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Herbal Medicine – A natural cure to arthritis

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Arthritis is a chronic disease condition and a major cause of disability throughout the world. The pathophysiological phenomenon of arthritis involves dysregulation of pro-inflammatory cytokines and pro-inflammatory enzymes which results in elevated levels of prostaglandins, leukotriene and nitric oxide; additionally, there is also expression of an adhesion molecule, matrix metalloproteinase and hyper proliferation of synovial fibroblasts. Regulation of all these factors is maintained through transcription factor called nuclear factor $\kappa\beta$. Thus, agents that can suppress either one or multiple of these pathological modulators could serve as a potential treatment for arthritis. As synthetic molecules have not been proven to provide adequate therapy due to toxicity, side effects or reappearing of symptoms on discontinuation, there is urgent need to have alternative options for arthritis. A large flora of herbal medicines is available in traditional medicine and basic scientific research has provided an understanding of the efficacy of these remedies in treating arthritis. In recent years, there has been boom in research and industries focusing on herbal remedies to treat a variety of diseases including arthritis. Several developments in clinical studies in carefully designed clinical trials have made the way easier to include herbs as arthritis therapy. This review is focused on the potential role of herbs in treating arthritis and prospects for the future.

Keywords: Herbs, Cytokines, Matrix metalloproteinase, Nitric oxide, Complementary and alternative medicine, Natural cure, Arthritis.

IPC code; Int. cl. (2011.01) –A61K 36/00, A61P 19/02

Introduction

Arthritis is a musculoskeletal system disorder following mechanical and biological events that destabilize normal coupling between degradation and synthesis within articular cartilage¹. Arthritis can affect individuals of any age but is more predominant in the age range of 25 and 50 years with a peak in the age range of 40-50 years. There are about 100 types of arthritis of which the most commonly occurring include osteo-arthritis, rheumatoid arthritis, ankylosing spondylitis, systemic lupus erythematosus and juvenile arthritis². It is estimated that the highest incidences of arthritis are found in Indians followed by Americans. The prevalence of main two types of arthritis that is osteo-arthritis and rheumatoid arthritis in Indian population is 22-39 and 5%, respectively³⁻⁵. The joints most commonly affected by arthritis are weight bearing joints such as feet, knees, hips, spine and other joints which finally results in mainly

inflammation, pain, joint stiffness and loss of mobility⁶. Along with weight bearing joints, arthritis also affects peri-articular bone, synovial joint lining and adjacent supporting connective tissue elements⁶. The worsening condition of arthritis requires proper therapy for arthritis along with better economical consideration for chronic treatment. Even though synthetic drugs are available in the market for the treatment of arthritis their use is limited due to serious side effects upon chronic use⁴.

Traditionally, herbal plants were used both externally as well as internally for treating inflammatory conditions like arthritis (Table 1 & Table 2)^(Ref.7-17). The positive influence of herbal medicine in modifying pathophysiology of arthritis has resulted in a substantial increase in their use as a treatment for arthritis. While an abundant number of herbal drugs are available to effectively reduce chronic joint inflammation in case of arthritis there should be emphasis to prove their therapeutic effects through basic scientific research. This paper deals with the review on herbs showing potential for the treatment of arthritis.

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Table 1—Traditionally used plants for arthritis (externally)

