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THERAPEUTIC PROPERTIES OF MEDICINAL PLANTS: A REVIEW OF PLANTS WITH ANTI-INFLAMMATORY, ANTIPYRETIC AND ANALGESIC ACTIVITY (PART 1)

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ABSTRACT

The previous studies showed that a wide range of medicinal plants exerted antiinflammatory, antipyretic and analgesic effects. These plants included: *Achillea santolina*, *Althaea officinalis*, *Adiantum capillus-veneris*, *Alhagi maurorum*, *Ailanthus altissima*, *Allium cepa*, *Alpinia galanga*, *Ammanniabaccifera*, *Ammi majus*, *Anchusaitalica*, *Andrachne aspera*, *Anethum graveolens*, *Anthemis nobelis*, *Apium graveolens*, *Arachis hypogaea*, *Arctium lappa*, *Aristolochia maurorum*, *Asclepias curassavica*, *Asparagus officinalis*, *Astragalus hamosus*, *Avena sativa*, *Bacopa monnieri*, *Bauhinia variegata*, *Bellis perennis*, *Benincasa hispida*, *Betula alba*, *Bidens tripartita*, *Brassica nigra*, *Brassica rapa*, *Bryonia dioica*, *Bryophyllum calycinum*, *Caesalpinia crista*, *Calendula officinalis*, *Calotropis procera*, *Canna indica*, *Capparis spinosa*, *Capsella bursa-pastoris*, *Capsicum annuum*, *Capsicum frutescens*, *Carthamus tinctorius*, *Carum carvi*, *Cassia occidentalis*, *Centaurea cyanus* and *Chenopodium album*. This review will highlight the antiinflammatory, antipyretic and analgesic effects of these medicinal plants.

Key words: Pharmacology, Therapeutic, Pharmacognosy, Medicinal plants, Anti-inflammatory, Antipyretic, Analgesic.

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INTRODUCTION

Medicinal plants are the backbone of traditional medicine, more than 3.3 billion people in the less developed countries utilize medicinal plants on a regular basis [1]. Plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavours, fragrances, colours, biopesticides and food additives. Many previous studies showed that a wide range of medicinal plants exerted antiinflammatory, antipyretic and analgesic effects [2-54]. This review will highlight the antiinflammatory, antipyretic and analgesic effects of medicinal plants.

Achillea santolina

A. santolina ethanolic extract exerted anti-inflammatory and antidiuretic activity[55, 56]. Tekieh *et al* showed that methanolic extract of *A. santolina* caused significant reduction in the edema, hyperalgesia and serum IL-6 level in complete Freund's adjuvant induced inflammation in hind paw of rats [57]. Zaringhalam *et al* found that the methanolic extract of *A. santolina* exhibited significant antihyperalgesic and anti-inflammatory effects during pretreatment and short-term treatment at dose of 200 mg/kg and there was no significant difference between 200 and 400 mg/kg doses of this extract. Defatted extract of *A. santolina* did not show significant effect on CFA-induced inflammation during different stages of treatment ($P>0.05$). Short-term treatment with methanolic extract at dose of 200 mg/kg was found more effective than indomethacin in edema, hyperalgesia and serum IL-6 level reduction ($P<0.01$, $P<0.01$ and $P<0.05$ respectively) [58].

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Althaea officinalis

Aqueous extracts of the roots of*Althaea officinalis* stimulated phagocytosis, and the release of oxygen radicals and leukotrienes from human neutrophils *in vitro*. The aqueous extract alsoinduced the release of cytokines, interleukin-6 and tumour necrosis factor from human monocytes in vitro, thereby exhibiting anti-inflammatory and immune stimulant activity [59]. A polysaccharide fraction (500mg/ml) isolated from a root extract had anticomplement activity in human serum *in vitro* [29]. Marshmallow mucilage polysaccharides administered intraperitoneally to mice at a dose of 10 mg/kg produced a 2.2-fold increase in phagocytic activity of macrophages in the carbon-clearance test[60].However, with a dry 80% ethanolic extract administered orally (100 mg/kg b.w.), no inhibition of carrageenan induced rat paw oedema has been proved[61]. Hypolaetin 8-glucoside has been tested for its anti-inflammatory, analgesic and anti-ulcer activity in rats. This flavonoid (30, 60 and 90 mg/kg i.p.) was more potent than phenylbutazone (30, 60 and 90 mg/kg ip) in suppressing the acute phase of adjuvant carrageenan-induced inflammation but had less effect in the prolonged inflammatory phase. In contrast to phenylbutazone, it did not cause gastric erosions. Analgesic activity of hypolaetin 8-glucosid has been found to be lower than the one of phenylbutazone**.** Hypolaetin 8-glucoside was also more potent than troxerutin (both at the doses of 100, 200, 300 and 400 mg/kg s.c.) in inhibiting histamine-induced capillary permeability in rats [62].An ointment containing an aqueous marshmallow root extract (20%) applied topically to the external ear of rabbits reduced irritation induced by UV irradiation or by tetrahydrofurfuryl alcohol. The ointment has been compared to pure dexamethasone 0.05% ointment and a combined marshmallow and dexamethasone product. The anti-inflammatory effect of marshmallow ointment was lower than that of a dexamethasone ointment. The combined product had higher anti-inflammatory effect than the ointments with the individual ingredients [20].Scopoletin exert anti-inflammatory activity in croton oil induced mouse ear edema [63].

Adiantum capillus-veneris

Alcoholic extract of *Adiantum capillus-veneris* and its hexane fraction exerted significant anti-inflammatory activity against formalin induced inflammation. The hexane fraction showed topical anti-inflammatory activity after 6h and continued for 30h in croton oil- induced inflammation. The ethyl acetate fraction of the ethanolic extract of *Adiantumcapillus-veneris* showed significant inhibition of hind paw edema induced by carrageenan. The chronic anti-inflammatory activity of the ethanol extract was also evaluated by carrageen-induced paw edema method. The results, at the two dose levels tested in rats, indicate significant anti-inflammatory activity. The maximum inhibition of inflammation (71.15 %) was recorded with 100 mg/kg of plant extract. The analgesic activity of the ethanolic extract of *Adiantumcapillus-veneris* and its fraction carried out by tail flick method and writhing test, the result showed significant analgesic activity with insignificant gastric ulceration as compared to the standard anti-inflammatory analgesic antipyretic drugs [64-66]. The anti-inflammatory and anti-nociceptive activities of the crude ethanolic extract of*Adiantum capillus veneris* and its various fractions was studied using carrageenan induced hind paw edema, tail-flick method and writhing test at a dosage of 300 mg/kg po. Gastric ulceration studies have been further carried out for the ethanolic extract and its various fractions at dose of 900 mg/kg body weight. Amongst the tested fractions, the ethyl acetate fraction exhibited better anti-inflammatory effect (67.27%) at 300 mg/kg po dosage when compared to the standard drug, indomethacin (63.63%) after 3h in the carrageenan induced hind paw edema. The anti-inflammatory activity of the ethanolic extract and its various fractions appear to be related to the inhibition of NO release, and the decreasing TNF-α level. The ethanolic extract and all its fractions especially the ethyl acetate ($p<0.01$) showed significant analgesic activity with insignificant ulceration as compared to the standard drug, ibuprofen. The histopathological study of the effect of ethanolic extract and its fractions in the stomach, reveals that none of them cause ulcer[65]. The anti-inflammatory effect of ethanolic extracts of *Adiantum capillus-veneris* and the involvement of NF-κB signaling in the regulation of inflammation was studied. The plant ethanolic extracts effectively suppressed PGE2, IL-6 and TNFα release with an IC_{50} less than 50 µg/ml. Moreover, luciferase expression could be specifically blocked in HepG2 cells, showing that the plant extracts displayed a cell-specific pattern on NF-κB gene transcription. The assayed biological activity also depended on the order of adding TNF-α and the plant extracts because the plant extracts could only block the NF-κB activation if added earlier but were unable to stop the signal when added after TNF-α. However, the plant extracts did not exert any effect on ubiquitination which regulates several steps in the NF-κB pathway. Additionally, the plant extracts down-regulated phosphorylation of IKKα/β at S176/180, p38 at T180/Y182 and p65 at S536, but not p65 at S276. This was confirmed by their ability to selectively abrogate the induction of IL-8 transcription, whereas the ICAM-1 gene, which is not transcribed selectively by an NF-κB complex containing a form of p65 phosphorylated on Ser536, did not change. Finally, the plant extracts at 200 µg/mg could normalize the LPS-induced elevation of spleen index as well as NF-κB and p38 activations in CD1 mice [67].

