Praveen K Dixit and Suchita Mittal. / *International Journal of Phytopharmacology*, 4(3), 2013, 158-165.

e- ISSN 0975 – 9328
Print ISSN 2229 – 7472

International Journal of Phytopharmacology

Journal homepage: www.onlineijp.com

IJP

HERBAL SOURCES OF ANTI-INFLAMMATORY POTENTIAL: A REVIEW

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ABSTRACT

Inflammation is usually regarded as a pathological state. It is a physiological response of the living tissue to injury, provided the injury is not of such a degree as to cause necrosis or loss of viability. Inflammation is characterized by redness, pain and swelling. There are many drugs available for inflammation like Non-steroidal anti-inflammatory drug (NSAID). But these drugs have many adverse effects like peptic ulceration, Na+ and water retention, raised transaminases, mental confusion, etc. While the drugs obtained from plant source (herbal drug) have fewer side effect. The main aim of this review to summarize the herbal plants used in inflammation.

Key words: Inflammation, Anti-inflammatory activity, Herbal plants.

INTRODUCTION

Pain and inflammation are some of the most common manifestations of many diseases afflicting millions of people worldwide. (Raghav *et al*., 2006; *Rang et al*., 2011). Even though there are effective orthodox medicines used to alleviate these manifestations (South African Medicines Formulary, 2010). Traditional medicine practitioners, in mainly, developing countries have used herbal medicines to treat various ailments including pain and inflammation (Martini-Bettolo, 1980).

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. Vasodilation and its resulting increased blood flow cause the redness (rubor) and increased heat (calor). Increased permeability of the blood vessels results in an exudation (leakage) of plasma proteins and fluid into the tissue (edema) which manifests itself as swelling (tumor). Some of the released mediators such as bradykinin increase the sensitivity to pain (hyperalgesia, *dolor*). The mediator molecules also alter the blood vessels to permit the migration of leukocytes, mainly neutrophils, outside of the blood vessels (extravasation) into the tissue. The neutrophils migrate along a chemotactic gradient created by the local cells to reach the site of injury. The loss of function (*functio laesa*) 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. These include the complement system activated by bacteria and the coagulation and fibrinolysis systems activated by necrosis, e.g. a burn or a trauma (Cotran *et al*., 1999).

NSAIDs are among the most commonly used drugs worldwide. They are prescribed for orthopaedic conditions such as osteoarthritis, soft-tissue injuries and fractures etc (Boursinos *et al*., 2009). NSAIDs are one of the best classes of drug to prevent and treat postoperative pain (Luna *et al*., 2007). The greatest disadvantage in

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presently available potent synthetic drugs lies in their toxicity and reappearance of symptoms after discontinuation. Therefore, the screening and development of drugs for their anti-inflammatory activity is the need of hour and there are many efforts for finding anti-inflammatory drugs from indigenous medicinal plants (Srinivasan *et al*., 2001). The use of NSAIDs is associated with many side effects, but their unwanted effects on the gastrointestinal tract, the kidney and the cardiovascular system are considered as major issues with the use of these drugs (Alexandrina, 2010).

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' (Chatterjee *et al*., 1984).

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 *et al*., 2009). Since ancient times herbal plants are known for their medicinal values and in rural areas they have been used tremendously. In 21st century there are so many drugs available for the treatment of various types of inflammatory disease but along with their therapeutic effect they all posses several adverse effect. In such condition there is need to explore the herbal resources for treatment of such disease because they have comparatively less side effects.

Plants with anti-inflammatory activity

Drugs which are obtained directly from plant source have been used all over the world from last many centuries for many diseases like inflammation, rheumatism, depression, diabetes, etc. In this review, an effort has been made to collect those plants which possess anti-inflammatory activity.

Aegle marmelos

Aqueous extract of root bark of *Aegle marmelos* was prepared and tested for anti-inflammatory activity in albino rats weighing 150-280 grams. The *in vivo* anti-inflammatory activity was studied using the acute (Carrageenan induced paw edema) and chronic (Cotton pellet induced granuloma) animal models. The PI with indomethacin and Bilwa in carrageenan induced paw edema were 52.7% and 46% and in cotton pellet induced granuloma were 24.7% and 9.2% respectively. Indomethacin showed highly significant anti-inflammatory activity in both the models. However, Bilwa showed highly significant activity in acute model and but a trend of anti-inflammatory activity in chronic model studied (Benni *et al*., 2011).

