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Anti-inflammatory activity of medicinal plants: A review

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Abstract

Medicinal plants continue to be of interest for several reasons including lack of availability of a satisfactory therapy of several clinical conditions inflammatory disorders being one of them. Inflammation is a defensive response that is characterized by redness, pain, heat, and swelling and loss of function in the injured area. Inflammation is body's nonspecific internal systems of defense, the response of a tissue to an accidental cut is similar to the response that results from other types of tissue damage, caused by burns due to heat, radiation, bacterial or viral invasion. Anti-inflammatory drugs like NSAIDs used to reduce the swelling and pain of inflammation. Long-term uses of NSAID cause adverse side effects and damage human biological system such as liver, gastrointestinal tract etc. The management of inflammation related diseases is a real issue in the rural community; the population in these areas uses many alternative drugs such as substances produced from medicinal plants. Herbal products from medicinal plants are playing a major role to cure many diseases associated with the inflammation. Many conventional drugs are available in the market to treat the inflammation which produces various side-effects. Due to these side-effects there is need for the search of newer drugs with less or no side-effects. In this review an attempt has been made to investigate the anti-inflammatory activity of some medicinal plants. It can be helpful to researchers in the study of anti-inflammatory substances from plants. This also may serve as a guide for pharmacologists studying the mechanisms of action and anti-inflammatory effects of these substances.

Keywords: Medicinal plants, Phytoconstituents, Pharmacology, Anti-inflammatory activity

Introduction

Inflammation is a part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells or irritants. It is characterized by redness, swollen joints, joint pain, its stiffness and loss of joint function. Inflammation is either acute or chronic inflammation. Acute inflammation may be an initial response of the body to harmful stimuli. In chronic inflammation, the inflammatory response is out of proportion resulting in damage to the body. Cyclooxygenase (COX) is the key enzymes in the synthesis of prostaglandins, prostacyclins and thromboxanes which are involved in inflammation, pain and platelet aggregation [3].

Inflammatory diseases are common in the aging society of developed and developing countries; yet, the drugs used to combat inflammatory diseases like rheumatoid arthritis often have serious side-effects. Despite the progresses in modern medicine, it has been reported that more than 70% of the developing world's population still depends on complementary and alternative systems of medicine, otherwise known as traditional medicine [4]. Some herbs possess anti-inflammatory properties and have the ability to reduce both internal and external swelling and inflammation. Herbal drugs have gained importance and popularity in recent years because of their safety, efficacy and cost effectiveness. There are a number of anti-inflammatory herbs that could help to achieve similar results without the harmful effect [5]. Most of the researchers concluded their study by mentioning that the anti-inflammatory activity may be due to inhibition of the enzyme cyclooxygenase leading to inhibition of prostaglandin synthesis. The crude extracts of the various parts or the whole plants of the medicinal plants and isolated compounds from the medicinal plants showed statistically significant anti-inflammatory activity both in *in vivo* and *in vitro* assay. Several leads from plant sources, like curcumin, resveratrol, baicalein, boswellic acid, betulinic acid, ursolic acid and oleanolic acid are now studied as possible drugs for the future against inflammatory [6]. This review will help the recent and future researchers in their research work as they could select the anti-inflammatory medicinal plants from which they can isolate active constituents and unveil some new molecules which help us to fight against inflammatory disorders.

Ancient and modern approach to inflammation

The basic concepts of Ayurvedic physiology provide the linkage between inflammation, lipid metabolism, diabetes, and cancer using its three dynamic pathophysiological entities called "Doshas" [7]. The three Doshas are termed as Vata, Pitta and Kapha, respectively. At the cellular level, Doshas can be associated with signaling pathways regulating cell growth, differentiation, cell death, actions of enzymes, growth

