DOI: 10.5281/zenodo.17805392

CHAPTER 9

Medicinal Plants in the Management of Rheumatoid Arthritis: Insights from the Oriental Region

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Received: 20 November 2025; Accepted: 25 November 2025; Available online: 3 December 2025

Abstract: Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by persistent joint inflammation, synovial hyperplasia, and progressive cartilage destruction. While conventional therapies, such as corticosteroids, DMARDs, and biologics, have improved disease management, their high cost and adverse effects have driven a resurgence of interest in medicinal plants, particularly from the Oriental region. This chapter explores the phytotherapeutic potential of oriental medicinal flora in mitigating RA pathophysiology through immunomodulatory, antioxidant, and anti-inflammatory pathways. Integrating molecular pharmacology, traditional knowledge systems, and sustainable bioresource management, this chapter underscores the interdisciplinary bridge between ethnomedicine and modern life sciences.

Interdisciplinary Research in Life Sciences: A Path Towards Sustainability (Vol. 3) - Jayvardhan V. Balkhande & Jalander Vaghmare (Eds.)

ISBN: 978-93-95369-86-2 (paperback) 978-93-95369-58-9 (electronic) | © 2025 Advent Publishing.

https://doi.org/10.5281/zenodo.17805392

Keywords: Rheumatoid arthritis, Medicinal plants, Oriental region, Immunomodulation, Phytotherapy, Sustainability

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disorder marked by chronic synovial inflammation, progressive joint destruction, and diverse extra-articular complications. Its global burden has more than doubled since 1990, with nearly 18 million individuals affected, contributing substantially to morbidity and healthcare costs.[1,2] RA arises from dysregulated immune responses involving pro-inflammatory cytokines, synovial hyperplasia, and subsequent cartilage and bone damage.[3] Although disease-modifying antirheumatic drugs and biologics, particularly methotrexate and tumour-necrosis factor inhibitors, have improved clinical outcomes, they remain limited by variable efficacy,[4] high cost, adverse effects, and incomplete disease control, leaving significant therapeutic gaps, especially in resource-constrained regions.

Growing interest in plant-derived therapeutics reflects the need for safe, accessible, and multi-targeted interventions. Medicinal plants contain diverse bioactive compounds, including polyphenols, flavonoids, terpenoids, and alkaloids, which modulate key inflammatory pathways such as NF-κB and MAPK. Many of these species have long-standing traditional use for arthritis and related inflammatory disorders, demonstrating both cultural relevance and pharmacological promise.[5] The Oriental region, encompassing South, East, and Southeast Asia, serves as a biodiversity hotspot and a repository of rich ethnomedical knowledge preserved in systems such as Ayurveda and Traditional Chinese Medicine.[6] This ecological and cultural wealth provides fertile ground for identifying novel anti-arthritic agents, while also underscoring the importance of sustainable harvesting, conservation, and equitable benefit-sharing.

Addressing the complexity of RA requires an interdisciplinary framework that integrates ethnobotany, phytochemistry, pharmacology, rheumatology, and sustainability sciences. Such an approach supports evidence-based innovation while aligning with broader goals of ecological stewardship and culturally respectful utilisation of traditional knowledge.

Rheumatoid Arthritis: Immunopathogenesis and Molecular Targets

Rheumatoid arthritis is a systemic autoimmune disorder driven by complex dysregulation of innate and adaptive immunity, leading to persistent synovial inflammation, cartilage degradation, and bone erosion. Central to its development is the early appearance of autoantibodies such as Rheumatoid Factor and Anti-Citrullinated Protein Antibodies (ACPA), which signal a loss of immune tolerance and form pathogenic immune complexes that activate complement pathways

and recruit inflammatory cells.[7,8] This response is reinforced by aberrant antigen-presenting cells and autoreactive lymphocytes, promoting the formation of ectopic germinal centres and sustaining chronic synovial inflammation. The disease environment is further shaped by an amplified cytokine network dominated by TNF-α, IL-6, and IL-17, which drive endothelial activation, osteoclastogenesis, and matrix degradation, largely through the JAK–STAT signalling axis.[9,10] Excessive production of reactive oxygen and nitrogen species by synovial macrophages, neutrophils, and fibroblasts induces oxidative damage, chondrocyte apoptosis, and NF-κB activation, perpetuating a cycle of inflammation and tissue injury.[11] Macrophage polarization toward the pro-inflammatory M1 phenotype, alongside hyperactivated fibroblast-like synoviocytes, accelerates joint destruction through sustained cytokine release and degradative enzyme production. Given the multifaceted nature of rheumatoid arthritis pathogenesis, phytochemicals such as flavonoids, terpenoids, polyphenols, and alkaloids offer promising multi-target therapeutic potential. They exert their effects by modulating cytokine signalling, inhibiting NF-κB and JAK–STAT pathways, reducing oxidative stress, and promoting anti-inflammatory M2 macrophage polarization. These properties support the exploration of medicinal plants from the Oriental region as sustainable and effective adjuncts in rheumatoid arthritis management.[12]

