
**HERBAL PLANTS IN THE MANAGEMENT OF RHEUMATOID
ARTHRITIS: A COMPREHENSIVE REVIEW**

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disorder characterized by joint synovial inflammation, progressive cartilage degradation, and bone erosion, ultimately leading to joint deformity and functional disability. Although conventional therapies such as non-steroidal anti-inflammatory drugs and disease-modifying antirheumatic drugs are commonly prescribed, their long-term use is frequently limited by associated adverse effects. In recent years, natural plant extracts and phytoconstituents have gained considerable attention as potential therapeutic agents for RA due to their diverse pharmacological properties. Evidence from various studies indicates that these bioactive compounds exert significant anti-inflammatory and immunomodulatory effects by inhibiting key pro-inflammatory cytokines such as tumour necrosis factor-alpha (TNF- α), interleukin-1 (IL-1), and interleukin-6 (IL-6), thereby reducing inflammation and disease progression. In addition, herbal therapies are considered relatively safe, cost-effective, and may offer opportunities for individualized treatment approaches. However, additional studies are required to confirm clinical efficacy, establish safety profiles, and develop standardized formulations for the successful incorporation of herbal therapies into rheumatoid arthritis management.

KEYWORDS: Rheumatoid arthritis, Autoimmune disorder, Inflammation, Immunomodulation, Cytokines, TNF- α , IL-6.

1. INTRODUCTION

Rheumatoid arthritis (RA), a chronic systemic autoimmune disorder, is characterized by persistent inflammation of synovial joints and is often accompanied by extra-articular manifestations. It is a chronic inflammatory disease driven by a complex interplay of genetic and environmental factors, including smoking or tobacco exposure^[1]. Persistent synovial inflammation is a hallmark feature of RA, leading to progressive joint damage, structural deformity, and functional impairment over time. Clinically, RA typically begins in small peripheral joints in a symmetrical pattern and progressively involves proximal joints if left untreated^[3]. Persistent inflammation leads to cartilage degradation, bone erosion, and ultimately joint deformity and functional impairment. Based on symptom duration, RA is classified as early-stage when symptoms persist for less than six months and established-stage when they extend beyond six months^[4]. The disease follows a progressive course associated with increased morbidity and mortality in the absence of appropriate management^[5]. Patients often require significant lifestyle modifications to manage disease burden^[6]. Current therapeutic approaches include glucocorticoids, disease-modifying antirheumatic drugs, and non-steroidal anti-inflammatory drugs; however, these treatments are associated with limitations and potential adverse effects during long-term use^[7]. **(Fig 1)** In recent years, natural plant extracts and compounds (NPECs) have gained considerable attention due to their diverse pharmacological activities and demonstrated efficacy in preclinical studies for reducing RA progression^[8,9]. These bioactive agents offer promising therapeutic potential through their multi-targeted mechanisms, supporting the growing interest in their development as alternative or complementary treatments for RA.

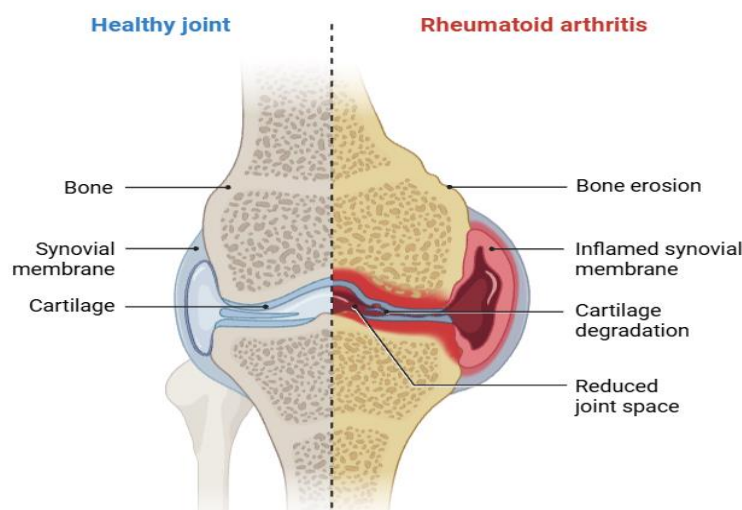


Fig.no 1: Diagrammatic Representation of Pathological Changes in Rheumatoid Arthritis.