factors, hormones, energy homeostasis, maintenance of basal metabolism, anabolic processes (such as biosynthesis of macromolecules), coordination of gene and protein function [8]. Most of the Ayurvedic drugs are based on plants, herbo-mineral in the form of poly herbal formulations and very few as single. The selection of herb in formulation is based on their capability to balance the Doshas. Several herbs from these Indian classical Ayurvedic text texts viz. "Charak Samhita", "Sushurt Samita" and "Bhavaprakash Nigantu" have been studied for their anti-inflammatory properties and have the potential to provide new scaffolds for safer and synergistic drugs. Over the past two decades, many studies reveal that chronic inflammation is a critical component in many human diseases and conditions, including obesity, cardiovascular diseases (atherosclerosis, coronary diseases, cerebrovascular disorder, heart failure and cardiomyopathy), neurodegenerative diseases (Alzheimer & Parkinson), diabetes, aging, metabolic disorder and cancers. Epidemiological studies provide convincing evidence that natural dietary compounds that humans consume as food possess many biological activities. Among these natural bioactive compounds, flavonoids are widely recognized for their biological and pharmacological effects, including antiviral, anti-carcinogenic, antioxidant, antimicrobial, anti-inflammatory, anti-angiogenic and anti-thrombogenic properties [9-11]. Epidemiologic studies indicate that the incidence of chronic disease and cancer is inversely correlated with the consumption of fruits and vegetables rich in phenolics [9] and this is attributed to their possible anti-inflammatory activities. Unlike modern Allopathic drugs which are single active compounds that can specifically target one pathway, herbal remedies work in a way that depends on orchestral approach. A plant contains a multitude of several molecules that synergistically act on targeted elements of the cellular complex pathway. Medicinal herbs have been source of wide range of biologically active compounds for many centuries and they have been used extensively as crude drugs or as pure components for treating varieties of disease conditions. When compared to synthetic ones, natural remedies are having less side effects and toxicity. So, now days the usages of herbal remedies are increased when compared to allopathic drugs.

Phytoconstituents reported to have anti-inflammatory activity

Natural chemical agents extracted from plants that can modulate the expression of pro-inflammatory signals clearly have potential against arthritis. These include flavonoids, terpenes, quinones, catechins, alkaloids, anthocyanins, polyphenols and anthoxanthins, all of which are known to have anti-inflammatory effects. The phytoconstituents which have been attributed with anti-inflammatory activity are:

Alkaloids

Thalicsiline (diterpenoid alkaloid), cycleanine and tetranidrine, rohutkin alkaloid, trilobine and isotrilobine etc [12, 13].

Triterpenoids and their glycosides

Aescin (β-amyrin), chiisanosides (lupine triterpenoids), dysobinin, boswellic acid and pentacyclic triterpenoid acids, α-amyrin & taxifolin 3, sorghumol, bassic acid etc [14].

Flavonoids and coumarins

Hypoleitin & sideritoflavone, baicalin, baicalein, 5, 7-dimethoxyflavone, osthol (coumarin), quercetin-3-o-rhamnoglucoside, kaempferol, hedychinone (flavonoid), marmin (coumarin) etc [15].

Saponin and sapogenins

Phytolaccoside B (saponin), panax saponin, misaponins, saikogenin, glycyrrhytinic and glycyrrhizinic acids etc [16].

Steroidal components

Spinasterol, β-sitosterol, steroidal components of *Boughainwellia glabra* etc [17].

Xanthones & their glycosides

Calophyllolide, magniferin, A xanthone, C glycoside, xanthorhamnin etc [16].

Others

Magnoshinin, hematoxylin, copaifera oleoresin, pinens, benzoxacinoid compounds, bavachinin, gangetin, embelin, epicatechin etc [18].

Reported pharmacological studies

Akah *et al.* considered that egg albumin induced inflammation model is a significant predictive test for anti-inflammatory activity. These results are an indication that *Jatropha curcas* can be effective in acute inflammatory disorders [19].

Iwueke *et al.* showed that the leaves of *Vitex doniana* possess anti-inflammatory and analgesic properties mediated by prostaglandin synthesis inhibition. Membrane stabilization may contribute to the anti-inflammatory effect. The study also provides empirical evidence for the use of the leaves of *V. doniana* in folkloric treatment of inflammatory disorders and pain [20].

The anti-inflammatory activity of low dose of the aqueous extract of *T. procumbens* and ethanolic extract of *C. gigantea* were assessed on carrageenan induced paw edema and compared with standard drug ibuprofen [21]. The oral administrations of 400 mg/kg of *C. gigantea* and 300 mg/kg of *T. procumbens* have showed significant anti-inflammatory activity more than that of 100 mg/kg of ibuprofen. This study also proved the greater anti-inflammatory action due to the combined effect of *C. gigantea* and *T. procumbens* with ibuprofen than ibuprofen alone.