Oriental Medicinal Systems and Rheumatoid Arthritis

The Oriental region hosts long-established medical systems such as Ayurveda, Traditional Chinese Medicine (TCM), Unani, and Siddha, all of which provide plant-based strategies for RA grounded in principles of systemic balance, detoxification, and immune modulation (Figure 1).[13] Contemporary immunology increasingly validates these traditional insights. In Ayurveda, RA corresponds to Amavata, arising from Ama accumulation and Vata imbalance,[14] paralleling modern concepts of metabolic dysfunction, cytokine overproduction, and oxidative stress. Rasayana herbs, including *Withania somnifera*, *Tinospora cordifolia*, and *Zingiber officinale*, exhibit anti-inflammatory and immunomodulatory actions through NF-κB, TNF-α, and IL-6 regulation.[15,16] TCM interprets RA-like symptoms as 'Bi syndrome', resulting from Wind, Cold, and Damp obstruction, and treats them with formulations such as Du Huo Ji Sheng Tang and Gui Zhi Shao Yao Zhi Mu Tang, which modulate cytokine profiles and T-cell responses.[17,18] Unani and Siddha traditions attribute RA to humoral or doshic imbalances and employ herbs like *Boswellia serrata*, *Commiphora mukul*, and *Curcuma longa*, known to reduce oxidative stress and inflammatory mediators.[19,20] Integrating these frameworks with modern immunology supports sustainable ethnopharmacological discovery and strengthens the scientific basis for plant-derived therapeutics.

Phytotherapeutic Agents from the Oriental Region

Medicinal plants from the Oriental region have played a longstanding role in the management of RA, offering anti-inflammatory, immunomodulatory, and antioxidant benefits. These therapeutic properties are well documented across Ayurveda, Traditional Chinese Medicine (TCM), and Southeast Asian ethnomedicine (Table 1). Contemporary studies increasingly validate their ability to modulate cytokines, regulate immune cell function, and reduce oxidative tissue damage.

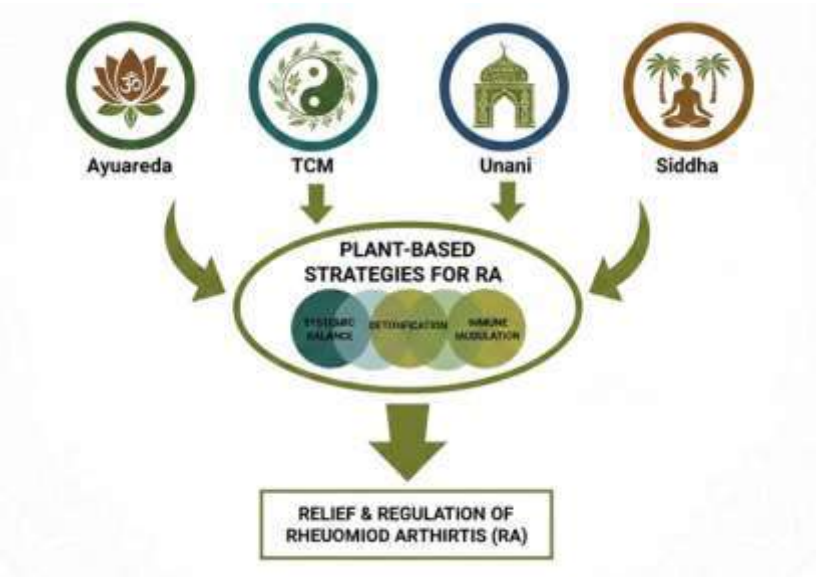

Figure 1. Overview of traditional medical systems of the Oriental region. Ayurveda, Traditional Chinese Medicine (TCM), Unani, and Siddha, highlighting their shared principles of systemic balance, detoxification, and immune modulation in the plant-based management of rheumatoid arthritis.

