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ANTIARTHRITIC ACTIVITY OF SOME INDIGENOUS PLANTS: A REVIEW

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ABSTRACT

Arthritis is a chronic, inflammatory, systemic autoimmune disease characterized by pain, swelling and stiffness. Allopathic medications have been prescribed to alleviate symptoms of this disease which results into associated side effects like heart attack, stroke, stomach ulcers, bleeding from the digestive tract, and kidney damage etc. Hence the use of herbal medicine is becoming popular due to toxicity and side effects of allopathic medicines. The plant, as one of the important sources, still maintains its original place in the treatment of various diseases, including arthritis, with minimum side effects. Considerable studies have been carried out on ethno medicinal plants; however, only few medicinal plants have attracted the interest of scientists, to investigate them as a remedy for arthritis. In this review an attempt has been done to highlight the work on indigenous medicinal plants having Anti-arthritic potential.

INTRODUCTION: Arthritis is inflammation of one or more joints. Arthritis involves the breakdown of cartilage. Cartilage normally protects a joint, allowing it to move smoothly. Cartilage also absorbs shock when pressure is placed on the joint, such as when you walk. Without the normal amount of cartilage, the bones rub together, causing pain, swelling (inflammation), and stiffness. 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 [1].

In India more than about 20% of total population is suffering from arthritis. 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. Symptoms of arthritis can include reduced ability to move the joint, stiffness, especially in the morning, difficulty performing daily activities, disability, long-term (chronic) pain etc. The key risk factors of arthritis includes age, gender, excess weight, injury, dietary pattern, consumption of excess alcohol, life style, heredity, hormonal factors, environmental factors and lack of physical activity. There are four main groups of drugs used to treat arthritis: Pain killers (analgesics), non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs) and corticosteroids (steroids) [2].

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. The modern medicine has also started admitting that ayurveda and herbal medicine, has a lot of positive influence on the treatment of arthritis. A large number of medicinal plants have been tested and found to contain active principles with curative properties against arthritis. Antiarthritic plants contain a variety of chemical constituents like phenols, coumarins, essential oils, monoterpenes, catechins, quinones, carotinoids, flavanoids, alkaloids, anthocyanins and xanthenes [3]. This paper deals with the study of indigenous herbs showing potential for treatment of arthritis.

Antiarthritic plants :

***Ajuga bracteosa*:** The antiarthritic activity of 70 % ethanolic extract of *Ajuga bracteosa* (EEAB) was evaluated against turpentine oil and formaldehyde induced acute nonimmunological and complete freund's adjuvant (CFA) induced chronic immunological arthritis in albino rats. EEAB showed a significant and dose dependant inhibitory effect against acute and chronic models of arthritis. EEAB exhibited better antiarthritic activity than the standard aspirin. Treatment with EEAB (5, 10 and 20 mg/kg) exhibited 64.55 %, 73.42 %, and 81.01 % of protection against joint oedema in comparision to standard aspirin (i.e. 40.51 % inhibition) after 6 days of treatment. The secondary inflammatory response observed from 9th to 14th day was also inhibited much more effectively by EEAB at a dose of 20 mg/kg (68.31 %) when compared with aspirin (60.49 %).The data support the traditional use of *Ajuga bracteosa* for rheumatism and other inflammatory diseases [4, 5].

***Alangium salvifolium*:** The anti-arthritic activity of stem barks of *Alangium salviifolium* wang belonging to family Alangiaceae was studied in rats. The barks of *Alangium salviifolium* wang were collected and dried in shade and subjected for successive extraction with petroleum ether, Ethyl acetate, chloroform, methanol using soxhlet apparatus and distilled water by maceration. Each extracts were then subjected for preliminary phytochemical studies and pharma-cological investigation. Study of anti-arthritic activity was carried out by following Fruends adjuant arthritis model. All the extracts of *Alangium salviifolium* wang showed potent anti-arthritic activity and the potency of the activity follows the order standard > chloroform > ethyl acetate > aqueous > pet. ether > methanol [6, 7].

***Alpinia galanga*:** The petroleum ether, chloroform, alcoholic extracts of the *A. galanga* rhizomes were evaluated for their antiarthritic activity by using Complete Freund's Adjuvant (CFA) induced rat model. Application of all the three extracts exhibited statistically significant edema inhibition when compared with the arthritic control group. Sub planter injection of Freund's Complete Adjuvant in the rat hind paw led to the development of arthritis which reached a peak edema on 28 days of the injection. The test extracts petroleum ether, chloroform and alcoholic application of *A. galanga* showed 48.69, 44.63 and 54.68% inhibitions of this oedema respectively. The studies reveal that the petroleum ether is better than that of chloroform and alcoholic extracts of *A. galanga* rhizomes in respect to their antarthritic activity [8].

