



# “ANTI-INFLAMMATORY ACTIVITY OF HERBAL PLANTS: A REVIEW”

*Shifali Verma<sup>1</sup>, Diksha Gupta<sup>1\*</sup>, Dr.Ujjwal Nautiyal<sup>2</sup>,*

*<sup>1</sup>Student, <sup>\*1</sup>Assistant Professor of Pharmaceutics, <sup>2</sup>Principal,*

*<sup>\*1</sup>Assistant Professor of Pharmaceutics*

*Genba Sopanrao Moze College of Pharmacy, Wagholi, Pune.*

## ABSTRACT:

In this review article we have discuss about the overview of inflammation and herbal plants which are used in the treatment of inflammation. Numerous diseases, including rheumatic and immune-mediated ailments, diabetes, cardiovascular accidents, and other conditions, are included in the broad category of pathologic states known as inflammation. We have discuss few plants whose anti-inflammatory properties have been proven in both clinical and experimental research. For a very long time, medicinal plants were the primary treatment for a wide range of illnesses. Nowadays, many medications have been created from the principles of conventional medicine. This essay examines a few medicinal plants and their primary ingredients that have anti-inflammatory properties that can be used to treat various inflammatory diseases. Here, we give a succinct summary of the subject for quick and simple reading on the significance of medicinal plants .We anticipate that this analysis will help to clarify how these natural anti-inflammatory substances work and spark the curiosity of researchers working to develop cutting-edge therapeutic strategies for the treatment of a variety of inflammatory disorders.

**Keywords:** *Herbal drugs, Anti inflammation, Mediators, Curcumin ,Ginger.*

## INTRODUCTION:

An vital immunological response, inflammation is a host defence mechanism of the body that helps it survive infections and injuries while preserving tissue homeostasis under toxic situations. Modern thinking holds that inflammation is a good process that develops as a result of a disturbance or illness. A typical reaction to any unpleasant stimuli that endangers the host is inflammation, which can range from a localised to a broad response [1 ].Or, to put it another way, "Inflammation is the major and complex response of the body against infection upon tissue injury."Today, there is a greater understanding of both the aggressive and restorative functions of inflammation. But in some cases, there doesn't seem to be any improvement, and an on-going state of inflammation develops that could last the rest of the person's life. Rheumatoid arthritis, osteoarthritis, inflammatory bowel illnesses, retinitis, multiple sclerosis, psoriasis, and atherosclerosis are a few examples of these inflammatory diseases. Aspirin and other nonsteroidal anti-inflammatories are only a few of the safe and efficient anti-inflammatory medications that are now on the market to treat this issue. Many more are also being researched and developed. Therefore, these substances are referred to be anti-inflammatory agents since they serve to lessen the inflammatory response [2]. There are a wide range of pathological and physiological responses to inflammation.

## TYPES OF INFLAMMATION

Acute inflammation- Acute inflammation usually has becoming within minutes or at most hours after tissue injury, and may be characterized by the classical symptoms of redness, heat, oedema[3].It's a short term process. It is characterized by the exudation of fluids[4] and plasma proteins and the migration of leukocytes, most importantly neutrophils into the injured area. This acute inflammatory response is useful to the defence mechanism aimed at killing of bacteria, virus and parasites while still facilitating wound repairs.

Chronic inflammation - Chronic inflammation is of a more prolonged duration and histologically by the presence of lymphocytes and macrophages, resulting in fibrosis and tissue necrosis. The chronic inflammation increases the development of the degenerative diseases such as rheumatoid arthritis, atherosclerosis, heart disease, Alzheimer, asthma, acquired immunodeficiency disorder (AIDS), cancer, congestive heart failure, multiple sclerosis, diabetes, infections, gout, IBD-inflammatory bowel disease, aging and other neurodegenerative CNS depression, Chronic inflammation also has been implicated as part of the cause of the muscle loss that occurs with aging all of which are associated with immunopathological that appears to play a key role in the onset of the condition[5]. **Figure 1:** indicates the health complications associated with acute and chronic inflammations.

