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Anti-Inflammatory Activity of Ethanobotnical Plants Used as Traditional Medicine: A Review.

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Review Article

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ABSTRACT

Herbs are staging a comeback and herbal 'renaissance' is happening all over the globe. The herbal products today symbolise safety in contrast to the synthetics that are regarded as unsafe to human and environment .Inflammation is one of the body unique mechanisms that help body to protect itself against infection, burn, toxic chemicals, allergens or other noxious stimuli. However, over reaction of the body reaction may be harmful or undesirable. This has lead to extensive development of anti-inflammatory drugs. Now a day world population moves towards herbal remedies for treatment of such ailments. The several side effects of steroidal and nonsteroidal anti-inflammatory drugs evoked us to search for new anti-inflammatory agents from natural botanical sources that may have minimal side effects. The number of plants has been screened for their anti-inflammatory, but only few of them reached up to the clinical level. This review article focuses on our current knowledge of plants which have anti-inflammatory activity and discusses their potential therapeutic use in the management relevant inflammatory diseases.

INTRODUCTION

During the past decade, the therapeutic use of herbal medicine is gaining considerable momentum in the world. The use of herbal medicine due to toxicity and side effects of allopathic medicines has led to sudden increase in the number of herbal drug manufactures. Herbal medicines as the major remedy in traditional system of medicine have been used in medical practices since antiquity. The practices continue today because of its biomedical benefits as well as place in cultural beliefs in many parts of world and have made a great contribution towards maintaining human health [1]. Ayurveda the "science of life" or longevity, is the holistic alternative science from India, and is more than 5,000 years old. It is believed to be the oldest healing science in existence. Ayurveda said to be a world medicine, is the most holistic/comprehensive medical system available. Naturally healthy living is the principle of Ayurveda [2].

Inflammation

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 joint that is warm to touch, joint pain, its stiffness and loss of joint function. Inflammation is either acute or chronic. Under specific circumstance, it could turn into a chronic state and subsequently become a causative factor in the pathogenesis. Inflammation is a self-defence reaction in its first phase, hence regarded as the main therapeutic target and often, the best choice to treat the disease and alleviate the symptoms [3]. The process of Inflammation is shown in Figure 1. Inflammation is a defence reaction caused by tissue damage or injury. The primary objective of inflammation is to localize and eradicate the irritant and repair the surrounding tissue [4]. There are basic two types of inflammation Acute and chronic inflammation.

Acute inflammation

Acute inflammation is of short duration and represents the early body reactions. Acute inflammation may be an initial response of the body to harmful stimuli. An increased movement of plasma and leukocytes, especially

granulocytes from the blood into the injured tissues is observed. A cascade of biochemical events propagates and matures the inflammatory response, involving the local vascular system, the immune system and various cells within the injured tissue. Mast cells in the tissues, the key players of inflammation, are loaded with mediators of inflammatory response. When their toll-like receptors interact with pathogen associated molecular patterns these cells discharge the chemical mediators recruiting white blood cells to the site of inflammation. These include neutrophils, monocytes (that become macrophages when they leave the blood and enter the tissue), antigen-presenting dendritic cells, lymphocytes (B cells and T cells leading to an adaptive immune response) and natural killer cells. The Inflammatory response stimulates release of TNF-α from stimulated mast cells. Other cells involved in inflammation have receptors for TNF-α. They are activated by the binding of TNF-α. Activation of these recruited cells produces their own mediators of inflammation. This positive feedback quickly amplifies the response. Phagocytes (macrophages and neutrophils) produce reactive oxygen species (ROS). Macrophages and activated platelets release interleukin (IL)-1, a cytokine. IL-1 causes fever by stimulating the release of prostaglandins (PGs), which act on the temperature control canter of the hypothalamus. IL-1 is synthesized from a larger precursor that is cleaved by a caspase-1. Caspase-1 is part of two (or more) multiprotein complexes in the cytosol of macrophages and neutrophils that are called inflammasomes. Inflammasomes are activated by several different products produced by invading bacteria that interact with toll-like receptors (TLRs) thus providing a link between the innate immune system and inflammation. Chemical mediators such as histamine and bradykinin induce the production of PGs and leukotrienes with a role to potentiate the plasma exudation. These potent mediators of inflammation are derivatives of arachidonic acid (AA), Arachidonic acid released from membrane phospholipids is catalyzed by phospholipase A2 (PLA2) esterified at the second carbon in the glycerol backbone. It is subsequently metabolized by COX and LOX. The COX-1 is constitutively expressed and produces PGs involved in basic housekeeping for normal functioning of the body. The COX-2 is inducible and expressed in response to cytokines, mitogens and endotoxins [3].

