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A Comprehensive Review on Natural Products and Anti-Inflammatory Activity

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Authors' contributions

This work was carried out in collaboration among all authors. Authors FA and RA designed the study, performed the literature search wrote the first draft of the manuscript. Author BKD review and update the manuscript. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Natural plants various metabolites are widely utilized in a different kind of infections and inflammation as traditional medication. The inflammatory response is a reaction always effects in daily life and physical issue and activity of herbal complex act through of blood vessels. Inflammation is a pathologic issue that incorporates a wide scope of sicknesses, for example rheumatic, diabetes, cardiovascular accident and chronic kidney disease. We present a few herbal spices which their metabolites that have been assessed in clinical and test. The review includes number of various herbal plants with their families, parts utilized, k concentrate utilized, bioassay models and their usages in medicinal activities.

Keywords: Anti-inflammatory activity; inducers of inflammation; natural products; medicinal plants; review.

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1. INTRODUCTION

Inflammation has been studied molecular level concentrated trying to manage it without side effect for huge number of years. Inflammation or flogose is a response of the tissue blood vessels against the aggressor agent characterized by access of liquids and of cells to interstice. The inflammatory response is effected by become blush, heat, tumor, pain, and lost cell function. Celsius (in 30 A.D.) described in his study that the four signs of inflammation includes [(rubor, calor, dolor, and tumor or redness), heat, pain and swelling] and he utilized willow leaves as concentrated form to relieve them. Inflammation may occurs as result of contact with infectious microorganisms such as viruses, bacteria or fungi to a specific tissues. [1-3] and this infection progressions lead to a tissue injury, cell death, cancer, ischemia and degeneration of cell wall causes inflammation on that particular area. [4-6]. This process was best represented for microbial contamination (particularly bacterial), in which various receptors of the intrinsic resistant framework, for example, Toll-like receptors (TLRs) and NOD (nucleotide-binding oligomerization-domain protein)-like receptors (NLRs). This early acknowledge of diseases is intervened by tissue inhabitant macrophages and mast cells, this lead to produce variety of inflammatory mediators, including chemokines, cytokines, vasoactive amines, eicosanoids and products of proteolytic falls. Mostly, inflammation progress includes both the innate immune responses as well as the adaptive immune response [7]. The innate immune system is the primary defense mechanism against entering different microorganisms and carsigenic cells, including macrophages, mast cells and dendritic cells. The adaptive immune systems involve the activity of more immune response cells for example, B and T cells whos mechanism activate for eradicating invading pathogens and cancer cells by creating specific receptors and antibodies. The aggravation reaction is synchronized by a huge scope of go between that structure complex administrative reaction systems. In order to analyze these complex networks, it is important to put these signals into specific functional categories and isolate the inflammatory between inducers and mediators. Inducers are the signals which induce the response to infammation. They trigger pecific sensors, which then cause the production of exact mediator. The mediators, respose to the functional states of different tissues and organs (which are effectors of inflammation) in such a way to indicated that the particular inflammation inducer adapt them to the singiling condition. Consequently, a nonspecific inflammatory 'pathway' consists of inducers, sensors, mediators and effectors, each which determining the type of inflammatory response.

1.1 Inducers and Sensors of Inflammation

Inducers induce inflammation can be exogenous or endogenous (Fig. 1).

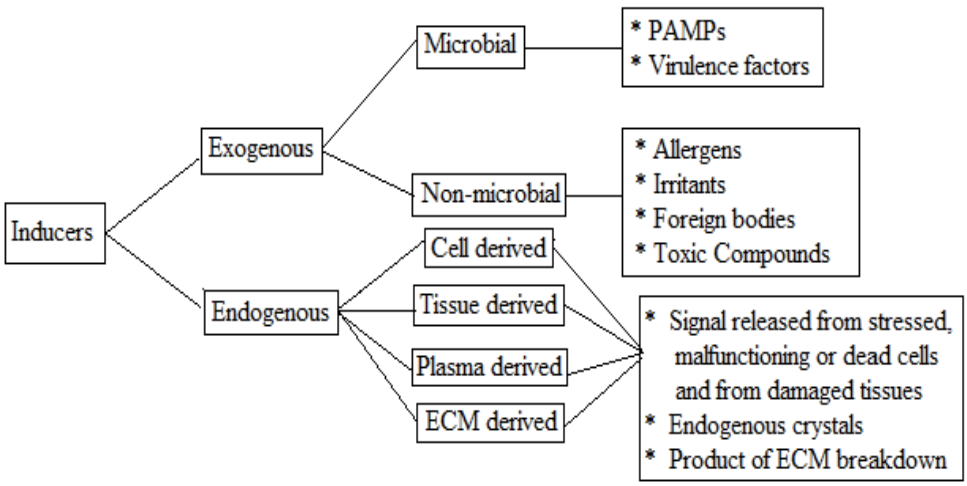


Fig. 1. Inducers of inflammation

1.1.1 Endogenous inducers of inflammation

Endogenous inflammation inducers that are signals produced in connection with stressed, Injured or otherwise malfunctioning tissues. The identity of the inflammations signals and their characteristic are not well discovered. They probably belong to various functional classes according to the nature and the degree of tissue anomalies [8].

One specific method in the detecting of acute tissue injury is the identifying of active molecules that are normally kept separate in intact tissue and cells. Activated components are separated by the various forms of compartmentalization process that exist in normal tissues. The cellular membranes sequestration (especially the plasma membrane), basement membranes, surface epithelium and vascular endothelium [9]. During necrotic cell death, plasma membrane integrity is impaired its activity, resulting in the release of certain cellular chemical mediator, including ATP, K^+ ions, ,HMGB1 (high-mobility group box 1 protein), uric acid and several S100 calcium-binding protein family (S100A8, S100A9 and S100A12) [10]. The ATP molecule attached to purinoceptors (including P2X7) on the macrophages , subsequently in K^+ ion efflux, and may activated the signaling pathway to inflammatory NALP3 activation [11]. ATP also activates nociceptors, which produces tissue injury to the nervous system. S100A12 and HMGB1 involve the RAGE receptor (advanced glycation end-product-specific receptor; also known as AGER), which lead to (at least in the case of HMGB1) cooperates with TLRs to induce an inflammatory action [11,12].

1.1.2 Exogenous inducers of inflammation

Exogenous inducers are two groups inducers includes microbial and nonmicrobial. The microbial inducer in process existing pathogen-associated molecular patterns (PAMPs) and virulence factors [13,14]. The PAMPs microbial inducer is a partial and specific set of conserved molecular forms that is carried by most of the microorganisms (whether pathogenic or commensal) [15]. PAMPs are represented in the sense of a corresponding set of a receptors (known as pattern-recognition receptors). It has been evolved continuously and detect in presence. The second class of microbial inducer includes a variety of virulence factors and its pathogenesis. PAMPs are dedicated receptors do not specifically rather than the effects of their operation on host tissues. PAMPs particularly shows their adverse effects and responsible for activating the inflammatory pathway to produces inflammation [11]. Specialized sensors are determine to detect selective behavior of various virulence factors. For example, Bacteria that from pore-producing exotoxins (gram positive bacteria) are detected by the NALP3 (NACHT-, leucine-rich repeat- and pyrin-domain containing protein) inflammasome, which is also sensitive to the efflux of K^+ ions produces by pore formation., the proteolytic activity of helminthes also produce proteases is which is sensed by an unknown sensor of basophiles [16]. Notably, this functional also mimics can be unintentionally activate this sensing mechanism of inflammation, so an allergens of proteases pathway normally induced by helminths. This substitute approached to sensing virulence activity is non-specific, also by detecting the cell death and tissue damage results. In this case, endogenous toxins products damaged cells and tissue are the real inducers of the inflammatory response [17]. Importantly, the inflammatory responses induced by these two of virulence mediator activity sensing mechanism in their specificity, since the former is characteristic of pathogens (and in some cases, pathogen classes), but the latter is not. These inflammatory responses are likely to have different characteristics, and it will be interesting to investigate whether they result in distinct physiological and pathological outcomes [18].

