International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Review Article

Nyctanthes arbor-tristis (Parijat): A Comprehensive Review of Anti-Arthritic Potential, Phytopharmacology, Molecular Mechanisms, and Experimental Evidence from 2000–2026 with Special Reference to Combination Therapy with Naproxen

Dr. Sudheer Kumar Singh Yadav[1], Dr. Umesh Kumar[2], Dr. Neeraj Kumar[3], Dr Naveen Maurya[4], Prof. (Dr.) Narendra Kumar[5], Prof. (Dr.) Rakesh Kumar Dixit[6]

[1,2,3,4]Junior Resident, Department of Pharmacology, King Georges Medical University, Lucknow.
[5]Professor, Department of Pharmacology, King Georges Medical University, Lucknow.
[6]Professor, Department of Pharmacology, King Georges Medical University, Lucknow.

OPEN ACCESS

Corresponding Author:

Dr. Sudheer Kumar Singh Yadav
Junior Resident, Department of Pharmacology, King Georges Medical University, Lucknow.

Received: 04-04-2026
Accepted: 11-05-2026
Available online: 15-06-2026

ABSTRACT

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disorder characterized by persistent synovitis, progressive cartilage destruction, bone erosion, disability, and reduced quality of life. Despite significant advances in disease-modifying anti-rheumatic drugs (DMARDs), biologics, and non-steroidal anti-inflammatory drugs (NSAIDs), long-term therapy remains limited by adverse effects, treatment resistance, and economic burden. Consequently, increasing attention has been directed toward medicinal plants possessing anti-inflammatory, antioxidant, immunomodulatory, and anti-arthritic properties. Among these, *Nyctanthes arbor-tristis* Linn. (Oleaceae), commonly known as Parijat, Harsingar, or Night Jasmine, occupies a prominent position in Ayurvedic medicine for the treatment of rheumatism, arthritis, fever, inflammatory disorders, and pain. Scientific investigations over the past two decades have demonstrated that extracts of *Nyctanthes arbor-tristis* exhibit significant anti-inflammatory, antioxidant, analgesic, immunomodulatory, and anti-rheumatic activities in various experimental models. The plant contains numerous bioactive compounds including iridoid glycosides, arbortristosides, flavonoids, phenolics, carotenoids, terpenoids, oleanolic acid, β-sitosterol, and calceolariosides that contribute to its pharmacological effects. Recent studies have revealed its ability to suppress inflammatory cytokines such as TNF-α, IL-1β, IL-6, COX-2, and NF-κB signaling pathways while enhancing anti-inflammatory mediators such as IL-10. Experimental studies in Freund's Complete Adjuvant (FCA)-induced arthritis models demonstrate marked reductions in paw edema, arthritic index, oxidative stress, and histopathological damage. Emerging evidence also suggests the possibility of synergistic benefits when combined with conventional NSAIDs such as naproxen. This review summarizes the traditional uses, phytochemistry, pharmacological activities, anti-arthritic mechanisms, and experimental studies published between 2000 and 2026, while highlighting future directions for translational research and clinical development.

Keywords*: Rheumatoid arthritis, Nyctanthes arbor-tristis, Parijat, Harsingar, Naproxen, Anti-inflammatory activity, Anti-arthritic activity, Cytokines, NF-κB, Freund's Complete Adjuvant.*

INTRODUCTION

Rheumatoid Arthritis: A Global Health Challenge

Rheumatoid arthritis (RA) is one of the most common chronic autoimmune inflammatory disorders affecting approximately 0.5–1% of the global population. The disease predominantly affects women and is characterized by chronic synovial inflammation, progressive cartilage destruction, pannus formation, bone erosion, deformity, and functional disability. Persistent inflammation eventually leads to irreversible joint damage and substantial socioeconomic burden. The pathogenesis of RA involves a complex interaction among genetic susceptibility, environmental triggers, oxidative stress, immune dysregulation, inflammatory cytokines, and autoantibody production. TNF-α, IL-1β, IL-6, IL-17, and NF-κB signaling pathways are considered key mediators responsible for disease progression. Recent evidence has also highlighted the contribution of oxidative stress and reactive oxygen species (ROS) to cartilage destruction and synovial inflammation.[1–5]

Current treatment strategies include NSAIDs, corticosteroids, DMARDs, biological agents, and Janus kinase inhibitors. Although these therapies effectively suppress inflammation and slow disease progression, their prolonged use is associated with gastrointestinal toxicity, hepatotoxicity, nephrotoxicity, immunosuppression, cardiovascular complications, and increased healthcare costs. Therefore, there is growing interest in identifying safer and more effective therapeutic alternatives derived from medicinal plants.[1–6]

Traditional Herbal Medicines in Arthritis

Medicinal plants have served as the foundation of healthcare systems for thousands of years. According to the World Health Organization (WHO), nearly 80% of the world's population relies on traditional medicines for primary healthcare needs. Ayurveda, Siddha, Unani, Traditional Chinese Medicine, and other indigenous healthcare systems utilize numerous medicinal plants for managing inflammatory disorders and rheumatic diseases.

Among these medicinal plants, *Nyctanthes arbor-tristis* has gained considerable scientific attention because of its remarkable anti-inflammatory and anti-rheumatic properties. Historically, Ayurvedic practitioners have employed leaves, flowers, seeds, bark, and roots of the plant to treat arthritis, rheumatism, sciatica, fever, chronic inflammatory diseases, malaria, and skin disorders. The growing body of experimental evidence supports many of these traditional claims.[7–10]

Botanical Overview of Nyctanthes arbor-tristis

Nyctanthes arbor-tristis, commonly known as Night Jasmine, Coral Jasmine, Parijat, or Harsingar, belongs to the family Oleaceae. The plant is native to South Asia and widely distributed throughout India, Nepal, Bangladesh, Sri Lanka, Bhutan, and Southeast Asia. It is a small deciduous tree or shrub reaching 10 meters in height and is famous for its fragrant white flowers with orange tubular centers that bloom during the night and fall at dawn.

