Mechanism-First Phytochemical Therapeutics: Integrating Target Prediction, Pathway Enrichment, Phenotypic Effects, and Disease Network Biology

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ABSTRACT

Phytochemical therapeutics occupy a difficult translational space because structurally diverse natural compounds often generate broad biological signals before their mechanisms are clearly established. Target prediction, pathway enrichment, phenotypic screening, and disease-network analysis each contribute useful mechanistic clues, but none can independently justify a therapeutic claim. This article develops an original mechanism-first framework for phytochemical therapeutics that prioritizes construction of testable mechanistic hypotheses before claims of efficacy, safety, or clinical relevance. The framework synthesizes four central evidence domains: predicted or associated targets, enriched or annotated pathways, observed phenotypic effects, and disease-network biology. It proposes that these evidence streams should be interpreted through contextual checks, uncertainty mapping, contradiction visibility, and validation-readiness assessment. The principal contribution is a qualitative mechanistic architecture that distinguishes predicted targets from target engagement, pathway enrichment from pathway modulation, phenotypic response from mechanism, and disease-network association from causal disease biology. The framework is intended to help researchers move from isolated computational or phenotypic outputs toward validation-ready therapeutic hypotheses, while remaining explicitly conceptual rather than experimentally validated.

Key Words: *Phytochemicals, Mechanism-first discovery, Target prediction, Pathway enrichment, Phenotypic screening, Disease networks*

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INTRODUCTION

Phytochemical therapeutics increasingly sit at the intersection of natural product chemistry, pharmacology, computational biology, and translational drug discovery. Their mechanistic interpretation is difficult because a structurally defined compound, compound class, extract, or formulation may generate multiple biological associations across targets, pathways, cell states, and disease contexts. Systems pharmacology has helped frame this complexity by emphasizing integration of heterogeneous molecular and pharmacological data rather than isolated target interpretation [1].

For phytochemical research, the implication is not that complexity itself establishes mechanism, but that mechanism must be constructed from coordinated evidence.

The central difficulty is that many phytochemicals are biologically pleiotropic, chemically diverse, and frequently studied through incomplete evidence streams. A target prediction result may appear mechanistically persuasive even when no target engagement experiment has been performed; a phenotypic improvement may

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appear therapeutic even when its causal target remains unknown. Quantitative systems pharmacology has shown that model-informed discovery depends on explicit assumptions, biological context, and translational decision logic rather than uninterpreted model outputs [2]. This principle is especially important for phytochemical therapeutics, where incomplete chemical definition or broad bioactivity can easily encourage overinterpretation.

Computational and experimental evidence streams now make it possible to generate mechanistic hypotheses at several levels. Target prediction can suggest candidate protein interactions, pathway enrichment can organize target or gene lists into functional themes, phenotypic assays can show cellular or disease-model responses, and disease networks can contextualize molecular relationships in pathobiology. Recent work combining systems pharmacology and machine-learning perspectives illustrates that such evidence must be interpreted through disease-specific assumptions and model boundaries [3]. Mechanism-first phytochemical therapeutics therefore requires more than accumulating positive signals across platforms.

The main risk is interpretive inflation. A predicted target is not a confirmed target; a docking or affinity estimate is not target engagement; pathway enrichment is not pathway modulation; a phenotype is not necessarily a mechanism; and network proximity is not therapeutic efficacy. These distinctions are not semantic details. They define whether a phytochemical claim remains a computational hypothesis, becomes a validation-ready mechanism, or becomes an unsupported therapeutic assertion.

This article proposes a mechanism-first framework for phytochemical therapeutics that coordinates target prediction, pathway enrichment, phenotypic effects, and disease-network biology. The objective is not to review every method in these fields, but to develop a decision architecture for converting heterogeneous evidence into appropriately qualified mechanistic hypotheses. The framework emphasizes context definition, evidence filtering, cross-domain alignment, contradiction mapping, and validation readiness. Its original contribution is a structured interpretive model that prevents any single computational or phenotypic output from dominating therapeutic interpretation.

Mechanism-first therapeutic discovery

Mechanism-first therapeutic discovery begins by defining the biological question before ranking compounds, targets, pathways, or disease modules. In phytochemical research, this means specifying the compound or phytochemical class, the disease or phenotype of interest, the relevant tissue or cell context, and the expected biological direction of effect. Without these boundaries, the same predicted target or enriched pathway can be interpreted differently across inflammatory, metabolic, neurodegenerative, antimicrobial, or oncological contexts. A mechanism-first approach therefore treats context as the condition that makes evidence interpretable.

