

Herbal Treatment for Rheumatoid Arthritis

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ABSTRACT

Rheumatoid arthritis is basically an autoimmune disease that causes chronic inflammation of joints and other areas of the body. It is known to affect people of all ages but the main cause of rheumatoid arthritis is still not known precisely among individuals. In RA the joints are damaged to a huge extent that ultimately leads to its destruction and deformity. Although RA has no proper cure it can be treated well under good medications with sufficient rest and regular exercises and occasionally surgery.

Arthritis is still a challenge for medical research. Pharmaceutical research has resulted in several new approaches for treatment/management of arthritis including drugs like the biologic disease modifying anti-rheumatic drugs (DMARDs). Several disadvantages like serious side effects, high costs and requirement of parenteral administration still invite more research in this area to provide a convenient, affordable therapy with lesser or no side effects. Traditionally used herbal medicines, due to their anti-inflammatory and immune modulatory properties, have potential to be a therapy of choice for arthritis patients and are now extensively being studied. Although a number of these medicines are being used traditionally for their therapeutic activity, development of their novel drug delivery systems was not attractive to the scientists due to insufficient knowledge about their exact mechanism of action and difficulties in processing, standardising, extracting and identification of active constituents. The present manuscript focuses on herbal medicines for arthritis along with various strategies adopted by scientists so as to improve the bioavailability, stability and to reduce the side effects of these medicines so as to provide consistently effective alternative medication for arthritis. A possible way to achieve this is designing novel drug delivery systems for herbal constituents. Novel drug delivery systems help to reduce toxicity and increase the bioavailability thereby improving the therapeutic value of the active constituent.

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Introduction

'Rheumatism' means Musculo Skeletal illness, 'Arth' means joint and 'itis' means inflammation.

Rheumatoid arthritis is the most common inflammatory arthritis and is a major cause of disability. It was known to exist in early Native American populations about several hundred years ago but might not have appeared in Europe until the seventeenth century. Early theories on the pathogenesis of Rheumatoid arthritis focused on autoantibodies and immune complexes and the contribution of autoantibodies has returned to the forefront more recently. Based on the pathogenic mechanisms specific therapeutic interventions can be designed to suppress synovial inflammation and joint destruction in rheumatoid arthritis. There are so many medicinal plants that have shown anti-rheumatoid arthritis properties. So the plants and plant products with significant advantages are used for the treatment of Rheumatoid arthritis (1).

Pathophysiology

The pathophysiology of OA and RA is distinct although the primary manifestations of both involve the joints. OA is characterized by progressive cartilage loss. Increased thickness of the subchondral plate, osteophytes and subchondral bone cysts are the characteristic features. Vascular invasion and further calcification of nearby

articular cartilage may occur as the disease progresses, leading to decreased thickness of articular cartilage. Bone remodeling and enhanced cartilage deterioration takes place over time. The inflammation is generally milder in severity than that observed in rheumatoid arthritis and typically involves the periarticular tissues.

Rheumatoid arthritis is a chronic, autoimmune syndrome. Autoimmune inflammation is a result of a response to self-antigens. Thus, a dysregulated immune system results in autoimmune diseases. Synovial inflammation leading to cartilage and bone damage is characteristic of the disease. Persistent inflammation leads to progressive destruction of articular and periarticular structures which in turn, lead to deformity. Morning stiffness is a common problem for patients with rheumatoid arthritis. Characteristic features of RA pathophysiology are increased angiogenesis, cellular hyperplasia, influx of inflammatory cells, changes in the expression of cell surface adhesion molecules and presence of many cytokines. Tumour necrosis factor (TNF) and interleukin-1 are in abundance in the joints. They are the stimulators of proliferation, metalloproteinase expression, adhesion molecule expression, and further secretion of other cytokines. CD4 T cells, mononuclear phagocytes, fibroblasts, osteoclasts, and neutrophils play major role in pathophysiology of rheumatoid arthritis. Presence of anti-cyclic citrullinated protein antibody (ACPA) and rheumatoid factor (RF) is highly specific for RA (2).

Features of Rheumatoid Arthritis

- Warm, swollen joints
- Symmetrical pattern of affected joints
- Fatigue, occasional fevers, loss of energy.
- Joint inflammation often affecting the wrist and finger joints
- Joint inflammation sometimes affecting the joints in the neck, shoulders, elbows,
- hips, knees, ankles and feet (3).