Alchornea cordifolia

Aqueous decoction and methanol leaf extracts were tested for their ability to reduce Croton oil-induced oedema in the mouse ear, after topical application. The methanol leaf extract dose-dependently inhibited the Croton oil-induced ear oedema in mice *(ID (*50)<500 microg/cm) (Manga *et al*., 2004).

Aloe barbadensis

The anti-inflammatory and analgesic activities of aqueous extract of *Aloe barbadensis* was investigated in rats. Formalin- induced hind paw oedema was used to assess the anti- inflammatory activity of the extract while acetic acid-induced abdominal writhing was used for analgesic activity. The results of the anti-inflammatory study revealed that 25, 50 and 100 mg/kg of the extract reduced the formalin-induced oedema significantly ($P<0.05$) at the beginning of 3 hours when compared to the control group. In the analgesic study, 25, 50 and 100 mg/kg of extract significantly ($P<0.5$) reduced the number of writhes induced by a 0.6% Acetic acid solution with an approximately 66.49%, 57.59% and 68.06% inhibition respectively (Egesie *et al., 2011*).

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: carrageenin-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 standard drug, indomethacin, which was 88.89% (Hemamalini *et al*., 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 *et al*., 2009).

Bauhinia variegata

Methanolic and aqueous fraction of the bark of *Bauhinia variegata* was investigated for its acute inflammation potential in animals. The aqueous fraction of the methanol extract significantly inhibited carrageenan induced paw edema in rat at 250 mg/kg. Significant activity against dextran induced paw edema in rats was

exhibited by both methanol extract and aqueous extract when administered orally at 200 mg/kg and 250 mg/kg (Bairagi *et al*., 2012).

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 *et al*., 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 *et al*., 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 *et al*., 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 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 *et al*., 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 compared with control in cotton pellet granuloma (Borhade *et al*., 2012).

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 *et al*., 2008).

Mirabilis Jalapa Linn

Alcoholic extract and successive petroleum ether fractions of leaves of *Mirabilis Jalapa Linn* were screened for its anti-inflammatory activity using carageenan 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 *et al*., 2010).

***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 carageenan induced hind paw oedema and cotton pellet granuloma in rats (Goli *et al*., 2011).