This orientation differs from compound-first screening. Compound-first workflows may begin with broad bioactivity and only later search for molecular explanations. Such workflows can be productive, but they become mechanistically weak when the observed effect is retrofitted to a convenient target or pathway. Mechanism-first reasoning does not require complete certainty at the beginning. It requires that uncertainty be visible and that each claim remain proportional to the evidence supporting it.

Mechanism-first discovery also differs from target-list accumulation. In phytochemical therapeutics, a long predicted target list can create an impression of systems-level activity, yet target quantity is not mechanistic strength. A useful mechanism links a compound or class to plausible target modulation, pathway-level consequence, phenotypic effect, disease-network relevance, and validation requirement. The relevant question is not how many targets are predicted, but whether a coherent and testable target–pathway–phenotype–disease chain can be constructed.

Pathway-list interpretation creates a parallel risk. Enrichment outputs often contain biologically familiar terms such as inflammation, apoptosis, oxidative stress, metabolism, or immune response, but such terms can be too broad to establish mechanism. A pathway becomes mechanistically informative only when its relation to the target set, assay system, disease context, and phenotypic direction is explained. Mechanism-first reasoning therefore treats pathway enrichment as an interpretive layer rather than a causal conclusion.

Phenotypic evidence is equally important and equally limited. A phenotypic effect can constrain mechanistic hypotheses by showing whether the biological response is compatible with a proposed target and pathway chain. However, phenotype alone cannot identify the target, prove direct pathway control, or establish therapeutic relevance. The conceptual differences between mechanism-first discovery and weaker mechanism-inference practices are summarized in **Table 1**.

Table 1. Conceptual Distinctions between Mechanism-First Discovery and Weak Mechanism Inference in Phytochemical Therapeutics

Inference practice	Intended role	Common overinterpretation	Missing mechanistic requirement	Risk for phytochemical therapeutics	Required mechanism-first correction
Target prediction	Generate candidate target hypotheses	Predicted target is treated as confirmed mechanism	Target engagement and functional modulation evidence	Inflated target lists create false mechanistic confidence	Filter targets by applicability, prior evidence, disease relevance, and validation need
Docking-informed inference	Assess binding plausibility	Docking score is treated as target engagement	Biophysical or cellular engagement evidence	Apparent affinity substitutes for pharmacology	Treat docking as supportive plausibility only
Pathway enrichment	Organize targets or genes into functional themes	Enriched pathway is treated as modulated pathway	Directional and context-specific pathway perturbation evidence	Generic pathways are overread as therapeutic mechanisms	Interpret enrichment relative to context, topology, and phenotype
Phenotypic observation	Show biological response	Phenotype is treated as mechanism or therapeutic effect	Causal connection to target and pathway	Broad bioactivity is mistaken for disease-relevant action	Anchor phenotype to target, pathway, exposure, and disease model
Disease-network proximity	Contextualize targets in disease biology	Network proximity is treated as efficacy	Causal disease relevance and compound-action evidence	Disease association becomes therapeutic claim	Integrate network evidence with target, pathway, and phenotype alignment
Natural-product origin	Provide chemical and discovery context	Natural origin is treated as relevance or safety	Mechanistic and safety validation	Traditional or natural status substitutes for evidence	Separate discovery value from mechanistic and therapeutic validation

Target prediction and pathway enrichment

Target prediction provides one entry point into phytochemical mechanism construction because it can nominate proteins that may plausibly interact with a compound or compound class. Current approaches include ligand similarity, chemogenomic inference, deep-learning drug–target interaction prediction, graph-based affinity prediction, machine-learning target classification, docking-informed hypotheses, and polypharmacology-oriented target prediction [4–10]. In a mechanism-first framework, these approaches are valuable because they generate structured target hypotheses. They are not sufficient to establish binding, cellular engagement, functional modulation, or disease relevance.

The first interpretive requirement is target credibility. A predicted target should be assessed in relation to chemical-space applicability, training-set bias, target-class bias, compound quality, prior pharmacology, and biological context. Chemically similar molecules may diverge biologically, and benchmark performance may not generalize to structurally unusual phytochemicals. A predicted target can therefore be upgraded only when additional evidence supports plausibility, while targets outside the model's credible domain should remain provisional. This filtering prevents the framework from treating target abundance as mechanistic depth.

