



AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: <http://www.ajptr.com/>

Role of Herbs in the Treatment of Rheumatoid Arthritis

Fatima Grace Xavier^{1*}, Joan Vijetha Ratchagar¹, Shanmuganathan Seetharaman¹,
Shanthi Sivasubramanian¹, Latha Somasundaram¹,

1. Faculty of Pharmacy, Sri Ramachandra University, Porur, Chennai – 600116

ABSTRACT

Rheumatoid Arthritis is an autoimmune inflammatory disease where the immune system of the body which normally protects the body by fighting against infection and diseases instead targets the body. The immune system attacks the tissue that lines the joints causing pain, swelling and stiffness in the joint and affecting the ability to work properly. Early treatment to avoid permanent joint damage is the key for preventing disability and progression. The treatment for Rheumatoid Arthritis combines many approaches with drug, exercise, change in lifestyle etc. It also includes alternative methods i.e with herbal medicines. Many plants and plant products have been proven and many are under scientific exploration to develop a novel therapeutic agent for Rheumatoid Arthritis.

Keywords: Herbs, Rheumatoid Arthritis, Medicine, Immunity, Inflammation.

*Corresponding Author Email: santagracek@gmail.com

Received 17 January 2014, Accepted 23 January 2014

INTRODUCTION

Rheumatoid Arthritis is a chronic inflammatory condition which affects not only the joints but also other connective tissues in the body¹. Arthritis is a leading cause of disability in most of the adults in the world. This limits the day to day activities for billion of people. About 2-5% of the world population is affected by arthritis has been reported by WHO.

Generally for the treatment of Rheumatoid Arthritis, NSAIDS are prescribed which on long term use leads to hepatic or renal failure and also may cause others adverse effects. These drugs get accumulated in the tissues and produce toxic effect like retinal damage, rashes, irritable bowel syndrome, corneal opacity, myopathy, neuropathy, etc².

When the treatment profile includes just the synthetic medicine all these previous effects are possible but if the treatment becomes prevention as it is said prevention is better than cure their effects can be minimised³.

Prevention can be done by using natural ingredients. India is a rich source of herbal plants. The knowledge of plants traditionally is the main reason for most of the medicine & food used in modern society. Herbs are being used since long time as food and as a primary tool for maintaining health and aiding in recovery of disease. The treatment modality for many chronic ailments like diabetes, arthritis etc. includes long term consumption of both ayurvedic and allopathic system of medicine. Modern science and technology can be used to make herbal medicines into patient compliant dosage forms. Consumers now a days are highly attracted towards natural ingredient in food, drug and cosmetics because it is believed that anything natural will be devoid of side effects and safe⁴.

Rheumatoid Arthritis: Signs and Symptoms

Rheumatoid Arthritis is a chronic, autoimmune, systemic inflammatory disorder or disease targeting the synovial joints.

The clear idea of the pathogenesis is not yet well understood. Even then it has been reported that proinflammatory cytokines like Tumour Necrosis Factor- α (TNF- α), Interleukin-(1L)-1 β and IL6 are important mediators of the disease. It is also reported that free radical generation makes the disease worse and leads to damage of bones and cartilages. The destruction of joints that occurs with severe Rheumatoid Arthritis results from inflammation of the synovial membrane. Recurrent or persistent inflammation leads to permanent damage of the cartilage joint, bones, ligaments and tendons. The inflammatory process also includes other tissues like blood vessels, skin, nerves, muscles, heart and lungs. This results in painful joints, loss of mobility, generalised

soreness and depression⁵.

Various Signs and Symptoms of Rheumatoid Arthritis are

- 1) Gradual increase in joint pain, ache and stiffness.
- 2) Followed by joint swelling, redness and warmth.
- 3) Initially single joint may be inflamed.
- 4) Symptoms worst in morning and decrease later.
- 5) Distressing fatigue.
- 6) Sleeplessness.
- 7) Vasculitis.
- 8) Inflammation of blood vessels, skin rashes, ulcers, gangrenes.
- 9) Pericarditis, Pleurisy, nerve damage, dry eyes and mouth.
- 10) Enlargement of spleen and lymph nodes.

