Translational Readiness in AI-Discovered Phytotherapeutics: Evidence Gates from In Silico Discovery to Preclinical and Clinical Decision-Making

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ABSTRACT

AI-assisted discovery is increasingly used to identify phytochemicals, predict biological targets, prioritise mechanisms, and screen safety-related properties of natural product candidates. However, computational outputs can easily be overinterpreted when they are not connected to transparent translational criteria. This article develops an original translational readiness framework for AI-discovered phytotherapeutics, positioning in silico evidence as hypothesis-generating rather than clinically confirmatory. The framework organises candidate advancement through staged evidence gates that begin with botanical and phytochemical identity, data provenance, model transparency, target plausibility, molecular docking, molecular dynamics, network pharmacology, ADMET screening, reproducibility checks, and mechanistic hypothesis quality. It then connects these computational gates to preclinical validation requirements, including in vitro confirmation, mechanism testing, target engagement, pathway validation, in vivo relevance, pharmacokinetic evidence, formulation standardisation, toxicity assessment, interaction screening, and reproducibility controls. The clinical decision pathway component emphasises that phytotherapeutic candidates should not enter clinical interpretation unless evidence quality, safety, uncertainty, patient context, therapeutic indication, interaction risk, formulation consistency, and clinical evidence alignment are explicitly evaluated. The main contribution is a staged evidence-gate model that clarifies when AI-discovered phytotherapeutic candidates should advance, pause, or be revised. The framework is designed to reduce translational overclaiming, distinguish computational novelty from biological readiness, and support responsible movement from in silico discovery toward preclinical testing and cautious clinical decision-making.

Key Words: *AI drug discovery, Phytotherapeutics, Natural products, Translational readiness, Network pharmacology, ADMET*

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INTRODUCTION

AI-assisted natural product discovery has expanded the capacity to identify candidate phytochemicals, predict compound–target associations, prioritise biological mechanisms, and organise complex molecular evidence. This computational expansion is valuable because natural products remain a major source of pharmacologically relevant chemical diversity, yet the translation of AI-derived candidates requires evidence standards that are different from discovery-stage ranking alone [1, 2].

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The long-standing contribution of natural products to drug discovery demonstrates that botanical and phytochemical sources can yield clinically relevant pharmacological agents, but this historical contribution should not be interpreted as evidence that any newly predicted phytotherapeutic candidate is ready for clinical use. Each candidate must still pass through identity, quality, mechanism, pharmacokinetic, safety, formulation, and clinical-evidence checks before translational claims become responsible [3].

Deep learning and related computational methods can accelerate discovery by learning chemical representations, predicting molecular properties, and helping prioritise hypotheses from large chemical and biological datasets. Nevertheless, computational prediction is not equivalent to biological validation, and model outputs require interpretation in relation to data quality, domain applicability, reproducibility, and experimental confirmation [4].

This article therefore proposes a translational readiness framework for AI-discovered phytotherapeutics. The aim is not to review AI, docking, network pharmacology, or phytotherapy as isolated fields, but to define staged evidence gates that connect computational discovery to preclinical validation and clinical decision-making. The central premise is that readiness depends on evidence progression: an AI-supported candidate becomes more translationally plausible only when botanical identity, phytochemical composition, computational transparency, mechanistic plausibility, reproducibility, safety, formulation, pharmacokinetics, and clinical relevance are addressed in sequence.

Translational readiness in phytotherapeutics

Translational readiness in phytotherapeutics can be defined as the staged accumulation of evidence required to move from candidate identification toward responsible preclinical and clinical interpretation. Traditional herbal knowledge may guide hypothesis generation and prioritisation, but modern translational evaluation must convert such knowledge into testable evidence about composition, mechanism, exposure, safety, and clinical relevance [5].

A distinctive feature of phytotherapeutic research is that the tested material is often more complex than a single purified molecule. Phytotherapeutic candidates may involve extracts, fractions, multi-component preparations, or formulations with variable phytochemical composition, and therefore experimental design, controls, reporting quality, and interpretation must be especially rigorous before biological findings can be considered translationally meaningful [6].

