



# Natural Medicinal Resources for Treating Inflammatory Conditions

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## ABSTRACT

Inflammation is a part of the intricate biological response of vascular tissues to undesirable stimuli such as infections, damaged cells, or irritants. Symptoms include redness, swollen joints, joint soreness, stiffness, and loss of joint function. Inflammation is now treated using non-steroidal anti-inflammatory drugs (NSAIDs). These drugs, however, increase the chance of blood clots, which may lead to heart attacks and strokes. As a consequence, the development of effective anti-inflammatory drugs based on natural substances is being studied. Natural products are a great source for the creation of innovative medications due to their chemical diversity. Many inflammation-related disorders may be treated with a natural product made from medicinal plants. The most often prescribed anti-inflammatory medicine has a slew of undesirable side effects. Because of these negative effects, researchers are looking for novel medications that have fewer or no side effects. Hundreds of phytoconstituents have been reported to have a range of pharmacological effects, however most of these researches are just of academic interest, and only a few make it into clinical trials. The purpose of this research is to assemble data on phytochemicals from herbal plants that have been tested in inflammatory models using cutting-edge scientific approaches.

**Key Words:** Herbal Medicine, Inflammation, Natural Resources, Medicinal Plants, Cyclooxygenase, Anti-inflammatory

## INTRODUCTION

An uncontrolled inflammatory response is the root cause of a wide range of disorders, including autoimmune diseases, allergies, metabolic syndrome, cancer, and cardiovascular dysfunctions, all of which place a significant financial burden on individuals and, as a result, on society. Cyclooxygenases (COXs), also known as cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2), are the main enzymes involved in the formation of prostaglandins, prostacyclins, and thromboxanes, which are involved in inflammation, pain, and platelet aggregation (COX-2). Despite their negative renal and stomach side effects, steroidal and non-steroidal anti-inflammatory medicines (SAIDs and NSAIDs, respectively) are presently the most often prescribed treatments for acute inflammatory disorders. These drugs stop COX-1 and COX-2 enzymes from working. Humans have traditionally utilized non-steroidal anti-inflammatory drugs (NSAIDs). As a result, long-term usage of these pharmaceuticals results in undesirable side effects (gastric lesions, cardiovascular, renal,

and gastrointestinal damage) as well as damage to human biological systems including the liver and gastrointestinal tract. [1]

## Process of Inflammation

Inflammation is the body's localized defence reaction to irritation, injury, and/or infection caused by allergies or chemicals. Inflammation causes pain, heat, redness, swelling, and loss of function via dilatation of blood vessels, which increases blood flow, and expanded intracellular spaces, which enable leukocytes, protein, and fluids to enter the inflamed tissues. It's crucial to understand how chemical mediators of inflammation work. Plasma proteins or chemicals generated by cells such as mast cells, platelets, neutrophils, and monocytes/macrophages are examples of these mediators. They may be triggered by allergies or chemicals, as well as traumas and illnesses. These mediators, also known as pro-inflammatory basic factors, have an impact on the severity of inflammation based on the degree of damage. By

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binding to specific target receptors on cells, these substances may increase vascular permeability, promote neutrophil chemotaxis, induce smooth muscle contraction, raise direct enzymatic activity, cause pain, and/or mediate oxidative damage. Chemical mediators include prostaglandins, nitric oxide (NO), vasoactive amines (serotonin, histamine, etc.), leukotrienes, and cytokines. Some cytokines (IL-3, IL-4, IL-5, IL-6, IL-10, and IL-13) are beneficial because they act as anti-inflammatory mediators inside the cells. [2]

