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Commentary

From ethnomedicine to precision rheumatology: a translational framework for prioritizing medicinal plants in rheumatoid arthritis drug discovery

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Abstract

Despite advances in disease-modifying therapies, rheumatoid arthritis (RA) continues to impose a substantial clinical and socio-economic burden. Ethnobotanical studies have identified numerous medicinal plants for inflammatory disorders, yet only a few have progressed to systematic scientific evaluation or therapeutic development. A major limitation is the absence of a structured approach for prioritizing medicinal plants with the greatest translational potential. This commentary proposes a translational prioritization framework that integrates ethnobotanical evidence, phytochemical information, mechanistic plausibility, safety, computational approaches, and experimental validation to guide the selection of promising medicinal plants for RA. Rather than treating ethnobotanical knowledge as an end point, the proposed framework positions it as the starting point for evidence-based drug discovery. By linking indigenous knowledge with modern biomedical research, this approach provides a practical strategy for improving the efficiency and translational value of plant-based therapeutic development in rheumatoid arthritis.

Keywords: Rheumatoid arthritis, Ethnobotany, Plant-derived therapeutics, Translational prioritization, Precision rheumatology, Drug discovery

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disorder characterized by chronic inflammation of the synovium, leading to progressive destruction of cartilage and bone, and ultimately resulting in joint dysfunction. Despite significant advances in therapeutic interventions, including disease-modifying antirheumatic drugs (DMARDs), biologic agents, and targeted therapies, many patients continue to experience inadequate clinical response, adverse effects, or limited access to treatment because of cost and the need for long-term therapy [1]. These challenges have intensified the search for safer, affordable, and mechanism-based therapeutic options, including plant-derived candidates with the potential to modify disease progression [2].

Indigenous communities have long relied on medicinal plants to relieve joint pain, swelling, and stiffness through traditional knowledge passed down across generations [3,4]. However, documenting their traditional use alone is not enough to support their development into clinically useful therapies. This raises an important question: which medicinal plant candidates should be prioritized for further scientific investigation? At present, there is no widely accepted strategy for selecting the most promising candidates. As a result, a few well-known medicinal plants continue to receive disproportionate scientific attention, while many ethnobotanically important but poorly investigated species remain overlooked within drug discovery programs [5]. The real challenge is not the lack of

ethnobotanical evidence, but the absence of a systematic approach for translating that evidence into clinically relevant therapeutic research. This translational gap between ethnobotanical documentation and therapeutic development is illustrated in **Figure 1**.

Much of the existing ethnobotanical research has focused on documenting medicinal plants [6], whereas the perspective presented in this commentary shifts the focus towards evidence-based translational prioritization as the first step in rheumatoid arthritis drug discovery [7]. Rather than presenting another catalogue of medicinal species, this commentary proposes a practical framework that integrates ethnobotanical evidence with phytochemical profiling, mechanistic plausibility, computational prioritization, experimental validation, and clinical translation. **Figure 2** presents the proposed translational prioritization framework for advancing indigenous knowledge towards evidence-based therapeutics for rheumatoid arthritis.

The Translational Gap: From Ethnobotanical Documentation to Drug Discovery

Ethnobotanical investigations have substantially expanded the knowledge base of medicinal plants traditionally used for the management of RA. Across different geographical regions, Indigenous communities have reported numerous medicinal plants in their indigenous knowledge systems for managing joint pain, inflammation, and other musculoskeletal problems, which may represent potential sources of novel therapeutic candidates [8,9]. However, only a small proportion of these plants have been extensively investigated for their phytochemical composition, mechanisms of action, or clinical potential [10]. As a result, this knowledge has rarely been translated into evidence-based therapeutic development for RA.