EPIDERMIOLOGY

Rheumatoid arthritis (RA) is a chronic, progressive autoimmune disorder that imposes a significant global health burden, affecting approximately 0.5–1% of the population worldwide and occurring at any age, although it most commonly presents between the fourth and fifth decades of life ^[10]. The prevalence and incidence of RA increase with advancing age ^[11], and the disease is classified as early-onset when it occurs before 65 years and late-onset when it develops thereafter ^[12]. Epidemiological studies indicate that women are affected two to three times more frequently than men, highlighting the influence of hormonal, genetic, and environmental factors in disease pathogenesis. The onset of RA may be either gradual or acute, with nearly half of cases exhibiting an insidious progression, and the disease course remains highly variable and unpredictable, ranging from mild forms to severe, debilitating conditions ^[13]. Notably, disease activity often improves during pregnancy and exacerbates in the postpartum period, further supporting the role of hormonal influences ^[14]. In the Indian population, the prevalence of RA is comparable to global estimates, representing a considerable public health concern. Genetic predisposition, particularly a positive family history, along with environmental triggers such as smoking, significantly increases the risk of disease development. RA is associated with substantial morbidity and mortality, with disability rates reaching up to 30% and mortality rates up to 52% in severe cases ^[15]. Overall, RA remains a major contributor to global disability, underscoring the need for early diagnosis, effective management, and continued research into improved therapeutic strategies.

PATHOPHYSIOLOGY

The pathophysiology of RA is heavily influenced by monocytes and macrophages, which secrete pro-inflammatory cytokines such as TNF, IL-1, and IL-6. In RA, the CD14+ population of synovial macrophages and peripheral monocytes expressed more of the chemokine receptor CCR9, which is crucial for leukocyte migration to and retention in RA joints. Both RA patients and controls have macrophages colocalised with CCL25 (a CCR9 ligand) in the synovium. In comparison to controls, treatment with CCL25 in vitro often caused RA monocytes to differentiate more strongly from monocyte to macrophage. According to numerous studies, adiponectin can play a significant pro-inflammatory role in the development of RA, particularly in the joints, by activating synovial fibroblasts that express adiponectin receptors and causing them to secrete inflammatory mediators. In RA synovium, particularly in FLSs and macrophage-like synoviocytes, Angptl2 and its mRNA

are abundantly expressed. In addition, in vitro, Angptl2 enhances the chemotaxis of CD14⁺CD16⁻ monocytes, hence boosting chronic inflammation. TNF signalling has numerous roles in the etiology of RA. (Fig 2) It recruits proinflammatory cells, including synovial fibroblasts and macrophages, which release proinflammatory cytokines like IL-6, IL-1, and TNF. The IL-1, and TNF can trigger the transcription of IL-6. One of the characteristics of RA is the sustained production of IL-6 in synovial fibroblasts following stimulation with TNF. RA is characterized by an increase in IgM and IgG rheumatoid factors as well as antibodies to citrullinated peptides^[16, 17, 18].

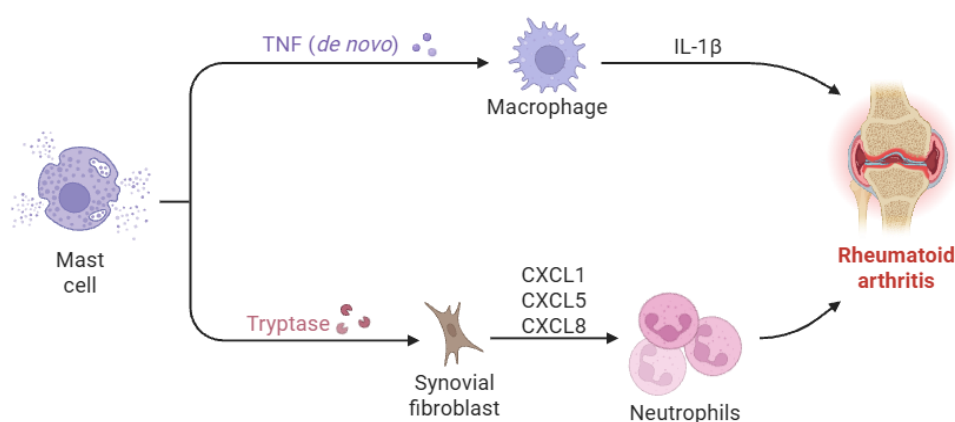


Fig.no 2: Cytokine-Mediated Pathogenesis of Rheumatoid Arthritis.

