



## **MEDICINAL PLANTS USED FOR THE TREATMENT AND MANAGEMENT OF RHEUMATOID ARTHRITIS**

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### **ABSTRACT**

Rheumatoid arthritis is an autoimmune disease. Patients suffering from rheumatoid arthritis experience severe pain in their joints. The joint pain is basically caused by systemic inflammation in joints and damaged cartilage and bones around the joint. The disease persists and develops in a patient resulting into disabilities. It affects the internal organs such as lung, heart and eyes. There is no known effective treatment that can cure rheumatoid arthritis. Modern medications are being used to treat only the symptoms associated with the disease albeit, modern medicines possess numerous disadvantages. Modern medicines can temporarily give relief the patient and the symptoms reappear upon discontinuation. The adverse effects of the modern medicines can hamper the therapeutic treatments also. The herbs and plants are proved to be a better alternative to treat pain and inflammation around the joints. In nature there is an abundance of medicinal plants that shows anti rheumatoid arthritis properties. So the plants and plant products with great advantages are utilized and used to treat rheumatoid arthritis. The aim of this review article is to update information on rheumatoid arthritis including causes, epidemiology, symptoms, diagnosis and classification of rheumatoid arthritis. The present review also highlights the medicinal plants having anti rheumatoid arthritis property.

### **INTRODUCTION**

Rheumatoid arthritis is one of the oldest known diseases that have been found in people with almost all age groups. Most patients of rheumatoid arthritis are found to be in the age group of 20 to 40. In India about 20% of the population has been recorded as arthritis patient. It is an autoimmune disease and can be characterized by the synovial inflammation of the joints and pain in the joints. The aetiology of this chronic autoimmune disease is still unknown. The characteristic joint pain of the

disease is caused by the damage of cartilage and bone around the joints [1]. The damage of the bone is progressive and eventually it results into the deformation and immobility of the bone. The arthritis initiates from the smaller joints of the limbs and gradually escalates to the larger joints, synovial extends and then erodes the particular cartilage and bone, causing joint deformity and progressive physical disability. Extra-articular features include nodules, pericarditis, pulmonary fibrosis, peripheral neuropathy and amyloidosis.

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The actual cause of rheumatoid arthritis is still undiscovered. However, autoimmunity plays the key-role in both chronicity and progression of health. In autoimmune diseases, immune system of the body gets misguided and thus attacks on the healthy tissues. Interleukin-1 (IL-1) and tumour necrosis factor alpha are such immune system tools that play an important role in Rheumatoid Arthritis.

Traditional rheumatoid arthritis (RA) treatments face numerous challenges in terms of both safety and efficacy. Rheumatoid arthritis management is a multidisciplinary approach to pain relief, inflammation reduction, and joint function restoration. Intensive therapy's practical goal is to suppress inflammation. Man was utterly dependent on medicinal plants for disease treatment prior to the discovery of synthetic drugs. Everyone in society used to acknowledge plants' medicinal value. In the 19th century and earlier generations, natural product extracts, particularly those derived from botanical species, were the primary source of traditional medicinal. However, bioactive organic molecules were isolated in considerably pure form for medicinal use in the late 19th century. Salicylic acid, the precursor to aspirin, for example, was isolated from willow bark in 1874. Many synthetic drugs are used as standard treatment for rheumatoid arthritis, but they have side effects that can interfere with the therapeutic treatment; these negative effects increase the likelihood of using herbal plants for rheumatoid arthritis treatment. [2][3]

