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Review Article

Anti-inflammatory agents of herbal origin: An overview

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ABSTRACT

Inflammation is a pathological state characterized by redness, pain and swelling which is probably the result of leucocyte infiltration. Various agents such as Non-steroidal anti-inflammatory drug (NSAID's) have potent anti-inflammatory activity that are accompanied by various adverse effects like peptic ulceration, increase Na+ and water retention, raised transaminases, mental confusion, etc. Contrary to that the drugs obtained from plant source (herbal drug) have fewer side effects. The main objective of this review is to abridge the herbal plants used in inflammation and to seek their anti-inflammatory potential.

Keywords: Inflammation; Anti-inflammatory activity; Herbal agents.

INTRODUCTION

Inflammation is the reaction of living tissues to injury, infection or irritation. Lysosomal enzymes released during inflammation produce a variety of disorders which leads to the tissue injury by damaging the macromolecules and lipid peroxidation of membranes which are assumed to be responsible for certain pathological conditions as heart attacks, septic shocks and rheumatoid arthritis etc. (Chippada 2011) These inflammatory mediators come from plasma proteins or cells including mast cells, platelets, neutrophils and monocytes/macrophages. (Kumar 2012).

Prolonged inflammation leads to the rheumatoid arthritis, atherosclerosis, hay fever, ischemic heart diseases etc (Rahman 2012). Traditional medicine practitioners, in mainly, developing countries have used herbal medicines to treat various ailments including pain and inflammation. (Amabeoku 2012).

Vasodilation and its resulting increased blood flow cause the redness and increased heat. Increased permeability of the blood vessels results in an exudation of plasma proteins and fluid into the tissue which manifests itself as swelling. Some of the released mediators such as bradykinin increase the sensitivity to pain. The process of acute inflammation is initiated by cells already present in all tissues, mainly resident macrophages, dendritic cells, histiocytes, kupffer cells and mastocytes. These cells present on their surfaces certain receptors named pattern recognition receptors (PRRs), which recognize molecules that are broadly shared by pathogens but distinguishable from host molecules, collectively referred to as pathogen-associated molecular patterns (PAMPs). At the onset of an infection, burn, or other injuries, these cells undergo activation (one of their PRRs recognizes a PAMP) and release inflammatory mediators responsible for the clinical signs of inflammation. The neutrophils migrate along a chemotactic gradient created by the local cells to reach the site of injury. The loss of function is probably the result of a neurological reflex in response to pain. In addition to cell-derived mediators, several acellular biochemical cascade systems consisting of preformed plasma proteins act in parallel to initiate and propagate the inflammatory response. (Cotran 1999).

NSAIDs are the most commonly used drugs throughout the world. They are prescribed for osteoarthritis, and fractures etc. (Boursinos 2009). These are one of the best classes of drugs to prevent and treat postoperative pain. (Vikrant 2011) Most of the anti-inflammatory drugs, particularly steroids and cyclooxygenase inhibitors are often associated with adverse side effects including GI irritation, ulcers, hypertension and cardiac abnormalities. Drugs from plant sources have been used for the treatment of various disorders and diseases since ancient times. Nowadays, the use of herbal drugs to cure inflammation and pain is gaining popularity due to their effectiveness, fewer side effects, low cost and availability. (Ajay 2012) Conventional drugs treatments are limited in their effectiveness in managing the incidence and outcome of many inflammatory diseases. They also present a significant number of side effects in patients. (Amdekar 2012).

Inflammatory diseases including different types of rheumatic diseases are a major cause of morbidity of the working force throughout world. This has been called the 'King of Human Miseries'. (Shah 2006).