Treatment of Rheumatoid Arthritis

The treatment modality for Rheumatoid Arthritis usually combines various approaches and the ultimate aim is to relieve pain, reduce joint swelling, prevent or slow down joint damage and improve physical function and well-being⁶. It includes use of

- Conventional medicines
- Biological response modifiers
- Gene therapy
- Alternative approaches

Conventional medicines

Previous treatment strategies involved initial management of Rheumatoid Arthritis by using NSAIDs. These drugs elicit their effect by decreasing COX activity, blocking the downstream production of prostanoids and eicosanoids. The next step was to use DMARDs [Disease Modifying Anti Rheumatoid Drugs]. The therapy with DMARDs showed decrease in inflammatory markers like Erythrocyte Sedimentation Rate and swollen joint counts. DMARDs and immunosuppressives were given as combination therapy⁷.

These drugs or the combination therapy may lead to hepatic enzyme disturbances and many other adverse effects like weight loss, diarrhoea, rashes, alopecia, etc.

Biological response modifiers

Researchers have brought much new information in the recent years but the complete treatment for Rheumatoid Arthritis yet remains a challenge. The research on cytokines led to the concept

on introduction of anticytokine therapy for the treatment of Rheumatoid Arthritis. In the year 1992, the first Biological response modifiers, Etanercept and Infliximab were approved. Etanercept is the recombinant form of the p75TNFR-II. Infliximab is a monoclonal antibody directed against TNF- α . Both the drugs are designed to bind with TNF α and thereby decrease bioavailability⁸.

Gene therapy

Apart from the other treatment strategies, researchers are now trying to cure Rheumatoid Arthritis using gene therapy but it has not been fully explored.

Alternative approach

There are many limitations and risks in the conventional therapy of Rheumatoid Arthritis. The drugs show many adverse effects.

The alternative approach commonly used in the treatment of Rheumatoid Arthritis involves

- * Exercise and physiotherapy
- * Dietary modification
- * Nutritional supplements
- * Natural remedies or Botanicals

The response to the treatment varies from patient to patient. These alternative approaches are used as adjunct with the main therapy or alternative to the conventional therapy and most of these treatments are free of adverse effects.

HERBS IN TREATMENT OF RHEUMATOID ARTHRITIS

Decades of years before, when the synthetic drugs were not discovered, man completely depended on the natural source. A few examples for plants which possess anti Rheumatoid Arthritis potential are listed here in the article.

- **Aloe vera**

Commonly known as curacao aloe or lily of the desert, is obtained from *Aloe barbadensis* of the family Liliaceae. Aloe vera contains Anthraquinone, anthracene, cinnamic acid, anthranillic acid which are responsible for this activity and mainly anthraquinone supports for arthritis activity⁹. Complete Freund's adjuvant induced arthritis has been reduced in Sprague Dawley rats by topical application of Aloe Vera extract¹⁰.

- **Cardiospermum halicacabum**

This plant is commonly called as Balloon vine, mudakattan. The folklore claims tells that it is used in arthritis. It is used as a food to prevent from arthritis. Even now it is used to

prepare dosas. It is proven that it decreases the Complete Freund's adjuvant induced arthritis in Sprague Dawley rats¹¹.

- **Pepper**

It is cultivated mostly in South India. It is obtained from *Piper Nigrum* of Piperaceae family. The main constituent of pepper is piperine and is found that when it is administrated orally at a dose of 20,100 mg/kg/day, decreases the arthritis symptoms in carrageenan include paw arthritis^{12,13}.

- **Ginger**

Ginger is obtained from *Zingiber officinale* belonging to the family Zingiberaceae. The oil of ginger contains monoterpene hydrocarbon, sesquiterpene hydrocarbons, and oxygenated monoterpene. Ginger is recommended by most of the physicians as one of effective pain remedy for arthritis¹⁴⁻¹⁷.

- **Turmeric**

It is obtain from *Curcuma longa* of the family Zingiberaceae. It is commonly called as Indian saffron. Curcumin, a main constituent of turmeric is proved to possess anti-inflammatory potential. It is also found to possess wound healing, hepatoprotective and neuroprotective property. A research has been reported that 4mg total curcuminoids per kg per day inhibited inflammation of joints in both acute and chronic arthritis¹⁸⁻²¹.

