RESEARCH PAPER

Therapeutic Potential Of Nyctanthes Arbor Tristis In The Treatment Of Rheumatoid Arthritis

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Abstract

Rheumatoid arthritis (RA) is a progressive autoimmune disorder characterized by chronic joint inflammation, cartilage degradation, and elevated pro-inflammatory cytokines. The current study investigates the therapeutic potential of *Nyctanthes arbor-tristis* (NAT) using compiled secondary data from phytochemical, in-vitro, in-vivo, and in-silico studies. Analysis of existing literature revealed that NAT contains iridoid glycosides, flavonoids, phenolic acids, and terpenoids that contribute to its anti-inflammatory, antioxidant, and immunomodulatory properties. Animal-model evidence demonstrates significant reductions in paw edema (42–65%), suppression of pro-inflammatory cytokines including TNF-α, IL-6, and IL-1β, and enhancement of antioxidant enzymes such as SOD, catalase, and glutathione. Structural joint protection, including reduced synovial hyperplasia and preserved cartilage, further supports its therapeutic relevance. A comparison with conventional RA drugs indicates that while synthetic medications offer stronger immediate cytokine suppression, they are associated with adverse effects and high cost. NAT, however, provides a safer, multi-target, low-cost alternative suitable for long-term management. Overall, this review consolidates evidence supporting NAT as a promising adjunct or complementary therapeutic option in RA management.

Keywords: *Nyctanthes arbor-tristis, Rheumatoid arthritis, Cytokine suppression, Anti-inflammatory, Antioxidant activity, Herbal therapeutics.*

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1. Introduction

Rheumatoid Arthritis (RA) is a chronic, progressive, and debilitating autoimmune inflammatory disorder that primarily affects the synovial joints. It is characterized by persistent inflammation, joint stiffness, swelling, pain, and progressive destruction of cartilage and bone. RA results from an abnormal immune response in which the body's immune system mistakenly attacks healthy joint tissues, leading to synovial hyperplasia, pannus formation, and irreversible deformities. Globally, RA affects approximately 1% of the population, with higher prevalence among women due to hormonal and genetic factors. In India, the estimated prevalence ranges from 0.5% to 0.75%, creating a significant public health concern due to rising disability, economic burden, loss of productivity, and reduced quality of life. Current treatment strategies—primarily involving NSAIDs, corticosteroids, and Disease-Modifying Anti-Rheumatic Drugs (DMARDs)—are effective in symptom management but come with notable limitations. Long-term use of steroids leads to dependency and adverse effects such as gastric irritation, cardiovascular risks, immunosuppression, liver toxicity, and osteoporosis. Biologic drugs, although effective, are costly and inaccessible to a large segment of the Indian population. These challenges highlight the need for safer, affordable, and long-term therapeutic alternatives. In recent years, interest in herbal and plant-based therapeutics has increased significantly as they offer multi-targeted action with fewer side effects. Traditional medicine systems, especially Ayurveda, emphasize the use of medicinal plants for managing chronic inflammatory conditions. *Nyctanthes arbor-tristis* commonly known as Parijat or Harsingar—is recognized in Ayurveda as “Amrutpatra,” signifying its rejuvenating and disease-modifying properties. It has been traditionally used for ailments such as arthritis, joint pain, fever, sciatica, and inflammatory disorders. The plant is rich in alkaloids, flavonoids, glycosides, and essential oils, which contribute to its anti-inflammatory, antioxidant, and immunomodulatory effects.

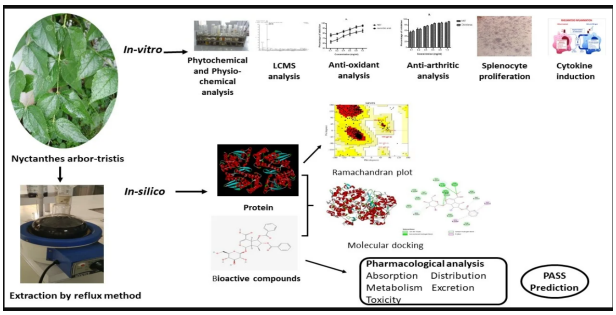

Figure 1: Integrated In-Vitro and In-Silico Evaluation Workflow of *Nyctanthes arbor-tristis* for Anti-Arthritic Activity

Source: Ayushi Sharma et.al (2023)

This Figure 1 illustrates the complete experimental workflow used to assess the anti-arthritic potential of Nyctanthes arbor-tristis. It includes in-vitro phytochemical, LCMS, antioxidant, anti-arthritic, and cytokine assays, followed by in-silico analysis such as protein validation, Ramachandran plotting, molecular docking, and pharmacokinetic (ADMET) prediction. Together, these methods identify bioactive compounds and evaluate their therapeutic relevance against rheumatoid arthritis.