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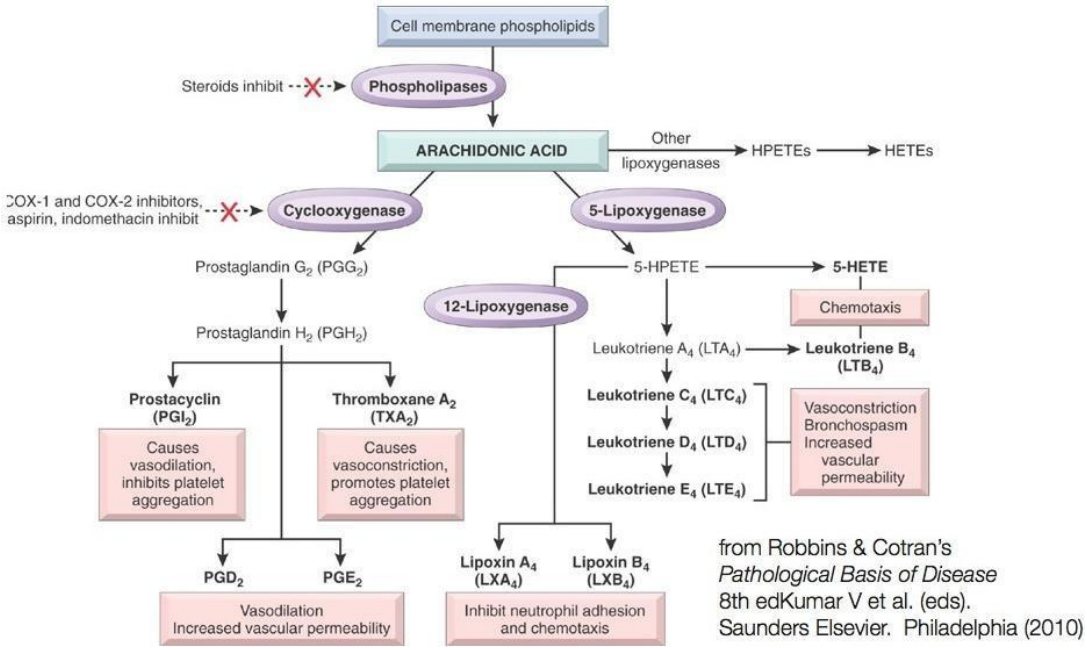

Figure 1: Role of Arachidonic acid metabolites in Inflammation

Natural products in general and medicinal plants in particular, are believed to be an important source of new chemical substances with potential therapeutic efficacy (Ameh 2009).

Natural products of plant origin are still a major part of traditional medical system in developing countries. Now-a-day's interest in natural products as potent therapeutic agent has increased tremendously, the modern clinicians are now inclined towards the use of herbal medicine. WHO estimate that 65-80% of the world population uses traditional medicine as their primary form of healthcare and about 85% of the traditional medicine involve the use of herbal preparation fully aware of the importance of the herbal medicine as a valuable answer readily available resources for primary health care and has endorsed there safe and effective use. (Patil 2012).

Plants with anti-inflammatory activity

Plants are well known for their medicinal values with lesser side effects. Drugs which are obtained directly from plant source have been used throughout the world from many centuries for the treatment of many diseases like rheumatism, depression, diabetes, etc. In this overview, an attempt has been made to bring together those plants which acquire anti-inflammatory activity.

Abbreviations: HIPE- histamine induced paw edema, CIAP-carrageenan indused air pouch, PE- Paw edema, UA- Ulcerogenic assay, CIP-carragenan induced peritonitis, TEME-Topical edema of mouse ear, CPIG-Cotton pellet induced granuloma, Zymogen induced paw edema, CIEP-carragenan induced ear pouch, FIAI-Formalin induced acute inflammation, VP- Vascular permeability, MDLA-Monocyte dependent leucocyte adhesion, CIPE-Carrageenan induced paw edema, FIPE-Formalin induced paw edema, ZIPE- XIPE-Xylene induced paw edema.

Aconitum heterophyllum

The anti-inflammatory activity of ethanolic root extract of *Aconitum heterophyllum* (225, 450 and 900mg/kg p.o) has been evaluated in cotton pellet-induced granuloma in rats. The extract has reduced inflammation as evidenced by decreased weight of cotton pellet in cotton pellet-induced granuloma in rats. The results demonstrate the anti-inflammatory properties of extract and the effects were comparable to diclofenac sodium, a standard non-steroidal anti-inflammatory drug. (Verma 2010).

Coriandrum sativum

Ethanolic extracts of fruits of *Coriandrum sativum*, leaves were subjected to preliminary screening for anti-inflammatory activity in albino rats. Ethanolic extracts (200mg/kg) exhibited significant anti-inflammatory activity comparable to the standard drug Diclofenac sodium(5mg/kg) against carrageenan induced rat paw edema method.(Gupta 2010).

Anogeissus acuminata

The methanolic extracts of *Anogeissus acuminata* leaf were ingested orally (p.o.) in the form of suspension in 0.5% Tween 80 in two different doses, 200 and 400 mg/kg body weight. The anti-inflammatory effect of *A. acuminata* was tested in: carrageenan-induced paw oedema in wistar albino rats and formalin-induced paw oedema in Swiss albino mice and compared with the standard, indomethacin (5 mg/kg body weight) showed that *A. acuminata* has significant reduction in inflammation i.e. 66.67 % (200 mg/kg body weight) and 77.78% (400 mg/kg body weight) as compared to the

