Therapeutic potential of Indian plants for the treatment of rheumatoid arthritis

Priyanka Pandey and Sugandha Tiwari

Abstract
Immune system of the body is very important. It protects our body from many diseases but hypersensitivity of the immune system causes many diseases like allergies and several autoimmune diseases. Rheumatoid arthritis is an autoimmune disease. It causes inflammation, swelling and redness of the affected joints. It also affects blood vessels and lymphatic tissues. The main aim of the treatment of RA is to eliminate the symptoms of the disease or to slow down the development of the disease. Presently many types of drugs are used for the treatment of this disease like disease modifying antirheumatic drugs (DMARDs), glucocorticoids and non-steroidal anti-inflammatory drugs (NSAIDs). Long term usage of these drugs causes many adverse effects. Use of plants for the treatment of the disease causes no side-effects. India has blessed with enormous wealth of medicinal plants. Since ancient time, herbal drugs are used for the treatment of various disorders in India. In the present review many plants having antirheumatic property are mentioned.

Keywords: Autoimmune disease, inflammation, rheumatoid arthritis, hypersensitivity, herbal treatment

Introduction
The word rheumatism is derived from the Greek word ‘rheuma’, which means swelling. Rheumatism or rheumatic disorder is a nonspecific term for medical problems affecting the joints and connective tissue. Rheumatoid arthritis is a type of inflammatory arthritis. Rheumatism is characterized by redness, heat, swelling and pain, fever, intense soreness, swelling, stiffness of the affected muscles, pain in eyes, loss of sleep and improper urination. About 1% of the world’s population is afflicted by rheumatoid arthritis. Rheumatic disorder is commonly found in middle aged and elderly people, it also involves problems in the internal organs, such as heart, skin, kidneys and lungs. The disease can affect the person at any age but chances of the occurrence of the disease increases with the age. It is a very painful disease. The disease badly affects the life of a person.

Causes
It is an autoimmune disorder. The real cause of the disease is yet not known. The possibility of occurrence of disease is three times more in females than males. More than 20% of total population of India is suffering from arthritis. Arthritis involves the breakdown of cartilage. Cartilage normally protects a joint, allowing it to move smoothly. The process produces an inflammatory response of the synovial (sinusitis) secondary to hyperplasia of synovial cells, excess synovial fluid, and the development of panes in the synovial. The pathology of the disease process often leads to the destruction of articular cartilage and alkalosis of the joints. Rheumatoid arthritis can also produce diffuse inflammation in the lungs, pericardium, pleura, and sclera, and also nodular lesions, most common in subcutaneous tissue. Although the cause of rheumatoid arthritis is unknown, autoimmunity plays a pivotal role in both its chronicity and progression, and RA is considered a systemic autoimmune disease. Many immune-mediated compounds are the main cause of inflammation in synovial joints.

Symptoms
Symptoms include joint swelling, pain, morning joint stiffness, and poor sleep, and fatigue, loss of weight and feeling of having flu symptoms. Rheumatoid arthritis is diagnosed by rheumatoid factor, these are abnormal antibodies (IgG) which are present in blood. These are reacted with antigen and form antigen-antibody complex that leads to pain and inflammation of synovial membrane. The American College of Rheumatology requires at least four of the following seven criteria to confirm the diagnosis.
- Morning stiffness around the joint that lasts at least 1 hour
- Arthritis of three or more joints for at least 6 weeks
- Arthritis of hand joints for at least 6 weeks
- Rheumatoid nodules under the skin
- Rheumatoid factor present in blood testing
- Evidence of rheumatoid arthritis on X-rays

**Diagnosis**
RA can be hard to detect because it may begin with subtle symptoms, such as achy joints or a little stiffness. The stiffness seen in active RA is most often worst in the morning. Stiffness for a long time in the morning is a clue that one may have RA. Methods to detect RA include clinical assessment, imaging and laboratory tests. Clinical assessment and opinion is considered the ‘gold standard’ [29]. 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-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.

**Therapy**
For the treatment of the RA many synthetic drugs are prescribed by the physician (Table 1).

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Drug</th>
<th>Toxocities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Methotrexate(DMARDs)</td>
<td>Stomatitis, rash, hepatotoxicity, rare but potentially life-threatening pulmonary toxicity</td>
</tr>
<tr>
<td>2.</td>
<td>Oral gold salts</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>3.</td>
<td>Injectable gold salts</td>
<td>Stomatitis, myelosuppression, rash, thrombocytopenia</td>
</tr>
<tr>
<td>4.</td>
<td>Cyclosporine</td>
<td>Renal impairment, hypertension, gingival overgrowth</td>
</tr>
<tr>
<td>5.</td>
<td>D-penicillamine</td>
<td>Rash, Stomatitis, dysgeusia, proteinuria, myelosuppression</td>
</tr>
<tr>
<td>6.</td>
<td>Non-steroidal Anti-inflammatory Drugs(NSAIDs)</td>
<td>Gastro intestinal symptoms (indigestion, ulceration, hemorrhage, stomatitis); renal abnormalities, pulmonary neurological abnormalities, displacement of protein bound drugs, dermatologic abnormalities, hematologic abnormalities, possible systemic complications</td>
</tr>
</tbody>
</table>

India is a rich source of medicinal plants (Table 3). A large number of medicinal plants are found in India. More than 2000 plants are described in ancient Indian medicinal systems such as Ayurveda, Siddha, Unani, homeopathy and naturopathy [10].