Fig.1. Role of Prostaglandins in Inflammation

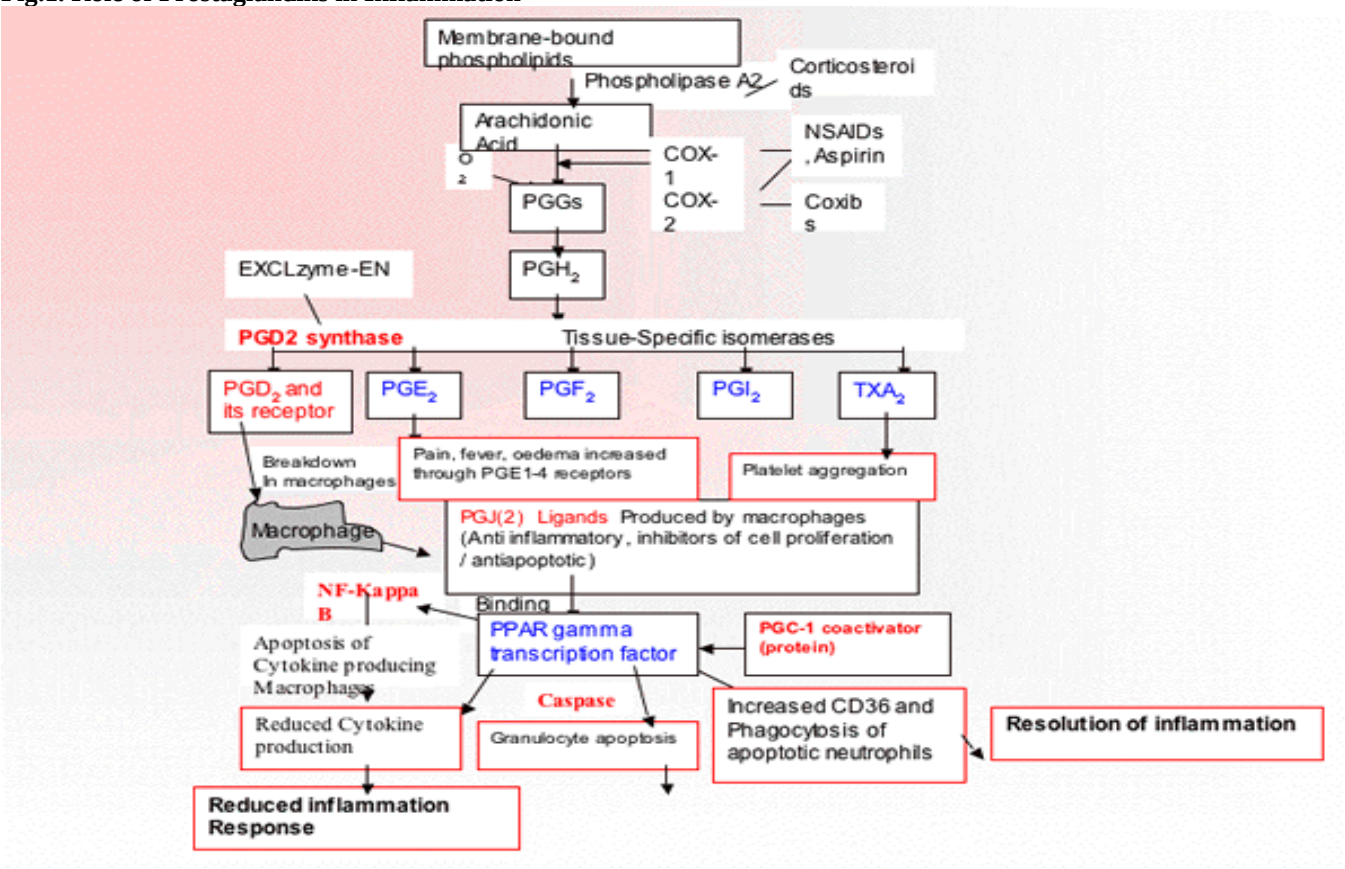

Fig.2. Pathogenesis of Inflammation

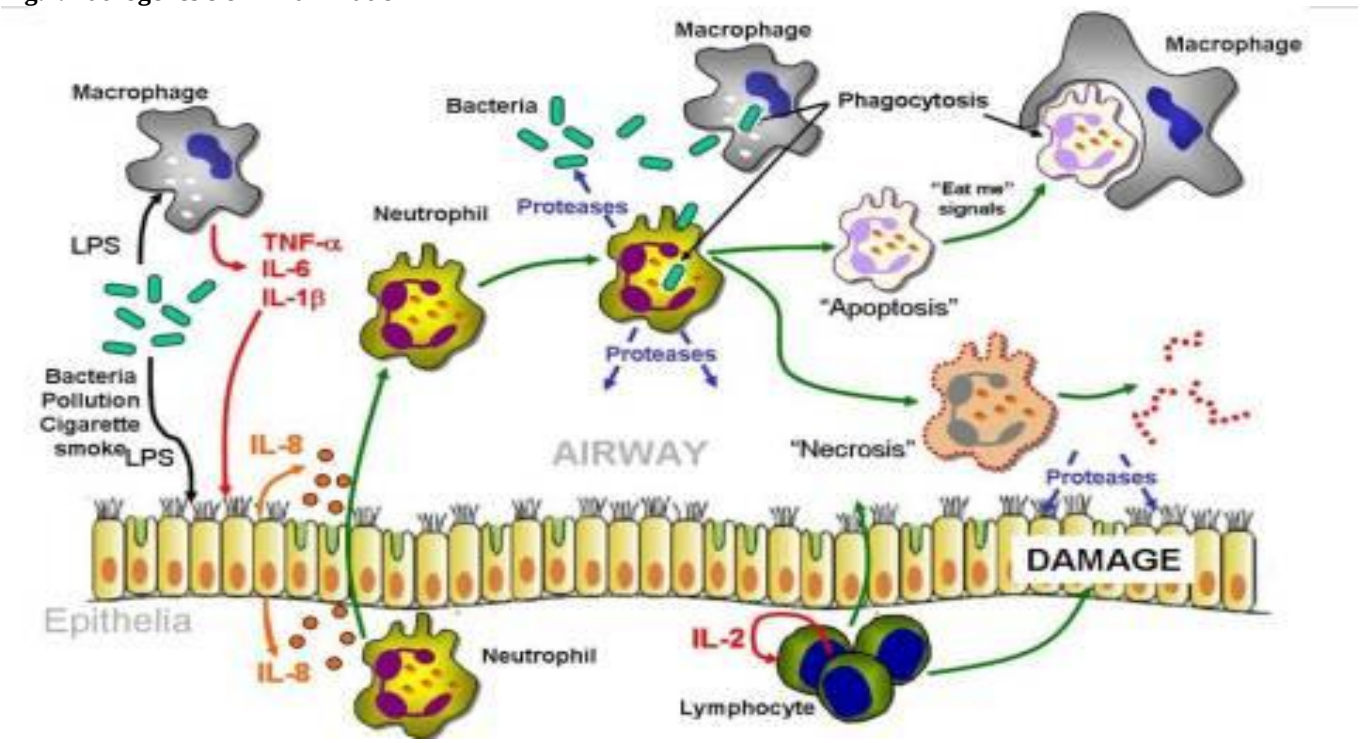

Table 1. Herbal plants with anti-inflammatory property

S.No	Botanical Name and family	Common name	Plant Part used	Extract used	Experimental model used	References
1.	*Aegle marmelos* Rutaceae	Bel	Root bark	Aqueous	PE,CPIG	Benni *et al*., 2011
2.	*Alchornea cordifolia* Euphorbiaceae	Christmas tree	Leaves	Aqueous decoction and methanol	COIEE	Manga *et al*., 2004
3.	*Aloe barbadensis* Liliaceae	Aloe Vera	Juice of leaf	Aqueous	PE	*Egesie et al., 2011*
4.	*Arctostaphylos uva-ursi* Ericaceae	Bearberry	Leaves	Aqueous	CIPE	Matsuda *et al*., 1992
5.	*Anogeissus Acuminate* Combretaceae	Buttontree	Leaves	Methanolic	CIPE,FIPE	Hemamalini *et al*., 2010
6.	Albizia lebbeck Leguminosae	Siris Tree	Bark	Petroleum ether, ethanol	CIPE	Babu *et al*., 2009
7.	*Borassus flabellifer L.* Asteraceae	Palmyra Palm	Male flower	Ethanol	PE,CPIG, CIAP	Paschapur *et al*., 2009
8.	*Bauhnia variegate* Caesalpiniaceae	Mandarai	Bark	Methanol and aqueous	CIPE, DIPE	Bairagi *et al*., 2012
9.	*Berberis vulgaris L.* Berberidaceae	Barberry root	Root	ethanol	CIPE,ZIPE	Ivanovska *et al*., 1996
10.	*Bambusa vulgaris* Poaceae	Bamboo	Leaves	Methanolic	FIAI,VP,CPIG, CIP	Carey *et al*., 2009
11.	*Curcuma longa Linn.* Zingiberaceae	Haldi	Rhizomes	Petroleum ether	CPIG	Kohli *et al*., 2005