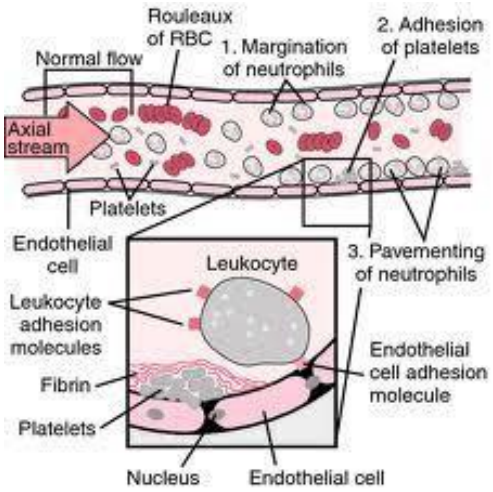

Figure 2: Steps involved in Inflammation

standard drug, indomethacin, which was 88.89%. (Hemamalini 2010).

Albizia lebbeck

The anti-inflammatory activity of *Albizia lebbeck* was studied using the carrageenan, dextran, cotton pellet and freund's complete adjuvant induced rat models. The petroleum ether and ethanol extracts at 400mg/kg, showed maximum inhibition of inflammation induced by carrageenan (petroleum ether-48.6%; ethanol-59.57%), dextran (petroleum ether-45.99%; ethanol-52.93%), cotton pellet (petroleum ether-34.46%; ethanol-53.57%) and freund's adjuvant (petroleum ether-64.97%; ethanol-68.57%).(Babu 2009).

Bambusa vulgaris

The anti-inflammatory effect is investigated employing acute inflammatory models: formaldehyde-induced paw edema, acetic acid-induced vascular permeability, subacute anti-inflammatory model: cotton pellet granuloma, estimation of plasma MDA and carrageenan-induced peritonitis. MEBV (100, 200 and 400 mg/kg, p.o) exhibited a dose-dependent and significant inhibition in all the experimental models. (Carey 2009).

Cordia dichotoma forst

The effects of *Cordia dichotoma forst f.* seeds extracts on different phases of acute inflammation were examined using different phlogistic agents-induced paw edema *viz*., Carrageenan-induced paw oedema and Dextran- induced paw oedema in rats. Various extracts (ethanol and aqueous) of *C. dichotoma forst* seeds at a dose of 250 mg/kg and 500 mg/kg orally were tested. Diclofenac sodium at the dose of 10mg/kg was used as standard. Both the extracts showed significant activity compared with the control in both of these models. (Sharma 2010).

***Caesalpinia pulcherrima* Linn**

Anti-inflammatory action of the ethanolic and aqueous extracts of *C. pulcherrima* (100 and 200 mg/kg b.w.) (CPE and CPA) were evaluated by cotton pellet granuloma models. The ethanolic and aqueous extracts of *C. pulcherrima* significantly decreased the granuloma tissue development. (Sharma 2011).

Ichnocarpus frutescens

The effect of methanolic extract of *Ichnocarpus frutescens* (MEIF) was evaluated for its anti-inflammatory activity by using carrageenan, and cotton pellet induced granuloma tests for its effect on acute and chronic phase inflammation models in rat. Maximum inhibition (54.63 %) was obtained at the dose of 100 mg/kg after 3 h of drug treatment in carrageenan induced paw oedema, whereas indomethacin produced 57.65 % of inhibition. In the chronic model the MEIF 300 mg/kg, indomethacin and dexamethasone standard drug showed decreased formation of granuloma tissue by 22.64, 29.63 % and 34.84 % respectively. (Pandurangan 2008).

***Mimosa pudica* Linn**

The anti-inflammatory activity of the various extracts of leaves of *Mimosa pudica* Linn was studied based on their effects on carrageenan-induced paw oedema and cotton pellet granuloma in rats. The extracts in dose levels of 50,100 and 200 mg/kg orally were used for anti-inflammatory studies. The ethanol and aqueous extracts significant inflammatory activities in a dose-dependent manner to that of standard drug indomethacin, while petroleum ether extract exhibit minimum inhibitory effect in carrageenan induced hind paw oedema and cotton pellet granuloma in rats.(Goli 2011).

