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ANTI-INFLAMMATORY HERBS: A REVIEW

Baheti J. R.*¹, Awati S.T.², Navale S.D.², Sonawane A.A.², Dama G.Y.², Bidkar J.S.², Deore S. R.²

1. SSDJ College of Pharmacy, Chandwad, Nashik, Maharashtra, India
2. SGMSPM's Sharadchandra Pawar College of Pharmacy, Otur, Pune, Maharashtra, India

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For Correspondence:

Dr. Baheti J.R.

Dept. of Pharmacognosy,

SSDJ College of
Pharmacy, Chandwad,
Nashik, Maharashtra,
India

E-mail:

jbaheti@gmail.com

ABSTRACT

Inflammatory diseases including arthritis and rheumatism are major group of prevalent diseases. Inflammation is the complex biological response of vascular tissues to harmful stimuli including pathogens, irritants or damaged cells. Many substances, interfering with the inflammatory response have been isolated from medicinal plants. The review analyses the herbal plants, their extracts, isolated Phytoconstituents derived from medicinal plants evaluated for possible anti-inflammatory activity by using experimental animal model. Natural products with anti-inflammatory activity mainly contain active principles viz. Flavonoids, terpenoids, steroids, Phenolic compounds, saponins, alkaloids. In present study we have focused on some of the important medicinal plants reported for their anti-inflammatory action.

INTRODUCTION

Inflammation is protective and defense mechanism of the body. It is the reaction of vascularized living tissue to local injury. Inflammation is the complex biological response of vascular tissues to harmful stimuli including pathogens, irritants or damaged cells.¹ During inflammatory conditions various pathological changes are take place. The production of active inflammatory mediators is triggered by microbial products or by host proteins, such as proteins of the complement, kinins and coagulation systems that are themselves are activated by microbes and damaged tissues.^{2,3}

Acute inflammation is characterized by classical sign- edema, pain, heat and loss of function. The classical sign are triggered by the infiltration of the tissue but serum and white blood corpuscles (leucocytes).Chronic inflammation results in a progressive shift in type of cells, present at site of inflammation. It is characterized by simultaneous destruction and healing of the injured tissue from incidence of inflammation. The cellular process of inflammation falls into four distinct categories: a) Changes in blood flow caused by changes in smooth muscle

cell function causing vasodilation. b) Alteration in vascular permeability engendered by cytoskeleton contraction in endothelial cells. c) Migration of phagocytic leucocytes to the site of inflammation. d) Phagocytosis.^{4,5}

Early inflammatory changes in damaged tissue are now known to involve the release of various biologically active materials from polymorph nuclear leukocytes, lysosomal enzymes and others. The vascular effects are primarily mediated by kinins, prostaglandins and vasoactive amines cause increased vascular permeability leading to plasma exudation. The inflammatory process involves a complex interplay between cell of the blood, the blood vessels themselves and the cells of the involved tissue. The process can be seen as a coordinated response of a large number of cells to an initial stimulus.⁶ Inflammation research involves number of experimental models to study the anti-inflammatory activity. These models are of two types: 1) acute inflammatory models and 2) Chronic inflammatory models.⁷

Acute models are designed to test drugs that modulate erythema, changes in vascular permeability, leukocyte migration and chemotaxis, phagocytosis-

polymorphonuclear leukocytes and other phagocytic cells, measurement of local pain, and rat paw edema.⁸ Chronic models are designed to find drugs that may modulate the disease process and these includes sponge and pellet implants and granuloma pouches which deposits granulations tissue, adjuvant induced arthritis.⁷ It is well known that several physiological changes play key role in initiating inflammation disorders like arthritis and rheumatism. These response to inflammation include hyperpyrexia, increased total leukocyte count (TLC), differential leukocyte count (DLC), elevated erythrocytic sedimentation rate (ESR) and creative proteins. These are referred to as markers of acute inflammation.⁶

Natural products have been long recognized as an important source of therapeutically effective anti-inflammatory medicine. Different approaches used to analyze the anti-inflammatory potential of plant and plant derived compounds have been developed in the past years. Further, traditional herbal medicines like *Curcuma amada*, *Dichrostachys cinera*, *Gymnema sylvestre* have been used for anti-inflammatory activity.^{9,11,12,15}

HERBS WITH ANTI-INFLAMMATORY ACTIVITY

Alstonia scholaris (Apocynaceae)

