

COPING WITH ARTHRITIS USING SAFER HERBAL OPTIONS**SUNETRA K PATWARDHAN*, KAUMUDEE S BODAS, SAMEER S GUNDEWAR**

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ABSTRACT

Arthritis, generally inflammation of joints is a one of the oldest known diseases occurring almost in all age groups. In India, more than about 20% of total population is suffering from arthritis. Many arthritic patients may not have reported to be arthritic as they may not have detected their problem of arthritis due to illiteracy, poverty and unaffordability for medical check ups. Forty-six million Americans report that they have arthritis or other rheumatic conditions. One in 6 people in the US has arthritis. The use of alternative therapies, such as acupuncture and medicinal herbs, is on the rise because of many side effects and toxicities associated with the synthetic drugs. Despite considerable progress in the treatment of arthritis by NSAIDs and other drugs, search for newer drugs continues because the existing synthetic drugs have several limitations. According to reports approximately 60-90% of dissatisfied arthritis patients are likely to seek the option of complementary and alternative medicine (CAM).

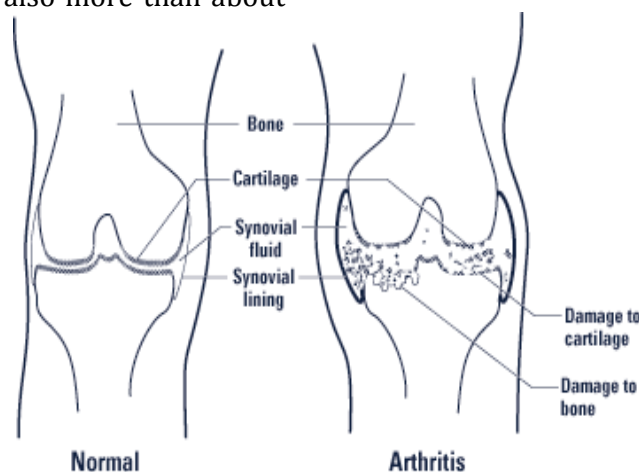
This paper reviews the efficacy of some of valuable herbs like guggul, bhallataka, ginger, ashwagandha etc. that have a history of human use and their anti-inflammatory or anti-arthritic properties have been evaluated preclinically and clinically. Basic scientific research has uncovered the mechanisms by which some plants afford their therapeutic effects. The present literature emphasizes on causes for arthritis, its signs, symptoms, preventive measures as well as its safer options of treatments. Available data suggests that the extracts of most of these herbs or compounds derived from them may provide a safe and effective adjunctive therapeutic approach for the treatment of arthritis.

INTRODUCTION

Arthritis is a chronic, inflammatory, multisystem autoimmune disease. The individuals of any age can be affected with Arthritis; the usual age of onset is between 25 and 50 with a peak in the 40s and 50s. At any given time approximately two million individuals in the US are affected by Rheumatoid Arthritis. In India also more than about

20% of total population is suffering from arthritis.

Arthritis is due to the wearing down of cartilage, which cushions the ends of the bones which is depicted in figure no. 1. The joints most commonly affected by arthritis are weight-bearing joints, such as feet, knees, hips, spine and other joints, such as finger and thumb joints^{1,2}.

**Fig. 1: Arthritic changes as compared to normal pattern**

Warning Symptoms

The warning symptoms include pain is a result of inflammation of the joint lining. It is the body's natural response to injury. The other signs that inflammation presents are redness, swelling, heat and pain. When a joint becomes inflamed, it may get any or all of these symptoms. This prevents the normal use of the joint due to stiffness and therefore it can cause the loss of function of that joint^{3, 4}.

Risk factors of Arthritis

The key risk factors includes age, gender, excess weight, injury and complications from other conditions, dietary pattern, consumption of excess alcohol, life style, heredity, hormonal factors, environmental factors and lack of physical activity⁴.