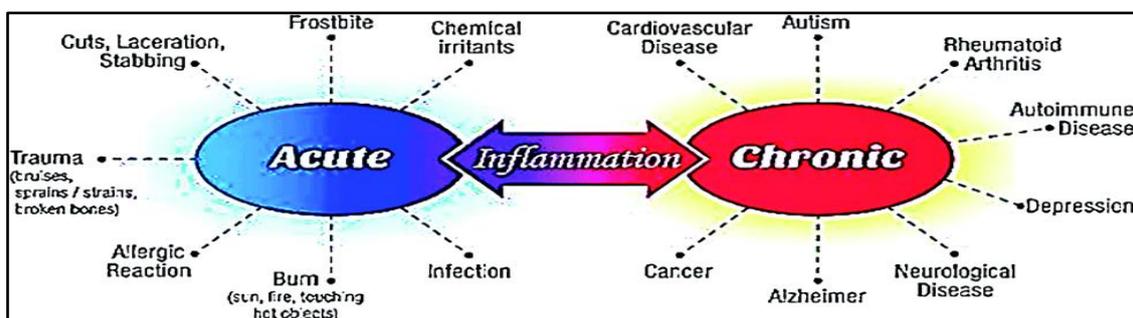


fig. 1 : serious health problems resulting from acute and chronic inflammations.

## PROCESS OF INFLAMMATION

A localized protective response of the body's cells and tissues to an allergic or chemical irritant, damage, and/or infections. Pain, heat, redness, swelling, and loss of function are the hallmarks of inflammation, which are brought on by dilated blood vessels that increase blood flow and by expanded intracellular spaces that allow leukocytes, protein, and fluids to move into the inflamed areas [6,7]. This is very necessary to understand the role of chemical mediators of inflammation. These mediators are the substances released as plasma proteins, or that come from cells like mast cells, platelets, neutrophils and monocytes/macrophages. They are triggered by allergic or chemical irritation, injury and infections. These mediators, depending on the duration of injury determine the severity of inflammation and are termed pro-inflammatory fundamental factors. These chemicals may improve vascular permeability, encourage neutrophil chemotaxis, stimulate smooth muscle contraction, boost direct enzymatic activity, generate discomfort, and/or mediate oxidative damage[8] because they bind to specific target receptors on the cells. Nitric oxide, prostaglandins, leukotrienes, vasoactive amines (histamine, serotonin), and cytokines are a few examples of chemical mediators. Even However, some of the cytokines (IL-3, 4, 5, 6, 10, and 13) released are advantageous since they function as anti-inflammatory mediators within the cells[9].

## 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 [10]. We discussed about herbs which have been tested for anti-inflammatory activity in clinical and laboratory studies. Also, other listed herbs have demonstrated good anti-inflammatory activity in clinical and experimental design [11,12]. 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) [13,14].

### 4.1 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 [15,16,17].

### 4.2 Bradykinin

Bradykinin 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 [18,19]. After immunological challenge, kinins chemical mediators are also present in nasal secretion and kininogens is produced from mast cells of the lung [20,21,22,23].

### 4.3 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 [24]. In other words, NSAIDs drugs inhibit the release of PGs chemical mediators that contributes to inflammation, fever, and pain.

#### 4.4 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 [25]. Through this pathway aspirin prevented the formation of the intermediate endoperoxide (Fig. 3) [26]. The TXA2 chemical mediator is another prostaglandin chemical exhibited opposite behavior to that of TXA2 [27]. 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 [28,29].