2.MEDICINAL PLANTS USED FOR RHEUMATOID ARTHRITIS

2.1 CINNAMOMUM CASSIA



Fig.no 3: Dried Bark of *Cinnamomum cassia*. (Chinese Cinnamon)

Cinnamomum cassia, (Fig 3) commonly known as Chinese cassia or Chinese cinnamon, is an evergreen plant belonging to the Lauraceae family, which comprises approximately 250 species distributed across Asia, South America, and other tropical regions. The plant is

characterized by leathery, oppositely arranged leaves measuring up to 10 cm in length with an acuminate tip. It contains several bioactive constituents, including cinnamaldehyde, cinnamic acid, and coumarin, which contribute to its pharmacological properties. Traditionally, *C. cassia* has been used in Chinese medicine for the treatment of gastrointestinal disorders, circulatory disturbances, and inflammatory conditions. Pharmacological studies have demonstrated that the bark extract exhibits significant anti-inflammatory and antimicrobial activities, including effectiveness against antibiotic-resistant strains such as *Bacillus megaterium* and *Enterococcus faecalis*. Among its active components, cinnamaldehyde plays a major role in mediating antioxidant, anti-tyrosinase, and anticancer effects. In addition, *C. cassia* has been reported to reduce triglyceride and low-density lipoprotein levels in hypercholesterolemic animal models^[19]. Furthermore, it has shown the ability to modulate inflammatory responses by downregulating the expression of vascular cell adhesion molecule-1 (VCAM-1) in TNF- α -stimulated endothelial cells, highlighting its potential role in the management of inflammatory conditions such as rheumatoid arthritis.

2.2 LIGUSTICUM CHUANXIONG HORT



Fig.no 4: Dried Rhizome of *Ligusticum chuanxiong*. (Chuanxiong)

Ligusticum chuanxiong Hort.(Fig 4) (Umbelliferae), commonly known as Chuanxiong Rhizoma, is a well-established medicinal herb widely used in the treatment of various disorders. The plant contains several bioactive constituents, including ligustilide, 3-butyrolactone, cypressene, ferulic acid, tetramethylpyrazine (ligustrazine), palmitic acid, carotene, and β -sitosterol, which contribute to its diverse pharmacological activities. Numerous biomedical and clinical studies have demonstrated its antioxidant, neuroprotective, anti-fibrotic, antinociceptive, anti-inflammatory, and antineoplastic properties. In experimental studies, *L. chuanxiong* has shown significant anti-arthritic potential by reducing joint swelling in collagen-induced arthritis models. Furthermore, treatment with ligustrazine has been reported to decrease serum levels of pro-inflammatory cytokines such as

interleukin-1 (IL-1) and interleukin-6 (IL-6), while increasing interleukin-2 (IL-2) levels, thereby contributing to the modulation of the inflammatory response^[20]. These findings suggest that ligustrazine exerts its therapeutic effects by restoring cytokine balance and regulating immune responses, indicating its potential role in the management of rheumatoid arthritis.