1.2 Mediators of Inflammation

There are various herbal products are for controlling and prevents inflammatory crisis. Herbal medicine is widely popular and one of traditional medicine's most significant aspect. The role of anti-inflammatory remission herbs has been asserted in many scientific studies [19-21]. We discussed about herbs which have been tested for anti-inflammatory activity in clinical and laboratory studies. The clinical result are significantly improve condition of inflammation; among our research data, the *Curcuma longa* had shown the most significant clinical benefits in the management of disorders such as RA, uveitis, and IBD. Also, other listed herbs have demonstrated good anti-inflammatory activity in clinical and experimental design [22,23]. Consequently, the inflammation process has shown different mechanisms and multiple method of treatment. usually cytokines are involved in enzyme activation (such as phospholipase A2), mediator release, fluid

extravasation and vasodilation, blood cell migration, and eventually inflammation tissue damage (Fig. 2) [24,25].

1.3 Histamine

The production of the histamine from mast cells during the antigen-antibody reactions, as is its active role in cell membrane damage lead to inflammatory process. In the rheumatoid synovium and in the asthmatic lung, increase numbers of mast cells are also present, associated with elevated histamine levels [26-28].

1.4 Bradykinin

Bradykini is a chemical association with pain, vasodilatation, and edema, resulting in inflammatory reaction. Mediator–like immunoreactivity of bradykinin chemicals has been found in inflammatory pleural rat exudates [29,30]. After immunological challenge, kinines chemical mediators are also present in nasal secretion and kininogens is produced from mast cells of the lung [31-34].

1.5 The Prostaglandins

Beside non-nucleated erythrocytes, all kind of other cells are synthesizing PGs as per need basis, usually released in response to many types of cell membrane disruption. Aspirin was discovered by Vane in 1971 acting on this pathway and similar other drugs inhibit PGs, biosynthesis and predicted that his would explain their mechanism of action [35]. In other words, NSAIDs drugs inhibit the release of PGs chemical mediators that contributes to inflammation, fever, and pain.

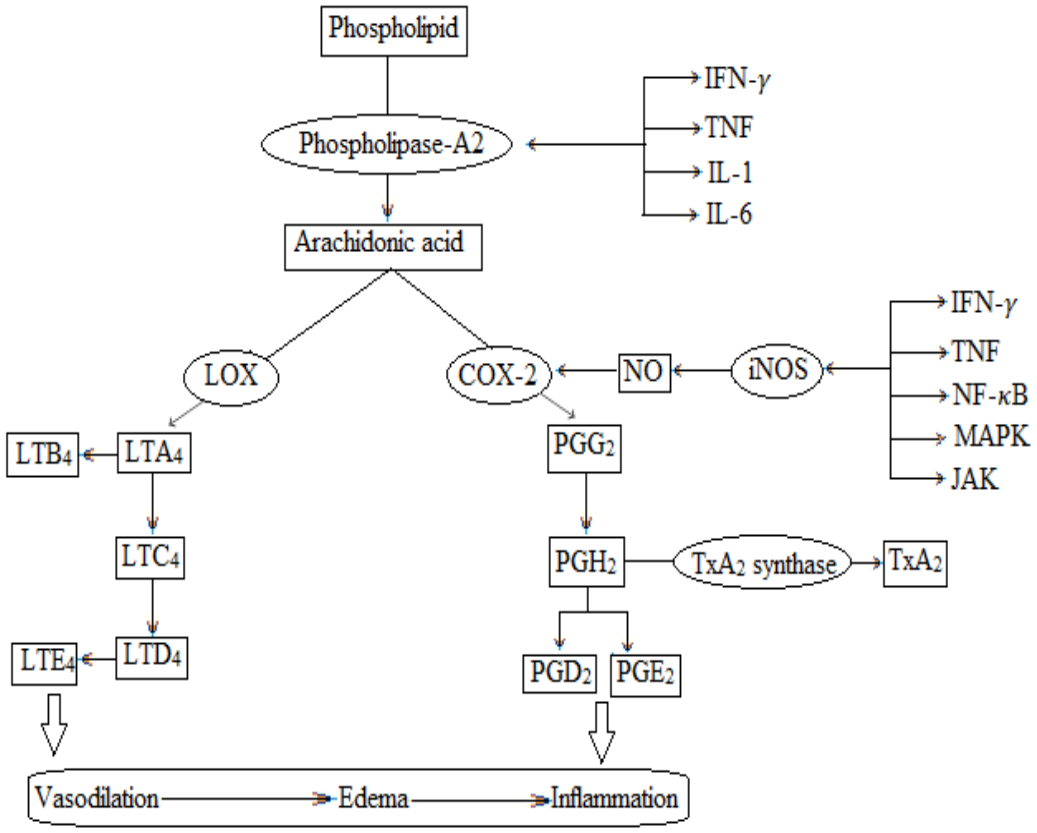


Fig. 2. Inflammation pathway. COX [cyclooxygenase]; IL [interleukin]; LT [leukotriene]; LOX [lipoxygenase]; PG [prostaglandin]; TX [thromboxane]; NO [nitricoxide]; iNOS [inducibleNOsynthase]; IFN [interferon]; TNF [tumornecrosisfactor]; NF-κB[nuclearfactor-κB]; MAPK [mitogenactivated proteinkinase]; JAK [januskinase]; IL [interleukin]

1.6 Thromboxane A2 and Prostacyclin

Aspirin's antiplatelet properties could not be explained by inhibiting the chemical mediator of PGE2 or PGF2a, because these PGs have no significant effect on platelet aggregation. However, in 1975 Samuelsson found that arachidonic acid (AA) is metabolized in platelets into pro aggregatory thromboxane (TX) A2 [36]. Through this pathway aspirin was prevented the formation of the intermediate endoperoxide (Fig. 3) [37]. The TXA2 chemical mediator is a another prostaglandin chemical exhibited opposite behavior to that of TXA2 [38]. Prostacyclin, as it was later named prostacyclin also relaxes blood vessels and prevents platelets aggregation. The chemical synthesis is of particular importance in the endothelial cells of blood vessel walls [39,40].

1.7 Leukotrienes

The leukotriences Slow-reacting anaphylaxis substance (SRS-A) was identified as a product of AA metabolism's 5-lipoxygenase pathway [41,42], and Samuelsson termed the chemical constituents of SRS-A as leukotrienes (LTs). In its inhibitory effects on cyclo-oxygenase, aspirin does not inhibit 5-lipoxygenase and, therefore, neither does it inhibit LT synthesis (Fig. 4) [43]. There's some evidence that lipo-oxygenase products leads to inflammatory vascular changes.

1.8 Platelet-Activating Factor (PAF)

The phospholipid PAF-acether is produced from the most proinflammatory cells, through the action of phospholipaseA2 mediated through vascular endothelial cells and platelets [44]. It usually cased inflammatory response in various species of animals and human skin [45].