Sharma *et al.* examined the effects of *Cordia dichotoma* forst f. seed extracts on different phases of acute inflammation. The dry powdered seeds were found to contain alkaloids, glycosides, saponins, tannins and carbohydrates. Thus, it is revealed from the screening model used that the ethanol

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extract and aqueous fraction of this plant possess acute anti-inflammatory activity [22].

Abdullahi *et al*. suggested that the activity of the leaves could be associated with the type of phytochemicals such as flavonoids, alkaloids and saponins isolated from some members of the Asteraceae (compositae) family that were found to exhibit analgesic and anti-inflammatory activities [23].

Vijaya *et al.* stated that the alcohol extract of *Achyranthus aspera* was evaluated for anti-inflammatory activity in wistar rats using the carrageenan induced paw edema test with oral administration. It resulted in promising anti-inflammatory activity against acute inflammation [24].

Owoyele *et al.* reported that the plant crude extract of *L. owariensis* exhibited very high anti-inflammatory activity. This may be linked with the presence of polyphenolic compounds present in the extract [25].

Ami *et al.* evaluated the fruit of *Trapa natans* traditionally used as anti-inflammatory for its activity by *in vivo* study. *Trapa natans* aqueous extract of pericarp and seed has shown significant anti-inflammatory activity by decreasing mean paw volume compared with control [26].

Ravi *et al*. described that the ethanol, chloroform and aqueous extracts of the leaves of *Abutilon indicum* were screened for anti-inflammatory activity. The prevention of hypotonicity induced HRBC membrane lysis was taken a measure of anti-inflammatory activity. All three fractions showed a biphasic effect on the membrane stabilization. Their activities are comparable to that of standard drug diclofenac sodium. However, their activities decreased with time [27].

Arunachachalam *et al.* investigated anti-inflammatory activity methanolic extract of leaves of *Eclipta prostrata* Linn in albino wistar rats. Anti-inflammatory activity of the tested extract was comparable with that of the standard drug indomethacin and cyproheptadine. The results lend support to the traditional use of *E. prostrata* in the treatment of inflammatory diseases. The preliminary phytochemical screening of leaves of *E. prostrata* indicated the presence of steroids, triterpenoids, flavonoids, tannins, reducing sugar and saponins. The steroids, alkaloids and triterpenoids present in the extract may be responsible for the anti-oedematous effect [28].

Warrier *et al.* reported that the seeds of *Cordia dichotoma* are antiinflammatory. The fruits of the plant are used as astringent, expectorant, anthelmintic, purgative and diuretic [29].

Parmar *et al.* have reported the anti-inflammatory activity of Gossypin (bioflavonoid) isolated from *Hibiscus vitifolius* in comparison with the standard non-steroidal anti-inflammatory drug (NSAID) phenylbutazone against various experimental models of inflammation and increased vascular permeability. It produced significant inhibition of the accumulation of pouch fluid and granulation tissue formation in the carrageenan induced granuloma pouch in rats, which could be attributed to the decreased formation of collagen tissue. It was found to significantly reduce the rat paw oedema and the increased vascular permeability induced by various phlogistic agents [30].

Sashida *et al.* reported the use of *Smilax china* in the treatment of rheumatoid arthritis, gout and other inflammatory ailments. *Smilax china* contains saponins, like smilaxin, prosapogenin A of dioscin, gracillin, dioscin, pseudoprotodioscin, methygracillin and methylprotodioscin [31].

Chattopadhyay *et al*. evaluated the effect of *Azadirachta indica* leaf extract on inflammatory oedema induced by chemical mediators (5-HT, histamine, bradykinin and PGE1) to find out its possible mechanism of reported anti-inflammatory effect against carrageenan-induced rat hind paw oedema. The leaf extract showed significant anti-inflammatory effect against 5-HT and PGEI induced inflammation, but not on the inflammation induced by histamine and bradykinin. Their study suggests that *Azadirachta indica* extracts anti-inflammatory effect may be due to antagonism of the deleterious effect of 5-HT and PGEI on blood vessels [32].