### Mechanism of inflammation

Prostaglandin synthesis, interleukin or other chemo toxin generation, adhesive protein receptor activation, and platelet-activating factors are all involved in the inflammatory process (PAFs). They're all capable of acting as chemotactic agonists. Phospholipase A hydrolyzes membrane phospholipids into arachidonic acid, which subsequently acts as a substrate for cyclooxygenase and lipoxygenase enzymes, resulting in prostaglandins PGE<sub>2</sub>, PGH<sub>2</sub>, and leukotrienes such as LTC<sub>4</sub>, LTB<sub>4</sub>, and others. Interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF- $\alpha$ ) are two cytokines that play essential roles in the inflammatory process. IL-1 and TNF are considered to mediate physiologic responses to bacterial lipopolysaccharide (LPS, also called endotoxin). They're made by monocytes and macrophages, as well as adipocytes and other cells. They work along with a variety of cytokines and growth factors to induce gene expression and protein synthesis in a variety of cells, mediating and enhancing inflammation (including IL-8 and granulocyte-macrophage colony-stimulating factor). By assisting in the creation of nitric oxide from endothelium-derived releasing factor, which promotes vasodilatation and assists in the adhesion of platelets and other chemotoxins, the generation of prostaglandin (PGE<sub>2</sub>) or prostacyclin (PGI<sub>2</sub>) enhances blood flow and blood vessel permeability (bradykinin, histamine). Despite the fact that polymorphonuclear leukocytes, eosinophils, and monocytes are generally pro-inflammatory, LTB<sub>4</sub> is a potent chemotactic agent. At higher dosages, LTB<sub>4</sub> causes polymorphonuclear leukocyte aggregation, as well as degranulation and superoxide generation. LTB<sub>4</sub> promotes neutrophil adhesion to vascular endothelial cells and trans-endothelial migration, as well as the production of pro-inflammatory cytokines by macrophages and lymphocytes [3].

### Types of inflammation

Acute inflammation occurs minutes or hours after tissue injury and is characterized by redness, heat, and edema. It's a simple technique. It is defined by the exudation of fluids and plasma proteins, as well as the migration of leukocytes, especially neutrophils, into the injured area. The defense mechanism's objective of removing bacteria, viruses, and parasites while enabling wound healing to progress is aided

by this first inflammatory response. Chronic inflammation is marked by the presence of lymphocytes and macrophages in the histology, which leads to fibrosis and tissue necrosis. Heart disease, rheumatoid arthritis, Alzheimer's disease, atherosclerosis, acquired immunodeficiency syndrome (AIDS), asthma, congestive heart failure, cancer, diabetes, multiple sclerosis, gout, infections, ageing, inflammatory bowel disease (IBD), and other neurodegenerative CNS depressions are all promoted by chronic inflammation. Chronic inflammation has also been related to muscle mass loss as individuals become older. They're all connected to immunopathological variables that seem to have a part in the disease's onset. [4]

