Polypharmacology by Design: Prioritizing Plant-Derived Compounds Across Inflammation, Oxidative Stress, Metabolic Dysfunction, and Immune Modulation

Rafael Mendoza[1]*, Isabela Cruz[1], Carlos Lopez[2]

[1]Department of AI for Anti-Inflammatory Phytochemicals, Faculty of Pharmacy, National Autonomous University of Mexico, Mexico City, Mexico.
[2]Department of Computational ADMET Prediction for Plant-Based Drugs, Faculty of Pharmacy, Monterrey Institute of Technology, Monterrey, Mexico.

ABSTRACT

Plant-derived compounds are frequently described as multi-target agents, yet broad claims of activity across many pathways do not by themselves establish therapeutically meaningful polypharmacology. This Original Conceptual Model Article develops a mechanism-centered framework for prioritizing plant-derived compounds across inflammation, oxidative stress, metabolic dysfunction, and immune modulation. The article positions polypharmacology as a design logic in which candidate compounds are prioritized when reported target or pathway activities converge across biologically connected mechanisms, rather than when they simply accumulate predicted targets or unspecific bioactivity claims. The proposed approach integrates compound identity, phytochemical class, source context, evidence type, target and pathway convergence, mechanistic coherence, exposure plausibility, safety considerations, disease-context relevance, translational readiness, and validation needs. Inflammation and oxidative stress are treated as interdependent regulatory domains involving inflammatory signaling, cytokine networks, redox balance, and antioxidant-response pathways, while metabolic dysfunction and immune modulation are framed through immunometabolic crosstalk, gut–metabolic interactions, and context-dependent immune regulation. The main contribution is a structured prioritization logic that distinguishes confirmed mechanisms, pathway associations, predicted targets, phenotypic observations, and conceptual hypotheses. Practically, the model is intended to support more disciplined phytochemical screening, systems pharmacology interpretation, and translational candidate selection without implying that multi-target activity, antioxidant capacity, or natural origin is sufficient evidence of efficacy or safety.

Key Words: *Polypharmacology, Plant-derived compounds, Phytochemicals, Inflammation, Oxidative stress, Metabolic dysfunction*

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INTRODUCTION

Polypharmacology is increasingly relevant to complex biological systems because inflammatory signaling, oxidative stress regulation, metabolic dysfunction, and immune modulation rarely operate as isolated mechanisms. In a design-oriented interpretation, polypharmacology refers to purposeful engagement of multiple biological targets or pathways in a mechanistically coherent manner, rather than broad molecular promiscuity or an unstructured list of possible interactions [1–3].

Corresponding author: Rafael Mendoza
Address: Department of AI for Anti-Inflammatory Phytochemicals, Faculty of Pharmacy, National Autonomous University of Mexico, Mexico City, Mexico.
E-mail: ✉ rafael.mendoza@unam.mx
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This distinction is especially important when plant-derived compounds are discussed as multi-target agents, because a compound may appear biologically active across several assays without necessarily showing coherent, exposure-relevant, or translatable pharmacology.

Natural products continue to occupy an important place in drug discovery because they provide structurally diverse chemical matter and have historically contributed to therapeutic innovation, but this discovery relevance should not be confused with proof that any individual phytochemical is clinically effective [4]. For plant-derived compounds, the central challenge is not simply to document that many targets or pathways have been reported. The more rigorous task is to ask whether those reported activities converge around disease-relevant mechanisms at plausible exposures and under conditions where safety, specificity, and validation can be assessed.

This article develops a mechanism-centered conceptual model for prioritizing plant-derived compounds as multi-target candidates across four interconnected domains: inflammation, oxidative stress, metabolic dysfunction, and immune modulation. The aim is not to provide a generic review of phytochemicals or to rank compounds by popularity. Instead, the article proposes a structured logic for deciding when reported activity across these domains should be interpreted as potentially useful polypharmacology, when it should remain a mechanistic hypothesis, and when it should be treated as a low-priority or caution signal.

The model-building focus is therefore translational and methodological. It distinguishes confirmed targets, predicted targets, pathway associations, phenotypic effects, network-inferred mechanisms, preclinical evidence, clinical evidence, and conceptual prioritization logic. By doing so, it frames plant-derived polypharmacology as a disciplined process of evidence integration that requires target relevance, pathway convergence, mechanistic coherence, exposure plausibility, safety evaluation, and validation feasibility.