Sarkar *et al.* reported the effect of leaf exudates of *Aloe vera* on nitric oxide production by macrophages during inflammation. *Aloe vera* leaves (25 mg/kg) significantly reduced carrageenan and dextran induced oedema in rats by 61.9% and 61.7% respectively and 10 µg/mL caused a decrease in nitric oxide production in macrophages without causing toxicity [33].

Speroni *et al.* have studied the effect of various extracts of *Verbena officinalis* (petroleum ether, chloroform, methanol extract, flavonoids enriched extract and a CO_2 extract) on carrageenan-induced rat paw oedema. The strongest inhibition was achieved with the CO_2 extract [34].

Ilavarasan *et al.* reported bark extracts of *Cassia fistula* possess significant anti-inflammatory effect in the acute and chronic anti-inflammatory model of inflammation in rats. The main constituents responsible for anti-inflammatory activity of *Cassia fistula* were flavonoids and bioflavonoids [35].

Verma *et al.* reported that the ethanolic extract of root of *A. heterophyllum* contains alkaloids, glycosides, flavonoids and sterols. It has been reported that plants with these chemical classes of compounds possess potent anti-inflammatory effects through inhibition of prostaglandin pathways. In literature, it has been reported that an ethanolic root extract of *A. heterophyllum* has potential to inhibit sub-acute inflammation by interruption of the arachidonic acid metabolism [36].

Ahmed *et al.* have reported that the ethanolic extract of *Caralluma tuberculata* possesses significant anti-inflammatory and analgesic activities. Experimental data

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indicated that the ethanolic extract significantly inhibited carrageenan-induced inflammation in rats. The extract also decreased granuloma formation by cotton pellets in treated rats [37].

Chamomilla recutita which is an annual herbaceous plant has been reported to possess good anti-inflammatory, antibacterial and antifungal properties [38].

The ethanolic bark extract of *Plumeria rubra* also exhibits anti-inflammatory activity. The various phytochemicals responsible for activity include flavonoids, tannins, alkaloids and terpenoids [39].

Konan *et al.* reported that mice treated with the extracts of *Gomphrena celosioides* at dose of 100 mg/kg showed significant anti-inflammatory activity [40].

Plants as sources of anti-inflammatory agents

Medicinal plants remain a promising source of anti-inflammatory agents [40]. Current anti-inflammatory therapies mostly involve classes of drugs that produce serious side effects such as gastric intolerance, bone marrow depression and water and salt retention, resulting from prolonged use of these drugs [39]. Medicinal plants are believed to be an important source of new chemical substances that are safer and with fewer side effects. A considerably large number of plants have been scientifically validated to exhibit anti-inflammatory activity.

Aegle marmelos

The aqueous extract of the root bark of Bilwa was prepared and tested for anti-inflammatory activity in albino rats using carrageenan induced paw edema model and cotton pellet induced granuloma and the standard drug was taken indomethacin and Bilwa. The result revealed that anti-inflammatory activity was expressed the inhibition [41].

Azardirachta indica

The anti-inflammatory potential of *Azardirachta indica* was using carbon tetrachloride extract of *Azadirachta indica* fruit skin and its isolated constituent azadiradione a two different dose levels (50 and 100 mg kg^{-1} body weight). Anti-inflammatory activity was observed using carrageenan-induced paw oedema model. The results concluded that the animals treated with 100 mg kg^{-1} dose of carbon tetrachloride extract and azadiradione exhibited significant anti-nociceptive and anti-inflammatory activities [42].

Albizia lebbeck

The bark extract of *Albizia lebbeck* Benth obtained by cold extraction of mixture of equal proportions of petroleum ether, ethyl acetate and methanol was chosen for pharmacological screening. In rat paw edema model induced by carrageenan, the extract at the 200 and 400 mg/kg dose level showed 27.51% and 36.68% ($P<0.001$) inhibition of edema volume at the end of 4 h [43].