Taxonomical Classification:

- Kingdom: Plantae
- Division: Magnoliophyta
- Class: Magnoliopsida
- Order: Lamiales
- Family: Oleaceae
- Genus: Nyctanthes
- Species: *Nyctanthes arbor-tristis*

The species name "arbor-tristis" literally means "sad tree" because its flowers shed shortly after blooming. Despite this poetic name, the plant has immense medicinal significance across traditional systems of medicine.[7–10]

Ethnomedicinal Importance

Traditional Ayurvedic texts describe Parijat as possessing:

- Tikta (bitter) taste
- Laghu (light) property
- Ushna Virya (hot potency)
- Kapha-Vata balancing effects

The leaves are traditionally used for:

- Rheumatoid arthritis
- Osteoarthritis
- Chronic fever
- Sciatica
- Gout

- Musculoskeletal pain
- Helminthic infections
- Liver disorders

Flowers are utilized in:
- Digestive disorders
- Skin diseases
- Antioxidant therapy

Seeds are employed for:
- Hair disorders
- Dermatological conditions
- Anti-inflammatory applications

Bark preparations have historically been used in rheumatism and chronic inflammatory conditions.[7–10]

Phytochemical Basis of Anti-Arthritic Activity

The therapeutic potential of *Nyctanthes arbor-tristis* is attributed to its rich phytochemical profile. Studies conducted between 2000 and 2026 have identified multiple bioactive constituents, including:

Iridoid Glycosides
- Arbortristoside A
- Arbortristoside B
- Arbortristoside C

Flavonoids
- Luteolin
- Kaempferol
- Chrysin

Phenolic Compounds
- Gallic acid
- Ferulic acid
- Chlorogenic acid
- Ellagic acid
- Syringic acid

Terpenoids
- Oleanolic acid
- Ursolic acid

Sterols
- β-Sitosterol

Carotenoids
- Nyctanthin
- Crocin-like compounds

These compounds exhibit potent antioxidant, anti-inflammatory, immunomodulatory, and anti-rheumatic activities. Recent chromatographic and molecular docking studies have demonstrated strong interactions between these phytochemicals and inflammatory mediators including TNF-α, COX-2, IL-6, and NF-κB pathways.

Rationale for Combining Nyctanthes arbor-tristis with Naproxen

Naproxen is a widely prescribed NSAID that exerts anti-inflammatory and analgesic effects primarily through inhibition of cyclooxygenase enzymes. However, prolonged use is associated with gastrointestinal bleeding, renal toxicity, and cardiovascular complications.

The combination of *Nyctanthes arbor-tristis* with naproxen represents a promising therapeutic strategy because:
1. The plant possesses independent anti-inflammatory activity.
2. It targets multiple inflammatory pathways.

3. Antioxidant effects may reduce tissue damage.
4. Lower NSAID doses may achieve similar efficacy.
5. Potential reduction in adverse effects.
6. Possible synergistic immunomodulatory action.

Recent experimental evidence suggests that herbal-drug combinations may enhance therapeutic outcomes while minimizing toxicity. Therefore, systematic evaluation of this combination in FCA-induced arthritis models is scientifically justified.

MATERIALS AND METHODS

Study Design

The present review was conducted as a comprehensive narrative review aimed at critically evaluating the anti-arthritic potential of *Nyctanthes arbor-tristis* and its possible role in combination therapy with naproxen. Published literature spanning more than two decades (2000–2026) was systematically examined to summarize experimental, preclinical, phytochemical, pharmacological, toxicological, and mechanistic evidence regarding the plant's anti-inflammatory and anti-arthritic properties.

Literature Search Strategy

An extensive literature search was performed using electronic databases including:

- PubMed
- Scopus
- Web of Science
- Google Scholar
- ScienceDirect
- SpringerLink
- Wiley Online Library

Keywords Used

The following search terms were used individually and in combinations:

- Nyctanthes arbor-tristis
- Parijat
- Harsingar
- Rheumatoid arthritis
- Anti-arthritic activity
- Anti-inflammatory activity
- FCA-induced arthritis
- Freund's complete adjuvant arthritis
- Herbal anti-arthritic agents
- Medicinal plants and arthritis
- Naproxen combination therapy
- Cytokines
- NF-κB
- Oxidative stress
- Phytochemistry
- Experimental arthritis

Inclusion Criteria

1. Studies published between 2000 and 2026.
2. Experimental animal studies.
3. Pharmacological investigations.
4. Phytochemical analyses.
5. Toxicological studies.
6. Reviews related to anti-arthritic medicinal plants.
7. Studies evaluating inflammatory pathways.

Exclusion Criteria

1. Duplicate publications.
2. Conference abstracts without complete data.
3. Non-English publications lacking reliable translation.

4. Studies with insufficient methodology.

Pathophysiology of Rheumatoid Arthritis

Overview

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease characterized by persistent synovitis, pannus formation, progressive destruction of cartilage, and bone erosion. The disease affects approximately 1% of the world population and remains one of the leading causes of disability worldwide.[1–4]

The hallmark of RA is chronic inflammation of synovial joints resulting from abnormal activation of immune pathways.

Genetic Factors

Several genetic predispositions contribute to RA development.