Pathway enrichment then asks whether candidate targets or perturbation-derived genes can be organized into meaningful biological functions. Functional enrichment platforms support conversion of gene or target lists into interpretable categories, biological processes, and pathway terms [11]. This function is useful because target prediction alone often produces a list that is too fragmented to support mechanistic reasoning. The framework therefore uses enrichment to identify candidate functional structure, not to declare causal pathway control.

Curated pathway resources further support this interpretive step by providing structured biological knowledge. Reactome offers pathway and reaction-level annotations that can help position molecular entities within organized biological processes [12]. Such resources are essential for translating target lists into mechanistic language, but their presence in a pathway database does not prove that a phytochemical activates or inhibits that pathway in a given cell type. The pathway resource provides a map; it does not itself provide the perturbation evidence.

KEGG similarly supports pathway-level mapping across cellular and organismal systems [13]. For phytochemical therapeutics, these resources can help identify whether predicted targets cluster around metabolism, inflammation, stress responses, signal transduction, or other processes. However, pathway redundancy, incomplete annotation, pathway overlap, and context-free interpretation can

distort mechanistic conclusions. A pathway that is richly annotated may appear important because it is well represented in the database, not because it is pharmacologically controlled in the biological system under study.

The strongest target-to-pathway inference is not the most statistically striking term, but the most biologically coherent and contextually relevant explanation of the evidence. Enrichment methods and results are affected by input gene lists, background selection, database choice, statistical assumptions, and biological question framing [11, 14–16]. Directionality is especially important: overrepresentation does not show whether a pathway is activated, inhibited, compensated, or merely annotated. The methodological roles and interpretation limits of target prediction and pathway enrichment are organized in **Table 2**.

Table 2. Methodological Roles and Interpretation Limits of Target Prediction and Pathway Enrichment

Evidence stream	Intended mechanistic contribution	Key methodological input	Major interpretive risk	Required contextual check	Validation requirement	Inappropriate inference to avoid
Ligand-based target prediction	Nominate plausible targets from chemical similarity	Chemical structure and known ligand-target relationships	Similarity may not preserve biological action	Applicability to phytochemical scaffold and target class	Binding or engagement testing	Similar compound means same mechanism
Machine-learning target prediction	Rank candidate interactions	Molecular representation and trained prediction model	Training-set and target-class bias	Model domain, benchmark setting, and uncertainty	Independent target evidence	Model prediction confirms target
Graph-based affinity prediction	Estimate interaction plausibility from molecular graphs	Compound graph and protein representation	Predicted affinity lacks cellular context	Chemical novelty and protein-class coverage	Biophysical and cellular validation	Predicted affinity equals functional modulation
Docking-informed target hypothesis	Explore binding plausibility	Structural model and docking protocol	Score overinterpretation	Protein structure quality and binding-site relevance	Target engagement assay	Docking score proves engagement
Target-to-pathway mapping	Organize targets into functional themes	Candidate target list and pathway resource	Target-list inflation drives broad enrichment	Filtered target evidence and disease context	Perturbation-based pathway assessment	Target list proves pathway control
Gene-set enrichment	Interpret omics or target lists	Gene list, background set, statistical method	Database and background dependence	Cell type, disease stage, directionality	Orthogonal pathway readout	Enrichment proves pathway modulation
Pathway topology interpretation	Add structural pathway context	Pathway graph or interaction topology	Topology mistaken for causality	Upstream/downstream direction and phenotype match	Functional perturbation testing	Topological position proves causal role

Phenotypic effects and disease networks

Phenotypic evidence provides a second kind of constraint because it asks what biological response is actually observed after exposure to a compound or phytochemical class. Phenotypic drug discovery has produced important therapeutic insights, but mechanism elucidation often remains necessary after a phenotype is observed [17]. In phytochemical therapeutics, this distinction is crucial because anti-inflammatory, antioxidant, cytotoxic, metabolic, neuroprotective, antimicrobial, or immunomodulatory effects can arise through multiple direct and indirect mechanisms. A phenotype can support a mechanistic hypothesis only when it is interpreted in relation to target and pathway evidence.

High-content screening expands phenotypic evidence by measuring cellular features that are not captured by single endpoint assays. Image-based high-content approaches can quantify complex cellular states and response patterns relevant to drug discovery [18]. These data can help identify whether a phytochemical response is specific, broad, toxic, adaptive, or compatible with a proposed pathway. Yet the image-derived phenotype still does not identify the causal target without further evidence.