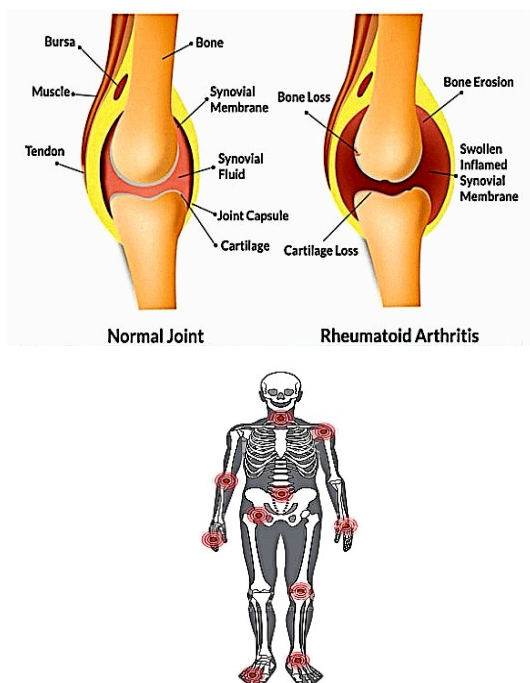


Figure 1: Normal joint and arthritic joint [18]

From clinical and radiological studies it has been found that the progression of rheumatoid arthritis can be classified into 4 stages [4]. The stages are discussed below-

Table 1: Stages of rheumatoid arthritis

Stages	Explanation
Stage I	This is the early stage of rheumatoid arthritis. In this stage, no destructive changes are seen upon radiographic examination. There is a possibility of finding radiographic evidences of osteoporosis.
Stage II	This stage is considered to be the moderate stage of the disease. The radiographic evidences of periarticular osteoporosis, with or without subchordal bone destructions are found in this stage. Adjacent muscle atrophy is present, extra-articular soft tissues lesion are possible.
Stage III	This stage is severe progression radiographic evidence of cartilage and bone destructions are seen. Peri-articular osteoporosis, joint deformity (e.g., subluxation, ulnar deviation or hyperextension) without fibrous or bony ankylosis, excessive muscle atrophy, extra-articular soft tissue lesions are possible in this condition.
Stage IV	This stage is terminal progression stage. Presences of fibrous or bony ankylosis along with the other criterions of stage III are supposedly found in this stage.

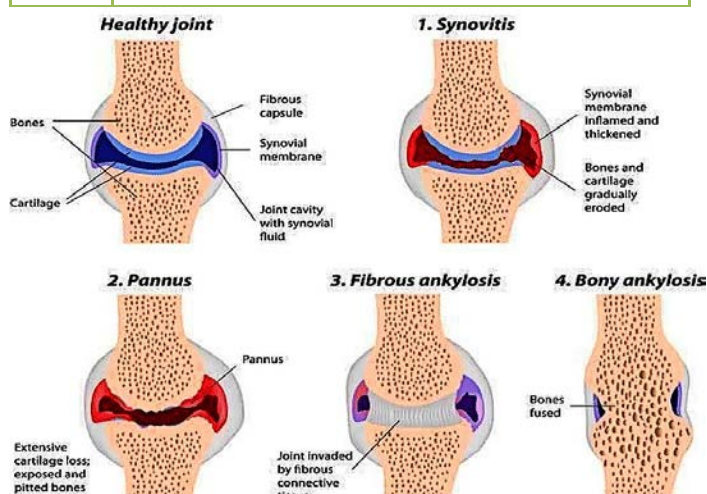


Figure 2: Stages of rheumatoid arthritis [19]

**Epidemiology:** These days rheumatoid arthritis is found in about 1% of the world's total population. Women are three times more tend to be afflicted by rheumatoid arthritis than men.

Arthritis represents one of the most prevalent chronic health problems and is a leading cause of disability. In USA 43 millions of adults were affected by rheumatoid arthritis in the year 2002. The numbers of affected people have reached 60 million by the year 2020. Rheumatoid arthritis is three times more common in smokers than non-smokers, particularly in men, those who have rheumatoid factor positive. A study in 2010 found that those who drank modest amounts of alcohol regularly were four times less likely to get rheumatoid arthritis than those who never drank [5].