Plant	Family	Part used in arthritis	Reference
<i>Abutilon indicum</i> L.	Malvaceae	Leaves	7
<i>Acacia leucophloea</i> Willd.	Mimosaceae	Bark	8
<i>Acalypha indica</i> L.	Euphorbiaceae	Whole plant	9
<i>Adansonia digitata</i> L.	Malvaceae	Leaves	8
<i>Allium cepa</i> L.	Liliaceae	Roots	8
<i>Alangium salviifolium</i> (Linn.f.) Wang.	Alangiaceae	Roots	10
<i>Anisomeles malabarica</i> R. Br.	Lamiaceae	Leaves	8
<i>Bacopa monnieri</i> (L.) Penn.	Scrophulariaceae	Leaves	11,12
<i>Brassica alba</i> (L.) Rabenh.	Brassicaceae	Seed	13
<i>Cadaba indica</i> Lam.	Capparidaceae	Leaves	8
<i>Calophyllum inophyllum</i> L.	Clusiaceae	Seed	8
<i>Cassia fistula</i> L.	Caesalpinaceae	Fruit	8
<i>Peucedanum graveolens</i> Benth.	Apiaceae	Seed, roots	8
<i>Pongamia glabra</i> Vent.	Fabaceae	Roots	16
<i>Salvadora indica</i> Royle	Salvadoraceae	Fruit, flower	8
<i>Tamarindus indica</i> L.	Caesalpinaceae	Leaves	8
<i>Vitex negundo</i> L.	Verbenaceae	Leaves	8
<i>Ziziphus jujuba</i> Mill.	Rhamnaceae	Root, bark	14

Table 2—Traditionally used plants for arthritis (Internally)

Plant	Family	Part used in arthritis	Reference
<i>Argyreia speciosa</i> Sweet	Convolvulaceae	Roots	10
<i>Asarum europaeum</i> L.	Aristolochiaceae	Roots	8
<i>Azima tetraacantha</i> Lam.	Salvadoraceae	Leaves, roots	8
<i>Boerhaavia diffusa</i> L.	Nyctaginaceae	Roots	14
<i>Cardiospermum helicacabum</i> L.	Sapindaceae	Leaves	10,11
<i>Celastrus paniculatus</i> Willd.	Celastraceae	Seed	8
<i>Cephalandra indica</i> Naud.	Curcubitaceae	Roots	8
<i>Citrullus colocynthis</i> Schard.	Cucurbitaceae	Roots	8
<i>Cleodendrum phlomidis</i> L.	Verbenaceae	Leaves	9
<i>Cleome viscosa</i> L.	Capparidaceae	Leaves	8
<i>Cocculus villosus</i> DC.	Menispermaceae	Roots	8
<i>Corallocarpus epigaeus</i> Benth. ex Hook. f.	Cucurbitaceae	Roots	8
<i>Cuminum cyminum</i> L.	Apiaceae	Seed	9
<i>Curcuma zedoaria</i> Rosc.	Zingiberaceae	Roots	8
<i>Daemia extensa</i> R. Br.	Asclepiadaceae	Leaves, roots	15,16
<i>Enicostemma littorale</i> Blume	Gentianaceae	Roots	8,10
<i>Glycyrrhiza glabra</i> L.	Fabaceae	Roots	8
<i>Gmelina asiatica</i> L.	Verbenaceae	Roots	10
<i>Indigofera aspalathoides</i> Vahl. ex DC.	Papilionaceae	Roots	8
<i>Myristica fragrans</i> Houtt.	Myristicaceae	Fruit	8
<i>Ocimum gratissimum</i> L.	Lamiaceae	Leaves, roots	8
<i>Pavonia zeylanica</i> Cav.	Malvaceae	Whole plant	8
<i>Plumbago zeylanica</i> L.	Plumbaginaceae	Roots	14
<i>Randia dumetorum</i> Lam.	Rubiaceae	Bark, roots	8
<i>Ricinus communis</i> L.	Euphorbiaceae	Seed	9
<i>Semecarpus anacardium</i> Linn.f.	Anacardiaceae	Seed	9,17
<i>Sida acuta</i> Burm.f.	Malvaceae	Roots	10
<i>Smilax china</i> L.	Liliaceae	Roots	8
<i>Terminalia chebula</i> Retz.	Combretaceae	Seed	9
<i>Tribulus terrestris</i> L.	Zygophyllaceae	Whole plant	8
<i>Withania somnifera</i> Dunal	Solanaceae	Roots	8,10,12
<i>Zingiber officinalis</i> Roxb.	Scitamineae	Roots	12,16