2.3 ALOE VERA



Fig.no 5: Fresh Leaves of *Aloe barbadensis*. (Aloe vera)

Aloe barbadensis (**Fig 5**) (family Liliaceae), commonly known as Aloe vera, Curacao aloe, or “lily of the desert,” is widely cultivated in Europe and various parts of India, including the north-western Himalayan region. It is one of the most important medicinal plants used in traditional and folk medicine. The plant contains several bioactive constituents such as anthraquinones, anthracene derivatives, cinnamic acid, and anthranilic acid, which are responsible for its pharmacological activities. Aloe vera is commonly used in the treatment of various skin conditions, including minor cuts, insect bites, bruises, poison ivy, and eczema, and it also exhibits antibacterial and antifungal properties. In addition to its dermatological applications, Aloe vera has gained attention for its potential role in the management of inflammatory disorders, including rheumatoid arthritis. The anti-arthritic activity of Aloe vera is primarily attributed to anthraquinone compounds, which possess potent anti-inflammatory and immunomodulatory effects. It has been reported to stimulate the immune system and reduce inflammation^[21]. Experimental studies have demonstrated that topical application of Aloe vera extract significantly reduces inflammation and arthritic symptoms in adjuvant-induced arthritis models in Sprague–Dawley rats.

2.4 WITHENIA SOMNIFERA LINN



Fig.no 6: Dried Roots of *Withaniasomnifera*. (Ashwagandha)

Withaniasomnifera L. Dunal, (Fig 6) commonly known as Ashwagandha or Indian ginseng, is a prominent medicinal plant widely used in Ayurvedic, Siddha, and Unani systems of medicine. It belongs to the family Solanaceae and is well known for its diverse pharmacological properties. The plant exhibits antioxidant, anti-stress, adaptogenic, neuroprotective, anxiolytic, anti-inflammatory, hypolipidemic, hepatoprotective, and antibacterial activities. Several studies have demonstrated the immunomodulatory and antitumor effects of *W. somnifera* root extracts, highlighting their therapeutic potential in various disorders. Traditionally, the plant has been used in the management of conditions such as neurological disorders, including Parkinsonism and neuropathy, as well as paralysis and certain tumors, including uterine fibroids and other proliferative disorders. Owing to its significant anti-inflammatory and immunomodulatory properties, *W. somnifera* shows promising potential in the management of rheumatoid arthritis [22].

2.5 CALOTROPIS PROCERA LINN



Fig.no 7: Leaves and Latex Source of *Calotropis procera*. (Swallow Wort)

Calotropis procera Linn., (Fig 7) commonly known as Swallow wort, belongs to the family Asclepiadaceae and is an important medicinal plant used in traditional Ayurvedic medicine. In India, it is represented by two species, *C. procera* and *C. gigantea*. Traditionally, the plant has been used for the treatment of ulcers, leprosy, cancer, piles, and liver disorders. It possesses a wide range of pharmacological activities, including purgative, anthelmintic, analgesic, anti-inflammatory, anticoagulant, antipyretic, and antimicrobial effects. The latex of *C. procera* has been extensively studied for its hepatoprotective, anti-inflammatory, anthelmintic, anticonvulsant, and antimicrobial properties. Moreover, it has been traditionally recognized for its beneficial effects in the management of inflammation and arthritis^[23]. Experimental studies have demonstrated significant anti-inflammatory activity of the latex in various animal models, and its extracts have shown protective effects against inflammation and oxidative stress in monoarthritis induced by different inflammatory mediators.

2.6 SARACA ASOCA ROXB:



Fig.no 8: Bark/Flowers of *Saracaasoca*Roxb.(Ashoka Tree)

Saracaasoca Roxb., (Fig 8) commonly known as Asoka or Ashoka, belongs to the family Caesalpiniaceae and is widely distributed in the foothills of the central and eastern Himalayas as well as in scattered regions of the northern plains of India. Phytochemical analysis of its methanolic and ethanolic extracts has revealed the presence of various bioactive constituents, including carbohydrates, tannins, flavonoids, saponins, glycosides, proteins, and steroids. The plant is traditionally known for its diverse pharmacological properties, such as spasmogenic, uterotonic, antibacterial, anti-implantation, antitumor, anti-progestational, anti-estrogenic, and anti-inflammatory activities. Notably, *S. asoca* has demonstrated potential anti-arthritic effects, with methanolic extracts reported to significantly reduce paw edema in adjuvant-induced arthritic rat models^[24]. These findings suggest its therapeutic potential in the management of rheumatoid arthritis.