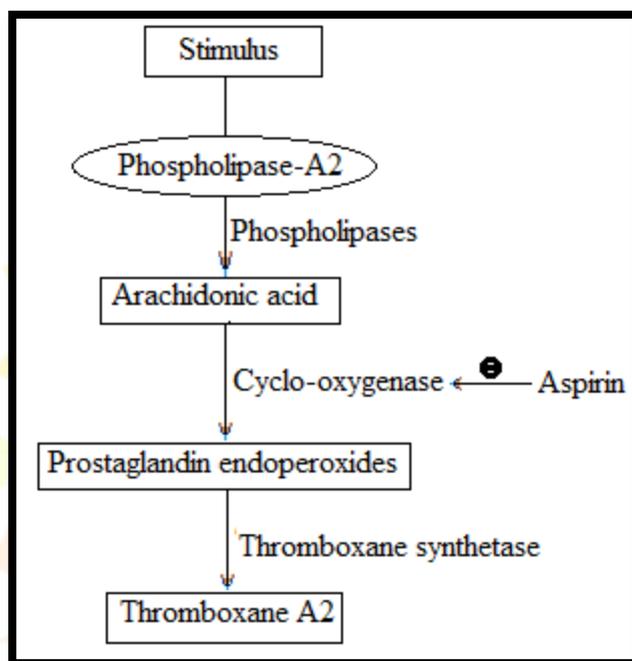


fig.3: action of aspirin on platelets

#### 4.5 Leukotrienes

The leukotrienes Slow-reacting anaphylaxis substance (SRS-A) was identified as a product of AA metabolism's 5-lipoxygenase pathway [30,31], 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) [32]. There's some evidence that lipo-oxygenase products leads to inflammatory vascular changes.

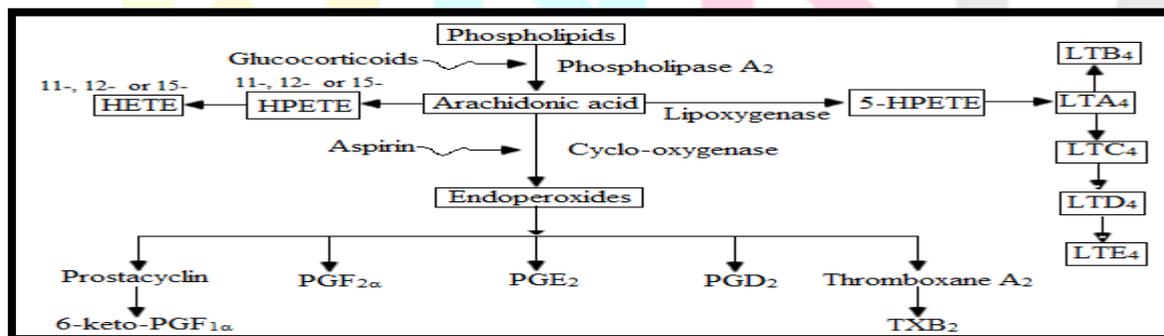


fig. 4: catabolic pathways of aa

#### 4.6 Platelet-Activating Factor (PAF)

The phospholipid PAF-acether is produced from the most proinflammatory cells, through the action of phospholipase A2 mediated through vascular endothelial cells and platelets [33]. It usually causes inflammatory response in various species of animals and human skin [34].

#### 4.7 Interleukin-1

IL-1 is a polypeptide formed by activated macrophages mimicking chronic inflammation symptoms [35,36]. It also called as endogenous pyrogen. IL-1-like activity (equivalent to 1.69 U/mi) was observed in synovial fluids of rheumatoid arthritis patients [37]. Its actions include lymphocytes activation and fever production which is mediated by release of PGE<sub>2</sub>.