Plant-derived compounds and polypharmacology

Plant-derived compounds represent chemically diverse molecules embedded in specific phytochemical, botanical, and preparation contexts. Prioritization should therefore begin with compound identity, compound class, source context, chemical characterization, and evidence type rather than with broad assumptions about botanical origin [5]. A compound-level framework is particularly important because crude-extract activity, traditional-use context, predicted targets, and isolated-compound pharmacology do not provide equivalent evidence for mechanism-centered prioritization.

In silico polypharmacology can help organize compound-target-pathway hypotheses for natural products, but predicted networks should be interpreted as prioritization tools rather than confirmed biological mechanisms [6]. A compound with numerous predicted targets is not automatically a high-priority polypharmacological candidate. Its priority depends on whether those targets are biologically relevant, whether they converge on disease-associated pathways, whether the evidence is reproducible, and whether downstream validation is feasible.

Curcumin illustrates why prominent plant-derived compounds require careful medicinal-chemistry and exposure-aware interpretation. Although curcuminoids are often discussed in relation to inflammatory and redox pathways, medicinal chemistry concerns such as assay interference, instability, and limited exposure can weaken unsupported claims of broad mechanism or therapeutic relevance [7]. This example supports a general principle: multi-target potential must be filtered through chemical tractability, evidence quality, and plausible biological exposure.

Plant-derived immunomodulating compounds also require careful framing because immune regulation is context-dependent. Natural product-derived immunomodulators may support drug-discovery hypotheses when target engagement, pathway relevance, safety, and translational validation are considered together [8]. However, immune modulation should not be treated as inherently beneficial, because suppressing or stimulating immune processes can have different implications depending on disease context, immune state, dose, exposure, and safety profile.

Table 1 summarises major plant-derived compound classes and their relevance to mechanism-centered polypharmacology.

Table 1. Plant-Derived Compound Classes Relevant to Mechanism-Centered Polypharmacology: Representative Phytochemical Groups, Multi-Target Potential, Pathway Relevance, Evidence Considerations, Exposure Constraints, Safety Issues, and Translational Limitations

Compound class	Representative compound examples	Reported multi-target relevance	Primary pathway domains	Evidence type commonly reported	Exposure or bioavailability concern	Safety consideration	Polypharmacology prioritization relevance
Polyphenols	Broad dietary and plant phenolics	Often discussed through pathway	Inflammation, oxidative stress, metabolism,	Reviews, mechanistic	Variable absorption, metabolism,	Interaction and context-specific safety	Useful for convergence mapping when

		convergence and systems-level effects	immunometabolism	studies, pathway-oriented synthesis	and microbiota-dependent transformation	issues require evaluation	exposure and metabolite identity are considered
Flavonoids	Quercetin and related flavonoids	Reported relevance to inflammatory and metabolic contexts	Chronic inflammation, metabolic dysfunction, redox-associated pathways	Mechanistic and disease-context reviews	Bioavailability may differ by structure, food matrix, and metabolism	Not inherently safe; interactions and context require assessment	Prioritized when inflammatory and metabolic mechanisms converge with plausible exposure
Alkaloids	Berberine	Reported relevance to metabolic and immune-inflammatory mechanisms	Metabolic syndrome-related pathways, inflammatory signaling, immune regulation	Mechanistic reviews and disease-context synthesis	Exposure and formulation context may influence interpretation	Safety, interaction, and tolerability issues require specific assessment	Relevant when metabolic and immune-inflammatory effects are supported by coherent evidence
Terpenoids	Plant terpenoid classes	Potential multi-target relevance in natural product discovery	Context-dependent inflammatory, redox, metabolic, or immune domains	Discovery-oriented and pharmacology reviews	Compound-specific exposure constraints should be assessed	Compound-specific toxicity cannot be inferred from class identity	Lower priority without compound-level characterization and pathway-specific evidence
Organosulfur compounds	Sulforaphane	Reported pathway convergence across redox, inflammation, and metabolic health	Nrf2-related antioxidant response, inflammation, metabolic regulation	Narrative and mechanistic reviews	Bioavailability and metabolite context require interpretation	Safety assessment should remain compound- and context-specific	Strong candidate class for redox-inflammation-metabolism convergence analysis
Stilbenes	Resveratrol	Reported anti-inflammatory and immune-response relevance	Inflammatory signaling, immune response, metabolism-related contexts	Mechanistic reviews	Exposure limitations and metabolic transformation may constrain interpretation	Effects should be interpreted in context rather than generalized	Prioritized only when immune and inflammatory claims are exposure-aware and validated
Catechins	Epigallocatechin-3-gallate	Reported relevance to inflammation, oxidative stress, and apoptosis-related pathways	Inflammatory signaling, oxidative stress regulation, apoptosis pathways	Pathway-focused reviews	Stability, dose, and exposure context require evaluation	Safety should not be assumed from dietary origin	Useful for pathway mapping when claims remain mechanistic and cautious
Curcuminoids	Curcumin	Frequently reported across inflammatory and redox pathways but requires caution	Inflammation, oxidative stress, broad pathway associations	Health-effect reviews and medicinal-chemistry critique	Limited exposure, instability, and assay concerns may affect interpretation	Assay interference and translational uncertainty are key caution signals	Prioritization requires stricter evidence, exposure, and validation filters