1.9 Interleukin-l

IL-I is a polypeptide formed by activated macrophages mimicking chronic inflammation symptoms [46,20]. It also called as endogenous pyrogen. IL-I-like activity (equivalent to 1.69 U/mi) was observed in synovial fluids of rheumatoid arthritis patients [47]. Its actions include lymphocytes activation and fever production which is mediated by release of PGE2.

1.10 Mechanism of Action of Non Steroid Anti-Inflammatory Agents

The PGE2-like chemicals composition presents in synovial fluid of rheumatoid arthritis legs is around 20 ng/ml. This chemical reduce to zero in patients who used aspirin and its clinical proves effect on PG synthesis [48]. Polyester sponges impregnated with carrageenan injection s.c. experimental inflammation was induced in rats [49]. The inflammatory mediator examination contained within the sponges showed an increase in PGE2 concentration throughout the 24-h experiment. Additionally, the TXA2 and LTB4 usually showing peak after 4-6 h and then decreased over the rest of the experiment (Fig. 5). PGE2 induces hyperalgesia and vasodilatation. The chemical property of LTB4 is likely to draw polymorphonuclear leukocytes to the area [50]. However, the role of TXA2 in the process inflammation not well conventional.

Evidence has been shown that role of PGs in the inflammation producer usually cased by carrageenan to cause inflammation in the rat paw. Aspirin clinically proven suppression of endogenous PGs and then the administration of low doses of exogenous PGE2 (1.0 ng) or prostacyclin (10 ng) caused an increase in edema [51]. The ability for aspirin-like drugs to affect the release of certain compound, such as histamine and bradykinin, has been experimentally dismissed and further experiments have been planned to demonstrate that the anti-enzyme activity of aspirin-like drugs associated with their anti-inflammatory effect [52].

1.11 The Mechanism of Action of Steroids in Inflammation

Steroids clinically demonstrated the inhibit phospholipase A2 activity, which is precursor for the release of AA. Thus, corticosteroids mechanism of inhibit the complex of PGs, TX, and the LTs. Anti-inflammatory properties of steroids prevent phospholipase A2 release by producing inhibitory protein. This has been inhibitory proteins called as macrocortin, lipomodulin, or renocortin, and its molecular sizes ranges 15, 30, and 40 kDa have been identified by scientific studies. There is some dispute with respect to its mode of action of lipocortins appear due to similar identical to calpactins [54]. Calpactins usually bind calcium ion and also phospholipid ion. it has been

suggested that this property of Calpacitns direct inhibition of phospholipase A2, and also responsible for the reduction in eicosanoid formation [55-57].

2. METHODS

In this study, all the data from internet search engines were generated as follows: Pub Med, Science Direct, Google Scholar, web of science and Cocraine review. We used several keywords for searching in the database, “anti-inflammatory”, “herbs”, “herbal”, “herbal medicine”, and “Herbal Anti-Inflammatory medication”.

All the references within include publish this descriptive review article was written in English as a standard format, this review attempts to includes all the articles from 1980 to the present. Table 1 summarizes selected articles which report (2010–2016) on the anti-inflammatory effects of herbal plants materials and Table 2 contains summary of relevant research articles reporting on the anti-inflammatory effects of some selected herbs.

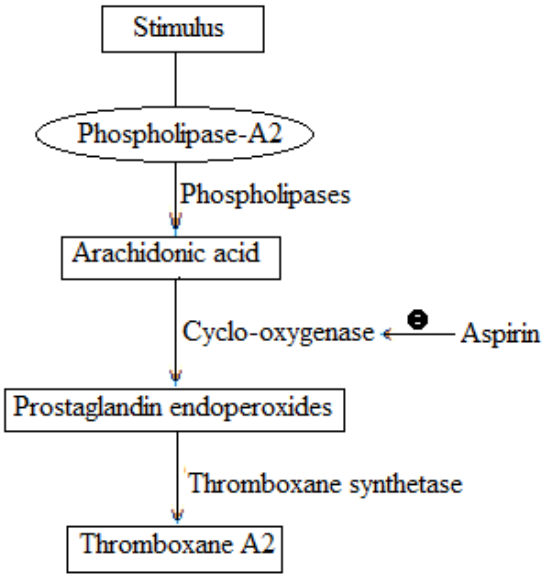


Fig. 3. Action of aspirin on platelets

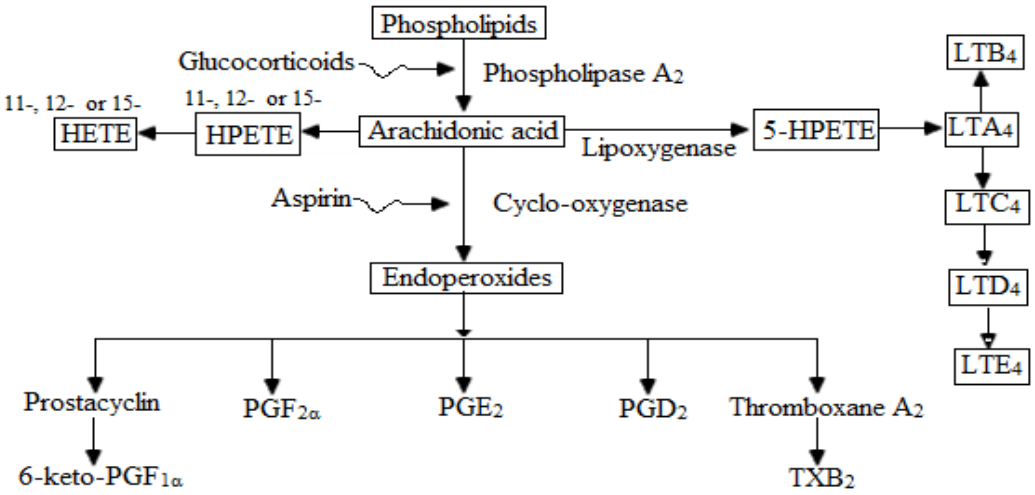


Fig. 4. Catabolic pathways of AA

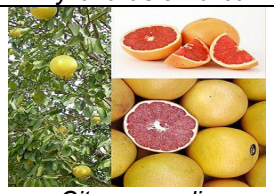
Table 1. Summarizes selected articles which report (2010–2016) on the anti-inflammatory effects of herbal plants materials