Types

There are about 100 types of arthritis; but most common are described below:

1. Osteoarthritis⁵⁻⁸

It is called degenerative joint disease affecting bone cartilage. In osteoarthritis, the surface layer of cartilage breaks down and wears away. This allows bones under the cartilage to rub together, causing pain, swelling, and loss of motion of the joint. Over time, the joint may lose its normal shape. Also, small deposits of bone called osteophytes or bone spurs may grow on the edges of the joint. Bits of bone or cartilage can break off and float inside the joint space. This causes more pain and damage. It mostly often affects the hands and weight-bearing joints such as the knee, hip and facet joints (in the spine). The common signs and symptoms are stiffness in a joint after getting out of bed or sitting for a long time, swelling in joints, crunching feeling or the sound of bone rubbing on bone.

2. Rheumatoid Arthritis⁵⁻¹⁰

A long lasting disease that can affect joints in any part of the body, most commonly the hands, wrists, and knees. The immune system mistakenly attacks itself and causes the joint lining to swell by targeting the thin membrane (synovium) that lines the joints. The inflammation then spreads to the surrounding tissues, and can eventually damage cartilage and bone. Other than genetic (inherited) factors and environmental factors, hormonal factors are also involved. Women are more likely to develop rheumatoid arthritis than men, pregnancy may improve the disease, and the disease may flare after a pregnancy. Breastfeeding may also aggravate the disease. Contraceptive use may alter a person's likelihood of developing rheumatoid arthritis¹¹. The common signs & symptoms often affects the wrist joints and the finger joints closest to the hand, also other parts of the body besides the joints and causes pain, swelling, stiffness, and loss of function in the joints.

3. Gout^{5, 6, 12}

It results from deposits of needle-like crystals of uric acid in connective tissue, in the joint space between two bones, or in both. These deposits lead to inflammatory arthritis and development of hyperuricemia. Gout accounts for approximately 5 percent of all cases of arthritis. It is more common in men than in women and more common in adults than in children. Eating too many foods rich in purines and exposure to lead can cause or aggravate gout. The common symptoms are Hyperuricemia, attack of acute arthritis in only one joint, usually the toe, ankle, or knee.

4. Systemic Lupus Erythematosus^{6, 13, 14}

In this autoimmune disease, the immune system turns against parts of the body it is designed to protect. Lupus

can affect many parts of the body, including the joints, skin, kidneys, heart, lungs, blood vessels, and brain. At present, there is no cure for lupus but can be controlled by drugs. It is characterized by additional symptoms like unexplained fever, red rashes, most commonly on the face, chest pain upon deep breathing, unusual loss of hair, pale or purple fingers or toes from cold or stress (Raynaud's Phenomenon), sensitivity to the sun, swelling (edema) in legs or around eyes, mouth ulcers, swollen glands and extreme fatigue.

5. Fibromyalgia ^{6, 15}

It refers to muscle and connective tissue pain characterised by widespread muscle pain, fatigue, and multiple tender points. Tender points are specific places on the body, on the neck, shoulders, back, hips, and upper and lower extremities where people with fibromyalgia feel pain in response to slight pressure. In addition, it causes sleep disturbances, morning stiffness, headaches, irritable bowel syndrome, painful menstrual periods, numbness or tingling of the extremities, restless legs syndrome, temperature sensitivity, cognitive and memory problems (sometimes referred to as "fibro fog").

Preventive Measures for Arthritis:

- Healthy lifestyle
- Exercise (such as walking, cycling and swimming) to strengthen supporting muscles and maintain joint mobility.
- Weight control
- Medication to alleviate pain.
- Severe, advanced arthritis may be treated with surgery.

People all over the world prefer to use allopathic medicines especially, Non-steroidal anti-inflammatory drugs (NSAIDs) as prescribed by doctors. The

greatest disadvantage in presently available potent synthetic drugs lies in their toxicity, side effects and reappearing of symptoms after discontinuation^{11, 16}. The common side effects are stomach irritation, kidney malfunction, urticaria, hepatic dysfunction, haematological abnormalities, bronchospasm and serious gastrointestinal problems including ulcers, bleeding, heartburn, diarrhea, fluid retention and perforation of the stomach or intestine⁵. Hence the use of alternative therapies, such as acupuncture and medicinal herbs, is on the rise and according to reports approximately 60-90% of dissatisfied arthritis patients are likely to seek the option of complementary and alternative medicine (CAM) ¹⁷.