Botanical and phytochemical identity should be treated as an early evidence gate rather than as background information. Without documented botanical source, plant part, extraction method, preparation context, chemical characterisation, and batch-level consistency, downstream AI predictions, bioassays, and safety interpretations may refer to an inadequately defined intervention rather than a reproducible candidate [7].

Translational readiness also requires a development logic that connects standardisation, formulation, safety, and clinical evidence. Botanical drug development illustrates that complex natural products can be advanced responsibly only when composition, manufacturing consistency, pharmacological rationale, clinical evidence, and risk assessment are aligned rather than handled as separate or optional domains [8].

In silico evidence gates

The first computational gate concerns ADMET and safety-risk screening, which should be interpreted as an early exclusion and prioritisation step rather than as evidence of actual safety. In silico ADME/Tox profiling can help identify potential liabilities and guide candidate refinement, but predicted absorption, distribution, metabolism, excretion, and toxicity properties must remain provisional until supported by experimental pharmacokinetic and toxicological evidence [9].

Target prediction forms a second in silico gate by estimating plausible protein targets for phytochemicals or phytochemical-like structures. Such predictions can strengthen prioritisation when the chemical input is well curated and the predicted targets are biologically relevant to the intended therapeutic context; however, predicted targets should not be described as confirmed mechanisms without target engagement, pathway, or phenotypic validation [10].

Molecular docking provides a third gate by assessing whether a candidate may plausibly interact with a target binding site under modelled conditions. Its translational value depends on appropriate protein preparation, ligand representation, binding-site rationale, control comparisons, and cautious interpretation, because docking can generate plausible binding hypotheses without proving efficacy, selectivity, target engagement, or cellular mechanism [11]. Molecular dynamics can refine docking-derived hypotheses by examining conformational stability and interaction persistence under simulated conditions, but the results remain dependent on force fields, system preparation, simulation length, and sensitivity analysis [12]. Network pharmacology can then organise multi-target and pathway-level hypotheses, while ADMET screening and provenance checks help identify whether the resulting mechanism model is biologically plausible,

safety-aware, and sufficiently traceable for preclinical prioritisation [9, 13].

Table 1 summarises the in silico evidence gates required before AI-discovered phytotherapeutic candidates can be considered translationally plausible.

Table 1. In Silico Evidence Gates for AI-Discovered Phytotherapeutics: Botanical and Phytochemical Identity, Data Provenance, Target Prediction, Docking Plausibility, Molecular Dynamics, Network Pharmacology, ADMET Screening, Reproducibility, and Mechanistic Hypothesis Quality

Evidence gate	Core question	Required evidence	Minimum documentation	Common failure risk	Translational readiness signal	Recommended caution	Next validation step
Botanical and formulation identity	Is the candidate intervention clearly defined?	Botanical source, plant part, preparation method, extraction context, formulation context, and batch description	Taxonomic identity, voucher or source traceability where applicable, preparation protocol, and batch identifiers	Treating a vague plant name or product label as a pharmacologically defined intervention	Candidate material can be reproduced and linked to downstream evidence	Do not infer mechanism or safety from an undefined preparation	Chemical profiling and composition verification
Phytochemical curation	Are the candidate compounds chemically plausible and traceable?	Curated phytochemical list, identifiers, structural information, and source evidence	Compound names, structural identifiers, database/source provenance, and uncertainty notes	Including predicted or misannotated compounds as confirmed constituents	Candidate compounds are linked to credible chemical evidence	Separate measured constituents from predicted constituents	Analytical confirmation and prioritisation of measurable markers
Data provenance and model transparency	Are computational inputs and models traceable?	Source databases, model type, training domain, input assumptions, and evidence origin	Dataset names, version/date where available, preprocessing description, model rationale, and limitations	Black-box outputs without source or domain explanation	Computational output can be audited and repeated	Avoid translational claims from opaque or poorly matched models	Independent model replication or external dataset checking
Target prediction	Are predicted targets biologically plausible?	Compound–target predictions connected to disease biology or mechanism rationale	Prediction method, confidence category where available, target identifiers, and biological context	Treating predicted targets as experimentally confirmed	Prioritised target hypotheses match relevant biology	Predictions should guide experiments, not replace them	Target engagement or pathway assay
Docking plausibility	Is the proposed ligand–target interaction structurally plausible?	Docking protocol, binding-site rationale, controls, and qualitative interaction interpretation	Protein preparation, ligand preparation, binding-site definition, control compounds, and reproducibility notes	Overclaiming mechanism from docking pose or score	Docking supports a testable binding hypothesis	Do not equate docking with efficacy or selectivity	Orthogonal binding or functional assay
Molecular dynamics	Is the docked interaction stable under simulation assumptions?	Simulation protocol, stability assessment,	Force field, system preparation, simulation	Presenting one simulation as definitive mechanism proof	Dynamic behaviour does not immediately	Interpret as model-dependent support only	Experimental confirmation of target engagement