While most ethnobotanical studies conclude by cataloguing medicinal plants, they rarely provide an objective basis for prioritising candidates for drug development [11]. Ethnobotanical consensus can provide an important first-level signal for candidate selection, particularly when therapeutic use is repeatedly reported across independent communities. However, frequency of citation or use does not necessarily establish pharmacological efficacy, safety, bioavailability, or clinical relevance. Conversely, plants with limited documentation should not automatically be considered scientifically unimportant. A prioritization framework should therefore balance traditional evidence with phytochemical, mechanistic, toxicological, pharmacokinetic, and translational evidence rather than treating any single criterion as decisive. Without clear criteria for prioritization, a medicinal plant candidate is more likely to be selected on the basis of its availability, frequent mention in the literature, or the investigator preference rather than its scientific merit [12]. As a result, only a few well-known medicinal plants have received considerable research attention, whereas many traditionally used plants are still poorly studied. Therefore, the selection of medicinal plant candidates should not depend only on their traditional use, but should also take into account their phytochemical composition, mechanism of action, safety, and ability to influence disease-related pathways. This commentary argues that documenting medicinal plants should mark the beginning rather than the endpoint of drug discovery (**Figure 1**). The following section outlines a translational prioritization framework to address this gap.

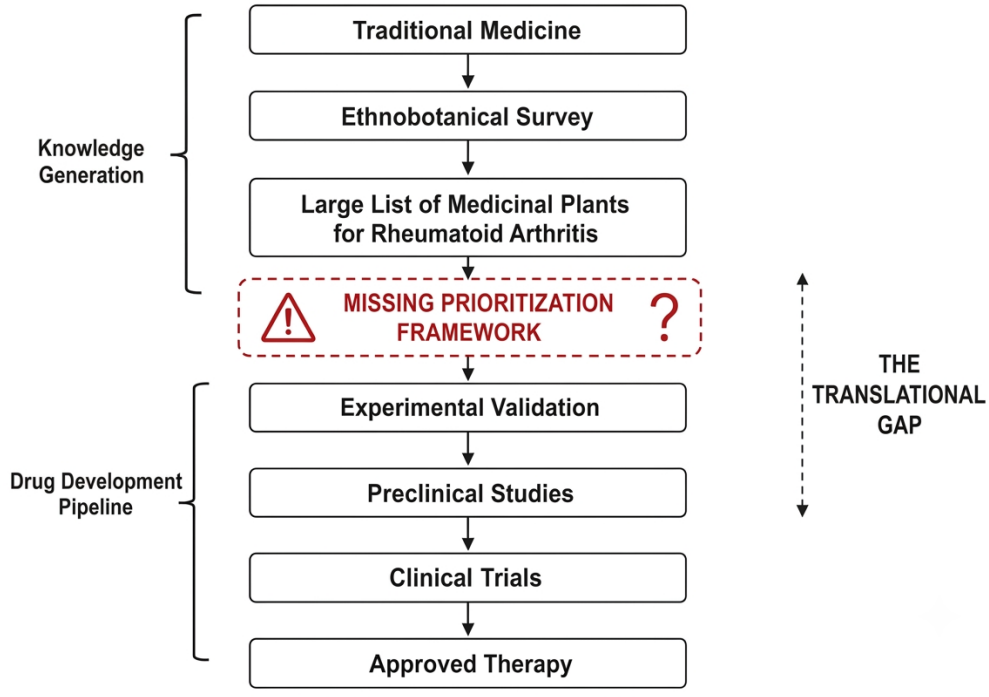

Figure 1. The translational gap in ethnobotanical drug discovery for rheumatoid arthritis. Schematic representation of the gap between ethnobotanical documentation of medicinal plants and their progression to mechanism-based drug discovery and clinical translation, highlighting the need for a standardized translational prioritization framework.

A Conceptual Framework for Translational Prioritization

The conceptual framework proposed in this commentary (**Figure 2**) addresses this need by introducing translational prioritization as the critical first step in RA drug discovery. Rather than replacing traditional research and pharmaceutical science, it enhances the initial candidate-selection stage by supplementing traditional knowledge with computational and clinical evidence [13]. Emerging technologies such as network pharmacology, molecular docking, artificial intelligence, multi-omics and other cutting-edge technologies can be used as additional decision support tools in the framework to support evidence-based therapeutic development.