Alhagi maurorum

Pharmacological screening of extract of *Alhagi*

maurorum has revealed that it possesses anti-inflammatory effect; the extract inhibited the release of pro-inflammatory mediators of acute inflammation such as histamine and prostaglandin[68]. The anti-inflammatory activity of an aqueous extract of *Alhagi maurorum* was examined in mice by formalin induced paw edema assay. The extract was also significantly reduce the thickness of paw edema induced by formalin at dose –dependent manner in both phase I, and phase II[69]. Zakaria *et al.* also found that *Alhagi maurorum* extract exerted significant anti-inflammatory activity in acutepaw edema and significant anti-inflammatory activity in sub-acute cotton pellet model [70]. By using a spontaneous flinching of the formalin injected mice paw method. The aqueous extract at doses of 125, 250, 500 µg/animal caused significant decrease in frequency of licking of the formalin- injected paw [69].The aqueous extract of *Alhagi maurorum* was evaluated in mice at doses of 125, 250 and 500µg/animal, for its anti-inflammatory and analgesic effects. The extract and the reference drug (Diclofenac sodium 1 µg/animal) were significantly reduce the thickness of paw edema induced by formalin at dose -dependent manner in both phase I and II. The analgesic effect of the aqueous extract of *Alhagi maurorum* at doses of 125, 250 and 500µg/animal and diclofenac sodium(1µg/animal), on licking frequency was estimated, in the phase 1 (0-5 min.) and in phase II (15-20 min) after formalin administration. The extracts induced analgesic effects and the 500µg/ animal, showed the most potent effect [71]. Administration of the ethanolic extract of *Alhagi maurorum* powdered roots in doses of 0.25 and 0.5 g/kg (IP) into mice did not induce any changes in the rectal temperature. However, administration of the extract in doses of 1 g/kg (IP) decreased the body temperature with a maximum of 3.3 °C 60 min after administration of the extract. Thereafter the temperature started to rise again [72]. The antinociceptive effect of methanolic extracts (200 and 400 mg/ kg) of *Alhagi maurorum* was studied using acetic acid-induced writhing and tail-flick test in mice. Oral administration of methanolic extracts of *Alhagi maurorum*significantly inhibited the nociception to acetic acid-induced writhe even in low dose. In the tail-flick test, methanolic extracts of *Alhagi maurorum*in a dose of 400 mg/ kg produced significant increase in the latency to response of tail to thermal stimulation [73]. Intraperitoneal administration of glyceryl-n-tetracosan-17-ol- 1-oate (a new aliphatic ester isolated from the root of the plant) in mice at a dose of 200 mg/ kg of body weight reduced body temperature by 4.1 and 5.2 after one and two hoursrespectively [74]. The effect of both *Alhagi maurorum*extracts on xanthine oxidase activity was studied. The addition of the leaves extract showed a dose-dependent inhibition of xanthine oxidase activity, but the addition of flowers extract exhibited a lower effect. Higher concentrations showed more efficient inhibitory action on xanthine oxidase activity than the lower concentration. The inhibition activities were (92.00 and 80.00%, for the leaves and flowers extracts, respectively) [75].

Ailanthus altissima

Ailanthus altissima stem bark of Egyptian origin were evaluated for their analgesic, antipyretic and antiulcer activities. Analgesic and antipyretic activities were evaluated by hot plate test at doses of 50 mg/ kg and 100 mg/kg of the extracts. The extracts have similar analgesic activity and the ether extract showed good analgesic activity at 30min. Also extracts showed a decrease on rectal temperature that means an hypothermic activity of the plant extracts with longer effect for the ether extract. Ether extracts showed a gastric ulcer protection activity and cytoprotection activity in a doses of 100 mg/kg as well as 50 mg/kg in ethanol induced ulcer in mice [76]. Luteolin-7-O-glucoside (L7G), isolated from *Ailanthus altissima*, inhibited 5-lipoxygenase (5-LOX)-dependent leukotriene C_4 (LTC_4) production in bone marrow-derived mast cells (BMMCs) in a concentration-dependent manner with an IC_{50} of 3.0 µM. To determine the action mechanism of L7G, immunoblotting for cytosolic phospholipase A2 (cPLA2) and mitogen-activated protein kinases (MAPKs) following c-kit ligand (KL)-induced activation of BMMCs with or without L7G were performed. Inhibition of LTC_4 production by L7G was accompanied by a decrease in cPLA2 phosphorylation, which occurred via the extracellular signal-regulated protein kinase-1/2 (ERK1/2) and p38 and c-Jun N-terminal kinase (JNK) pathways. In addition, L7G also attenuated mast cell degranulation in a dose-dependent manner (IC_{50}, 22.8 µM) through inhibition of phospholipase Cγ1 (PLCγ1) phosphorylation. Accordingly, the authors suggested that the anti-asthmatic activity of L7G may be mediated in part via the inhibition of LTC_4 generation and mast cell degranulation [77]. The Antiinflammatory effect of an ethanol extract from the parts of *Ailanthus altissima* was evaluated in both *in vitro* and in *in vivo* system. The ethanol extract of *Ailanthus altissima*(EAa) inhibited generation of the cyclooxygenase-2 (COX-2) dependent phases of prostaglandin D2 in bone marrow-derived mast cells (BMMC) in a concentration-dependent manner with an IC_{50} value of 214.6 microg/ml. However, this compound did not inhibit COX-2 protein expression up to a concentration of 400 microg/ml in the BMMC, indicating that EAa directly inhibits COX-2 activity. In addition, EAa inhibited leukotriene C4 production with an IC_{50} value of 25.7 microg/ml. Furthermore, this compound inhibited degranulation reaction in a dose dependent manner, with an IC_{50} value of 27.3 microg/ml. When ovalbumin (OVA)-sensitized mice were orally pretreated with EAa before aerosol challenges. EAa reduced the eosinophil infiltration into the airway and the eotaxin, IL-4, and IL-13 mRNA expression levels [78]. The ethanol extract of *Ailanthus altissima*showed antiinflammatory activity in an ovalbumin (OVA)-sensitized murine asthmatic model. To

determine the anti-inflammatory compounds in the plant, luteolin-7-O-glucoside (L7G) was isolated and its antiasthmatic activity was evaluated in an *in vivo* murine asthmatic model. L7G (10 to 100 mg/kg, po) reduced the amount of eosinophil infiltration in bronchoalveolar lavage (BAL) fluid in a dose-dependent manner. L7G inhibited both the prostaglandin E2 (PGE2) and serum immunoglobulin E level in BAL fluid in a dose-dependent manner. In addition, L7G inhibited the transcript profiles of interleukin IL4, IL5, and IL13 mRNA expression levels in the murine asthma model [79].

Allium cepa

Hot plate and formalin tests were used to study the analgesic effect of fresh onion juice (7.5 ml/kg) in mice during acute and chronic pain stages modeling. A significant analgesic property for fresh onion juice in both pain phases was recorded, the effect was similar to that of morphine (5 mg/kg). Fresh onion juice also decreased the hind paw thickness significantly. In the mean time, it also demonstrated better results than the standard treatment, diclofenac[80]. Ethanol (75%) extract of the fixed oil inhibited lipoxygenase in the polymorphonuclear leukocytes of guinea pigs[81]. The anti-inflammatory effect of an aqueous extract of Welsh onion green leaves (WOE) was investigated in mice. Administration of WOE, in the range of 0.25–1 g/kg, showed a concentration dependent inhibition on paw edema development after carrageenan treatment. The anti-inflammatory effects of WOE were closely attributed to decreased levels of tissue NO and tumor necrosis factor-α (TNF-α). Further evidence for WOE's protection is shown in the reduction of lipid oxidation and the increase of antioxidant enzyme activities, including catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPX) *in vivo*. WOE also decreased the number of acetic acid-induced writhing responses and formalin-induced pain in the late phase in mice. Overall, the results showed that WOE might serve as a natural source of anti-inflammatory compounds[82]. Seven different synthetic thiosulfinates, and cepaene- and/or thiosulfinate-rich onion extracts were found to inhibit *in vitro* the chemotaxis of human granulocytes induced by formyl-methionine-leucinephenylalanine in a dose-dependent manner at a concentration range of 0.1–100 μ*M*. Diphenylthiosulfinate showed the highest activity and was found to be more active than prednisolone. The anti-inflammatory properties of onion extracts are related, at least in part, to the inhibition of inflammatory cell influx by thiosulfinates and cepaenes[83]. In addition, ajoene inhibited the pain receptors at dorsal root of spinal cord, thus resulting in an inhibition of pain signal transduction[84].

Alpinia galanga

A significant analgesic effect in formalin test was produced bytopical preparation containing methanolic extract of*Alpinia galanga* rhizome [85]. A polyherbal formulation (JointCare B) containing A. galanga, exerteddose-dependent inhibition of inflammation in carrageenan induced paw and granuloma weight in croton oil-induced granuloma pouch model in rats [86]. In a randomized double-blind placebo controlled study,patients with osteoarthritisof the knee and moderate-to severe pain, the concentrated extract has been found significantly reduce symptoms of osteoarthritis [87].

Ammannia baccifera

Gopalakrishnan *et al* evaluated the anti-inflammatory and anti-arthritic activities of different extracts of *Ammannia baccifera* Linn. in acute inflammation induced by carrageenan in rat hind paw and in chronic inflammation induced by Freund's adjuvant induced arthritis models in comparison with indomethacin (10 mg/kg bw) as a standard drug. The ethanol extract of *Ammannia baccifera* exhibited significant dose dependent activity in acute inflammation and the doses of 100 mg/kg and 200 mg/kg bw produced 38.27% and 43.39% inhibition respectively after 3 h as compared with that of the standard drug which showed 48.52% inhibition. In Freund's adjuvant induced arthritis model, the doses of 100 mg/kg and 200 mg/kg bw of the ethanol extract produced (38.83%) and (44.08%) inhibition respectively after 19 days when compared with that of the standard drug (55.47%)[88]. The ethanolic extract of the *Ammannia baccifera* (whole plant) at doses of 200, 400 and 600mg/kg ip produced an inhibition of 20.7%, 43.4% and 72.9%, respectively, of the abdominal writhes induced by acetic acid in mice. In the formalin test, the administration of 200,400 and 600mg/kg ip had no effects in the first phase (5 min) but produced a dose dependent analgesic effect on the second phase (1540 min) with inhibitions of the licking time of 27.3%, 47.7% and 57.4%, respectively [89]. The methanolic extract exhibited significant anti-inflammatory and analgesic activities at the dose of 100 and 200 mg/kg po. The analgesic effect of the higher dose of the extract (200 mg/kg) was comparable with the standard drugs aspirin and morphine [90].Tripathy *et al* found that ethanol extract of aerial parts of*A. baccifera*exhibited better anti arthritic activity than aqueous extract on cotton pallet induced granuloma and complete Freund'sadjuvant induced arthritis models in albino rats[91].

