framework for Phytopharmacological Discovery

Alt-text description

A left-to-right conceptual framework showing medicinal plants and phytochemical data entering three coordinated analytical domains: network-based computational pharmacology, structure-based phytochemical screening, and omics-driven mechanistic discovery. Outputs converge in an evidence-integration layer that supports mechanism hypotheses, compound prioritization, target prioritization, and biomarker identification before progressing through in vitro, in vivo, and translational validation. Feedback arrows return validated evidence to computational model refinement.

The synthesis also shows that different computational domains can generate both concordant and conflicting evidence. A target predicted by similarity-based methods may not be structurally plausible for a phytochemical; a favorable docking pose may not correspond to measured cellular response; and an omics signature may implicate a pathway that is absent from the initial network model. Such conflicts are not failures of the scoping framework but important signals that computational outputs require staged interpretation and experimental resolution [30].

The comparatively mature part of the field is the availability of databases, target-prediction tools, pathway resources, network visualization workflows, docking pipelines, and omics platforms. The less mature part is the systematic connection of these outputs to transparent validation, reproducible reporting, exposure-relevant pharmacology, botanical standardization, and translational decision-making. Cross-strategy synthesis is therefore most valuable when it produces a ranked validation agenda rather than a claim that computational convergence alone has established mechanism, efficacy, or safety [32].

Research gaps

A central research gap concerns reproducibility and transparency in network pharmacology of natural products. Future studies should report database versions, compound-selection rules, target-prediction thresholds, disease-gene sources, PPI confidence settings, enrichment parameters, negative controls, and sensitivity analyses so that inferred mechanisms can be independently inspected rather than accepted as opaque network outputs [33].

A second gap concerns phytopharmacological translation. Computational workflows often begin with plant names, extract descriptions, or phytochemical lists, but translation requires standardized botanical identity, preparation methods, chemical characterization, dose and exposure context, pharmacokinetic plausibility, safety assessment, and alignment between computational targets and biologically achievable concentrations [34].

A third gap lies in the overinterpretation of convergent computational outputs. Future network–structure–omics workflows should explicitly quantify uncertainty, test whether conclusions change under alternative databases or thresholds, include negative or decoy comparisons where appropriate, and distinguish concordance from causality. Hub nodes, enriched pathways, docking poses, stable simulations, and omics signatures should be framed as prioritization evidence unless supported by direct pharmacological testing [33].

A fourth gap concerns the need for experimentally anchored computational pharmacology. Future research should prioritize prospective validation, orthogonal assays, causal perturbation, transparent benchmarking, open workflows, code and data availability, external validation datasets, standardized multi-omics integration, and feedback loops in which experimental results refine computational assumptions. Such priorities are essential for moving computational phytopharmacology from attractive mechanism maps toward reliable, reproducible, and translationally meaningful evidence [34].

CONCLUSION

This scoping review maps the convergence of computational pharmacology and phytopharmacology across network-based, structure-based, and omics-driven discovery strategies. These approaches can support hypothesis generation, compound prioritization, target

prioritization, pathway interpretation, mechanism mapping, biomarker discovery, and evidence integration, but they do not independently establish pharmacological mechanism, therapeutic efficacy, safety, or clinical utility. Reliable translation depends on data quality, methodological transparency, reproducibility, uncertainty awareness, botanical standardization, pharmacological context, orthogonal experimentation, and multi-level validation. The most productive future direction is not to replace experimental pharmacology with computational inference, but to use computational methods to design clearer, more testable, and more translationally responsible phytopharmacological research.

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