Inflammatory and oxidative stress pathways

Inflammatory signaling and oxidative stress regulation form a central convergence zone for plant-derived compound prioritization because cytokine networks, inflammatory mediators, redox balance, and stress-response pathways can influence one another. Curcumin, resveratrol, and quercetin provide commonly discussed examples of compounds reported in relation to inflammatory, redox, immune, or metabolic pathway relevance, but their interpretation should remain compound-specific and evidence-dependent [9–11]. These examples are best used to illustrate pathway convergence

rather than to imply therapeutic equivalence across compounds or disease contexts.

Sulforaphane provides a useful example of a plant-derived organosulfur compound discussed across inflammation, oxidative stress, and metabolic health, particularly through redox-responsive regulatory logic such as antioxidant-response pathway activation [12]. In a prioritization model, such a compound would not be advanced simply because it is associated with redox biology. It would be prioritized only if the redox mechanism is linked to relevant inflammatory or metabolic disease biology, supported by appropriate evidence, and compatible with plausible exposure and safety assessment.

Epigallocatechin-3-gallate illustrates catechin-level pathway mapping because it has been reviewed in relation to molecular pathways controlling inflammation, oxidative stress, and apoptosis [13]. This supports a pathway-domain view in which plant-derived compounds are assessed by whether reported activities occupy connected biological modules. However, pathway presence alone is insufficient; the model requires evaluation of whether a reported effect is direct or indirect, experimentally observed or inferred, and biologically meaningful in the disease context under consideration.

The conceptual risk in this domain is overinterpreting antioxidant or anti-inflammatory activity. Antioxidant capacity in a chemical or simplified biological setting does not establish clinical benefit, and anti-inflammatory signaling does not necessarily imply therapeutic value. A mechanism-centered prioritization logic should therefore ask whether inflammatory and oxidative stress pathways are linked to target convergence, disease-context relevance, exposure plausibility, safety, and validation feasibility. Claims should remain cautious when evidence is limited to pathway association, phenotypic change, or computational inference.

Metabolic and immune modulation targets

Metabolic dysfunction and immune modulation are closely connected because metabolic stress can influence inflammatory tone, immune-cell behavior, and tissue-level homeostasis. Berberine provides a plant-derived alkaloid example with reported relevance to metabolic syndrome-related contexts [14]. Its prioritization value increases when metabolic relevance is not treated as a standalone claim but is linked to pathway coherence, disease-context fit, and plausible biological mechanisms.

The same compound class can also intersect with immune-inflammatory mechanisms. Berberine has been discussed in relation to autoreactive T-cell activation and autoimmune inflammation, supporting the idea that candidate prioritization may need to bridge metabolic and immune-inflammatory domains rather than assign compounds to a single pathway category [15]. This does not mean that a compound has broad immune benefit; rather, it indicates that immune-related evidence should be interpreted according to immune context, target specificity, and validation strength.

Gut–metabolic interactions create another important prioritization layer because microbial metabolism can influence phytochemical exposure, metabolite formation, and downstream biological interpretation. Curcumin, quercetin, and catechins have been reviewed in relation to gut microbiota and metabolic disease, indicating that the active entity may not always be the parent compound alone [16]. For prioritization, this means that compound identity should include metabolite-aware interpretation when microbiota-dependent transformation is relevant.