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		sensitivity checks, and qualitative interpretation	parameters, replicate or sensitivity information		contradict the proposed interaction		
Network pharmacology and pathway plausibility	Does the candidate fit a coherent multi-target mechanism hypothesis?	Target network, pathway mapping, evidence provenance, and disease-context rationale	Node and edge sources, evidence type, pathway databases, and filtering criteria	Dense networks without biological prioritisation or source quality	Multi-target hypothesis is interpretable and evidence-ranked	Avoid assuming multi-target effects are automatically beneficial	Focused pathway and phenotypic validation
ADMET and safety-risk screening	Are there early pharmacokinetic or toxicity liabilities?	Predicted ADME properties, toxicity alerts, interaction flags, and uncertainty notes	Prediction tools, input structures, assumptions, and flagged liabilities	Treating predicted safety as confirmed safety	Candidate has no unresolved computational safety signal that blocks testing	ADMET prediction does not replace toxicity or PK studies	In vitro toxicity, metabolic stability, and interaction assays
Reproducibility and sensitivity checking	Are outputs robust to reasonable workflow changes?	Repeated analyses, parameter sensitivity, alternative tools, and input-quality checks	Workflow description, software/tool settings, random seeds where relevant, and comparison outputs	Candidate ranking changes substantially across minor assumptions	Candidate remains plausible under transparent sensitivity checks	Weak reproducibility should trigger revision	Independent computational replication before wet-lab prioritisation
Mechanistic hypothesis quality	Does the combined evidence justify preclinical testing?	Integrated identity, target, docking, dynamics, network, ADMET, and reproducibility evidence	Evidence summary, uncertainty grading, stop-or-revise decisions, and proposed validation assays	Moving to experiments because the candidate is computationally attractive rather than biologically justified	A clear, testable, safety-aware mechanism hypothesis is ready for preclinical evaluation	Mechanistic plausibility is not clinical readiness	In vitro and mechanistic validation study design

Figure 1 illustrates the staged in silico evidence-gate pathway from AI-assisted phytochemical discovery to mechanistic plausibility and preclinical prioritisation.