Medicinal plants for arthritis treatment

Complementary/alternative medicine use is prevalent in medicine even in USA¹⁸. Today's present scenario reveals that herbal therapies contribute approximately 25% of currently used crude drugs and another 25% is derived from chemically altered natural products¹⁹. Efficacy of these herbs is attributable to complex phytochemicals, viz. alkaloids, glycosides, flavonoids, tannins, resins and many other components which are also reported to have different pharmacological activities. There are many plants which can treat arthritis, few of them which have been recently claimed for their effectiveness are: *Bidens pilosa* L., *Boerhaavia diffusa* L., *Boswellia serrata* Roxb., *Cayaponia tayuya* (Vell.) Cogn., *Maytenus krukovii* A.C. Sm., *Mikania guaco* Humb. & Bonpl., *Persea americana* Mill., *Pongamia pinnata* (L.) Pierre, *Smilax officinalis* Kunth, *Terminalia chebula* Retz. and *Uncaria tomentosa* (Willd. ex Schult.) DC.

Pongamia pinnata (L.) Pierre (Family-Fabaceae; Karanja)²⁰

It is medium sized glabrous, perennial, nitrogen fixing tree, grows in the littoral regions of South eastern Asia and Australia²¹. Seeds, roots, flowers, bark and leaves of this tree are used for medicinal purpose²². Seeds contains phytochemicals such as sterol and its derivatives, while leaves and stem contains flavone and chalcone derivatives like pongone, galbone, pongalabol, pongagallon A & B²³. As a crude drug this plant is traditionally used in tumors, piles, skin diseases, wounds and ulcers²¹. Pharmacologically it has been studied for its anti-ulcer, anti-diarrhoeal, antioxidant, anti-plasmodium, anti-hypoglycemic, anti-viral, anti-bacterial and anti-inflammatory activities^{23, 24}. Anti-arthritis activity of Karanja has been proven by using different animal models like carrageenan induced paw edema and formaldehyde induced paw edema²².

Boerhaavia diffusa L. (Family-Nyctaginaceae; *Punarnava*)

It is creeping, ascending weed, having a height of about one meter with spread and occurs in all seasons of the year²⁵. It is distributed throughout regions of the world including Australia, China, Egypt, and Pakistan, Sudan, Srilanka, South Africa, USA and

other countries of Middle East²⁵⁻²⁷. Leaves, seeds and roots of the plant are used for medicinal purposes²⁶. Many phytochemicals are present in *Punarnava* which include glycosides, alkaloids, steroids, triterpenoids and flavonoids and amongst these punarnavoside, boeravinone G & H are prominent^{26, 27}. In traditional systems of medicine like Ayurveda and Unani, roots of *Punarnava* is described for its use in dyspepsia, jaundice, entanglement of spleen, abdominal pain and stress, while seeds are used as tonic, expectorant, carminative, lumbago, scabies, blood purifier and muscular pain^{25,26}. Alcohol extract of the *Punarnava* have shown various pharmacological activities like anti-bacterial, hypoglycemia, anti-proliferative, anti-estrogenic, anti-stress and immunomodulatory activity while aqueous extract had been studied for its hepatoprotective activity²⁸. *Punarnava* has good free radical and nitric oxide scavenging activity. In addition to these effects its anti-inflammatory activity aids in its use in arthritis²⁷.

Terminalia chebula Retz. (Family-Combretaceae; *Haritaki*)²⁹

It is medium to large deciduous tree having height of approx. 30 m with spread branches. It is native to Asian countries mainly India, Pakistan, Nepal and South China. Fruits of this plant are used for medicinal purpose³⁰. Chemical constituents of *T. chebula* include tannins, alkaloids, flavonoids, terpenoids, steroids, carbohydrate, protein and saponins³¹. *Haritaki* is a part of Ayurvedic formulation '*Triphala Churna*' and used for sinusitis, allergies, piles, constipations, high cholesterol, rheumatism, mal absorption and blood purification³². Plant extract has been proved for its antibacterial and anti-convulsant activity^{30,31}. One of the chemical moieties present in *T. chebula* has been found to show effective against enzymes like elastase and hyaluronidase as well it also affects collagen-II expression³³. This herbal drug has also been proven for its anti-arthritis activity by Freund's adjuvant induced arthritis model³⁴.