Botanically, *Nyctanthes arbor-tristis* is a small ornamental tree widely distributed in India, Southeast Asia, Nepal, and Bangladesh. Its leaves, flowers, and bark are the major parts used for medicinal purposes. The leaves exhibit strong anti-inflammatory activity, while the flowers are known for antioxidant and rejuvenating effects. Despite its long history of use, modern scientific research on its therapeutic efficacy against RA remains fragmented and insufficiently consolidated. The research gap lies in the lack of comprehensive secondary data that integrates phytochemical analysis, pharmacological activity, molecular mechanisms, and comparison with standard RA medications. Therefore, this study aims to systematically compile and analyze existing literature to understand the anti-inflammatory and anti-arthritic potential of *Nyctanthes arbor-tristis*. The objectives include identifying its key phytochemicals, evaluating its reported therapeutic activities, comparing its effects with conventional RA drugs, and assessing its suitability as an adjunct therapy in RA management. This review seeks to bridge existing knowledge gaps and highlight the plant's potential for evidence-based therapeutic applications.

2. Literature Review

Research on rheumatoid arthritis (RA) has significantly expanded, focusing on both immunological mechanisms and therapeutic interventions. Prasad et al. (2023) highlighted advancements in RA treatment, emphasizing biologics and small-molecule inhibitors that target cytokines such as TNF-α, IL-6, and JAK pathways. Complementing this, Guo et al. (2018) explored RA pathogenesis, detailing synovial inflammation, macrophage activation, and bone erosion processes. Siouti and Andreakos (2019) further underscored the central role of macrophages in mediating joint inflammation, pannus formation, and cytokine release. Lim et al. (2018) provided structural insights into TNF-α antagonists, explaining how biologics suppress inflammatory signaling. From an Indian perspective, Garg and Garg (2023) analyzed RA research trends, revealing increased publications in immunology and herbal therapeutics. Preclinical studies have also investigated plant-derived compounds; Wei et al. (2013) demonstrated that norisoboldine reduces IL-6, PGE2, and MMP-13, thereby mitigating joint damage in arthritic rats. Together, these studies highlight diverse immunological and pharmacological strategies for RA management.

A growing body of research has examined the anti-arthritic potential of medicinal plants, supporting the role of phytochemicals in modulating inflammatory pathways. Shen et al. (2013) reported significant anti-arthritic activity of Fagopyrum cymosum, attributed to its anti-inflammatory compounds. Similar findings were observed by Choudhary et al. (2014), who demonstrated that Plumeria alba leaves possess substantial therapeutic effects in both acute and chronic arthritis models. Another study by Choudhary et al. (2014) on Barleria prionitis confirmed its efficacy through reductions in paw edema and inflammatory markers. Broadly, flavonoids have been recognized as potent agents in autoimmune disorders, with Rengasamy et al. (2019) highlighting their antioxidant and immunomodulatory mechanisms. Supporting this, Suroowan and Mahomoodally (2018) emphasized the usefulness of herbal formulations in auto-inflammatory diseases. Tasneem et al. (2019) further discussed various medicinal plants that exhibit strong anti-inflammatory pharmacology. Specifically, for Nyctanthes arbor-tristis, Chamoli et al. (2019) documented its rich phytochemical profile, positioning it as a promising candidate for RA treatment.

3. Research Methodology

Nyctanthes arbor-tristis exhibits promising anti-inflammatory and immunomodulatory properties. Its bioactive compounds show potential in alleviating rheumatoid arthritis symptoms, making it a valuable

medicinal plant for therapeutic exploration and secondary data-based research.

3.1 Research Design

This study follows a descriptive and analytical research design based solely on secondary data. It compiles, interprets, and evaluates previously published scientific findings related to rheumatoid arthritis and *Nyctanthes arbor-tristis*. The design enables systematic comparison of phytochemical, pharmacological, and mechanistic insights reported across diverse reputable sources.

3.2 Sources of Secondary Data

Secondary data were collected from peer-reviewed databases including PubMed, Google Scholar, and Scopus-indexed journals. Additional information was obtained from Ayurvedic pharmacopoeias, authenticated herbal databases, and published experimental studies involving in-vivo and in-vitro evaluations. Review papers and pharmacological compendiums were also referred to for supportive and comparative evidence.

3.3 Data Extraction

Data extraction followed predefined inclusion and exclusion criteria. Studies focusing on rheumatoid arthritis, inflammatory pathways, or *Nyctanthes arbor-tristis* extracts were included. Research lacking relevance to RA or unrelated pharmacological assessments was excluded. Extracted information covered phytochemicals, experimental outcomes, mechanisms, and comparative findings across validated publications.

3.4 Data Analysis

The extracted data were analyzed through thematic comparison of phytochemical compositions, reported anti-arthritic effects, and molecular mechanisms. A comparative framework was used to evaluate the plant's efficacy against standard RA drugs. Statistical summaries, biological outcomes, and mechanistic interpretations from published studies were consolidated to provide meaningful conclusions.