Carica papaya

The anti-inflammatory activity of an ethanolic extract of *Carica papaya* leaves was investigated in rats using carrageenan induced paw oedema, cotton pellet granuloma and formaldehyde induced arthritis models and animals received 25–200 mg/Kg (orally) of the extracts or saline (control group) and the reference group received 5 mg/ Kg of indomethacin. The results show that the extracts significantly reduced paw oedema in the carrageenan test. Likewise the extract produced significant reduction in the amount of granuloma

Table 1: List of few herbal sources having potent anti-inflammatory activity

S. No	Botanical Name	Family	Plant Part used	Extract used	Experimental model used	References
1.	*Aconitum hetero-phyllum*	Valeraneaceae	Root	Ethanolic	CPIG,	Verma 2010
2.	*Coriandrum Sati-vum*	Umbelliferae	Fruit	Ethanolic	CIPE	Gupta 2010
3.	*Cicer arietinum*	Fabaceae	Seeds	Methanolic and ethanolic	CIPE, HIPE	Doppalapudi 2012
4.	*Cussonia panicu-lata*	Araliaceae	Stembark	Aqueous	CIPE, HIPE	Adeolu 2008
5.	*Anogeissus acuminata*	Combretaceae	Leaves	Methanolic	CIPE,FIPE	Hemamalini 2010
6.	*Albizia lebbeck*	Leguminosae	Bark	Petroleum ether, ethanol	CIPE	Babu 2009
7.	*Bambusa vulgaris*	Poaceae	Leaves	Methanolic	FIAI,VP,CPIG,CIP	Carey 2009
8.	*Borassus flabellifer* L.	Asteraceae	Male flower	Ethanol	PE,CPIG,CIAP	Paschapur 2009
9.	*Euphorbia neriifo-lia* Linn	Euphorbiaceae	Leaves	Hydroalcoholic	CIPE	Gaur 2009
10.	*Curcuma longa* Linn.	Zingiberaceae	Rhizomes	Petroleum ether	CPIG	Kohli 2005
11.	*Centaurea cyanus*	Asteraceae	Flowers	Aqueous	ET IPE	Talhouk 2008
12.	*Cordia dichotoma forst f.*	Boraginaceae	Seeds	Ethanol and aqueous	PE	Sharma 2010
13.	*Caesalpinia Pulcherrima*	Leguminosae	Bark	Ethanolic and aqueous	CPIG ,CIPE	Sharma 2011
14.	*Curcuma amada* Roxb.	Zingiberaceae	Rhizome	Ethyl alcohol.	PE,CPIG,	Mujumdar 2000
15.	*Citrullus colocyn-this*	Cucurbitaceae	Fruit and seed	Aqueous	PE,CIAP	Marzouk 2011
16.	*Carica papaya*	Caricaceae	Leaves	Ethanolic	CPIG,CIPE	Owoyele 2008
17.	*Gendarussa vul-garis Nees*.	Apocyanaceae	Leaves	Alcoholic and aqueous	CIPE	Saleem 2011
18.	*Ficus bengalensis*	Moraceae	Stembark	Aqueous and methanolic	CIPE, CPIG, VP	Thakare 2010
19.	*Garcinia man-gostana*	Guttiferae	Fruit hull	Ethanolic	PE	Geeng 2007
20.	*Hygrophila spinosa T.*	Acanthaceae	Leaves	Petroleum ether, chloro-form	PE,	Patra 2009
21.	*Ichnocarpus Frutescens*	Apocynaceae	Roots,	Methanolic	CIPE, CPIG	Pandurangan 2008
22.	*Leucas aspera* Spreng.	Labitae	Leaves	Suspensions of powders with 2% gum acacia were prepared	CIPE, CPIG	Srinivas 2000

Abbreviations: **HIPE**- Histamine induced paw edema, **CIAP**-Carrageenan induced air pouch, **PE**- Paw edema, **UA**- Ulcerogenic assay, **CIP**-Carrageenan induced peritonitis, **TEME**-Topical edema of mouse ear, **CPIG**-Cotton pellet induced granuloma, **ZIPE**- Zymogen induced paw edema, **CIEP**-Carrageenan induced ear pouch, **FIAI**-Formalin induced acute inflammation, **VP**- Vascular permeability, **MDLA**-Monocyte dependent leucocyte adhesion, **CIPE**-Carrageenan induced paw edema, **FIPE**-Formalin induced paw edema, **XIPE**-Xylene induced paw edema.