Author Name	Article topic	Major Method(s) of Testing	Main Effects on Inflammation*
Aravindaram, et al. 2010	Plant based natural products	in vitro and in vivo models of inflammation (LPS-induce lipopolysaccharide) and cancer.	Important reduction of cytokines levels; inhibition of development of COX-2, iNOS, NFκB and STAT (signal transducers and transcription activators) [58].
Arya et al. 2011	Plant barks	Different form of *in-vivo* inflammation (paw edema caused by carrageenan).	Significant COX and iNOS inhibition; pow edema attenuation of [59].
Shah, et al. 2011	Medicinal plants (General)	Different models of *in-vivo* (paw edema caused by carrageenan)	Inhibition of development in COX, iNOS, 5-LOX and PLA2 ; attenuation of paw edema [60].
Beg, et al. 2011	Herbal drugs (Medicinal plants)	Various models of inflammation *in-vitro* and *in-vivo* (animals); clinical humans trials with health and efficacy test.	Significant decrease in levels of cytokines, PGs, LTs, and NO; inhibition of development of COX, 5-LOX, PLA2, iNOS, and NFκB ; Humans: different effects of analgesicpain states, edema reduction, attenuation of inflammatory mitigation [61].
Lucas et al. 2011	Virgin olive oil	Similar *in-vitro* and *in-vivo* inflammation models.	Important reduction in levels cytokines, LTs, NO and PGs levels; inhibition of development of COX, iNOS and 5-LOX activity [62].
Sengupta et al. *2012*	Medicinal plants	Similar *in-vitro* and *in-vivo* inflammation models.	Analgesic effects and inflammatory action reduction [63].
Shilpi et al. *2012*	Mangrove plants	Similar *in-vitro* and *in-vivo* inflammation models.	Decrease levels of cytokines, LTs, NO and PGs levels; inhibition of development of COX, iNOS, 5-LOX and NFκB activity [64].
S. Kumar et al. 2013	Herbal plants	Similar *in-vitro* and *in-vivo* inflammation models.	Significant decrease in the levels of cytokines, LTs, NO and PGs levels; COX, iNOS and 5 LOX activity [65].
Wei et al. 2013	Marine natural products from soft corals	Various *in-vitro* and *in-vivo* models of inflammation (LPS-induced inflammation)	Reduction in levels of cytokines, NO and PGs; inhibition of COX and iNOS activity [66].
Lee et al. 2013	Marine natural products of algal origin	Various *in-vitro* and *in-vivo* models of inflammation (LPS-induced inflammation)	Decrease in level of IL-6, TNF-α, NO and PGs ; inhibition of development COX, iNOS, NFκB and STAT activity [67].
Bajpai et al. 2014	Ethnobotanical plants	Carrageenan induced paw edema	The effects were similar to those of other anti-inflammatory drugs like aspirin, diclofenac, valdecoxib, sulindac, ibuprofen, phenylbutazone and indomethacin [68].

Author Name	Article topic	Major Method(s) of Testing	Main Effects on Inflammation*
Furst et al. 2015	Plant derived compounds	Various *in-vitro* and *in-vivo* models of inflammation; pre-clinical tests and clinical trials in humans.	Decrease levels of cytokines, LTs and PGs; activation of COX-2, 5-LOX and NFκB in humans: attenuation of inflammatory factors such as CRP, IL-1β, IL-6, and TNF-α [69].
Schafer et al. 2014	Active organosulfur compounds in garlic	Various *in-vitro* and *in-vivo*animals models (LPS-induced inflammation); studies in human volunteers and pre-clinical studies.	Anti-inflammatory: reduction of the levels PGs, NO, IL-1β, IL6 and TNF-α increase of the of IL-10 levels; inhibition of COX-2, iNOS and NFκB activity Pro-inflammatory: opposite effects of the mentioned above [70].
Arreola et al. 2015	Active organosulfur compounds and extracts of garlic	Various *in-vitro* and *in-vivo*animals models (LPS-induced inflammation); studies in human.	Anti-inflammatory: reduction in IL-1β, IL-6 and TNF-α rise in levels; increase in IL-10 levels; inhibition of NFκB activity Pro-inflammatory: increase in NO, IFN-γ and TNF-α levels [71].
Bhagyasri et al. 2015	Indian medicinal plants	Various *in-vitro* and *in-vivo* models	Decrease levels of TNF-α and other cytokines; PLA2 inhibition; general–anti-inflammatory, analgesic and anti-allergic effects [72].
González et al. 2015	Marine diterpenoids	Various *in-vitro* and *in-vivo* models (LPS-induced inflammation)	Substantial reduction in rates IL-6, TNF-α, NO, PGs and LTs levels; substantial inhibition of COX-2, 5-LOX,NFκ B and iNOS activity , some of which were equivalent to those of anti-inflammatory drugs such as indomethacin [73].
Parhiz et al. 2015	Citrus flavonoids	Various *in-vitro* and *in-vivo* animal models (e.g., LPS-induced inflammation), healthy human volunteers	Decreased levels IL-1β, IL-6, TNF-α, PGs and NO levels; inhibition of COX-2, NFκB activity, iNOS , reduction in human plasma CRP levels [74].
Karunaweera et al. 2015	Plant polyphenols	Various *in-vitro* and *in-vivo* animal models (LPS induced inflammation)	Reduction in rates IL-1β, IL-6, TNF-α, NO and PGs levels; inhibition of development of COX-2, iNOS and NFκB activity [75].
Cheung et al. 2016	Marine natural products	Various *in-vitro* and *in-vivo* animal models (carrageenan or LPS-induced inflammation)	Important reduction in rates IL-1β, IL-6, TNF-α, NO and PGs; substantial inhibition of development COX-2, iNOS and NFκB activity [45].
Maione et al. 2016	Medicinal plants	Diverse animal models *in-vitro* and *in-vivo* (LPS induced inflammation)	Decrease in rates IL-1β, IL-6, TNF-α, NO and PGs levels; inhibition of development of COX-2 and iNOS activity [76].

Table 2. Comprehensive summary of research articles reporting on the anti-inflammatory effects of plant products

Plant Name	Family	Extracting Solvent(s)	Major Method(s) of Testing	Main Effects on Inflammation
 *Portulaca oleracea*	*Portulacaceae*	10% C_2H_5OH in H_2O	Hot-plate method for assessing analgesia activity; carrageenan-induced paw edema	A significant reduction in paw edema and an analgesic effect, similar to that of diclofenac [77].
 *Salvia officinalis*	*Lamiaceae*	n-Hexane, $CHCl_3$, MeOH	Croton oil-induced ear edema in mice	n-Hexane and $CHCl_3$ extracts prominently decreased ear edema; MeOH extract had a weak effect while the essential oil was ineffective; the significant effect of ursolic acid was 2-fold stronger in reducing the edema than indomethacin [78].
 *Salvia fruticosa*	*Lamiaceae*	$CHCl_3$, CH_3OH, $C_2H_5OCH_3$,n-butyl alcohol	Carrageenan-induced paw edema in mice	A significant reduction in paw edema similar to that seen under treatment with diclofenac [79].
 *Corchorus olitorius*	*Malvaceae*	H_2O	Yeast-induced pyrexia and carrageenan-induced paw edema and in rats	A significant reduction in paw edema which was stronger than that of aspirin; attenuation of hyperthermia (fever) [80].
 *Carica papaya*	*Caricaceae*	C_2H_5OH	Cotton pellet -induced granuloma and Carrageenan-induced paw edema in rats	A significant reduction in paw edema and pellet granuloma; effects were similar to those of indomethacin [81].

Plant Name	Family	Extracting Solvent(s)	Major Method(s) of Testing	Main Effects on Inflammation
 *Vitex agnus-castus*	*Lamiaceae*	CH_3OH	In-vitro assays for measuring neutrophils inflammation and lipoxygenase activity	Three compounds had a significant anti-inflammatory activity; two compounds inhibited the activity of lipoxygenase [82].
 *Origanumsyriacum*	*Lamiaceae*	Essential oils	LPS-induced inflammation in RAW 264.7 cells	*Origanumsyriacum*caused a significant decrease in NO production [83].
 *Phyllanthus emblica*	*Phyllanthaceae*	H_2O	carrageenan-induced paw edema, Ethyl phenylpropiolate and arachidonic acid-induced ear edema and cotton pellet-induced granuloma in rats	Significant reduction in a paw edema, inhibition of ear inflammation, and pellet granuloma-effects were similar to those of aspirin; the extract exerted an analgesic effect [84].
 *Citrus paradis*	*Rutaceae*	CH_3OH	LPS-induced inflammation in RAW 264.7 cells	A significant, dose-dependent reduction in PGE2 and NO levels; a significant decrease in COX-2 and iNOS expression [85].
 *Mangiferaindica*	*Anacardiaceae*	CH_3OH	Carrageenan-induced paw edema in rats; Acetic acid-induced writhing in mice.	A non-significant reduction in paw edema; a significant analgesic effect similar to that of diclofenac [86].