12.	*Centaurea cyanus* Asteraceae/Compositae	Cornflower	Flowers	Aqueous	ET IPE	Talhouk *et al*., 2008
13.	*Cordia dichotoma forst f.* Boraginaceae	pink pearl	Seeds	Ethanol and aqueous	PE	Sharma *et al*., 2010
14.	*Curcuma amada Roxb.* Zingiberaceae	Mango Ginger	Rhizome	Ethyl alcohol.	PE,CPIG,	Mujumdar *et al*., 2000
15.	*Citrullus colocynthis* Cucurbitaceae	Bitter apple	Fruit and seed	Aqueous	PE,CIAP	Marzouk *et al*., 2011
16.	*Caesalpinia Pulcherrima* Leguminosae	Gulmohar	Bark	Ethanolic and aqueous	CPIG, CIPE	Sharma *et al*., 2011
17.	*Carica papaya* Caricaceae	Papaya	Leaves	Ethanolic	CPIG, CIPE	Owoyele *et al*., 2008
18.	*Cassia Auriculata* Caesalpiniaceae	Tanner's cassia.	Flowers	Methanolic	AIPE, CPIG	Doshi *et al*., 2011
19.	*Garcinia mangostana* Guttiferae	Mangosteen	Fruit hull	Ethanolic	PE	Lih-Geeng Chen *et al*.,
20.	*Gendarussa vulgaris Nees*.Apocyanaceae	Justicia gendarussa	Leaves	Alcoholic and aqueous	CIPE	Saleem *et al*., 2011
21.	*Hygrophila spinosa T.* Acanthaceae	Gokulakanta	Leaves	Petroleum ether, chloroform	PE	Patra *et al*., 2009
22.	*Hibiscus tiliaceus* Malvaceae	Bola	Wood	Methanolic	CPIG, CIPE	Borhade *et al*., 2012
23.	*Hedychium coronarium* koen Zingiberaceae	Butterfly ginger	Rhizome	Hexane, chloroform, methanol	CIPE	Shrotriya *et al*., 2007
24.	*Ichnocarpus Frutescens* Apocynaceae	Shyamlata	Roots,	Methanolic	CIPE, CIPG	Pandurangan *et al*., 2008