The Plant *Alstonia scholaris linn.* (Family- Apocynaceae) grows throughout mainly in deciduous and evergreen forests, the plant traditionally used in rheumatic pains, malarial fever, cardiogenic, anthelmintic, laxative, snake-bite, and ulcer. Phytochemical investigation shows presence of triterpenoids, tannins, flavonoids, Ethanolic extract of *A.scholaris linn.* Leaves produced significant anti-inflammatory effect at dose (200mg/kg and 400mg/kg) using animal model Carrageenan induced rat paw edema for acute inflammation in rats and Diclofenac sodium (10mg/kg) as standard have been studied. Result showed significant anti-inflammatory effect as compared to that of standard.¹³

Stachytarpheta indica (Verbenaceae)

The Plant *Stachytarpheta indica linn.* (Family Verbenaceae), is a annual herb or shrub mainly found in Karnataka, Brazil, traditionally widely used for the treatment of ulcer, fever, rheumatic inflammation, constipation, diuretic, diarrhoea. Phytochemical investigation shows presence of irridoid glycosides tarphetalin, steroidal

saponins torvonin-A and iplomide. Alcoholic extract of *S. Indica linn.* leaves produced anti-inflammatory action at dose (500mg/kg) using animal model Carrageenan induced rat paw edema for acute inflammation in rats and Diclofenac sodium (100mg/kg) as standard have been studied. Result showed that it might proved to be an effective anti-inflammatory agent.¹⁴

Dichrostachys cinera (Mimosaceae)

The Plant *Dichrostachys cinera linn* (Family-Mimosaceae) is a medium sized thorny shrub occurs in tropical regions of India. it is widely used for the treatment of diuretics, urinary calculi, Kapha, Vata. Anti-inflammatory like effect of alcoholic extract of leaves of *D.cinera linn.* at (200 mg/kg) by using animal model Carrageenan induced rat paw edema for acute inflammation and cotton pellet granuloma for chronic inflammation in rats and indomethacin (10 mg/kg) as reference standard have been studied. Result showed that anti-inflammatory effect due to presence of flavonoids.¹⁵

Sapindus trifoliatus (Sapindaceae)

The Plant *Sapindus trifoliatus linn.* (Family-Sapindaceae) mainly occurs near to the

Mangalore, Karnataka; it is commonly used for treatment of expectorant, emetics, abortificant, spermicidal, epilepsy. Anti-inflammatory effect of methanolic extract of leaves of *S.trifoliatus linn.* at (400 mg/kg) by using carrageenan induced rat paw oedema model for acute inflammation and cotton –pellet granuloma model for chronic inflammation in rats and indomethacin (10mg/kg) as reference standard have been studied. Result showed that it posse’s significant anti-inflammatory activity.¹⁶

Biophytum sensitivum (Oxalidaceae)

The Plant *Biophytum sensitivum linn.*(Family-Oxalidaceae) is a mesophytic under shrub and grows in slightly moist places as well as in tropical and sub- tropical regions of world, the plant is ethno botanically and traditionally used for treatment of various diseases like abdominal pain, worm infestation, convulsion, muscular cramp. Anti-inflammatory effect of methanolic extract of leaves of *B.sensitivum linn.* at (200mg/kg) by using histamine,dextran,and Carrageenan induced rat paw oedema model in rats and indomethacin(10mg/kg) as standard have been studied. Result showed that anti-inflammatory effect due to presence of steroids and flavonoids.¹⁷

Scoparia dulcis (Scrophulariaceae)

The Plant *Scoparia dulcis* linn. (Family-Scrophulariaceae) is found in abundance in south America and in the Amazon rainforest and widely spread in India, the plant traditionally and ethno botanically used in the treatment of fever, cough, bronchitis, antifungal, antidiabetic, antibacterial. Anti-inflammatory like effect of aqueous extract of whole plant of *S.dulcis* linn. at (500 mg/kg) by using Carrageenan, histamine, dextran induced rat paw oedema model for acute inflammation and cotton pellet induced granuloma model for chronic inflammation in rats and indomethacin (10mg/kg) as reference standard have been studied. Result showed that the plant possess anti-inflammatory effect by inhibiting synthesis of prostaglandin due to presence of flavonoid.¹⁸