However, these approaches should be considered complementary rather than definitive evidence of therapeutic potential. Ethnobotanical use may be influenced by cultural, geographical, and documentation-related factors, while phytochemical richness does not necessarily indicate therapeutic efficacy or safety. Similarly, network pharmacology, molecular docking, artificial intelligence, and multi-omics analyses mainly generate mechanistic hypotheses and

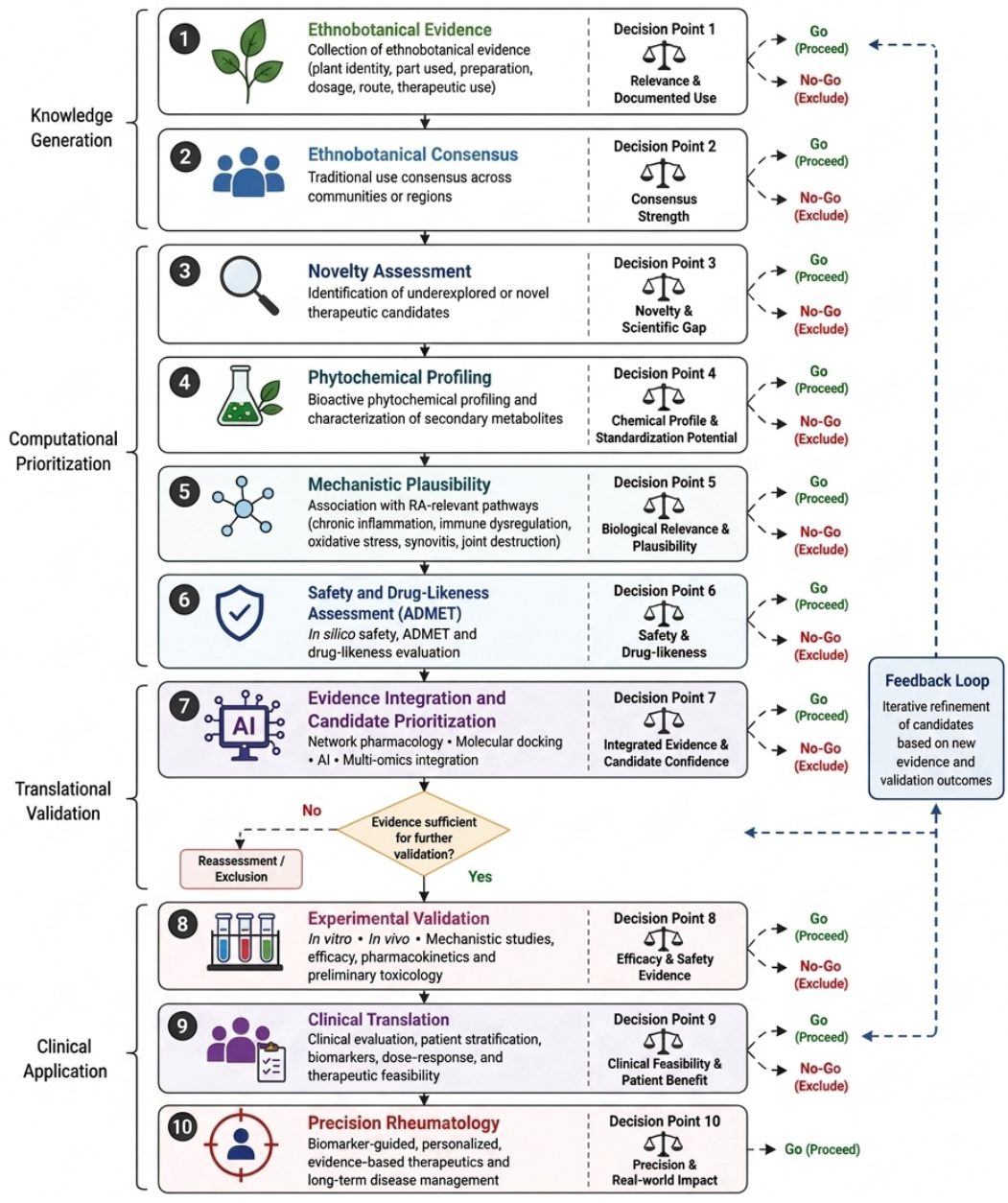

Figure 2. A translational framework for prioritizing medicinal plants in rheumatoid arthritis drug discovery. The framework integrates ethnobotanical, phytochemical, mechanistic, safety, computational, experimental, and clinical evidence to support evidence-based candidate selection. Defined Go/No-Go decision points and iterative feedback enable refinement of candidate prioritization towards precision rheumatology. Abbreviations: ADMET: Absorption, Distribution, Metabolism, Excretion, and Toxicity; AI: Artificial Intelligence; RA: Rheumatoid Arthritis.

require experimental validation. Therefore, candidate prioritization should be based on the combined strength of independent evidence rather than on any single criterion.

Proper documentation of the medicinal plant, including its correct botanical identity, the part used, preparation method, dosage, and traditional therapeutic use, forms the basis for subsequent scientific validation. However, traditional use alone should not justify translational commitment. Greater confidence may be obtained when similar therapeutic uses are independently reported by different indigenous communities or geographical regions [14]. While intensive investigation of a small group of well-established medicinal plants can be useful, it also takes away focus from numerous highly reputed traditional species whose scientific potential has not been sufficiently explored. Prioritizing these candidate plants will give a better chance of discovering bioactive compounds that can be further developed into effective medicines.

Once primary prioritization is completed, mechanistic plausibility and phytochemical characterization provide the scientific basis for assessing therapeutic relevance. Understanding the secondary metabolites produced by a plant helps determine its chemical characteristics and supports its standardization for further investigation [15]. However, phytochemical richness alone is insufficient without biological plausibility and evidence of safety. Candidate plants should demonstrate activity against pathways relevant to chronic inflammation, immune dysregulation, oxidative