Chronic Inflammation

Chronic inflammation is most appropriately defined in terms of the process, in which continuing inflammation and attempted tissue healing by repair occur simultaneously. Although it is often defined simply in terms of time course, with lesions of over 6 weeks' duration traditionally being regarded as chronic, any such definition is entirely arbitrary. At a microscopic level, chronic inflammation is sometimes defined in terms of the pattern of cellular response, although this is variable and not altogether reliable. Involving tissue regeneration or repair, chronic inflammation is characterized by inflammation and repair occurring concurrently, rather than consecutively. Note that repair is always a feature of chronic inflammation because it is associated with irritants that cause destruction of tissue architecture. Repair is typically achieved by in growth of granulation tissue, which includes macrophages, fibroblasts and new blood vessels. Because the irritant fails to be eliminated in chronic inflammation (either because of its innate characteristics or because of an ineffective host response) it may cause continuing tissue damage in its own right. In addition, most persistent irritants are recognized as foreign antigens by the host immune response, which contributes to the chronic inflammatory process and may add to the tissue destruction. This is well illustrated in diseases such as tuberculosis and hepatitis B, where the inciting agents persist in the host and continue to evoke a chronic inflammatory response. Other important distinctions between acute and chronic inflammation relate to the relative balance between exudation and cellular recruitment, as well as the types of cells that predominate in the inflammatory response. In chronic inflammation there is typically a less pronounced oxidative response (although this is still in evidence) and increased inflammatory cellular recruitment, which may be accompanied by local cellular proliferation. In contrast to acute inflammation, which is usually characterized by recruitment of large numbers of neutrophil leucocytes, the dominant infiltrating cell in all forms of chronic inflammation is the macrophage. Depending on the nature of the irritant, different profiles of inflammatory mediators and growth factors (collectively referred to as cytokines) are generated locally, giving rise to different morphological patterns of chronic inflammation (see below). The systemic effects of inflammation are more pronounced in chronic inflammatory diseases and may contribute significantly to the clinical consequences. These systemic effects are largely mediated by cytokines. Whereas the most prominent systemic effects of acute inflammation are fever and leucocytosis, chronic inflammation is usually associated with fatigue, sleepiness and weight loss and wasting.

Role of Persistent Irritant

Chronic inflammation may be caused by:

- An irritant that usually evokes an acute inflammatory response, which fails to be eliminated or continues to be generated locally; or
- Self antigens that induce an autoimmune response; or
- An irritant of low intensity but long persistence, which does not evoke a significant acute inflammatory reaction [5].

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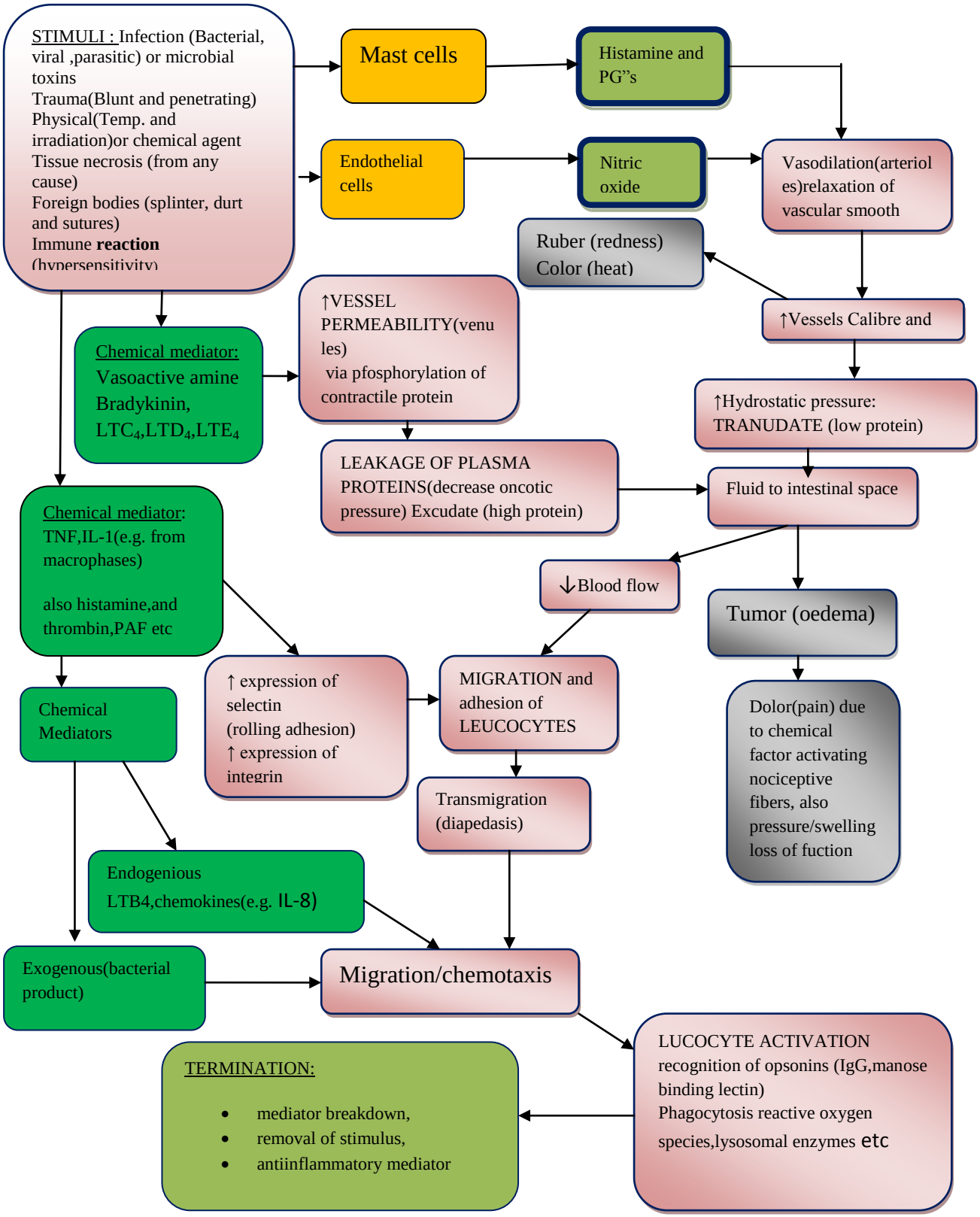