Immune modulation should also be interpreted through immunometabolic balance rather than through a simple beneficial-or-harmful binary. Resveratrol has been discussed in relation to immune-response modulation, while broader polyphenol literature links immunonutrient concepts to immunometabolism in chronic disease contexts [17]. Immunometabolism provides a conceptual bridge between metabolic dysfunction and immune regulation, but its use in prioritization requires careful distinction between mechanistic plausibility, disease-context relevance, and evidence strength [18].

Table 2 maps inflammation, oxidative stress, metabolic dysfunction, and immune modulation domains relevant to plant-derived compound prioritization.

Table 2. Mechanistic Domains for Prioritizing Plant-Derived Multi-Target Compounds: Inflammatory Signaling, Oxidative Stress Regulation, Metabolic Dysfunction, Immune Modulation, Target Crosstalk, Pathway Convergence, and Validation Needs

Mechanistic domain	Representative targets or pathways	Relevance to polypharmacology	Potential compound-interaction logic	Evidence interpretation requirement	Risk of overclaiming	Validation need	Prioritization implication
Inflammatory signaling	NF-κB-related signaling, cytokine networks,	Central domain for pathway convergence when linked to disease biology	Candidate compounds may be assessed for coherent	Distinguish direct target evidence from pathway association or	Treating any anti-inflammatory signal as	Target engagement, pathway validation, disease-	Higher priority when inflammatory relevance converges with

	inflammatory mediators		modulation of inflammatory mediator networks	phenotypic anti-inflammatory effects	therapeutic proof	context testing	redox, metabolic, or immune evidence
Oxidative stress regulation	Redox balance, ROS regulation, antioxidant-response pathways, Nrf2-related logic	Relevant when redox mechanisms connect to inflammatory or metabolic pathways	Candidate compounds may influence stress-response pathways or redox-sensitive signaling	Distinguish chemical antioxidant activity from biologically meaningful pathway modulation	Assuming antioxidant activity predicts clinical benefit	Exposure-aware redox assays and pathway-specific validation	Higher priority when redox effects are biologically plausible and not limited to nonspecific antioxidant claims
Metabolic dysfunction	Metabolic syndrome-related pathways, gut–metabolic interactions, lipid and glucose homeostasis contexts	Provides disease-context relevance for compounds with metabolic and inflammatory links	Candidate compounds may be prioritized when metabolic relevance aligns with inflammatory or immune mechanisms	Clarify whether evidence concerns parent compound, metabolites, microbiota effects, or broad phenotypes	Inferring disease improvement from pathway association	Metabolic pathway assays, metabolite-aware testing, relevant disease models	Higher priority when metabolic evidence is mechanistically coherent and exposure-aware
Immune modulation	T-cell modulation, immune-response pathways, immune-inflammatory signaling	Important when immune effects align with inflammatory or metabolic disease context	Candidate compounds may influence immune balance rather than simply suppress or stimulate immunity	Interpret immune effects according to disease context and immune state	Assuming immune modulation is always beneficial	Immune-cell and context-specific validation	Higher priority when immune effects are specific, contextualized, and safety-aware
Immunometabolic crosstalk	Links between metabolism, inflammation, and immune regulation	Integrates metabolic dysfunction with immune modulation	Candidate compounds may be assessed for convergence across metabolic and immune pathways	Determine whether evidence supports crosstalk or only separate pathway observations	Presenting separate mechanisms as integrated without evidence	Models that capture metabolic–immune interactions	Higher priority when metabolic and immune evidence supports a coherent shared mechanism
Gut–compound–metabolism axis	Microbiota-mediated phytochemical metabolism and metabolic effects	Adds exposure plausibility to multi-target interpretation	Parent compounds and metabolites may differ in biological relevance	Identify whether active entities are parent compounds, metabolites, or microbiota-modified products	Ignoring transformation and assuming parent-compound activity in vivo	Metabolite profiling and microbiota-aware experiments	Higher priority when exposure and metabolite identity are integrated
Target and pathway convergence	Overlapping targets, shared pathway nodes, disease-relevant modules	Core requirement for designed polypharmacology	Multi-target activity is prioritized when targets converge on coherent	Separate confirmed targets from predicted or network-inferred targets	Counting targets rather than evaluating biological coherence	Orthogonal target validation and pathway perturbation tests	Higher priority when convergence is mechanistically interpretable

			disease mechanisms				
Evidence and translation domain	Evidence strength, exposure plausibility, safety, validation feasibility	Determines whether mechanistic plausibility can move toward translational prioritization	Candidate status depends on evidence quality, achievable exposure, and safety profile	Grade evidence type and avoid treating hypotheses as validation	Presenting conceptual prioritization as experimental proof	Stepwise experimental and translational validation	Higher priority when evidence strength and feasibility align with mechanism