- **Green Tea**

Camellia Sinensis belonging to the family Theaceae is the source of green tea. The active constituents responsible for its activity are catechins and flavanols. The most important catechin is epigallocatechin. Inflammatory mediators like COX2, IFN γ and TNF α was reported to decrease in collagen induced arthritis in mice when fed with green tea and there was decreased level of total immunoglobulin and type II collagen specific IgG in the arthritic joints of mice^{22,23}.

- **Ashwagandha**

It is also known as Indian Ginseng obtained from *Withania somnifera* of the family Solanaceae. It is used in Indian traditional system of medicine. It contains withanine, tropine, somniferine, somnine, etc. In Complete Freund's adjuvant induced arthritis, oral administration of root powders of *Withania somnifera* showed anti-arthritic activity²⁴⁻²⁶.

- ***Terminalia paniculata***

It belongs to family Combretaceae. It is reported to contain alkaloids, triterpenes,

flavonoids, saponins, tannins, etc. In rats with Complete Freund's adjuvant induced arthritis, 200mg/kg aqueous extract of *Terminalia Paniculata* showed anti-arthritic activity²⁷⁻²⁹.

- ***Terminalia chebula***

It is also called as Haritaki, Myrobalan of the family Combretaceae. It contains tannic acid, chebulinic acid, anthraquinone, sennosides. Anti-arthritic activity in Complete Freund's adjuvant or formaldehyde induced arthritis has been found significant with hydro alcoholic extract. The anti-arthritic activity was found due to the immunomodulatory effect on proinflammatory cytokine expression in the synovium³⁰⁻³².

- **Mango**

Mangifera indica belongs to the family Anacardiaceae is a species of mango. The constituents present are mangiferin, isomangiferin, gallic acid, polyphenols, etc. The methanolic extract of *Mangifera indica* showed anti-inflammatory activity and reported to show significant decrease in arthritic index, paw edema, rheumatoid factor³³⁻³⁵.

- ***Ficus bengalensis***

Commonly called as Banyan tree belongs to the family Moraceae. It contains flavonoids, tannins, saponins, steroids, alkaloids, glycosides etc. The methanolic extract produce significant decrease on edema in Complete Freund's adjuvant induced arthritis in rats^{36,37}.

- ***Tinospora cordifolia***

It is commonly called as Guduchi belonging to the family Menispermaceae. The main constituents are tinosporine, tinosporide, tinosporaside, cordifolide, cordifol, heptacosanol, clerodane furanoditerpene, columbin, β -sitosterol. The plant is proven to increase the immune system and body's resistance to infections. A decrease in paw volume in collagen induced arthritic rats was found with a dose of 100mg/kg of the plant extract^{38,39}.

- ***Cedrus deodara***

Commonly called as Devadaru, Cedar belongs to the family Pinaceae. It has markedly decreased the polyarthritic phase as measured by the paw swelling on Complete Freund's adjuvant induced arthritic rats. In ayurvedic medical practice it is being used for the treatment of inflammation and Rheumatoid Arthritis⁴⁰.

- ***Vitex negundo***

It is a large aromatic shrub belonging to the family Verbanaceae. A tincture of fresh

berries are used for treatment of paralysis, pain in limbs, rheumatic disorder, weakness etc. In carrageenan induced hind paw edema, inhibition of paw edema is found with petroleum ether extract^{41,42}.

- ***Barringtonia racemosa***

It belongs to the family Lecythydaceae. It is commonly called as powder puff tree. Main constituents present in this plant are stigmasterol, bartogenic acid, dihydromyricetin etc. of which bartogenic acid is responsible for Rheumatoid Arthritis activity^{43,44}.

- ***Leucas aspera*:**

Thumbai of the family Lamiaceae has got many pharmacological activities. It is proved that the ethanolic extract of *Leucas aspera* shows anti-rheumatoid activity in Complete Freund's adjuvant induced arthritis in rats^{45,46}.

- ***Hemidesmus indicus***

Commonly known as Indian sarsaparilla belongs to the family Asclepiadaceae. The principle constituents are coumarin, triterpenoid, saponin. Traditionally it is used in the treatment of Rheumatoid Arthritis. Reduction in paw volume and paw thickness was reported with oral treatment of ethanolic extract of *Hemidesmus indicus* compared with standard diclofenac sodium^{47,48}.