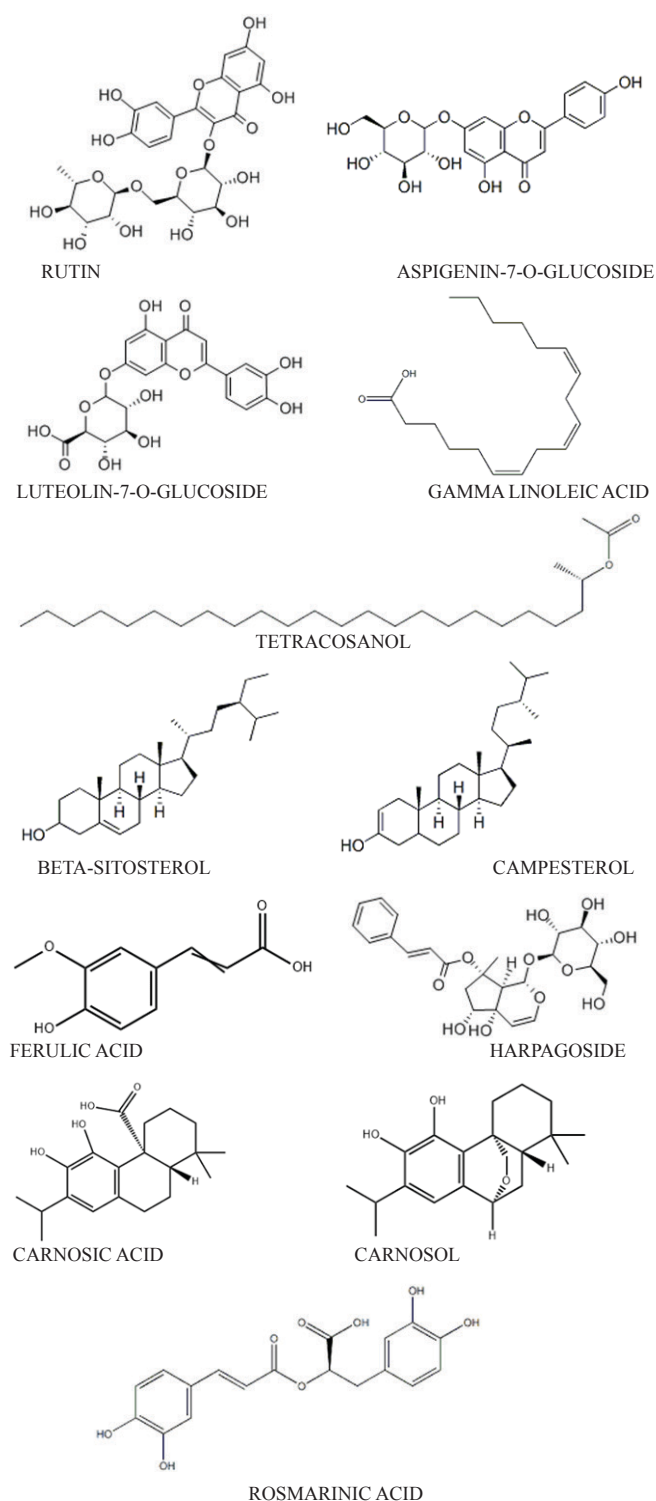
### Approaches for treatment

SAIDs, NSAIDs, and immunosuppressants are among the drugs used to control and inhibit inflammatory crises, but they all have side effects, while our major goal in practice is to employ the lowest effective dosage with the maximum effectiveness and fewest side effects. As a result, natural anti-inflammatory components must be added in drug treatment in order to improve pharmacological effectiveness while reducing unpleasant side effects. Herbal medications are causing medical problems, thus we need to learn more about them. Although most herbal prescription suggestions come from complementary, alternative, and traditional medicine, contemporary medicine must confirm these prescriptions using scientific means before employing them in practice.[5] In this study, we looked into the plants and found the greatest clinical evidence of their anti-inflammatory qualities.

## NATURAL RESOURCES WITH ANTI-INFLAMMATORY POTENTIALS

### Achilleamillefolium (Asteraceae)

Achilleamillefolium L. is a perennial plant native to Europe that is well-known in traditional medicine for its anti-inflammatory properties. The plant has traditionally been used to treat wounds, burns, edema, and irritated skin on the outside. In investigations, isoprenoids and phenolics, two forms of secondary metabolites, were shown to have a significant role in anti-inflammatory effects. Aqueous and alcoholic extracts of A. millefolium are used to treat gastrointestinal, hepatobiliary, and antiphlogistic disorders internally in traditional medicine. The topical anti-inflammatory activity of sesquiterpenes is related to the inhibition of arachidonic acid metabolism. The three flavonoids discovered in the crude extract and concentrated in the flavonoid fraction are rutin, aspigenin-7-O-glucoside, and luteolin-7-O-glucoside. Human neutrophil elastase and matrix metalloproteinases (MMPs), which are connected to anti-inflammatory activities, are inhibited in vitro



**Figure 1:** Phytoconstituents mediating prominent anti-inflammatory activity.

by the crude plant extract and two fractions enriched in dicaffeoylquinic acids and flavonoids. [6]

**Aconitum heterophyllum (Ranunculaceae)**

*Aconitum heterophyllum* is a plant that is also known as

‘Ativisha’ or ‘Patis’ in Ayurveda. It’s used to treat disorders of the neurological system, digestive system, fever, and rheumatism. The ethanolic extract of *A. heterophyllum* root contains alkaloids, glycosides, flavonoids, and sterols. By blocking prostaglandin pathways, plants with various chemical families of compounds have been proven to have potent anti-inflammatory capabilities. A typical approach for assessing the transudative and proliferative components of chronic inflammation is cotton pellet-induced granuloma. The weight of the wet cotton pellets determines the amount of granulomatous tissue. The weight of wet cotton pellets was demonstrated to be suppressed in a dose-dependent way by the administration of *A. heterophyllum* extract, with the higher dosage of this extract demonstrating inflammatory inhibition remarkably comparable to that of diclofenac sodium. The ability of the ethanolic root extract to prevent sub-acute inflammation by altering arachidonic acid metabolism has been shown in the literature. [7]