Table 1. Selected Oriental medicinal plants used for rheumatoid arthritis (RA)

Scientific name	Region (Oriental)	Plant part used	Current status / remarks	Ref.
Withania somnifera	South Asia (India)	Root, whole plant	Strong preclinical evidence (CIA models); immunomodulatory and anti-inflammatory (↓ TNF-α, IL-1β). Candidate for adjunct therapy.	21
Boswellia serrata	South Asia (India)	Resin (gum)	Boswellic acids inhibit 5-LOX; clinical/preclinical studies show reduced pain/stiffness in arthritic conditions.	22

Curcuma longa	South Asia (India)	Rhizome (curcumin)	Extensive evidence (mechanistic, animal, clinical): NF-κB inhibition, cytokine modulation, promising adjunct.	23
Tinospora cordifolia	South Asia (India)	Stem, whole plant	Immunomodulatory; reduces oxidative stress and arthritis signs in animal models.	24
Zingiber officinale	South / SE Asia	Rhizome	Gingerols/shogaols inhibit COX/LOX; analgesic/anti-inflammatory actions in preclinical and clinical OA/RA contexts.	25
Tripterygium wilfordii	East Asia (China)	Root / root extract (triptolide)	Potent immunosuppressant; multiple RCTs/meta-analyses show efficacy, but toxicity (hepato/renal) restricts use, derivatives under study.	26
Paeonia lactiflora (TGP)	East Asia (China)	Root (total glucosides of paeony — TGP)	Clinical trials & meta-analyses: TGP has immunomodulatory efficacy as adjuvant therapy; generally good safety in trials.	27
Panax ginseng	East Asia (China, Korea)	Root	Ginsenosides (various) modulate macrophages, Th17/Treg balance; preclinical RA models support benefit, clinical data mixed.	28
Angelica sinensis	East Asia (China)	Root (polysaccharides, ferulic acid)	Polysaccharides/ferulic acid reduce proinflammatory cytokines in arthritis models; commonly included in TCM anti-arthritic formulas.	29
Andrographis paniculata	Southeast Asia (Thailand, Indonesia)	Whole plant / leaves (andrographolide)	Andrographolide inhibits NF-κB and inflammatory cytokines; promising preclinical anti-inflammatory/autoimmune data.	30
Curcuma xanthorrhiza(Java turmeric)	Southeast Asia (Indonesia)	Rhizome	Rich in xanthorrhizol; antioxidant and anti-inflammatory properties suggest potential for chronic inflammatory disease.	31

Boesenbergia rotunda (finger root)	SE Asia (Thailand, Indonesia)	Rhizome	Panduratin A and chalcones (anti-inflammatory, NO inhibition); active in vitro/in vivo anti-inflammatory studies.	32
Nigella sativa (black seed)	South / West Asia	Seeds / oil (thymoquinone)	RCTs and meta-analyses indicate adjunctive benefit (↓ oxidative markers, improved cytokine profile) in RA; safe in studied doses.	33
Nyctanthes arbortristis (night-jasmine)	South / SE Asia	Leaves (extracts)	Animal and in-vitro RA models show ↓ paw edema, ↓ proinflammatory cytokines (TNF-α) and ↑ IL-10; active constituents under study.	34
Melicope pteleifolia	SE Asia (Malaysia, Vietnam)	Leaves	Active β-GP compound shows anti-arthritic effects in murine CIA models (preclinical evidence).	36
Achyranthes bidentata	East & South Asia	Root (radix)	Traditional use in TCM and Ayurveda for rheumatism; several preclinical anti-inflammatory studies.	37
Plectranthus amboinicus	SE Asia / India	Leaves	Traditional anti-arthritic use; patent literature and preclinical reports indicate anti-inflammatory potential.	38
Kadsura coccinea	China (Tujia/ethnic medicines)	Stem / triterpenoids	Triterpenes suppress IL-6/TNF in macrophage models; in vitro activity on synoviocytes reported.	39
Artemisia ordosica	East Asia (China, Mongolia)	Aerial parts	In CIA rats, extracts reduced paw swelling and cytokines (TNF-α, IL-1β, IL-6); mechanistic links to STAT3 pathway reported.	40
Camellia sinensis (green tea - EGCG)	East & South Asia (China, India)	Leaves (EGCG)	EGCG inhibits synovial fibroblast growth, modulates apoptosis and NF-κB; evidence from in vitro and animal RA studies.	41

