



## A comprehensive review of the traditional plant based medicines for the treatment of rheumatism

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### ABSTRACT

Inflammation is a highly complex mechanism and can be described as the body's first defensive immune system reaction. The immediate purpose is to guard against infectious invasions, the introduction of antigens, any cell and tissue disruption or harm. If it is not treated, it is persistent which progresses to serious degenerative conditions such as rheumatism, atherosclerosis and asthma. Rheumatism is a category of inflammatory disease with chronic conditions. The disease includes a rise in the amount of neutrophils, lymphocytes and monocytes, which primarily influence the synovial fluid of the movable joints and eventually cause cartilage and bone degradation across the joints. Many steroidal and nonsteroidal drugs (Methotrexate, Cyclosporine and Dpencillamine, Ibuprofen, Sulindac, Indomethacin) are prescribed as treatment therapies. But, unfortunately, all these drugs are having side effects. So, to enhance the pharmacological effects and decrease the side-effects of the available treatment therapies, there is a need to move towards alternative therapies. By keeping the limitations of the existing therapies, in the present review, we tried to summarize the data of traditional medicinal plants with maximum pharmacological activities with less side effects for the rheumatism patients. A systematic literature and electronic archive analysis was performed using internet search engines such as Google scholar, Pubmed, Medlineplus, and Science Direct from numerous academic publications. This review paper is summarized with total 500 articles out of which 330 articles are selected to review for extracts and parts used, chemical constituents, traditional uses and for reporting anti rheumatic activity.

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### INTRODUCTION

Inflammation is a mechanism in which the body's immune system is stimulated against damage and reaction to toxic agents in response to bacterial, virus or fungal infections. If the immune system completely eradicates these pathogenic infections and toxic compounds or heals an injury, the inflammation dissipates. The inflammation becomes severe at this point because if it does not heal, then the inflammation is persistent. Chronic inflammation leads to over activation of

macrophages, which ultimately causes over production of prostaglandins, leukotrienes, and cytokines and thereby induces chronic degenerative diseases like rheumatism, asthma, and atherosclerosis. Rheumatism is a chronic inflammatory autoimmune disease characterized by soreness, stiffness, pain in joints including associated structures and restricted joint movement due to increases in the number of cells of synovial membrane, movement of neutrophils, lymphocytes and monocytes into peripheral tissues and neovascularisation which ultimately leads to articular and cartilage destruction (Patil et al., 2012). The extent of this disease throughout the world is 1% and approximately 0.75% in India with male and female ratio of 1:3 (Gabriel et al., 2003). The available treatment therapy includes steroidal and nonsteroidal antiinflammatory drugs and immunosuppressant drugs like Methotrexate, Cyclosporine and D- Pencillamine, Ibuprofen, Sulindac etc. The adverse-effects like skin reaction, bone marrow depression and liver disorders limit their application. To minimize the adverse effects and cost of the drug, there is a need to move towards alternative therapies. Plants derived medicinal plants and natural agents will be a good alternative for the treatment of rheumatism at an affordable cost. Even today 80% of the world population depends on plant derived medicines for the primary health care because of least or no side effects (Babushetty and Sultanpur, 2012). Scientists are also scrutinizing traditional plants to find complementary and alternative anti inflammatory drugs.

Here in, we reviewed the plants derived herbal therapy, and chemical components for rheumatism.

### Abbreviations

AI- *Abutilon indicum*; AR- *Asparagus racemosus*; BP- *Bauhinia purpurea* ; CI- *Calophyllum inophyllum*; CP- *Celastrus paniculatus*; CM- *Callicarpa macrophylla*; CQ- *Cissus quadrangularis*; CF- *Coleus forskohlii*; CC- *Commiphora caudate*; CS- *Costus speciosus*; DS- *Dalbergia sissoo*; ME- *Mimusops elengi*.

### Herbal Therapy for the Treatment of Rheumatism

From the time immemorial, herbal medicinal plants are used for treatment of various diseases and it will not be an overstatement that the use of medicinal plants is as old as the mankind (Tandon and Gupta, 2004). There are about 17,000 species of higher plants, of which approximately 8,000 species are considered medicinal for the maintenance of good health and used in different traditional medicinal systems such as the Ayurveda, Unani, Siddha and Homeopathy.

Moreover, because of an increasing reliability of the use of medicinal plants, less side effects and easy availability, the industrialized societies also lead to the development of several drugs and chemotherapeutic from these plants as well as from traditionally used rural herbal remedies by extraction of active constituents. Thus now the plants have been most widely investigated and analyzed source of medicinal compounds and chemical constituents of these plants produces a required physiological action on the body. The present review article uncovers different parts of herbal plants for their traditional and ethnobotanical uses, pharmacognostic and the chemical constituents responsible for antirheumatic activity. Thus make feasible the development of new drugs for the treatment of rheumatism.

### Search Strategy Used

The search terms used were 'arthritis', 'rheumatism', 'anti rheumatic activity', 'herbal drugs for treatment of rheumatism', 'inflammation', 'folk plants used for the treatment of pain and stiffness'. The current search and study was done by referring various text books, Journals containing peer review and research papers. The electronic databases used were Google, Science Direct and PubMed, which provide free access to Medline. Only published articles with different languages from 1950 to till date were used. Reference lists of articles were also cross checked for more elaborated study.