Herbs on Arthritis

The modern medicine has also started admitting that Ayurveda and Herbal medicine, Yoga and Pranayam has a lot of positive influence on the treatment of Arthritis. There are a number of herbs that work synergistically to reduce chronic joint inflammation in cases such as osteoarthritis, rheumatoid arthritis and other types of arthritis. Basic scientific research has uncovered the mechanisms by which some plants afford their therapeutic effects. This paper deals with the study of herbs showing potential for treatment of arthritis.

Commonly cited herbs for treatment of Arthritis

1. Guggul (*Commiphora mukul*, *Burseraceae*) ^{18, 19}

Guggul has a complex structure made up of various compounds such as lignans, lipids, diterpenoids and steroids. Ten steroids have been isolated from the resin, among these; Z-guggalsterone and E-guggalsterone have hypolipidemic effects. The other components of the

ethyl acetate extract exert a synergistic activity²⁰. It is carminative, antispasmodic, disphoretic, ecobolic, anti-supportive and emmenagogue. It is a potent drug for cardiac disorders high cholesterol²¹.

Pharmacological Findings related to arthritis

1. In rat paw edema and induced-adjutant arthritis, guggul extract showed anti-inflammatory activity equal to phenylbutazone and ibuprofen and one-fifth as compared to hydrocortisone. In chronic inflammation model, it proved to be more effective than hydrocortisone, phenylbutazone and ibuprofen in reducing the severity of secondary lesions. It may be due to immune modulation and inhibition of delayed hypersensitivity reactions. Guggul extract stops the formation of these immune complexes around joints, regulates blood supply and stops the hypersensitivity reactions, thereby reducing the inflammation²².

2. According to one research work on both preclinical and clinical investigations of guggul indicated significant improvement in patients of osteoarthritis of the knee with no reported side effects. The study was conducted using an outcome, quasi-experimental model. Thirty male and female participants meeting the inclusion/exclusion criteria, with a score of 2 or more on the Kellegran-Lawrence scale for at least 1 knee, were admitted in the study. Guggul was administered in capsule form (500 mg concentrated exact delivered TID) along with food. The WOMAC Total Score was used as a primary outcome measure. VAS scales, 6-minute walk-test, and WOMAC subscales were used as outcome measures. On the primary measure, WOMAC total score, participants were significantly improved ($P < 0.0001$) after taking the

supplement for 1 month and continued to improve at the 2-month marker and follow-up. Secondary measures of pain in the VAS format demonstrated participant improvement; however, mood state, and current pain were not significantly different ($P < 0.05$) than baseline until the 2 month assessment ($P < 0.001$)²³.

2. Bhallataka (*Semecarpus anacardium* (SA), Linn, *Anacardiaceae*)^{18, 24}

Kernel of the nut contains a small quantity of sweet oil. Pericarp of fruit contains a bitter and astringent principle. The black corrosive juice of the pericarp contains tarry oil consisting of 90% of oxy-acid anacardic acid and 10% of higher nonvolatile alcohol called cardol, also contains catechol and a mono-hydroxyphenol called as anacardol²⁵. It acts as anti-asthmatic, stimulant, digestive, escharotics, carminative, antiseptic, demulcent, rheumatism, piles and in dyspepsia, swallowed with ghee or cream.

Pharmacological Findings related to arthritis:

1. In this study, ethanol extract of nuts inhibited the spontaneous and LPS induced production of proinflammatory cytokines IL-1 β and IL-12p40 but had no effect on TNF- α and IL-6 production, both at protein and mRNA level²⁶.