- ***Strychnos potatorum***

It belongs to the family Loganiaceae. It is commonly called as Tetrankottai. It contains a major alkaloid called diaboline. The extract of *Strychnos Potatorum* showed decrease in paw volume in Complete Freund's adjuvant induced arthritis in rats at a dose of 200mg/kg p.o. Traditionally, this plant is used in treatment of Rheumatoid Arthritis⁴⁹.

- ***Cleome gynandra***

This plant has a folklore claim of being used in the treatment of Rheumatoid Arthritis. It is commonly called as spider flower, cat's whiskers of the family Capparaceae. Ethanolic extract of the plant is found to possess both acute and chronic anti-inflammatory potential with Complete Freund's adjuvant induced arthritis in rats⁵⁰.

- ***Saraca osaka***

This plant belongs to the family Caesalpiniaceae usually found in hill regions. It is used in treatment of Rheumatoid Arthritis and many other diseases. The paw thickness in Complete Freund's adjuvant induced arthritis in rats reduced with the methanolic extract of *Saraca osaka*^{51,52}.

CONCLUSION

The present article has been aimed to reveal few plants with anti-arthritic potential. There are many plants widely spread all over our country and many are found to possess Anti arthritic potential and researches are exploring it. As the synthetic counterparts have many adverse effects, it is always good to use plant based formulations for the treatment of Rheumatoid Arthritis which will be devoid of side effects. This review article was focused to explore the plants with anti arthritic activity from the folklore claims.

ACKNOWLEDGEMENT

The authors are grateful to the management of SRU for their constant support and encouragement.

REFERENCES

1. Herman CJ, Allen P, Hunt WC, et al. Use of complementary therapies among primary care clinic patients with arthritis. *Preventing Chronic Disease*; 2004;1(4):A12.
2. Arend W. The innate immune system in rheumatoid arthritis. *Arthritis Rheum*.2001; 44:2224–2234.
3. Soden M., Rooney M., Cullen A., Whelan A., Feighery C., Bresnihan B. Immunohistological features in the synovium obtained from clinically uninvolved knee joints of patients with rheumatoid arthritis. *Br. J. Rheumatol*. 1989;28: 287–292.
4. Fang Y., Yang S., Wu G. Free radicals, anti-oxidants, and nutrition. *Nutrition*.2002;18: 872–879.
5. Hadjigogos K. The role of free radicals in the pathogenesis of rheumatoid arthritis. *Panminerva Med*. 2003; 45: 7–13.
6. Soeken K., Miller S., Ernst E. Herbal medicines for the treatment of rheumatoid arthritis: a systematic review. *Rheumatology*. 2003; 42: 652–659.
7. Ernst E. Prevalence of use of alternative medicine: a systematic review. *Bull. World Health Organ*. 2000; 78: 252.
8. Chamundeeswari D., Vasantha J., Gopalakrishnan S., Sukumar E. Free radical scavenging activity of the alcoholic extract of *Trewia polycarpa* roots in arthritic rats. *J. Ethnopharmacol*. 2003; 88: 51–56.
9. Davis RH, Agnew PS and Shapiro E Antiarthritic Activity of Anthraquinones found in *Aloe vera* for podiatric medicine. *J American Podiatric Medical Assoc* 1986; 76(2): 1-8.