Figure 1: Flow chart of inflammation

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Animal models

Inflammation research involves a number of experimental models that can be broadly classified into two types: acute inflammatory models and chronic inflammatory models. Acute models are designed to test drugs modulating erythema, changes in vascular permeability, leukocyte migration, and measurement of local pain, local analgesic action and rat paw edema. Chronic models are designed to find drugs modulating disease process induced by sponge, pellet implants, granuloma pouches and adjuvant induced arthritis [5].

Ethanobotnical plants with anti-inflammatory activity

Table 1, showed the Ethnobotanical data of the studied plants which have anti-inflammatory activity.

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 [6].

Argyreia speciosa

The anti-inflammatory activity of hydroalcoholic extract of *Argyreia speciosa* root using various experimental models. The anti-inflammatory effect was evaluated for plant extracts (100, 200 and 500 mg/kg) orally using acute inflammatory model, carrageenan induced paw oedema in rats. *Argyreia speciosa* extract in the highest tested dose (500 mg/kg p.o.) was found to inhibit rats paw oedema significantly after 1 h (60.15%) and 3 h (44.79%) of carrageenan injection. The extract was also significantly inhibited rat paw oedema in oral dose of 200 mg/kg after 3 h (46.87%) of carrageenan injection. The extract at the dose 100 mg/kg, p.o. did not produce significant anti-inflammatory activity. Furthermore, *Argyreia speciosa* extract exhibited were significantly (P<0.05) reduced rat paw edema [7].

Sphearanthus indicus

The anti-inflammatory activity of hydroalcoholic extract of *Sphearanthus indicus* herb was done by using various experimental models.The anti-inflammatory effect was evaluated for plant extracts (100,200 and 500 mg/kg) orally using acute inflammatory model, carrageenan induced paw oedema in rats. 500mg/kg oral dose of hydroalcoholic extract of *Sphearanthus indicus* was found to inhibit rats paw oedema significantly after 1 h (43.48%) and 3 h (65.11%) of carrageenan injection. The hydroalcoholic extract of *Sphearanthus indicus* in other two tested doses (100 and 200 mg/kg, p.o.) was found to inhibit rat paw oedema formation to the extent 68.75% and 67.71% respectively at 3 h of carrageenan injection. Furthermore the extract exhibited were significantly (P<0.05) reduced rat paw edema induced by sub plantar injection of carrageenan [7].

Barleria prionitis

B.prionitis roots were extracted with petroleum ether, chloroform, ethyl acetate, ethanol and Water. These extracts were screened for anti-inflammatory activity using caragennan induced rat paw edema at the dose of 200 and 400 mg/kg orally. The aqueous extract was found most active, it was then fractionated into four major fractions (FR) and were screened. In the test for acute inflammation, FR-III(Methanol: Water) & IV(Water), 200 mg/kg with 45.51% & 52.56% inhibition of edema respectively at the end of 4 h showed significant (P<0.01). At a dose of 400mg/kg FR-III (Methanol: Water) & IV (Water) with 50.64% & 55.76% inhibition of edema respectively at the end of 4 h) showed significant (P<0.01) as compared with reference drug indomethacin with 60.25% inhibition of edema (P<0.01). Aqueous extracts fractions showed significant dose dependant anti-inflammatory activity in rat model [8].