Epidemiology

- Affects 1-3% of the population world wide
- With the peak prevalence between the ages of 30 to 50 years
- Women's are affected 3 or 4 times more commonly than men.
- Arthritis represents one of the most prevalent chronic health problems and is a leading cause of disability.
- Arthritis affected 43 million U.S. adults in 2002 and by the year 2020, this number is expected to reach 60 million. It is up to three times more common in smokers than non smokers, particularly in men, heavy smokers, and those who are 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 (4).

Causes

There is no definite cause of arthritis. Causes of arthritis depend upon the particular form of arthritis. Probable of arthritis cause are:

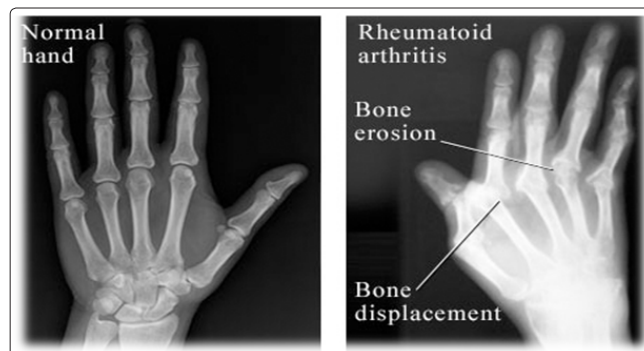
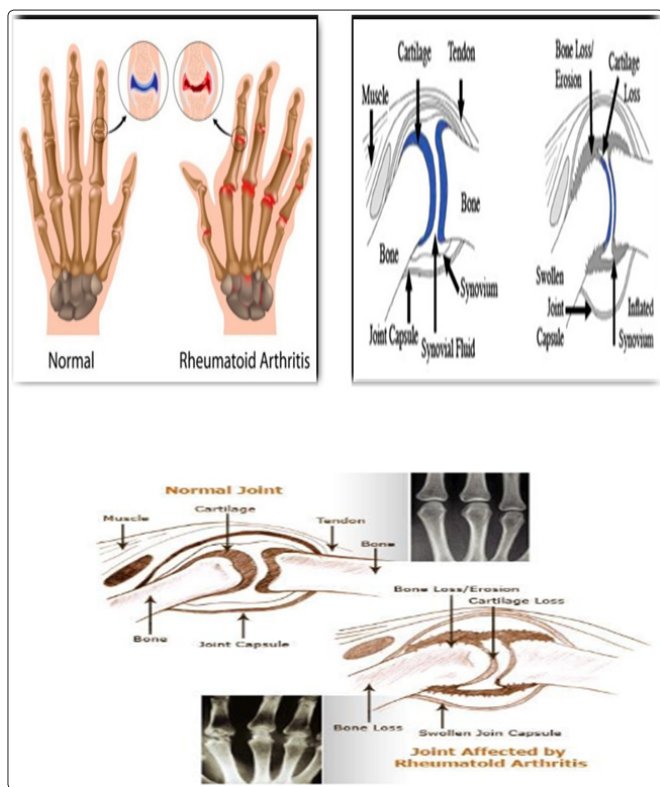
- Genetic susceptibility
- An immunological reaction: possible involving a foreign antigen, preferentially focused on synovial tissue
- An inflammatory reaction in joints and tendons sheaths
- The appearance of rheumatoid factor in the blood and synovium
- Articular cartilage destruction

Symptoms

- Swelling: Arthritis causes an abnormal enlargement of a part of the body. This is due to the accumulation of fluid.
- Pain: The feeling of constant pain in the many parts of the body.
- Stiffness: Stiffness in the muscle upon waking up, or sitting at one place for long or after sitting at a desk. One may feel stiffness in the fingers, wrist, elbow, knees, ankles, shoulders or in any other joints.
- Fever, chills, fatigues, loss of appetite and headache are some other common symptoms of arthritis (5).