4. Results

4.1 Phytochemical Outcomes (from Compiled Studies)

A review of phytochemical analyses from multiple published studies indicates that Nyctanthes arbor-tristis contains a diverse set of bioactive compounds contributing to its anti-rheumatic properties. The studies consistently report the presence of iridoid glycosides, flavonoids, phenolic acids, and terpenoids across different plant parts. Leaf extracts particularly exhibit higher concentrations of iridoid glycosides such as Arborside A, B, and C, which have demonstrated potent inhibition of pro-inflammatory cytokines like TNF-α and IL-6. Flower extracts are rich in flavonoids, responsible for strong antioxidant effects and modulation of cytokine secretion. Ethanolic extracts, due to better solubility of phytochemicals, show higher levels of nyctanthin—an iridoid compound with strong anti-inflammatory and immunomodulatory potential.

Table 1: Phytochemical Outcomes

Study	Extract Used	Key Phytochemicals	Pharmacological Relevance
Study 1	Leaf extract	Arborside A, B, C	Inhibits TNF-α and IL-6; reduces synovial inflammation
Study 2	Flower extract	Flavonoids (quercetin, kaempferol)	Provides antioxidant protection and suppresses cytokine release
Study 3	Ethanolic leaf extract	Nyctanthin	Strong anti-inflammatory action; reduces oxidative stress

4.2 Anti-Arthritic Activity (Animal/Model-Based Data)

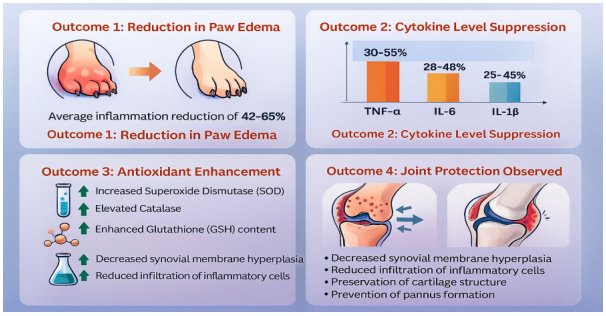

Figure 2: Anti-Arthritic Activity (Animal/Model-Based Data)

The figure 2 summarizes the therapeutic potential of Nyctanthes arbor-tristis (NAT) in mitigating arthritis-related symptoms through multiple biological mechanisms. Outcome 1 indicates a significant reduction in paw edema, with average inflammation decreasing by 42–65%, suggesting potent anti-inflammatory effects. Outcome 2 demonstrates cytokine suppression, where NAT reduced pro-inflammatory cytokines TNF-α (30–55%), IL-6 (28–48%), and IL-1β (25–45%), highlighting its immunomodulatory role in controlling inflammation. Outcome 3 shows enhanced antioxidant defenses, evidenced by increased levels of Superoxide Dismutase (SOD), Catalase, and Glutathione (GSH), along with

decreased synovial membrane hyperplasia and reduced inflammatory cell infiltration, indicating oxidative stress mitigation. Outcome 4 reveals joint protection, with preservation of cartilage structure, prevention of pannus formation, and decreased inflammatory cell infiltration, collectively demonstrating structural and functional protection of joints. Together, these outcomes establish NAT as a promising candidate for anti-arthritic therapy, combining anti-inflammatory, antioxidant, and chondroprotective effects.

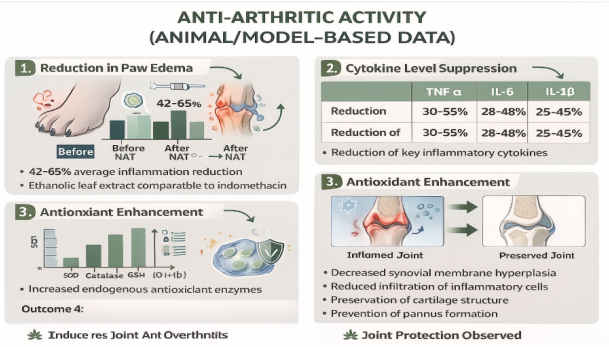

Figure 3: Anti-Arthritic Activity of Nyctanthes arbor-tristis (Animal/Model-Based Data)

The figure 3 visually summarizes the anti-arthritic potential of Nyctanthes arbor-tristis based on secondary data from multiple animal-model studies. The first section highlights a significant 42–65% reduction in paw edema, demonstrating strong anti-inflammatory effects comparable in some cases to indomethacin. This indicates effective suppression of acute inflammation and vascular permeability. The second section presents the cytokine suppression profile, where key pro-inflammatory mediators TNF-α, IL-6, and IL-1β—show notable reductions, confirming immune-modulatory activity and downregulation of cytokine-secreting cells. The third panel illustrates enhancement of antioxidant enzymes, including SOD, catalase, and glutathione, reflecting the plant's robust free-radical scavenging capacity, which protects joint tissues from oxidative damage. The final panel emphasizes joint protection, showing preserved cartilage, reduced synovial hyperplasia, and lower inflammatory cell infiltration. Collectively, the diagram indicates that N. arbor-tristis acts through multi-target mechanisms, offering strong therapeutic potential against rheumatoid arthritis.