Transcriptomic phenotyping adds another layer by describing compound-induced molecular signatures. Large-scale perturbational resources such as L1000 demonstrate how gene-expression profiles can connect compounds, biological states, and inferred mechanisms [19]. For mechanism-first phytochemical therapeutics, transcriptomic signatures can test whether the observed phenotype is compatible with the predicted target and enriched pathway pattern. Their limitation is that

association or reversal of a signature does not prove direct pathway control.

Morphological profiling can also contribute to mechanism comparison. Cell Painting datasets show that small-molecule treatments can produce high-dimensional morphology profiles useful for grouping perturbations and comparing cellular responses [20]. These profiles may reveal whether a phytochemical resembles known perturbation classes or produces a distinct phenotype. However, morphological similarity does not establish therapeutic relevance, target engagement, or disease mechanism.

The interpretive problem becomes more difficult when phenotypic evidence is strong but molecular anchoring is weak. A robust cellular response may be biologically meaningful while still leaving target identity unresolved. High-content imaging and data science approaches show that assay design, feature extraction, and interpretive context strongly influence the meaning of phenotypic profiles [21]. The framework therefore treats phenotypes as constraining evidence: they can support, weaken, or redirect a proposed mechanism, but they should not replace mechanism construction.

Disease-network biology provides the fourth evidence domain by locating targets, pathways, and phenotypes in disease-relevant molecular architecture. Interactome models, disease modules, drug-repurposing proximity, multi-layer network signatures, and topological measures can contextualize candidate mechanisms, but they do not independently prove causal disease biology or therapeutic efficacy [22–27]. The strongest mechanistic pattern arises when predicted or associated targets map to contextually meaningful pathways, the phenotype is compatible with that pathway logic, and the target–pathway–phenotype chain is positioned plausibly within disease-network biology. The evidence architecture connecting predicted targets, enriched pathways, phenotypic effects, and disease networks is shown in **Figure 1**.