Diagnosis

- Blood culture: Diagnosis of RA depends on the symptoms and some blood tests can also help to confirm RA. Telltale signs include: Anemia (a low red blood cell count); rheumatoid factor (an antibody, or blood protein, found in about 80% of patients with RA in time, but in as few as 30% at the start of arthritis); antibodies to cyclic citrullinated peptides (pieces of proteins), or anti-CCP for short (found in 60-70% of patients with RA); Elevated erythrocyte sedimentation rate (a blood test that, in most patients with RA, confirms the amount of inflammation in the joints).
- X-Ray: X-rays can help in detecting RA, but may not show anything abnormal in early arthritis. Even so, these first X-rays may be useful later to show if the disease is progressing.
- Often, MRI and ultrasound scanning are done to help judge the severity of RA.
- There is no single test that confirms an RA diagnosis for most patients with this disease



Generally, over-the-counter medications are recommended first:

- Acetaminophen (Tylenol) is usually tried first. It is advisable not to take more than the recommended dose or do not take the drug along with a lot of alcohol. Doing so may damage liver.
- Aspirin, ibuprofen, or naproxen are nonsteroidal anti-inflammatory drugs (NSAIDs) that can relieve arthritis pain. However, they have many potential risks, especially if used for a long time. Potential side effects include heart attack, stroke, stomach ulcers, bleeding from the digestive tract, and kidney damage.

Figures: show comparison of normal joint and joint affected by rheumatoid arthritis.

Treatment	Drugs
Over The Counter	Acetaminophen (Tylenol), Aspirin, ibuprofen, or naproxen
Disease-modifying anti-rheumatic drugs (DMARDs)	Methotrexate, gold salts, penicillamine, sulfasalazine, and hydroxychloroquine. Common combinations of DMARDs include methotrexate –hydroxychloroquine, methotrexate –sulfasalazine, sulfasalazine –hydroxychloroquine, and methotrexate –hydroxychloroquine –sulfasalazine.
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Paracetamol, ibuprofen, naproxen, meloxicam, etodolac, nabumetone, sulindac, toleminin, choline magnesium salicylate, diclofenac, diflusal, indomethacin, ketoprofen, oxaprozin, and piroxicam.
Biological agents	Tumor necrosis factor alpha (TNF α) blockers-etanercept (Enbrel), infliximab (Remicade), adalimumab (Humira), certolizumab pegol (Cimzia), golimumab (Simponi) Monoclonal antibodies against B cells – rituximab (Rituxan)

Home Remedies for Arthritis

Exercise Regularly: Gentle exercise can help to strengthen muscles around joints and also helps to fight fatigue.

Relax: Techniques such as hypnosis, guided imagery, deep breathing and muscle relaxation can be done to control.

Yoga: Yoga can help to improve strength and flexibility. The exercises should be performed with caution by people with rheumatoid arthritis who have spinal problems (6).

Surgery and other Treatments

In some cases, surgery may be done if other treatments have not worked. This may include:

- Arthroplasty to rebuild the joint
- Joint replacement, such as a total knee joint replacement

Need for Herbal Drugs for the Management of RA:

Conventional treatments for rheumatoid arthritis (RA) present a number of problems, in terms of both safety and efficacy. Owing to side effects of synthetic drugs as shown in table many patients look for complementary and alternative medicine (CAM) options in coping with this debilitating disease.

Sr no:	Drug	Toxicities
1.	Methotrexate (DMARD's)	Stomatitis, rash, alopecia, infrequent myelosuppression, hepatotoxicity, rare but potentially life-threatening pulmonary toxicity
2.	Oral Gold Salts	Diarrhoea
3.	Injectable Gold Salts	Stomatitis, myelosuppression, rash, thrombocytopenia
4.	Cyclosporine	Renal impairment, hypertension, gingival overgrowth
5.	D-penicillamine	Rash, stomatitis, dysgeusia, proteinuria, myelosuppression
6.	Nonsteroidal Anti-inflammatory Drugs	Gastrointestinal symptoms (indigestion, ulceration, hemorrhage, stomatitis); renal abnormalities; pulmonary neurological abnormalities; abnormalities; dermatologic abnormalities; hematologic abnormalities; hepatic abnormalities; displacement of protein-bound drugs; possible systemic complication

Research has indicated that people suffering from chronic pain, as in RA, and those dissatisfied with current treatment are very likely to seek alternative treatments, and an estimated 60–90% of persons with arthritis use CAM. With the growing interest in herbal therapies among persons with rheumatoid arthritis, there exists a need for investigation into their safety and efficacy. The management of rheumatoid arthritis is a multidisciplinary approach in order to lessen the pain, reduction of inflammation and restoration of joints function. In practical terms suppression of inflammation is the target intensive therapy. Herbal medicines have become popular for the treatment of rheumatoid arthritis worldwide recently (7).