Plant Name	Family	Extracting Solvent(s)	Major Method(s) of Testing	Main Effects on Inflammation
 *Urgineaindica*	*Liliaceae*	CH_3OH	Hot-plate method in mice; carrageenan-induced paw edema and cotton pellet granuloma in rats	Anti-inflammatory and analgesic effects, a significant reduction in paw edema; effects were similar to those of ibuprofen [87].
 *Desmodiumgangeticum*	*Fabaceae*	C_2H_5OH	Carrageenan-induced paw edema in rats	A significant reduction in paw edema [88]
 *Crataegus pinnatifida*	*Rosaceae*	70% MeOH in H2O, in different solvents	LPS-induced inflammation in RAW 264.7 cells	The aqueous extract caused a significant reduction in NO levels; and, a significant dose-dependent reduction in COX-2, IL-1β, IL-6 and TNF-α expression [89]
 *Mentha spicata*	*Lamiaceae*	CH_3OH	Hot-plate test & acetic acid-induced writhing in mice; yeast-induced pyrexia in rats; carrageenan-induced paw edema in rats;	Significant dose-dependent analgesic effect, anti-inflammatory effect (decrease in paw edema) and antipyretic effect; effects were parallel to those of reference drugs such as ketorolac and paracetamol [90].

Plant Name	Family	Extracting Solvent(s)	Major Method(s) of Testing	Main Effects on Inflammation
 *Malva sylvestris*	*Malvaceae*	C_2H_5OH	12-O-tetradecanoylphorbol-acetate-induced ear edema in mice	A significant dose-dependent decrease in ear edema; a reduction in IL-1β levels, and leukocytes relocation to the tissue; effects were less effective than those of dexamethasone [91].
 *Abutilon indicum*	*Malvaceae*	C_2H_5OH	5-LOX activity in lung malignance cell line A549	A significant reduction in 5-LOX activity [92].
 *Capsicum annuum*	*Solanaceae*	C_2H_5OH	Adjuvant-induced arthritis in mice	A significant decrease in CRP, IL-1β, IL-6 and TNF-α levels; a significant reduction in arthritis [93].
 *Morindacitrifolia*	*Rubiaceae*	H_2O	Carrageenan-induced paw edema in mice	A significant reduction in TNF-α levels; a significant decline in leukocytes migration; effects were comparable to those of indomethacin [94].

Plant Name	Family	Extracting Solvent(s)	Major Method(s) of Testing	Main Effects on Inflammation
 *Solanum lycocarpum*	*Solanaceae*	C_2H_5OH and fractionation with n-hexane, CH_2Cl_2, $C_2H_5OCH_3$	Carrageenan-induced paw edema in mice	A significant reduction in paw edema which was similar to that seen under treatment with indomethacin [95].
 *Rosmarinus officinalis*	*Lamiaceae*	CH_3OH	LPS-induced inflammation in RAW 264.7 cells; dextran sulfate sodium-induced colitis in mice	A significant dose-dependent decrease in nitrites, IL-6 and TNF-α levels; a significant reduction in COX-2 and iNOS expression; a significant decline in NFκB activity, among other inflammatory markers that were attenuated [96].
 *Eriodictyonangustifolium*	*Boraginaceae*	90% C_2H_5OH in H_2O	LPS-induced inflammation in human gingival fibroblasts.	A significant reduction in IL-6, IL-8 and MCP-1 levels [97].
 *Droseraburmannii*	*Droseraceae*	70% CH_3OH in H_2O	LPS-induced inflammation in RAW 264.7 cells	A significant dose-dependent decrease in nitrites and TNF-α levels; a significant dose-dependent reduction in COX-2 and iNOS expression [98].

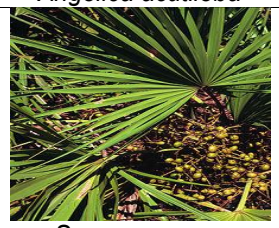
Plant Name	Family	Extracting Solvent(s)	Major Method(s) of Testing	Main Effects on Inflammation
 *Angelica acutiloba*	*Apiaceae*	CH_3OH	LPS-induced inflammation in RAW 264 cells	A significant decrease in NO, PGE2, IL-6 and TNF-α levels; a significant increase in heme oxygenase-1 expression, suggesting enhanced anti-inflammatory activity [99].
 *Serenoarepens*	*Arecaceae*	H_2O, C_2H_5OH	A testosterone-induced benign prostatic hyperplasia model in obese rats.	A significant reduction in IL-1β, IL-6, NO, and TNF-α levels [100].
 *Picrorhizakurroa*	*Plantaginaceae*	C_2H_5OH in H_2O	Formaldehyde and adjuvant-induced Arthritis in rats	A significant reduction in synovial expression of IL-1β, IL-6, and TNF-α; a significant decrease in paw edema; a significant decline in NO levels and leukocytes infiltration to the inflamed joints; all the effects were comparable to those of indomethacin [101].

Table 3. Mechanisms of anti-inflammatory action of the medicinal plants mentioned in this review article

Herb	TNF-α	COX-2	iNOS	NF-κB	Inhibition of PGE_2	NO	LOX	Complement	IFN-γ
Curcuma longa	√	√	√	---	---	---	√	---	---
Zingiber officinalis	√	√	---	---	---	√	√	√	---
Rosmarinus officinalis	√	---	---	---	---	---	---	---	---
Boragoofficinalis	√	---	---	---	√	---	---	---	---
Oenothera biennis	√	√	---	---	---	√	---	---	√
Harpagophytumprocumbens	√	√	√	---	√	---	---	---	---
Boswellia serratsa	√	---	---	---	√	√	√	√	√
Rosa canina	---	√	---	---	√	√	√	---	---
Urticadioica	---	√	---	---√	---	---	---	---	---
Uncariatomentosa	√	√	√	√	√	---		---	---
Salvia officinalis	---		---	---	√	---	√	---	---
Ribes nigrum	√	√	---	√	√	---	√	---	---
Persea americana	---	---	---	√	---	---	---	---	---
Glycine max	√	√	√	---	√	√	---	---	√
Elaeagnus angustifolia	√	√	---	---	---	---	---	---	---
Vaccinium myrtillus	√		√	---	---	---	---	---	---
Olea europaea	---	√	√	---	---	---	√	---	---

Note: Other mechanisms may also exist, but we could not cover all of them

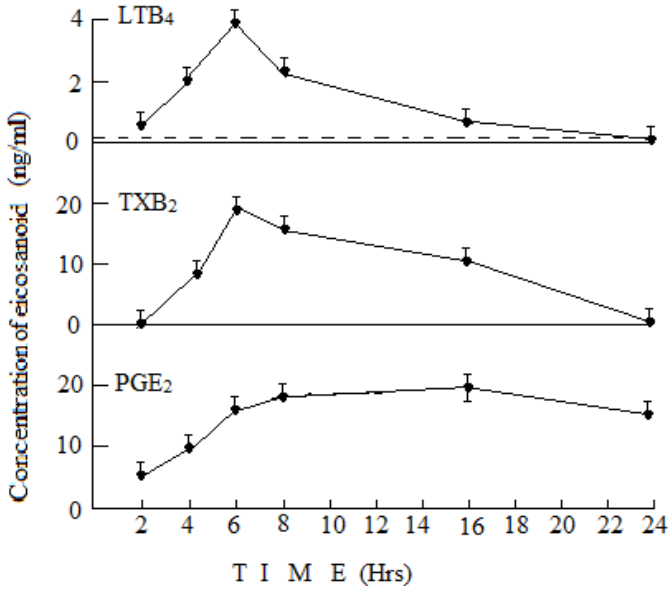


Fig. 5. Concentrations of eicosanoids in inflammatory exudates with the minimum concentration level (------) [53,49]