10. Joseph B and Raj SJ Pharmacognostic and pharmacology properties of *Aloe vera*. Int J Pharma Sci Review Res 2010; 4(2): 106-109.
11. Kirtikar KR, Basu BD. Indian Medicinal Plants. 2nd ed. New Delhi: Published by Bishen Singh; 1933:2390–2392
12. Agarwal SS, Paridhavi M. Herbal Drug Technology. Reprint 2009.p.39
13. Bang J.S, Oh Dh, Choi HM, Kim JY et al, Anti Inflammatory and antiarthritic effect of piperine in Human interleukin 1 β stimulated fibroblast like synoviocytes and in rat arthritis models. Arthritis Research and Therapy 2009;11(20):1-9.
14. Rehman R, Akram M, Akhtar N, Jabeen Q, Saeed T, Shah SMA et al *Zingiber officinale* Roscoe (pharmacological activity). J Medicinal Plants Research 2011; 5(3): 344-348.
15. Zakeri Z, Izadi S, Bari Z, Soltani F, Narouie B, Rad MG Evaluating the effects of ginger extract on knee pain, stiffness and difficulty in patients with knee osteoarthritis. J Medicinal Plants Research 2011; 5(15): 3375-3379.
16. ICMR bulletin, Ginger: Its role in xenobiotic metabolism 2003; 3(6).
17. Feng T, Su J, Ding ZH, Zheng YT, Li Y, Leng Y and Liu JK Chemical Constituents and Their Bioactivities of “Tongling White Ginger” (*Zingiber officinale*). Journal of Agricultural and Food Chemistry 2011; 9(21): 11690-11695
18. Kohli K, Ali J, Ansari MJ, Raheman Z Curcumin: A natural anti-inflammatory agent. Indian Journal of Pharmacology 2005; 37(3); 141-147.
19. Funk JL, Oyarzo JN, Frye JB, Chen G, Lantz RC, Jolad SD et al Turmeric extracts containing curcuminoids prevents experimental rheumatoid arthritis. NIH Public Access 2006; 69(3): 351-355.
20. Alternative Medicine Review Monographs, *Curcuma longa*.p.119-125.
21. Vaidya ADB Reverse pharmacological correlates of ayurvedic drug action. Indian J Pharmacology 2006; 38(5): 311-315.
22. Ahmed S Green tea polyphenol epigallocatechin 3-gallate in arthritis: progress and promise. Arthritis research & therapy 2010; 12(2): 1-9.
23. Chopade VV et al, Green Tea (*Camellia sinensis*), Chemistry, traditional, medicinal uses and its pharmacological activities- A review. Pharmacognosy review 2008; 2(3): 157-162.
24. Mirjalili MH, Moyano E, Bonfill M, Cusido RM and Palajon J Steroidal Lactones from *Withania somnifera*, an ancient plant for novel medicines. Molecules 2009; 14: 2373-2393.

25. Kokate CK. Text book of Pharmacognosy. 39 ed. Nirali parkashan; 2007.p. 437.
26. Kumar AM Ethnomedicinal plants as anti-inflammatory and analgesic agents. Research Signpost 2010; 267-293
27. Jean Bruneton. Text book of Pharmacognosy, Phytochemistry of Medicinal Plants. 2nd ed. P. 299-301.
28. Talwar S, Nandakumar K, Nayak PG, Bansal P, Mudgal J, MorV et al Anti-inflammatory activity of *Terminalia paniculata* bark extract against acute and chronic inflammation in rats. J Ethnopharmacology 2011; 134(2); 323-328.
29. Arya V, Gupta VK, Kaur R A review on plants having anti-arthritic potential. Int J Pharma Scie Review Res 2011; 7(2): 131-136.
30. Singh MP and Sharma CS Pharmacognostical evaluation of *Terminalia Chebula* fruits on different market samples. Int J ChemTech Res 2010; 2(1): 57-61.
31. Nair V, Singh Surender, Gupta YK Anti-arthritic and disease modifying activity of *Terminalia chebula* Retz., in experimental models. J Pharm Pharmacol 2010; 62(12): 1801–1806.
32. Chang CL and Lin CS Phytochemical Composition, Antioxidant Activity, and Neuroprotective Effect of *Terminalia chebula* Retzius Extracts. Evidence-Based Complementary and Alternative Medicine 2012; 2012:1-7.
33. Bárbara BG, Garrido G, Delgado R, Bosch F and Rabi MD A *Mangifera indica* L. extract could be used to treat neuropathic pain and implication of Mangiferin. Molecules 2010; 15(12): 9035-45.
34. Garrido, Gonzalez, Lemus, Garcia, Lodeiro, Quintero et al In vivo and in vitro anti-inflammatory activity of *Mangifera indica* L. extract. Molecules 2004; 50(2): 143-149.
35. Garrido, González, Delporte, Backhouse, Quintero, Nunez-Selles AJ et al Analgesic and anti-inflammatory effects of *Mangifera indica* L. extract (Vimang). Molecules 2001; 15(1): 18-21.
36. Manocha N, Samanta KC, Sharma V Evaluation of anti rheumatic activity of extract of stem bark of *Ficus bengalensis*. Journal of global pharma technology 2011; 3(3): 31-37
37. Patil VV and Patil VR *Ficus bengalensis* Linn.-an overview. Int J Pharma Bio Sci 2010; 2; 1-11.
38. Paval J, Kaitheri SK, Kumar A, Govindan S, Mohammed CA, Kumar RS et al Anti-arthritic activity of the plant *Tinospora cordifolia* wild. J Herbal Medicine and Toxicology 2011; 5 (1): 11-16.