Prioritization logic for multi-target compounds

Prioritizing plant-derived compounds for mechanism-centered polypharmacology requires more than documenting activity across several pathways. A candidate should move forward only when its target or pathway activities can be interpreted in relation to achievable exposure, metabolite formation, safety, and interaction risk [19–21]. This gate is especially important for polyphenols and related phytochemicals, because absorption, metabolism, microbiota-mediated transformation, and herb-drug interaction concerns can substantially influence whether reported mechanisms are biologically plausible.

Chemical diversity is valuable only when connected to mechanism and disease context. Plant natural products provide diverse chemical scaffolds, but diversity alone does not justify prioritization [22]. A compound should be considered higher priority when its chemical identity is clear, its compound class is relevant to the intended mechanism, its target or pathway evidence is interpretable, and its reported activities converge across disease-relevant inflammatory, redox, metabolic, or immune modules.

Computational and in silico methods can support candidate ranking by linking compounds to possible targets, pathways, and disease modules, but they also introduce risks related to database incompleteness, target-prediction uncertainty, structural annotation quality, and weak experimental follow-up [23]. Therefore, predicted target number should not be used as a surrogate for polypharmacological value. A compound with fewer but better-supported and biologically coherent target-pathway links may be more suitable for prioritization than a compound with many uncertain predicted interactions.

The proposed prioritization logic uses seven linked questions. First, is the compound identity sufficiently resolved? Second, are reported targets or pathways relevant to the disease mechanism? Third, do inflammatory, oxidative, metabolic, or immune domains converge in a biologically coherent way? Fourth, is the evidence type strong enough for the claim being made? Fifth, is exposure plausible for the proposed mechanism? Sixth, are safety and interaction risks acceptable for further investigation? Seventh, is the candidate ready for validation, or should it remain a mechanistic hypothesis? This logic turns polypharmacology from a descriptive claim into a structured decision process.

Proposed conceptual model

The proposed conceptual model prioritizes plant-derived compounds through a sequence of evidence-sensitive filters rather than through a simple accumulation of reported targets. Its first stage is compound identity, which includes compound class, source or phytochemical context, chemical characterization, and distinction between isolated compound, metabolite, extract constituent, or computationally predicted entity. Its second stage is mechanism mapping, where candidate targets and pathways are organized around disease-relevant modules rather than treated as isolated annotations. Network pharmacology is useful here when it focuses on causal or mechanistically relevant modules rather than on treating broad network connectivity as evidence of efficacy [24].

The third stage is pathway convergence analysis. Systems pharmacology can help organize compound-target-pathway relationships in natural product research, particularly when it distinguishes bioactive compounds, predicted interactions, and mechanism-of-action hypotheses [25]. In silico medicinal-plant workflows can also support screening and candidate ranking, but such outputs should be interpreted as hypothesis-generating and should be followed by experimental validation when a candidate is advanced [26]. In the present model, convergence means that evidence from inflammatory signaling, oxidative stress regulation, metabolic dysfunction, or immune modulation points toward a coherent biological rationale, not merely that several pathways are mentioned in the literature.

The fourth stage is exposure and safety filtering. A candidate with plausible target convergence may still be low priority if the active compound or metabolite is unlikely to reach relevant biological compartments, if the proposed mechanism depends on unrealistic exposure, or if safety and interaction concerns are insufficiently characterized. Immune-relevant natural product networks may support prioritization when compound-target-response relationships are used cautiously and linked to immune-context interpretation [27]. However, immune-related network outputs should not be presented as

confirmed immunomodulatory mechanisms without appropriate validation.