Persea americana Mill. (Family-Lauraceae; Avocado)

It is medium sized evergreen tree having 10-20 cm long, elliptic leaves and it is found in many places all around the world including North, Central and South America and in East and South East Asia³⁵. Almost 30 to 40 chemical compounds are found in Avocado but

among those the major compounds are alkanols, terpenoid glycosides and furan containing derivatives, flavonoid and coumarin which are having many medicinal properties³⁶. An aqueous extract of leaves of this plant has been shown to possess antihypertensive activity³⁷ and also the oil extracted from seed has been used for treatment of skin eruptions. In addition to these properties its pharmacological profile includes vasorelaxant, analgesic and anti-inflammatory activity, anti-convulsant activity, anti-viral, wound healing, hepatoprotective, anti-oxidant and hypoglycemic activity³⁶.

In animal models it has been found that Avocado decreases cartilage breakdown by reducing collagen degradation and also reduces chondrocyte hyperplasia as well as its cloning. Treatment with Avocado reduces the synthesis of proteases like MMP-13 in deeper zone of cartilage³⁸. Avocado also possesses inhibitory activity on inducible nitric oxide synthase (iNOS) enzyme and thus is very useful in arthritis³⁸.

Uncaria tomentosa Willd. (Family-Rubiaceae; Cat's Claw)

It is found in South America and tropical Amazon rainforest³⁹ and grows up to 30 m, having elliptic leaves with smooth edge. Bark and roots are normally used for medicinal purposes^{40,41}. Chemical constituents found in this plant are oxindole alkaloid, quinovic acid, glycosides, plant sterol and catechins⁴². In addition to this it has been proved for their anti-inflammatory activity. This plant has been used for many years by native people to cure many of the diseases like intestinal disorders, wounds, fever, ulcers, cancer, diabetes and many other diseases. In recent research it has shown effective activity against allergic conditions, acne, chronic fatigue, menstrual disorders, hormonal imbalance, viral infection and even depression⁴³.

The potential of Cat's claw for treating arthritis hide in its anti-inflammatory activity. The inhibitory activity against cytokines like interleukins (IL-1 β) and tumor necrosis factor alpha (TNF α) are more prominent during arthritis. In addition it promotes cartilage repair by stimulating the production of insulin like growth factor⁴³.

Cayaponia tayuya (Vell.) Cogn. (Family-Curcubitaceae; Tayuya)

It is native of Brazil but also found in many parts of the Amazon rain forest⁴⁴. This plant is

mainly characterized by its long tuberous roots⁴⁵. Traditionally infusion made from these roots was used to relieve pain, epilepsy, for metabolism regulation, backache, sciatic pain, headaches, gout, neuralgia, constipation, anaemia, cholera, dyspepsia, stomach problems and fatigue⁴⁴. Phytochemicals found in the Tayuya are flavones, glycosides, curcubitacin and terpenes, which have been proved for their anti-oxidant, anti-inflammatory, analgesic and anti-cancerous activities⁴⁴⁻⁴⁶. The rationale behind using this plant in arthritis is effective role of its chemical constituent dihydro-curcubitacin β in the synthesis, release and activity of pro-inflammatory enzymes like elastase, cyclooxygenase and NO synthase as well as its effect on different inflammatory mediators like IL-1 β and TNF α ⁴⁵⁻⁴⁷.

Maytenus krukovii A.C. Sm. (Family-Celastraceae; Chuchuhuasi)

This plant is normally found in Amazon rain forest and grows up to 30 m high, having large leaves, small white flowers and extremely tough heavy reddish brown bark. Mainly leaves roots and barks are used for medicinal purposes. Alcoholic extract has evidenced for its anti-mutagenic, anti-oxidant, anti-microbial, analgesic, anti-inflammatory and hypotensive properties. Chuchuhuasi contains wide variety of chemical constituents, triterpenes, favonols and sesquiterpene alkaloids⁴⁸⁻⁵⁰. The alkaloids are responsible for its anti-arthritic activity as they are capable of inhibiting enzyme protein kinase C which is involved in pathophysiology of arthritis⁵¹.