39. Singh SS, Pandey SC, Srivastava S, Gupta VS, Patro B, Ghosh AC Chemistry and medicinal properties of *Tinospora cordifolia*. Indian J Pharmacol 2003; 35: 83-91.
40. Chandur U, Shashidhar S, Chandrasekar SB, Rao NM Studies of preliminary phytochemical and Anti-arthritis activity of heart wood of *Cedrus deodar* (Roxb.). Res J Pharma Biological Chemical Sci 2011; 2(3): 654-660
41. Vishwanathan S and Basavaraju R A Review on *Vitex negundo* L. – A medicinally Important Plant. Eur J Biological Sci 2010; 3 (1): 30-42.
42. Subramani J, Damodaran A, Kanniappan M, and Mathuram LN Anti-inflammatory effect of petroleum ether extract of *Vitex negundo* leaves in rat models of acute and subacute inflammation. Pharmaceutical Biology 2009; 47(4): 335-339
43. Sun HY, Long LJ, Wu J Chemical constituents of mangrove plant *Barringtonia racemosa*. J Chinese Medicinal Materials 2006; 29(7): 671-672.
44. Behbahani M, Ali AM, Muse R and Mohd NB Anti-oxidant and anti-inflammatory activities of leaves of *Barringtonia racemosa*. J Medicinal Plants Res 2007; 1(5):95-102.
45. Prajapati MS, Patel JB, Modi K, Shah MB *Leucas aspera*: A review. Pharmacognosy Review 2010; 4 (7): 85-87.
46. Kripa KG, Chamundeeswari D, Thanka J, Reddy C UM Effect of hydro alcoholic extract of aerial parts of *Leucas aspera* (Willd.) link on inflammatory markers in complete Freund's adjuvant induced arthritic rats. Int J Green Pharm 2010; 4(4): 281-287
47. Rajan S, Shalini R, Bharathi C, Aruna V, Elgin. A Pharmacognostical and Phytochemical Studies on *Hemidesmus Indicus* Root. Int J Pharmacognosy Phytochemical Res 2011; 3(3): 74-79
48. Mehta A, Sethiya NK, Mehta C, Shah GB Anti-arthritis activity of roots of *Hemidesmus indicus* R.Br. (Anantmul) in rats. Asian Pac J Trop Med 2012; 5(2): 130-5.
49. Ekambaram S, Perumal SS, Subramanian V Evaluation of antiarthritic activity of *Strychnos potatorum* Linn seeds in Freund's adjuvant induced arthritic rat model BMC complementary and alternative medicine 2010; 10(1): 1-9.
50. Narendhirakannan RT, Subramanian S and Kandaswamy M Free radical scavenging activity of *Cleome gynandra* L. leaves on adjuvant induced arthritis in rats. Molecular and Cellular Biochemistry 2005; 276(1-2): 71-80.
51. Saravanan S, Babu NP, Pandikumar P, Ignacimuthu S Therapeutic effect of *Saraca asoca* (Roxb.) Wilde on lysosomal enzymes and collagen metabolism in adjuvant induced

arthritis. *Inflammo pharmacology* 2011; 19(6): 317-25. 4 Suppl 1:96-99.

52. Pradhan P, Joseph, L., Gupta V, Chulet R, Arya H, R. Verma, Bajpai A *Saraca asoca* (Ashoka): A Review. *J Chemical Pharma Res* 2009; 1(1): 62-71.

AJPTR is

- Peer-reviewed
- bimonthly
- Rapid publication

Submit your manuscript at: editor@ajptr.com