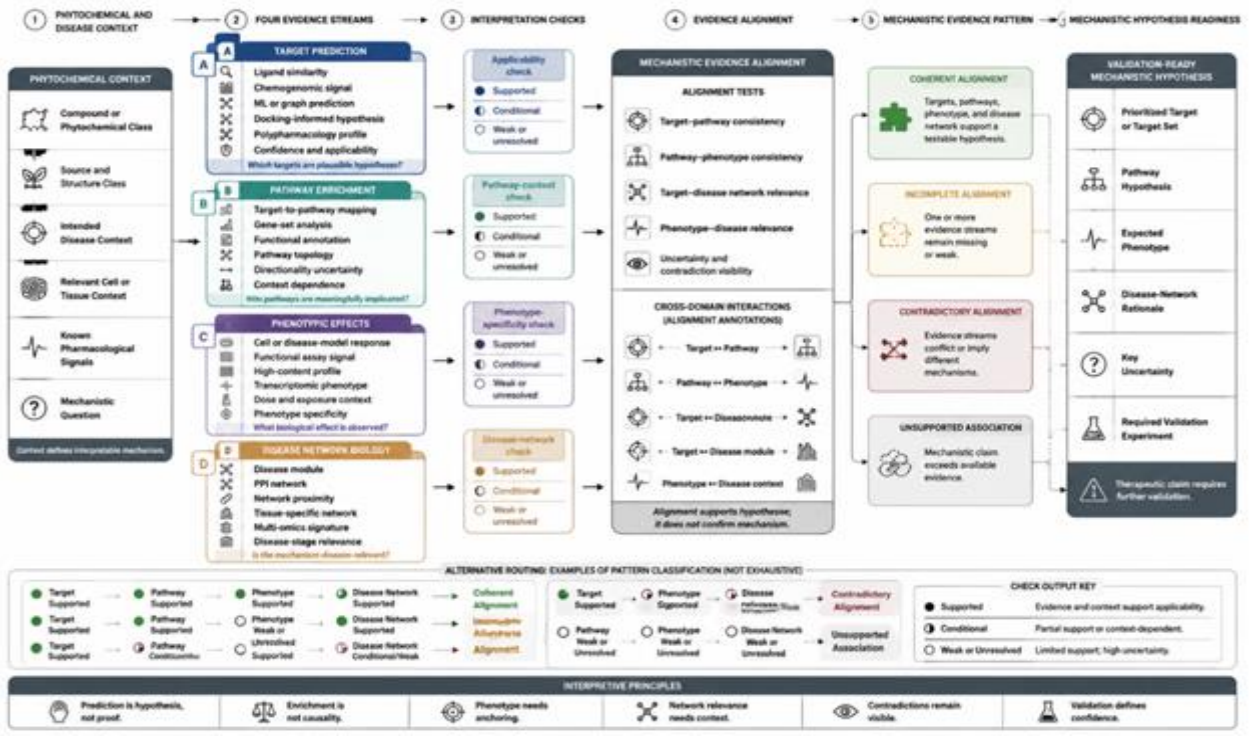

Figure 1. Mechanism-First Evidence Architecture for Phytochemical Therapeutics

Alt-text

A wide left-to-right evidence architecture begins with a phytochemical or phytochemical class and therapeutic context. Four evidence streams evaluate predicted targets, enriched pathways, observed phenotypic effects, and disease-network relevance. Each stream includes uncertainty and interpretation checks. The streams converge into an alignment layer that identifies coherent, incomplete, contradictory, or unsupported mechanism patterns before recommending validation priorities.

Mechanistic evidence integration

Mechanistic evidence integration begins when the four evidence domains are interpreted together rather than sequentially stacked. In phytochemical therapeutics, computational polypharmacology can be useful because it identifies possible target distributions and multi-target hypotheses for natural products [28]. Yet the integration step must ask whether those targets form a biologically interpretable chain with pathways, phenotypes, and disease-network relevance. A predicted multi-target profile

without functional coherence remains a set of hypotheses, not a mechanism.

Herbal and phytochemical systems pharmacology approaches are valuable because they encourage organization of multi-component and multi-target evidence into structured biological models [29]. Their limitation is that systems-level language can sometimes obscure uncertainty if every target, pathway, or network association is treated as equally meaningful. The proposed integration logic therefore distinguishes between evidence accumulation and evidence alignment. Only aligned evidence can justify a validation-ready mechanistic hypothesis.

The first integration criterion is target–pathway alignment. A predicted or associated target should map to a pathway in a way that is biologically plausible for the defined context. If the enriched pathway is generic, redundant, or unsupported by target relevance, the pathway should remain conditional. If pathway evidence is coherent but directionality is unknown, the framework should describe a pathway hypothesis rather than pathway activation or inhibition.

The second integration criterion is pathway–phenotype alignment. A phenotype strengthens a mechanism when it is compatible with the expected biological consequence of the target–pathway chain. For example, a disease-relevant phenotype may support a predicted inflammatory or metabolic pathway hypothesis only if the assay context and exposure conditions make that interpretation plausible. Conversely, a strong phenotype with unclear target identity should not be converted into a target mechanism by narrative inference.

The third integration criterion is disease-network contextualization. Network proximity, disease-gene overlap, or module membership may increase plausibility when they align with target, pathway, and phenotype evidence, but they should not be interpreted as therapeutic proof. Contradictory evidence should remain visible, because conflict may indicate model dependence, tissue specificity, dose dependence, off-target toxicity, or an unsupported mechanism. The proposed mechanistic evidence-integration criteria and their interpretive consequences are presented in **Table 3**.

Table 3. Proposed Mechanistic Evidence-Integration Criteria for Phytochemical Therapeutics

Integration criterion	Evidence question	Favorable evidence pattern	Conditional evidence pattern	Concerning evidence pattern	Interpretive consequence	Validation requirement
Target credibility	Are candidate targets plausible hypotheses?	Predicted target is supported by applicability, prior pharmacology, and disease relevance	Prediction is plausible but model domain or target class is uncertain	Target list is unfiltered or outside credible applicability	Target remains prioritized, conditional, or downgraded	Binding, target engagement, or functional modulation testing
Target–pathway alignment	Do targets map to meaningful pathways?	Filtered targets converge on contextually relevant pathway logic	Pathway term is relevant but broad or directionally unclear	Enrichment is generic, redundant, or target-list driven	Pathway hypothesis is strengthened, held, or downgraded	Perturbation-based pathway readout
Pathway–phenotype alignment	Does phenotype match pathway logic?	Phenotype is compatible with expected pathway consequence	Phenotype is relevant but nonspecific or assay-limited	Phenotype contradicts pathway interpretation	Mechanism becomes coherent, incomplete, or contradictory	Orthogonal phenotype and pathway assays
Disease-network relevance	Does evidence connect to disease biology?	Target–pathway–phenotype chain maps plausibly to disease module or network context	Disease connection exists but is not tissue- or stage-specific	Network evidence is limited to overlap or centrality alone	Disease relevance is strengthened, conditional, or unsupported	Disease-model and tissue-context validation
Contradiction visibility	Are conflicts explicitly preserved?	Evidence streams converge or conflicts are biologically explainable	Conflicts may reflect model or context dependence	Conflicts are ignored or hidden	State assignment remains transparent	Replication in relevant biological context
Validation readiness	Is the mechanism specific and testable?	Target, pathway, phenotype, and disease context define a focused test	One evidence stream remains missing but addressable	Claim exceeds available evidence	Mechanism is prioritized, held, refined, or rejected	Target engagement, pathway perturbation, and disease-model testing