3. CONCLUSION

The herbal plants which have been claimed to have an anti-inflammatory effect are many and including all in a single paper is beyond the limit; therefore we have gathered articles refer to the herbs those data is available and clinically significant. Herbal medicine in the treatment of inflammation is widely popular in Indian traditional system of medicine and the most important aspects of modern medicines. Since scientific clinical studies have demonstrated the important of herbs in inflammation remission. we reviews some herbs activities which had been tested in clinical and laboratory studies for anti-inflammatory activities. we focused on more clinical result than others studies; among our research data, the Curcuma longa has the most clinical significant for management of various inflammatory disorders. we also listed herbs that have demonstrated efficacy in clinical and experimental anti-inflammatory tests. Inflammation process has numerous mechanisms and their treatment includes variety of drugs. Number of cytokines and enzyme activation (such as phospholipaseA2), mediator release, vasodilation, cell migration, and finally tissue damage which have been enlisted as inflammatory mediator (Fig. 1). The experimental animal studies demonstrated that the potential role of herbal active compounds are responsible for inhibition of pro-inflammatory chemicals such as cytokines, PG2 etc. (Table 3), although geographical based clinical studies with larger participants, meta analyses and randomized control trials could provide clear overview and minimized conflicts. The enlisted plants in this review believed to have an anti-inflammatory effect and significant for anti-inflammatory effects. Although more evidence-based research are needed for exploit mechanism of action of such herbs in a border demographic population to offer health actioners a consistent approach.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Artis D, Spits H. The biology of innate lymphoid cells. Nature. 2015; 517(7534):293-301.

2. Isailovic N, Daigo K, Mantovani A, Selmi C. Interleukin-17 and innate immunity in infections and chronic inflammation. Journal of Autoimmunity. 2015;60:1-11.
3. Pedraza-Alva G, Pérez-Martínez L, Valdez-Hernández L, Meza-Sosa KF, Ando-Kuri M. Negative regulation of the inflammasome: keeping inflammation under control. Immunological Reviews. 2015;265(1):231-57.
4. Fernandes JV, Cobucci RN, Jatobá CA, Fernandes TA, de Azevedo JW, de Araújo JM. The role of the mediators of inflammation in cancer development. Pathology Oncology Research: POR. 2015;21(3):527-34.
5. Heppner FL, Ransohoff RM, Becher B. Immune attack: the role of inflammation in Alzheimer disease. Nature reviews Neuroscience. 2015;16(6):358-72.
6. Loane DJ, Kumar A. Microglia in the TBI brain: The good, the bad, and the dysregulated. Exp Neurol;275 Pt. 2016; 3(03):316-27.
7. Waisman A, Liblau RS, Becher B. Innate and adaptive immune responses in the CNS. The Lancet Neurology. 2015;14(9): 945-55.
8. Jang J, Park S, Hur HJ, Cho H-J, Hwang I, Kang YP, et al. 25-hydroxycholesterol contributes to cerebral inflammation of X-linked adrenoleukodystrophy through activation of the NLRP3 inflammasome. Nature communications. 2016;7(1):1-11.
9. Yurchenco PD. Basement membranes: cell scaffoldings and signaling platforms. Cold Spring Harbor Perspectives in Biology. 2011;3(2):a004911.
10. Sims GP, Rowe DC, Rietdijk ST, Herbst R, Coyle AJ. HMGB1 and RAGE in inflammation and cancer. Annual Review of Immunology. 2009;28:367-88.
11. Medzhitov R. Origin and physiological roles of inflammation. Nature. 2008; 454(7203):428-35.
12. Zong W-X, Thompson CB. Necrotic death as a cell fate. Genes & Development. 2006;20(1):1-15.
13. Hannoodee S, Nasuruddin DN. Acute Inflammatory Response. StatPearls [Internet]: StatPearls Publishing; 2020.
14. Wilmanski JM, Petnicki-Ocwieja T, Kobayashi KS. NLR proteins: integral members of innate immunity and mediators of inflammatory diseases. Journal of Leukocyte Biology. 2008; 83(1):13-30.
15. Boller T, Felix G. A renaissance of elicitors: Perception of microbe-associated molecular patterns and danger signals by pattern-recognition receptors. Annual Review of Plant Biology. 2009;60:379-406.
16. Kasper CA. Amplifying the innate immune response: cell-cell propagation of proinflammatory signals during bacterial infection: University_of_Basel; 2012.
17. Poon IK, Lucas CD, Rossi AG, Ravichandran KS. Apoptotic cell clearance: basic biology and therapeutic potential. Nature Reviews Immunology. 2014;14(3):166-80.
18. Costantini C, Renga G, Sellitto F, Borghi M, Stincardini C, Pariano M, et al. Microbes in the era of circadian medicine. Frontiers in Cellular and Infection Microbiology. 2020;10:30.
19. Ting EY-C, Yang AC, Tsai S-J. Role of Interleukin-6 in depressive disorder. International Journal of Molecular Sciences. 2020;21(6):2194.
20. Yang L, Wen M, Liu X, Wang K, Wang Y. Feikang granules ameliorate pulmonary inflammation in the rat model of chronic obstructive pulmonary disease via TLR2/4-mediated NF-κB pathway. BMC Complementary Medicine and Therapies. 2020;20:1-11.
21. Yasueda A, Kayama H, Murohashi M, Nishimura J, Wakame K, Komatsu K-i, et al. Sanguisorba officinalis L. derived from herbal medicine prevents intestinal inflammation by inducing autophagy in macrophages. Scientific Reports. 2020; 10(1):1-13.
22. Mattai SA. Turmeric: Anti-inflammatory Effects and Evidence for Use in Osteoarthritis. Proceedings of UCLA Health. 2020;24.
23. Rajabiesterabadi H, Hoseini SM, Fazelan Z, Hoseinifar SH, Doan HV. (2020)Effects of dietary turmeric administration on stress, immune, antioxidant and inflammatory responses of common carp (Cyprinus carpio) during copper exposure. Aquaculture Nutrition.
24. Ghasemian M, Owlia S, Owlia MB. Review of anti-inflammatory herbal medicines. Advances in Pharmacological Sciences; 2016.
25. Mehrzad J. Molecular aspects of neutrophils as pivotal circulating cellular innate immune systems to protect mammary gland from pathogens. Recent Advances in Immunology to Target