Ammi majus

Ammi majus coumarins were evaluated for anti-inflammatory activity by the carrageenan induced rat paw edema method. They possessed anti-inflammatory effects at a dose of 0.01 mg/100 g [92].

Anchusaitalica

The anti-inflammatory activity of different extracts from the aerial parts and the roots of

*Anchusaitalica*was investigated in rats using carrageenan-induced acute inflammation. The methanolic extract from the aerial parts, its *n*-butanol fraction, and rosmarinic acid, which was isolated from the *n*-butanol fraction of the methanol extract, showed significant dose-dependent anti-inflammatory activity. During the acute phase of inflammation, the anti-inflammatory activity of rosmarinic acid was comparable to that of ibuprofen[93].

Andrachne aspera

The antinociceptive effect of different oral doses of*Andrachne aspera* methanolic root extract was assessed in the writhing, the tail flick and the hot plate tests in mice. The extract produced significant antinociception in all the tests .The antinociception produced was dose-dependent in the tail flick test [94].

Anethum graveolens

The hydro alcoholic extract of the *Anethum graveolens* seed caused significant decrease in the inflammation and pain in rats [95]**.** *Anethum graveolens* oil and diclofenac-gel showed a significant ($p < 0.001$) decrease in the paw volume in rats compared to the blank group. *Anethum graveolens* oil showed even more decrease in the paw volume compared to the diclofenac [96].A single topical application of an ethanol extract of the fruits to the inner and outer surface of the ear of mice inhibited ear inflammation induced by 12-*O*- etradecanoylphorbol-13 acetate by 60% [97]. A 10% aqueous extract of the fruits and 5% aqueous solution of the essential oil had analgesic effects in mice pain induced by hot plate and acetic acid writhing models. The effect of the fruits (1.0 g/kg body weight) was comparable to 200 mg / Kg body weight of acetyl salicylic acid [98].

Anthemis nobelis

Thevolatile oil have been documented as having anti inflammatory activity (carrageenan rat paw odema test) and produced antidiuretic and sedative effects following intraperitoneal administration of doses up to 350 mg/kg to rats. The mechanism of antiallergic and anti inflammatory effects of azulenes is thought to involve inhibition of histamine release [99]. Two varieties of *Anthemis nobilis*, named (white-headed) or double flowered and (yellow-headed) yield essential oils with different composition. These essential oils proved to possess interesting anti-inflammatory and sedative properties, especially that derived from the (White-headed) variety. The oils caused 22.8 to 38.7% inhibition of the carrageenan induced increase in paw volume [100].Six octulosonic acid derivatives were isolated from the flower heads of Roman chamomile (*Chamaemelum nobile*). The biological activity of the isolated compounds was evaluated toward multiple targets related to inflammation and metabolic disorder such as NAG-1, NF-κB, iNOS, ROS, PPARα, PPARγ, and LXR. Similar to the action of NSAIDs, all the six compounds increased NAG-1 activity 2-3-fold. They also decreased cellular oxidative stress by inhibiting ROS generation. Three of the compounds activated PPARγ 1.6-2.1-fold, while PPARα was activated 1.4-fold by compounds two compounds. None of the compounds showed significant activity against iNOS or NF-κB [101].

Apium graveolens

Apium graveolens exerted anti-inflammatory effects in the mouse ear test and against carageenan induced rat paw odema [102], therefore *Apium graveolens* was recommended in arthritis and back pain [103, 104].

Arachis hypogaea

The anti-inflammatory effects of proanthocyanidins isolated from peanut skin were tested on inflammatory cytokine production and melanin synthesis in cultured cell lines. Peanut skin extract (PSE, 200 μg/mL) decreased melanogenesis in cultured human melanoma HMV-II co-stimulated with phorbol-12-myristate-13-acetate. It also decreased production of inflammatory cytokines (PSE at 100 μg/mL), tumor necrosis factor-α and interleukin-6, in cultured human monocytic THP-1 cells in response to lipopolysaccharide. Proanthocyanidins of peanet showed suppressive activities against melanogenesis and cytokine production at concentrations ranging from 0.1-10 μg/mL. Among the tested compounds, the suppressive activities of proanthocyanidin dimers or trimers in two assay systems were stronger than those obtained with monomer or tetramers. These data indicate that proanthocyanidin oligomers from peanut skin have the potential to reduce dermatological conditions such as inflammation and melanogenesis [105, 106]. Cho-K1 cells stably transfected with opioid receptor subtypes μ, Δ, and κ was used to assay the affinity of peanut constituents to opioid receptors. Compound GC-143-8 was run in competition binding against all three opioid subtypes (μ, κ, and Δ). One of peanet stilbenoidsshowed opioid recetor affinity . Combined use of this compound and analgesic agents may result in lower amounts of the latter needed to block pain . However, it is likely that the specific position and number ofhydroxy groups in the structure of the stilbenoid may be responsible for opioid receptor binding [107].

Arctium lappa

*Arctium lappa*decreased edema in the rat-paw model of carageenan-induced inflammation. Its extract was significantly reduce the release of inflammatory mediators through inhibition of degranulation and cys-leukotriene release [109]**.** Cultured macrophage RAW 264.7 was used to investigate the anti-inflammatory mechanism of arctigenin of *A. lappa* . Arctigenin suppressed lipopolysaccharide (LPS)-stimulated NO production and pro-inflammatory cytokines secretion, including TNF-a

and IL-6 in a dose-dependent manner. Arctigenin also strongly inhibited the expression of iNOS and iNOS enzymatic activity, whereas the expression of COX-2 and COX-2 enzymatic activity were not affected by arctigenin [110].Chlorogenic acid, as one of the constituents of *A. lappa*, inhibited lipopolysaccharide (LPS)-induced inflammatory response in RAW 264.7 cells, inhibited staphylococcal exotoxin-induced production of IL-1β, TNF, IL-6, INF-γ, monocyte chemotactic protein-l, macrophage inflammatory protein (MIP)-lα, and MIP-lβ in human peripheral blood mononuclear cells. Chlorogenic acid also inhibited lipopolysaccharide (LPS)-induced inflammatory response in RAW 264.7 cells, and decreased LPS-induced up-regulation of cyclooxygenase-2 at the protein and mRNA levels resulting in the inhibition of prostaglandin E2 release from LPS-treated RAW 264.7 cells [111-112].Butanol extract of *A. lappa* caused significant inhibition of β-hexosaminidase release in RBL-2H3 cells and suppressed mRNA expression and protein secretion of IL-4 and IL-5 induced by ConA-treated primary murine splenocytes. 100 μg/ml of butanol extract of *A. lappa* suppressed not only the transcriptional activation of NF-κB, but also the phosphorylation of MAPKs in ConA-treated primary splenocytes [113]. When BALB/C female mice were treated with *Arctium lappa* L polysaccharide(ALP) at low, medium and high dose, the immunological analysis showed that the number of antibody-producing cells at all doses, the phagacytosis index at medium dose and the weight of spleen and thymus at all doses was significantly increased after 20 days [114].

Aristolochia maurorum

Xanthine oxidase inhibitors which block the terminal step in uric acid biosynthesis, can lower the plasma uric acid concentration, and are generally employed for the treatment of gout [115].

Asclepias curassavica

Hydroalcoholic extract of the aerial part (95%) of plant showed anti-inflammatory activity [116]. The analgesic (flick method on mice) and antipyretic (Brewer's yeast induced pyrexia in rats) effects of the alcoholic and aqueous extracts of the stem of the plant were studied. The aqueous and alcoholic extracts of stem of *Asclepias curassavica* Linn showed significant anti-pyretic and analgesic activity[117].

Asparagus officinalis

Jang *et al.*, examined *Asparagus officinalis* for its inhibitory effects against both cyclooxygenase-1 and -2. They found that linoleic acid was the most active compound[118].

Astragalus hamosus

Astragalus hamosus pod extract showed anti-inflammatory activity , it induced significant reduction in the size of rats' hind paws 3 hours after injection. The aqueous and alcoholic extracts of the pod exhibit a similar significant effect [119].The anti-inflammatory effect of the hydro-alcoholic extract of the pods of *Astragalus hamosus* (HAAH)was evaluated by the rat paw edema induced by formalin. Also the analgesic effect was examined by the acetic-acid-induced writhing response and hot plate test. The analgesic effects of chloroform, hexane, ethyl acetate and aqueous fractions were evaluated by the hot-plate method. The hydroalcoholic extract of *Astragalus hamosus* could reduce the edema in a dose-dependent manner ($P<0.05$). In the acute phase, the result of 1000 mg/Kg and in the chronic phase, the result of 100 and 300 mg/Kg of the extract were more significant and comparable with the effect of sodium salicylate. Also application of different doses of HAAH had significant anti-nociceptive effects on both animal models. The findings showed that HAAH at doses of 700 and 1000 mg/Kg produced analgesic effects comparable to sodium salicylate. The hexane and ethyl acetate (but not the other fractions) showed significant analgesic activity in hot plate test, when compared to morphine [120].An aqueous and alcoholic extract of *Astragalus hamosus* (0.58 gm/kg) once a day for 13 days, orallyproduced highly significant anti-inflammatory effect in comparison to the control [119].