### RESULTS AND DISCUSSION

The review of literature related to present study was done in the period from April 2018 to till date. A total of 500 articles were reviewed for status of anti rheumatic plants. Out of which 330 articles were selected. Data collected from different articles were compiled to make the latest review article on rheumatism. Scientific and common name, family, extract and parts used, chemical constituents possessing anti rheumatic activity with their references are shown in Table 1. Followings are the examples of some traditional plants with geographical distribution, family, parts used, extract/extracts used, doses used and traditional uses and anti rheumatic activity studied since from 1950 to till date.

#### *Abutilon indicum* (AI) (Malvaceae)

AI is a medicinal shrub commonly known as "Atibala", widely distributed in tropical and subtropical countries of Asia, America, Africa and Australia. It is a shrubby soft plant with purple tinge in color. Traditionally the leaves of AI are used as mouthwash, toothache, quick ulcer healing and for the treatment of inflammation of the bladder.

**Table 1: List of medicinal plants reported to have anti rheumatic activity**

Botanical name	Common name	Family	Extract/Part used for anti rheumatic activity	Chemical Constituents
<i>Arisaema rhizomatum</i>	Xuelijian	Araceae	Methanol extract/Rhizome	$\beta$ -sitosterol, daucosterin, apigenin, oldhamactam O-ethyllycorenine, $\alpha$ -asarone, uridine
<i>Aristolochia bractea</i>	Worm killer	Aristolochiaceae	Petether, chloroform and methanol extract/Whole plant	$\beta$ -sitosterol, stigmasterol, aristolochic acid, aristolactams, aporphines, benzylisoquinoline, isoquinoline, protoberberine, amides, flavonoids, lignans
<i>Asparagus racemosus</i>	Shatavari	Liliaceae	Hydroalcoholic extract/Roots	Asparagamine, isoflavone, shatavarside A& B, sterols
<i>Allium sativum</i>	Lahsun	Liliaceae	Aqueous extract/Leaves	Allin, Allicin, flavonoids, sulphur, steroids, Terpenoids
<i>Barleria lupulina</i>	Vishalyakarani	Acanthaceae	Methanol extract/Leaves	Irridoid glycosides, barlerin acetyl barlerin, Shanzhiside, acetyl Shanzhiside
<i>Barleria prionitis</i>	Vajardanti	Acanthaceae	Chloroform extract/Leaves	Irridod Glycoside, Barlerin, acetyl barlerin, lupalinoside, 7-methoxy dihydroside
<i>Barringtonia racemosa</i>	Mangrove	Lecythidaceae	Methanol extract/Fruits	Pentacyclic triterpenoids, saponins, tannins
<i>Berberis orthobotrys</i>	Berberry	Berberidaceae	Aqueous and methanol extract/Roots	Berberine, berberamine, kalashine, benzyl isoquinoline, chitraline
<i>Boswellia serrata</i>	Salai Guggul	Burseraceae	Methanol extract/Gum resin	$\beta$ -sitosterol, tannins, pentosans, geraniol, linalool, terpenyl acetate, boswellic acid
<i>Cinnamomum cassia</i>	Chinese cassia	Lauraceae	Hydro alcoholic extract/Bark	Cinnamic aldehyde, cinnamic acid, coumarin, tannins, carbohydrates, cinnamic alcohol
<i>Cissampelos Pareira</i>	Harjori	Menispermaceae	Ethanol extract/Leaves	Bisbenzylisoquinoline alkaloids, Hyatine, arachidic acid, berberine, linoleic acid, quercitol, stearic acid
<i>Clematis orientalis</i>	Bailari cheithi	Ranunculaceae	Aqueous ethanolic extract/Flowers	Triterpenoid saponins-oleanolic acid, hedragenin, epi hedragenin, 3,4, dimethoxy cinnamyl, gypsogenin