2.7 PREMNA SERRATIFOLI LINN



Fig.no 9:*Premnaserratifolia* Linn. (Agnimantha)

Premnaserratifolia Linn.(Fig 9) (family Verbenaceae) is an important medicinal shrub widely distributed in the deciduous forests of India and is also known by the synonym *Premna integrifolia*. Commonly referred to as “Munney” in Tamil and “Agnimantha” in Ayurveda, it is a well-recognized herb in traditional medicine. The plant possesses a broad spectrum of pharmacological activities, including cardi tonic, anticoagulant, anti-inflammatory, antihyperglycemic, antiparasitic, antioxidant, and antimicrobial properties. Various parts of the plant have been traditionally used to treat a range of conditions such as cardiovascular disorders, skin diseases, inflammatory conditions, arthritis, rheumatism, anorexia, and jaundice. Notably, its anti-inflammatory and antioxidant properties contribute to its therapeutic potential in the management of rheumatoid arthritis. Experimental models, such as adjuvant-induced arthritis, which closely resemble human rheumatoid arthritis, have been used to evaluate its efficacy^[25]. These findings support the traditional use of *P. serratifolia* in alleviating inflammatory symptoms associated with rheumatoid arthritis, suggesting its potential as a complementary therapeutic agent.

2.8 SHALLAKI



Fig.no 10: *Boswellia serrata* Roxb.(Indian Frankincense)

Boswellia serrata Roxb., (**Fig 10**) commonly known as Indian frankincense, is widely used in Ayurvedic medicine for its potent anti-inflammatory properties. The resinous gum obtained from its bark, often referred to as “guggulu,” is extensively utilized in traditional and modern phytomedicine. It contains bioactive compounds, particularly boswellic acids, which are responsible for its therapeutic effects. *B. serrata* has been reported to exhibit anti-inflammatory, analgesic, sedative, and anticancer activities. Notably, it provides anti-inflammatory effects without causing gastrointestinal irritation commonly associated with non-steroidal anti-inflammatory drugs. The resin is traditionally recommended for the management of rheumatoid arthritis, osteoarthritis, fibromyositis, and spondylitis^[26]. Clinical studies have shown that treatment with *B. serrata* leads to a reduction in joint pain and swelling, along with improvements in joint flexibility and physical function, including increased walking distance.

2.10 MYROBALAN



Fig.no 11: Fruits of *Terminalia chebula* Retz. (Chebulic Myrobalan)

Terminalia chebula Retz., (**Fig 11**) widely used in traditional medicine across India, China, and other Asian countries, is a well-known medicinal plant valued for its diverse therapeutic properties. In traditional Chinese medicine, particularly in Tibetan and Mongolian systems, it is referred to as the “king of medicines” due to its broad spectrum of pharmacological activities, including anticancer, antioxidant, antidiabetic, anti-inflammatory, antimicrobial, and immunomodulatory effects. The fruit of *T. chebula* contains several bioactive compounds that contribute to its medicinal value. Experimental studies have demonstrated that hydroalcoholic extracts of *T. chebula* exhibit significant anti-arthritic activity in formaldehyde-induced and complete Freund’s adjuvant-induced arthritis models^[27]. This activity is primarily attributed to its ability to modulate the expression of pro-inflammatory cytokines within the synovial tissue, thereby reducing inflammation and disease progression.

2.11 TURMERIC



Fig.no 12: Dried Rhizome of *Curcuma longa*.(Turmeric)

Curcuma longa (turmeric)(**Fig 12**), a perennial herb belonging to the family Zingiberaceae, is widely recognized for its medicinal properties. The principal bioactive compound, curcumin, is responsible for its diverse pharmacological effects, including antioxidant, anti-inflammatory, anti-angiogenic, and anticancer activities, with relatively low toxicity [28]. Curcumin has been shown to effectively inhibit inflammatory pathways, thereby reducing symptoms such as pain and swelling. It exerts its therapeutic effects by modulating key inflammatory mediators and signaling pathways involved in autoimmune conditions. Recent studies have demonstrated that curcumin can alleviate symptoms associated with autoimmune diseases, including rheumatoid arthritis and inflammatory bowel disease, highlighting its potential as a complementary therapeutic agent [29].