Bidens pilosa Linn. (Family-Asteraceae; Carrapicho)

It is small erect annual herb grows up to 1m high and normally found in Amazon rain forest, tropical areas like South-America, Africa, the Caribbean and Philippine. The plant chemicals in Carrapicho are phenylpropanoids, glucosides, polyacetylenes, diterpene flavonoids and flavone glycoside⁵²⁻⁵⁴. Plant extract has been reported for use in diabetes, hypertension, inflammation, immunosuppression, cancer and malaria⁵²⁻⁵⁴. It is capable of showing its anti-arthritic activity because of its free radical scavenging and nitric oxide synthase inhibition activity⁵⁵.

Mikania guaco Humb. & Bonpl. (Family- Asteraceae; Guaco)

Plant is 2-2.5 m wide and having height of around 2 m. Medicinally used part of the plant is

leaf which is bright green in colour and heart shaped. Plant is grown in South America, Brazil, Peru, Venezuela and Colombia⁵⁶. It is beneficial in the treatment of cough, asthma, pain, infections and inflammation⁵⁷. It contains variety of phytochemicals mainly steroids, campesterol, stigmasterol and β -sitosterol, diterpenes, triterpenes: α -amyrin, β -amyrin, α -amyrin acetate, β -amyrin acetate, lupeol, lupeol acetate and friedelin, coumarin: scopoletin, flavonoid: quercetin and caffeoylquinic acid⁵⁷. Amongst this caffeoylquinic acid has been proved for its *in-vitro* anti-inflammatory activity. Anti-inflammatory profile of Guaco may be responsible for its anti-arthritic activity⁵⁸.

Boswellia serrata Roxb. (Family-Burseraceae; Salai Guggal, Indian Frankincense)

The tree grows on dry hilly areas throughout India. It is also found in South America, North Africa and Arabica⁵⁹. The main chemical found in Salai guggal is gum resin but along with it there are other chemicals like volatile oil, terpinols, arabinose, xylose, uronic acid, β -sitosterin and phlobaphenes⁶⁰. It has been proved to show its anti-inflammatory and anti-arthritic activity through animal studies in rats. Boswellic acid is having inhibitory activity against 5-lipoxygenase enzyme and thus it prevents the synthesis of leucotriens^{59,60}.

Smilax officinalis Griseb. (Family-Smilacaceae; Sarasaparilla)

This plant is long, tuberous and spreads 2-3 m. It is native to South-America, Jamaica, The Caribbean, Mexico and West Indies. Root of Sarasaparilla is used for medicinal purpose. Chemically it contains flavonol, steroidal glycoside, saponins, phenylpropanoids and phenolic compounds⁶¹. Its therapeutic category includes diuresis, immunomodulation, antibacterial and blood purifier. Aqueous extract of the plant has been studied for its anti-inflammatory, analgesic and anti-pyretic activity^{61,62}. It is also proven to reduce inflammation in Freund's adjuvant induced arthritis in rats⁶³.

Along with above mentioned plants, the other plants which have been experimentally proved for their anti-arthritic activity are listed in Table 3. Even though traditional systems of medicine claim their effectiveness, the use of herbs should be supported with clinical studies. Well designed clinical trials can help prove the safety and efficacy of herbal products in treating arthritis and help understand whether there is loss or alteration of the efficacy of these herbal products upon chronic use. Regulatory requirements also demand the necessity of validated clinical data of different diseases collected through properly conducted