***Anisomeles malabarica*:** Anti-arthritic activity of Anisomeles malabarica was studied by the inhibition of protein denaturation method. The methanolic extract of the plant exhibited significant activity at 97.47% at 250µg/ml by inhibition of protein denaturation and its effect was compared with the standard drug Diclofenac sodium. The production of auto antigen in certain arthritic disease may be due to denaturation of protein. From the results of present study it can be stated that methanolic extract of *Anisomeles malabarica* is capable of controlling the production of auto antigen and inhibits denaturation of protein in rheumatic disease [9, 10].

***Aristolochia bracteata* -** Anti arthritic activity of Aristolochia bracteata was evaluated using Freund's complete adjuvant in rats, the course of treatment was followed for 4 weeks post inoculation period using health parameters, clinical and behavioural methods of study. Estimation of blood Hb, ESR (Erythrocyte sedimentation rate) and change in body weight were considered as health parameters and clinical observations included paw edema volume, thermal hyperalgesia, radiological and histomarphological analysis and exploratory behavior was studied in behavioral observations.

The results indicates that, regular treatment of adjuvant induced arthritic rats with A. bracteata extracts improves ESR, Hb value and also restores body weight. Significant inhibitory effect was observed with *A. bracteata* extract on Freund's complete adjuvant induced paw edema throughout the study. On the basis of the results obtained in the study, it was concluded that possibly, the potent anti-arthritic effect of *Aristolochia btracteata* chloroform extract may be through maintenance of synovial membrane and vascular permeability, thereby inhibiting cytokines and leukotriene infiltration inhibition as evidenced in paw edema volume [11].

***Bacopa monniera*:** The methanolic extract of B. monniera has showed significant activity at various concentrations and its effect was compared with the standard drug Diclofenac sodium. The maximum percentage inhibition of protein denaturation and membrane stabilisation of *B. monniera* was observed as 90.34±0.83% and 93.67±1.34% at 2000µg/ml respectively. When compared to standard Diclofenac sodium was found out to be 96.52±1.25% and 98.76±1.67% respectively at a dose of 2000 µg/ml. The production of auto antigen in certain arthritic disease may be due to denaturation of protein and membrane lysis. From the results, it can be stated that methanolic extracts are capable of controlling the production of auto antigen and inhibits denaturation of protein and membrane lysis in rheumatic disease [12, 13].

***Barringtonia racemosa*:** Bartogenic acid (BA) isolated from the fruits of *Barringtonia racemosa* was evaluated for effectiveness against CFA-induced arthritis in rats. The results indicate that at doses of 2, 5, and 10mg/kg/day, BA protects rats against the primary and secondary arthritic lesions, body weight changes and haematological perturbations induced by CFA. The serum markers of inflammation and arthritis, such as C-reactive protein and rheumatoid factor, were also reduced in the BA-treated arthritic rats. The overall severity of arthritis as determined by radiological analysis and pain scores indicated that BA exerts a potent protective effect against adjuvant-induced arthritis in rats [14].

***Cedrus deodar*:** The petroleum ether, chloroform and alcoholic extracts of the heart wood of *Cedrus deodar* were examined for its external anti arthritic activity in rats using the freunds adjuvant method. Application of all the three extracts exhibited significant inhibition of CFA (Complete Freund's Adjuvant) induced rat paw edema when compared with the arthritic control group. The effect of *C. deodara* on adjuvant induced arthritis in rats showed that it effectively inhibited the polyarthritis phase as measured by the paw swellings on the injected limbs. It also inhibited the acute phase of CFA induced response (measured by the response every day from the first day 1 following the injection of CFA), confirming its activity against the acute and chronic inflammatory response.

The studies reveal that the petroleum ether is better than that of chloroform and alcoholic extracts of *C. deodara* heart wood in respect to their antiarthritic activity [15].