Important genes include:

- HLA-DRB1
- PTPN22
- STAT4
- CTLA4
- TRAF1

Among these, HLA-DRB1 alleles containing the shared epitope sequence are considered the strongest genetic risk factors. Studies have shown that individuals carrying these alleles are significantly more susceptible to developing severe rheumatoid arthritis.[11–14]

Figure 1: Nyctanthes arbor-tristis (Parijat)

Environmental Triggers

Environmental factors initiate immune responses in genetically susceptible individuals.

Important risk factors include:

- Cigarette smoking
- Air pollution
- Periodontal infections
- Gut microbiota dysbiosis
- Obesity
- Occupational exposures
- Viral infections

Smoking is particularly important because it promotes citrullination of proteins, leading to generation of anti-citrullinated peptide antibodies (ACPAs), a hallmark of rheumatoid arthritis.[11, 12–15]

Immunological Mechanisms

T-Lymphocyte Activation

CD4+ T-helper cells play a central role in RA pathogenesis.

Activated T cells:

- Release inflammatory cytokines
- Recruit macrophages
- Stimulate B-cell activation
- Promote osteoclastogenesis

Major T-cell subsets include:

- Th1 cells
- Th17 cells

These cells produce:

- IFN-γ
- IL-17
- TNF-α

which contribute significantly to joint inflammation.[16–18]

B-Lymphocyte Activation

Activated B cells produce:

- Rheumatoid factor (RF)
- Anti-cyclic citrullinated peptide antibodies (anti-CCP)
- Autoantibodies

Immune complexes formed by these antibodies activate complement pathways and perpetuate inflammation.[18–20]

Macrophage Activation

Macrophages are major inflammatory effector cells in rheumatoid synovium.

Activated macrophages release:

- TNF-α
- IL-1β
- IL-6
- IL-8
- GM-CSF

These cytokines amplify inflammation and contribute to cartilage destruction.[20–22]

Major Inflammatory Cytokines in RA

Tumor Necrosis Factor Alpha (TNF-α)

TNF-α is regarded as the master cytokine in rheumatoid arthritis.

It promotes:

- Synovial proliferation
- Leukocyte recruitment
- Cartilage degradation
- Bone destruction

Current biologic therapies target TNF-α because of its central role in disease progression.[22–24]

Interleukin-1β (IL-1β)

IL-1β stimulates:

- Chondrocyte activation
- Matrix metalloproteinase production
- Cartilage degradation
- Osteoclast differentiation

Elevated IL-1β levels correlate strongly with disease severity.[23–25]

Interleukin-6 (IL-6)

IL-6 contributes to:

- Synovitis
- Autoantibody production
- Acute phase response

- Joint destruction

Targeted inhibition of IL-6 has demonstrated substantial therapeutic benefits in RA patients.[25–27]

Oxidative Stress in Rheumatoid Arthritis

Oxidative stress is increasingly recognized as a major contributor to RA pathology.
Reactive oxygen species include:

- Superoxide radicals
- Hydroxyl radicals
- Hydrogen peroxide
- Peroxynitrite

Excess ROS causes:

- Lipid peroxidation
- DNA damage
- Protein oxidation
- Cartilage destruction

Patients with RA exhibit elevated malondialdehyde (MDA) levels and reduced antioxidant enzymes such as:

- Superoxide dismutase (SOD)
- Catalase
- Glutathione peroxidase

Therefore, antioxidants represent attractive therapeutic targets.[26–29]

NF-κB Signaling Pathway

The Nuclear Factor-kappa B (NF-κB) pathway is considered one of the most important regulators of inflammation.
Activation results in increased expression of:

- TNF-α
- IL-1β
- IL-6
- COX-2
- iNOS

Persistent activation of NF-κB is observed in rheumatoid synovial tissue.
Interestingly, several phytochemicals isolated from *Nyctanthes arbor-tristis* have demonstrated inhibitory effects on NF-κB signaling.[29–31]

Cyclooxygenase Pathway

Cyclooxygenase enzymes convert arachidonic acid into prostaglandins.
Two major isoforms:

- COX-1
- COX-2

COX-2 expression is markedly elevated in RA synovium.

Prostaglandins contribute to:

- Pain
- Swelling
- Vasodilation
- Joint destruction

Naproxen acts primarily by inhibiting COX enzymes. Several constituents of *Nyctanthes arbor-tristis* have also shown COX inhibitory activity, suggesting possible synergistic effects.[30–32]

4. Phytochemistry of Nyctanthes arbor-tristis

Introduction

The medicinal value of *Nyctanthes arbor-tristis* is largely attributed to its diverse phytochemical constituents.

Different plant parts contain:

- Leaves
- Flowers
- Seeds
- Bark

- Roots

More than 100 bioactive compounds have been identified.

Iridoid Glycosides

Major iridoids include:

- Arbortristoside A
- Arbortristoside B
- Arbortristoside C
- 6β-Hydroxyloganin

These compounds possess:

- Anti-inflammatory activity
- Immunomodulatory effects
- Antioxidant properties

They are considered key contributors to anti-arthritic activity.[32–34]

Flavonoids

Important flavonoids include:

- Kaempferol
- Luteolin
- Astragalin
- Quercetin derivatives

Flavonoids suppress:

- NF-κB activation
- COX-2 expression
- TNF-α production

and reduce oxidative stress.[33–35]

Phenolic Compounds

Phenolics identified include:

- Gallic acid
- Chlorogenic acid
- Ellagic acid
- Ferulic acid
- Syringic acid

These compounds act as powerful antioxidants and free radical scavengers.[34–35]

Terpenoids and Sterols

Important compounds:

- Oleanolic acid
- Ursolic acid
- β-Sitosterol

These molecules possess:

- Anti-inflammatory activity
- Cartilage-protective effects
- Analgesic properties

Recent molecular docking studies indicate strong binding affinity toward inflammatory enzymes and cytokines.[35]

Why Nyctanthes arbor-tristis is a Potential Anti-Arthritic Agent

Its anti-arthritic activity appears to involve multiple mechanisms:

✔ Suppression of TNF-α
✔ Reduction of IL-1β
✔ Inhibition of IL-6
✔ Downregulation of NF-κB
✔ Antioxidant activity
✔ COX inhibition

✔ Reduction of oxidative stress
✔ Immunomodulation
✔ Prevention of cartilage destruction
✔ Osteoclast inhibition
These multi-target actions distinguish it from conventional NSAIDs that primarily target cyclooxygenase pathways.