Avena sativa

The anti-inflammatory activities from whole oat groats of seven common varieties were evaluated. Oat variety CDC Dancer inhibited tumor necrosis factor-α induced nuclear factor-kappa B activation by 27.5% at 2 mg/ml, whereas, variety Deiter showed 13.7% inhibition at a comparable dose. Avenanthramide levels did not correlate with the observed anti-inflammatory activities[121].Avenanthramides have been reported to exhibit anti-inflammatory activity on the skin. At concentrations as low as 1 part per billion, it inhibited the degradation of inhibitor of nuclear factor kappa B-alpha (IkappaB-alpha) in keratinocytes which correlated with decreased phosphorylation of p65 subunit of nuclear factor kappa B (NF-kappaB). Furthermore, cells treated with avenanthramides showed a significant inhibition of tumor necrosis factor-alpha (TNF-alpha) induced NF-kappa B luciferase activity and subsequent reduction of interleukin-8 (IL-8) release. Additionally, topical application of 1-3 ppm avenanthramides mitigated inflammation in murine models of contact hypersensitivity and neurogenic inflammation and reduced pruritogen-induced scratching in a murine itch model [122].

Bacopa monnieri

Bacopa monniera effectively suppressed experimentally induced inflammatory reaction effect by inhibiting the prostaglandins synthesis and partly by stabilizing lyosomal membranes and didn't cause gastric irritation at anti-inflammatory doses[123].The ethanol

extract of the whole plant of *Bacopa monnieri* produced significant writhing inhibition in acetic acid induced writhing in mice at the oral dose of 250 and 500 mg/kg (P<0.001) comparable to diclofenac sodium 25mg/kg [124]. The anti-inflammatory effects of the many extracts of *Bacopa monnieri* were investigated on carrageenan induced edema in rat's hind paws**.** The methanol extract and aqueous fractions (100 mg/kg) showed a significant reduction in the edema paw volume, while, petroleum ether and hexane extracts didn't reduced inflammation[125].Human red blood cell (HRBC) membrane stabilization method was used to assay the in vitro anti-inflammatory activity of *Bacopa monnieri*. Methanolic extract and the callus (100, 200, 300 µg) produced membrane stabilization better than diclofenac sodium [126]. The anti-inflammatory activity of *Bacopa monnieri* is due to the triterpenoid and bacoside present in the plant. *Bacopa monniera* has the ability to inhibit inflammation through modulation of pro-inflammatory mediator release. The fractions containing triterpenoids and bacosides inhibited the production of pro-inflammatory cytokines such as tumor necrosis factor-alpha and interleukin-6 [127].

Bauhinia variegata

Phytochemical analysis of non woody aerial parts of *Bauhinia variegata* yielded 6 flavonoids with one triterpene caffeate. These seven compounds showed anti-inflammatory activity, they inhibited the lipopolysaccharides and interferon γ induced nitric oxide (NO) and cytokines[128]**.**

Bellis perennis

In two placebo-controlled studies, Traumeel injections, (which contains *Bellis perennis*) was used in patients with hemarthrosis. It showed that Traumeel injections improved joint and mobility, and decreased intensity of pain and effusion[129, 130].

Benincasa hispida

The preliminary investigations of aqueous extract of *Benincasa hispida* showed that it exhibited anti-inflammatory properties. Petroleum ether and methanolic extract of *Benincasa hispida* fruit, at the dose of 300 mg/kg bw, produced dose dependent and significant inhibition of carrageenan- induced paw edema, histamine induced paw edema and cotton pellet induced granuloma in rat model. In carrageenan- induced paw edema model, petroleum ether and methanolic extracts showed maximum inhibition in inflammation (0.270 ± 0.063 and 0.307 ± 0.043 respectively) as compared to control group (1.27 ± 0.059) and standard valdecoxib (0.247 ± 0.033). In histamine-induced paw edema, both extracts showed (62.86% and 54.84% respectively) inhibition as compared to control. The effects were comparable with that of standard drug cetrizine (95.24%). Petroleum ether and methanolic extracts showed slight insignificant reduction in granuloma tissue formation in cotton pellet implanted rats[131]. The mechanism of anti-vascular inflammatory activity of an aqueous extract of *B. hispida* (ABH) in human umbilical vein endothelial cells (HUVECs) was investigated. ABH inhibited high glucose-induced cell adhesion molecules (CAMs) surface and protein expression, resulting in reduced adhesion of U937 monocytes. ABH also inhibited the mRNA expression level of monocyte chemoattractant protein-1 (MCP-1) and interleukin-8 (IL-8). High glucose-induced ROS production was also inhibited by ABH. Pretreatment of HUVECs with ABH blocks NF-κB activation via blocking phosphorylation and degradation of its inhibitory protein, IκB-α . ABH also reduced NF-kB promoter activity[132].The methanolic extract of *Benincasa hispida* at doses of 250 and 500 mg/kg bw, significantly (P<0.05) increased the antinociceptive effective (as determined by analgesiometer which exerts force at a constantly-increasing rate on the rat paw) in a dose dependent manner in rats. Similarly, at doses of 250 and 500 mg/kg bw, the extract significantly (P<0.05) decreased the Brewer'syeast induced pyrexia in rats [133].

Betula alba

Betulinic acid was found a moderate inhibitors of COX-1, COX-2 and Leukotriens formation *in vitro* with IC_{50} values of >125, >125 and 102.2 µM, respectively [134].It also produced anti-inflammatory activity in the carrageenan and serotonin paw edema and TPA and EPP ear edema[135]. It was also produced an *in vivo* anti-inflammatory effect on TPA-induced model of inflammation in mice.Betulinic acid showed pronounced antinociceptive properties in the writhing test and formalin test in mice [136].

Bidens tripartita

The anti-inflammatory potential of three doses of an aqueous infusion of aerial parts *Bidens tripartita* L. was investigated against carrageenan-induced acute paw edema in rats. Infusion doses of 20ml/k bw exhibited significant anti-inflammatory activity in rats, as compared with indomethacin. In addition, the infusion showed analgesic properties in a hot-plate test and antipyretic properties in carrageenan-induced local hyperthermia in rats. The effects were dose-dependent [137].

Brassica nigra

The effect of *Brassica nigra* seed extracts on arthritic rats were assessed by the various models. In arthritic rats, inflammation reached maximum on day 3 and maintained till day 9. Paw maintained its inflammation till day 14. A significant reduction was recorded in the extracts treated group. Ankle diameter reached maximum on day 7 and maintained its inflammation till day 14. A non-significant reduction was observed in the extracts treated

group [138]. *In vivo* and *in vitro* anti-inflammatory activity of the crude extract was evaluated using carrageenan induced rat paw edema and protease enzyme inhibition assay. *In vivo* anti-inflammatory test of the ethanolic extract of *Brassica nigra* (500 mg/kg) gave 17.9% inhibition whereas standard phenylbutazone (100mg/kg) gave 39.38%. *In vitro* anti-inflammatory test of *Brassica nigra* by protease inhibition method also gave 42.57% inhibition of trypsin at dose 250 µg/ml[139].Volatile oil of mustard is an extremely diffusible and penetrating irritant, quickly exciting heat and burning pain through its dilating action upon the peripheral vessels and irritation of the sensory nerve endings. If too long applied it will blister, and cause inflammation, sloughing and deep ulceration; and not infrequently gangrene. To a degree local anesthesia is produced in some instances and the patient is then not aware of the possible destruction of tissue. When the treatment removed in time only induration is caused, followed sometimes by desquamation. Mustard applied in the same manner acts similarly but more slowly and with gradually increased intensity [140].

Brassica rapa

Arvelexin also inhibited LPS-induced NO and prostaglandin E2 production through the suppression of iNOS and COX-2 at the level of gene transcription. In addition, arvelexin inhibited NF- κB dependent inflammatory responses by modulating a series of intracellular events of IκB kinase (IKK)-inhibitor κBα (IkBα)- NF- κB signaling. Moreover, arvelexin inhibited IKKβ -elicited NF- κB activation as well as iNOS and COX-2 expression. Serum levels of NO and inflammatory cytokines and mortality in mice challenged injected with LPS were significantly reduced by arvelexin[141].

Bryonia dioica

Bryonia dioica revealed interesting anti-inflammatory and antioxidant properties. Its anti-inflammatory effects provide the scientific evidence for its folk uses as anti-inflammatory[142]. The triterpene-glycosides, bryonioside B, C, E and G, cabenoside D and bryoamaride inhibited TPA-induced mouse ear oedema. The antiphlogistic activity of these triterpene glycosides (ID50 = 0.2–0.7 mg/ear) was stronger than the reference quercetin (ID50 = 1.6 mg/ear) and comparable to indomethacin (ID50 = 0.3 mg/ear [143].Triterpene glycosides were evaluated for their inhibitory effects on 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation (1 µg/ear) in mice and on Epstein−Barr virus early antigen (EBV-EA) activation induced by TPA. All the tested compounds showed marked anti-inflammatory effects, with 50% inhibitory doses (ID_{50}) of 0.2−0.6 mg/ ear. In addition, all of the tested compounds ,except one, showed potent inhibitory effects on EBV-EA induction (100% inhibition at 1×10^3 mol ratio/TPA) [144].

Bryophyllum calycinum

The plant extract significantly inhibited fresh egg albumin-induced acute inflammation and significantly exhibited antinociceptive effectsagainst thermally- and chemically-induced nociceptive pain stimuli in mice[(145)]. Stigmast-4, 20 (21), 23-trien-3-one, a steroidal derivative obtained from the leaves extract of the plant , also possessed anti-inflammatory effects [146].

The aqueous extract of *Bryophyllum calycinum* leaves were showed antinociceptive, anti-inflammatory and antidiabetic activity. The antinociceptive effect was evaluated by the hot-plate and acetic acid test models of pain in mice. The anti-inflammatory and antidiabetic effects were investigated in rats, using fresh egg albumin-induced pedal (paw) odema, and streptozotocin -induced diabetes mellitus [145].