Annona squamosa

Caryophyllene oxide was isolated from an unsaponified petroleum ether extract of the bark of *Annona squamosa* and studied for its analgesic and anti-inflammatory activity. Caryophyllene oxide at the doses of 12.5 and 25 mg/kg body wt and unsaponified petroleum ether extract at a dose of 50 mg/kg body wt showed significant central as well as peripheral analgesic, along with anti-inflammatory, activity. These activities of caryophyllene oxide were comparable with the standard drug used in the respective experiments [44].

Achillea millefolium

The anti-inflammatory potential of aqueous extract *Achillea millefolium* was investigated and measured by the mouse paw edema test. The result revealed the isolation of a material which reduces inflammation by 35% [45].

Abrus precatorius L

Abruquinone A is a naturally occurring isoflavoquinone isolated from the roots of *A. precatorius*. The anti-inflammatory effect of Abruquinone A was found to be partly via prevention of vascular permeability and inhibition of platelet aggregation. It could influence the release of chemical mediators from mast cells in vitro and to suppress plasma extravasation caused by these chemical mediators *in vivo* [46].

Acacia catechu L

Catechin, a natural flavonoid isolated from *A. catechu* was tested for COX-2 and 5-LOX inhibition via enzyme, cellular and *in vivo* models. Catechin inhibited both ovine COX-1 and COX-2 at IC_{50} of 15 mg/mL [47]. In *in vivo* studies, human osteosarcoma cells expressing COX2 showed decreased production of PGE2. It could also inhibit leukotriene production in human cell lines viz., immortalized THP-1 monocyte and HT-29 colorectal adenocarcinoma [48]. *A. catechu* flavans (epicatechin, quercetin, catechin) with reported anti-inflammatory activity had dual specificity for inhibiting COX-2 and 5-LOX experimented in air pouch model created on the back of Balb/C mice [49, 50].

Alstonia scholaris (L.)

Three main alkaloids, picrinine, vallesamine and scholaricine from *A. scholaris* leaf produced anti-inflammatory and analgesic effect. In *in vitro* tests, alkaloids inhibited inflammatory mediators viz., COX-1, COX-2 and 5-LOX [51]. Further indole alkaloids, 16-formyl5a-methoxystrictamine, picralinal, and tubotaiwine isolated from this plant exhibited COX-2/5-LOX dual inhibition. They reduced inflammatory symptoms in xylene-induced ear edema and carrageenan-induced air pouch inflammatory model in mice [52].

Andrographis paniculata Wall

A. paniculata was reported to exhibit analgesic, anti-pyretic and anti-inflammatory effect [53]. Bioactivity guided chromatographic fractionation was applied to identify bioactives with anti-inflammatory activity. They were analyzed for anti-inflammatory activity in *in vitro* studies using RAW

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264.7 (Mouse leukaemic monocyte macrophage cell line) stimulated for inflammatory response by LPS/interferon (IFN)-g [54]. A significant decrease in the levels of NFkB mRNA, tumor necrosis factor (TNF)-α, IL-6, MIP-2 and nitric oxide (NO) was recorded [55, 56].

Artocarpus heterophyllus Lam

Three phenolic compounds viz., artocarpesin [5,7,2,4-tetrahydroxy-6-(3-methylbut-3-enyl) flavone] [57], norartocarpetin (5,7,2,4-tetrahydroxyflavone) and oxyresveratrol [trans-2,4,3,5-tetrahydroxystilbene] were reported from *A. heterophyllus* [58, 59]. Among them, artocarpesin suppressed the LPS-induced production of NO and PGE2 through the down-regulation of iNOS and COX-2 protein expressions in LPS-activated RAW 264.7 murine macrophage cells [60].

Bauhinia variegata L

Six flavonoids, namely kaempferol, ombuin, kaempferol 7, 4-dimethyl ether 3-O-β- dglucopyranoside, kaempferol 3-O-β-d-glucopyranoside, isorhamnetin 3-O-β-d-glucopyranoside and hesperidin, together with one triterpene caffeate, 3β-trans-(3,4- dihydroxycinnamoyloxy)olean-12-en-28-oic acid were isolated from the non-woody aerial parts of *B. variegate*. All the seven compounds were tested in LPS/IFN-g induced macrophages. These compounds inhibited LPS and IFN-g induced NO and cytokines (TNF-α and IL-12) production all of which play a crucial role in inflammation [61].