**Symptoms:** The prevalent nature of arthritis symptoms have a discouraging impact on physical, social and occupational activities, which may result into psychological sequel such as anxiety, depression and helplessness [6]. The other signs and symptoms of rheumatoid arthritis includes, joint pain and swelling, reduced ability to move the joint, redness of skin around the joint, warmth around the joint, loss of energy and appetite, low fever dry eyes and mouth, Jorgen's syndrome, firm lumps called rheumatoid nodules (grows under the skin in places like elbow, hands)

**Diagnosis:** Diagnosis of RA can be a bit difficult as it begins with very mild symptoms like achy joints and little stiffness. The stiffness is mostly experienced by the patients during the first few hours of the morning. In some cases, it may even last for the whole day. Methods through which RA can be detected include clinical assessment, imaging and laboratory tests. In early arthritis the diagnosis tests may not show anything abnormal. Diagnosis of RA depends on the symptoms and X-rays can help in detecting RA. Even if it goes undetectable in the early stage X-ray reports, the report may help letter to examine if the disease is progressing or not. To judge the severity of the disease is often judged by the MRI and ultrasound scanning [7]. Also there are some specific blood tests that help rheumatologist determine the presence of RA. These tests are explained in table 2.

**Classification:** The American Rheumatism Association (ARA) first proposed the Rheumatoid Arthritis classification criteria in 1958. The 1958 ARA were revised in 1987 by the American College of Rheumatology (ACR).

**Medication:** Along with lifestyle changes, medications are also provides during the treatment of rheumatoid arthritis [8]. There is an abundance of plants and herbs having anti-arthritis property in our surroundings. These plants are rich in bioactive elements

and possess several medicinal properties. From an ancient time these herbs and plants are being used in the practice of traditional medicines. Some herbs having anti-arthritis property are discussed in following section

**Table 2: List of tests to diagnose RA**

Name of test	Explanation
<b>Rheumatoid factor test</b>	The RF blood test looks for rheumatoid factor, which is a protein. High levels of rheumatoid factor have been linked to autoimmune diseases, particularly RA.
<b>Anti-citrullinated protein antibody test (anti-CCP)</b>	This test is to examine an antibody that is associated with RA. A person having this antibody is considered to be affected by the disease. However, not everyone with RA tests positive for this antibody. The anti-CCP Ab is more specific for RA than the RF test.
<b>Antinuclear antibody test</b>	The antinuclear antibody panel determines whether the immune system is producing antibodies or not. The body may produce antibodies in response to several of conditions, which may include RA too.
<b>Erythrocyte sedimentation rate</b>	The ESR test assists in determining the level of inflammation in the body. The outcome indicates whether inflammation is present or not. However, it does not clarifies the cause of the inflammation.
<b>C-reactive protein test</b>	The liver can produce C-reactive protein in response to a severe infection or significant inflammation anywhere in the body. A high level of this inflammatory marker is associated to RA.

**Ginger-** Ginger is obtained from the plant *Zingiber officinale*. It belongs to the family Zingiberaceae. For the management of rheumatoid arthritis mainly the root part (rhizome) is used. The Rhizome is rich in bioactive substances. Apart from the anti-arthritis property, ginger root possesses so many other medicinal properties also. Ginger extract acts as a remedy for inflammation. Main constituents present in ginger are sesquiterpenoids with zingiberene. Sesquiterpene Lactones (SLs) are natural products responsible for its anti-inflammatory activity [9].

**Table 3: Classifications of RA**

Condition	Definition
<b>Morning sickness</b>	Morning sickness in and around the joints, lasting at least 1 hour before maximal improvement.
<b>Arthritis of 3 or more joint areas</b>	Areas simultaneously have had soft tissue swelling or fluid. The possible areas are right or left PIP, MCP, wrist, elbow, knee ankle and MTP joints.
<b>Arthritis of hand joints</b>	At least 1 area swollen: wrist, MCP or PIP joint.
<b>Symmetric Arthritis</b>	Simultaneous involvement of the same joint areas on both sides on both sides of the body (bilateral involvement of PIPs, MCPs, MTPs).
<b>Rheumatoid nodule</b>	Subcutaneous nodule, over body prominences or extensor in juxta articular regions, observed by a physician.
<b>Serum rheumatoid factor</b>	Demonstration of abnormal amounts of rheumatoid factor or any method for which the result has been positive in <5% of normal control subjects.
<b>Radiographic changes</b>	Radiographic changes typical of rheumatoid arthritis on postero-antero hand and wrist radiographs, which must include erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joint (osteoarthritis changes alone do not qualify)