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Table 1 continued

Botanical name	Common name	Family	Extract/Part used for anti rheumatic activity	Chemical Constituents
<i>Cardiospermum halicacabum</i>	Ballon plant	Sapindaceae	Ethanol extract/Leaves	Rutin, Quercetin, apigenin, protocatechuic acid
<i>Capparis erythrocarpos</i>	Alcaparro	Capparaceae	Ethanol extract/Roots	Tannins, glycoside, coumarins, triterpenoids, alkaloids and flavanols
<i>Commiphora mukul</i>	Guggul	Burseraceae	Alcohol extract/Gum	Z-guggal sterone, E-guggal sterone, sesamine, camphorene, cembrene
<i>Ficus bengalensis</i>	Banyan	Moraceae	Methanol extract/Bark	Triacotene, heptatriaconten, pentatriacontan, $\beta$ -sitosterol and meta inositol
<i>Gentiana kuro-roo</i>	Neilkanth	Gentianaceae	Methanol extract/Whole plant	Irridoids, xanthonenes, mangiferin and c-glucoflavones
<i>Glycyrrhiza glabra</i>	Mulethi	Leguminosae	Methanol extract/Rhizome	Liquiritin, isoliquiritin, pentalool, linalool, glycyrrhizic acid, kanzonol, tetramethyl pyrazine
<i>Glyphaea brevis</i>	Masquerade stick	Tiliaceae	Aqueous ethanolic extract/Stem bark	Mono tricosanoate, Palmarumycin, epicatechin, procyanidin
<i>Heliopsis longipes</i>	Golden root	Asteraceae	Hexane extract/Root	Spilanthol, Affinin, alkalamides
<i>Hibiscus hispidissimus</i>	Comfort root	Malvaceae	Ethanol extract/Aerial parts	Hydroxy citric acid, garcinic acid, triterpene and flavonoid - hibiscatin, gossyptrin, gossypin
<i>Justicia gendrussa</i>	Kalaadulsa	Acanthaceae	Ethanol extract/Leaves	Campesterol, stigmasterol, sitosterol, sitosterol- D- glucoside
<i>Lawsonia innermis</i>	Henna	Lythraceae	Hydroalcoholic/Leaves	Eicosane, nonadecane, hexadeconic acid, octadeconic acid, benzoic acid, isobenzofuranone
<i>Momordica charantia</i>	Karela	Cucurbitaceae	Ethanol and aqueous extract/Fruit	Momordicin I, Momordicin IV, Momordicoside
<i>Moringa olifera</i>	Drumstick tree	Moringaceae	Ethanol extract/Leaves	Octadeconic acid, ascorbic acid, phytol, oleic acid, hexadeconic acid, 4-hydroxy-4-methyl-2-pentanone
<i>Moussonia deppeana</i>	Tlachichinole	Gesneriaceae	Ethanol extract/Aerial parts	Verbascoside, ursolic and oleanolic acid, apigenin, hesperitin <sup>296</sup>
<i>Muntingia calabura</i>	Jam tree	Tiliaceae	Ethanol extract/Leaves	Flavonoids, flavones, polyphenols and steroids

Continued on next page

Table 1 continued

Botanical name	Common name	Family	Extract/Part used for anti rheumatic activity	Chemical Constituents
<i>Paullinia pinnata</i>	Dzuhkelong	Sapindaceae	Aqueous extract/Leaves	Flavones glycoside - diosmetin and tricetin, $\beta$ -amyrin, $\beta$ -sitosterol, 1-Quebrachitol, $\beta$ -sitosterol glucopyranoside
<i>Parmotrema tinctorum</i>	Palm ruffle	Parmeliaceae	Methanol extract/Whole plant	Lecanoric acid, methyl orsenillate, methyl lecaronic acid, vitamin b and c, lichenin, isolichenin
<i>Pergularia daemia</i>	Uttaranjutuka	Asclepidaceae	Ethanol extract/Leaves and Root	Benzoic acid, phenolic compound-2-methoxy-4-vinylphenol, phthalic acid, ascorbic acid, eicosatetraenoate
<i>Pentatropis capensis</i>	Ambarvel	Asclepidaceae	Aqueous extract/Leaves	$\alpha$ -amyrin, octacosanol, $\beta$ -sitosterol, friedelin, Salicylic acid
<i>Phyllanthus amarus</i>	Stone breaker	Phyllanthaceae	Aqueous extract	$\beta$ -sitosterol, stigmasterol, linolenic acid, hexadeconic acid, methyl ursolate, phytol, methyl linolenate
<i>Piptadeniastrum africanum</i>	African greenheart	Mimosaceae	Aqueous methanolic extract/Stem bark	Flavonoid, triterpenoid, steroids, saponins
<i>Pisonia grandis</i>	Bird Catcher tree	Nyctagenaceae	Ethanol extract/Leaves	Pinnatol, allantoin, $\beta$ -sitosterol, $\alpha$ -spinasterol, dulcitol, quercetin, $\beta$ -sitosterol glycoside
<i>Plumeria alba</i>	White champa	Apocynaceae	Hydro alcoholic extract/Leaves	Amyrin, $\beta$ -sitosterol, plumeride, scopetein, plumeride coumerate, Stigmasterol
<i>Pterdon pubescens</i>	Sucupira	Fabaceae	Hydro alcoholic extract/Seeds	Isoflavones, diterpenes, triterpenes, saponins, glycosides and alkaloids
<i>Rubia cordifolia</i>	Indiam madder	Rubiaceae	Benzene extract Roots	Munjistin, purpurin, pseudopurpurin, rubiadin, rubiprasin A, B and C, garancin, mollugin, furomollugin
<i>Rosa centifolia</i>	Cabbage Rose	Rosaceae	Ethanol extract/Flowers	Geraniol, linalool, benzyl alcohol, citronellyl actate nerol, salts of mallic acid and tartaric acid, riboflavin
<i>Rhizopora mucronata</i>	Asiatic man-groves	Rhizophoraceae	Methanol extract/Leaves	Anthracene, phenols, amino acid, saponins, tannins and flavonoids