***Cleodendron inermae*:** The Petroleum ether, Chlorofrom, Ethyl acetate, Ethanol and water fractions of the leaves of *Clerodendron inerme* were subjected to *in-vitro* anti-arthritic activity by protein denaturation method. From the result of the study, it can be stated that all the extracts of *Clerodendron inerme* leaves is capable of controlling the production of auto antigen and thereby, it inhibits the denaturation of proteins and its effect was compared with the standard drug diclofenac sodium.

The percentage protection was found to be 78.94% (Petroleum ether), 88.46 % (Chloroform), 89.25% (Ethyl acetate), 87.10% (ethanol), 82.31% (water) and 92.20% (Diclofenac sodium). All the extracts showed dose dependant response. This effect may be due to the presence of steroids, alkaloids and flavonoids present in various fractions. The effect was represented as follows - Ethyl acetate> Chloroform> Ethanol> Water> Petroleum ether [16].

***Cleome rutidosperma*:** The various extracts of Cleome rutidosperma were investigated for its anti-arthritic activity in male albino rats. The evaluation of anti-arthritic activity was carried out using cotton pellet granuloma method and Freund's adjuvant induced arthritis model. Prednisolone (5 mg/kg bw) was used as a standard drug. The ethanolic extract of *Cleome rutidosperma* exhibited significant anti-arthritic activity as compared to other extracts.

The doses of 200 mg/kg bw of the ethanolic extract of *Cleome rutidosperma*, in chronic model of granuloma pouch in rats produced 48.0% and in arthritis model produced 44.0 % inhibition respectively with that of the standard drug Prednisolone (5 mg/kg) which produced 58.5% and 59% inhibition. All the extracts of *Cleome rutidosperma* showed potent antiarthritic activity and the potency of the extracts follows the order - standard>ethanolic extract>petroleum ether extract>di-ethyl ether extract>ethyl acetate extract [17, 18].

***Cocculus hirsutus*:** The anti-arthritic effect of oral administration of methanolic and aqueous extracts of root (100 and 200 mg/kg) of *Cocculus hirsutus* was evaluated using Freund's adjuvant arthritis model in Wistar albino rats. Arthritis was induced by injecting 0.1ml of complete Freund's adjuvant below the plantar aponeurosis of the right hind paw. Treatment with the extracts and standard started on the day of induction of inflamogens and continue up to 21 days. The body weight loss that was found during the arthritic condition was corrected on treatment with methanolic extracts of root of *Cocculus hirsutus* Linn. The swelling of the paw during the secondary lesions was also markedly reduced. Various hematological parameters like total WBC count, ESR and RBC were also estimated. The results of the study support the traditional use of this plant as anti-arthritic drug. Antiarthritic activity of methanolic extract was dose dependant and the dose of 200mg/kg was more effective than 100mg/kg bodyweight whereas methanolic extracts were more effective than aqueous extracts [19].

***Cyperus rotundus*:** The anti-arthritic activity of Cyperus rotundus was evaluated by using formaldehyde induced arthritis model in Wistar albino rats. The assessment made on the 10th day showed that, treatment with Cyperus rotundus (500 mg/kg) significantly reduced the swelling in the injected (left) hind paw as compared to Diclofenac sodium treated group. On the 10th day the % inhibition of paw edema exhibited by Cyperus rotundus (500 mg/kg) was 75.54%, while Diclofenac sodium treated animals showed maximum % of inhibition of paw edema 81.37 on 21st day [20].

***Glycine max*:** The antiarthritic activity of *Glycine max* seeds was evaluated in adjuvant induced arthritis in rats. Antiarthritic activity was assessed based on the paw volume, biochemical parameters, haematological parameters and histological parameters. The changes in these parameters were reversed by the *G. max* seed extract administered at the dose of 60 mg/kg orally. The biochemical parameters showed that the parameters such as total protein. Alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase levels were increased significantly at ($P<0.05$) in the arthritic control group than normal group, while the level of serum albumin was reduced significantly ($P<0.05$). After treatment with *G. max* extract in treatment group, the parameters were reduced significantly than the arthritic control group ($P<0.05$). This results showed that the extract of G. max possess anti arthritic activity [21, 22].

***Hybanthus enneaspermus*:** The effect of alcoholic and aqueous extracts of the whole plant of *Hybanthus enneaspermus* on freund's adjuvant induced arthritis in male albino mice was evaluated. Both the extracts significantly decrease the paw thickness at the end of 30 days treatment. Though in acute phase inflammation both of them show the same potency, in chronic phase, alcoholic extract exhibit more potency than the aqueous extracts. At the end of the studies the alcoholic extract shows more pronounce effect (59.4%) as comparable to aqueous extract (57.4%).