**Turmeric-** The root part of *Curcuma longa* plant is used in the management of rheumatoid arthritis. It belongs to the family Zingiberaceae. A yellow colour substance present in the curcuma longa rhizome shows anti-inflammatory property. Daily administration of the low dose of purified curcuminoids (4 mg total curcuminoids/kg/d) inhibited joint inflammation in both the acute and chronic phases of arthritis [8].

**Aloe Vera-** *Aloe barbedensis* is the botanical name for aloe vera. Aloe vera has been a very important and most widely used medicinal plant in the practice of folk medicines. Anthraquinone, anthracene, cinnamic acid and anthranilic acid are found in the aloe Vera plants that are responsible for its activity. The anti-arthritis property of aloe vera is due to the

Anthraquinone compound. Aloe Vera stimulates the immune system and it is a powerful anti-inflammatory agent. Topical application of aloe vera extract result in the reduction of inflammation and arthritis in adjuvant induced arthritis in Sprague Dawley rats [3].

**Table 4: Medications for RA**

Treatment	Drugs
<b>Over-the-counter (OTC)</b>	Acetaminophen (Tylenol), Aspirin, Ibuprofen or naproxen.
<b>Disease-modifying-anti-rheumatic drugs (DMARDs)</b>	Methotrexate, gold salt, penicillamine, sulfasalazine, hydroxy-chloroquine. Common combination of DMARDs includes: Methotrexate-hydrochloroquine, Methotrexate- sulfasalazine, sulfasalazine-hydroxychloroquine and Methotrexate-hydroxychloroquine-sulfasalazine.
<b>Non-steroidal anti-inflammatory drugs (NSAIDs)</b>	Paracetamol, ibuprofen, naproxen, meloxicam, etodolac, nabumetone, sulindac, toleminin, choline magnesium, salicylate, diclofenac, indomethicin, ketoprofen, oxaprozin and Piroxicam.
<b>Biological agents</b>	Tumor necrosis factor alpha (TNF- $\alpha$ ) blocker, infliximab (Remicade), adalimumab.

**Ashwagandha-** Ashwagandha, also known as Indian ginseng, is a very ancient plant. It belongs to the family Solanaceae. The roots of Ashwagandha have been used in Indian traditional systems of medicine. The alkaloids and steroidal lactones in the root are responsible for its pharmacological activity. Withanine, pseudo-Withanine, tropine, pseudo-tropine, somniferine, and somnine are the most abundant alkaloids. Roots have yielded two acyl glucosides, sitoindoside-7 and sitoindoside-8. Oral administration of *Withania somnifera* L, root powder showed the anti-arthritis effect in adjuvant induced arthritic rats [3] [8].

**Black Pepper-** *Piper nigrum* L is an indigenous plant cultivated in south India, which belongs to the family Piperaceae. A bioactive substance namely piperine, isolated from black pepper is basically responsible for its anti-arthritis property. Piperine administered orally at a dose of 20 and 100 mg/kg/day for eight days cause decrease in the arthritic symptoms in carrageenan-induced acute paw arthritis [8].

**Night Jasmine-** *Nyctanthes arbortristis* L is a shrub and belongs to the family Oleaceae. The leaves of *Nyctanthes arbortristis* Linn have anti-inflammatory property. It contains mannitol, b-amyrin, b-sitosterol, benzoic acid and benzoic ester of nycthanic acid. Acute inflammatory edema produced by different phlogistic agents such as, carrageenin, formalin, histamine, 5-hydroxytryptamine and hyaluronidase in the hind paw of rats was inhibited after the application of night jasmine leaves. *Nyctanthes arbortristis* Linn, also found to inhibit the inflammation produced by immunological methods such as, Freund's adjuvant arthritis [10].