Table 2: List of few herbal sources having potent anti-inflammatory activity

23.	*Hibiscus tiliaceus*	Malvaceae	Wood	Methanolic	CPIG,CIPE	Borhade 2012
24.	*Hedychium coronarium* koen	Zingiberaceae.	Rhizome	Hexane, chloroform , methanol	CIPE	Shrotriya 2007
25.	*Lantana camara*	Verbenaceae	Aerial part	Aqueous	PE	Gidwani 2009
26.	*Stellaria media*	Caryophyllaceae	Whole herb	Methanol	AIPE	Oyebanji 2012
27.	*Mirabilis jalapa Linn.*	Nyctaginaceae	Leaves	Alcoholic	PE,CPIG,	Nath 2010
28.	*Murraya koenigii Spreng*	Rutaceae	Leaves	Petroleum ether, ethanol chloroform,	PE	Darvekar 2011
29.	*Pfaffia glomerata*	Amaranthaceae	Root	Hydroalcoholic extract	PE	Neto 2005
30.	*Medicago sativa L.*	Fabaceae	Dried leaves, stems,	Ethyl acetate	LPS-II	Yong-Han 2009
31.	*Mimosa pudica*.	Fabaceae	Leaves	Petroleum ether, alcoholic, aqueous	CIPE,CPIG	Goli 2011
32.	*Ocimum Sanctum*	Lamiaceae	Leaves	Paste of tulsi leave	CIPE.	Kalabharathi 2011
33.	*Pinus roxburghii Sarg.*	Pinaceae	Dried leaves	Alcoholic, petroleum ether	CIPE,CPIG	Kaushik 2012
34.	*Wigandia urens*	Hydrophyllaceae	Aerial parts	Methanolic, aqueous, chloroform	CIPE	Zavala-Sánchez 2009
35.	*Psoralea Corylifolia* Linn.	Leguminosae	Seed	Hexane	CIPE	Gidwani 2010
36.	*Phyllanthus amarus* Euphorbiaceae		Whole plant	Methanol	PE,CPIG,CIAP	Mahat 2007
37.	*Solanum nigrum* Linn	Solanaceae	Berries	Methanolic	CIPE	Ravi 2009
38.	*Terminalia arjuna*	Combretaceae	Leaf	Methanolic, petroleum ether	CIPE	Biswas 2011
39.	*Strophanthus hispidus*	Apocynaceae	Root	Aqueous	CIPE,XIPE	Agbaje 2012
40.	*Wigandia urens*	Hidrofilaceae	Aerial part	Chloroform, methanol, aqueous	CIPE	Zavala-Sánchez 2009
41.	*Securidaca longipedunculata Fres*	Polygalaceae	Root, Bark	Methanol, petroleum ether	TEME,PE,UA	Okoli 2006
42.	*Plumbago zeylanica*	Plumbaginaceae	Root	Methanol	CIPE	Arunachalam 2010
43.	*Trigonella foenum graceum*	Leguminosae	Seeds	Alcoholic	CIPE	Datta 2010

formed from 0.58 ±0.07 to 0.22 ±0.03 g. In the formaldehyde arthritis model, the extracts significantly reduced the persistent oedema from the 4th day to the 10th day of the investigation. (Owoyele 2008).

***Hibiscus tiliaceus* Linn**

Methanolic wood extract of Hibiscus tiliaceus Linn in experimental acute and chronic inflammatory animal models was studied using the acute (Carrageenan induced paw edema) and chronic (Cotton pellet induced granuloma) animal models. Only the 200 and 4000 mg/kg body weight extracts exhibited significant result when compared with control. The rats exhibited 6.71 %, 31.79 % and 44.03 % inhibition of granuloma mass formation after the 7 days treatment with 100, 200 and 400 mg/kg body weight of extracts when com-

pared with control in cotton pellet granuloma. (Borhade 2012).

Mirabilis Jalapa Linn

Alcoholic extract and successive petroleum ether fractions of leaves of *Mirabilis Jalapa Linn* were screened for its anti-inflammatory activity using carrageenan induced rat paw edema and cotton pellet induced granuloma models. The total alcoholic extract at the dose of 300 mg/kg p.o and successive petroleum ether fraction at the dose of 200 mg/kg exhibited significant anti-inflammatory activity in carrageenan induced paw edema model. In cotton pellet granuloma model, the total alcoholic extract at the dose of 300 mg/kg and successive petroleum ether fraction at the dose of 200 mg/kg inhibited granuloma formation significantly. (Nath 2010).

Plumbago zeylanica

The study of anti inflammatory on the root of *P. zeylanica* with methanolic extracts at 300 and 500 mg/kg produced 31.03 and 60.3% inhibition of acute inflammation, respectively, in Carrageenan induced raw paw oedema confirming that *P. zeylanica* roots are effective against acute inflammation. (Arunachalam 2010).

CONCLUSION

These are the few herbal plants which are formerly explored for their anti-inflammatory activity. But in the lap of the nature there are so many plants which are remaining unexplored and need to study for their therapeutic value, so that they can also be used as herbal medication. Herbal medications have lesser or no side effects and frequent toxicity unlike the allopathic medicines. So this review is merely an initiation to provide options of herbal source for the treatment of various types of inflammatory diseases.

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