stress, synovitis, synovial hyperplasia, and progressive joint destruction [16]. This integrated approach combines ethnobotanical evidence, phytochemical profiling, mechanistic plausibility, safety assessment, computational analysis, experimental validation, and clinical considerations within a single evidence-based continuum. Such cumulative evaluation enables researchers to prioritize medicinal plants on the basis of scientific merit rather than convenience, familiarity, or availability [17]. By providing a transparent and reproducible pathway from indigenous knowledge to clinical investigation, the proposed framework offers a practical strategy for accelerating evidence-based drug discovery in RA.

Precision Rheumatology: Why the Framework Matters

Individual patient-related parameters, including genetic background, immune signature, disease activity, and response to treatment, increasingly require personalized therapeutic strategies in RA [1]. The proposed conceptual framework strengthens this concept by extending translational prioritization to the early stages of plant-based drug discovery. To date, plant-derived compounds or whole plant extracts have largely been investigated for broad-spectrum properties such as analgesic or anti-inflammatory activity, without specifically targeting the complex molecular pathways underlying RA [18]. Rather than serving solely as sources of isolated bioactive compounds, medicinal plants should be viewed as multicomponent therapeutic interventions capable of modulating several interconnected disease pathways simultaneously [19].

In the future, precision rheumatology will increasingly rely on matching therapeutic options to disease-specific molecular signatures and individual biomarker profiles. Better understanding of molecular signaling pathways and cellular biomarkers is improving our knowledge of disease heterogeneity and therapeutic response in RA [20]. Although the proposed framework does not directly identify plant-based therapies for individual patients, it provides a systematic approach for prioritizing medicinal plant candidates with highest potential to modulate relevant pathways. By integrating scientific information obtained from ethnobotanical study, phytochemical analysis, mechanistic evaluation, preclinical studies, and clinical translation, this framework connects indigenous knowledge with modern rheumatology. Consequently, precision rheumatology encompasses not only the clinical selection of targeted therapies for individual patients, but also the systematic identification of therapeutic candidates through transparent, evidence-based research strategies [21].