***Rhododendron dauricum* Linn.** (Ericaceae)

The Plant *Rhododendron dauricum* linn. (Family-Ericaceae) is an evergreen shrub widely distributed in India, china, Korea. Traditionally it has been used in treatment of skin diseases, inflammation and bronchitis. The aqueous extract of leaves of *R. dauricum* linn. produced anti-inflammatory effect at dose (80mg/kg) using animal model like Lipopolysaccharide (LPS) induced

septic shock and LPS induced micro vascular permeability in mice and Pentoxifylline (100mg/kg) as standard drug have been studied. Result suggested that it might proved to be an effective anti-inflammatory agent.¹⁹

Delonix elata (Caesalpiniaceae)

The Plant *Delonix elata* linn. (Family-Caesalpiniaceae) is a small sized tree found in Gujarat and southern india, the plant traditionally used for inflammatory joint disorders, methanolic extract of *D.elata* linn. Leaves produced anti-inflammatory effect at dose (300mg/kg) using animal model Carrageenan induced rat paw oedema for acute inflammation and cotton pellet granuloma for chronic inflammation in rats and valdecoxib (0.14mg/kg) as standard drug have been studied. Result suggested that it might proved to be an effective anti-inflammatory agent.²⁰

Lippia alba (Verbenaceae)

The Plant *Lippia alba* linn. (Family-Verbenaceae) is an aromatic shrub, traditionally used in many countries of the American continent for the treatment of asthma, cold, bronchitis, grippe (influenza). Topical anti-inflammatory effect of hydro-

alcoholic and diethyl ether extract of *L.alba linn.* Leaves at dose (0,15mg/ μ l) by using animal model 12-0-tetradecanoylphorol-13-acetate (TPA) and arachidonic acid (AA) induced mouse ear edema and Dexamethasone (4 μ g/ μ l) as standard drug have been studied. Result suggested that it possess significant topical anti-inflammatory activity.²¹

Spilanthes acmella (Compositae)

The Plant *Spilanthes acmella linn.* (Family-Compositae) is an indigenous annual herb grown throughout the tropics, the whole plant is claimed to possess medicinal properties widely used traditionally for the treatment of rheumatism, skin diseases. Anti-inflammatory effect of aqueous extract of aerial parts of *S.acmella linn.* at dose (400mg/kg) by using animal model Carrageenan induced rat paw oedema for acute inflammation in rats and Aspirin(100mg/kg) as standard drug have been studied. Result suggested that it might proved to be an effective anti-inflammatory agent.²²

Blechnum occidentale (Blechnaceae)

The Plant *Blechnum occidentale linn.* (Family-Blechnaceae) is a terrestrial fern

that ranges from the United States to South America and is employed in Brazilian folk medicine, traditionally this fern has been used to treat pulmonary and inflammatory diseases. Anti-inflammatory effect of methanolic extract of *B.occidentale linn.* Leaves at dose (100mg/kg and 300mg/kg) by using animal model Carrageenan induced rat paw oedema in rats and neutrophil migration method in mice and Dexamethasone (0.7mg/kg) as standard have been studied. Result suggested that it posses significant anti-inflammatory activity.²³

Miscellaneous plants

Several other plants that have significant anti-inflammatory activity that been reported in the literature. Some of these plants like *Brazillian propolis*, *Cassia angustifolia* and *Gymnema sylvestre* along with other plants reportedly possessing anti-inflammatory action are summarized in Table 1. Some of these herbal drugs characterized chemically along with used of experimental animal models.

Table1. Herbal plants with anti-inflammatory activity ¹¹⁻⁴²

BOTANICAL NAME	PART	DOSE	CHEMICAL CONSTITUENTS	ANIMAL MODEL
<i>Alstonia scholaris</i> (Apocynaceae)	Leaves	400mg/kg	Triterpenoids, bioflavonoid, tannins, quercetin, luteolin, hesperidins	INVIVO- Carrageenan induced rat paw oedema model
<i>Baliospermum montanum</i>	Root	200mg/kg	Tannins, saponins, flavonoids glycosides, proteins	INVIVO- Carrageenan induced rat paw oedema model
<i>Biophytum sensitivum</i> (Oxalidaceae)	Leaves	200mg/kg	Steroids, flavonoids terpenoids, tannins,	INVIVO- Carrageenan, Dextran, Histamine induced rat paw oedema model
<i>Blechnum occidentale</i> (Blechnaceae)	Leaves	300mg/kg	Flavonoids, saponins	INVIVO- Neutrophil migration model, Carrageenan induced rat paw oedema model
<i>Brazillian propolis</i>	Whole plant	500mg/kg	Phenolic acids, flavonoids, caffeic acid	INVIVO- Croton oil induced ear edema in mice
<i>Cassia angustifolia</i> (Leguminosae)	Leaves		Anthraquinone glycosides saponins, flavonoids, limonoids, magnoflorine	INVIVO- TPA induced mouse ear edema model Oxazolone induced contact-delayed type hypersensitivity
<i>Cassia grandis</i>	Leaves	125mg/kg	Saponins, triterpenoids, flavonoids	INVIVO- Carrageenan induced rat paw oedema model
<i>Delonix elata</i> (Caesalpinaceae)	Leaves	300mg/kg	Terpenoids saponins, flavonoids, Steroids	INVIVO- Carrageenan, Dextran, Histamine induced rat paw oedema model, Cotton pellet induced granuloma