Benincasa hispida

The anti-inflammatory activity of Petroleum ether and Methanolic extract of *Benincasa hispida* fruit. In carrageenan induced paw edema model, petroleum ether and methanolic extracts showed maximum inhibition in inflammation (0.270 ± 0.063, 0.307 ± 0.043 respectively) as compared to control group (1.27 ± 0.059) which were comparable with standard valdecoxib (0.247 ± 0.033). In histamine-induced paw edema, both the extract showed maximum inhibition (62.86% and 54.84% respectively) as compared to control group, which were comparable with that of standard drug cetrizine (95.24%). Petroleum ether and methanolic extracts showed slight reduction in granuloma tissue formation in cotton pellet implanted rats, which were not significant with that of standard drug diclofenac sodium. Both extracts at the dose of 300 mg/kg body weight, produced dose dependent

and significant inhibition (P<0.05) of carrageenan induced paw edema, histamine induced paw edema and cotton pellet induced granuloma in rat model [9].

Calendula officinalis

The ethyl alcohol extract of *Calendula officinalis* flower was used for anti inflammatory activity Administration of extract produced 50.6 and 65.9% inhibition in paw volume at the dose of 250 and 500 mg/kg body wt at 3 h significant inhibition (P<0.001).When dextran was used as a acute inflammatory agent there was 41.9 and 42.4% inhibition in paw volume at 3 h in the 250 and 500 mg/kg body wt. extract treated groups significant inhibition (P<0.001).Significant inhibition in paw edema was also seen in the treated groups in chronic inflammatory model using formalin which was 32.9 and 62.3% on the third day after treatment with 250 mg/kg significant inhibition (P<0.05) and 500mg/kg showed significant inhibition (P<0.001) of the extract [10].

Clerodendron infortunatum

The methanol extract of leaves of *Clerodendron infortunatum* Linn. was evaluated for anti-inflammatory activity against the carrageenan, histamine and dextran induced rat paw edema. The methanol extract of *Clerodendron infortunatum* showed maximum inhibition of 49.64 and 65.63% at the dose of 250 and 500 mg/kg body wt. respectively after 3 h of the extract treatment against carrageenan induced paw edema whereas the reference drug produced 76.29% of inhibition at the dose 100 mg/kg body wt. In case of histamine induced paw edema, the methanol extract produced 45.85 and 58.02% of inhibition at the dose of 250 and 500 mg/kg body wt. respectively. Whereas the reference drug produced 71.22% of inhibition in rats. In case of dextran induced paw edema, the methanol extract produced 39.65 and 57.90% of inhibition at the dose of 250 and 500 mg/kg body wt., respectively. The study revealed that after 3 h of carrageenan, histamine and dextran administration, the methanol extract of *Clerodendron infortunatum* at doses of 250 and 500 mg/kg body weight exhibited statistically significant (P<0.01) inhibition of paw volume respectively, which was less than that observed with standard drug phenylbutazone (P<0.01) given at a dose of 100 mg/kg body weight [11].

Cynodon dactylon

The anti inflammatory activity of aqueous extract of *Cynodon dactylon* at different doses using carrageenan, serotonin, histamine and dextran induced rat paw edema and cotton pellet method. The study was carried out in three different doses levels of 200,400 and 600 mg/kg orally. The maximum activity has been shown at a dose of 600 mg/kg, 47.69% as compared to Indomethacin 49.23% edema inhibition. In serotonin induced rat paw edema aqueous extract shown maximum activity at 600mg/kg, 50% as compared to Indomethacin, 53.12% edema inhibition. In histamine model the extract showed significant activity in all three doses but max activity has been shown at a dose of 600mg/kg, 45% as compared to Indomethacin, 50% edema inhibition. In dextran model all three doses showed significant activity. But max. activity has been shown at a dose 600 mg/kg ,42.18% edema inhibition at as compared to Indomethacin ,46.87% edema inhibition. In cotton pellet granuloma the % inhibition in the granuloma wt. shown by the extract at different doses was 13.12% at 200 mg/kg, 42.05% at 400 mg/kg and 46.40% at 600 mg/kg as compared to 46.27% shown by the Indomethacin. The Aqueous extract of *Cynodon dactylon* was found to be safe at all doses used and there is no mortality up to the dose of 4000mg/kg of extract when administered orally. *Cynodon 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 [12].