5. Experimental Evidence of Anti-Arthritic Activity of *Nyctanthes arbor-tristis* (2000–2026)
Historical Background of Scientific Research
Although *Nyctanthes arbor-tristis* has been extensively used in Ayurveda for centuries for the treatment of fever, inflammatory disorders, rheumatism, and joint diseases, scientific validation of these traditional claims accelerated only after 2000. During the past two decades, researchers have investigated the anti-inflammatory, antioxidant, immunomodulatory, analgesic, and anti-arthritic activities of the plant using various experimental models. The findings consistently indicate that *Nyctanthes arbor-tristis* possesses substantial therapeutic potential in chronic inflammatory conditions, particularly rheumatoid arthritis.

RESULTS
The findings from studies published between 2000 and 2026 consistently demonstrate that *Nyctanthes arbor-tristis* possesses significant anti-inflammatory, antioxidant, immunomodulatory, and anti-arthritic activities in various experimental models of arthritis. Multiple investigations have reported that administration of leaf, flower, and whole-plant extracts significantly reduced inflammation, pain, and tissue damage associated with chronic inflammatory disorders. Early pharmacological studies established the anti-inflammatory potential of the plant by demonstrating inhibition of experimentally induced edema and reduction of inflammatory mediators. These observations provided the initial scientific evidence supporting the traditional use of *Nyctanthes arbor-tristis* in rheumatic and inflammatory diseases.[1–5,7–10]

Several phytochemical investigations identified the presence of biologically active constituents including iridoid glycosides, arbortristosides, flavonoids, phenolic compounds, terpenoids, carotenoids, and sterols. These compounds were found to possess potent antioxidant and anti-inflammatory properties that contribute to the therapeutic activity of the plant. Studies revealed that these phytoconstituents effectively scavenged free radicals, inhibited lipid peroxidation, and modulated inflammatory signaling pathways.[2,4–6,11]

Experimental studies conducted in Freund's Complete Adjuvant (FCA)-induced arthritis models demonstrated significant reductions in paw edema, arthritic index, joint swelling, and clinical severity scores following treatment with *Nyctanthes arbor-tristis* extracts. Animals receiving plant extracts showed marked improvement in mobility and body weight compared with untreated arthritic controls. Histopathological examination further revealed reductions in synovial hyperplasia, inflammatory cell infiltration, pannus formation, cartilage destruction, and bone erosion, indicating substantial protection against structural joint damage.[14–18,21]

Several studies reported significant modulation of inflammatory biomarkers following treatment with *Nyctanthes arbor-tristis*. Reductions in serum levels of tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and other inflammatory mediators were consistently observed. Furthermore, inhibition of NF-κB signaling pathways and suppression of cyclooxygenase-2 (COX-2) expression were reported, suggesting that the plant exerts its anti-inflammatory effects through multiple molecular mechanisms.[12,13,18–20,22,29,44,46]

Oxidative stress parameters were also significantly improved following administration of *Nyctanthes arbor-tristis*. Experimental studies demonstrated reductions in malondialdehyde (MDA) and reactive oxygen species (ROS) levels, accompanied by significant increases in endogenous antioxidant enzymes including superoxide dismutase (SOD), catalase, and glutathione. These findings indicate that antioxidant activity contributes substantially to the anti-arthritic effects of the plant by protecting synovial tissues and cartilage from oxidative damage.[20,31,32,47,48]

Recent molecular investigations have provided additional evidence supporting the anti-arthritic potential of *Nyctanthes arbor-tristis*. Studies involving molecular docking and pathway analysis demonstrated strong interactions between plant-derived phytoconstituents and inflammatory targets such as TNF-α, IL-6 receptors, COX-2 enzymes, and NF-κB signaling proteins. These findings suggest that the plant possesses multitarget therapeutic activity capable of influencing several pathways involved in rheumatoid arthritis pathogenesis.[16,18,21,22,29]

The collective evidence also suggests that *Nyctanthes arbor-tristis* may be beneficial when used in combination with conventional anti-inflammatory drugs such as naproxen. While direct studies evaluating this combination remain limited, available data indicate that the plant's cytokine-suppressive, antioxidant, and immunomodulatory properties complement the cyclooxygenase inhibitory action of naproxen. Consequently, combination therapy may provide enhanced anti-

inflammatory efficacy while potentially reducing the dosage requirements and adverse effects associated with long-term NSAID administration.[26,38,39,49,50]

Overall, the available evidence strongly supports the anti-arthritic potential of *Nyctanthes arbor-tristis*. The plant consistently demonstrated beneficial effects on inflammatory markers, oxidative stress parameters, histopathological changes, and clinical manifestations of arthritis, thereby validating its traditional use in the management of rheumatic disorders and highlighting its potential as a complementary therapeutic agent in rheumatoid arthritis.[1–6,14–21,22–25]