Herbal Treatment

- Conventional treatments for rheumatoid arthritis (RA) present a number of problems, in terms of both safety and efficacy. Owing to side effects of synthetic drugs many patients look for complementary and alternative medicine (CAM) options.
- Herbal medicinal drugs that interact with the mediators of inflammation are used in the treatment of rheumatoid arthritis (RA).

Biological	Part used	Active ingredients	Therapeutic uses	Extract
Annona montana. (Annonaceae)	Leaves, fruit, seeds, bark, roots	Cyclomontanins A-D (1-4), annomuricin C (5), and (+)-corytuberine	Anti-rheumatic, anthelmintic, anticonvulsant, antidepressant, antimicrobial, antineoplastic, antiparasitic, antispasmodic, antiviral, astringent	methanol
Asparagus racemosus (Liliaceae)	Roots, Leaves, flowers and fruits	Steroidal glycosides including shatavarins I-IV, diosgenin and various sterols, alkaloid asparagine A, flavonoids: quercetin, rutin and hyperoside, an isoflavone, and a mucilage	Ulcerogenesis, antioxidant, treatment of thirst, fainting, dyspnoea, and gout	methanol
Boswellia serrata Roxb. (Burseraceae)	Oleogum resin	Resin which is pentacyclic triterpenoid in nature in which boswellic acids (β -boswellic acid, acetyl- β -boswellic acid, keto- β -boswellic acid and acetyl-11- keto- β -boswellic acid)	Cancer, inflammation, arthritis, asthma, psoriasis, colitis and hyperlipidemia	Petroleum ethre

Certain herbs may have anti-inflammatory properties that can help with rheumatoid arthritis [RA]

1. Aloe vera is one of the most commonly used herbs in alternative medicine. It's available in many forms, such as pills, powder, gels and as a leaf. Known for its healing properties, its popular for treating small skin abrasions, such sunburns, but it may also help with joint pain. Benefits: It has anti-inflammatory properties. It doesn't have the negative gastrointestinal effects of NSAIDs commonly used for arthritis pain.
2. Boswellia Serrata also called frankincense used for its anti inflammatory properties. Its derived from the gum of Boswellia trees, which are indigenous to India
 - Boswellic acid appears to have anti inflammatory effect that could help people with RA, OA and gout.
 - Results from human trials have suggested that frankincense capsule may help improve pain, function and stiffness due to OA
 - Its available in tablet form and topical cream



- Boswellia that is derived from a resin called salai guggal has been used for nearly thousand years in ayurvedic medicine and have been used historically for arthritis.
3. Ginger: many people use ginger in cooking, but it may also have medicinal benefits. The same compounds that give ginger its strong

flavor also have anti-inflammatory properties, studies have found.

- Ginger could be an alternative to NSAIDs
 - People have long used ginger in traditional medicine to treat nausea, but you can also use it for rheumatoid arthritis, osteoarthritis and pain in the joints and muscles.
 - Here are some ways to consuming ginger: make tea of fresh ginger in boiling water for 5mins or add powdered ginger to savory dishes.
4. Turmeric: turmeric is a yellow powder made from a flowering plant. its main ingredient curcumin has anti-inflammatory properties.
 - It helps with RA, OA and other arthritis conditions
 5. Willow bark: it is an ancient treatment for pain and inflammatory. it is used as either tea or tablet form.
 - It may help in relieve joint pain related to RA and OA. However results have been conflicting, it may not be safe for everyone
 - Common side effects include: stomach upset and high blood pressure
 6. Arnica: Chronic arthritis with a feeling of bruising and soreness may be helped by this remedy. The painful parts feel worse from being moved or touched. The gels and ointments of Arnica may help to soothe arthritic pain when applied externally to areas of inflammation and soreness (8).

List of Homeopathic Remedies

- Arnica
- Aurum metallicum
- Bryonia
- Causticum
- Calcarea fluorium
- Kalmia latiflora
- Ledum palustre
- Rhododendron

Arnica

Chronic arthritis with a feeling of bruising and soreness may be helped by this remedy. The painful parts feel worse from being moved or touched. The gels and ointments of Arnica may help to soothe arthritic pain when applied externally to areas of inflammation and soreness.