Cancer, Inflammation and Infections Rijeka/Shanghai: InTech. 2012;383-422.
26. Hanuskova E, Plevkova J. The role of histamine H4 Receptors as a Potential Targets in Allergic Rhinitis and Asthma; 2013.
27. Holgate STJA, actions. The pathophysiology of bronchial asthma and targets for its drug treatment. 1986;18(3-4):281-7.
28. Nigrovic PA, Lee DM. Mast cells in inflammatory arthritis. Arthritis Res Ther. 2004;7(1):1.
29. Gholamreza-Fahimi E, Bisha M, Hahn J, Straßen U, Krybus M, Khosravani F, et al. Cyclooxygenase activity in bradykinin-induced dermal extravasation. A study in mice and humans. Biomedicine & Pharmacotherapy. 2020;123:109797.
30. Gonçalves EC, Vieira G, Gonçalves TR, Simões RR, Brusco I, Oliveira SM, et al. Bradykinin Receptors play a critical role in the chronic post-ischaemia pain model. Cellular and Molecular Neurobiology; 2020.
31. Barnes PJJBJOHM. Mediators and asthma. 1985;34(6):339-44.
32. Challenge A. Elevation of tissue kallikrein and kinin in the airways of asthmatic subjects after Endobronchial; 2020.
33. Patrekar PV, Mali SS, Kashid K, More S, Mali SS, Dongare SD. A overview: non-steroidal anti-inflammatory drugs and mechanisms. Indian Journal of Pharmaceutical and Biological Research. 2014;2(04):94-103.
34. Proud D. Kinins. Asthma and COPD: Elsevier. 2002;237-42.
35. Vane JRJNNB. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. 1971;231(25):232-5.
36. Hamberg M, Svensson J, Samuelsson B. Thromboxanes: a new group of biologically active compounds derived from prostaglandin endoperoxides. Proc Natl Acad Sci U S A. 1975;72(8):2994-8.
37. Roth GJ, Majerus PW. The mechanism of the effect of aspirin on human platelets. I. Acetylation of a particulate fraction protein. The Journal of Clinical Investigation. 1975;56(3):624-32.
38. Moncada S, Gryglewski R, Bunting S, Vane JJN. An enzyme isolated from arteries transforms prostaglandin endoperoxides to an unstable substance that inhibits platelet aggregation. 1976;263(5579):663-5.
39. Fodor P, White B, Khan R. Inflammation—The role of ATP in pre-eclampsia. Microcirculation. 2020;27(1):e12585.
40. Gryglewski RJ, Bunting S, Moncada S, Flower RJ, Vane JRJP. Arterial walls are protected against deposition of platelet thrombi by a substance (prostaglandin X) which they make from prostaglandin endoperoxides. 1976;12(5):685-713.
41. Chakrin L. The leukotrienes: Chemistry and biology: Elsevier; 2012.
42. Samuelsson B, Borgeat P, Hammarström S, Murphy RJP. Introduction of a nomenclature: leukotrienes. 1979;17(6): 785-7.
43. Heymann MA. The role of eicosanoids in the fetal and perinatal circulations. Eicosanoids in Reproduction. 2020;285.
44. Morley J. Platelet activating factor and asthma. Agents Actions. 1986;19(1-2): 100-8.
45. Cheung RCF, Ng TB, Wong JH, Chen Y, Chan WYJAm, biotechnology. Marine Natural Products with Anti-Inflammatory Activity. 2016;100(4):1645-66.
46. Dinarello CAJRoid. Interleukin-1. 1984; 6(1):51-95.
47. Nouri A, Panayi G, Goodman SMJC, immunology e. Cytokines and the chronic inflammation of rheumatic disease. I. The presence of interleukin-1 in synovial fluids. 1984;55(2):295.
48. Higgs G, Vane J, Hart F, Wojtulewski JJPsi. Effects of anti-inflammatory drugs on prostaglandins in rheumatoid arthritis. 1974;165-73.
49. Simmons PM, Salmon JA, Moncada SJBP. The release of leukotriene B4 during experimental inflammation. 1983;32(8): 1353-9.
50. Ford-Hutchinson A, Brunet G, Savard P, Charleson SJP. Leukotriene B4, polymorphonuclear leukocytes and inflammatory exudates in the rat. 1984;28(1):13-27.
51. Moncada S, Ferreira S, Vane JJN. Prostaglandins, aspirin-like drugs and the oedema of inflammation. 1973;246(5430): 217-9.
52. Chan MM, Fong D. Anti-Inflammatory Therapeutics. Pharmaceutical Sciences Encyclopedia: Drug Discovery, Development, and Manufacturing; 2010.
53. Norling L, Serhan C. Profiling in resolving inflammatory exudates identifies novel anti-inflammatory and pro-resolving mediators and signals for termination.

Journal of Internal Medicine. 2010;268(1): 15-24.
54. Willis AL. CRC Handbook of Eicosanoids, Volume II: Prostaglandins and Related Lipids: CRC Press; 2017.
55. Balsinde J, Dennis EA. Role of Phospholipase A2 Forms in arachidonic acid mobilization and eicosanoid generation. Handbook of Cell Signaling: Elsevier. 2010;1213-7.
56. Davidson F, Dennis E, Powell M, Glenney JJJoBC. Inhibition of phospholipase A2 by" lipocortins" and calpactins. An Effect of Binding to Substrate Phospholipids. 1987;262(4):1698-705.
57. Dhananjaya BL, Shivalingaiah S. The anti-inflammatory activity of standard aqueous stem bark extract of Mangifera indica L. as evident in inhibition of Group IA sPLA2. Anais da Academia Brasileira de Ciências. 2016;88(1):197-209.
58. Aravindaram K, Yang N-SJPM. Anti-inflammatory plant natural products for cancer therapy. 2020;76(11):1103-17.
59. Arya V, Arya ML. A review on anti-inflammatory plant barks. International Journal of PharmTech Research. 2011;3:899-908.
60. Shah B, Seth A, Maheshwari KJRJMP. A review on medicinal plants as a source of anti-inflammatory agents. 2011;5(2):101-15.
61. Beg S, Swain S, Hasan H, Barkat MA, Hussain MSJPR. Systematic review of herbals as potential anti-inflammatory agents: Recent advances. Current Clinical Status and Future Perspectives. 2011; 5(10):120.
62. Lucas L, Russell A, Keast RJCPD. Molecular mechanisms of inflammation. Anti-inflammatory Benefits of Virgin Olive Oil and the Phenolic Compound Oleocanthal. 2011;17(8):754-68.
63. Sengupta R, Sheorey SD, Hinge MAJIJOPSR, Research. Analgesic and anti-inflammatory plants: An Updated Review. 2012;12(2):114-9.
64. Shilpi J, Islam M, Billah M, Islam K, Sabrin F, Uddin S, et al. Antinociceptive, anti-inflammatory, and antipyretic activity of mangrove plants: A Mini Review; 2012.
65. Kumar S, Bajwa B, Kuldeep S, Kalia AJIJAPBC. Anti-inflammatory activity of herbal plants: A Review. 2013;2(2):272-81.
66. Wei W-C, Sung P-J, Duh C-Y, Chen B-W, Sheu J-H, Yang N-SJMd. Anti-inflammatory activities of natural products isolated from soft corals of Taiwan between 2008 and 2012. 2013;11(10): 4083-126.
67. Lee J-C, Hou M-F, Huang H-W, Chang F-R, Yeh C-C, Tang J-Y, et al. Marine algal natural products with anti-oxidative, anti-inflammatory, and anti-cancer properties. 2013;13(1):1-7.
68. Bajpai S, Pathak R, Hussain TJRRJBS. Anti-inflammatory activity of ethnobotanical plants used as traditional medicine: A Review. 2014;3:8-18.
69. Fürst R, Zündorf IJMoi. Plant-derived anti-inflammatory compounds: hopes and disappointments regarding the translation of preclinical knowledge into clinical progress. 2015;2014.
70. Schafer G, H Kaschula CJA-CAiMC. The immunomodulation and anti-inflammatory effects of garlic organosulfur compounds in cancer chemoprevention. 2014;14(2):233-40.
71. Arreola R, Quintero-Fabián S, López-Roa RI, Flores-Gutiérrez EO, Reyes-Grajeda JP, Carrera-Quintanar L, et al. Immunomodulation and anti-inflammatory effects of garlic compounds; 2015.
72. Bhagyasri Y, Lavakumar V, Divya Sree M, Ashok Kumar CJIJRPNS. An overview on anti-inflammatory activity of Indian herbal plants. 2015;4:1-9.
73. González Y, Torres-Mendoza D, Jones GE, Fernandez PLJMOI. Marine diterpenoids as potential anti-inflammatory agents; 2015.
74. Parhiz H, Roohbakhsh A, Soltani F, Rezaee R, Iranshahi MJPR. Antioxidant and anti-inflammatory properties of the citrus flavonoids hesperidin and hesperetin: an updated review of their molecular mechanisms and experimental models. 2015;29(3):323-31.
75. Karunaweera N, Raju R, Gyengesi E, Münch GJFIMN. Plant polyphenols as inhibitors of NF-κB induced cytokine production—A Potential Anti-inflammatory Treatment for Alzheimer's Disease? 2015;8:24.
76. Maione F, Russo R, Khan H, Mascolo NJNPR. Medicinal plants with anti-inflammatory activities. 2016;30(12):1343-52.
77. Chan K, Islam M, Kamil M, Radhakrishnan R, Zakaria M, Habibullah M, et al. The analgesic and anti-inflammatory effects of *Portulaca oleracea* L. subsp. sativa (Haw.) Celak. 2000;73(3):445-51.