The fifth stage is translational prioritization and validation planning. Network pharmacology applications in traditional medicine and natural product research can support integrative interpretation, but their outputs should remain distinct from experimentally confirmed mechanisms [28]. The model therefore assigns candidates to conceptual tiers: high-priority candidate, conditional-priority candidate, mechanistic hypothesis, or low-priority or caution candidate. These tiers are not claims of efficacy; they are structured judgments about whether available evidence justifies further mechanistic or translational investigation.

Table 3 presents the proposed prioritization model for plant-derived compounds with multi-target activity across inflammation, oxidative stress, metabolic dysfunction, and immune modulation.

Table 3. Proposed Prioritization Model for Plant-Derived Multi-Target Compounds: Mechanistic Convergence, Evidence Strength, Exposure Plausibility, Safety Considerations, Disease-Context Relevance, Translational Readiness, and Validation Priorities

Model component	Core question	Assessment criterion	Evidence required	High-priority signal	Low-priority or caution signal	Failure risk	Recommended validation step
Compound identity	What exactly is being prioritized?	Clear chemical identity, class, and source context	Compound characterization, phytochemical context, distinction between parent compound and metabolite	Well-defined isolated compound or clearly characterized constituent	Vague extract-level claim or unclear active entity	Misattributing effects to the wrong compound	Chemical characterization and metabolite-aware annotation
Compound class	Does class identity help interpret mechanism?	Class-specific relevance to inflammatory, redox, metabolic, or immune pathways	Mechanistic literature linked to compound class and representative compounds	Compound class supports plausible pathway-domain relevance	Class identity used as a substitute for direct evidence	Overgeneralizing from one compound to an entire class	Compound-specific mechanism testing
Target relevance	Are reported targets biologically meaningful?	Alignment between targets and disease-relevant mechanisms	Confirmed target data or cautious interpretation of predicted targets	Targets converge on relevant mechanism modules	Long target lists without biological coherence	Target-count inflation	Orthogonal target-engagement assays
Pathway convergence	Do pathways connect mechanistically?	Coherence across inflammation, oxidative stress, metabolism, and immunity	Pathway-level evidence and mechanistic synthesis	Multiple domains converge around a plausible disease mechanism	Separate pathway claims presented as integrated without support	False systems-level interpretation	Pathway perturbation and module-level validation
Evidence strength	What type of evidence supports the claim?	Separation of confirmed targets, predicted targets, pathway associations, phenotypes, and network inferences	Evidence grading by study type and claim type	Mechanistic evidence matches the strength of the manuscript claim	Computational or phenotypic evidence presented as confirmation	Unsupported mechanistic certainty	Evidence-tiered validation plan
Exposure plausibility	Can the proposed mechanism occur at plausible exposure?	Consideration of absorption, metabolism, metabolites,	Bioavailability, metabolism, microbiota, or	Mechanism is plausible for parent compound or	Mechanism depends on unrealistic or	Translation failure from exposure mismatch	Pharmacokinetic and metabolite-aware

		and biological compartment	exposure-relevant evidence	relevant metabolite	unspecified exposure		experimental design
Safety considerations	Are safety and interaction risks addressed?	Compound-specific risk, interaction potential, and context-dependent immune effects	Safety literature, interaction assessment, tolerability signals when available	Safety issues acknowledged and testable	Natural origin used as a safety argument	Underestimated toxicity or interaction risk	Safety pharmacology and interaction screening
Disease-context relevance	Does the mechanism fit the intended biological context?	Match between pathway module and disease biology	Disease-relevant mechanism evidence	Mechanism aligns with inflammatory, redox, metabolic, or immune disease context	Broad claims without disease-context specificity	Mechanistic relevance without translational relevance	Disease-relevant cellular, tissue, or model-system testing
Translational readiness	Is the candidate ready for further development?	Integration of identity, mechanism, exposure, safety, and feasibility	Cross-domain evidence synthesis	Candidate can be assigned to a clear validation pathway	Major uncertainty across several model components	Advancing weak candidates prematurely	Stage-gated translational evaluation
Validation needs	What must be tested next?	Identification of the weakest unresolved gate	Target, pathway, exposure, safety, or disease-context validation	Clear next experiment addresses a defined uncertainty	No feasible validation route	Conceptual model becomes untestable	Prioritized validation sequence before efficacy claims

Figure 1 illustrates the proposed mechanism-centered prioritization model for plant-derived compounds across inflammation, oxidative stress, metabolic dysfunction, and immune modulation.