Desmostachya bipinnata

The petroleum ether, benzene, chloroform, ethanol and aqueous extracts of *Desmostachya bipinnata Stapf* (300 mg/kg, orally) shown percentage inhibition 47.69%, 43.07%, 46.15%, 53.84% and 38.46% respectively and gave significant (P<0.05) reduction of rat paw edema at all assessment times. The maximum inhibition was shown by the ethanol extract 53.84% whereas the standard drug showed 32.30% of inhibition. As per we can say ethanol extract significantly (P<0.05) reduce inflammation [13].

Euphorbia heterophylla

The aqueous and methanolic extract of leaves of *E. heterophylla* were used for anti-inflammatory activities by carrageenan-induced rat paw oedema method At the different dose range used (50, 100 and 150 mg/kg), there was no significant differences in their anti-inflammatory activity hence they were not dose-dependent. However, the methanolic extract did not show any appreciable activity (20-24% inhibition) and were not dose-dependent. The results obtained the aqueous extract showed significant activity (P<0.001) comparable to the reference drug used [14].

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Garcinia mangostana

The acetone extract of fruit of *Garcinia mangostana* was used to anti inflammatory activity. The anti-inflammatory effects of α and γ mangostins were evaluated by carrageenan-induced paw edema in mice. At doses 20 mg/kg both α mangostin and sulindac treatment showed significant difference on paw edema inhibition when compared with control group (α mangostin vs. control, P = 0.001; sulindac vs. control, P = 0.006). α Mangostin and sulindac exhibited a potent inhibition on paw edema at 3 and 5 h, respectively. Therefore, we suggested the on-set time of paw edema inhibition from the α-mangostin was more quickly than that of sulindac. However, γ-mangostin did not significant inhibit the paw edema in mice. The data demonstrated that α-mangostin has more anti-inflammatory activity than γ-mangostin *in vivo* [15].

Gymnema sylvestre

The aqueous extract of leaves of *G. sylvestre* was used for two anti inflammatory activity model like Carrageenan induced paw oedema and Cotton pellet-induced granuloma. The three doses of extract was used 200,300 and 500 mg/kg, but 500 mg/kg decreased the paw oedema by 48.53% within 4 h. After administration, while standard drug decreased the paw oedema volume by 57.6%.When compared with paw oedema volume of control. The aqueous extract at the dose 300 and 500 mg/kg produced significant reduction (P<0.01) in granuloma volume when compared with control group [16].

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 by17.12 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<0.001) anti-inflammatory activities against all the agents used [17].

Indigofera tinctoria

The ethanol extract of leaves *Indigofera tinctoria* (250, 500 & 1000 mg/kg b.wt, p.o.) reduced acute paw oedema volume induced by sub-planter injection of carrageenan (0.1ml of 1% solution) in wister Albino rats. Ethanolic extracts of the dose of 500 and 1000 mg/kg body weight showed inhibition of paw edema after 2 h 48.43%, 61% and 3 h 51%, 62% respectively. This anti-inflammation activity was dose dependent and found to be statistically significant (P<0.01). Ethanolic extracts of leaves of *Indigofera tinctoria Linn.* (500 & 1000 mg/kg bwt) showed potent anti-inflammatory activity when compared to control as well as positive control Ibuprofen (standard drug) group. The low doses of ethanolic extract (250 mg/kg bwt) did not show significant inhibition of inflammation. The result showed that ethanolic extract of *Indigofera tinctoria Linn* dose dependently improve the potent anti-inflammatory activity [18].

Kaempferia galangal

The three doses, 300, 600 and 1200 mg/kg of alcoholic extract of *Kaempferia galanga* was tested for anti-inflammatory activity. Acute and sub acute inflammatory activities were studied in rats by carrageenan induced paw edema and cotton pellet induced granuloma models respectively. After 1 and 3 h of carrageenan administration, *K.galanga* exhibited maximum % inhibition of paw volume 36.95%, 33.55% and 42.31%, 44.19%, at the higher two doses of plant extract 600 mg/kg and 1200 mg/kg body weight respectively, however % inhibition of paw volume was less than that of standard drug aspirin 54.96%, 69.59% (P<0.001) at the dose of 100 mg/kg body weight. In carrageenan induced rat paw edema test, the two doses plant extract showed statistically significant (P<0.001) inhibitory effect on mean increase in paw volume at all the time intervals up to 6 h. In the cotton pellet induced granuloma model two doses of *K. Galangal* 600 mg/kg and 1200 mg/kg was used and the % of inhibition of paw volume 27.305 and36.70% significant (P<0.001), and aspirin showed % of inhibition 42.17% significant (P<0.001) activity in inhibiting dry weight of granuloma. The extract administered at p.o. had a greater anti-granulation effect but less than aspirin [19].