25.	*Lantana camara* Verbenaceae	Chaturangi	Aerial part	Aqueous	PE	Gidwani *et al*., 2009
26.	*Mirabilis jalapa Linn*. Nyctaginaceae	Marvel of Peru	Leaves	Alcoholic	PE,CPIG	Nath *et al*., 2010
27.	*Murraya koenigii Spreng* Rutaceae	Curry Leaf	Leaves	Petroleum ether, chloroform,ethanol	PE	Darvekar *et al*., 2011
28.	*Medicago sativa L*. Fabaceae or Leguminosae	Alfalfa	Dried leaves, stems,	Ethyl acetate	LPS-II	Yong-Han Hong *et al*., 2009
29.	*Mimosa pudica*. Fabaceae	Humble plant	Leaves	Petroleum ether, alcoholic, aqueous	CIPE, CPIG	Goli *et al*., 2011
30.	*Ocimum Sanctum* Lamiaceae	Tulsi	Leaves	Paste of tulsi leave	CIPE	Kalabharathi *et al*., 2011
31.	*Pfaffia glomerata* Amaranthaceae	Brazilian Ginseng	Root	Hydroalcoholic extract	PE	Neto *et al*., 2005
32.	*Pinus roxburghii Sarg.* Pinaceae	Chir pine	Dried leaves	Alcoholic, petroleum ether	CIPE, CPIG	Kaushik *et al*., 2012
33.	*Psoralea Corylifolia* Linn. Leguminosae	Babchi	Seed	Hexane	CIPE	Gidwani *et al*., 2010
34.	*Phyllanthus amarus* Euphorbiaceae	Bahupatra	Whole plant	Methanol	PE,CPIG, CIAP	Mahat *et al*., 2007
35.	*Solanum nigrum* Linn Solanaceae	Black Nightshade.	Berries	Methanolic	CIPE	Ravi *et al*., 2009
36.	*Strophanthus hispidus* Apocynaceae	Arrow poison	Root	Aqueous	CIPE, XIPE	Agbaje *et al*., 2012
37.	*Securidaca longipedunculata Fres* Polygalaceae	Violet tree	Root, Bark	Methanol, petroleum ether	TEME,PE, UA	Okoli *et al*., 2006
38.	*Stellaria media* Caryophyllaceae	Chickweed, Starweed	Whole herb	Methanol	AIPE	*Oyebanji et al*., 2012
39.	*Terminalia arjuna* Combretaceae	Arjuna	Leaf	Methanolic, petroleum ether	CIPE	Biswas *et al*., 2011
40.	*Wigandia urens* Hydrophyllaceae	stinging tree	Aerial parts	Methanolic, aqueous, chloroform	CIPE	Zavala-Sánchez *et al*., 2009

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

CONCLUSION

These are the few herbal plants which are previously explored for their anti-inflammatory activity. But in the heart of the nature there are still so many plants which are unexplored and need to study for their therapeutic value, so that they can also be used as herbal medication for betterment of human being. Herbal medications are free from side effects and frequent toxicity unlike the allopathic medicines. So this review is merely an initiation to provide wide options of herbal source for the treatment of various inflammatory diseases.

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