**Table 1: Medications available for treatment of rheumatoid arthritis [24]**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease modifying anti rheumatic drugs(DMARDs)</td>
<td>Methotrexate, gold salt, penicillamine, and hydroxychloroquine, Common combinations of DMARDs include methotrexate-hydroxychloroquine, methotrexate-sulfasalazine, sulfasalazine-hydroxychloroquine, and methotrexate-hydroxychloroquine-sulfasalazine.</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs (NASIDs)</td>
<td>Paracetamol, ibuprofin, naproxen, meloxicam, etodolac, nabumeton, sulindac, tolemiten, choline magnesiunm-salicylate, diflunisal, diltisnual, ketoprofen, oxaprozin, and piroxicam.</td>
</tr>
<tr>
<td>Biological agents</td>
<td>Tumor necrosis factor alpha(TNF-α) blockers etanercept (Enbrel), infliximab (Remicade), adalimumab (Humira), certolizumab pegol (Cimzia), golimumab (Simponi). Monoclonal antibody against B cells-rituximab (Rituxan).</td>
</tr>
</tbody>
</table>

**Table 2: Toxicity of allopathic anti rheumatic drugs [7]**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Botanical name</th>
<th>Family</th>
<th>Plant part used</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Aloe vera(L),Burmk</td>
<td>Liliaceae</td>
<td>Leaves</td>
</tr>
<tr>
<td>2.</td>
<td>Asparagus racemosus wild.</td>
<td>Asparagaceae</td>
<td>Whole plant, root</td>
</tr>
<tr>
<td>3.</td>
<td>Achyranthes aspera L.</td>
<td>Amaryllidaceae</td>
<td>Root, stem and leaves</td>
</tr>
<tr>
<td>4.</td>
<td>Ajuga bracteosa Wallich ex Benth.</td>
<td>Lamaceae</td>
<td>Whole plant</td>
</tr>
<tr>
<td>5.</td>
<td>Argemone mexicana L.</td>
<td>Papaveraceae</td>
<td>Seed</td>
</tr>
<tr>
<td>6.</td>
<td>Boerhavia diffusa L.</td>
<td>Nyctaginaceae</td>
<td>Root</td>
</tr>
<tr>
<td>7.</td>
<td>Boswellia serrata Roxb.</td>
<td>Burseraceae</td>
<td>Olegum, resin</td>
</tr>
</tbody>
</table>
Many plants or plant extracts have been used as anti-rheumatic agents. Use of plants or plant extracts as antirheumatic agents/drugs is based on the presence of antirheumatic phytochemical compounds in them. Many active chemicals are found in antirheumatic plants. These phytochemicals include alkaloids, tannins, steroids etc. These chemicals play an important role in reducing the symptoms of the disease. Bromelain extracted from the pineapple stem has anti-inflammatory property. Many active compounds found in Bromelain (Sulphydryl proteolytic enzyme) are peroxidase, acid phosphates and several protease inhibitors. [12]

Vitex negundo originate in southern India and Burma, [147] this plant has its traditional use in rheumatism, headache, syphilis, diarreha and cholera. Leaves of this plant along with garlic, rice and gu is a remedy for rheumatism [146, 36]. In Ayurvedic, Chinese and Unani medicine system the leaves extract of this plant is used for the treatment of rheumatism [48, 35]. The chemical compounds present in the plant are, nishindine, flavones, luteolinβglucoside, casticin, iridoid glycosides, vitamin C, β-sitosterol, and phthalic acid [16, 28, 15]. Xanthium is commonly found in the tropical parts of India. In Chinese and Ayurvedic medicine system the plant infusion is used for the treatment of rheumatism p [49, 25]. The main chemical constituents present in the plant are alkaloids; sesquiterpenes, lactones such as xanthinin, xanthumin, xanthatin; sulphated glycoside such as xanthatin; sulphated glycoside such as xanthostrumarin, xanthomin, xanthan, xanthanolides, and deacetylxanthumin [44,18, 31]. 22 Trionella is commonly used as food and food additive Fenugreek seeds have high content of mucilage, choline and trigonelline. Extract of this plant possess anti-inflammatory and antirheumatic activity [44, 17, 51]