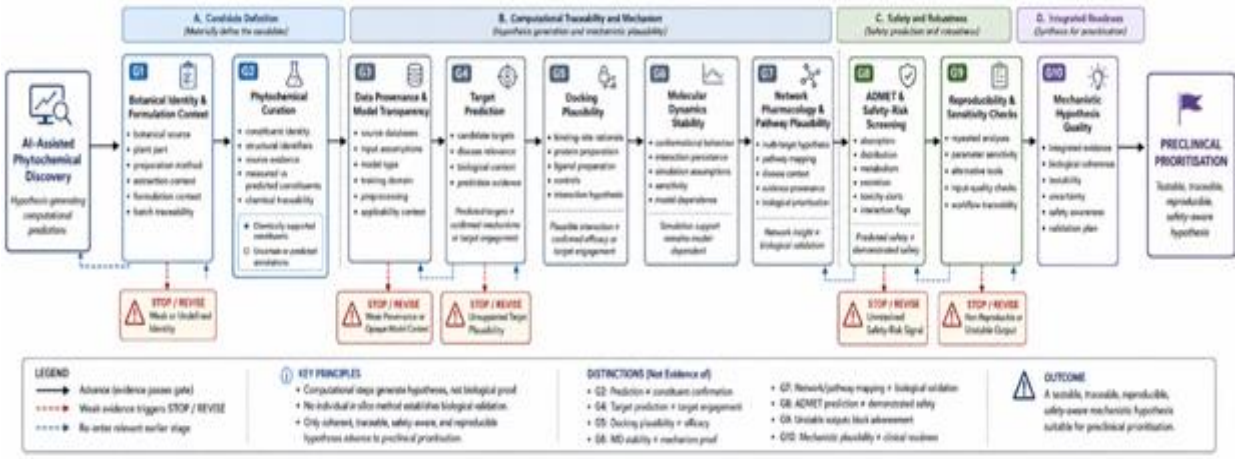

Figure 1. In Silico Evidence-Gate Pathway for AI-Discovered Phytotherapeutics

Alt-text description

A left-to-right evidence-gate pathway diagram showing AI-assisted phytochemical discovery moving through botanical identity, phytochemical curation, data provenance, target prediction, docking, molecular dynamics, network pharmacology, ADMET screening, reproducibility checks, and mechanistic plausibility before entering preclinical validation.

Preclinical validation requirements

Preclinical validation is the stage at which computationally prioritised phytotherapeutic candidates must be tested against biological reality. Natural bioactive products may have development potential, but a candidate emerging from AI prediction, docking, molecular dynamics, network pharmacology, or ADMET screening should advance only when a clear biological validation plan tests the proposed mechanism rather than merely seeking confirmatory results [14].

In vitro validation should include fit-for-purpose assays, appropriate controls, reproducible exposure conditions, and reporting sufficient to evaluate whether the observed biological effect corresponds to the proposed computational hypothesis. Experimental design and reporting quality are therefore not administrative details; they are core readiness criteria because weak controls, unclear replication, or selective reporting can transform a plausible computational hypothesis into a misleading translational claim [15].

Mechanistic testing should also consider whether conventional cell assays are sufficient for the biological question. Human-relevant experimental systems, including advanced microphysiological platforms where appropriate, may strengthen the bridge between simplified in vitro testing and more complex organism-level responses, particularly when the proposed phytotherapeutic mechanism involves tissue context, metabolism, barrier function, or multi-organ toxicity concerns [16].

Pharmacokinetic and formulation readiness are essential because phytochemicals may show limited solubility, instability, poor bioavailability, or delivery-related constraints that alter the relevance of computational target predictions [17]. In vivo preclinical validation must then be designed and reported transparently, with attention to animal model relevance, dose rationale, randomisation, blinding where feasible, outcome definition, and reproducibility, so that animal evidence is interpreted as a translational test rather than as a guaranteed predictor of clinical benefit [18].

Table 2 maps the preclinical validation requirements needed to move AI-discovered phytotherapeutics beyond computational plausibility.

Table 2. Preclinical Validation Requirements for AI-Discovered Phytotherapeutics: In Vitro Confirmation, Mechanistic Testing, In Vivo Evidence, Pharmacokinetics, Formulation Standardisation, Toxicity Assessment, Interaction Screening, and Reproducibility Controls

Validation domain	Purpose	Evidence required	Methodological consideration	Readiness contribution	Risk if absent	Quality-control requirement	Decision implication
In vitro biological confirmation	Test whether the predicted biological effect is observable in a controlled system	Phenotypic or functional assay evidence linked to the proposed mechanism	Use relevant cell type, exposure duration, concentration rationale, positive and negative controls	Moves candidate beyond computational plausibility	Computational hypothesis remains untested	Replication, assay validation, and transparent reporting	Advance only if biological signal is reproducible and interpretable
Target engagement	Determine whether the predicted target is affected under biological conditions	Direct or indirect target engagement evidence	Select assay appropriate to target class and compound complexity	Connects target prediction to biological mechanism	Predicted target may be irrelevant	Orthogonal confirmation where feasible	Revise mechanism if target engagement is unsupported
Pathway or mechanism testing	Evaluate whether downstream pathway effects match the proposed mechanism	Pathway markers, functional readouts, or mechanistic perturbation evidence	Avoid relying on a single marker as proof of mechanism	Strengthens mechanism plausibility	Effects may be nonspecific or unrelated to predicted pathway	Predefined pathway readouts and controls	Advance to broader validation only if mechanism remains coherent

