Review Article

Medicinal Plants having Anti-arthritic Potential: A Review

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ABSTRACT

Arthritis, literally meaning "inflammation of the joint," encompasses over 100 rheumatic diagnoses, with osteoarthritis and rheumatoid arthritis being the most prevalent. Rheumatoid arthritis is a systemic autoimmune disease with chronic inflammation characterized by hyperplasia of synovial cells and angiogenesis in affected joints, which ultimately leads to the destruction of cartilage and bone. Plants have been used since prehistoric times for treatment of various ailments. The uses of traditional medicines are widely spread and plants represent a large source of natural chemicals that might serve as leads for the development of the novel drugs. In this review, an attempt has been made to highlight the work on medicinal plants having anti-arthritic potential. This review may be helpful for the researchers for further research on the potential use of medicinal plants having anti-arthritic property.

Keywords: Rheumatoid arthritis, Medicinal plants, Anti-arthritic potential, Herbal medicine.

INTRODUCTION

Plants are the only economic source of a number of well established and important drugs. In addition, they are also the source of chemical intermediates needs for the production of some drugs.[1] Herbal medicine is the root of various traditional medicine systems around the world. Ayurvedic medicine in India has proven track record of 5000 years and forms part of the National Health Service, offered alongside conventional medicine. The ayurvedic national formulary lists some 8000 well proven ayurvedic formulation described in dravyaguna (ayurvedic pharmacology). Remedies are made from single or multiple herbs and minerals for various medical conditions like asthma, flu, diabetes, arthritis, heart disease, digestive problems, mental health and skin problems. Herbal medicines yielding about 25% of currently used crude drugs with another 25% derived from chemically altered natural products. In ancient texts about 500 plants have been indicated in the treatment of arthritis; however only little number of plants have been evaluated scientifically.[2] Herbal products are often perceived as safe because they are "natural". In recent years, there is increased research on traditional ayurvedic herbal medicines on the basis of their known effectiveness in the treatment of ailments for which they have been traditionally applied.[3]

Rheumatoid arthritis (RA) is a chronic inflammatory condition of the connective tissues throughout the body, but especially around the joints. RA is the most common inflammatory arthritis and affects about one percent of the population[4]. RA affects three times more women than men.[5]

Arthritis is classified as an autoimmune, inflammatory arthritis; the disease comprises three basic interrelated processes- Inflammation, synovial proliferation and joint tissue destruction. In the early stages of RA, the synovial membrane begins to invade the cartilage. In established RA, the synovial membrane becomes transformed into inflammatory tissue, the pannus. This tissue invades and destroys adjacent cartilage and bone. The interface between pannus and cartilage is occupied predominantly by activated macrophages and synovial fibroblasts that express matrix metalloproteinases.

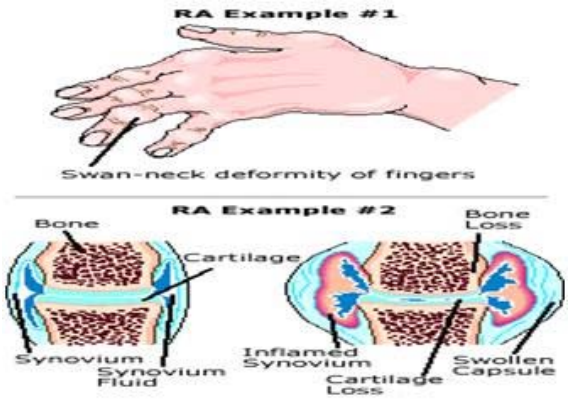

Figure 1: Joint deformity in fingers and bone

Interleukin-1 (IL-1) and tumour necrosis factor-α (TNF-α) stimulate the expression of adhesion molecules on endothelial cells and increase the recruitment of neutrophil into the joints. TNF-α causes bone destruction in RA (Figure 1). Neutrophil release elastase and proteases, which degrade proteoglycan in the superficial layer of cartilage. The depletion of proteoglycan enables immune complexes to precipitate in the superficial layer of collagens and exposes chondrocytes. Chondrocytes and synovial fibroblasts release matrix metalloproteinase (MMPs) when stimulated by IL-1, TNF- α, or activated CD4+ T cells. MMPs, in particular stromelysin and collagenases, are enzymes that degrade connective-tissue matrix and are thought to be the main mediators of joint

damage in RA. Thus result cartilage and bone destruction and to the fibrosis.[6-8]