**Adhatodavasica (Acanthaceae)**

The Acanthaceae family includes *Adhatodavasica* L., a native plant. In traditional systems of medicine all throughout the world, the plant has been used as herbal remedy for coughs, colds, chronic bronchitis, whooping cough, sedative expectorant, asthma, anthelmintic, antispasmodic, rheumatic unpleasant inflammatory swellings, and rheumatism. Fresh juice, decoction, infusion, and powder are all available forms of the drug. It may also be found as an alcoholic extract, a liquid extract, or syrup. This plant contains alkaloids, tannins, flavonoids, terpenes, sugars, and glycosides. The anti-inflammatory activities of ethanolic extract were investigated using a carrageenan-induced paw edema test and a formalin-induced paw edema test in albino rats. In a dose-dependent manner, the ethanolic extract of *A. vasica* reduced carrageenan-induced paw edema and formalin-induced paw edema. [8]

**Bacopamonnieri (Scrophulariaceae)**

*Bacopamonnieri* is a creeping, glabrous, succulent plant that roots at nodes and thrives in marshes and muddy shorelines. It has long been used as a brain tonic to aid memory, learning, and concentration. In India and Pakistan, the plant is also used as a heart tonic, digestive aid, and to improve respiratory function in cases of bronchoconstriction. In carrageenan-induced rat paw edema, the plant has an anti-inflammatory effect, decreasing edoema by 82 percent when compared to indomethacin. *B. monnieri* significantly reduced the activities of 5-lipoxygenase (5-LOX), 15-lipoxygenase (15-LOX), and COX-2. The presence of triterpenoid and bacoside in the plant extract has anti-inflammatory characteristics, which may explain its usage in traditional medicine to treat a variety of inflammatory illnesses by lowering TNF- $\alpha$  and IL-6 levels. This was investigated in vitro using lipopolysaccharide-

activated peripheral blood mononuclear cells and peritoneal exudate cells. As a consequence, *B. monnieri* has the ability to modulate the release of pro-inflammatory mediators and thereby decrease inflammation. [9]

### **Boragoofficinalis (Boraginaceae)**

The gamma-linoleic acid (GLA) content of this plant (also known as borage) is significant (approximately 25 percent). GLA functions as a potent TNF-suppressor because it boosts prostaglandin-E (PGE) levels, which increases cyclic adenosine monophosphate (cAMP). Borage is not suggested for usage during pregnancy due to the risk of miscarriage. The anti-rheumatoid arthritis (RA) properties of borage seed oil were investigated in two RCTs: the first compared 1.4 g/day borage seed oil versus placebo in RA patients, with the treated group showing a 36.8% improvement after six months of treatment. Patients were given 2.8 g of borage seed oil per day for six months in the second study, and there was a considerable improvement in RA manifestation at the conclusion of treatment: 64 percent in the treatment group compared to 21 percent in the control group. In atopic dermatitis sufferers, the anti-inflammatory benefits of borage oil were also examined. To investigate the effectiveness of this herb in treating atopic dermatitis, a total of 12 clinical investigations were done. Five of them showed an anti-inflammatory effect, and two of them saw some patients improve, while the other five trials found no evidence of remission. [10]

### **Boswelliaserrata (Burseraceae)**

The efficacy of *Boswelliaserrata* extract in osteoarthritis patients has been shown; at the end of the treatment period, there was a significant decrease in the incidence of soreness and joint swelling, as well as an improvement in joint flexibility and walking distance. Another clinical trial revealed that individuals with rheumatoid arthritis had a lower erythrocyte sedimentation rate (ESR), morning stiffness, and the need for NSAIDs throughout therapy. In one pilot study on patients with chronic polyarthritis, no significant remission in patient symptoms was identified after 12 weeks of therapy with this extract; only a modest decrease in the demand for NSAIDs was noted. Collagenous colitis is an IBD, and *B. serrata* has been demonstrated to be clinically beneficial in the treatment of this illness when compared to a placebo. After 4 weeks, the treatment group exhibited a significant drop in plasma levels of leukotriene C4 (LTC4), NO, and malondialdehyde, indicating that the combination of *B. serrata*, *Curcuma longa*, and *Glycyrrhizaglabra* relieved asthmatic patient symptoms. *B. serrata* extract has been demonstrated to alter inflammatory mediators (TNF- $\alpha$ , IL-1, IL-6, IFN- $\gamma$ , and PGE2) in vivo and in vitro studies. Boswellic acid is the main component of this gum, and it inhibits C3 convertase and suppresses the conventional

complement pathway. It also possesses cutaneous anti-inflammatory properties as well as systemic effects. [11]