Astragalus membranaceus	East Asia (China)	Root (polysaccharides, saponins)	Polysaccharides show anti-inflammatory/immunomodulatory action (OPG/RANKL/NF-κB pathways) in arthritis models.	42
Glycyrrhiza glabra(licorice)	West / South / East Asia	Root (glycyrrhizin, glycyrrhetinic acid)	Glycyrrhizin/derivatives modulate immune responses and inflammatory mediators; possible adjunct in RA (toxicity/standardization considerations).	43
Scutellaria baicalensis	East Asia (China)	Root (baicalin, baicalein)	Baicalin/baicalein inhibit FLS proliferation, induce apoptosis, modulate PI3K/Akt/NF-κB — promising preclinical evidence & small clinical signals.	44
Alpinia galanga(greater galangal)	SE Asia (India, Thailand)	Rhizome	Traditional use for joint pain; recent studies (preclinical/quasi-clinical) show analgesic and anti-inflammatory effects.	45
Curcuma zedoaria(white turmeric)	South / SE / East Asia	Rhizome	Anti-inflammatory sesquiterpenes and antioxidant activity documented; preclinical RA relevance.	46

South Asia

Ayurveda identifies several key botanicals for RA. *Withania somnifera* (ashwagandha) reduces TNF-α and IL-1β via withanolides, supporting relief from joint inflammation.[47] *Boswellia serrata* provides boswellic acids that inhibit 5-lipoxygenase, with clinical evidence of reduced pain and stiffness.[48] *Curcuma longa* suppresses NF-κB and cytokine activation through curcumin,[49] while *Tinospora cordifolia* enhances phagocytic activity and decreases oxidative stress.[50] *Zingiber officinale* adds COX and LOX inhibition via gingerols and shogaols.[51]

East Asia

TCM offers potent immunoregulatory agents. *Tripterygium wilfordii* exerts strong T-cell and cytokine suppression through triptolide, with clinical benefits despite toxicity concerns.[52] *Panax ginseng* regulates macrophage activity and oxidative stress via ginsenosides.[53] *Angelica sinensis*

provides phthalides and ferulic acid with antioxidant and vasomodulatory effects,[54] while *Paeonia lactiflora* modulates T-cell differentiation through paeoniflorin.[27]

Southeast Asia

Regional ethnomedicine contributes *Andrographis paniculata*, which inhibits NF-κB and pro-inflammatory cytokines.[55] *Curcuma xanthorrhiza* supplies xanthorrhizol with broad anti-inflammatory activity,[56] and *Boesenbergia rotunda* offers panduratin A, an inhibitor of nitric oxide synthase and related mediators.[57] Collectively, these botanicals reflect significant, multi-target potential for sustainable complementary RA therapeutics (Figure 2).

Figure 2. Oriental Medicinal Plants in RA Therapy. SWOT analysis of phytochemical-based interventions for rheumatoid arthritis, highlighting strengths (anti-inflammatory effects), weaknesses (safety issues), opportunities (enhanced bioavailability), and threats (regulatory hurdles) within therapeutic development.

Mechanistic Insights and Molecular Docking Evidence

Understanding the mechanistic basis of Oriental medicinal plants in RA is essential for translating traditional knowledge into evidence-based therapeutics. Advances in molecular biology, computational chemistry, and systems analytics show that key RA-related pathways, including JAK/STAT, NF-κB, and MAPK, are major phytochemical targets, with in silico tools like docking and molecular dynamics offering strong mechanistic support (Figure 3). Curcumin from *Curcuma longa* and andrographolide from *Andrographis paniculata* inhibit NF-κB activation and downregulate TNF-α and IL-6.[55,58] Withanolides from *Withania somnifera* and boswellic acids from *Boswellia serrata* suppress MAPK signalling by reducing ERK, JNK, and p38 phosphorylation.[59,60] Triptolide from *Tripterygium wilfordii* inhibits STAT3 activation, limiting Th17 differentiation, while paeoniflorin and ginsenosides modulate cytokine-driven STAT responses.[27,36,61] Computational studies demonstrate high binding affinity of curcumin, boswellic acids, paeoniflorin, and xanthorrhizol to JAKs, COX-2, TNF-α, and IL-1β,[62] with curcumin forming stable interactions in the JAK2 ATP-binding pocket[63] and andrographolide favourably docking with NF-