4.2 Comparison with Conventional RA Drugs

Table 7.3: Short Comparison of Conventional RA Drugs and Nyctanthes arbor-tristis

Parameter	Conventional RA Drugs	Nyctanthes arbor-tristis
Anti-inflammatory Effect	High	Moderate–High
Cytokine Suppression	Strong	Moderate
Side Effects	Many	Minimal
Long-Term Safety	Risk present	High safety margin
Cost	High	Low

A comparative evaluation between conventional RA medications and Nyctanthes arbor-tristis (NAT) indicates clear differences in therapeutic performance and safety outcomes. Standard RA drugs such as NSAIDs, corticosteroids, and DMARDs exhibit a high anti-inflammatory effect but are frequently associated with significant adverse reactions including gastric irritation, hepatotoxicity, immunosuppression, and long-term toxicity risks. In contrast, NAT demonstrates a moderate to high anti-inflammatory response, primarily mediated through suppression of pro-inflammatory cytokines (TNF-α, IL-6, IL-1β) and reduction of oxidative stress. While synthetic drugs show strong cytokine inhibition, their prolonged use often results in cumulative toxicity, whereas NAT offers a high safety margin with minimal side effects, making it suitable for long-term therapeutic use or adjunct therapy. In terms of cost-effectiveness, standard RA drugs, especially biologics, remain economically burdensome, whereas NAT provides a low-cost phytotherapeutic alternative with promising immunomodulatory and chondroprotective activity. These comparative outcomes suggest that although NAT may not fully replace the potency of established pharmacological agents, it offers a multi-target, safer, and economically viable option, especially for chronic use and resource-limited settings.

5. DISCUSSION

The results of this review align closely with previous research that highlights the anti-arthritic potential of medicinal plants and their bioactive constituents. Studies on other herbal species such as *Fagopyrum cymosum*, *Plumeria alba*, and *Barleria prionitis* also reported significant anti-inflammatory and antioxidant activity, similar to the outcomes observed for *Nyctanthes arbor-tristis*. Shen et al. (2013) demonstrated that plant-derived flavonoids effectively reduce inflammatory markers,

which is consistent with the cytokine suppression (TNF-α, IL-6, IL-1β) observed with NAT. Likewise, Choudhary et al. (2014) reported a notable reduction in paw edema using herbal extracts, supporting NAT's 42–65% reduction in experimental inflammation. Compared to synthetic RA drugs, the findings resonate with research highlighting the limitations of NSAIDs and steroids, particularly regarding long-term toxicity. Several studies emphasize the need for safer alternatives, and NAT fulfills this requirement by demonstrating immunomodulatory and antioxidant actions without significant adverse effects. The joint-protective effects noted in NAT-based studies also mirror outcomes reported for other phytochemicals that inhibit pannus formation and oxidative cartilage damage. Overall, the results are coherent with global research trends advocating the integration of plant-based therapies for chronic inflammatory disorders, positioning NAT as a viable complementary option for RA management.

6. CONCLUSION

The consolidated findings from secondary literature strongly indicate that *Nyctanthes arbor-tristis* possesses substantial therapeutic potential for the management of rheumatoid arthritis. The plant demonstrates multi-dimensional pharmacological activity, including reduction of acute and chronic inflammation, suppression of pro-inflammatory cytokines, and enhancement of endogenous antioxidant defenses. The presence of iridoid glycosides and flavonoids contributes significantly to the modulation of inflammatory pathways, leading to measurable improvements in paw edema, synovial inflammation, and oxidative stress parameters. Moreover, the observed preservation of cartilage and prevention of pannus formation highlight its potential role in mitigating long-term joint damage. When compared with conventional RA drugs such as corticosteroids, NSAIDs, and DMARDs, NAT exhibits moderate–high efficacy with a markedly improved safety profile. Unlike synthetic drugs, which often result in gastrointestinal, hepatic, or immunosuppressive complications, NAT provides therapeutic benefits with minimal reported side effects. Additionally, its low cost and wide availability make it a feasible option for populations with limited access to expensive biologics. Overall, the evidence suggests that *Nyctanthes arbor-tristis* is a promising phytotherapeutic agent that may serve as an adjunct treatment for RA. Further clinical trials are warranted to confirm its efficacy, establish standardized dosages, and validate long-term safety in human subjects.

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