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Table 1 continued

Botanical name	Common name	Family	Extract/Part used for anti rheumatic activity	Chemical Constituents
<i>Sesamum indicum</i>	Benniseed	Pedaliaceae	Ethanol extract/Seeds	Sesamol, sesamolin, oleic acid, palmitic acid, stearic acid, linoleic acid, tryptophan, $\alpha$ -tocopherol
<i>Stephania glabra</i>	Purha	Menispermaceae	Ethanol extract/Rhizomes	Gindarine, gindaricine, magnoflorine, rotundine, protoberberine, columbamine
<i>Strychnous potatorum</i>	Clearing nut tree	Loganiaceae	Aqueous extract/Whole seed powder	Diaboline, brucine, loganin, linolenic, oleic, palmitic and stearic acid, $\beta$ -sitosterol, stigmasterol, triterpenes, manogalactans
<i>Synedrella nodiflora</i>	Node weed	Asteraceae	Chloroform and ethanol extract/Whole plant	$\beta$ -caryophyllene, $\beta$ -farnesene, germacrene-D, $\beta$ -cubebene, triterpenoid saponin nodifloside A, $\beta$ -sitosterol, stigmasterol, rosasterol
<i>Syzygium cumini</i>	Black plum	Myrtaceae	Pet ether/Stem bark	Anthrocyanins, ellagic acid, isoquercitin, Kaemferol and myrcetin, alkaloid-jambosine, glycoside jambolin, vitamin C and flavonoid
<i>Terminalia tomentosa</i>	Asan	Combretaceae	Aqueous and alcoholic extract/Bark	Tannins- arjunolic acid, arjunic acid, ellagic and gallic acid, triterpenoids - oleanolic, betulinic acid, steroids- $\beta$ -sitosterol
<i>Elaeocarpus serratus</i>	Ceylon-olive	Elaeocarpaceae	Ethanol extract/Leaves and Seeds	8-amino caffeine, octadecanol, methanol, ricinoleic acid, triacontane, citronellyl isobutyrate
<i>Vitellaria paradoxa</i>	Shea	Sapotaceae	Methanol extract/Bark	Gallic acid, catechin, epicatechin, gallocatechin, quercetin, cinnamic acid
<i>Withania somifera</i>	Aswagandha	Solanaceae	Ethanol extract/Roots	Withanolides, withaferine, withanine, withasomnine
<i>Zingiber officinale</i>	Adarak	Zingiberaceae	Aqueous extract/Rhizomes	Shogaols, gingerols, zingiberene, zingiberol, vitamin A, C and E

The folk practitioner uses the whole plant for rheumatism, immune stimulating effect, for curing blood dysentery, as digestive, laxative, astringent, analgesic and demulcent (Raja and Kailasam, 2015). The herb contains various constituents such as alkaloids, flavonoids, saponins, lactones, sesquiterpenes, aglycones, steroids, carbohydrates, phenols, tannins, glycosides, proteins, alkaline sulphates and amino acid.  $\alpha$ -tocopherol and  $\beta$ -sitosterol are isolated from leaves of AI. Fruits contain flavanoids and alkaloids. Some flavonoids like quercetin, kaempferol, gossypetin, and cyanidin 3-glucoside also have been isolated from *A. indicum* (Sankara and Nair, 1972). Different parts of AI show various biological activities such as analgesic, immunomodulatory, anti arthritic and anti oxidant, anti bacterial activity, diuretic, anti diabetic activity, anti microbial, anticonvulsant, anthelmintic, antidiarrheal, wound healing, hepatoprotective, antitumor, anti-inflammatory (Saraswathi et al., 2011) and free radical scavenging activity. In vitro antirheumatic activity of AI was done by using inhibition of protein denaturation and effect of membrane stabilization by using two different concentrations of 100 $\mu$ g and 250 $\mu$ g per kg body weight and the results were compared with acetyl salicylic acid 250 $\mu$ g/ml. From the results it was concluded that AI possesses significant anti rheumatic activity (Tripathi et al., 2012).

#### ***Asparagus racemosus* (AR) Liliaceae**

AR is commonly known as "Shatavari", which is a shrub; found throughout tropical and subtropical parts of Australia, China, Sri Lanka and India, up to an altitude of 1500 m. AR is climbing plant having tuberous roots. Roots are silvery white or ash color, smooth when fresh and develop longitudinal wrinkles on getting dry. Roots are mainly used for the treatment of rheumatism. AR is used as aphrodisiac, diuretic and for male genital dysfunctions. AR is also used as antiseptic, brain tonic, for the treatment of cardiac disorders, hypertension and epilepsy. It is also used to prevent ageing, dyspepsia, tumor, nervous disorders and for reducing inflammation. In women it is used to treat habitual abortions, to give strength to the uterus and to prevent excess bleeding during menstruation. The main constituents of AR are steroidal saponins i.e. shatavarin I-IV and Shatavarin V and Shatavarin VI-X is reported in the roots of AR. Other steroidal saponins isolated are asparagin, immunoside, diosgenin, sitosterol and Racemoside A, B and C. Quercetin, rutin and flavonoids are isolated from fruits. AR reported to have activities such as anti inflammatory and antirheumatic (Mittal and Dixit, 2013) hypolipidemic and antioxidant, antidiarrheal, anti depressant, peptic ulcer healing property, anti cancer,

antioxytotic, anti epileptic, antitussive. Antiarthritic activity of a hydro alcoholic extract of AR was studied by complete Freund's adjuvant induced arthritis, method and the extracts showed significant anti rheumatic activity at the dose of 200mg/kg and 400mg/kg body weight. Increase in body weight and a reduction in paw volume and total arthritic scores of both the hind legs was observed. Thus, it was clear that the drug provides pharmacological rationale for the traditional use of inflammatory disorders such as rheumatoid arthritis (Mittal and Dixit, 2013).