2.12 Medicinal Plants Used in the Management of Rheumatoid Arthritis

Table 1: Herbal Plants with Anti-Arthritic Activity in Rheumatoid Arthritis.

S. N O.	PLANT NAME (COMMON NAME)	FAMILY	KEY PHYTOCONSTITUENTS	PHARMACOLOGICAL ACTIVITIES	ANTI-ARTHRITIC MECHANISM / EVIDENCE
1	<i>Cinnamomum cassia</i> (Chinese cinnamon)	Lauraceae	Cinnamaldehyde, cinnamic acid, coumarin	Anti-inflammatory, antimicrobial, antioxidant, anticancer	Downregulates VCAM-1 expression; reduces inflammatory response in TNF- α -stimulated cells

2	<i>Ligusticum chuanxiong</i> (Chuanxiong)	Umbelliferae	Ligustilide, ligustrazine, ferulic acid, β -sitosterol	Anti-inflammatory, antioxidant, neuroprotective, antinociceptive	Reduces IL-1 & IL-6; increases IL-2; modulates cytokine balance
3	<i>Aloe barbadensis</i> (Aloe vera)	Liliaceae	Anthraquinones, anthracene derivatives, cinnamic acid	Anti-inflammatory, antibacterial, antifungal, immunomodulatory	Reduces inflammation in adjuvant-induced arthritis models
4	<i>Withania somnifera</i> (Ashwagandha / Indian ginseng)	Solanaceae	Withanolides, alkaloids	Adaptogenic, anti-inflammatory, antioxidant, immunomodulatory	Modulates immune response and reduces inflammation
5	<i>Calotropis procera</i> (Swallow wort)	Asclepiadaceae	Latex proteins, flavonoids	Anti-inflammatory, analgesic, antimicrobial, hepatoprotective	Reduces inflammation and oxidative stress
6	<i>Saraca asoca</i> (Ashoka tree)	Caesalpinaceae	Flavonoids, tannins, saponins, glycosides	Anti-inflammatory, antibacterial, antitumor	Reduces paw edema in arthritis models
7	<i>Premna serratifolia</i> (Agnimantha)	Verbenaceae	Flavonoids, glycosides	Anti-inflammatory, antioxidant, antimicrobial	Effective in adjuvant-induced arthritis
8	<i>Boswellia serrata</i> (Indian frankincense)	Burseraceae	Boswellic acids	Anti-inflammatory, analgesic, anticancer	Improves joint mobility; reduces swelling
9	<i>Terminalia chebula</i> (Chebulic myrobalan)	Combretaceae	Polyphenols, tannins	Antioxidant, anti-inflammatory, antimicrobial, immunomodulatory	Modulates pro-inflammatory cytokines
10	<i>Curcuma longa</i> (Turmeric)	Zingiberaceae	Curcumin	Anti-inflammatory, antioxidant, anticancer	Inhibits TNF- α , IL-1, IL-6

CONCLUSION

This review provides a comprehensive overview of medicinal plants used in the management of rheumatoid arthritis, highlighting their pharmacological potential and therapeutic relevance. The discussed plants, including *Cinnamomum cassia*, *Ligusticum chuanxiong*, *Aloe barbadensis*, *Withaniasomnifera*, *Calotropis procera*, *Saracaasoca*, *Premnaserratifolia*, *Boswellia serrata*, *Terminalia chebula*, and *Curcuma longa*, are rich sources of bioactive compounds that exhibit significant anti-inflammatory, antioxidant, and immunomodulatory activities. These herbal agents primarily exert their effects by modulating key inflammatory mediators and cytokines involved in the pathogenesis of rheumatoid arthritis. The findings from various experimental studies support their role in reducing inflammation, joint damage, and disease progression. Furthermore, compared to conventional therapies, these herbal medicines may offer advantages such as reduced adverse effects and better suitability for long-term use. However, despite the promising evidence, further research, particularly well-designed clinical trials and standardization of formulations, is essential to establish their safety, efficacy, and clinical applicability. Overall, this review underscores the potential of medicinal plants as valuable complementary therapeutic options in the management of rheumatoid arthritis.

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