Leucas cephalotes

The crude methanolic alkaloid, aqueous, hexane, petroleum ether and non alkaloid fractions of the leaves were used for anti inflammatory activity with carrageenan induced rat paw edema method. The results showed that alkaloid fractions of the leaves causes significant reduction in inflammation 80% (100 mg/kg) followed by crude methanol extract 61% (100 mg/kg) and aqueous extract 58% (100 mg/kg) as compared to standard anti-inflammatory drug aspirin 68.62% (25 mg/kg). The values of reduction in paw volume, 0.11 ± 0.002, 0.14 ± 0.002, 0.16 ± 0.002 and 0.13 ± 0.004 were found significantly of alkaloidal fraction, methanol extract, aqueous extract

and aspirin, respectively at 4 h after carrageenan administration and statistical significant value was $P<0.05$. However, non alkaloidal, hexane and petroleum ether fractions did not show any anti-inflammatory activity irrespective of the time intervals. Thus crude methanolic extract and alkaloidal fractions of leaves of the plant can be fully explored for its anti-inflammatory potential [20].

Microtrichia perotitii

The n-butanol phase of the methanolic leaves extract of *Microtrichia perotitii* DC was used for anti-inflammatory activity. The doses of extract 25, 50 and 100 mg/kg were found significantly difference at $P<05$, $P<0.01$ and $P<0.001$ respectively in mean paw diameter in hours. The study has shown that the leaves have very strong activity to prevent the growth of oedema in the hind paw of the rats respectively [21].

Moringa oleifera

The aqueous and ethanolic extract of the stem bark of *Moringa oliefera* showed % inhibition after 5 h was maximum 27.27 and 30.30% significant reduction $P<0.01$and $P<0.05$ 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 $P<0.01$.The percentage of paw edema was found to be better with the alcoholic extract than the aqueous extract [22].

Pandanus odoritissimees

Crude acetone extract of whole plant of *pandanus odoritissimees linn* was used for anti-inflammatory activity against carrageenan induced rat paw edema, against mediator (histamine, and serotonin) induced inflammation in rats, it also used for the cotton pellet induced granuloma formation in rats, inhibits significantly where in phenyl butazone as the standard anti-inflammatory drug. In histamine induced hind paw edema the dose (250 and 500 mg/kg body wt.) of extract shown % of inhibition 38.9% and 51.8% respectively. In serotonin induced hind paw Oedema the doses (250 and 500 mg/kg body wt.) of extract shown % of inhibition 40.3% and54.4% respectively. In cotton pellet induced granuloma formation the dose (250 and 500 mg/kg body wt.) of extract shown % of inhibition28.80% and 47.90% respectively. The percentage of inhibition of *Pandanus odoritissimees* acetone extract at the dose level of 500mg/kg is nearer to the reference drug phenyl butazone. The present extract showed significant anti-inflammatory activity at both the tested dose (250 and 500 mg/kg) levels. Further the effect of the extract *Pandanus odoritissimees* acetone extract significantly inhibited the granuloma formation in rats ($P<0.001$) in a dose dependant manner [23].

Rubia cordifolia

The alcoholic extract of the stems of *Rubia cordifolia* was used for anti inflammatory activity. The standard NSAID indomethacin drug (10 mg/kg/ml/) was used orally. The low dose (20 mg/kg/ml) and high dose (40 mg/kg/ml) of alcoholic extract suspension of test drug *Rubia cordifolia* respectively orally. Indomethacin produced a 76.79% inhibition of paw oedema when observed after 3 hours of carrageenan injection. The alcoholic extract (high dose) of *Rubia cordifolia* significantly inhibited the paw oedema 39.13% inhibition when compared to the saline group after 3 h of carrageenan injection. In case of (low dose) of alcoholic extract of *Rubia cordifolia,* which gave a 29.01% inhibition of paw oedema, however, they didn't attain the statistical significant value compared to saline treated group. According to statistical analysis of anti-inflammatory data, we can say that the values were significantly different from the control or saline group at $P< 0.05$ [24].

Ruta graveolens

Aqueous, ethanolic and methanolic extracts of aerial part of *Ruta graveolens* was used for anti-inflammatory activity in carrageenan induced paw edema in wistar male rats, and compared to a positive control drug, Voveran. The extracts were tested at two different dose levels. The results showed that the methanolic extract with a dose of 20 mg/kg b.w and ethanolic extract with a concentration of 50 mg/kg b.w. showed 90.9% of inhibition on carrageenan induced rat paw edema at third hour. This result indicated that methanolic extract with a dose of 20 mg/kg b.w and ethanolic extract with a concentration of 50 mg/kg b.w. showed a maximum anti-inflammatory activity as compared to the reference drug Voveran, which showed only 72.72% inhibition. Methanolic extract with a dose 50 mg/kg b.wt produced 81.81% of inhibition and is also high as compared to the reference drug. Ethanolic extract with a dose of 50 mg/kg b.wt produced 63.6% of inhibition and is low as compared to the reference drug. Aqueous extract with two different doses 20 mg/kg b.w and 50 mg/kg showed only 18.2% and 36.3% inhibition respectively. The effect was significantly ($P<0.05$) higher than that of the standard drug Voveran (72.72%) It was lower as compared to the reference drug [25].