Extract and batch consistency	Confirm that the tested material is reproducible	Chemical profile, marker compounds, and batch-comparison documentation	Link biological assays to the exact tested batch	Ensures biological findings are tied to defined material	Results cannot be reproduced across preparations	Batch records and analytical profile	Stop or revise if composition is unstable
In vivo relevance	Test whether effects persist in organism-level context	Animal-model evidence where justified by mechanism and safety question	Use relevant model, ethical design, and transparent reporting	Provides organism-level plausibility	In vitro findings may not translate	Randomisation, blinding where feasible, sample-size rationale, and outcome transparency	Do not infer clinical benefit from animal data alone
Pharmacokinetics	Determine whether active constituents or relevant metabolites reach plausible exposure	Absorption, distribution, metabolism, excretion, and exposure evidence	Consider parent compounds, metabolites, matrix effects, and route of administration	Links mechanism to achievable exposure	Target effects may occur only at unrealistic concentrations	Validated analytical method and exposure reporting	Revise dose rationale or formulation if exposure is inadequate
Formulation standardisation	Improve consistency, stability, delivery, and interpretability	Formulation composition, stability, release, and batch consistency evidence	Address solubility, degradation, excipient effects, and delivery route	Converts candidate into testable intervention	Variable formulation undermines validation and safety interpretation	Defined formulation protocol and stability testing	Advance only with reproducible formulation
Toxicity assessment	Identify biological safety concerns before clinical interpretation	Cytotoxicity, organ-relevant toxicity, genotoxicity where relevant, and in vivo safety evidence where justified	Match toxicity model to expected exposure and intended use	Provides safety-risk boundary for further testing	Candidate may advance despite unresolved harm signals	Dose-response design and adverse-effect reporting	Stop or revise if safety signal is unresolved
Interaction screening	Evaluate herb-drug and compound-drug risk	Enzyme, transporter, pharmacodynamic, or clinical interaction evidence where relevant	Consider common co-medications and vulnerable populations	Supports safer clinical decision pathways	Hidden interaction risk may be missed	Interaction assay documentation and uncertainty notes	Require clinical caution unless interaction risk is clarified
Reproducibility controls	Confirm that findings are robust	Replication, independent confirmation where feasible, sensitivity analysis, and transparent methods	Avoid selective confirmation of expected computational results	Builds confidence across computational and biological domains	False-positive translational signal	Full method reporting and data traceability	Advance only when reproducibility supports the gate decision

Clinical decision pathways

Clinical decision pathways for AI-discovered phytotherapeutics must integrate pharmacokinetic interaction evidence, toxicity and interaction forecasting, and decision-support safeguards before any candidate is interpreted in relation to patient care [19-21]. This means that clinical relevance is not achieved by computational plausibility or preclinical activity alone; it depends on whether the candidate has sufficient evidence to inform a specific indication, patient context, safety profile, uncertainty boundary, and comparison with existing therapeutic options.

Patient communication is a central element of phytotherapeutic decision-making because complementary medicine use may be undisclosed, fragmented across providers, or separated from conventional medication review. A translational readiness framework must therefore treat disclosure, medication reconciliation, and patient-context documentation as safety-relevant decision gates rather than as peripheral clinical details [22].

Clinical evidence alignment requires attention to botanical-specific development challenges, including the definition of the intervention, composition consistency, comparator selection, clinically meaningful endpoints, dose rationale, safety monitoring, and interpretability of trial evidence. A candidate should not be presented as clinically ready unless the clinical evidence corresponds to the same material, formulation, indication, and patient context under consideration [23].

Clinical decision support readiness is therefore the final stage of translational interpretation, not a shortcut around missing evidence. A responsible decision pathway should state what is known, what remains uncertain, what safety concerns require review, whether the formulation is standardised, whether interactions are plausible, whether clinical evidence exists for the intended use, and whether clinician oversight is necessary. In this framework, decision support is designed to clarify evidence status and uncertainty rather than to generate autonomous phytotherapeutic recommendations.