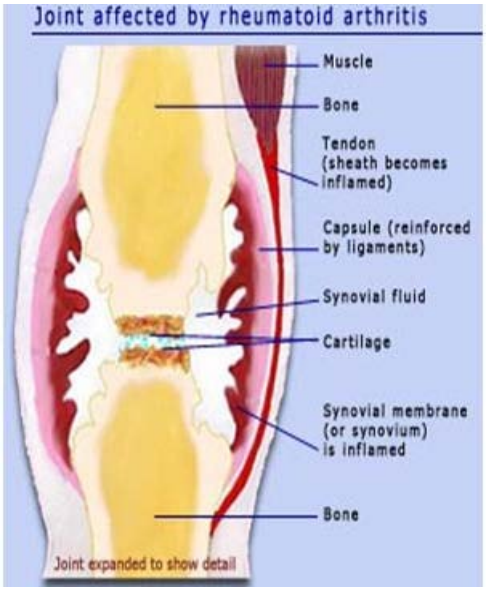

Figure 2: Joint affected by RA

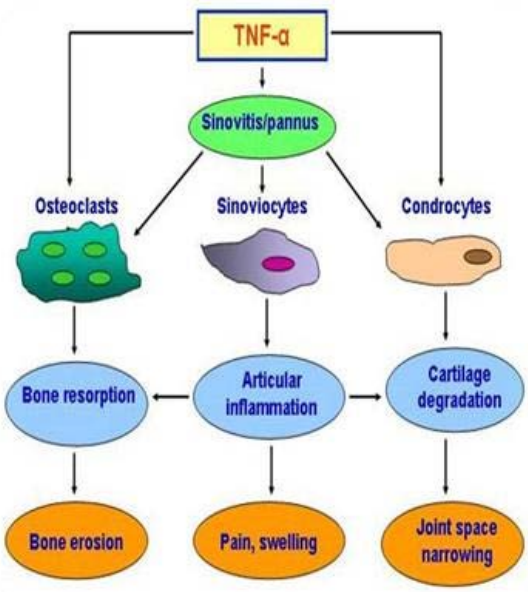

Figure 3: Role of TNF- α in RA

The production of auto antigens in certain arthritic diseases may be due to in vivo denaturation of proteins.[9] Onset of RA usually occurs between the ages of 25 and 50, although it may begin at any age. It affects anyone, including children. Animal models of arthritis are used to study pathogenesis of disease and to evaluate potential anti-arthritic drugs for clinical use.[6,10] A large numbers of herbal extracts are in vogue for the treatment of arthritis. The present study focus on different medicinal plants of anti-arthritic property. Plants part, extract and experimental models are used to evaluate anti arthritic activity also have been discussed.

Medicinal plants of anti-arthritic potential

Medicinal plants which are having anti-arthritic potential are provided in table 1.

DESCRIPTION OF SOME ENLISTED PLANTS

Cassia uniflora Mill.

Petroleum ether, ethyl acetate and methanolic extract of *Cassia uniflora* were screened for analgesic by Eddy's hot plate and acetic acid induced writhing, anti-inflammatory by carrageenan induced paw edema and anti-arthritic activity by complete Freund's adjuvant induced arthritis. In complete Freund's adjuvant arthritis model, degree of inflammation was evaluated by hind paw swelling, body weight and biochemical parameters, and supported by radiological analysis. Treatment with extracts of *C. uniflora* showed significant and dose dependent increase in paw licking time in Eddy's hot plate method. In writhing test, extracts significantly reduced the number of writhes. A dose dependent and significant inhibition of edema was observed in carrageenan induced paw edema. Petroleum ether extract at a dose of 100 mg/kg showed most potent and significant activity which was supported by the result of body weight, biochemical parameters and radiological analysis in CFA arthritic model.[24]

Cissampelos pareira

Cissampelos pareira showed the dose dependent significant protective effect against complete Freund's adjuvant induced arthritis.[27] Anti-arthritic nature of polyherbal formulation containing *C. Pereira* Linn, *Pongamia pinnata* (Linn) Pierre and *Vitex negundo* Linn. has been evaluated against Freund's complete adjuvant induced arthritis in rats. The degree of inflammation was evaluated by hind paw swelling, body weight and haematological study supported by histopathology of ankle joints and radiological study. Polyherbal formulation (200 mg/kg, 400 mg/kg and 600 mg/kg) reduced hind paw swelling and body weight along with significant improvement in haematological study, while histopathology revealed the significant reduction in mononuclear infiltration, pannus formation and bone erosion. The radiological pictures of the joints particularly metatarsal, phalanges and the ankle joint space of polyherbal formulation treated group animals showed protective effect against adjuvant induced arthritis.[54]