### **Cassia fistula (Caesalpinaceae)**

In India's forests, the *Cassia fistula* tree is one of the most prevalent. The whole plant contains medicinal properties that may be used to treat skin problems, inflammatory disorders, rheumatism, anorexia, and jaundice. The bark extracts show a significant anti-inflammatory effect in both acute and chronic anti-inflammatory inflammation models in rats. Reactive oxygen species (ROS) both endogenous and exogenous have been related to the pathophysiology of diseases including atherosclerosis, diabetes, cancer, arthritis, and the ageing process. The presence of reactive oxygen species (ROS) complicates inflammatory diseases. The anti-inflammatory activities of flavonoids and bio-flavonoids are the main components of *C. fistula*. [12]

### **Curcuma longa (Zingiberaceae)**

Curcumin, the major component of *Curcuma longa*, has been shown to have anti-inflammatory activities in various clinical studies. In contrast to the positive control, phenylbutazone, their data suggest that curcumin may be beneficial in reducing RA inflammation and clinical symptoms including joint swelling and morning stiffness. Curcumin was also tested in people with anterior uveitis, and they achieved full remission after two weeks. Curcumin's benefit in patients with dyspepsia and/or stomach ulcers was proven in another research trial. The participants in this study achieved remission after 12 weeks (maximum). Irritable bowel syndrome (IBS) and delayed graft rejection (DGR) following kidney transplant surgery may be helped by curcumin. Curcumin also aids in the prevention of IBD and the reduction of sedimentation rates in those who suffer from it. Psoriasis and ulcerative colitis have also been reported to benefit from it (by the discerning proscriptio of phosphorylase kinase). [13]

### **Daphne pontica (Thymelaeaceae)**

*Daphne* species have been regarded to have anti-cancer qualities since the 2nd century AD. The flavonoid component daphnodorins was extracted from the roots of *Daphne pontica*, a plant that has anti-tumor properties. Several *Daphne* species have been used to treat inflammation (rheumatic pain and inflammatory disorders) by reducing the generation of PGE2 and IL-1 $\beta$  over time. [14]

### **Elaeagnusangustifolia (Elaeagnaceae)**

The effectiveness of *Elaeagnusangustifolia* in the treatment of oral lichen planus (OLP) lesions was investigated in a 28-person RCT. There was a 75 percent decrease in pain and a 50 percent-75 percent reduction in lesion size in the case group, respectively. The active treatment group demonstrated



a significant decrease in pro-inflammatory mediators such as TNF- $\alpha$  and MMP-1, as well as an increase in IL-10, in another randomized clinical investigation including 90 female patients with knee osteoarthritis (OA) (an anti-inflammatory cytokine). *E. angustifolia* extract demonstrated an anti-inflammatory effect in an animal model, however this effect was not significant when compared to sodium salicylate. The anti-inflammatory properties of this fruit's aqueous extract have been proven in rats by suppressing COX-1 and COX-2; however, there is no evidence of a relationship between corticosterone levels and anti-inflammatory activity. [15]

### **Emblicoefficialis (Euphorbiaceae)**

The subtropical and tropical tree *Emblica officinalis* may be found in China, India, Indonesia, and the Malay Peninsula. It has been used for anti-inflammatory and anti-pyretic effects in certain areas. Recent study has shown that the water part of the leaves methanol extract has anti-inflammatory properties. The impact of the fraction on the production of inflammatory mediators such as leukotriene B<sub>4</sub>, PAF, and thromboxane was studied. At modest concentrations, the water part of methanol extract decreased human PMN migration. [16]

### **Garciniamangostana (Guttiferae)**

Traditional medicine has utilized the rinds of *Garciniamangostana* fruit to treat injuries and skin disorders. Mangosteen fruit hulls include the beneficial chemicals xanthenes and mangostins. Inhibition of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 by xanthenes demonstrates their biological effects (COX-2). PGE<sub>2</sub> levels have been demonstrated to be reduced by two mangostins that inhibit COX-2 activity and NO production. Mangostin reduces PGE<sub>2</sub> release more efficiently than either histamine or serotonin, according to research. [17]