Proposed mechanistic framework

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The proposed mechanistic framework begins with therapeutic context definition. Before interpreting any target prediction, pathway enrichment, phenotype, or disease network, the researcher defines the disease or phenotype, tissue or cell context, expected biological direction, and validation question. This step prevents post hoc interpretation, where a broad computational result is forced to fit a preferred therapeutic narrative. Context definition also establishes which evidence streams are relevant and which should be treated as exploratory.

The second component is phytochemical definition. A purified compound, phytochemical class, standardized extract, or multi-component formulation should not be treated as equivalent evidence objects. Compound identity, structural class, source context, exposure relevance, and known pharmacological signals determine how target predictions and phenotypes should be interpreted. If the chemical object is poorly defined, the framework does not reject the study automatically, but it lowers mechanistic specificity and limits claim strength.

The third component is target prediction followed by target evidence filtering. The framework accepts target prediction as hypothesis generation and then filters candidate targets by applicability, confidence, chemical plausibility, disease relevance, prior assay evidence, and potential functional role. It distinguishes predicted target, target association, confirmed binding, target engagement, and functional modulation. Only the last categories can support stronger mechanistic claims, and even they require connection to pathway, phenotype, and disease context.

The fourth component is pathway enrichment followed by pathway-context interpretation. Candidate targets or perturbation-derived genes may be mapped to pathways, but the framework treats enrichment as annotation and interpretation rather than causal proof. Pathway terms are evaluated for biological specificity, topology, redundancy, directionality, disease-stage relevance, and cell-context dependence. A pathway can therefore be coherent, conditional, generic, contradictory, or unsupported depending on how it relates to targets and phenotypes.

The fifth component integrates phenotypic evidence and disease-network relevance into a cross-domain decision architecture. Phenotypes constrain mechanistic claims by showing whether the predicted target–pathway chain produces a compatible biological effect, while disease networks test whether that chain is plausibly connected to disease biology. The framework then maps uncertainty and contradiction before assigning one of five states: Mechanistically Prioritized for Validation, Plausible but Incomplete Mechanism, Contradictory or Context-Dependent Mechanism, Evidence-Insufficient Mechanistic Hold, or Mechanistically Unsupported Claim. The proposed mechanism-first decision framework and its alternative mechanistic states are shown in **Figure 2**.