Caesalpinia crista

The anti-inflammatory effects of the ethanolic seed extract of *Caesalpinia crista* was investigated by carrageenan induced paw edema and the analgesic activity by writhing reflexes and tail immersion method in mice. The extract showed maximum inhibition of 74.2% at 300 mg kg-1 by carrageenan induced paw edema method as compared to standard, diclofenac. Furthermore, the extract also showed potent analgesic activity 71% at 300 µg/ml by writhing reflexes in mice, and the tail withdrawal latency of mice was 5.30±0.05 sec at 300 µg/ml by tail immersion method. The anti-inflammatory activity was also studied in rats using the formalin arthritis and granuloma pouch methods. At a dose of 250 mg/kg, the extract was found to be effective in the granuloma pouch model. The seeds showed a 50% inhibitory activity against carrageenan-induced oedema in the rat hind paw, at an oral dose of 1000 mg/kg when given 24 hours and 1 hour prior to carrageenan injection. On the other hand, *Caesalpinia crista* seed coat extracted by 95% ethanol was screened for anti-inflammatory and analgesic activity using carrageenan-induced paw edema, egg albumin-induced paw edema, Eddy's hot plate test and tail immersion method. It appeared that seed coat extract has the ability to decrease the induced inflammation at varied doses in carrageenan and egg albumin model in rats. The antinociceptive results indicate that the extract has the ability to increase the pain threshold of the animals, reduce the pain factor and induce analgesia [(147-149)].The antipyretic activity of ethanolic and aqueous extracts of seeds of *Caesalpinia crista* was evaluated in various experimental animal models including using Brewer's yeast induced pyrexia in rats, TAB-vaccine induced pyrexia in rabbits and boiled milk induced pyrexia in rabbits models.Ethanolic and aqueous seed extracts of *Caesalpinia crista* showed antipyretic activity, the antipyretic activity of the ethanolic extract of *Caesalpinia crista* was nearly equal to that of the standard drug, paracetamol[150].The analgesic and antipyretic activity of *Caesalpinia*

crista seed oil on acute and chronic inflammation was determined in experimental animal model. Doses of 100, 200 and 400 mg/kg of the seed oil of *Caesalpinia crista* were given orally in carrageenan induced rat paw oedema, brewer's yeast-induced pyrexia, acetic acid-induced writhing and hot plate reaction time in experimental rats. The paw volumes, pyrexia and writhes were reduced significantly ($p < 0.05$) in *Caesalpinia crista* treated rats as compared to that of control [151].

Calendula officinalis

Calendula officinalis flower extract possessed significant anti-inflammatory activity against carrageenan and dextran-induced acute paw edema. Oral administration of 250 and 500 mg/kg body weight Calendula extract produced significant inhibition (50.6 and 65.9% respectively) in paw edema of animals induced by carrageenan and 41.9 and 42.4% respectively with inflammation produced by dextran. Administration of 250 and 500 mg/kg body weight Calendula extract produced an inhibition of 32.9 and 62.3% compared to controls, respectively in chronic anti-inflammatory model using formalin. TNF-alpha production by macrophage culture treated with lipopolysaccharide (LPS) was found to be significantly inhibited by Calendula extract. Moreover, increased levels of proinflammatory cytokines IL- 1beta, IL-6, TNF-alpha and IFN-gamma and acute phase protein, C- reactive protein (CRP) in mice produced by LPS injection were inhibited significantly by the extract. LPS induced cyclooxygenase-2 (Cox-2) levels in mice spleen were also found to be inhibited by the extract treatment [(152)]. The hydroalcoholic plant extracts of *Calendula officinalis* suppressed the cell-free systems activities of 5-lipoxygenase (5-LO) and cyclooxygenase-2 (COX-2), the key enzymes in the formation of proinflammatory eicosanoids from arachidonic acid [153].

The inhibitory activity of nine oleanane-type triterpene glycosides isolated from Calendula officinalis was studied against 12-O-tetradecanoylphorbol-13-acetate (TPA) -induced inflammation (1 microg/ear) in mice, all of the compounds, except 1, exhibited marked anti-inflammatory activity, with ID_{50} values of 0.05-0.20 mg per ear [154]. The anti-inflammatory activity of the 3 main triterpendiol esters of marigold was tested against croton oil-induced edema of the ears in mice. Faradiol-3-myristic acid ester and faradiol-3-palmitic acid ester were found to have the same dose-dependent anti-inflammatory activity. The non-esterified faradiol was more active than the esters and had an equivalent effect on inflammation as an equimolar dose of indomethacin [155]. A dose of 1200 µg/ear of an aqueous-ethanol extract showed 20% inhibition in croton oil-induced mouse oedema. The activity was attributed to the presence of triterpenoids, the three most active compounds were the esters of faradiol-3-myristic acid, faradiol-3-palmitic acid and 4-taraxasterol [156, 157].The analgesic effects of *Calendula officinalis* was evaluated in thermal pain threshold in male rats. *Calendula officinalis* extract significantly increased the tail flick latency compared to the control group ($P<0.05$), indicating that the extract reduced pain threshold [158].

Calotropis procera

The anti-inflammatory effect of the chloroform (CH) and hydroalcoholic extract (HE) of the stem bark of *Calotropis procera* against carrageenan-induced paw oedema has been studied by using two acute models, aspirin (100 mg/kg, po) and ethanol (96%) in albino rats. CH and HE extracts showed significant anti-inflammatory activity at 200 and 400 mg/kg. As part of investigations to obtain compounds with anti-inflammatory effects, a bioassay was carried out with fractions obtained from the CH extract with n-hexane (NF1), 1-butanol (BF1), ethyl acetate (EF1) and chloroform (CF1). The HE extract of the stem bark was fractionated with n-hexane (NF2), 1-butanol (BF2), ethyl acetate (EF2), chloroform (CF2) and water (WF2). The fractions were evaluated for their anti-inflammatory effects. Fractions NF1, CF1, BF2 and EF2 (20 mg/kg) showed significant anti-inflammatory activity [159]. The latex of *Calotropis procera*, ethanol extract of its flowers and the chloroform soluble fraction of its roots possessed significant anti-inflammatory activity [160]. The methanolic extract of plant *Calotropis procera* roots has been reported to exhibit potent anti-inflammatory activity against carrageenan induced paw oedema and cotton pellet induced granuloma in albino Wistar rats. The different extracts of the roots of *C. procera* and standard anti-inflammatory drugs were administered orally 1 hour before inducing of inflammation. The methanolic extracts (180mg/kg, po) of roots of *C. Procera* has potential to inhibit sub-acute inflammation by interruption of the arachidonic acid metabolism in both paw oedema as well as cotton pellet model and showed inhibition of inflammation ($p<0.01$ and $p<0.001$) very close to the inhibitory effect of diclofenac sodium (25 mg/kg, ip) [161]. The ethanolic extract of root bark of *Calotropis procera* was investigated for its anti-inflammatory activity at different dose in the different animal models. The experimental paradigms used were complete Freunds adjuvant (CFA) induced arthritis (chronic inflammation), acetic acid induced vascular permeability model in mice for anti-inflammatory activity. The extract of *Calotropis procera* (CPE) exhibited significant anti-inflammatory effect at the dose 100 and 200 mg/kg. The extract showed 21.6 and 71.6% inhibition against CFA induced arthritis at the dose of 100 and 200 mg/kg after drug treatment, as compared to standard drug dexamethasone which produced 99% inhibition. The extract also exhibited significant inhibition in polyarthritic index in rats caused by CFA induced arthritic inflammation. In the acetic acid induced vascular permeability the CPE (100 and 200 mg/kg), significantly reduced dye leaking by 45.4% and 61.5% ($p<0.001$) respectiviley as compared to standard drug