### **Harpagophytumprocumbens (Pedaliaceae)**

Harpagoside, one of *Harpagophytumprocumbens*' numerous metabolites, has been demonstrated to be an anti-inflammatory component. Devil's claw root extract has been proven to decrease COX-2 and reduce inflammation by reducing inflammatory cytokines (IL-1, IL-6, and TNF- $\alpha$ ), NO levels, and PGE<sub>2</sub>, as well as blocking arachidonic acid metabolism and eicosanoid synthesis. Devil's claw showed no impact on carrageenan-induced edema in the rat's hind foot in another preclinical study. An RCT was conducted to determine the effectiveness of Devil's claw in osteoarthritis remission. At the end of the treatment period, anti-inflammatory properties of this herb were discovered. Researchers found no remission or subjective or objective improvement with 410 mg TDS of *H. procumbens* liquid extract in a 12-week pilot investigation on patients with arthritic illness (RA and psoriatic arthropathy). This plant's

most prevalent side effect is gastrointestinal pain, thus it's not recommended for persons who have stomach or duodenal ulcers, gallstones, or diabetes. [18]

### **Lantana camara (Verbenaceae)**

Many *Lantana* cultivars contain aerial parts that are often used in folk cancer and tumor therapies. Tea brewed from leaves and flowers was used to cure fevers, influenza, and stomachaches. Anti-malarial, anti-bacterial, and anti-diarrheal qualities are among the plant's other uses. The aqueous extract of *Lantana camara* leaves has been demonstrated to be exceedingly effective and safe in the treatment of hemorrhoids in clinical investigations. The extracts also have anti-inflammatory, anti-hemorrhoid, and analgesic effects. [19]

### **Lycopodiumclavatum (Lycopodiaceae)**

Wound-healing qualities have been discovered in *Lycopodiumclavatum*, often known as club moss. When compared to Indomethacin, only the alkaloid fraction from the aerial parts and the chloroform extract demonstrated substantial anti-inflammatory effect. [20]

### **Mangiferaindica (Anacardiaceae)**

*Mangiferaindica* is a tropical and subtropical plant whose extracts have long been used in traditional medicine to treat a variety of diseases. Traditional medicine has utilized the plant for a range of ailments, including monorrhagia, leucorrhoea, bleeding piles, and pulmonary hemorrhage. Calcinedidibs of the leaves are used to eradicate warts on the eyelids. Dried powdered leaves are used to treat diabetes. Dried flowers in decoction or powder may help with diarrhoea, chronic dysentery, and gleet. In comparison to traditional medicine, when compared to Diclofenac, ethyl acetate and ethanol extracts of the roots of *M. indica* have been demonstrated to have a considerable anti-inflammatory effect. Flavonoids, which decrease prostaglandin synthesis and have anti-inflammatory characteristics, were identified in phytochemical studies. [21]

### **Oenotherabiennis (Onagraceae)**

Evening primrose (*Oenotherabiennis*) oil includes GLA, linear aliphatic alcohols (e.g., tetracosanol), and a phenolic compound (ferulic acid), all of which have been found to reduce pro-inflammatory markers. Primrose oil includes sterols such as -sitosterol and campesterol, which have modulator effects on NO, TNF- $\alpha$ , IL-1, and thromboxane B<sub>2</sub> (TXB<sub>2</sub>), lowering COX-2 gene expression, and hence has a higher anti-inflammatory effect than borage oil. The effectiveness of evening primrose oil coupled with hemp seed oil has been experimentally evaluated in multiple sclerosis (MS), a chronic inflammatory condition. Patients with MS were randomly assigned to either hemp seed/

evening primrose oil or a placebo. IFN- $\alpha$  and IL-17 levels were significantly lower in the treatment group. The risk of sickness recurrence in the therapy group was similarly lowered, demonstrating the immunomodulatory effects of these oils and their components. In an RCT on RA, researchers discovered subjective improvement and a reduction in the usage of NSAIDs, but no change in clinical measurements. Patients have also reported less morning stiffness and no changes in articular index or pain. After 12 weeks, a clinical trial on 18 people with RA reported no significant improvement in the target therapy group. [22]

### **Oleaeuropaea (Oleaceae)**

In healthy persons and metabolic syndrome patients, extra virgin olive oil (EVOO) or Oleaeuropaea has been demonstrated to have a positive effect on postprandial plasma lipopolysaccharide, pro-inflammatory cytokines, TXB2 and LTB4, as well as a lower risk of coronary heart disease. In patients with second-degree and bigger burn burns, oral olive oil has accelerated wound healing and decreased hospitalization time when compared to sunflower oil (SFO). In addition, as compared to SFO-fed mice, EVOO enhanced food consumption lowered disease activity index, tumor incidence of ulcerative colitis-associated colon cancer, and pro-inflammatory cytokines. [23]