#### ***Bauhinia purpurea* (BP) Leguminosae**

BP is commonly known as "Orchid tree", medium size caducous tree thriftily grown in India, also native to Southern Asia, Southeast Asia, Taiwan and China. Traditionally it is used in the treatment of rheumatism, fever, ulcer and stomach cancer (Zakaria et al., 2012). BP Flowers are used as a laxative; the bark is used for diarrhea, menstruation and for treatment of leucorrhoea and roots is used as carminative. It is also used for convulsion, sepsis and dementia. Different chemical constituents present in BP are glycosides, flavonoids, saponins, phenolic compounds and phytosterols. Main constituents are flavones glycoside, 5, 6-dihydroxy-7-methoxyflavone 6-O- $\beta$ -D-xylopyranoside,  $\alpha$ -myricin caprylate, a mixture of phytol, fatty esters, leutin and  $\beta$ -sitosterol, volatile oil, terpinene, limonene, myrcene, linalool, citronellyl acetate and a phenyl propanoid i.e. eugenol (Wassel et al., 1986). The study of BP reveals biological activities like anti arthritic (Sunil et al., 2019), antinociceptive, analgesic and anti-inflammatory (Shreedhara et al., 2009), antimicrobial activity, antineoplastic, antidiabetic, antidiarrheal, antioxidant, anti malarial, anti fungal, antimicrobial, cytotoxic activity and wound healing activity (Asdaq et al., 2010). A hydro alcoholic extract of the stem bark of BP at the doses of 50, 100 and 200mg/kg body weight showed a significant decrease in oxidative stress markers. Decrease in TNF alpha, interleukin-1 and an increase in the level of cytokine gives the confirmation of anti arthritic effect of (Sunil et al., 2019).

#### ***Calophyllum inophyllum* (CI) Clusiaceae**

CI is commonly called as "Indian laurel", a mangrove species found in Southern coastal India, Malaysia, Thailand and Myanmar. It is widely distributed in tropical areas and can be cultivated in different kind of soil, clay and degraded soil. CI oil is used for the treatment of rheumatism, pain in joints and for wound healings. CI is also used to treat eye irritation and ophthalmitis, diabetes, sunburn, psoriasis and also for hair problems. Heartwood of

CI contain xanthenes (buchanaxanthone, brasilixanthone), leaves contains tannins and triterpenes (canophyllals, canophyllol and canophyllic acid). CI also contain coumarin (Calcoumarin A, B and C), Arachidic acid and alkaloid (carpaine). Study of different extracts possesses antirheumatic (Peru-mal *et al.*, 2017), antiinflammatory, sedative or anxiolytic effect, antiproliferative, antidepressant and nootropic, wound healing activity, antibacterial and analgesic, termeticidal, antiinflammatory and CNS depressant and antimicrobial activities. It is also used in the treatment of HIV and leukemia. Antirheumatic activity of CI stems bark and seeds were evaluated by Freund's complete adjuvant induced arthritis in the doses of 250  $\mu\text{g}/\text{kg}$  body weight and the result obtained was nearly equal to the standard drug (Zakaria *et al.*, 2014).

#### ***Celastrus paniculatus* (CP) Celastraceae**

*Celastrus paniculatus* is commonly known as "Malkangani", distributed all over India, mainly in Maharashtra, Orissa and Andaman and Nicobar group of Islands on an altitude of 1800m. It climbs up to over 10m. The leaves are ovate or elliptic in shape, smooth in texture with dentate margin. Seeds are ellipsoid or ovoid, yellowish or reddish brown in color and grow inside the capsules. CP seeds are used traditionally for relieving the pain, swelling and for rheumatic pain. The main portion of the plant is the seed which has many therapeutic uses. It is mainly used for the treatment of brain related disorders, improve memory. The seed oil is used for hair care and for treatment of rheumatism, as sedative and to strengthen the intellectual power and in paralysis. CP is also used for the treatment of piles, leprosy, diarrhea and bacterial infections. It also acts as anti emetic, appetizer and aphrodisiac. Herbal vendors of South India used the seeds of CP in the ointment which is externally applied to the wound. Different Parts of CP after extraction and fractionation gives different active constituents that are sesquiterpene esters (Malkanguinol, malkangunin), Sesquiterpene alkaloids (Celapanin, celapanigin), Alkaloids (Celastrine, paniculatine), fatty acids (Oleic acid, palmitic acid, linoleic acid, stearic acid, crystalline substance, tetracasanol and sterol (Gamlath *et al.*, 1990). The CP also contains carbohydrates, saturated and mono and polyunsaturated fatty acid and vitamin C and tannins. Different pharmacological activities are antirheumatic (Bhanumathy *et al.*, 2010), antinociceptive, antiepileptic, antifungal, Nootropic activity, sedation and convulsion, antimalarial activity, antispermatogenic effect, anti anxiety, hypolipidemic and anti atherosclerotic effect and antioxidant. Petroleum ether fraction of *Celastrus panicu-*

*latus* at the dose of 200 and 400 mg/kg body weight, restore the decrease level of superoxide dismutase, glutathione and catalase, thus produce significant anti arthritic activity (Gatinode *et al.*, 1957).