78. Baricevic D, Sosa S, Della Loggia R, Tubaro A, Simonovska B, Krasna A, et al. Topical anti-inflammatory activity of Salvia officinalis L. leaves: The Relevance of Ursolic Acid. 2011;75(2-3):125-32.
79. Boukhary R, Raafat K, Ghoneim AI, Aboul-Ela M, El-Lakany AJE-BC, Medicine A. Anti-inflammatory and antioxidant activities of Salvia fruticosa: An HPLC Determination of Phenolic Contents; 2016.
80. Zakaria Z, Sulaiman M, Arifah A, Mat Jais A, Somchit M, Kirisnaveni K, et al. The anti-inflammatory and antipyretic activities of Corchorus olitorius in rats. Journal of Pharmacology and Toxicology. 2016;1(2): 139-46.
81. Owoyele BV, Adebukola OM, Funmilayo AA, Soladoye AOJI. Anti-inflammatory activities of ethanolic extract of Carica papaya leaves. 2008;16(4):168-73.
82. Choudhary MI, Jalil S, Nawaz SA, Khan KM, Tareen RBJPRAIJDTP, Derivatives TEoNP. Antiinflammatory and lipoxygenase inhibitory compounds from vitex agnus-castus. 2009;23(9):1336-9.
83. Loizzo MR, Menichini F, Conforti F, Tundis R, Bonesi M, Saab AM, et al. Chemical analysis, antioxidant, antiinflammatory and anticholinesterase activities of Origanum ehrenbergii Boiss and Origanum syriacum L. essential oils. 2009;117(1):174-80.
84. Jaijoy K, Soonthornchareonnon N, Panthong A, Sireeratawong SJIJOARINP. Anti-inflammatory and analgesic activities of the water extract from the fruit of Phyllanthus emblica Linn. 2010;3(2):28-35.
85. Huang Y-S, Ho S-CJFC. Polymethoxy flavones are responsible for the anti-inflammatory activity of citrus fruit peel. 2010;119(3):868-73.
86. Islam M, Mannan M, Kabir M, Islam A, Olival KJJOTBAU. Analgesic, anti-inflammatory and antimicrobial effects of ethanol extracts of mango leaves. 2010;8(2):239-44.
87. Rahman MM, Chowdhury JA, Habib R, Saha BK, Salauddin A, Islam MKJIJOPS, et al. Anti-inflammatory, anti-arthritic and analgesic activity of the alcoholic extract of the plant urginea indica kunth. 2011;2(11):2915.
88. Yasmeen N, Sujatha KJIJOP. Evaluation of anti-inflammatory activity of ethanolic whole plant extract of *Desmodium gangeticum* L. 2013;5(3):347.
89. Li C, Wang M-HJNR, practice. Anti-inflammatory effect of the water fraction from hawthorn fruit on LPS-stimulated RAW 264.7 cells. 2011;5(2):101-6.
90. Yousuf PMH, Noba NY, Shohel M, Bhattacherjee R, Das BKJJOPRI. Analgesic, anti-inflammatory and antipyretic effect of Mentha spicata (Spearmint). 2013;854-64.
91. Prudente AS, Loddi AM, Duarte MR, Santos AR, Pochapski MT, Pizzolatti MG, et al. Pre-clinical anti-inflammatory aspects of a cuisine and medicinal millennial herb: *Malva sylvestris* L. 2013;58:324-31.
92. DSVGK K, Saranya K, Vadlapudi V, Yarla NJPELEoLCCLAfSNSJCST. Evaluation of Anti-inflammatory and Anti-proliferative Activity of *Abutilon indicum* L. 2014;6:195-201.
93. Tag HM, Kelany OE, Tantawy HM, Fahmy AA. Potential anti-inflammatory effect of lemon and hot pepper extracts on adjuvant-induced arthritis in mice. The Journal of Basic & Applied Zoology. 2014;67(5):149-57.
94. de Almeida Brito F, de Oliveira Barreto E, Serafini MR, dos Santos JPA, dos Santos Lima B, Walker CIB, et al. Anti-inflammatory property and redox profile of the leaves extract from *Morinda citrifolia* L. Journal of Medicinal Plants Research. 2015;9(24):693-701.
95. da Costa GAF, Morais MG, Saldanha AA, Assis Silva IC, Aleixo ÁA, Ferreira JMS, et al. Antioxidant, antibacterial, cytotoxic, and anti-inflammatory potential of the leaves of solanum lycocarpum A. St. Hil. (Solanaceae). Evid Based Complement Alternat Med. 2015;315987.
96. Medicherla K, Ketkar A, Sahu BD, Sudhakar G, Sistla R. *Rosmarinus officinalis* L. extract ameliorates intestinal inflammation through MAPKs/NF-κB signaling in a murine model of acute experimental colitis. Food & Function. 2016;7(7):3233-43.
97. Walker J, Reichelt KV, Obst K, Widder S, Hans J, Krammer GE, et al. Identification of an anti-inflammatory potential of Eriodictyon angustifolium compounds in human gingival fibroblasts. 2016;7(7): 3046-55.
98. Ghate N, Das A, Chaudhuri D, Panja S, Mandal NJCdd. Sundew plant, a potential source of anti-inflammatory agents, selectively induces G2/M arrest and apoptosis in MCF-7 cells through upregulation of p53 and Bax/Bcl-2 ratio. 2016;2(1):1-10.

99. Uto T, Tung NH, Taniyama R, Miyanowaki T, Morinaga O, Shoyama YJPR. Anti-inflammatory activity of constituents isolated from aerial part of Angelica acutiloba Kitagawa. 2015;29(12):1956-63.
100. III Colado-Velázquez J, Mailloux-Salinas P, Medina-Contreras J, Cruz-Robles D, Bravo GJPR. Effect of Serenoa repens on oxidative stress, inflammatory and growth factors in obese wistar rats with benign prostatic hyperplasia. 2015;29(10):1525-31.
101. Kumar R, Gupta YK, Singh S, Arunraja SJPr. Picrorhiza kurroa Inhibits Experimental Arthritis Through Inhibition of Pro-inflammatory Cytokines, Angiogenesis and MMPs. 2016;30(1):112-9.

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