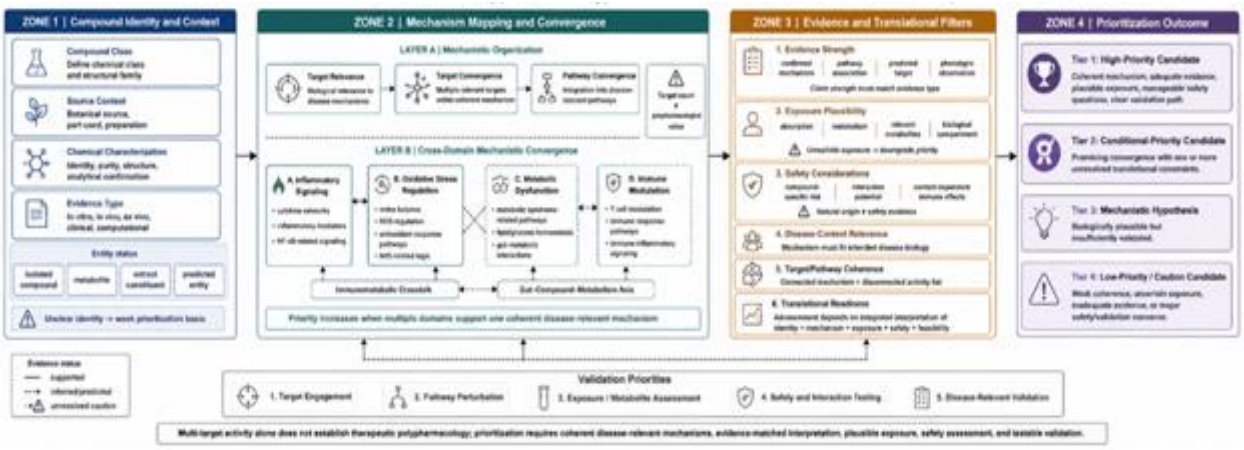

Figure 1. Mechanism-Centered Polypharmacology Prioritization Model for Plant-Derived Compounds

Alt-text description

A conceptual framework diagram showing plant-derived compounds entering a prioritization pipeline. The pipeline evaluates compound class, target convergence, pathway convergence, inflammation, oxidative stress, metabolic dysfunction, immune modulation, evidence strength, exposure plausibility, safety considerations, translational readiness, and validation needs before assigning candidate prioritization tiers.

Practical implications

For natural product pharmacology, the proposed model encourages clearer separation between discovery signals and mechanism claims. Practical implementation requires transparent reporting of compound identity, target-identification logic, experimental context, and evidence strength [29]. This is particularly relevant for studies that combine phytochemical screening, network

pharmacology, pathway analysis, and biological validation, because the weakest link in the evidence chain often determines whether a candidate should be advanced. For phytochemical screening and translational prioritization, the model can help avoid overclaiming by requiring that candidate selection be justified through mechanism, exposure, safety, and validation feasibility. Natural product discovery remains an active area of innovation, but advancement from discovery signal to credible candidate requires disciplined integration of chemistry, biology, pharmacology, and translational planning [30]. In this framework, a compound is not prioritized because it is natural, widely studied, or associated with many targets; it is prioritized because the evidence supports a coherent, testable, and context-relevant polypharmacological rationale.

Future research should apply the model prospectively in compound-selection workflows. Useful next steps include standardized compound characterization, metabolite-aware exposure assessment, pathway-specific validation, safety and interaction profiling, and disease-relevant experimental systems. The model may also support more careful interpretation of network pharmacology and systems pharmacology studies by forcing each inferred target, pathway, or module to be classified as confirmed evidence, plausible association, prediction, or validation need.

CONCLUSION

This article proposes a mechanism-centered conceptual model for prioritizing plant-derived compounds by polypharmacological relevance across inflammation, oxidative stress, metabolic dysfunction, and immune modulation. The model reframes polypharmacology as a design logic based on pathway convergence, target relevance, evidence strength, exposure plausibility, safety evaluation, disease-context fit, translational readiness, and validation discipline. It does not present multi-target activity as automatically beneficial, nor does it treat pathway modulation as proof of therapeutic efficacy. Instead, it offers a structured framework for deciding when plant-derived compounds should be advanced as high-priority candidates, conditional candidates, mechanistic hypotheses, or cautionary low-priority cases.

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