Securidaca longipedunculata

The extract and fractions of the root bark of *Securidaca longipedunculata* was used for anti inflammatory activity. The doses of extract were used 5 and 10 mg/kg body weight..The extract and fractions inhibited topical edema induced by xylene in the mouse ear. The petroleum ether fraction and methanol fraction caused greater inhibition than the methanol extract in the order PF>MF>ME the values were 65.63, 53.13 and 40.63% respectively. The methanol extract and methanol fraction suppressed the development of paw edema induced by egg albumin in rats. The methanol extract (ME) evoked a non-dose related inhibition while the methanol fraction (MF) caused the reverse from 2 h. The significant value $P<0.05$. The petroleum ether fraction (PF) was did not exhibit anti-inflammatory activity [26].

Solanum nigrum

The effect of methanolic extracts of berries of *Solanum nigrum* in carrageenan induced paw edema in rats is shown by the using of doses 125,250 and 375 mg/kg body weight .The % inhibition of paw edema was 17.08, 13.09 and 23.45% at the doses of 125,250 and 375 mg/kg body weight respectively. The methanolic extract of *Solanum nigrum* (375 mg/kg) prevented the formation of edema induced by carrageenan and thus showed significant anti-inflammatory activity ($P<0.05$). Diclofenac sodium at 10 mg/kg inhibited the edema volume by 12.60 %. On carrageenan induced acute inflammation model the methanolic extract (375 mg/kg) produced better inhibition of paw edema [27].

Trigonella-foenum-graceum

The alcoholic extract of seeds of *trigonella-foenum-graceum* (Fenugreek) was used to evaluate anti-inflammatory activity of on Wister strain rat. The doses (100 mg & 200 mg/kg b.w) were measured by using carrageenan as inflammatory agent, keeping indomethacin (10 mg/kg b.w) as reference standard. The maximum % of inhibition of alcoholic extract doses (100 and 200 mg/kg b.w.) after 6 h, 12.06 and 14.05% respectively. The (100 mg/kg b.w) had shown significant difference with control ($P<0.05$) at 3, 4 and 6 h.The (200 mg/kg b.w) and Indomethacin (10 mg/kg b.w) showed significant anti-inflammatory effect ($P<0.025$) up to 4 h. The study indicated that alcoholic extract of *Trigonella-foneum-graceum* exhibited anti-inflammatory effect on carrageenan induced paw oedema in rats at dosage of both at 100 mg & 200 mg/kg b.w. This low dose of fenugreek was more significant than Indomethacin. So the alcoholic extracts of fenugreek seeds can be used safely as anti inflammatory agent [28].

Callistemon lanceolatus

The methanolic extract of *C.lanceolatus* (200 and 400 mg/kg) showed paw volume after 1h (1.638 and 1.638), after 2 h (1.491 and 1.323) and after 3 h (1.412 and 1.270) respectively. *C. lanceolatus* methanolic leaf extracts (200 and 400 mg/kg) significantly inhibited carrageenan induced rat paw oedema formation the values are ($P<0.001$) and ($P<0.05$).the inhibition of extract was dose dependent. The diclofenac sodium (50 mg/kg) was used as standard drug [29].

Xeromphis spinosa

The bark of *Xeromphis spinosa* extracted by a mixture of equal proportions of petroleum ether, ethyl acetate and methanol was used for anti inflammatory activity. The anti-inflammatory activity of extract of *X. Spinosa* was evaluated by carrageenin induced paw edema method in Albino rats. In carrageenin induced paw edema model, *X. spinosa* at doses of 200 and 400 mg/kg caused significant inhibition of paw edema by 34.02% ($P<0.001$) and 26.80% ($P<0.001$) respectively, 4 h after carrageenin administration [30].

Ximenia Americana

The aqueous ethanol extract of root bark of the plant was used for the anti-inflammatory activity. From 3 h of challenge with extract, the swelling of paw were brought from 24.21% in control to 16.27, 9.82 and 5.68%, respectively in groups treated with 1, 10 and 100 mg/kg. That corresponded to 40, 56 and 73%, respectively of edema inhibition. The extract of *X. americana* (10 and 100 mg/kg b.w) significantly inhibited carrageenan provoked mice paw swelling $P<0.05$, $P<0.01$ respectively. The intensity of anti-edema effect of plant extract was proportional to the tested doses. The decrease of the edema caused by indomethacin and betamethasone was respectively, 38 and 93% [31].