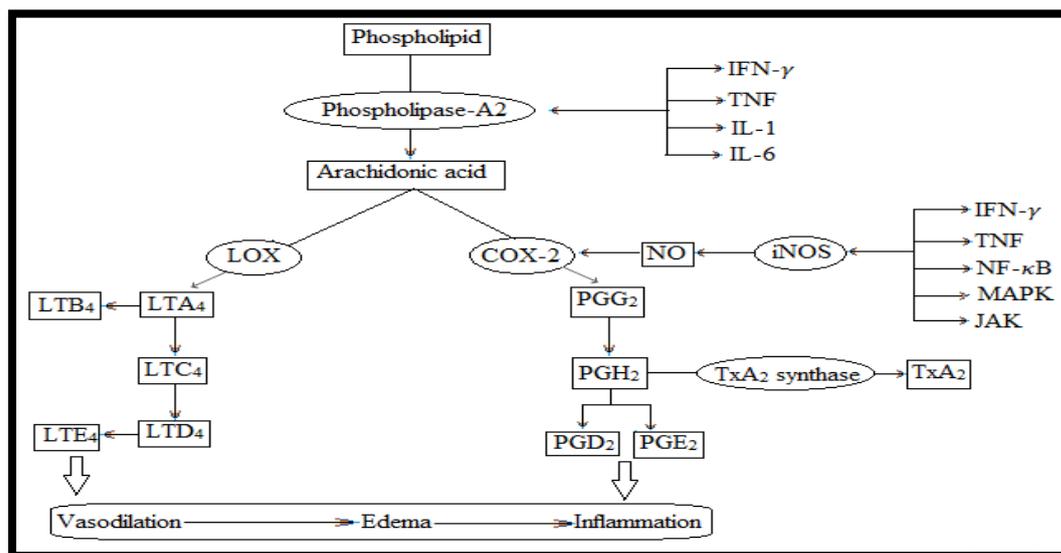


fig. 2:inflammation pathway

Now there is a need for the new safe, potent, nontoxic or less toxic anti-inflammatory drug. Plant medicines are great importance in the primary healthcare in many developing countries. In Ayurveda utilizing a large number of medicinal plants were used for the treatment of human diseases [38]. The medicinal plants occupied their exclusive place in human life. It provides more information about the use of plants or plant parts as medicine [39]. Plant-based drugs used in the traditional medicine have paid great attention because it is easily available, less expensive and also have no side effects [40]. Plants have the ability to synthesize a wide variety of phytochemical compounds as secondary metabolites. Many of the phytochemicals have been used to effectively treat the various ailments for mankind. Plants have a great potential for producing new drugs and used in traditional medicine to treat chronic and even infectious diseases [41]. In recent years, there is an increasing awareness about the importance of medicinal plants. Many medicinal plants have exhibit potent anti-inflammatory effect in the treatment of inflammation by using various experimental models.

#### Natural Source as an Anti-Inflammatory Agents:-

Different modern drugs which have single active components that target one specific pathway, moreover plants as a herbal medicines like Ayurvedic medicine work in a way like drug as a whole, that depends on an orchestral approach. A plant contains a massive amount of different molecules that act synergistically on targeted elements of the complex cellular pathway [42]. Medicinal plants have been source of wide variety of biologically active compounds for many centuries and used extensively as crude material or as pure compounds for treating various disease conditions [43]. By using of herbal medicines becoming popular due to toxicity and side-effects or adverse effect of allopathic medicines. Medicinal plants is a base for preparation of Ayurvedic formulation which play an important role in the development for drug discovery of effective therapeutic agents. There are over 1.5 million practitioners of traditional medicinal system using medicinal plants in preventive, promotional and curative applications [44,45].

#### HERBAL DRUGS USED FOR TREATMENT OF INFLAMMATION

**1) CURCUMA LONGA** (Turmeric in english) It is an indian indigenous plant. Curcumin is the most important secondary metabolite of curcuma longa, which is responsible for anti inflammatory effect of this plant. [46] Many clinical trials have been done for proving the anti inflammatory effect of curcumin. Curcumin can be effective in improving inflammation of rheumatoid arthritis (RA) and reducing clinical manifestation of RA, such as joint swelling and morning stiffness. [47] In treatment of irritable bowel syndrome (IBS) curcumin is beneficial. [48] Treatment with the C. longa methanolic extract (100 and 200 mg/kg, oral) reduced peribronchial inflammation, alveolar congestion, and intraluminal hemorrhage in the bronchus, total and differential WBC count as well as lung pathological changes in sensitized rats.



fig 5:curcuma longa

**2) ZINGIBER OFFICINALE** (common name is ginger in English) It is a native plant from south-east Asia. *Z. officinale* extract shows different and inconsistent effects when administered orally. In patients with osteoarthritis, ginger had efficacy in pain improvement identical to Diclofenac 100 mg and also no side effects [49] Ginger, has been used in folk medicine as a medicinal plant, as well as a spice and food in many countries. Numerous experimental and clinical trials have proven ginger for its range of therapeutic activities such as antibacterial, antiparasitic, antidiabetic, antiemetic, hypolipidaemic and hepatoprotective properties. The patients had musculoskeletal and rheumatism ginger powder had an ameliorative effect.[50]



a)Plant b) Rhizomes

fig 6:zingiber officinale

**3) ROSMARINUS OFFICINALIS** (common name is Rosemary in English) It belongs to the *Lamiaceae* family, is an aromatic evergreen plant and dark green leaves. It is commonly known as rosemary and is native in countries of the Mediterranean region. Fresh and dried leaves represent the most relevant part of the plant and can be used as a spice or to make herbal tea. The aerial parts of *Rosmarinus officinalis* have been widely used in different cultures as a food preservative and also as a flavoring agent in foods, beverages, and in cosmetics[51,52,53]