κB p65.[64] MD simulations confirm the stability of boswellic acid–COX-2 and triptolide–STAT3 complexes.[65] Synergistic combinations, such as *Curcuma longa* with *Zingiber officinale* or *Paeonia lactiflora* with *Angelica sinensis*, enhance bioavailability and broaden target profiles,[66] while metabolomics, proteomics, and network pharmacology continue to elucidate these multitarget interactions, guiding sustainable development of anti-arthritic therapeutics.[67]

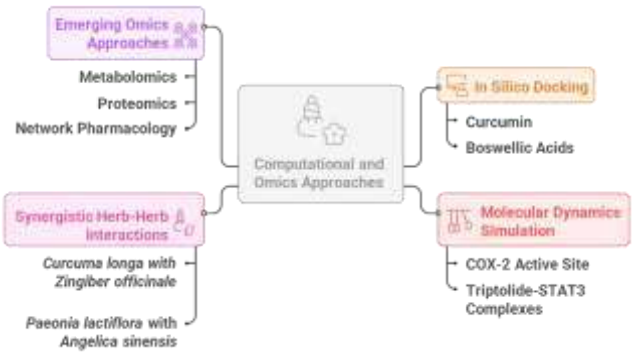

Figure 3. Computational and omics-based strategies in natural product research for rheumatoid arthritis. The diagram summarizes key integrative approaches, including emerging omics technologies (metabolomics, proteomics, and network pharmacology), in silico docking of bioactive compounds (e.g., curcumin, boswellic acids), molecular dynamics simulations of target–ligand interactions (e.g., COX-2 and STAT3 complexes), and synergistic herb–herb interactions (such as *Curcuma longa* with *Zingiber officinale*, and *Paeonia lactiflora* with *Angelica sinensis*). Together, these strategies enhance the understanding of phytochemical mechanisms and therapeutic potential in rheumatoid arthritis.

Preclinical and Clinical Evidence

The therapeutic potential of Oriental medicinal plants in RA is supported by growing preclinical and clinical evidence, although challenges in standardization, dosing, and safety remain. In vitro studies using LPS-stimulated macrophages and fibroblast-like synoviocytes have clarified key anti-inflammatory mechanisms. Curcumin from *Curcuma longa* and andrographolide from *Andrographis paniculata* inhibit NF-κB and MAPK signalling, reducing TNF-α, IL-6, and nitric oxide.[55,58] Triptolide from *Tripterygium wilfordii* suppresses fibroblast-like synoviocyte proliferation via STAT3 and NF-κB, while boswellic acids from *Boswellia serrata* lower matrix metalloproteinases, protecting cartilage.[59,68] Animal models, including collagen-induced and adjuvant-induced arthritis, further demonstrate systemic and joint-specific benefits; curcumin reduces swelling and cytokine expression,[44] withanolides from *Withania somnifera* decrease oxidative stress and improve histopathology,[69] and extracts of *Paeonia lactiflora* and *Angelica sinensis* alleviate inflammation.[27,70] Clinical trials show efficacy of *Boswellia*, *Tripterygium*, and

curcumin formulations; *Boswellia* improves pain and joint function[48] *Tripterygium* reduces disease activity but presents toxicity risks[52] and enhanced-bioavailability curcumin lowers pain and DAS28 scores with minimal adverse effects.[71] Persistent challenges include chemical variability, extraction-dependent composition, and poor bioavailability. Advances in nanoparticles, liposomes, and phytosomes, alongside integrated pharmacological, toxicological, and phytochemical evaluation, are crucial for ensuring the safe, effective, and standardized use of these herbal therapeutics in RA.

Sustainability and Ethnobotanical Conservation

Medicinal plants widely used for RA in the Oriental region, such as *Withania somnifera*, *Boswellia serrata*, *Curcuma longa*, *Zingiber officinale*, and *Tinospora cordifolia*, are increasingly threatened by overharvesting, habitat degradation, and climate variability, resulting in population decline and reduced natural regeneration.[72,73] Unsustainable extraction, often before reproductive maturity, endangers both biodiversity and the continuity of ethnomedical knowledge systems dependent on these species. Sustainable cultivation and biotechnological approaches, including micropropagation, tissue culture, and somatic embryogenesis, now support large-scale production of genetically uniform, disease-free plants with stable metabolite profiles, particularly for high-demand species such as *Boswellia serrata* and *Tinospora cordifolia*.[74,75] Good Agricultural and Collection Practices further enhance quality and phytochemical consistency. Interdisciplinary collaboration among ethnobotanists, pharmacologists, and conservation scientists strengthens the integration of traditional knowledge with modern validation and conservation frameworks.[76] Community participation in sustainable harvesting and benefit-sharing aligns with global conservation objectives.[77] Policy frameworks such as the Convention on Biological Diversity, the Nagoya Protocol, and relevant national regulations play a critical role in ensuring equitable bioprospecting, protecting intellectual property rights, and promoting sustainable regulation of the medicinal plant industry.[78,79] Together, these mechanisms strengthen long-term conservation efforts and facilitate the responsible and ethically grounded utilization of medicinal flora used in RA management.