<i>Dichrostachys cinera</i> (Mimosaceae)	Bark, Root	200mg/kg	β -amyrin, β -sitosterol, friedelin-3-one, n-octacosanol, hextriacontanol	INVIVO- Carrageenan induced rat paw oedema model, Cotton pellet induced granuloma
<i>Lippia alba</i> (Verbenaceae)	Whole plant	15mg/ μ l	Terpenoids essential oil contains carvone, limonene, sesquiterpens, myrecene, β - pinene	INVIVO- TPA and AA induced mouse ear edema model
<i>Prosthechea michuacana</i>	Bulb	200mg/kg	8-C-(6-deoxy- β -D-glucopyranosy)apigenina, 2-(4-hydroxybenzyl) malic acid	INVIVO- Cotton pellet induced granuloma Carrageenan induced rat paw oedema model
<i>Rhododendron dauricum</i> Linn. (Ericaceae)	Leaves	80 mg/kg	Flavonoids, saponins	INVIVO- LPS induced septic shock and LPS induced vascular permeability model
<i>Rubus ellipticus</i> (Rosaceae)	Root	500 mg/kg	Steroids, tannins, triterpenoids, flavonoids	INVIVO- Carrageenan induced rat paw oedema model
<i>Sapindus trifoliatus</i> (Sapindaceae)	Leaves	400 mg/kg	Triterpenoids, glycosides, flavonoids, saponins	INVIVO- Carrageenan induced rat paw oedema model
<i>Scoparia dulcis</i> (Scrophulariaceae)	Whole plant	500 mg/kg	Flavonoids, triterpenoids, steroids, saponins	INVIVO- Cotton pellet induced granuloma Carrageenan induced rat paw oedema model

<i>Spilanthes acmella</i> (Compositae)	Aerial parts	400mg/kg	Saponins, flavonoids, resins triterpenoids,	INVIVO - Carrageenan induced rat paw oedema model
<i>Stachytarpheta indica</i> (Verbenaceae)	Leaves	500 mg/kg	Irridoid glycosides tarphetalin, steroidal saponins torvonin-A and iplomide,	INVIVO - Carrageenan induced rat paw oedema model
<i>Stereospermum kunthianum</i> (Bignoniaceae)	Stem bark	400 mg/kg	Saponins, flavonoids triterpenoids, tannins	INVIVO - Carrageenan induced leucocytes migration method Carrageenan induced rat paw oedema model Granuloma air pouch model
<i>Sesbania sesban</i>	Leaves	200 mg/kg	Carbohydrates, steroidal saponins, glycosides, flavonoids, tannins	INVIVO - Carrageenan induced rat paw oedema model
<i>Trewia polycarpa</i>	Stem bark	500µg	Alkaloids, glycosides, tannins, phenols, flavonoids, steroids	INVITRO - Human RBC membrane stabilization
<i>Vitex leucoxylin</i> <i>Linn.</i> (Verbenaceae)	Bark	100mg/kg, 250mg/kg	β-sitosterol, diethyl terphthalate, vitexin, isovitexin, aucubin	INVIVO - Freund's complete adjuvant induced arthritis in rats model
<i>Gymnema sylvestre</i> (Asclepidaceae)	Leaves	300 mg/kg	Tannins, saponins, flavonoids, triterpenoids	INVIVO - Cotton pellet induced granuloma Carrageenan induced rat paw oedema model
<i>Curcuma amada</i> <i>roxb.</i> (Zingiberaceae)	Rhizome	200 mg/kg	Triterpenoids, curcuminoid derivatives, flavonoids, oleoresins, sesquiterpenes	INVIVO - Chronic granuloma pouch model Carrageenan induced rat paw oedema model

<i>Cordia dichotoma forst.</i>	Seed	500 mg/kg	Alkaloids, carbohydrates, flavonoids, saponins, tannins	INVIVO- Carrageenan, Dextran induced rat paw oedema model
<i>Cussonia paniculata</i> (Araliaceae)	Stem bark	200 mg/kg	Triterpenoids, saponins, tannins flavonoids	INVIVO- Histamine, Carrageenan, induced rat paw oedema model.