Biophytum sensitivum DC

Amentoflavone, a biflavonoid with anti-inflammatory activity isolated from *B. sensitivum*, downregulated COX-2 expression in TNFα-activated A549 cells with concomitant inhibition of NF-kB mediated signaling cascades. Amentoflavone inhibited NF-kB/ DNA binding activity with inhibition of degradation of IkBα and NF-kB translocation into nucleus in TNFα- activated A549 cells. It may be of therapeutic value for several lung diseases where COX-2 plays an important role [62].

Boswellia serrata Roxb

Frankincense, the gum resin of *B. serrata* and *B. carterii* has been used for the treatment of inflammatory diseases in the traditional medicine in many countries. Boswellic acid (BA), which belong to the ursane type pentacyclic triterpene saponines was identified as the active principle [63]. It could inhibit leukotriene biosynthesis in intact cells [64]. *In vitro*, BAs selectively blocked the leukotriene, IL-12 and IL-6 generation down regulating NFkB activation. In animal models of inflammation, BA has been shown to be an effective adjuvant mitigating BSA-induced arthritis [65].

Butea monosperma (Lam.) Taub

Butea monosperma is a well known medicinal plant in India used to treat cuts, wounds and skin diseases [66]. Anti-inflammatory activity was credited to the presence of polyphenols- butrin, isobutrin, isocoreopsin and butein. All these polyphenols could significantly reduce the phorbol 12-myristate 13-acetate and calcium ionophore A23187 induced inflammatory response in HMC-1 human mast cells. The anti-inflammatory potential was measured through decreased production of TNF-α, IL-6 and IL-8 in HMC1 cells mediated by inhibiting the activation of NF-kB. In addition, isobutrin was most potent in suppressing the NF-kB p65 activation by inhibiting IkBα-degradation, whereas butrin and butein were relatively less effective. Kinase activity assay revealed that isobutrin was a potent inhibitor of IKK (Inhibitor Kappa B Kinase) activity [67].

Bryophyllum pinnatum

The anti-inflammatory potential of *Bryophyllum pinnatum* was investigated using fresh egg albumin-induced pedal (paw) oedema model. The study results revealed that *Bryophyllum pinnatum* leaf aqueous extract possessed anti-inflammatory activity. The different flavonoids, polyphenols chemical constituents of the herb are speculated to account for the observed anti-inflammatory of the plant [68].

Cassia occidentalis

Anti-inflammatory potential of *Cassia occidentalis* ethanolic extract was evaluated. The result revealed that significant reduction in malondialdehyde levels of murine hepatic microsomes and significantly reduced carrageenan induced inflammation in mice at a dose of 250 mg/kg [69].

Cynodon dactylon

The anti-inflammatory activity of aqueous extract of *Cynodon dactylon* was evaluated at different doses (200, 400 and 600 mg/kg) using carrageenan, serotonin, histamine and dextran induced rat paw edema and cotton pellet method. The aqueous extract of *C. dactylon* was found to be safe at all doses used and there is no mortality up to the dose of 4000 mg/kg of extract when administered orally. *C. dactylon* showed significant anti-inflammatory activities in all model. The extract was found to reduce significantly ($P<0.001$) the formation of edema induced by carrageenan, serotonin, histamine and dextran after 3 and 5 h [70].

Embelia ribes Burm.

Embelin, identified primarily from *E. ribes*, exhibited chemopreventive, anti-inflammatory and apoptotic activities [71]. Embelin inhibited IL-1, IL-6, TNF-α binding TNF receptor (TNFR) and activation of NFkB. Embelin could also down regulate both inducible and constitutive NFkB activation when stimulated by diverse stimuli such as IL-1b, LPS, phorbol myristate acetate, okadaic acid, H_2O_2 and cigarette smoke condensate. A sequential inhibition of the TNF-α induced activation of the inhibitory subunit of NFkB, the IaBa kinase, IaBa phosphorylation, IaBa degradation and p65 phosphorylation and nuclear translocation were reported [72].