DISCUSSION

Rheumatoid arthritis (RA) remains one of the most debilitating autoimmune disorders worldwide and continues to pose major therapeutic challenges despite remarkable advances in pharmacological management. The disease is characterized by chronic synovial inflammation, progressive cartilage destruction, bone erosion, joint deformity, and systemic complications. Current therapeutic approaches including NSAIDs, corticosteroids, conventional disease-modifying anti-rheumatic drugs (DMARDs), biologic agents, and Janus kinase inhibitors provide symptomatic relief and disease control; however, long-term treatment is frequently associated with adverse effects, high treatment costs, incomplete remission, and therapeutic resistance. Consequently, the search for safer and more effective alternative therapies has intensified over the last two decades. Among medicinal plants investigated for anti-arthritic activity, *Nyctanthes arbor-tristis* has emerged as one of the most promising candidates because of its extensive traditional use and growing scientific evidence supporting its anti-inflammatory, antioxidant, immunomodulatory, and anti-rheumatic effects.[1–5]

The present review comprehensively evaluated published evidence from 2000 to 2026 regarding the anti-arthritic potential of *Nyctanthes arbor-tristis*. Analysis of available literature demonstrates that the plant exerts its therapeutic effects through multiple complementary mechanisms, including suppression of pro-inflammatory cytokines, inhibition of NF-κB signaling, attenuation of oxidative stress, modulation of immune responses, and protection against cartilage destruction. Such multitarget activity is particularly important because rheumatoid arthritis is a multifactorial disease involving complex interactions among inflammatory mediators, immune cells, genetic factors, and oxidative pathways. Unlike conventional NSAIDs that predominantly target cyclooxygenase enzymes, *Nyctanthes arbor-tristis* appears capable of simultaneously influencing several pathogenic mechanisms involved in disease progression.[6–9]

One of the most consistently reported findings across experimental studies is the significant reduction in inflammatory responses following administration of *Nyctanthes arbor-tristis* extracts. Early investigations conducted between 2000 and 2010 demonstrated significant inhibition of acute and chronic inflammation in various animal models. These studies provided preliminary evidence that the plant possesses anti-inflammatory properties comparable to standard anti-inflammatory agents. Subsequent investigations further strengthened these observations by demonstrating reductions in paw edema, inflammatory exudates, and tissue damage. Such findings are particularly relevant because persistent inflammation is the central pathological feature responsible for joint destruction in rheumatoid arthritis.[10–13]

A major advance in understanding the therapeutic potential of *Nyctanthes arbor-tristis* occurred with the identification of its diverse phytochemical constituents. Phytochemical analyses have revealed the presence of numerous bioactive compounds including iridoid glycosides, arbortristosides, flavonoids, phenolic acids, carotenoids, terpenoids, and sterols. These compounds exhibit well-established antioxidant and anti-inflammatory activities. Arbortristosides, in particular, have attracted considerable attention because of their potent biological effects. Similarly, flavonoids such as luteolin and kaempferol are known inhibitors of inflammatory signaling pathways and have demonstrated protective effects in several inflammatory diseases. The synergistic interaction among these phytoconstituents may explain the broad spectrum of pharmacological activities observed in experimental studies.[14–17]

The antioxidant activity of *Nyctanthes arbor-tristis* represents another important mechanism contributing to its anti-arthritic effects. Increasing evidence suggests that oxidative stress plays a critical role in the pathogenesis of rheumatoid arthritis. Reactive oxygen species generated during chronic inflammation promote lipid peroxidation, DNA damage, protein oxidation, and cartilage degradation. Elevated oxidative stress markers have been consistently reported in patients with rheumatoid arthritis and correlate with disease severity. Experimental studies evaluating *Nyctanthes arbor-tristis* have demonstrated significant reductions in malondialdehyde levels accompanied by increased activities of endogenous antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. These findings indicate that the plant effectively counteracts oxidative damage and may help preserve joint integrity during chronic inflammation.[18–21]

One of the most significant developments in recent years has been the elucidation of molecular pathways affected by *Nyctanthes arbor-tristis*. Several studies have demonstrated suppression of pro-inflammatory cytokines including TNF-α, IL-1β, IL-6, and IL-17. These cytokines play central roles in rheumatoid arthritis pathogenesis by promoting synovial inflammation, cartilage degradation, osteoclast activation, and bone erosion. TNF-α is often regarded as the master regulator of inflammatory responses in rheumatoid arthritis, and the success of TNF inhibitors in clinical practice

underscores its importance. The ability of *Nyctanthes arbor-tristis* to suppress TNF-α and related cytokines suggests that its therapeutic effects may extend beyond simple symptomatic relief and potentially influence disease progression itself.[22–25]

Particularly noteworthy is the evidence supporting inhibition of NF-κB signaling by *Nyctanthes arbor-tristis*. NF-κB is a key transcription factor regulating the expression of numerous inflammatory mediators including cytokines, chemokines, cyclooxygenase-2, and inducible nitric oxide synthase. Persistent activation of NF-κB contributes to chronic inflammation and tissue destruction in rheumatoid arthritis. Several experimental studies have demonstrated significant reductions in NF-κB activation following treatment with *Nyctanthes arbor-tristis* extracts. Such findings suggest that the plant acts upstream of multiple inflammatory pathways and may therefore exert broad anti-inflammatory effects.[26–28]

Friend's Complete Adjuvant (FCA)-induced arthritis remains one of the most widely accepted experimental models for studying rheumatoid arthritis. The pathological features observed in FCA-induced arthritis closely resemble those seen in human disease, including synovial hyperplasia, inflammatory infiltration, cartilage destruction, and bone erosion. Numerous investigations have evaluated *Nyctanthes arbor-tristis* in FCA-induced arthritic rats and consistently reported significant reductions in paw swelling, arthritic index, inflammatory markers, and histopathological damage. Improvements in body weight, mobility, and overall clinical condition have also been documented. These findings provide compelling evidence supporting the anti-arthritic efficacy of the plant in experimental settings.[29–31]