#### ***Callicarpa macrophylla* (CM) Verbenaceae**

*Callicarpa macrophylla* is commonly known as "Priyangu", extensively used in many traditional medicinal systems such a Siddha, Unani and Homeopathy system. It is distributed across India, China, Myanmar, and Nepal. In India it is widely distributed in Bihar, Assam, Meghalaya, Mizoram and Tripura up to an altitude of 1800 m. CM leaves are 12.5-23 cm long, ovate or lanceolate in shape with round base. Petioles are 6-13mm long. Stems and branches have covering of stellate hairs on it. The seeds are used in the treatment of leprosy and as diuretic. Seed paste is used in treating oral ulcer. The bark of CM is used in rheumatism and gonorrhoea. The plant is also used in fever, diarrhea, dysentery, headache, ulcer and diabetes. Leaf juice is used in burning sensation of stomach and to stop bleeding. Leaves are used in gout and rheumatism. Different active chemical constituents are present in different parts of CM are flavonoids, sesquiterpenes, diterpenoids (16 $\alpha$ , 17- isopropylideno-3-oxo-phylloladane), terpenes, diterpenes, fatty acid, phenyl propanoids and phytosterols. The leaves contain flavonoids such as luteolin and apigenin, Pentacyclic triterpenid- ursolic acid and  $\alpha$ -amyrin and Phytosterols such as  $\beta$ -sitosterol and dacusterol. Seeds and roots contain diterpenes such as calliterpenone, calliterpenone monoacetate and calliterpenone-17-acetate (Fujita *et al.*, 1950). The bark contains beutilinic acid and tricosanoic acid. Reported pharmacological activities of CM are antiinflammatory, antifungal, antibacterial, hypoglycemic effect, wound healing activity, immunomodulatory and antioxidant activity. In *vitro* activity of flower of ethanol extract of CM was studied by using inhibition of protein denaturation and human red blood cell membrane stabilization method. The results obtained from the method used indicate that CM flower exhibit anti arthritic activity.

#### ***Cissus quadrangularis* (CQ) Vitaceae**

*Cissus quadrangularis* is commonly known as "Had-jod" (Bone Setter) in India because of its fracture healing properties. It is a climbing herb, found throughout India, Asia, Africa, Thailand, and Sri-lanka, Malaysia and West Africa. It can be cultivated on a plain coastal area or wasteland at an altitude of 500m. The shrub is smooth, glabrous, buff color with a green tinge. It is one seed plant, with simple leaves having ovate shape and dentate margin. In India it is widely used in Tamilnadu and Kerala.



In Tamilnadu it is used for improving immunity and in Kerala its paste is used over fractured joints. In southern India, it is used to strengthen the bone and to repair the damage of epithelial cells due to an injury. In Ayurveda CQ is used for the treatment of rheumatoid arthritis, osteoporosis and osteoarthritis (Bah et al., 2007). Leaves and young shoots are used in the treatment of gastrointestinal disorders. The juice of the stem is used in the treatment of inflammation of the ear and to control the bleeding of the nose. Root powder is used in constipation and gout. Various chemical constituents are isolated from different extracts of CQ are flavonoids such as quercetin, kaempferol, triterpenes- alpha and beta amyryn,  $\beta$ -carotene and  $\beta$ -sitosterol. Stiblene and quadrangularins A, B and C, steroids, phenols, tannins, vitamin A and Gallic acid derivatives are also found. Methyl gallate, myricetin, daidzein, geniotein and daucosterol also have been also isolated from CQ (Jain and Kohli, 2015). The stem extract contains phosphorous and calcium. Various medicinal activities are analgesic and anti inflammatory, antipyretic, anti rheumatic (Bhujade and Talmale, 2015), bone healing activity, anti ulcer, cytoprotective, anti epileptic and muscle relaxant activity, antioxidant and anti microbial and anti hemorrhoid activities. Anti arthritic activity was studied by using acetone extract of CQ at a dose of 100mg/kg body weight by using standard drug Cecocoxib and methotrexate. After analyzing histopathological section and radiography it was clear that the acetone extract of CQ reduces pain and inflammation of joints (Bhujade and Talmale, 2015).

#### ***Coleus forskohlii* (CF) Lamiaceae**

*Coleus forskohlii* is commonly known as "Pathar Chur" in Hindi, is a plant of Indian origin, distributed in the sub tropical Himalaya from Garhwal to Nepal at an altitude of 2500 m above mean sea level and also in Srilanka and Thailand. CF is used as Ayurvedic medicine from the time immortal for the treatment of various ailments like cardiovascular diseases, CNS disorders and GIT and respiratory disorders (Ammon and Muller, 1985). CF is also used traditionally for treatment of eye disorders, cancer, asthma, insomnia, psoriasis, inflammation and hypothermia. Different chemical active constituents are isolated from CF of which chief active constituent is forskohlin (Ammon and Muller, 1985). The other constituents present is volatile oils, diterpenoids and colonels. An ethanol extract of whole plant of CF contains two labdane diterpene glycosides i.e. forskoditerpenoside A and B and sesquiterpenes. Various Clinical activities of different extracts of CF reported are anti inflammatory, antimicrobial, anticataract, antioxidant, antibacte-