fig 7:rosmarinus officinalis

**4) OLEA EUROPEA** (Common name olive in English) The whole plant is useful for heart, blood pressure, cholesterol diseases. It is also prevent viral infection. It diminished performance in risk of coronary heart disease has been demonstrated in healthy individuals and metabolic syndrome patients.[54,55] Oral olive oil has accelerated wound healing process and has alleviated hospitalizing duration in deep second-degree and more burn wound patients in comparison with sunflower oil (SFO).[56]



fig 8: olea europea

**5)GLYCINE MAX** (common name soyabean in english) It protects against shock caused either by blood loss or endotoxin. It reduces alcohol levels in the stomach and improves recovery from alcoholic hepatitis.[57] Glycine may be useful clinically for the treatment of sepsis, adult respiratory distress syndrome, arthritis, and other diseases with an inflammatory component. And dietary glycine is protective in the kidney against cyclosporin A toxicity and ischemia-reperfusion injury.



fig 9: glycine max

**6)RIBES NIGRUM** (common name is black-currant in English) The blackcurrant bud extract is indicated in Allergic rhinitis: it, also often called “hay fever” is characterized by an inflammation of the nasal mucosa. In 2000 its gain popularity in the U.S. It contains high phenolic compounds like anthocyanins. And the major anthocyanins in blackcurrant are delphinidin-3-rutinoside, cyanidin-3-rutinoside, delphinidin-3-glucoside, and cyanidin-3-glucoside. These all anthocyanins contains antioxidant, anti-inflammatory, and anti-microbial properties[58.59.60.61]. Polyphenol-rich blackcurrant extract (BCE) prevent inflammation in the liver and adipose tissue of diet-induced obesity (DIO) mice.



fig 10: ribes nigrum

**7)SALVIA OFFICINALIS** (commonly known as sage in english) Chloroform extract of sage leaves has shown atopic anti-inflammatory effect in mice. The plant of salvia officinalis represent basis for phytochemical products with beneficial effects for health or play an active role in improving the state of health.[62] This plant has also been used for a long time in traditional medicine to fight fever, rheumatism, perspiration, sexual malfunction, as well as in the treatment of chronic bronchitis or of various mental diseases[63]. The best known species are Salvia Officinalis, Salvia Fruticosa and Salvia Lavandulifolia[64].



fig 11: salvia officinalis

**8) BORAGO OFFICINALIS** (common name is Borage in English) Gamma linoleic acid (GLA) is a rich source of this plant, which contains 25% of GLA, by elevating prostaglandin-E (PGE) level that leads to cyclic adenosine monophosphate (cAMP) augmentation; GLA could count as a strong suppressor of  $\text{TNF-}\alpha$ . In rheumatoid arthritis (RA) borage oil shows anti-inflammatory effect [65]. In asthma and allergic reactions these herbs are used.



fig 12: borago officinalis

**9) OENOTHERA BIENNIS** (common name is evening primrose in English) GLA, linear aliphatic alcohols (e.g., Tetracosanol), and phenolic compound (ferulic acid) are the active components of evening primrose oil which have had protective roles against pro-inflammatory markers [66]. Primrose oil has a greater anti-inflammatory effect than borage oil because primrose oil has sterols such as  $\beta$ -Sitosterol and Campesterol that have had modulator effect on nitric oxide (NO),  $\text{TNF-}\alpha$ ,  $\text{IL-1}\beta$ , and thromboxane B2 (TXB2) leading to suppressing COX-2 gene expression [67]. Multiple sclerosis patients (a chronic inflammatory disorder) have taken primrose oil because of the clinical effectiveness of the oil. In an RCT on RA, researchers have recorded subjective improvement and reduction in using NSAIDs without any improvement in clinical measurements [68].



fig 13: oenothera biennis

**10)HARPAGOPHYTUM PROCUMBENS (DEVIL CLAW)** Harpagophytumprocumbens (Devil’s Claw) It contains abundant metabolites so substantiated as an anti-inflammatory component[69]. In another preclinical study, devil’s claw has shown no efficacy in improving carrageenan-induced edema in the hind foot of the rat[70]. Over an RCT, the effectiveness of Devil’s claw in osteoarthritis remission has been assessed. At the end of treatment period, anti-inflammatory effects of H. procumbens have been observed[71]. Devil’s Claw produces a strong anti-inflammatory action. It reduces swelling and pain in the joints and improves their flexibility and range of movements. It also acts as an antioxidant and prevents damage to the joint tissues caused by free radicals.