2. Arthritis was induced in rats by injecting Freund's complete adjuvant containing 10 mg of heat killed mycobacterium tuberculosis in 1 ml paraffin oil (0.1 ml) into the left hind paw of the rat intradermally. After 14 days of induction, SA (150 mg/kg body weight/day) was administered orally by gastric intubations for 14 days. Decreased levels of collagen and glycosaminoglycans (GAGS) components (chondroitin sulphate, heparan

sulphate, hyaluronic acid) and increase in the levels of connective tissue degrading lysosomal glycohydrolases observed in arthritic Wistar Rats were reverted back to near normal levels upon treatment with milk extract of nut. Thus it very effectively regulates the collagen metabolism that derange during arthritic condition²⁷.

3. The effect of Bhallataka nut milk extract on the metabolism of bone turnover has been studied by analyzing various markers of bone turnover and by histological and radiological analysis of the joints in adjuvant arthritis in rats. It significantly reverted the alterations in the bone turnover observed in arthritic animals by modulating the levels of calcium, phosphorus and the activities of the enzymes names tartrate resistant acid phosphatase, acid phosphatase and alkaline phosphatase. The drug increased the bone weights²⁸.

4. A significant increase in the level of Lipid peroxides LPO, reactive oxygen species ROS and decreased levels of antioxidant enzymes in arthritic rats were observed. On treatment with Bhallataka, the above changes were reverted back to near normal levels as conducted in one study. The increment in C-reactive protein CRP level and Erythrocyte sedimentation rate ESR observed in arthritic animals were found to be significantly restored in drug treated rats²⁹.

5. The in vivo carrageenan induced paw edema assay resulted in dose dependent anti-inflammatory effect of major COX inhibitory principle of Bhallataka seeds, tetrahydroamentoflavone (THA) and the activity was comparable to that of ibuprofen, one of the well-known NSAIDs³⁰.

6. A Siddha preparation of its nut extract called Serankottai Nei was tested for its capacity to stabilize lysosomes obtained

from liver and kidney of adjuvant-induced arthritic animals. Significantly increased lysosomal membrane fragility as observed in arthritic condition was reduced in drug-treated animals. Antiarthritic activity of the drug through its stabilizing action on lysosomal membranes could be inferred from this study³¹. In another work of same preparation, attempts have been made to study the potency of a milk extract of SA (Serankottai Nei), a Siddha preparation from SA nut, which has been shown to have antiarthritic effects³².

8. A chloroform extract of SA nut significantly reduced acute carrageenan-induced paw oedema in rats and was active against the secondary lesions of adjuvant-induced arthritis. Delayed hypersensitivity induced in mice by sheep red blood cells as an antigen was potentiated by the extract³³.

3. Ginger (*Zingiber Officinale*, *Zingiberaceae*)^{18, 34}

It contains, 1 to 5%, light yellow colour aromatic volatile oil having a characteristic odour containing camphene, phallandrene, zingibreine, cineol, borneol, gingerol, gingerin and starch. Ginger has actions like aromatic, carminative, stimulant to gastrointestinal tract, stomachic, digestive, externally used as stimulant, rubefacient and anti-rheumatic.

Pharmacological findings related to arthritis:

1. Protocol Ginger extract was compared to placebo and Ibuprofen in patients with osteoarthritis of the hip or knee in a controlled, double blind, double dummy, cross-over study with a wash-out period of one week followed by three treatment periods in a randomized sequence, each of three

weeks duration. Acetaminophen was used as rescue medication throughout the study.

A ranking of efficacy of the three treatment periods: Ibuprofen>ginger extract>placebo was found for visual analogue scale of pain (Friedman test: 24.65, $P < 0.00001$) and the Lequesne-index (Friedman test: 20.76, $P < 0.00005$). In the cross-over study, no significant difference between placebo and ginger extract could be demonstrated (Siegel-Castellan test), while explorative tests of differences in the first treatment period showed a better effect of both Ibuprofen and ginger extract than placebo (Chi-square, $P < 0.05$)³⁵.

2. In this study, 156 patients (28 with rheumatoid arthritis, 18 with osteoarthritis and 10 with muscular discomfort) used powdered ginger against their afflictions. Amongst the arthritis patients more than three-quarters experienced, to varying degrees, relief in pain and swelling with no adverse effects during the period of ginger consumption which ranged from 3 months to 2.5 years. At least one of the mechanisms by which ginger shows its ameliorative effects could be related to inhibition of prostaglandin and leukotriene biosynthesis, thus it works as a dual inhibitor of eicosanoid biosynthesis³⁶.