Interdisciplinary Integration and Future Prospects

The integration of traditional Oriental medicinal knowledge with artificial intelligence (AI) is reshaping research on RA by linking ethnopharmacological wisdom with computational precision. Ayurveda, Traditional Chinese Medicine, Siddha, and Unani provide extensive documentation of multi-herb formulations with potent anti-inflammatory and immunomodulatory effects. AI-driven phytochemical screening now accelerates the discovery of bioactive compounds, molecular targets, and toxicity profiles (Figure 4). Natural language processing enables systematic mining of classical medical texts to identify synergistic herb combinations, while neural network–based virtual

screening strengthens lead identification. Additionally, cheminformatics tools support molecular docking, ADMET prediction, and structure-activity relationship analyses, thereby enhancing the precision and efficiency of natural product research. Systems biology and computational immunology deepen understanding of RA pathogenesis by integrating multi-omics data to reveal how phytochemicals influence NF-κB, JAK/STAT, MAPK, and NLRP3 inflammasome pathways.[81,82] Network pharmacology highlights multi-target actions of compounds such as curcumin, quercetin, sinomenine, and berberine on immune cell modulation and cytokine suppression. Personalized herbal medicine incorporating pharmacogenomics, metabolomics, and AI supports biomarker-guided therapeutic stratification.[83,84] Sustainable cultivation, biosynthetic engineering, and community-based supply chains further align these innovations with global health and ecological priorities.

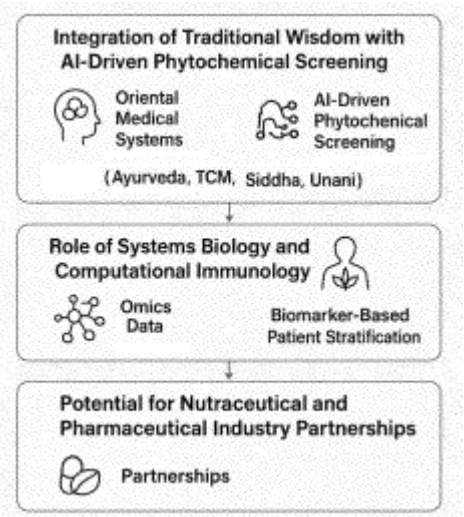

Figure 4. Interdisciplinary integration and future prospects in natural product–based immunology research. The figure highlights three emerging directions, (1) integrating traditional Oriental medical systems (Ayurveda, TCM, Siddha, Unani) with AI-driven phytochemical screening to accelerate discovery of bioactive compounds; (2) leveraging systems biology and computational immunology, including multi-omics data and biomarker-based patient stratification, to improve mechanistic understanding and precision in therapy; and (3) fostering nutraceutical-pharmaceutical industry partnerships to translate phytochemical insights into clinically relevant interventions.

Conclusion

Medicinal plants from the Oriental region offer a rich source of bioactive compounds capable of modulating RA through multi-target mechanisms addressing inflammation, oxidative stress, immune dysregulation, and joint degeneration. Their ability to regulate signaling pathways such as

NF-κB, JAK/STAT, and MAPK, alongside cytokine suppression and antioxidant activity, positions them as promising adjuncts or alternatives to conventional RA therapies.[85] Sustainable and ethical utilization requires robust scientific validation, including standardization of phytochemical profiles, clinical efficacy, and safety assessment, alongside conservation strategies to mitigate biodiversity loss and overharvesting.[54] The future of plant-based RA therapeutics lies in interdisciplinary integration, combining traditional herbal knowledge with molecular pharmacology, systems biology, computational immunology, and sustainable biotechnology. Such convergence ensures that innovation in RA management preserves ecological integrity while translating Oriental medicinal wisdom into safe, effective, and environmentally responsible therapies.[13]

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