Proposed translational readiness framework

The proposed framework begins with data provenance and model transparency because AI-derived phytotherapeutic claims cannot be evaluated if the input chemistry, training domain, model logic, or prediction context is opaque. Explainability is not required to make every model fully interpretable, but it should make the basis of prioritisation sufficiently understandable for scientific review, error detection, and validation planning [24]. Computational reproducibility is a parallel requirement because a candidate that cannot be reproduced under transparent workflow conditions should not advance to biological testing as a high-confidence translational lead [25].

The second stage is evidence-source assessment, which asks whether predicted targets, bioactivities, and mechanistic links are supported by traceable assay or database evidence. Curated bioactivity resources can help organise compound–target evidence, but translational interpretation requires attention to assay context, data quality, chemical identity, and biological relevance rather than treating database presence as proof of mechanism [26].

The third stage is model-performance and domain-fit review. Molecular machine-learning predictions may be useful for property estimation or candidate ranking, but their reliability depends on representation quality, training data, benchmark performance, and applicability to the chemical space being evaluated [27]. For phytotherapeutics, this is especially important because complex extracts, mixtures, stereochemical ambiguity, metabolites, and poorly characterised constituents may fall outside the domain in which many molecular models perform best.

The fourth stage integrates safety and interaction evidence into the same readiness pathway as mechanism evidence. Knowledge-graph approaches can support structured representation of natural product–drug interaction evidence, helping connect compounds, enzymes, transporters, drugs, evidence sources, and clinical risk concepts in a way that is more transparent than isolated prediction outputs [28]. In the proposed framework, such integration is used to flag uncertainty and interaction risk, not to declare clinical safety.

The fifth stage links ADME prediction, pharmacokinetic readiness, and translational-risk assessment. Tools for estimating pharmacokinetic and drug-likeness properties can support early screening, but predicted ADME properties should be separated from measured pharmacokinetic evidence and formulation-specific exposure data [29]. The final framework stage therefore asks whether AI has meaningfully increased the probability of responsible translation or merely produced attractive hypotheses that remain biologically, chemically, or clinically under-supported [30].

Table 3 presents the proposed translational readiness framework for AI-discovered phytotherapeutics from computational discovery to clinical decision-making.

Table 3. Proposed Translational Readiness Framework for AI-Discovered Phytotherapeutics: Evidence Gates, Readiness Criteria, Validation Requirements, Safety Controls, Clinical Decision Relevance, Implementation Risks, and Advancement Logic

Framework stage	Evidence gate	Readiness criterion	Required validation	Safety or interaction consideration	Clinical decision relevance	Failure risk	Advancement condition	Stop-or-revise trigger
Stage 1: Candidate definition	Gate 1: Botanical and phytochemical identity	Candidate material is clearly defined and chemically traceable	Botanical authentication, preparation documentation, chemical profiling	Misidentified or variable material may produce misleading safety interpretation	Clinical evidence cannot align with undefined intervention	Product label is mistaken for pharmacological identity	Advance when source, preparation, and composition are documented	Stop if botanical identity or chemical profile is unclear