Harpagophytum procumbens

Harpagophytum procumbens known as "devil's claws," is a plant, originated from Southern Africa, specifically, from the Kalahari Desert and Namibia steppes. Ethanolic extract of *H. procumbens* root has been evaluated for its anti-inflammatory and analgesic activity in rat by Freund's adjuvant-induced arthritis both in the acute and chronic phases. Behavioral test, body weight, Hot-plate test and paw volume were measured. The results showed that the extract increased the animals 'latency of paws' withdrawal, indicating a protective effect against the pain induced by the thermal stimulus, both in acute and chronic treatments.[32]

Table 1: The commonly used plants

S. no	Name of Plant	Family	Part used	Experimental models	Extract used	Ref
1.	*Acanthopanax chiisanensis*	Araliaceae	Leaves	CFA	Methanolic, butanolic	11
2.	*Ajuga bracteosa*	Labiatae	Whole plant	FIA	Ethanolic	12
3.	*Alpinia galanga*	Zingiberaceae	Rhizomes	CFA	Ether (60-80), chloroform, alcohol	13
4.	*Alangium salviifolium*	Alangiaceae	Stem bark	CFA	Ethyl acetate, petroleum ether, chloroform, methanol	14
5.	*Albizia lebbeck*	Mimosaceae	Bark	CFA	Methanolic	15
6.	*Ammania baccifera*	Lythraceae	Whole plant	CFA	Ethanolic, aqueous	16
7.	*Alstonia scholaris*	Apocaynaceae	Leaves	FCA	Ethanolic	17
8.	*Asystasia dalzelliana*	Acanthaceae	Leaves	PD, HRBC-MS	Methanolic (fraction)	18
9.	*Aristolochia bracteata*	Aristolochiaceae	Whole plant	FCA	Methanolic	19
10.	*Boswellia carteri*	Burseraceae	Dried gum resin	CFA	Acetone	20
11.	*Boswellia serrata*	Burseraceae	Whole plant	CFA	n-Hexane	21
12.	*Bridelia ferruginea*	Euphorbiaceae	Stem bark	CFA	Aqueous	22
13.	*Capparis spinosa*	Capparidaceae	Fruit	CFA	Ethanolic	23
14.	*Cassia uniflora*	Caesalpiniaceae	Leaf	CFA	Petroleum ether, ethyl acetate, methanolic	24
15.	*Cedrus deodara*	Pinaceae	Stem bark	FCA	Aqueous	25
16.	*Centella asiatica*	Mackinlayaceae	Leaves	PD	Methanolic	26
17.	*Cissampelos pareiro*	Menispermaceae	Root	CFA	Aqueous, ethanolic	27
18.	*Clematis vitalba*	Ranunculaceae	Aerial parts	CFA	Methanol	28
19.	*Cleome rutidosperma*	Capparidaceae	Aerial parts	CFA	Ethanolic, petroleum ether, diethyl ether, ethyl acetate	29
20.	*Delonix elata*	Fabaceae	Bark	CFA	Ether, chloroform, 40% hydroalcohol	30
21.	*Euphorbia atiquorum*	Euphorbiaceae	Whole plant	CFA	Aqueous, alcoholic	31
22.	*Glycyrrhiza glabra*	Fabaceae	Rhizomes	CFA	Methanolic extract	21
23.	*Harpagophytum procumbens*	Pedaliaceae	Root	CFA	Ethanolic	32
24.	*Hemidesmus indicus*	Asclepiadaceae	Roots	CFA	Hydroalcoholic extract, ethyl acetate, chloroform	33
25.	*Hybanthus enneaspermus*	Violaceae	Whole plant	CFA	Aqueous, alcoholic	34
26.	*Hippocratea excels*	Celastraceae	Bark	FIA , AIA	Ethanolic	35
27.	*Kalopanax pictus*	Araliaceae	Stem bark	FCA	Chloroform, ethylacetate, *n*-butanol fractions of the methanol	36, 37
28.	*Lawsonia inermis*	Lythraceae	Leaves	FIA, FCA	Hydroalcoholic	38
29.	*Merremia tridentate*	Convolvulaceae	Whole plant	CFA	Benzene,water, ethanol, choloroform	39
30.	*Newbouldia laevis*	Bignoniaceae	Stem bark	CFA	Hydroalcoholic extract	40
31.	*Nyctanthes arbortristis Linn.*	Nyctanthaceae	Leaves	FIA ,FCA	Ethanolic	41
32.	*Palisota hirsute*	Commelinaceae	Leaves	CFA	Ethanolic	42
33.	*Phyllanthus amarus*	Euphorbiaceae	Herbs	CFA	Aqueous	43
34.	*Pleurotus sajorcaju*	Polyporaceae	Mycelium	CFA	Water, methanol	44
35.	*Pistio stratiotes*	Araceae	Leaf	CFA	Aqueous, ethanolic	45
36.	*Ricinus communis*	Euphorbiaceae	Leaves	CFA	Hydroalcoholic	46
37.	*Rubia Cordifolia*	Rubiaceae	Roots	FCA ,CIA	Ethanolic	47
38.	*Strychnos potatorum*	Loganiaceae	Seed	CFA	Aqueous	48
39.	*Ulmus davidiana*	Ulmaceae	Bark	CIA	Aqueous	49
40.	*Urginea indica*	Liliaceae	Bulb	CPM	Methanolic	50
41.	*Urtica pilulifera*	Urticeacae	Leaves	FCA	Methanolic extract	51
42.	*Vernonia anthelmintica*	Asteraceae	Seed	CFA	Water extract	52
43.	*Wedelia calendulacea*	Asteraceae	Leaf	CFA	Petroleum ether, ethyl acetate, methanol	53