ACTIVE PRINCIPLES WITH ANTI-INFLAMMATORY ACTIVITY:

Flavonoids

Flavonoids are a group of compounds with a wide range of biological effects, including anti-inflammatory activity. Various mechanisms have been proposed to explain the anti-inflammatory effect of flavonoids; these include inhibition of inflammatory mediators, inhibition of hydroxyl and lipid peroxide free radicals also, flavonoids have been found to be free radical scavengers. free radicals play an important role in inhibition of synthesis of prostaglandin by inhibiting the enzyme prostaglandin synthetase. The most commonly anti-inflammatory Flavonoids viz. flavonol, flavonones, flavones (luteolin), quercetin, rutin, hesperidins, silymarin derivatives. flavonoids isolated from the aqueous extract of aerial parts of *Spilanthes acmella linn.*

(Compositae) mainly targets prostaglandin which involved in late phase of acute inflammation.²² Moreover, several extracts containing flavonoids have been found to exert anti-inflammatory and antioxidant activity.⁴³

Steroids

Steroids are widely distributed in plants and are in a particular form of glycosides. The oleoresins fraction of *Curcuma amada linn.* (Zingiberaceae) possesses significant anti-inflammatory and anti-arthritic activities.¹¹ β -sitosterol isolated from *Dichrostachys cinera linn.* (Mimosaceae) possesses potent anti-inflammatory activity against Carrageenan induced rat paw edema and Cotton pellet-induced granuloma model in rats.¹⁵ α -spinasterol obtained from the stem bark of *Symplocos spicata linn.* Showed a significant activity against acute inflammation induced by Carrageenan in

rats.²⁴ Several plants containing high amounts of steroids have been shown to possess anti-inflammatory activity in several experimental anti-inflammatory models.

Terpenoids

The triterpenoids of the oleanene and ursene series were found to be active against Carrageenan induced edema and formaldehyde-induced edema and arthritis in rats. It has been suggested that the anti-inflammatory activity of the triterpenoids of the oleanene series with the polarity of compounds which is enhanced by the number of hydroxyl groups in the molecule.²⁵ Two oleanane type triterpenes saponin, Zanthosaponins A and B and the cyclitol pinitol isolated from the methanolic extract of root bark of *Zanha Africana linn.* (Sapindaceae) were active as inhibitors of phospholipase A2.²⁶ Pentacyclic triterpenes from the 11-keto-boswellic acid series were identified as the active principle ingredients of *Boswellia* resin, inhibiting the key enzymes of leukotrienes biosynthesis, 5-lipoxygenase, of the genuine boswellic acid.²⁷

Phenolic compounds

The petroleum ether extract of the rhizomes of *Curcuma longa linn.* (Turmeric) showed

significant anti-inflammatory activity and was effective in delayed hypersensitivity. In granuloma pouch method, the aqueous extract was the most potent with activity comparable to indomethacin.^{28,29} Epicatechin isolated from seed coat of *Anacardium occidentale linn.* appears to be effective as Phenylbutazone against various test models.³⁰ Bergen isolated from the pods of *Peltophorum pterocarpum linn.* was found to be equipotent to phenylbutazone in rats against Carrageenan induced edema.³¹

CONCLUSION:

Rheumatism and arthritis are the major prevalent inflammatory disorders, It is interesting to note that a large number of plants have been studied and these investigations suggest selective anti-inflammatory activity of the said plants in experimental animal models of inflammation. There are several natural products with potential therapeutic applications because of their high efficacy and low toxicity. The non-steroidal anti-inflammatory drugs (NSAIDs) inhibit the biosynthesis of inflammatory mediators such as (prostaglandin, bradykinin, and leukotrienes) which is supposed to be the principal mode of action of these drugs.

Finally, it should be noted that Phytoconstituents such as flavonoids, terpenoids, steroids, saponins, alkaloids that possess anti-inflammatory activity. It is believed a superior therapeutically effective anti-inflammatory drug can be obtained from this natural source.

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