Future Perspectives and Research Priorities

The future of plant-derived therapeutics for RA will rely less on documenting additional medicinal species and more on improving the quality, reproducibility, and translational relevance of subsequent investigations. A major research priority is the development of standardized criteria for translational prioritization, enabling medicinal plant candidates to be selected using objective and reproducible scientific evidence rather than availability or investigator preference [22]. **Table 1** summarizes the principal criteria proposed to support this systematic prioritization. Future progress will also depend on integrating ethnobotanical knowledge with contemporary biomedical research. Interconnected databases that comply with

Table 1. Proposed criteria for translational prioritization of plant-derived therapeutic candidates in rheumatoid arthritis drug discovery.

Prioritization criterion	Translational rationale	Expected contribution to drug discovery	Key limitations/consideration
Ethnobotanical consensus	Demonstrates repeated traditional use across communities or geographical regions	Strengthens initial confidence in candidate selection	Traditional use may be influenced by cultural, geographical and documentation-related factors
Novelty assessment	Identifies scientifically underexplored medicinal plants with potential translational value	Expands opportunities for discovering new therapeutic leads	Limited scientific information may reflect lack of research rather than therapeutic novelty
Phytochemical profiling	Characterizes the chemical composition of the plant	Supports identification and standardization of potentially active constituents	Phytochemical richness alone does not establish efficacy or safety
Mechanistic plausibility	Links plant constituents with pathways relevant to rheumatoid arthritis	Improves biological relevance of candidate selection	Predicted pathway associations require experimental confirmation

Prioritization criterion	Translational rationale	Expected contribution to drug discovery	Key limitations/consideration
Safety and ADMET assessment	Provides preliminary information on safety and pharmacokinetic properties	Helps identify candidates with better translational feasibility	In-silico or early-stage predictions cannot replace experimental toxicological and pharmacokinetic studies
Computational prioritization	Predicts molecular targets, pathway interactions and candidate ranking	Supports systematic and evidence-based candidate selection	Computational predictions are hypothesis-generating and require experimental validation
Experimental validation	Confirms pharmacological activity, mechanism and preliminary safety	Provides stronger preclinical evidence for therapeutic development	Findings may depend on the experimental model and may not directly translate to humans
Clinical feasibility	Considers human relevance, therapeutic applicability and available clinical evidence	Supports progression towards clinical investigation	Clinical relevance cannot be established without appropriately designed clinical studies

the FAIR (Findable, Accessible, Interoperable, and Reusable) principles should integrate ethnobotanical records, phytochemical data, pharmacological evidence, toxicity profiles, as well as clinical studies into a common research ecosystem [23,24]. Progress will also depend on multidisciplinary collaboration among ethnobotanists, rheumatologists, pharmacologists, phytochemists, computational scientists, medicinal chemists, and clinicians [25]. Scientific advances should also remain closely linked with environmental stewardship and ethical practice. Accordingly, sustainable harvesting, equitable benefit sharing, transparent documentation, and proper recognition of the traditional knowledge holders should remain integral to future translational research.

Conclusion

The future development of plant-derived therapeutics for rheumatoid arthritis should move beyond documentation alone towards systematic and evidence-based candidate prioritization. The framework proposed here integrates ethnobotanical evidence with phytochemical characterization, mechanistic assessment, computational analysis, safety evaluation, and experimental validation. Its value lies not in replacing traditional knowledge or established drug-discovery approaches, but in providing a transparent basis for deciding which candidates warrant further investigation. Future refinement and validation of such frameworks may improve the efficiency, reproducibility, and translational relevance of plant-based drug discovery in rheumatoid arthritis.

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Author Contribution Statement

Praveen Deepak: Conceptualization, literature review, framework development, writing – original draft preparation, writing – review and editing, and final approval of the manuscript.

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