Stage 2: Computational audit	Gate 2: Data provenance and model transparency	Inputs, models, databases, and assumptions are auditable	Workflow documentation, source traceability, model description	Opaque data may hide safety or quality limitations	Decision tools require evidence traceability	Black-box ranking without reviewable basis	Advance when predictions can be independently reviewed	Revise if provenance or model domain is unclear
Stage 3: Mechanism plausibility	Gate 3: In silico target and mechanism plausibility	Predicted targets and pathways are biologically coherent	Target prediction review, docking rationale, pathway mapping	Off-target or pathway mismatch may create risk	Mechanism must match intended indication	Network or docking output is overinterpreted	Advance when mechanism is testable and disease-relevant	Revise if target or pathway plausibility is weak
Stage 4: Early safety screen	Gate 4: ADMET and safety-risk screening	No unresolved computational safety signal blocks testing	ADMET prediction, toxicity alerts, interaction flags	Toxicity and interaction risks are identified early	Clinical interpretation requires safety awareness	Predicted safety is treated as confirmed safety	Advance when risk signals are documented and manageable for testing	Stop if major safety alerts remain unresolved
Stage 5: Computational robustness	Gate 5: Reproducibility and sensitivity checking	Candidate ranking and mechanism remain stable under transparent checks	Replication, alternative tools, sensitivity analysis	Irreproducible outputs may conceal false positives	Decision support cannot rely on unstable evidence	Results change with minor workflow changes	Advance when outputs are robust enough for preclinical testing	Revise if reproducibility is poor
Stage 6: Biological confirmation	Gate 6: In vitro biological validation	Biological effect is observed in relevant controlled assays	Phenotypic, functional, target-engagement, or pathway assays	Cytotoxicity and nonspecific effects are assessed	Provides first biological support for computational hypothesis	Activity is nonspecific or assay-dependent	Advance when effect is reproducible and mechanistically interpretable	Stop if in vitro evidence contradicts mechanism
Stage 7: Organism-level relevance	Gate 7: In vivo preclinical validation	Relevant organism-level evidence supports biological plausibility	Justified animal or alternative in vivo model evidence	Adverse findings and exposure limits are documented	Supports but does not establish clinical benefit	Animal findings are overextended to humans	Advance when in vivo evidence is transparent and relevant	Revise if model relevance or reporting is weak
Stage 8: Exposure and formulation	Gate 8: Pharmacokinetic and formulation readiness	Candidate can be delivered consistently at biologically plausible exposure	PK studies, formulation stability, batch consistency, dose rationale	Formulation may alter exposure and toxicity	Clinical decision relevance depends on reproducible intervention	Active constituents do not reach plausible exposure	Advance when exposure and formulation are coherent	Stop if formulation or PK evidence is inadequate
Stage 9: Safety boundary	Gate 9: Safety, toxicity, and interaction assessment	Toxicity and interaction risks are sufficiently characterised for next-stage evaluation	Toxicity testing, interaction assays, medication-risk review	Herb-drug interaction and vulnerable-population risks are addressed	Determines whether clinical interpretation is ethically plausible	Natural-origin safety assumption replaces evidence	Advance when safety uncertainties are explicit and acceptable for context	Stop if toxicity or interaction risk is unresolved
Stage 10: Evidence alignment	Gate 10: Clinical evidence alignment and decision relevance	Evidence matches intended indication, formulation, and patient context	Clinical literature assessment and endpoint relevance review	Safety evidence must correspond to same intervention context	Prevents extrapolation beyond evidence	Preclinical or traditional evidence is treated as clinical proof	Advance when evidence aligns with intended decision	Revise if clinical evidence is indirect or mismatched

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Stage 11: Risk synthesis	Gate 11: Translational risk assessment	Benefits, uncertainties, evidence gaps, and implementation risks are synthesised	Cross-gate evidence review and uncertainty grading	Safety, PK, formulation, and interaction risks are integrated	Supports cautious interpretation rather than recommendation	Evidence gaps are hidden by positive computational narrative	Advance when risks are transparent and manageable	Stop if uncertainty is too high for decision use
Stage 12: Decision readiness	Gate 12: Clinical decision support readiness	Candidate status can be communicated without overclaiming	Evidence summary, clinician-review logic, stop-or-revise status	Safety warnings and interaction caveats are visible	Supports clinician judgement without replacing it	Decision support becomes promotional or prescriptive	Advance only as evidence-status support, not autonomous recommendation	Revise if tool implies unsupported clinical action

Figure 2 displays the proposed translational readiness framework linking in silico discovery, preclinical validation, safety assessment, formulation readiness, and clinical decision relevance.