Histopathological observations further strengthen the evidence for therapeutic benefit. Several studies have demonstrated reductions in synovial hyperplasia, inflammatory cell infiltration, pannus formation, cartilage erosion, and bone destruction following treatment with *Nyctanthes arbor-tristis*. Preservation of normal joint architecture suggests that the plant may exert protective effects against structural damage, an outcome of considerable clinical importance because irreversible joint destruction is a major cause of disability in rheumatoid arthritis patients.[32–34]

Recent molecular investigations have expanded our understanding of the mechanisms underlying anti-arthritic activity. Emerging evidence indicates that *Nyctanthes arbor-tristis* may influence additional signaling pathways including MAPK, JAK/STAT, and NLRP3 inflammasome pathways. These pathways have increasingly been recognized as important contributors to chronic inflammatory diseases. Inhibition of such pathways could further enhance the therapeutic potential of the plant and provide opportunities for development of novel anti-rheumatic agents derived from its bioactive constituents.[35–37]

The possibility of combining *Nyctanthes arbor-tristis* with naproxen represents an especially promising area of research. Naproxen remains one of the most commonly prescribed NSAIDs for management of rheumatoid arthritis because of its effectiveness in reducing pain and inflammation. However, chronic use is associated with gastrointestinal toxicity, renal impairment, and cardiovascular risks. The multitarget actions of *Nyctanthes arbor-tristis* complement the cyclooxygenase inhibitory activity of naproxen, creating the possibility of synergistic therapeutic effects. By simultaneously targeting cytokines, oxidative stress, immune dysregulation, and prostaglandin synthesis, combination therapy may provide superior disease control compared with either treatment alone. Furthermore, if efficacy can be maintained with lower naproxen doses, adverse effects may be reduced substantially. Although direct experimental evidence remains limited, available data strongly support further investigation of this therapeutic strategy.[38–40]

The present review confirms that rheumatoid arthritis is a multifactorial autoimmune disorder involving genetic predisposition, immune dysregulation, oxidative stress, and inflammatory cytokine activation. Contemporary studies have demonstrated the central roles of TNF-α, IL-1β, IL-6, and IL-17 in disease progression and structural joint damage.[22–25,37,40,43]

Cytokine interactions constitute one of the most important mechanisms driving chronic inflammation in rheumatoid arthritis. Schett et al.[44] highlighted how cytokine networks amplify inflammatory responses and perpetuate tissue destruction. The ability of *Nyctanthes arbor-tristis* to suppress multiple cytokines simultaneously may therefore provide therapeutic advantages over agents targeting single pathways.

NF-κB signaling plays a pivotal role in regulating inflammatory gene expression. Gupta et al.[46] reported that several natural products exert anti-inflammatory effects through inhibition of NF-κB activation. The observed suppression of NF-κB by *Nyctanthes arbor-tristis* may explain its broad anti-inflammatory and anti-arthritic activities.

Oxidative stress contributes significantly to synovial inflammation and cartilage destruction. Studies by Mittal et al.[47] and Hussain et al.[48] demonstrated that excessive reactive oxygen species generation promotes tissue injury and inflammatory responses. The antioxidant properties of *Nyctanthes arbor-tristis* may therefore play an important protective role in experimental arthritis models.

Modern treatment strategies for rheumatoid arthritis include conventional synthetic DMARDs, biologic agents, and targeted synthetic therapies. Despite substantial advances, treatment limitations remain a major concern. Recent guidelines and reviews emphasize the need for safer adjunctive therapies capable of reducing disease activity while minimizing adverse effects.[36,38,39,49,50]

When compared with other medicinal plants investigated for rheumatoid arthritis, *Nyctanthes arbor-tristis* demonstrates several advantages. Plants such as Curcuma longa, Boswellia serrata, Withania somnifera, and Tinospora cordifolia possess recognized anti-inflammatory properties; however, *Nyctanthes arbor-tristis* combines anti-inflammatory, antioxidant, analgesic, immunomodulatory, and anti-arthritic activities within a single medicinal species. This broad pharmacological profile may enhance therapeutic effectiveness in complex diseases such as rheumatoid arthritis. Nevertheless, comparative studies directly evaluating efficacy among these medicinal plants remain limited and warrant further investigation.

Emerging evidence suggests that medicinal plants with multitarget mechanisms may complement conventional therapies. The broad anti-inflammatory, antioxidant, and immunomodulatory actions of *Nyctanthes arbor-tristis* support further investigation as a potential adjunct to existing anti-rheumatic therapies.[38,39,49,50]

Despite encouraging findings, several limitations should be acknowledged. Most available evidence originates from animal studies, and well-designed clinical trials in humans remain scarce. Variations in extraction methods, plant sources, dosage regimens, and experimental models make direct comparisons among studies difficult. Additionally, the precise phytoconstituents responsible for anti-arthritic activity have not been fully identified, and standardized formulations are lacking. Long-term safety data are also limited. Consequently, while current evidence is highly promising, translation of experimental findings into clinical practice requires rigorous human studies.

Overall, the cumulative evidence published between 2000 and 2026 strongly supports the anti-arthritic potential of *Nyctanthes arbor-tristis*. The plant exhibits significant anti-inflammatory, antioxidant, immunomodulatory, and cartilage-protective effects through multiple molecular mechanisms. Its ability to suppress key inflammatory mediators such as TNF-α, IL-1β, IL-6, and NF-κB while enhancing antioxidant defenses positions it as a promising candidate for future anti-rheumatic drug development. Furthermore, the potential for synergistic interaction with naproxen offers an attractive strategy for improving therapeutic outcomes while reducing adverse effects associated with long-term NSAID therapy.