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Table 1: Ethanobotnical data of medicinal plants with anti-inflammatory activity

S.no.	Plants (Family)	Part used	Extract	Doses (mg/kg)	Model
1	*Albizia lebbeck* (Leguminosae)	Bark	Pet. ether, ethyl acetate and methanol,	200 and 400 mg/kg	1
2	*Argyreia speciosa* (Convolvuceae)	Roots	Hydroalcoholic	100,200 and 500 mg/kg	1
3	*Barleria prionitis* (Acanthaceae)	Roots	Pet.ether, chloroform, ethyl acetate, ethanol and water	200 and 400 mg/kg	1
4	*Benincasa hispida* (Cucurbitaceae)	Fruit	Pet. ether and Methanol	300 mg/kg	1, 2 &3
5	*Calendula officinalis* (Compositae)	Flower	Ethyl alcohol	250 and 500 mg/kg	1, 4 & 5
6	*Clerodendron infortunatum* (Verbenaceae)	Leaves	Methanol	250 and 500 mg/kg	1
7	*Cynodon dactylon* (Poaceae)	Whole plant with roots	Aqueous	200,400 and 600 mg/kg	1, 2, 4 & 6
8	*Desmostachya bipinnata* (Poaceae)	Whole plant	Pet. ether, benzene, chloroform, ethanol and water	300 mg/kg	1
9	*Euphorbia heterophylla*, (Euphorbiaceae)	Leaves	Aqueous and methanolic	50,100 and150 mg/kg	1
10	*Garcinia mangostana* (Guttiferae)	Fruit	Acetone	20 mg/kg	1
11	*Gymnema sylvestre* (Asclepiadaceae)	Leaves	Aqueous	200,300 and 500 mg/kg	1, 3
12	*Hibiscus rosa- sinensis* (Malvaceae)	Leaves	Methanol	250and500 mg/kg	1, 4
13	*Indigofera tinctoria* (fabacae)	Leaves	Ethanol	250,500 and 1000 mg/kg	1
14	*Kaempferia galanga* (Zingiberaceae)	Rhizomes	Ethanol	600and1200 mg/kg	1, 3
15	*Leucas cephalotes* (Labiatae)	Leaves	Aqueous, methanolic, petroleum ether and hexane	100 mg/kg	1
16	*Microtrichia perotitii* (Asteraceae)	Leaves	Methanol (n-butanol)	25,50 and 100mg/kg	7
17	*Moringa oleifera* (Moringaceae)	Stem bark	Ethanolic and aqueous	300 mg/kg	1
18	*Pandanus odoritissimus* (Pandanaceae)	Whole plant	Acetone	250 and 500 mg/kg	1, 3 & 9
19	*Rubia cordifolia* ((Rubiaceae)	Stem	Ethanol	20 and 40mg/kg/ml	1
20	*Ruta graveolens* (Rutaceae)	Arial part	Aqueous, ethanolic and methanolic	20 and 50mg/kg	1
21	*Securidaca longipedunculata*, (Polygalaceae)	Root bark,	Methanol extract, petroleum ether and methanol fraction	5 and 10 mg/kg	1 & 8
22	*Solanum nigrum,* (Solanaceae)	Berries	Methanol	125,250 and 375 mg/kg	1
23	*Sphearanthus indicus* (Asteraceae)	Whole herb	Hydroalcoholic	100,200 and 500 mg/kg	1
24	*Trigonella foeum graceum* (Leguminosae)	Seeds	Alcoholic	100 and 200 mg/kg	1
25	*Callistemon lanceolatus* (Myrataceae)	Leaves	Methanolic	200 and 400 mg/kg	1
26	*Xeromphis spinosa* (Rubiaceae)	Bark	Mixture (petroleum ether, ethyl acetate and methanol)	200 and 400mg/kg	1
27	*Ximenia americana* (Olacaceae)	Root bark	hydro- alcohol	10,30 and 100mg/kg	1

Animal models

1-Carrageenan induced paw oedema
2-Histamine induced paw edema
3- Cotton pellet-induced granuloma
4-Dextran induced paw edema
5-Formalin induced paw edema
6-Serotonin induced paw edema
7-Formaldehyde induced oedema
8- Topical acute edema
9-Autocoids induced inflammation

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CONCULSION

The present review summaries that studies with new anti-inflammatory plants are important for the discovery of drug with less side effects, less costly, affordable and more effective in the treatment of inflammation. This type of study with medicinal plants will contribute to the benefit of the populations needing this type of health care. Researchers must pay attention to the scientific rigor of studies of herbal drugs in the future to improve the status. Further research is required to determine which ingredients are effective which will provide valuable clues for researching and developing anti-inflammatory drugs in the future.

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