dexamethasone and ibuprofen 23.7% and 67.4% respectively [162].Laticifer proteins (LP) of *Calotropis procera* were fractionated by ion-exchange chromatography, and the influence of a sub-fraction LP(PI)) on the inflammatory response of Swiss mice challenged by *Salmonella enterica Ser. Typhimurium* was investigated. The survival rate reached 100 % in mice treated with LP(PI) (30 or 60 mg/kg as a single inoculum by the intraperitoneal route 24 h before infection), whereas, the phosphate-buffered saline treated group died 1-3 days after infection. The neutrophil infiltration into the peritoneal cavity of pretreated mice was enhanced and accompanied by high bacterial clearance from the bloodstream. Tumor necrosis factor-alpha mRNA transcripts, but not interferon-gamma, were detected early in spleen cells of pretreated mice after infection; however, the nitric oxide contents in the bloodstream were decreased in comparison to the phosphate-buffered saline treated group [163]. The protective effect of latex of *Calotropis procera* in complete Freund's adjuvant (FCA) induced monoarticular arthritis was evaluated in rats. Arthritis was induced by a single intra-articular injection of 0.1 ml of 0.1% FCA in the right ankle joint. The effect of dried latex (DL, 200 and 400 mg/kg) and its methanol extract (MeDL, 50 and 500 mg/kg) following oral administration was evaluated on joint inflammation, hyperalgesia, locomotor function and histology at the time of peak inflammation. The effects of DL and MeDL were compared with antiinflammatory drugs phenylbutazone (100 mg/kg), prednisolone (20 mg/kg), rofecoxib (20 and 100 mg/kg) and immuno-suppressant methotrexate (0.3 mg/kg). Daily oral administration of DL and its methanol extract (MeDL) produced a significant reduction in joint inflammation (about 50% and 80% inhibition) and associated hyperalgesia. The antihyperalgesic effect of MeDL was comparable to that of rofecoxib. Both DL and MeDL produced a marked improvement in the motility and stair climbing ability of the rats. The histological analysis of the arthritic joint also revealed significant reduction in oedema and cellular infiltration by MeDL that was comparable to that of rofecoxib [164]. Oral mucositis is an important dose-limiting side effect of cancer chemotherapy. Soluble proteins of the latex of *Calotropis procera*, phytomodulatory laticifer proteins (LP) were challenged to regress the inflammatory events associated with 5-fluorouracil-induced oral mucositis. Oral mucositis was induced in hamsters by two injections of 5-fluorouracil (5-FU; 60 and 40 mg/kg, ip, on experimental days 1 and 2, respectively). LP (5 mg/kg, ip) was injected 24 h before and 24 h after mechanical trauma of the cheek pouches. The expression of pro-inflammatory cytokines and inducible enzymes, such as cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) were studied. On day 10, the cheek pouches were excised for macroscopic and histopathological analysis and immunohistochemical assessment of tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), iNOS, and COX-2. Proteins of the latex of *Calotropis procera* were significantly inhibited macroscopic histopathological scores and myeloperoxidase activity compared with the 5-FU control group. 5-Fluorouracil also induced marked immunostaining of TNF-α, IL-1β, iNOS, and COX-2 on inflamed conjunctive and epithelial tissue compared with the normal control group. Such damage was also significantly inhibited ($p < 0.05$) by LP treatment compared with the 5-FU group [165]. The non-dialysable protein fraction isolated from the latex (LP) of *Calotropis procera* was evaluated for its efficacy against inflammation in rats where paw edema was induced by sub-plantar injection of carrageenin and monoarthritis was induced by intra-articular injection of Freund's complete adjuvant (FCA). The effect of LP was evaluated on edema volume in the paw model and on joint diameter, stair climbing ability, motility, dorsal flexion pain, levels of oxidative stress markers and joint histology in arthritis model. The protection afforded by LP was compared with that of standard antiinflammatory drug, diclofenac (5 mg/kg). LP exhibited a dose-dependent antiinflammatory effect and produced 32% and 60% inhibition of paw edema at 10 and 25 mg/kg doses and 12% and 36% inhibition of joint inflammation at 50 and 150 mg/kg doses. The protective effect of LP was associated with normalization of joint functions, histology and levels of oxidative stress markers in joint tissue [166]. The effect of non-dialyzable protein (LP) sub-fractions on neutrophil functions and nociception in rodent models (the rat peritonitis model and on nociception in the mouse model) was investigated. LP sub-fractions exhibit distinct protein profile and produce a significant decrease in the carrageenan and DF induced neutrophil influx and exhibit anti-nociceptive property. The LP and its sub-fractions produced a marked reduction in the number of rolling and adherent leukocytes in the mesenteric microvasculature as revealed by intravital microscopy. The anti-inflammatory effect of LP(PI), the most potent anti-inflammatory fraction of LP, was accompanied by an increase in the serum levels of NO [167]. The latex protein fraction administered intraperitoneally to male mice at doses of 12.5, 25 and 50 mg/kg showed a dose-dependent antinociceptive effect compared with the controls. Inhibition of the acetic acid induced abdominal constrictions was observed at doses of 12.5 mg/kg (67.9 %), 25 mg/kg (85 %) and 50 mg/kg (99.5 %) compared with controls. Latex protein at doses of 25 mg/kg (39.8 %; 42 %) and 50 mg/kg (66.6 %; 99.3 %) reduced the nociception produced by formalin in the 1st and 2nd phases, respectively, and this effect was not reversed by pretreatment with naloxone (1 mg/kg). In the hot plate test, an increase in the reaction time was observed only at 60 min after treatment with latex at doses of 25 mg/kg (79.5 %) and 50 mg/kg (76.9 %), compared with controls. Naloxone was unable to reverse this effect. The antinociceptive effects of protein fraction of the latex of

Calotropis procera didn't depend of the opioid system [168]. A single oral dose of dry latex ranging (165 to 830 mg/kg bw) produced significant dose-dependent analgesic effect against acetic acid-induced writhing. The effect of a dose of 415 mg/kg was more pronounced than a 100 mg/kg oral dose of aspirin. Dry latex (830 mg/kg) produces marginal analgesia in a tail-flick model which was similar to that of aspirin [169]. The ethanol extract of *C. procera* produced significant reduction of yeast induced increase in body temperature. There was a significant increase in reaction time of the treated mice placed on hot plate confirming analgesic activity of the extract [170]. The ethanolic extract of the aerial parts also possessed antipyretic effect. Administration of yeast produced an increase in rectal temperature from 97.32 ± 0.19oF which reached to its maximum in 4 h (100.02 ± 0.27^{o}F). Administration of dry latex (DL)-250 mg/kg and 500 mg/kg at 4 h produced a significant (P <0.05) decline in rectal temperature to 98.50 ± 0.29^{o}F and 98.45 ± 0.60^{o}F respectively. The antipyretic effect was compared with that of aspirin, which was found to be more potent and brought down the temperature to 96.9 ±0.38 ^{o}F (P <0.001) [160].

Canna indica

The effect of benzene and methanolextracts of various parts of C. indica on nociceptive response using writhing test and hot plate method in mice was examined. All the extracts of C. indica showed significant central and peripheral analgesic activity in hot plate method and acetic acid-induced writhing test, respectively, at the dose of 50 mg kg(-1) intraperitoneally. Methanolic extract of leaves of C. indica showed highest increase in reaction time in hot plate method while benzene extract of leaves of C. indica showed more inhibitory effect on writhing induced by acetic acid [171].

Capparis spinosa

The anti-inflammatory effects of the flavonoids from caper fruits were evaluated by secreted placental alkaline phosphatase (SEAP) reporter assay, which was designed to measure nuclear factor-kappa B (NF-κB) activation. Isoginkgetin and ginkgetin showed inhibitory effects in initial screen at 20 μM, while the effect of ginkgetin was much greater than that of isoginkgetin. In a dose-response experiment, the IC_{50} value of ginkgetin was estimated at 7.5 μM, suggesting it could be a strong NF-κB inhibitor [172].The anti-inflammatory activities of *C. spinosa* L. fruit (CSF) aqueous extract was studied mice. The CSF aqueous extract were separated into three fractions (CSF1-CSF3) by macroporous adsorption resins. The fractions CSF2 and CSF3 effectively inhibited the carrageenan-induced paw edema in mice [173]. The extracts of *C. spinosa* were found to possess marked anti-inflammatory activity but devoid of analgesic activity in animal models, cappaprenol-13 isolated from *C. spinosa* showed significant anti-inflammatory activity[174]. The anti- arthritic active fractions of *Capparis spinosa* fruits was evaluated by adjuvant arthritic rat model..The fraction eluted by ethanol-water (50:50v/v) had the most significant anti- arthritic activity. The chemical constituents of this fraction showed that it contained seven known compounds: P-hydroxybenzoicacid, 5-(hydroxymethyl)furfura,l bis(5-for- mylfurfuryl) ether, daucosterol, α-D-fructo furanosidesmethyl, uracil, and stachydrine.Ethanol and ethanol-water extracts of *Capparis spinosa* fruits showed anti-arthritic effects due to the presence of an important chemical constituents such as P-hydroxy benzoic acid, 5-(hydroxymethyl) furfural, bis (5-formylfurfuryl) ether, daucosterol, α-D-fructofuranosides methyl, uracil and stachydrine [175, 176]. Plant extracts extracted with solvents of varying polarity were effective either in inhibiting the activity of xanthine oxidase or Cyt C. The IC_{50} ranges from 0.0226 ± 0.00019 to 4.32 ± 0.15g/l [177].

Capsella bursa-pastoris

The plant induced anti-inflammatory activity in carrageenan-induced and dextran-induced rat paw oedema. It also reduced capillary permeability in guinea-pig induced by histamine and serotonin. It also possessed anti-ulcer activity in rats following intraperitoneal injection. The extract did not affect gastric secretion, but accelerated recovery from stress-induced ulcers [178, 179]. The anti-inflammatory and antibacterial properties of a sulforaphane-containing solution (SCS) isolated from shepherd's purse (*Capsella bursa-pastoris*). SCS had significant anti-inflammatory activity indicated by the decreased levels of nitric oxide (NO), cytokines (interleukin 1β [IL-1β], IL-6, and IL-10), and prostaglandin E2 (PGE2) in lipopolysaccharide-stimulated RAW 264.7 murine macrophages. SCS also decreased the inducible NO synthase (iNOS) and cyclooxygenase 2 (COX-2) levels, which confirmed the anti-inflammatory activity of SCS [180].