Table 3—Herbal drugs reported pre-clinically for the treatment of arthritis

Herbal drug	Animal model used	Reference
<i>Commiphora mukul</i> (Hook.f. ex Stocks) Engl.	Rat paw oedema, adjuvant induced arthritis	64
<i>Semecarpus anacardium</i> L.f.	Freund's adjuvant induced arthritis	64
<i>Withania somnifera</i> Dunal	Carrageenan induced paw oedema	64
<i>Ricinus communis</i> L.	Freund's adjuvant induced arthritis	64
<i>Vitex negundo</i> L.	Freund's adjuvant induced arthritis	66
<i>Clematis vitalba</i> L.	Carrageenan induced paw oedema	67,68
<i>Harpagophytum procumbens</i> (Burch.) DC. ex Meisn.	Freund's adjuvant induced arthritis	69
<i>Acanthopanax chiisanensis</i> Nakai	Freund's adjuvant induced arthritis	70
<i>Tetrapleura tetraptera</i> Taub.	Egg albumin induced paw oedema	71
<i>Dorstenia barteri</i> Bureau	Carrageenan induced paw oedema	72
<i>Kalopanax pictus</i> Thunb.	Freund's adjuvant induced arthritis	73
<i>Bridelia ferruginea</i> Benth.	Adjuvant induced arthritis	74
<i>Hippocratea excelsa</i> Kunth.	Adjuvant induced arthritis	75
<i>Boswellia carteri</i> Birdw.	Adjuvant induced arthritis	76
<i>Sclerocarya birrea</i> (A. Rich.) Hochst.	Carrageenan induced paw oedema	77
<i>Ulmus davidiana</i> Planch.	Collagen induced arthritis	78
<i>Cissampelos pareira</i> L.	Freund's adjuvant induced arthritis	79

Table 4—Clinically proved plants for arthritis

Herb	Clinical trial design	Result	Reference
Combination of <i>Boswellia serrata</i> , <i>Withania somnifera</i> and <i>Curcuma longa</i>	Double-blinded, Cross-over, Placebo controlled	Significant improvement in pain in disability score	80
Combination of <i>Persea americana</i> and <i>Glycine max</i> Merr.	Double-blinded, placebo controlled, phase-iii, multi-centric	Significantly reduced NSAID consumption, pain and improved disability score	81
<i>Capsicum annuum</i> L.	Double-blinded, placebo controlled, multi-centric	Significantly reduced pain	82
<i>Harpagophytum procumbens</i>	Double-blinded, , placebo controlled	Significantly reduced pain	83
Combination of <i>Cyperus rotundus</i> L., <i>Tinospora cordifolia</i> Thumb., <i>Saussurea lappa</i> DC., <i>Picrorrhiza kurroa</i> Royle and <i>Zingiber officinalis</i>	Double blinded, comparative, parallel design	Significantly reduced pain	84
Combination of <i>Populus tremuloides</i> Michx., <i>Achillea millefolium</i> L.	Double blinded, double dummy, crossover	Insignificant reduction of pain	85
Combination of <i>Populus tremuloides</i> , <i>Fraxinus excelsior</i> L. and <i>Solidago virgaurea</i> L.	Three armed, double blinded against placebo	Significantly reduced pain	86
<i>Urtica dioica</i> L.	Double-blinded, , placebo controlled, cross over	Lowers pain and disability score significantly	87
Combination of <i>Salix alba</i> L., <i>Guaiacum officinale</i> L., <i>Cimicifuga racemosa</i> L., <i>Hemidesmus Indicus</i> L. and <i>Lirio dendron</i> L.	Double-blinded, placebo controlled	Significant mild analgesic effect	88

clinical trials. Some of the plants which have been studied in clinical trial are listed in Table 4.

Conclusion

The use of herbal medicines is wide spread among patients in treating variety of diseases. While already available older synthetic drugs may cause side effects, the herbal medicines could alternatively be introduced as natural cure for arthritis. Pharmacological properties and clinical studies have justified the positive influencing role of several herbal medicines in treating arthritis. Further research and development of herbal remedies may pave the way for new potential therapeutic agent for arthritis.

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