Experimental models – AIA or FCA or CFA - Adjuvant induced arthritis or Freund's complete adjuvant or complete Freund's adjuvant, CIA- Collagen-induced arthritis, CPM-Cotton pellet method, HRBC-MS –HRBC membrane stabilization, PD- Protein denaturation.

Hemidesmus indicus

The protective effects of hydroalcoholic and its fractions from roots of *Hemidesmus indicus* has been investigated by complete Freund's adjuvant model. Rats treated with hydroalcoholic extract (450 mg/kg), ethyl acetate (75 mg/kg), chloroform (60mg/kg) and residual fraction (270 mg/kg) showed significant decrease in physical and biochemical parameters compared with arthritic model rats. Hydroalcoholic extract and its ethyl acetate fraction

of *H. indicus* showed significantly higher anti-arthritic activity than chloroform and residual fraction. Histopathological analysis demonstrated that both of hydroalcoholic extract and its ethyl acetate fraction had comparable anti-arthritic activity with methotrexates.[33]

Phyllanthus amarus

Phyllanthus amarus Schum. and Thonn. (PA) (Euphorbiaceae) is a herb that grows in the tropics and subtropics in sandy regions as a weed in cultivated and waste lands. The aqueous extract of *P. amarus* extract (PAE) (2.5% Phyllanthin and hypophyllanthin) was tested against Freund's complete adjuvant (FCA) induced arthritic rats. Arthritis assessment, paw volume, joint diameter, mechanical hyperalgesia and nociceptive threshold were measured. PAE significantly decreased the arthritis which was evident with arthritis index, paw volume and joint diameter. It also significantly increased the mechanical hyperalgesia and nociceptive threshold. The histopathology also revealed the control in inflammation with PAE. [43]

Pleurotus sajorcaju

Pleurotus sajorcaju, is an edible and good source of carbohydrates, dietary fiber, essential amino acids, minerals,Vitamin B, folic acid and steroids. Aqueous and methanolic extracts of mycelium of *P. sajorcaju* were investigated for antiarthritic activity. Body weight, paw edema (inflammation), hematological parameter, spleen weight, radiological and histological analysis of bone damage were assessed in rats with Freund's adjuvant induced paw inflammation. Both extracts showed significant and dose-dependent anti-inflammatory and anti-arthritic effects compared to control group.[44]