**Indian sarsaparilla-** *Hemidesmus indicus*, commonly known as Indian sarsaparilla or Anantamul, is a species of plant that is found in south Asia. It belongs to the family Apocynaceae. Roots of Indian sarsaparilla are used in medicinal purpose. It contains coumarin, essential oil, starch, tannic acid, triterpenoid saponin. It is used in the treatment of rheumatoid arthritis, nephritic complaints, chronic skin disease [11] [12].

**Cat's claw-** *Uncaria tomentosa*, commonly known as Cat's claw is another anti-inflammatory herb that may reduce swelling in arthritis. It belongs to the family Rubiaceae. Stem and roots collected from the vines are used in the medicinal practice. It contains tannins and sterols which are responsible for its anti-inflammatory property. According to the Arthritis Foundation, a study showed cat's claw can help with RA swelling. But, it is not proved whether this herb can prevent further joint damage [13] [14].

**Eucalyptus-** *Eucalyptus oblique* is used in oral medications and topical oil extracts. Topical forms of eucalyptus leaves are used to treat arthritis pain. The plant leaves contain tannins, which may help reduce swelling and the pain arthritis causes [15].

**Green Tea-** *Camellia sinensis* has been used medicinally for centuries. It belongs to the family Theaceae. Made from unfermented tea leaves, it is a rich source of polyphenols. These plant compounds are powerful antioxidants. They fight free radicals which are compounds that can damage the cells. According to Arthritis Foundation, polyphenols have strong anti-inflammatory properties [15].

**Thunder god vine-** *Tripterygium wilfordii* is the scientific name for thunder god vine. It belongs to the family Celastraceae. It has

been used for hundreds of years in traditional Chinese medicine to treat swelling caused by inflammation. Extracts are prepared from the roots of thunder god vine. It is used in traditional Chinese medicine to treat swelling caused by inflammation. Thunder god vine is used orally as a dietary supplement for autoimmune diseases, such as rheumatoid arthritis. It is also used topically for rheumatoid arthritis [3].

**Willow bark-** Scientific name for willow bark is *Salix Alba* and it belongs to the family Salicaceae. Using willow bark is one of the oldest treatments for inflammation [8]. Willow bark acts a lot like aspirin, so it is used for pain, including muscle pain, rheumatoid arthritis (RA) and osteoarthritis. Salicin is the active ingredient in willow bark.

**Thyme-** Botanical name for thyme is *Thymus vulgaris* L. It belongs to the family Lamiaceae. The plant has an aroma and a warm pungent flavour. This plant's fragrance is due to essential oil, which provides flavouring value for culinary purposes as well as medicinal properties [16]. The studies showed that *T. vulgaris* has carminative, antimicrobial, muscle relaxant [16] and antioxidant properties [17].

### CONCLUSION

Though current medications are effective at managing rheumatoid arthritis, prolonged uses of these medicines are associated with various adverse effects. Natural products are claimed to have therapeutic properties against rheumatoid arthritis. In this review article 13 such herbs and plants are included, explaining their bioactive components and their therapeutic effects. Apart from these there are numerous such herbs and plants in the nature that shows anti-arthritic and anti-inflammatory property. Various phytochemical constituents of ginger have potential therapeutic roles in amelioration of RA symptoms and even possibly RA itself. The other herbs and plants that are included in this review contain certain phytochemicals which show anti-arthritic, anti-inflammatory and antimicrobial properties. Some of these phytoconstituents work as muscle reluctant and pain reliever also. It is expected that further elucidation of the molecular mechanisms behind the action of these phytochemical not only can lead to discovery of new drugs for symptomatic relief of RA conditions like inflammation and pain, but also may make it possible to stop further progress or even reverse the damage caused by RA. Based on reviewed cellular and animal studies, various active

phytochemical agents derived from mentioned medicinal plants are potentially efficacious on RA. Further research is mandatory to focus on bio-efficacy and safety aspects of these phytochemical agents for finding novel natural drugs.

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Nil

#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

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