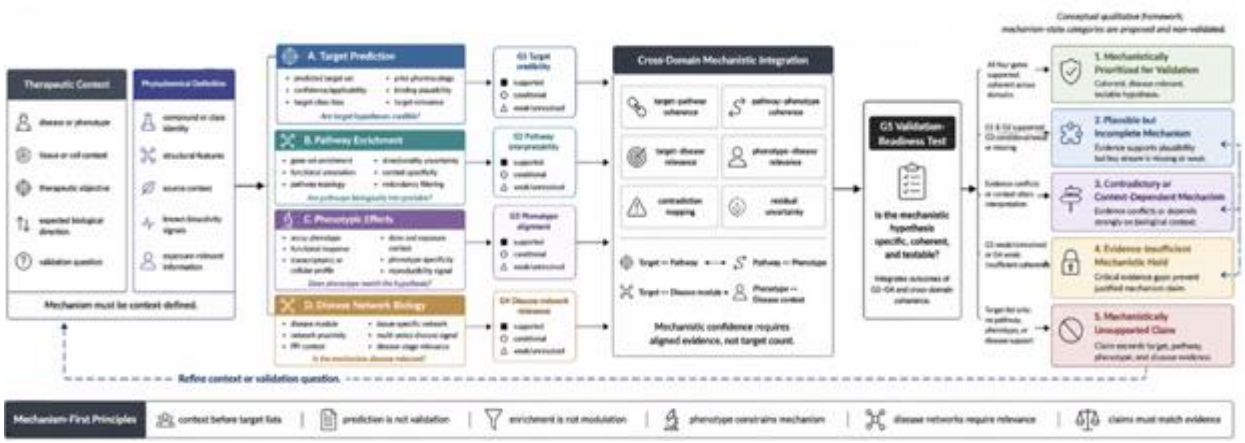

Figure 2. Proposed Mechanism-First Framework for Phytochemical Therapeutics

Alt-text

A wide left-to-right mechanistic framework begins with therapeutic context and phytochemical identity. Four evidence domains assess target prediction, pathway enrichment, phenotypic effects, and disease-network biology. Each domain passes through an evidence gate before converging in a cross-domain integration layer that checks coherence, uncertainty, contradiction, disease relevance, and validation readiness. The framework then assigns one of five mechanistic states ranging from prioritized for validation to unsupported claim.

Research implications

For phytochemical mechanism studies, the framework implies that chemical definition should be treated as part of mechanistic rigor. Natural products have historically contributed substantially to drug discovery, but that history does not justify assuming that a new phytochemical claim is mechanistically valid, therapeutically relevant, or safe [30]. Researchers should therefore report whether they are studying a purified compound, enriched fraction, phytochemical class, extract, or formulation. This

distinction determines how specifically target, pathway, phenotype, and network evidence can be interpreted.

For natural product and phytochemical discovery workflows, the framework supports opportunity while resisting mechanistic overreach. Modern natural product drug discovery increasingly benefits from chemical, biological, computational, and translational integration [31]. The practical implication is that target prediction, pathway enrichment, and disease-network analysis should be designed around explicit validation questions. They should not be used mainly to decorate a therapeutic narrative.

For target-evidence reporting, the framework encourages explicit separation of prediction, association, binding plausibility, engagement, and functional modulation. Target assessment guidance emphasizes that biological relevance, evidence strength, and validation discipline are central to credible target claims [32]. Phytochemical studies should therefore report why a target is retained, downgraded, or rejected. Negative and contradictory target evidence should be visible rather than omitted.

For computational reproducibility, the framework suggests that target-prediction workflows should report model choice, input chemistry, applicability concerns, benchmark context, and external evidence. Target-prediction validation guidance emphasizes that method evaluation and uncertainty assessment are necessary before prediction outputs are used as biological evidence [33]. This has direct implications for phytochemical studies because unusual scaffolds, mixtures, and underrepresented target classes may fall outside confident prediction domains. A validation-ready hypothesis should therefore specify the experiment that would test the predicted target rather than presenting the prediction as confirmation.

For translational prioritization, the framework supports more disciplined experimental planning. A mechanism-first study should identify the target-engagement assay, pathway perturbation readout, phenotypic assay, and disease-context model needed to test the proposed chain. Tissue-specific network interpretation, disease-stage annotation, exposure relevance, and contradiction reporting should be treated as research design elements rather than optional details. The framework does not claim to improve therapeutic success; it provides a structured basis for making mechanistic claims testable, limited, and transparent.

CONCLUSION

Mechanism-first phytochemical therapeutics requires a disciplined shift from evidence accumulation to evidence alignment. Isolated target prediction, pathway enrichment, phenotypic observation, or disease-network association can each contribute to hypothesis generation, but none is sufficient to establish a therapeutic mechanism. The central task is to construct a coherent target–pathway–phenotype–disease chain while preserving uncertainty and contradiction.

The proposed framework offers a qualitative architecture for that task. It defines how phytochemical identity, therapeutic context, target credibility, pathway interpretation, phenotypic evidence, and disease-network relevance can be integrated into mechanistic states. It also establishes interpretive boundaries that prevent predicted targets from becoming confirmed mechanisms, enriched pathways from becoming pathway modulation, phenotypes from becoming target identities, and network associations from becoming therapeutic proof.

The framework's original contribution is a mechanism-first decision model for organizing phytochemical therapeutic hypotheses before validation. It is intended to support transparent prioritization, evidence-gap mapping, and validation planning, not to replace experimental testing. Future work should evaluate whether such structured mechanistic reasoning improves reproducibility, interpretive quality, and translational decision-making in phytochemical therapeutic research.

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