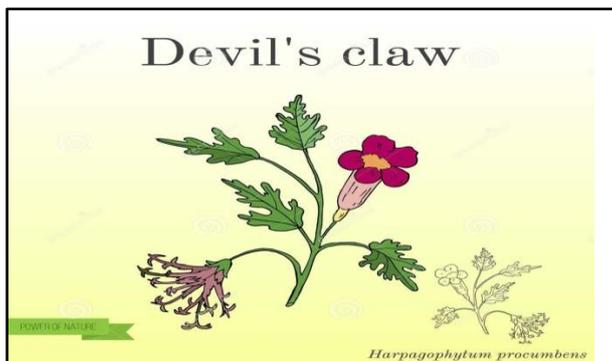


fig 14:harpagophytum procumbens

**11)BOSWELLIA SERRATA** ( common name is Indian olibanum in english) It is an oleo gum resin of *Boswellia* tree, which is native in India.In patients with osteoarthritis efficacy of *Boswelliaserrata* extract has been substantiated, dramatic alleviation in the frequency of joint swelling and pain and augmentation in joint flexibility and walking distance have been observed at the end of treatment period[72]. *B. serrata* has been clinically effective in the process of ameliorating the disease Collagenous colitis which is an inflammatory bowel disease (IBD) in target therapy group compared to the placebo group[73]. The combination of *B. serrata* with *C. longa* and *Glycyrrhizaglabra* has been effective on improvement of asthmatic patient’s symptoms[74]. and it has had topical anti-inflammatory impress as well as systemic effects[75].



fig 15: boswellia serrata

**12)ROSA CANINA**(common name is Dog rose in english) The Anti- inflammatory effect of rosehip refers to the seed. rosehip powder has reduced ESR and improved quality of life in RA patients; thus, it might be used as a supplement besides the standard treatment of RA.[76] Galactolipid is an active component in rosehip powder which its NO inhibitory potential has been confirmed through laboratory and in vitro studies[77,78]. On COX-1, COX-2, and LTB4 this plant’s fruit have had a downregulatory effect[79].



fig 16:rosa canina

**13)URTICA DIOICIA**(common name is stinging nettle in English) Nettle leaf has been investigated to prove its anti-inflammatory effect in a pilot study. When Urticadioica combined with NSAIDs give an outstanding synergistic effect[80]. Leaf extract of U. dioica has had inhibitory potential on proinflammatory transcription factor NF-κB (scientific studies have shown elevation in NF-κB in synovial fluid of RA patients)[81]. Leaf extract has had anti-inflammatory potential in allergic rhinitis by the following pathways: antagonizing H1-receptor, reducing of PGD2 production (allergy specific prostaglandin), and inhibitory effect on mast cell tryptase.



fig 17:urtica dioicia

**14)UNCARIA TOMENTOSA** (commonly known as cat’s claw in English) on 45 patients efficacy and safety of this plant have been tested in improving OA of the knee[82].Modest benefit of this herb in alleviating pain, swelling, and tenderness of joint has been shown in the treatment group in comparison with the placebo group[83], respiratory inflammation in mice cats claw extract has had protective action[84]. This plant’s bark has demonstrated anti-inflammatory action exactly the same as dexamethasone in an animal model.



fig 18:uncaria tomentosa: a) stem, b) thorns, c) abaxial face of leaves, (showing the ribs that seem " fine veins " ) d) inflorescence, and e) seeds. uncariaguianensis: f) stem, g) thorns, h) sheets, and i) fruit.

**15)ELAEAGNUS ANGUSTIFOLIA** (common name is oleaster in english) The effectiveness of Oleaster in the treatment of oral lichen planus (OLP) lesion has been evaluated in an RCT with 28 patients[85]. Calcium is also found with high levels in this plant and traditionally the flowers of Russian olive were considered a good source of Ca<sup>2+</sup> among people of Iran. In animal model oleaster extract has demonstrated an anti inflammatory effect and Aqueous extract of this fruit has shown anti-inflammatory properties in mice through COX-1 and COX-2 inhibition.[86,87].