4. Ashwagandha (*Withania Somnifera*, *Solanaceae*)^{18, 37}

It contains steroidal alkaloids, steroidal lactones (thirty-five withanolides), bitter alkaloid 'Somniferin' having hypnotic property along with other

contents like resin, fat, colouring matter, reducing sugar, phytosterol, Ipuranol, mixture of saturated and unsaturated acids³⁸. It is Tonic, adaptogen, immunomodulator, abortifacient, Astringent, Deobstruent, Nervine, Aphrodisiac and Sedative. It gives vitality and vigor and helps in building greater endurance. It has been used in diseases such as rheumatism, leprosy and arthritis³⁹.

Pharmacological findings related to arthritis:

1. In animal studies, Ashwagandha was found more effective than the prescription drug phenylbutazone in controlling inflammation. The Ashwagandha treated group completely reduced the inflammatory proteins, whereas animals treated with phenylbutazone as well as the control groups had increased inflammatory proteins. Similar results were achieved in carrageenan-induced inflammation. In another study, Ashwagandha extract showed far superior (almost double) results when compared to the drug hydrocortisone to reduce inflammation. One of the researches showed significant reduction in the swelling of arthritic paw due to Ashwagandha which may be due to cox-2 inhibition. The reduction in swelling and degeneration was better than hydrocortisone. In a different study, *Withania* root extract (1000 mg/ kg, orally daily for 15 days) caused significant reduction in both paw swelling and bony degenerative changes in Freund's adjuvant-induced arthritis in rats as observed by radiological examination. The reductions were

better than those produced by the reference drug, hydrocortisone⁴⁰. Hindawi et al found that *Withania* inhibited the granuloma formation in cotton-pellet implantation in rats and the effect was comparable to hydrocortisone sodium succinate (5 mg/kg) treatment⁴¹.

In another study, Ashwagandha root powder was given to 46 patients of rheumatoid arthritis with doses of 4, 6, or 9 grams for a period of 3-4 weeks. Pain and swelling disappeared completely in 14 patients, considerable improvement was noticed in 10 patients and 11 patients showed mild improvement. In one double blind, placebo control study, the combination of Ashwagandha with turmeric and zinc showed positive effects in osteoarthritis cases. Patients showed significant improvement in pain severity and disability score^{40, 41}. The free radical mechanism is one of the mechanisms considered to contribute to many inflammatory diseases. Oral administration of Ashwagandha has demonstrated powerful antioxidant action preventing lipid peroxidation^{40, 41}.

***Boswellia* (*Boswellia Serrata*, *Burseraceae*)^{18, 42}**

The bark is sweet, cooling and tonic containing boswellic acid. It is good in vitiated conditions of Pitta, cough, asthma. It is useful in fevers, urethrorrhea, diaphoresis, convulsions, chronic laryngitis, jaundice, analgesic, antihyperlipidemic, antiatherosclerotic and treatment of rheumatoid and osteoarthritis. Adults and children with

rheumatoid arthritis both experienced effective relief of their symptoms when treated with *Boswellia*, despite having responded poorly in the past to standard therapies such as NSAIDs or gold⁴³.

Pharmacological findings related to arthritis:

1. Its anti-inflammatory and anti-arthritic activities have been mainly attributed to a component in the resin containing [beta]-boswellic acid. In an animal-model study boswellic acids significantly reduced the infiltration of leukocytes into the knee joint, in turn significantly reducing inflammation-causing immune white blood-cell response⁴⁴.
2. A randomized double blind placebo controlled crossover study was conducted to assess the efficacy, safety and tolerability of *Boswellia serrata* extract in 30 patients of osteoarthritis of knee, 15 each receiving active drug or placebo for 8 weeks. All receiving *Boswellia* reported decrease in knee pain, increased knee flexion and decrease in the frequency of swelling in the knee joint⁴⁵.
3. The findings for studying mechanisms underlying the anti-inflammatory actions of boswellic acid derivatives in experimental colitis demonstrated that P-selectin-mediated recruitment of inflammatory cells is a major site of action for this novel anti-inflammatory agent⁴⁶.