Sida rhombifolia is commonly found in India and Ceylon [21]. The major chemical compounds present in plant are β-phenethylamine, N-methylβ-phenethylamine, S (pN-β- methyltryptophan methyl ester, vasicinol, vasicinone, vasicine, choline, hypaphorine methyl ester, hypaphorine, and betaine. In Indonesia and Johore whole plant juice is used for the treatment of rheumatism [3, 40]

Piper longum is commonly used for the treatment of the cold, cough, asthma and snake bite since ancient times. In rheumatism, roasted aments are bitten up with honey and taken in a prescribed dose. [9, 27] In Java and Indonesia, the whole plant was applied topically, as it relieves muscular pains and inflammation. Major constituents are piperine,
piperlongumine, piperlonguminine, and methyl 3, 4, 5-trimethoxyacinnamate. Others include resin, volatile oil, starch, fatty oil, and inorganic matter [23].

**Panica granatum** is a native of India, California, Asia and Africa. In Iranian medicinal system the seeds and juice are considered as a tonic for the treatment of rheumatism [48]. Some of the major chemical constituents present in the **Panica granatum** are aragellic acid, anthocyanins, ellagitannins, flavonies, flavonoids, anticatoydinids, sterols, quercitin, rutin, and other fatty acids. **Lantana camara** is an Indian native plant. In Ghana the plant infusion is used for the treatment of artritis. The active constituents are flavones, isoflavones, anthocyanins, coumarins, lignins, alkaloids, tannins, saponins, triterpenoids, catechins, and iso catechins [5, 6].

**Curcuma longa** is commonly found in the tropical and subtropical regions of the world. The major chemical constituents are curcumin, methylecumin, demethoxy curcumin, naldum curcuminate, and Arturmerone [20]. The essential oils of rhizome possess the anti-arthritic activity. An active compound found in turmeric is curcumin. This active compound reduce turmeric found in turmeric is curcumin. This active compound reduce morning stiffness and swelling around the affected joints.13 Coriander is a herbaceous plant distributed all over the India. Oil of this plant is very effective for the treatment of rheumatism [17].

Gingerol found in ginger rhizome inhibit the production of nitric oxide.50 **Curcuma longa** is widely used in the treatment of RA. In Indian medicinal system decoction of Nyctanthes leaves has been used from a very ancient times for the treatment of RA.17 Main active compounds found in Nyctanthes are nycanthic acid, crocin and arborrtriosides. In a clinical trial it has been reported that water soluble ethanolic extract of Nyctanthes leaves reduce the level of inflammatory cytokines (IL-1, TNF-α) [33].

Crocin and carotinoids are found in saffron stigma. These compounds have anti-inflammatory action [19].

**Gentiana macrophylla** root has anti-inflammatory action due to the presence of chemical compound Gentia. The anti-inflammatory action of the compound is as effective as the conventional drug Prednisone, used in the treatment of rheumatoid arthritis [52]. Tetrandrin is found in the root of *Stephania tetrandra & Stephania moore*. This chemical reduces the level of inflammatory cytokines, histamine and tumor necrotic factor. Anti-arthritic activity of *Capparis spinosa* L. fruits are due to the presence of Stachydrine (alkaloids). Colchicine is an alkaloid, having anti-inflammatory action. This alkaloid is found in corms of crocus like plants. In *Tinospora cordifolia* many active chemical compounds are found which plays an important role in the management of RA such as tinosporin, tinosporidine and tinosporasides. These chemicals have anti-inflammatory and antispasmodic properties. These chemicals also improve the immune system. Anti-arthritic and anti-inflammatory activity of Aloe vera is due to the presence of anthraquinone compounds. Boswelic acid, isolated from *Boswellia serrata*, has anti arthritic and anti inflammatory action [8].

**Conclusion**

From the very ancient time, the plants had been used for the treatment of rheumatoid arthiris. Different plant extract and plant product are found very effective against different diseases. Now a days, humans are moving towards the herbal therapy. At present investigation of anti-arthritic activity of traditional medicine led to the development and studies of many herbal preparations used for the treatment of arthiris. This information is very helpful in preserving folk medicinal plants having anti-arthritic potential. Use of plants is safe. It produces no side effects like the allopathic drugs. Herbal therapy is also very cheap in comparison to different medications used for the treatment of the disease. Much of the current research is focused on the identification, isolation and characterization of anti arthritic(s) from crude extracts of medicinal plants or herbs, often overlooking the fact that strong synergism of several constituents in the crude drug may prove more potent and effective than any single purified compound and this may help to nullify the toxic effects of individual constituents. This review reveals the importance of different plants used for the treatment and management of rheumatoid disease.

The aim of this review is to revive and explore the traditional medicinal knowledge of plants. Awareness among the people for the conservation of anti-rheumatic plants is very important and it is a demand of time because many plant species are decreasing very rapidly.

**References**