Capsicum annuum* and *Capsicum frutescens

Capsaicin reacts to transient receptor potential vanilloid 1 (TRPV1), previously known as the vanilloid receptor, which is mainly expressed in the sensory neurons. TRPV1 contained 838 amino acids and has a molecular weight of 95 kDa in both humans and rats, consisting of six transmembrane domains with a short pore-forming region between the fifth and sixth transmembrane domains. It was non-selective, ligand-operated cationic channel located primarily in the small fibers of nociceptive neurons. TRPV1 was also distributed in tissues of the brain, bladder, kidneys, intestines, liver, polymorphonuclear granulocytes, mast cells, keratinocytes, glial cells, and macrophages. It couples with a non-specific cation channel permeable to sodium and calcium ions, and is located in the plasma membrane and the endoplasmic reticulum where regulates intracellular calcium levels. Binding of

capsaicin with TRPV1 increases intracellular calcium, triggering release of substance P and the calcium gene-related peptide (CGRP). Contact between capsaicin and sensory neurons produces pain, inflammation and a localized heat sensation. When applied locally to skin, it promotes an analgesic response due to desensitizing of the sensory neurons caused by substance P depletion [181-186]. Capsaicin and its analogues were used topically to treat chronic pain syndromes musculoskeletal pain, osteoarthritis, rheumatoid arthritis, post-herpetic neuralgia and diabetic neuropathy [187, 188]. Topical application of capsaicin evokes burning pain, neurogenic inflammation (vasodilatation and plasma extravasation), and hyperalgesia to heat and mechanical stimuli [189-191]. The treated area becomes less sensitive to pain, after repeated applications, this effect made capsaicin a peripherally acting analgesic in chronic painful complains [192, 193]. The sensory dysfunction after capsaicin application to the skin resulted from rapid degeneration of intracutaneous nerve fibers.The effect of intradermal injection of capsaicin on morphological changes in cutaneous nerve fibers that would account for its analgesic properties was studied by comparing cutaneous innervation in capsaicin-treated skin with psychophysical measures of sensation. At various times after capsaicin injection, nerve fibers were visualized immunohistochemically in skin biopsies and were quantified. In normal skin the epidermis is heavily innervated by nerve fibers immunoreactive for protein gene product (PGP) 9.5, whereas fibers immunoreactive for substance P (SP) and calcitonin gene-related peptide (CGRP) are typically associated with blood vessels. There was nearly complete degeneration of epidermal nerve fibers and the subepidermal neural plexus in capsaicin-treated skin, as indicated by the loss of immunoreactivity for PGP 9.5 and CGRP. The effect of capsaicin on dermal nerve fibers immunoreactive for SP was less obvious. Capsaicin decreased sensitivity to pain produced by sharp mechanical stimuli and nearly eliminated heat-evoked pain within the injected area. Limited reinnervation of the epidermis and partial return of sensation occurred 3 weeks after treatment; reinnervation of the epidermis was; 25% of normal, and sensation improved to 50–75% of normal [193]. Topical preparations of capsaicinoids are widely used for musculoskeletal disorders as a complementary therapy. The potential effects of both topical capsaicinoids-containing patch and local subcutaneous capsaicin application on the anti-inflammatory action of NSAID were examined. Carrageenan-induced paw oedema of rats was used as the inflammation model. Topical capsaicinoids-containing patch application or local capsaicin injection (2, 10, 20 μg/paw) alone did not cause any effect on oedema volume and weight. However, the combination of diclofenac with topical capsaicinoids-containing patch significantly increased the effectiveness of diclofenac on inflammation. Evans blue content of the paws that represents plasma extravasation was decreased by capsaicinoids-containing patch with and without diclofenac [194].The anti-inflammatory activity of *Capsicum annuum* was assessed by inhibiting Soyal lipoxygenase (LOX) enzyme. The results showed higher % of LOX inhibition by green capsicum (46.12 %) followed by yellow (44.09 %) and red capsicum (32.18 %) [195]. Carotenoids extracted from dried *Capsicum annuum* were evaluated for their analgesic activities. Carotenoids extracts exhibited significant peripheral analgesic activity at 5, 20, and 80 mg/kg and induced central analgesia at 80 mg/kg. The guajillo pepper carotenoids extract was also exerted anti-inflammatory activity, they significantly inhibited oedema formation and progression at a dose of 5 mg/kg compared to the control treatment at 1, 3, and 5 hours after carrageenan injection ($p<0.05$). A similar response was obtained with indomethacin compared to the control treatment. Interestingly, at higher doses (20 and 80 mg/kg), the guajillo pepper extract significantly reduced oedema generated by the carrageenan at the 5 h time point ($p<0.05$) [196]. The anti-inflammatory effects of ethyl acetate extract of *Capsicum frutescens* (CFE) was examined on rat hind paw inflammation induced by subplantar injections of fresh egg albumin (0.5 ml/kg).Ethyl acetate extract of *Capsicum frutescens*produced anti-inflammatory effects that were comparable to diclofenac [197].

Carthamus tinctorius

Intragastric administration of 30 mg/kg bw of a 50% methanol extract of the flowers inhibited inflammation as measured by footpad oedema induced by carrageenan, serotonin, bradykinin, histamine or prostaglandin in mice. Intragastric administration of 30 g/kg bw of a 50% methanol extract of the flowers to mice also reduced writhing induced by acetic acid [124]. Subcutaneous administration of 10 g/kg bw of an aqueous or 50% methanol extract of the flowers inhibited carrageenan-induced footpad oedema in mice. Subcutaneous administration of 10.0 g/kg bw of an aqueous extract of the flowers to mice did not reduce pain perception as measured in the hot-plate test. Subcutaneous administration of 1.0–3.0 g/kg bw of a 50% methanol extract of the flowers to mice reduced writhing induced by acetic acid[198]. The effects of Hydroxysafflor yellow A (HSYA) on lipopolysaccharide (LPS)-induced inflammatory signal transduction in human alveolar epithelial A549 cells was studied. A549 cells stimulated with LPS were incubated with three doses of HSYA (1, 4 and 16μmol/l). HSYA suppressed the expression of TLR-4, Myd88, ICAM-1, TNFα, IL-1β and IL-6 at the mRNA and protein level, and inhibited the adhesion of leukocytes to A549 cells. HSYA treatment also decreased NF-κB p65 nuclear translocation and inhibited the phosphorylation of p38 mitogen-activated protein kinase (p38 MAPK) [199]. The effects of dried safflower petals aqueous extracts (SFA) and Carthamus yellow (CY) were investigated on

lipopolysaccharide (LPS)-induced inflammation using RAW264.7 macrophages. Treatment with SFA (1-1000 microg/ml and CY (1-2000 microg/ml does not cause cytotoxicity. SFA and CY inhibited LPS-stimulated nitric oxide (NO), prostaglandin E_2 (PGE_2), and interleukin 1β (IL-1β) release, through attenuation of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) protein expression. Furthermore, SFA and CY suppressed the LPS-induced phosphorylation of nuclear factor-κB, which was associated with the inhibition of IκB-α degradation[200]. N-(p-Coumaroyl)serotonin (CS) inhibited proinflammatory cytokine generation from human monocytes *in vitro*. CS augmented the proliferation of normal human and mouse fibroblast cells. The cells continued to proliferate in the presence of CS and form a transformed cell-like focus without transformation. CS, however, does not augment the proliferation of other cell types, either normal or tumor cells. CS augmented the proliferation of fibroblasts in synergy with basic fibroblast growth factor (bFGF) or epidermal growth factor (EGF), but not with acidic FGF(aFGF) or platelet-derived growth factor (PDGF)[201]. The inhibitory effect of HSYA was studied on the inflammatory signal transduction pathway related factors which were induced by permanent cerebral ischemia in rats. The result showed that intravenous injection of HSYA (10 mg/kg) to rats after cerebral occlusion, the p65 translocation activity and the phosphorylation of IkappaB-alpha were significantly inhibited. At the same time, HSYA suppressed p65 binding activity and the transcriptional level of pro-inflammatory cytokines including TNF-alpha, IL-1beta and IL-6, and promoted the mRNA expression of anti-inflammatory cytokine IL-10. The authors suggested that the anti-cerebral ischemic mechanism of HSYA may be due to its inhibition of NF-kappaB activity and the mRNA expression of cytokines in the inflammatory transduction pathway [202]. Alkane diols inhibited the inflammation induced by 12-0-Tetradecanoylphorbol-13-acetate (TPA, 1 microgram/ mice ear). The 50% inhibitory dose of these compounds for TPA-induced inflammation was 0.5-0.7 mg/ear [175]. A new bioactive triterpenoid saponin 3beta-O-[beta-D-xylopyranosyl(1→3)-O-beta-D-galactopyranosyl]-lup-12-ene-28oic acid-28-O-alpha-L-rhamnopyranosyl ester, isolated from the methanolic fraction of the roots of *Carthamus tinctorius*, showed anti-inflammatory activity [203]. All the polyacetylene glucosides compounds isolated from the florets of *Carthamus tinctorius* (11 compounds) were also tested for antinflammatory and inhibitory activities against LPS-induced NO production in murine macrophages, they showed weak activities at concentrations of 1×10^{-5}M[204]. The mechanism of anti-inflammatory effect of the methanol extracts of *Carthamus tinctorius* (MEC) was investigated. The results showed that the expression of HO-1 protein by MEC in macrophages was increased in a concentration- and time dependent manner. Treatment with MEC significantly inhibited upregulation of both iNOS and COX-2 in LPS-activated macrophages and consequently reduced production of NO and PGE2. The reduced expression of iNOS and COX-2 by MEC was reversed by siHO-1 RNA transfection. In addition, NF-E2-related factor (Nrf2) was translocated from cytosol to nucleus by MEC. The binding of NF-$_k$B as well as NF-$_k$B luciferase activity was also significantly diminished by MEC. Tumor necrosis factor (TNF)-α-mediated VCAM-1 expression in endothelial cell was significantly inhibited by MEC[205].