The important herbs used in arthritis control and treatment are summarized in table no. 1.

Table 1: The commonly used herbs for the treatment of arthritis

Sr.No	Name of Plant	Part used	Extract / Active content	Reference
1.	<i>Ricinus communis, Euphorbiaceae.</i>	Seed (oil)	Fixed oil, Celastrol (plant derived triterpene)	47
2.	<i>Vitex Negunda, Verbenaceae</i>	Leaf	Flavonoid fraction	18, 48,49
3.	<i>Thespesia Populnea, Malvaceae</i>	Bark	Ethanollic extract in higher doses	50
4.	<i>Clematis vitalba, Ranunculaceae</i>	Aerial parts	Vitalboside	51
5.	<i>Harpagophytum procumbens, Pedaliaceae</i>	Root	Harpagoside	52,53
6.	<i>Acanthopanax chiisanensis- Araliaceae</i>	Leaves	Methanolic extract	54
7.	<i>Tetrapleura tetraptera- Fabaceae</i>	fruit	Aqueous extract	55
8.	<i>Dorstenia barteri- Moraceae</i>	Leaf and twig	Alcoholic extract	56
9.	<i>Symphyti officinalis radix, Boraginaceae</i>	Root	Root extract ointment	57
10.	<i>Rosa canina, Rosaceae</i>	Fruits powder	Hyben Vital formulation	58
11.	<i>Kalopanax pictus, Araliaceae</i>	Stem bark	Methanolic extracts Kalopanaxsaponin-A and -I. chloroform, ethyl acetate and n-butanol fractions of the methanol extract	59, 60
12.	<i>Bridelia ferruginea, Euphorbiaceae</i>	Stem bark	Aqueous extract	61
13.	<i>Hippocratea excelsa, Celastraceae</i>	Bark	Ethanollic extract	62
14.	<i>Boswellia carteri, Burseraceae</i>	Dried gum resin	Acetone extract, Boswellic acid	63
15.	<i>Sclerocarya birrea (A. Rich.) Hochst., Anacardiaceae</i>	stem-bark	Aqueous and methanolic extracts	64
16.	<i>Tinospora cordifolia Menispermaceae</i>	Stem and root	Aqueous extract	18, 65, 66
17.	<i>Ulmus davidiana, Ulmaceae</i>	Bark	Aqueous extract	67, 68
18.	<i>Uncaria tomentosa, Rubiaceae</i>	Root bark	--	69
19.	<i>Cissampelos pareira, Menispermaceae</i>	Roots	50% Aqueous ethanollic extract	70
20.	<i>Nyctanthes arbortristis Linn. Nyctanthaceae</i>	Leaves	Water soluble portion of the alcoholic extract	71
21.	<i>Arnebia hispidissima, Boraginaceae</i>	Whole plant	Shikonin derivatives	72
22.	<i>Euphorbia tirucalli, Euphorbiaceae</i>	Whole plant	Biopolymeric fraction (BET)	73
23.	<i>Ananus comosus, Bromeliaceae</i>	Fruit and stem	Bromelain	74
24.	<i>Paeonia lactiflora- Ranunculaceae</i>	Root	Paeoniflorin	75
25.	<i>Trichodesma amplexicaule Roth, Boraginaceae</i>	Arial parts	Alkanoic acid	76

CONCLUSION

The use of complementary and alternative medical (CAM) therapies is widespread among patients, including those with rheumatic diseases. Herbal medications are often utilized with little

to no physician guidance or knowledge. An appreciation of this information will help physicians to counsel patients concerning the utility of CAM therapies. An understanding and elucidation of the mechanisms by which CAM therapies

may be efficacious, can be instrumental in discovering new molecular targets in the treatment of diseases. Available data suggests that the extracts of most of

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