Standard diclofenac sodium significantly decrease the paw thickness from the 1st day after induction of freund's adjuvant, where as the extracts significantly decrease the thickness after 4th day. Standard Diclofenac sodium decreases the paw edema by 72.4%. Standard drug, aqueous and alcoholic extract significantly suppressed the swelling of the paws in both acute and chronic phase which may be due to the suppression of inflammatory mediator released due to induction of freund's adjuvant. Though the actual mechanism of suppressing inflammation is not known but it can be correlated with the presence of alkaloids and flavonoids in suppressing the inflammation and antioxidant activity [23, 24].

***Merremia tridentata*:** The various extracts of *Merremia tridentata* were investigated for its anti-arthritic activities in male albino rats. The anti-arthritic activity was carried out using complete Freund's adjuvant induced arthritis model. Indomethacin (10 mg/kg bw) was used as a standard drug. The doses of 100 mg/kg bw and 200 mg/kg bw of the ethanol extract produced 49.0% and 51.7% inhibition respectively after 19 days when compared with that of the standard drug (55.5%). The anti-arthritic effect of the ethanol extract of *M. tridentate* started on day 3, which continued till day 19 when compared with that of the control. In the case of standard drug, maximum inhibition was observed on day 5 itself. Whereas in the case of 100 mg/kg bw and 200 mg/kg bw doses of the

test drug maximum inhibitions were noticed on day 9. In all the three cases the inhibition started decreasing after day 9 and again reached the maximum on day 19 [25].

***Premna serratifolia*:** Anti-arthritic activity of ethanol extract of *Premna serratifolia* Linn., wood was done by Freund's adjuvant induced arthritis model. Loss in body weight during arthritis condition was corrected on treatment with ethanol extract and standard drug, indomethacin. Biochemical parameters such as hemoglobin content, total WBC, RBC, erythrocyte and sedimentation rate were also estimated. The ethanol extract at the dose of 300 mg/kg body weight inhibited the rat paw edema by 68.32% which is comparable with standard drug indomethacin 74.87% inhibition of rat paw edema after 21 days. From the results it was concluded that anti-arthritic activity may be due to the presence of phytoconstituents such as alkaloids, steroids, flavonoids, phenolic compounds and glycosides specifically iridoid glycosides [26, 27].

***Strychnos potatorum*:** The study was carried out to evaluate the effect of the aqueous extract (SPE) and the whole seed powder (SPP) of *Strychnos 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. 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/ in both developing and developed phases of arthritis [28, 29].

***Vernonia anthelmintica*:** The experiment was undertaken to investigate the antiarthritic activity of ethanolic extract of seeds of *Vernonia anthelmintica* (EVA). The effect of EVA was evaluated for chronic inflammation in complete Freud's adjuvant (CFA) induced arthritis in rats. Further, the biochemical, histopathological and radiographic evaluation was performed. The treatment with EVA 250mg/kg showed significant prevention of the paw edema on 28th day, whereas the treatment with EVA 500 mg/kg showed significant prevention in the paw edema during 21st & 28th day as compared to the arthritis control. Methotrexate 0.75 mg/kg showed significant prevention in the paw edema on 21st & 28th day as compared to the arthritis control.

Percent inhibition of paw edema by methotrexate, EVA 250 and EVA 500 on 21st day was 72.72, 5.05 and 45.95 while on 28th day it was 97.00, 64.70 and 89.83. The ethanolic extract of seeds of *Vernonnia anthelmintica* may possibly act by decreasing synthesis or release of T cell mediators such as IL, TNF- α as evident from decreased in spleen weight. These effects may be attributed to phytochemicals alkaloids, steroids, flavonoids, triterpenoids, polyphenol and fatty acids present in EVA [30].

CONCLUSION : Arthritis stand as one of the foremost health troubles worldwide, leading cause of disability in western and developing countries. Therapies developed along the principles of western medicine are often limited in efficacy, carry the risk of adverse effects, and are often too costly, especially for the developing world. Therefore, treating arthritis with plant-derived compounds which are accessible and do not require laborious pharmaceutical synthesis seems highly attractive. In this review article, an attempt has been made to compile the reported antiarthritic plants from India and may be useful to the health professionals, scientists and scholars working in the field of pharmacognosy and therapeutics to develop evidence-based alternative medicine to cure different kinds of arthritis in man and animals.

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