Aurum Metallicum

This remedy is prescribed for wandering pains in the muscles and joints that are better from motion and warmth and worse at night. The person may experience deep pain in the limbs when trying to sleep. Therefore people who need this remedy are often serious and focused on work or career with a tendency to feel depressed.

Bryonia

Bryonia is an excellent remedy in cases of acute pains of rheumatoid arthritis. It helps in relieving the chest pains that gets worse while coughing. It may be given when the pains are worse by slightest touch and also when the pains are associated with swelling of the joints.

Causticum

Causticum that is used in homeopathic treatment of individuals suffering from rheumatoid arthritis has symptoms that include the development of deformities in the joints, contractures and weakness in the muscles of the body in general. These symptoms can be relieved through the use of warm applications and during conditions of cold weather it can lead to the worsening of the pain and the stiffness.

Calcarea Fluoricum

This medicine works for these patients of arthritis who tend to have large or medium joint infections such as knee joint, spine or shoulders. The patients will have pain in waking up in the mornings or while getting up from a sitting position. The joint pains are better by hot applications.

Kalmia Latiflora

Kalmia is extremely useful in rheumatism that effect the chest. Even inflammatory rheumatism shifting from joint to joint, which tends to attack the heart and also cause high fever and excruciating pain, will be benefitted by kalmia.

Ledum Palustre

The ledum rheumatism begins in the feet and travels upward. The pains of ledum and the purple mottling of the skin, which is a concomitant are almost entirely abated by putting the affected limb in cold water. Ledum maybe indicated in both acute and chronic form of this complaint.

Rhododendron

The patients experience rheumatism in hot season where their joints become swollen and there is rheumatic tearing in all

limbs. Rhododendron basically helps with rheumatic and gouty symptoms. It prevents stiffness of neck, pain in shoulders, arms, wrists. It also provides relief of swollen joints and gouty inflammation of the great-toe joint.



Herbal Drug Delivery for Arthritis

Plant preparations or their parts have been widely used in medicine since ancient times and till today use of phytomedicines is wide spread. Most of the biologically active constituents of plants are polar or water-soluble. However, water-soluble phytoconstituents are poorly absorbed due to macromolecular size, which cannot be absorbed by passive diffusion or due to their poor lipid solubility, thus severely limiting their ability to transport across lipid-rich biological membranes, resulting in their poor bioavailability.

Phytosomes are defined “Phyto” means plants and some means cell-like, which is a novel drug delivery system, Phytosome is a newly introduced patented technology developed to incorporate the water-soluble phytoconstituents into phospholipids to produce lipid compatible molecular complexes called phytosomes. provide better absorption and bioavailability than the conventional herbal drugs. When a stoichiometric amount of the phospholipid was made to react with purified herbal drug in an aprotic solvent, phytosomes were formed (9).

- Boswellic acid with lecithin delivery form (phytosome) significantly improved the absorption of BAs and promotes their tissue penetration, demonstrating for the first time the achievement of tissue concentrations of these compounds in the range of their anti-inflammatory activity (10).
- The Curcumin phytosomes were found to show better solubility and compatibility with the excipients, it is concluded that Curcumin phytosomes has better physical characteristics and improved permeability, solubility than that of curcumin drug to overcome ability to cross lipid-rich biological membranes and which results in increase oral bioavailability (11,12).

Marketed Phytosomal Preparations

1. Casperme™ Boswellia phytosome
2. Meriva™ Turmeric phytosome





List of Marketed Herbal Products

1. Cureveda joyful joints: it contains Boswellia, rose hip, turmeric
2. Health X Boswellia extract 600mg:contains 65% Boswellic acid
3. Arnica oil by herbs pharma:contains arnica oil and olive oil



Conclusion

These herbal treatments are therefore entirely natural and will definitely reduce the pain and inflammation in the joints. So taking good care of the joints and exercising regularly will help reduce the risk of rheumatoid arthritis. A large number of number of plants described in this , clearly demonstrated the importance of herbal plants in treatment of rheumatoid arthritis and also to consider one of good source for a new drug or a lead to make a new drug.

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