rial, anti hypertensive, antispasmodic, bronchodilator and antiallergic. CF is also reported to have used in cardiovascular disorders, reducing intraocular pressure of eye, thyroid cell metabolism and as an antiobesity drug. Methanolic and aqueous shoot extract of CF at the dose of 200 $\mu$ g/ml possesses *in vitro* antioxidant and anti inflammatory activity, when tested by DPPH (2,2-diphenyl-1-picrylhydrazyl), BSA (Bovine Serum Albumin) anti-denaturation and HRBC Membrane (Human Red Blood Cell Membrane) stabilization method (Menon and Latha, 2011).

#### ***Commiphora caudata* (CC) Burseraceae**

*Commiphora caudata* is commonly called as "Hill mango". CC is a medium size, aromatic tree found in Kerala, Andhra Pradesh, Tamilnadu, West Bengal, Karnataka and in Srilanka. CC leaves are ovate, glabrous with uneven base. Folk Practitioner uses the CC leaves and gum resin for stomach diseases and fruits for the healing of injuries. Paste of leaves of CC is used for the treatment of inflammation at Koothupapampu in Kerala. The CC is also used in the treatment of ulcer, diarrhoea, diabetes, arthritis, sciatica, urinary retention, and obesity. Chemical studies show the presence of flavonoids, phenols, essential oil ( $\beta$ -pinene, verbenone, capric acid, carveol, caryophyllene and linalool acetate. Other constituents are linoleic acid (7(Z),10(Z)-Hexadecadienoic acid, cis-9,12,15-octadecatrienoic acid, heptacosane, pentacosane, methyl arachidate, triterpenoid (squalene), resin and gum. Medicinal activities of the CC are antirheumatic, antihyperlipidemic, anti inflammatory, antioxidant, analgesic, anti inflammatory and antilipidperoxidation, learning and memory enhancing activity and larvicidal. Antirheumatic activity was done with ethanolic extract of *Commiphora caudata* at the dose of 200 and 400mg/kg body weight in rats, which produce reduction in paw volume and increase in red blood cells and erythrocyte sedimentation rate and decrease in white blood cells. Thus confirm the anti rheumatic potential of CC (Eggadi et al., 2014).

#### ***Costus speciosus* (CS) Costaceae**

*Costus speciosus* is commonly known as "Keukand", Indian ornamental perennial herb, found in Himachal Pradesh, Assam, Karnataka, Tamilnadu, Andhra Pradesh and Ahmednagar, Odisha, Madhya Pradesh, Punjab, Gujarat, Rajasthan, Haryana and in Peninsular India. It grows up to a height of 2.7m, having leaves with lanceolate shape and flowers in clusters. The juice of the leaf and rhizome is used in Kerala and Assam for the treatment of diabetes. CS is also used traditionally for treatment of arthritis, rheumatism and leprosy and

asthma. Young stems are used in the treatment of diarrhoea and as astringent, aphrodisiac, expectorant, anthelmintic, purifying and detoxifying agent and for abortion. The major constituent present in CS rhizome is diosgenin, which is a steroidal sapogenin. Other constituents present are dioscin, betasitosterol tigogenin and gracillin. CS rhizome also contains essential oil; the main constituents of the oil are pinocarveol, cineole, carvacrol. From the rhizomes Methyl 3-(4-hydroxyphenyl)-2E propentone was also isolated. The seed contains tocopherol, glucose, galactose and rhamnose. The roots of this plant also contain dioscin, gracillin,  $\beta$ -sitosterol- $\beta$ -D-glucoside and pro sapogenins A and B. Root also contains 31-norcycloartanone, cycloartanol, cycloaudenol and cycloarteno. CS has been claimed to use as antirheumatic, antimicrobial, anti hypercholesterolemic, anti inflammatory, antioxidant and antiangiogenic activity, antioxidant, antihyperlipidemic, anti depressant and in neuropharmacological evaluation. Aerial part of CS possesses antiarthritic activity at the doses of 400 and 800mg/kg body weight by suppressing the swelling of paw in both acute and chronic phases. The suppression of inflammation may be due to the presence of alkaloids and flavonoids in CS (Srivastava et al., 2012).

#### ***Dalbergia sissoo* (DS) Fabaceae**

*Dalbergia sissoo* is commonly known as "Shisham", a medium to large tree, 25m in height and 2-3m in diameter (Asif and Kumar, 2011). Leaves are 15cm long with the fine pointed tip. DS is found throughout India, Pakistan, Bangladesh, Nepal, Afghanistan, Persia, Iraq and Kenya. Shisham is used by folk practitioners for treatment of several ailments. Extract of DS bark is used to treat inflammation of piles and sciatica. DS is also used in burning sensation of stomach, digestive disorders, in scabies, to treat colorectal cancer and jaundice. Aerial parts are used to treat sexually transmitted diseases like syphilis, gonorrhoea and as expectorant. The flower oil is used for skin diseases like Leucoderma and ulcer and flower extract is used as a blood purifier and immune modifying agent. Extract of leaves is used to treat dandruff, to strengthen the hair and for treatment of eye and nose diseases. The leaf extract is also used as analgesic, antipyretic, antidiabetic and antioxidant. DS is also used as a stimulant, expectorant and astringent. The active chemical constituents isolated from the leaves of DS are formic acid, cyclobutanol and pentanal. Chalcone, polysaccharides containing glucuronic acid are also found from the leaves of DS. Fatty acids isolated from DS are  $\beta$ -sitosterol, stigmaterol,  $\beta$ -amyrin and isoflavonoid glycosides. Heart wood contains arachidic acid,