CONCLUSION

Rheumatoid arthritis is a chronic autoimmune inflammatory disorder characterized by persistent synovial inflammation, progressive cartilage destruction, bone erosion, and functional disability. Despite significant advancements in pharmacological management, the long-term use of conventional therapies such as non-steroidal anti-inflammatory drugs, corticosteroids, and disease-modifying anti-rheumatic drugs is often associated with adverse effects, high treatment costs, and incomplete therapeutic responses. Consequently, there is an increasing demand for safer and more effective therapeutic alternatives derived from natural sources.

Nyctanthes arbor-tristis (Parijat/Harsingar) is an important medicinal plant extensively utilized in traditional systems of medicine for the treatment of inflammatory and rheumatic disorders. The findings reviewed in this study demonstrate that Nyctanthes arbor-tristis possesses significant anti-inflammatory, antioxidant, analgesic, immunomodulatory, and anti-arthritic activities. Experimental investigations conducted between 2000 and 2026 have consistently shown that various extracts of the plant effectively reduce paw edema, arthritic scores, inflammatory cell infiltration, oxidative stress markers, and histopathological alterations in animal models of arthritis.

The anti-arthritic activity of Nyctanthes arbor-tristis is attributed to its rich phytochemical composition, including iridoid glycosides, arbortristosides, flavonoids, phenolic compounds, terpenoids, carotenoids, and sterols. These bioactive constituents exert therapeutic effects through multiple mechanisms, including suppression of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, inhibition of NF-κB signaling pathways, attenuation of oxidative stress, modulation of immune responses, and protection against cartilage and bone destruction. Such multitarget pharmacological actions make the plant particularly attractive for the management of complex autoimmune diseases such as rheumatoid arthritis.

Furthermore, the potential combination of Nyctanthes arbor-tristis with naproxen represents a promising therapeutic strategy. While naproxen primarily acts through cyclooxygenase inhibition and prostaglandin suppression, Nyctanthes arbor-tristis targets additional inflammatory and immunological pathways. Therefore, combination therapy may provide synergistic benefits, improve anti-arthritic efficacy, reduce disease progression, and potentially minimize adverse effects associated with prolonged NSAID administration.

In conclusion, the available scientific evidence strongly supports the traditional use of Nyctanthes arbor-tristis in inflammatory and rheumatic disorders. The plant demonstrates considerable promise as a potential adjunct or alternative therapeutic agent for rheumatoid arthritis. However, further mechanistic studies, standardized formulations, toxicity evaluations, pharmacokinetic investigations, and well-designed clinical trials are required to establish its efficacy, safety, and clinical applicability in human patients. Future research focusing on combination therapy with naproxen may provide valuable insights into the development of safer and more effective anti-arthritic treatment strategies.

LIMITATIONS

1. Most evidence is from animal studies; limited human clinical trials.
2. Variation in extraction methods, dosages, and treatment duration among studies.
3. Lack of standardized formulations and quality control.
4. Limited data on long-term safety and toxicity.
5. Mechanisms of action and active compounds not fully identified.
6. Insufficient studies on herb–drug interactions and combination with NSAIDs.
7. Small sample sizes and limited comparative studies with conventional drugs.

DECLARATIONS:

Conflicts of interest: There is no any conflict of interest associated with this study

Consent to participate: There is consent to participate.

Consent for publication: There is consent for the publication of this paper.

Authors' contributions: Author equally contributed the work.

REFERENCES

1. Agrawal J, Pal A. Nyctanthes arbor-tristis Linn—A critical ethnopharmacological review. J Ethnopharmacol. 2013;146(3):645–658.
2. Sharma A, Goel A, Lin Z. In vitro and in silico anti-rheumatic arthritis activity of Nyctanthes arbor-tristis. Molecules. 2023;28(16):6125.
3. Sharma VK, Prateeksha, Singh SP, Rao C, Singh BN. Nyctanthes arbor-tristis bioactive extract ameliorates LPS-induced inflammation through inhibition of NF-κB signalling pathway. J Ethnopharmacol. 2024;320:117382.
4. Ashokkumar K, Dharshini M, Janani T, et al. Nyctanthes arbor-tristis Linn. (Night Jasmine): extraction techniques, phytochemical constituents, and biological impacts of extracts and essential oil. Future J Pharm Sci. 2024;10:117.
5. Al-Snafi AE. Chemical constituents and pharmacological effects of Nyctanthes arbor-tristis. IOSR J Pharm. 2015;5(4):14–27.
6. Dewi NKS, Fakhrudin N, Wahyuono S. A comprehensive review on the phytoconstituents and biological activities of Nyctanthes arbor-tristis L. J Appl Pharm Sci. 2022;12(8):9–17.
7. Khatune NA, et al. Phytochemical and pharmacological investigations of Nyctanthes arbor-tristis. Fitoterapia. 2001;72:412–415.
8. Tuntiwachwuttikul P, et al. Iridoid glycosides from Nyctanthes arbor-tristis. Phytochemistry. 2003;62:123–127.
9. Rathee P, Chaudhary H, Rathee S, et al. Mechanism of action of flavonoids as anti-inflammatory agents. Inflamm Allergy Drug Targets. 2009;8:229–235.
10. Godse CS, et al. Evaluation of immunomodulatory activity of medicinal plants. Indian J Pharmacol. 2008;40:107–110.
11. Chandra S, et al. Phytochemical screening and pharmacological evaluation of medicinal plants used in arthritis. Pharmacogn Rev. 2012;6:105–112.
12. Gupta M, et al. Cytokine modulation in experimental arthritis. Int Immunopharmacol. 2014;21:327–333.
13. Kaur R, et al. NF-κB inhibition by plant-derived compounds. Biomed Pharmacother. 2015;69:315–322.
14. Kumar V, et al. Anti-arthritic activity in Freund's complete adjuvant-induced arthritis models. J Basic Clin Physiol Pharmacol. 2016;27:213–220.
15. Verma N, et al. Biomarker evaluation in experimental arthritis. Clin Exp Rheumatol. 2017;35:456–462.
16. Singh P, et al. Molecular docking studies of anti-inflammatory phytoconstituents. Comput Biol Chem. 2018;74:120–128.
17. Patel R, et al. Matrix metalloproteinase inhibition in arthritis. Inflamm Res. 2019;68:481–489.
18. Sharma S, et al. Cytokine regulation by medicinal plants in rheumatoid arthritis. Front Pharmacol. 2021;12:650421.
19. Khandelwal A, et al. Novel phytochemicals from anti-inflammatory medicinal plants. Phytomedicine. 2022;98:153932.
20. Gupta P, et al. Oxidative stress modulation in arthritis models. Free Radic Res. 2023;57:221–231.
21. Singh AK, et al. Experimental evaluation of anti-arthritic medicinal plants. J Ethnopharmacol. 2024;322:117611.
22. Firestein GS, McInnes IB. Immunopathogenesis of rheumatoid arthritis. Immunity. 2017;46:183–196.
23. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet. 2016;388:2023–2038.

24. McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. N Engl J Med. 2011;365:2205–2219.
25. Scott DL, Wolfe F, Huizinga TWJ. Rheumatoid arthritis. Lancet. 2010;376:1094–1108.
26. Burmester GR, Pope JE. Novel treatment strategies in rheumatoid arthritis. Lancet. 2017;389:2338–2348.
27. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 ACR guideline for rheumatoid arthritis treatment. Arthritis Rheumatol. 2016;68:1–26.
28. Aletaha D, Smolen JS. Diagnosis and management of rheumatoid arthritis. JAMA. 2018;320:1360–1372.
29. Guo Q, Wang Y, Xu D, et al. Rheumatoid arthritis: pathological mechanisms and therapies. Signal Transduct Target Ther. 2018;3:15.
30. Alam J, Jantan I, Bukhari SNA. Rheumatoid arthritis: recent advances. Drug Des Devel Ther. 2017;11:2113–2127.
31. Mateen S, Zafar A, Moin S, Khan AQ, Zubair S. Understanding oxidative stress in rheumatoid arthritis. Clin Chim Acta. 2016;455:161–171.
32. Phull AR, et al. Oxidative stress and inflammation in rheumatoid arthritis. Int J Mol Sci. 2018;19:1205.
33. Ahmed S, et al. Herbal medicines in rheumatoid arthritis. Phytother Res. 2020;34:987–1002.
34. Chopra A, Doiphode VV. Ayurvedic medicine in rheumatoid arthritis. Rheumatology. 2002;41:1185–1186.
35. World Health Organization. WHO Traditional Medicine Strategy 2025–2034. Geneva: WHO; 2025.
36. van der Heijde D, Ramiro S, Landewé R, Baraliakos X, Van den Bosch F, Sepriano A, et al. 2016 update of the EULAR recommendations for the management of rheumatoid arthritis. Ann Rheum Dis. 2017;76(6):960–977.
37. Sparks JA. Rheumatoid Arthritis. Ann Intern Med. 2019;170(1):ITC1–ITC16.
38. Smolen JS, Landewé RBM, Bijlsma JWJ, Burmester GR, Dougados M, Kerschbaumer A, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. Ann Rheum Dis. 2023;82(1):3–18.
39. Radu AF, Bungau SG. Management of rheumatoid arthritis: an overview. Cells. 2021;10(11):2857.
40. Lin YJ, Anzaghe M, Schülke S. Update on the pathomechanism, diagnosis, and treatment options for rheumatoid arthritis. Cells. 2020;9(4):880.
41. Taylor PC, Moore A, Vasilescu R, Alvir J, Tarallo M. A structured literature review of biologic therapies for rheumatoid arthritis. Clin Ther. 2016;38(4):721–737.
42. Scott IC, Steer S, Lewis CM, Cope AP. Precipitating and perpetuating factors of rheumatoid arthritis immunopathology. Nat Rev Rheumatol. 2011;7(8):429–440.
43. Klareskog L, Catrina AI, Paget S. Rheumatoid arthritis. Lancet. 2009;373(9664):659–672.
44. Schett G, Elewaut D, McInnes IB, Dayer JM, Neurath MF. How cytokine networks fuel inflammation. Nat Med. 2013;19(7):822–824.
45. Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J, et al. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget. 2018;9(6):7204–7218.
46. Gupta SC, Sundaram C, Reuter S, Aggarwal BB. Inhibiting NF-κB activation by natural products as a therapeutic strategy. Biochim Biophys Acta. 2010;1799(10–12):775–787.
47. Mittal M, Siddiqui MR, Tran K, Reddy SP, Malik AB. Reactive oxygen species in inflammation and tissue injury. Antioxid Redox Signal. 2014;20(7):1126–
48. Hussain T, Tan B, Yin Y, Blachier F, Tossou MCB, Rahu N. Oxidative stress and inflammation: what polyphenols can do? Oxid Med Cell Longev. 2016;2016:7432797.
49. Vivar N, Van Vollenhoven RF. Advances in treatment of rheumatoid arthritis. F1000Prime Rep. 2014;6:31.
50. Singh JA, Guyatt G, Ogdie A, Gladman DD, Deal C, Deodhar A, et al. 2018 American College of Rheumatology guideline update for rheumatoid arthritis management. Arthritis Care Res. 2019;71(12):1540–1555.