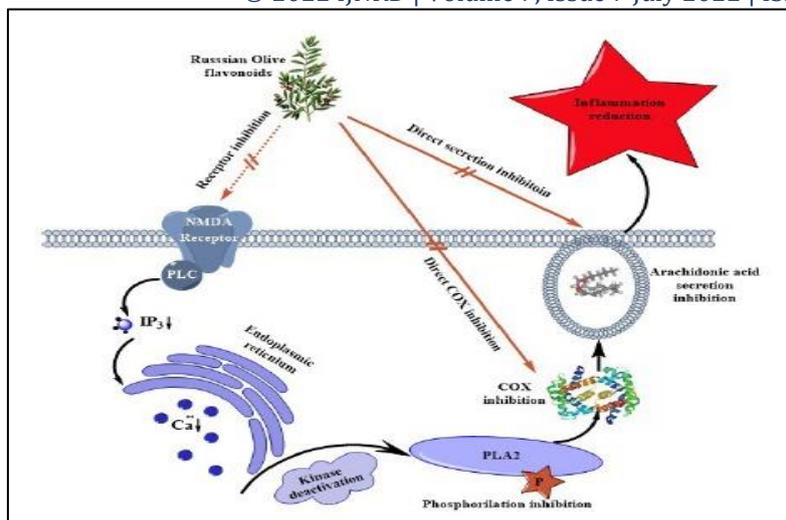


fig 19:anti-inflammatory mechanism of e. angustifolia

The above figure shows Anti-inflammatory mechanism of *E. angustifolia*: Flavonoids of *E. angustifolia* can directly block active sites of COX and the secretion of the arachidonic acid. Thus, arachidonic acid cannot change into prostaglandins and leukotrienes, the most important mediators of vasodilation, platelet activation and inflammation (filled arrows). Another proposed mechanism describes the importance of flavonoids in blocking NMDA receptors. NMDA receptor inactivation leads to a significant calcium secretion reduction from PLC pathway and finally no kinase, PLA2 and COX activation, respectively (dashed arrow).

**16)VACCINIUM MYRTILLUS** (commonly known as bilberry in English) It is one of the richest natural sources of anthocyanins. These polyphenolic components give bilberry its blue/black color and high antioxidant content, and they are believed to be the key bioactives responsible for the many reported health benefits of bilberry and other berry fruits. bilberry is widely used to improve night vision and to decrease vascular permeability and capillary fragility; moreover, the berry has various other reputed health benefits, like anthocyanin-related antioxidant effects and anti-inflammatory effects.[88,89,90,91]. The antioxidant properties of bilberry may be responsible for at least some of the anti-inflammatory effects reported[92,93].



fig 20:vaccinium myrtillus

**17)AZADIRACHTA INDICA** (common name in english is neem) Nimbidin, a component of *Azadirachta indica*, has been shown to possess potent anti-inflammatory and antiarthritic activity. Nimbidin suppresses the functions of macrophages and neutrophils involved in inflammation[94,95] Most important properties of *azadirachta indica* are immune stimulating properties. *Azadirachta indica* leaves early in the morn-ing for twenty four days protect the body from diseases like diabetics and hypertension[96]. *Azadirachta indica* twigs contain antiseptic ingredients necessary for dental hygiene and prevents tooth decay, periodontal diseases, infections, tooth decay, bleeding gums and sore gums[97].



fig 21:azadirachta indica

**CONCLUSION:**

Natural herbs offer a safer, more reliable alternative to pharmaceutical anti-inflammatory drugs. The phytoconstituents have an equivalent mode of action to synthetic compounds, making them just as effective. Future studies should concentrate on the molecular mechanisms behind the numerous therapeutic uses of these herbal plants for various ailments. Recent patents on herbal plants and anti-inflammatory medications have been covered, and they shed light on the situation now and the hopes for the future. Due to their accessibility, availability, inherited practise, economic viability, and perceived efficacy, medicinal plants have been used to treat a variety of diseases since ancient times. This review will aid current and upcoming researchers in their further study of these important medicinal plants.

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