Emblica officinalis

Anti-inflammatory effects of phenolic compounds from *Emblica officinalis* using carrageenan and cotton pellet

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induced acute and chronic inflammatory animal model was investigated. The compounds were studied for their acute and chronic anti-inflammatory activity at a dose level of 20 and 40 mg/kg against standard drug diclofenac. The results indicated reduction in the inflammation, but significant effects were observed only at high doses [73].

Garcinia indica (Thouars) Choisy

Garcinia indica extracts, especially from the rind, are rich in polyisoprenylated benzophenone derivatives such as garcinol. Garcinol shows strong antioxidant activity which has been credited to both phenolic hydroxyl groups as well as a β-diketone moiety. The effects of garcinol was associated with lowered concentrations of intracellular ROS, significant inhibition of 5-LOX and microsomal PGE2 synthase (mPGES)-1 in cell-free assays. Cell line studies recorded significant inhibition of COX-1 enzyme and as well as thromboxane B2 production by human platelets [74].

Hedera rhombea

The anti-inflammatory activity of methanol and butanol fractions of *Hedera rhombea* was investigated. Considerable analgesic activity, anti-inflammatory activity was found in the methanol, butanol and ether fractions by carrageenan induced edema method [75].

Hibiscus rosa- sinensis

The methanolic extract of *Hibiscus rosa- sinensis* leaves (250 and 500 mg/kg body weight orally) was used carrageenin and dextran induced rat paw edema anti-inflammatory model. Indomethacine was used as standard drug which showed significant anti-inflammatory activity. The inhibition of edema by 17.12 and 16.46% with 250 mg/kg, 45.35%, and 44.51% with 500 mg/kg body weight after 3 h with carrageenin, dextran respectively. The plant extract at the dose level of 250 and 500 mg/kg body weight by oral route exhibited significant ($P < 0.01$) anti-inflammatory activities against all the agents used [76].

Myristica fragrans Houtt

Macelignan was isolated from *M. fragrans*. It exhibited potent anti-inflammatory activity *in vitro* in microglial cells. One of the important features in neurodegenerative disease was the failure to regulate oxidative stress and inflammation. Macelignan could suppress COX-2 and iNOS expression in microglial cells activated by LPS. A subsequent reduction of NO and significant suppression of pro-inflammatory cytokine TNF-α and IL-6 was recorded [77].

Moringa oliefera

The aqueous and ethanolic extract of the stem bark of *Moringa oliefera* showed % inhibition after 5 h was maximum 27.27 and 30.30% and significant reduction $P<0.01$, $P<0.05$ in the edema volume at a dose of 300 mg/kg body weight, which is comparable to standard drug diclofenac sodium. The standard drug showed % inhibition 44.44% (25 mg/kg) body weight and significant value $P<0.001$. The percentage of paw edema was found to be better with the alcoholic extract than aqueous extract [78].

Pterocarpus marsupium Roxb

Pterostilbene was identified as an active principle of *P. marsupium* (PM) extract with potent anti-inflammatory activity. A decreased PGE2 production indicated specific COX-2 inhibition in LPS stimulated human peripheral blood mononuclear cells with IC50 of approximately 1.0mM. A short term human trial did not identify abnormal blood cell counts or blood chemistry. The authors suggest the need for clinical studies using the PM extract to corroborate the in vitro observed inhibitory activity on PGE2 production in order to resolve the potential use of PM extract in inflammatory disorders and/or inflammatory pain [79].

Piper ovatum

The anti-inflammatory potential of leaves of hydroalcoholic extract of *Piper ovatum* was evaluated. In this study, carrageenan-induced pleurisy in rats and croton oil-induced ear edema in mice were used as a model. The results indicate that the amide fractions piperovatine and piperlonguminine showed the greatest inhibitory activity of topical inflammation induced by croton oil [80].

Piper longum

Anti-inflammatory activity of the *Piper longum* was studied in rats using the carrageenan-induced right hind paw edema method was investigated. The activity was compared with that of standard drug ibuprofen. The result indicated to inhibit carrageenan induced rat paw edema and produced significant anti-inflammatory activity when compared with the standard and untreated control [81].