Pistia stratiotes

Antiarthritic activity of aqueous and ethanolic leaf extracts of *Pistia stratiotes* (AQPSE and ETPSE, respectively) has been investigated. Arthritis was induced in rats, paw swelling was measured, and arthritis indices were estimated in rats treated with AQPSE, ETPSE, methotrexate, diclofenac, dexamethasone, and normal saline-treated rats. Radiologic imaging, hematological assessment of red and white blood cells, C-reactive protein and erythrocyte sedimentation rate, as well as histopathological studies were also done. The 30, 100, and 300 mg/kg doses of AQPSE and the 30 and 100 mg/kg doses of ETPSE caused a significant reduction in ipsilateral paw swelling, similar to the effects of methotrexate, dexamethasone, and diclofenac. Only the 30 mg/kg dose of AQPSE caused a significant reduction in contralateral paw swelling. Arthritic indices reduced significantly at all drug doses, except for the 100 and 300 mg/kg doses of ETPSE. White blood cell levels decreased significantly in arthritic rats treated with the 30 mg/kg dose of AQPSE and those treated with methotrexate. Erythrocyte sedimentation rate and C-reactive protein levels were significantly lower in all the treatment groups except for the rats treated with AQPSE 300 mg/kg and ETPSE 100 and 300 mg/kg doses. The arthritic animals treated with 30 mg/kg of the aqueous extract showed no inflammatory changes in the ipsilateral paw, while the contralateral paw showed only foci of mild chronic inflammatory changes, as seen with the reference drug treatment in histopathological studied. [45]

Strychnos potatorum

Strychnos potatorum Linn (Loganiaceae) is a moderate sized tree found in southern and central parts of India, Sri Lanka and Burma. The effect of the aqueous extract (SPE) and the whole seed powder (SPP) of *S. potatorum* Linn seeds on the Freund's complete adjuvant (FCA) induced arthritic rat paw edema, body weight changes and alterations in haematological and biochemical parameters in both developing and developed phases of arthritis has been evaluated. Histopathology of proximal interphalangeal joints and radiology of hind legs were also studied. In FCA induced arthritic rats, there was significant increase in rat paw volume and decrease in body weight increment, whereas SPP and SPE treated groups, showed significant reduction in paw volume and normal gain in body weight. The altered haematological parameters (Hb, RBC, WBC and ESR) and biochemical parameters (blood urea, serum creatinine, total proteins and acute phase proteins) in the arthritic rats were significantly brought back to near normal by the SPP and SPE treatment at the dose of 200 mg/kg/p.o in both developing and developed phases of arthritis. Further the histopathological and radiological studies revealed the antiarthritic activity of SPP and SPE by indicating fewer abnormalities in these groups when compared to the arthritic control group.[48] The effect of crude powder (SPP) and aqueous extract (SPE) of *S. potatorum* Linn seeds on *in vivo* antioxidant defense system against FCA induced arthritis in rats at the dose of 200 mg/kg/p.o for 14 and 28 days and *in vitro* antioxidant activity against Ferrous thiocyanate (FTC) and Thiobarbiturate (TBA) induced lipid peroxidation also have been reported. The antioxidant defense system parameters studied in plasma and tissues of arthritic rats were found to be altered significantly.[55]

Wedelia calendulacea

The effect of *Wedelia calendulacea* leaves has been investigated alone or in combination with sub therapeutic dose of Methotrexate (1mg/kg) is salvaging, oxidative stress, anti-arthritic action and cardioprotective actin with Methotrexate. Rats were induced arthritis by sub plantar injection of 0.1 mL Complete Freund's adjuvant (CFA). Various hematological (RBC, WBC, Hb, ESR and RA Factor), biochemical parameters (Homocecytein, TNF-α, IL-2 and CRP) and tissue parameters (SOD, Catalase and Lipid peroxidation of aorta) were measured before initiation and after completion of treatment in all groups. Methanolic fraction of methanolic extract (Me-OH/Me-OH) of *W. calendulacea* showed significant anti-arthritic activity in CFA induced arthritic animals.[53]

CONCLUSION

The medicinal plants, which have been discussed, show promising role as anti-arthritic agents. Arthritis is one of the most common auto immune inflammatory disorders. The presently available pharmacological treatments in the market are not only causing economical exploitation but also associated with severe adverse effects. So these plants play efficient role for betterment of the treatment. The plants provide essential compounds with active principles, having minimal side effects and may be useful for arthritis control. In this article, it is attempted to compile reported plants of anti arthritic activity. It is concluded that isolation of lead compound which responsible for the activity, is required and it may be beneficial for improving the better treatment of the arthritis.

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