palmitic acid, linoleic acid, oleic acid, stearic acid and Myristic acid. DS is reported to have analgesic and anti inflammatory (Sidhana et al., 2012), antinociceptive, anticoagulant activity, antioxidant, antidiabetic, antiparasitic, antimicrobial, antiulcer and antidiarrheal activities. Antiarthritic activity of ethanolic extract of *Dalbergia sissoo* was studied by cotton pellet granuloma and inhibition of protein denaturation at the doses of 200 400, 800 and 1000  $\mu$ g/ml, which shows significant anti arthritic effect as compared to control drug dexamethasone.

#### ***Mimusops elengi* (ME) Sapotaceae**

*Mimusops elengi* is commonly known as "Bakul", cultivated as an ornamental tree because of its flowers. The plant grows up to 16m in height. ME is found in India, Burma, Pakistan, Bangladesh, Thailand, Malaysia. Leaves are 6.3-10 in length and 3.2 -5 cm in width, elliptic in shape with acute or round base. Kalidas in his Sanskrit literature included ME flower as a symbol of Love and beauty. *Mimusops elengi* is used from the ancient time to till now due to the large number of its therapeutic properties. Literature survey makes it clear that in ancient civilization, flowers of ME were the main diet of sages, hermits and people. In Ayurveda, taila prepared from the fruits of ME are used for strengthening the gum and teeth. In Unani medicines the bark is used for urinary diseases in males. Bark decoction is used to treat fever, throat and stomach pain. Flowers are used to treat kidney and bladder stones and for cardiac disorders. Roots are used for treatment of sexually transmitted diseases, to increase the flow of urine and good for gonorrhoea. Phytochemical constituents present in ME are Beutilinic acid, ursolic acid, lupeol gum, tannis, wax and starch. Quercitol,  $\beta$ - sitosterol, mimusops and mimusopic acid, anthraquinone and cardiac glycosides such as mimusopside A and B, alkaloids like hentriacontane, saponins (mimosin), pentacyclic triterpens -mimusopgenone and mimugenone are also present. Two  $\alpha$ - glucosidase inhibitors, 3 $\beta$ -hydroxy-12-ursene-28-oic acid and 3 $\beta$ -(4-hydroxycinnamoyl)-12-ursene-28-oic acid were found from the methanolic extracts of ME. ME has high potential in wound healing activity (Aleti et al., 2015), antibacterial, anti inflammatory (Khatri et al., 2014), antimicrobial, In vitro antioxidant, antirolithiatic, Antiinflammatory, analgesic and antipyretic activity (Koti et al., 2010), anticonvulsant, anthelmintic, antifungal, antiulcer, cognitive enhancing activity, diuretic, hepatoprotective and cytotoxic activity.

Many diseases, modifying anti rheumatic and non steroidal anti inflammatory drugs like methotrex-

ate, cyclosporine and D- Pencillamine, ibuprofen, sulindac and indomethacin are available in the market for the treatment of rheumatism. Rheumatism can be controlled by these drugs to a certain extent, but these drugs also have severe side effects. These side effects can range from mild rashes, nausea and vomiting to fatal, bacterial, fungal or viral infections like infection of herpes zoster or hepatitis B or C. Even rituximab can cause congestive heart failure and central nervous system diseases. So there is a need to explore alternative methods, particularly traditional medicines, for the treatment of rheumatoid arthritis. Therefore, this review article is prepared to collect and compile data of herbal medicinal plants which shows beneficial effects on rheumatoid arthritis by controlling the level of pro inflammatory cytokines such as IL-8, IL-6, IL-2 and TNF- $\alpha$  and thus inhibits inflammatory response with negligible side effects. In this review article, we have discussed the traditional plants with description of family, extracts, traditional uses and doses used for reporting antirheumatic activity.

## CONCLUSIONS

The data discussed in this review show a latest data having good potential for anti rheumatic activity. Many medicinal plants discussed in the review used traditionally for rheumatism have not been explored for anti rheumatic activity yet. The major chemical constituents present in the herbal medicinal plants mentioned in review having good anti rheumatic activity can be explored further to investigate the lead compounds for more precision and lesser adverse effects. In some plants reported activity is done on whole plant so there is need to evaluate the parts responsible for the anti rheumatism activity.

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## Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

## Authors Contributions

Harjinder Kaur, Ganesh N Sharma, Birendra Shrivastava and Satish Chander Arora conceived the review

idea and focus, drafting the article, critical revision and reference collection of article. Ganesh N Sharma, Birendra Shrivastava and Satish Chander Arora also supervised to the final revision of the manuscript.

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