Pluchea indica

The anti-inflammatory activity of the methanolic fraction of a chloroform extract of *Pluchea indica* roots was investigated. The extract showed significant inhibitory activity against carrageenan, histamine, serotonin, hyaluronidase and sodium urate induced pedal inflammation and also inhibited carrageenan and cotton pellet-induced granuloma formation [82].

Ricinus communis

Anti-inflammatory activity of methanolic extract of *Ricinus communis* Linn was investigated. The methanolic extract at doses 250 and 500 mg/kg of anti-inflammatory activity in carrageenan induced hind paw edema model. The results of the study indicate that the methanolic extract of *Ricinus communis* root possesses significant anti-inflammatory activity in acute and chronic inflammatory models in rats [83].

Sida cordifolia Linn.

Sida cordifolia is used in folk medicine for the treatment of inflammation of the oral mucosa, blenorrhea, asthmatic bronchitis and nasal congestion. It has been investigated as an antiinflammatory for preventing cell proliferation and for encouraging liver growth [84].

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Swertia chirata

The anti-inflammatory activity of ethanolic root extract of *Swertia chirata* was evaluated using the carrageenan-induced rat paw edema model. The result revealed that the extract was found to reduce significantly ($p<0.001$) the formation of edema at the 400 mg/kg dose level and showed 57.81% ($p<0.001$) inhibition of edema volume at the end of 3 h, the ethanolic extract of *Swertia chirata* reduced the inflammation [85].

Semecarpus anacardium Linn

Flavonoids viz., semicarpol and bhilawanol in *S. anacardium* extract inhibited acute tuberculin reaction in inflammatory and rheumatoid arthritis, these flavonoids inhibited the release of chemical mediators viz. histamine and serotonin reducing the symptoms. It was thought to be mediated through decreased monocyte infiltration and fibroblast proliferation, blocked TNF-α and inhibition of COX [86].

Terminalia chebula Retz

Preliminary studies have indicated anti-inflammatory activity for the ethanolic extracts of fruits of *T. chebula*. The extracts could inhibit COX1, COX-2 and 5-LOX. However the inhibitory quotient showed a strong preference to inhibit COX-2 and 5-LOX. Chebulagic acid was subsequently isolated from this extract. *In vitro* studies showed potent COX–LOX dual inhibition activity with IC50 values of 15 ± 0.288, 0.92 ± 0.011 and 2.1 ± 0.057mM for COX-1, COX-2 and 5-LOX respectively. Down regulation NFkB was observed [87].

Thespesia populnea

The aqueous and ethanolic extract of *Thespesia populnea* leaves were evaluated in animal models for anti-inflammatory activity. The extracts reduced paw oedema induced by carrageenan in rats. The results obtained in this study suggest that *Thespesia populnea* extracts have and anti-inflammatory properties [88].

Zingiber officinale

Anti-inflammatory effect of 40% ethanolic extract of *Zingiber officinale* was investigated. The study result showed potent suppressive effect on acute and chronic inflammation and inhibition of macrophage activation seems to be involved in this anti-inflammatory effect [89].

Conclusion

Since ancient times medicinal plants have been used to treat different ailments due to their accessibility, availability, inherited practice, economic feasibility and perceived efficacy. Several plants are promising as sources of anti-inflammatory drug targets. Inflammation is a pathological condition mediated through production of PGE2 from arachidonic acid (AA) generated by enzyme system PG synthetase, a complex enzyme including COX-2. Another group of compounds eliciting inflammatory condition are leukotrienes which are derived directly from AA by enzymatic action of lipoxygenase (LOX). The inflammatory response is controlled by the master regulator NFkB. Medicinal plants viz., *Andrographis paniculata*, *Biophytum sensitivum*, *Boswellia serrata*, *Butea monosperma*, *Embelia ribes*, *Terminalia chebula* and *Tribulus terrestries* have the reported ability to down regulate NFkB activation. *Acacia catechu*, *Alstonia scholaris*, *Artocarpus hirsutus*, *Bacopa monnieri* and *Myristica fragrans* have reported COX-2 inhibitory activity. Further *Acacia catechu*, *Alstonia scholaris*, *Bacopa monnieri* and *Garcinia indica* have LOX inhibitory activity. This review will help the recent and future researchers in more research work on these valuable medicinal plants.

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