Intragastric administration of 500 mg/kg body weight (bw) of a 95% ethanol extract of Flos Carthami reduced the responsiveness of mice as measured in the hot-plate test, indicating an analgesic effect, and also decreased yeast-induced fevers [206]. The effects of safflower yellow (SY) on pathologic changes in tendon, expression of basic fibroblast growth factor (bFGF) and collagen type I, and on the process of tendon injury-repair were investigated. The adhesion to surrounding tissues and tensile strength gradually increased after the injury and repair in control (no-SY) tendons, and were significantly greater by the sixth weeks than any other time. In the SY tendons, adhesion was significantly lower, and tensile strength significantly higher than in (no-SY) tendons at the same post-injury-suture time points. An inflammatory reaction was observed in the injury-repair areas of the tendon by the end of first week post-injury-suture, and reached its peak by the end of second week. The inflammatory reaction was significantly less in SY tendons than in controls. Immunostaining for bFGF in the tendon injury-repair areas by the end of first week, and the number of bFGF positive cells reached a peak by the end of second week, with a greater abundance in SY than control tendons from the second to sixth week. Expression of collagen type I protein was observed in the injury-repair areas as well, coincident with bFGF, and was remarkably higher in SY than in controls. The results indicated that SY promoted the repair of injured tendon by up-regulating expression of bFGF and collagen type I protein [207]. Safflower seed has been reported to have a protective effect against bone loss diseases. However, the precise molecular mechanisms underlying the inhibitory effect of safflower seed in osteoclast differentiation remain unclear. The probable inhibitory action of safflower seed extract (SSE) on the receptor activator of nuclear factor κB ligand (RANKL)-induced osteoclastogenesis in cultured mouse-derived bone marrow macrophages (BMMs) was investigated. SSE significantly inhibited the formation of tartrate-resistant acid phosphatase (TRAP)-positive multinucleated cells in BMMs without cytotoxicity. The gene expressions of nuclear factor of activated T-cells (NFATc1) and TRAP, which are genetic markers of osteoclast differentiation, were substantially decreased by SSE in a dose-dependent manner. Also, SSE diminished RANKL-mediated intracellular reactive oxygen species (ROS) generation on

osteoclastogenesis in a dose-dependent manner. The SSE, thereafter suppressed RANKL-induced p38 mitogen-activated protein kinase and IκBα kinase signalling activities which were activated by ROS generation for osteoclastogenesis. Additionally, SSE was found to decrease RANKL-induced actin ring formation, which is required for bone resorption activity[208]. Anti-bone resorption properties of the Korean herbal formulation, Honghwain (HHI; *Carthamus tinctorius* L. seed) was biochemically investigated. HHI inhibited *in vitro* and *in vivo* bone resorption by inhibition of phosphorylation of peptide substrates. HHI dose-dependently reduced the hypercalcemia induced in mice by IL-1b and partly prevented bone loss and microarchitectural changes in young ovariectomized rats, the protective effect on bone was exerted via the inhibition of bone resorption. The results indicated that the synergy between IL-b, TNF-a, IL-6 on PGE2 production is due to an enhanced gene expression of COX-2 and that tyrosine kinase(s) are involved in the signal transduction of COX-2 in mouse calvarial steoblasts [209]. The production of PGE2 is inhibited by 20-100 microg/ml HHI in nontransformed osteoblastic cells (MC3T3-E1 cells), indicating that HHI inhibited PGE2 production. The effect of HHI on the proliferation and osteoblastic differentiation in MC3T3-E1 was also studied. HHI dose-dependently increased DNA synthesis (significant at 20-100 microg/ml), and increased alkaline phosphatase (ALP) and prolyl hydroxylase activities of MC3T3-E1 cells (20-100 microg/ml), while anti-estrogen tamoxifen eliminated the stimulation of proliferation and ALP activity of MC3T3-E1 which was induced by HHI. The results indicated that HHI directly stimulates cell proliferation and differentiation of osteoblasts. Also, when the effects of HHI was examined on osteoblastic differentiation in MC3T3-E1, HHI enhanced ALP activity and mineralization in a dose- and time-dependent fashion. This stimulatory effect of the HHI was observed at relatively low doses (significant at 20-100 microg/ml and maximal at 100 microg/ml). Northern blot analysis showed that the HHI (60 microg/ml) increased bone morphogenetic protein-2 as well as ALP mRNA concentrations in MC3T3-E1 cells. HHI (100 microg/ml) slightly increased type I collagen mRNA abundance throughout the culture period, whereas it markedly inhibited the gene expression of collagenase-1 between days 15 and 20 of culture. The results also indicated that HHI has anabolic effect on bone through the promotion of osteoblastic differentiation, suggesting that it could be used for the treatment of common metabolic bone diseases [210]. The effects of Safflower (*Carthamus tinctorius*) seed oil (SSO) on osteoporosis induced-ovariectomized rats were investigated. Animals were administered SSO orally (1 ml/kg) daily for 30 days. IGF-I, IGF-II, IGBP-3 and BALP levels were significantly increased ($p<0.05$). The results showed that the safflower seeds have possible roles in the improvement of osteoporosis induced-ovariectomized rats [211]. The bone nodule formation, calcium uptake, alkaline phosphatase activity, and intracellular concentration of calcium ion Ca^{2+} was studied in murine osteoblastic cells of the MC3T3-E1 line, that were cultured on modified Eagle's minimal essential medium alone (controls) or with addition of 0.1% crude extract of safflower seed or 0.1% aqueous fraction of safflower seed. Fluorescence spectrometry measurement of Ca^{2+} showed significantly accelerated rates of osteoblast differentiation with 0.1% crude extract of safflower seed (3 microl of crude extract in 8 x 10^4 cells) and with 0.1% aqueous fraction of safflower seed (2 microl of aqueous fraction in 8 x 10(4) cells) compared to the control group [212].

Carum carvi

The analgesic effect of *Carum carvi* (CC) (100 and 500 mg/kg) was tested in acute and chronic pain in formalin test in mice. The results indicated that CC has analgesic effect in both doses in acute and chronic phases and the higher dose of the drug was more effective ($P<0.01$) [213].

Cassia occidentalis

The anti-inflammatory activity of *Cassia occidentalis* leaf powder was assayed in male albino rats using carrageenan-induced rat paw edema. *C. occidentalis* was maximally active at a dose of 2000 mg/kg. In the cotton pellet granuloma assay, *Cassia occidentalis* leaf powder was able to suppress the transudative, exudative and proliferative components of chronicinflammation.Furthermore,*Cassia occidentalis* leaf powder was able to lower the lipid peroxide content and gamma-glutamyl transpeptidase and phospholipase A2 activity in the exudate of cotton pellet granuloma. The increased alkaline phosphatase activity and decreased A/G ratio of plasma in cotton pellet granulomatous rats were normalized after treatment with *Cassia occidentalis* leaf powder. *C. occidentalis* powder was able to stabilize the human erythrocyte membrane against hypotonicity-induced lysis [214]. The ethanol and water extracts of *Cassia occidentalis* leaves were screened for antinociceptive activity using acetic acid induced writhing test, hot plate test and tail immersion test in mice. The antipyretic potential of the extract was evaluated using yeast induced pyrexia method in rats. The results showed that ethanol and water extracts had significant ($p<0.01$) dose dependent antinociceptive and antipyretic properties at a dose of 150 and 300 mg/kg. The inhibition produced by the highest dose (300 mg/kg) of the extracts was significantly ($P<0.01$) lower than that by acetylsalicylic acid (100 mg/kg). Both the ethanolic and water extracts of *Cassia occidentalis* showed significant ($P< 0.01$) effect on pyrexia induced by yeast [215].

Centaurea cyanus

Centaurea cyanus flower-heads had anti-inflammatory properties as shown by different pharmacological experiments including inhibition of carrageenan, zymosan and croton oil-induced edemas, inhibition of plasma hemolytic activity, and/or induction of anaphylatoxin activity [216]. Moschamine a safflomide-type phenylpropenoic acid amide found in *Centaurea cyanus* was a very potent COX-I inhibitor, it inhibited COX-I by 58% ($p < 0.012$) at the concentration of 0.1 μ mol /l [217].

C*henopodium album*

The topical anti-inflammatory activity for C*henopodium album* oil (5-0.625 mg) was evaluated by inhibition of the 12-O-tetradecanoylphorbol-13-acetate (TPA) induced ear edema in mice. The result revealed that the anti-inflammatory action of the oil is concentration dependent, the percentage reduction in the ear edema increases with increase in concentration of the oil. However, the oil caused significant reduction ($p < 0.05$) in the ear edema with all concentrations except at 0.625 mg [218]. The ethanolic extract from the fruits of *Chenopodium album*, 100-400 mg/kg orally, caused dose-dependently inhibition of scratching behavior induced by 5-HT (10 micro g per mouse, sc) or compound 48/80 (50 micro g per mouse, sc). But it failed to affect hind paw swelling induced by 5-HT or compound 48/80 in mice at doses of 100 and 200 mg/kg and only showed a relatively weak inhibition on the swelling at a higher dose of 400 mg/kg [219]. The role of NF kappa B (NFκB) in the antiarthritic potential of extracts of aerial parts of *Chenopodium album* was explored and evaluated. The result indicated that the acetone extract of *Chenopodium album* (ACCA) has shown significant reduction in rat paw edema (80.13%) at dose level of 200mg/kg orally in 21 days of the experiment. On 22nd day, it was observed that the altered hematological parameters (Hb, RBC, WBC and ESR), biochemical parameters (serum creatinine, total proteins and acute phase proteins) and loss in body weight in the arthritic rats were significantly brought back to near normal level by the ACCA extract. ACCA extract significantly decreased the NFκB expression in paraventricular nucleus of hypothalamus and this effect is comparable with standard indomethacine [220]. Significant analgesic effect was observed for the crude extract at 500 mg/kg dose from 30 min - 210 min using tail flick method in mice [221].

CONCLUSION

The paper reviewed the anti-inflammatory, antipyretic and analgesiceffects of the medicinal plants to open the door for their utilization in medical applications as a result of effectiveness and safety**.**

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