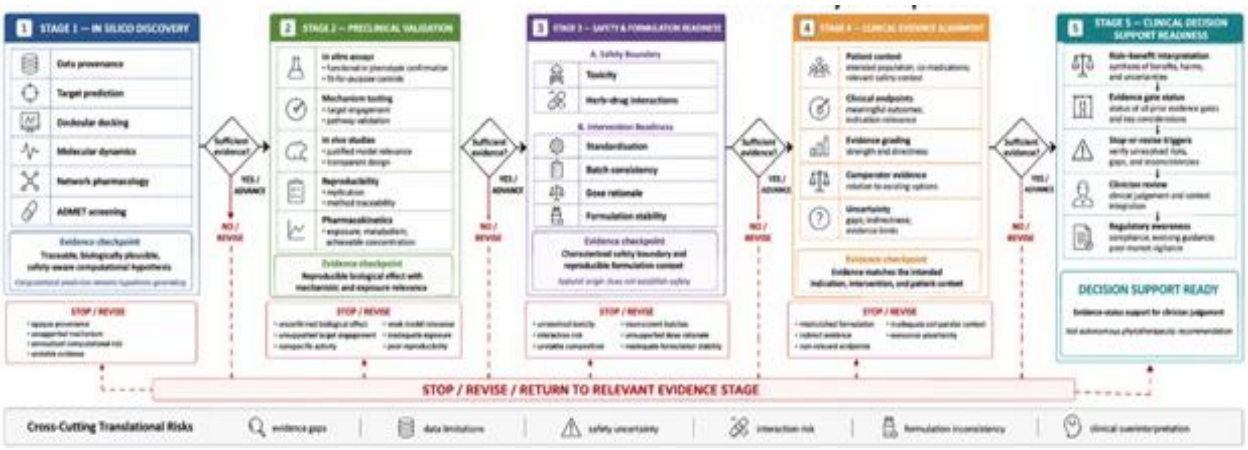

Figure 2. Translational Readiness Framework for AI-Discovered Phytotherapeutics

Alt-text description

A layered translational readiness framework diagram showing in silico discovery feeding into evidence gates, preclinical validation, safety and toxicity assessment, pharmacokinetic and formulation readiness, clinical evidence alignment, decision support readiness, implementation risk review, and stop-or-revise feedback loops.

Implementation risks

The first implementation risk is that AI-assisted phytotherapeutic discovery may inherit data limitations from both chemical and biological sources. Poor annotation, biased datasets, structurally ambiguous phytochemicals, inadequate negative data, and weak biological relevance can all create predictions that appear precise while remaining translationally fragile [31]. The framework addresses this risk by requiring data provenance, model-domain review, reproducibility checks, and stop-or-revise triggers before computational outputs are used to justify experimental advancement.

The second implementation risk concerns safety evidence. Herbal medicine adverse-event data can inform risk awareness, but pharmacovigilance evidence is often shaped by reporting heterogeneity, incomplete product characterisation, variable causality assessment, and uneven documentation of concomitant medicines [32]. For AI-discovered phytotherapeutics, this means that the absence of a strong safety signal should not be mistaken for evidence of safety, especially when the candidate formulation, dose, patient population, or co-medication context differs from available evidence.

The third implementation risk is clinical overinterpretation. Spontaneous adverse-event reporting can identify important safety concerns associated with herbal products, but such data are limited by underreporting, incomplete exposure information, and uncertainty about causality [33]. A translational readiness framework can reduce overclaiming by requiring every candidate to pass through identity, provenance, mechanism, reproducibility, biological validation, formulation, pharmacokinetic, toxicity, interaction, and

clinical-evidence gates before it is positioned as decision-relevant.

CONCLUSION

This article proposes a translational readiness framework for AI-discovered phytotherapeutics that connects in silico discovery to preclinical validation and clinical decision-making through staged evidence gates. The framework distinguishes computational prediction from biological validation, mechanistic plausibility from demonstrated effect, and preclinical promise from clinical decision readiness. Its central contribution is a structured advancement logic in which botanical and phytochemical identity, data provenance, model transparency, reproducibility, target plausibility, ADMET screening, biological validation, pharmacokinetics, formulation standardisation, safety assessment, interaction review, clinical evidence alignment, and implementation-risk evaluation are treated as connected requirements. Responsible translation of AI-discovered phytotherapeutics depends not on computational novelty alone, but on whether evidence is sufficiently traceable, reproducible, biologically meaningful, safety-aware, formulation-specific, and clinically contextualised.

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