### **Perseaamericana (Lauraceae)**

153 OA patients were recruited and treated with soybean unsaponifiables (SU) of Perseaamericana and NSAIDs in a prospective multicenter, 3-month randomized control research; after 45 days of therapy, the requirement for NSAIDs reduced, but there were no significant changes in patients' pain levels. Three clinical investigations on OA patients have shown the usefulness of ASU. Two of them showed reductions in Lequesne's functional index (LFI), pain, and disability; additionally, 71 percent of patients in the case group versus 36 percent in the control group had a 50 percent reduction in NSAID requirement; however, there were no intergroup changes in joint space width (JSW), which was considered the primary endpoint, in the last trial. During three years of hip follow-up in OA patients who used SU, there was no improvement in JSW, however there was a 20% decrease in JSW aggravation. A total of 100 people with linear scleroderma and morphea were given SU, and the results showed that if administered early enough in the disease, SU may help prevent atrophy, deformity, and contracture. Individuals with moderate to severe vulvar lichen sclerosus have been given soybean extract as a topical and dietary therapy (VLS). At the end of the 24-week treatment period, the principal signs and symptoms of disease were significantly decreased. [24]

### **Phyllanthuspolyphyllus(Euphorbiaceae)**

In the tropical and subtropical parts of India and Sri Lanka, Phyllanthuspolyphyllus is used in anti-inflammatory traditional medicine. One benzenoid and three aryl-naphthalidelnans isolated from the entire plant inhibited the production of NO and cytokines (TNF- $\alpha$  and IL-12), the main pro-inflammatory cytokines released during the early stages of acute and chronic inflammatory disorders like asthma, rheumatoid arthritis, and septic shock. These compounds may explain why P. polyphyllus has been used as an anti-inflammatory therapy in traditional medicine. [25]

### **Ribesnigrum (Grossulariaceae)**

In a 6-week clinical investigation, researchers looked at the effects of Ribesnigrum or blackcurrant oil (BCO) on RA patients; the findings showed a reduction in morning stiffness in the experimental group and a drop in pro-inflammatory mediators like IL-1 and TNF- $\alpha$  in peripheral blood monocytes. After a 24-week treatment with BC seed oil, the RA patients' disease activity symptoms were reduced. Between the placebo and case groups, there were no significant differences in clinical signs and symptoms. BC seed oil has a slight reinforcing effect on the immunological response and an inhibitory effect on PGE2 synthesis in 40 healthy volunteers over the age of 65. Another clinical research in which 12 healthy volunteers drank BC oil showed a reduction in LTB4 synthesis by polymorphonuclear neutrophils (PMN) and an increase in dihomolinoleic acid in PMN phospholipids. The plant skin extract lowered heat shock protein (HSP-70 and HSP-90), COX-2, and NF- $\kappa$ B expression in rats exposed to diethylnitrosamine (a hepatocarcinogen). [26]

### **Ricinuscommunis (Euphorbiaceae)**

Ricinuscommunis Linn. is a tropical and subtropical plant that may be found almost everywhere in the globe. In Wistar albino rats, researchers looked at the anti-inflammatory and free radical scavenging effects of a methanolic extract of the root. The methanolic extract demonstrated significant anti-inflammatory activity in a carrageenan-indexed hind paw edema model. The methanolic extract revealed significant free radical scavenging action by decreasing lipid peroxidation. The presence of phytochemicals in the plant extract, such as flavonoids, alkaloids, and tannins, might explain the observed pharmacological effect. [27]

### **Rosa canina (Rosaceae)**

The effectiveness of Rosa canina, often known as Rosehip, has been studied in patients with OA and RA. Individuals with OA had pain alleviation, decreased rescue drug usage, and stiffness, as well as a significant decline in CRP after treatment with this plant, according to the results of these trials. It's important to note that rosehip's anti-inflammatory qualities are found in the seed, not the shell. The latter assumption has been supported by two clinical studies

including OA patients. Rosehip powder has also been proven to reduce ESR and improve quality of life in RA patients, indicating that it might be taken as a supplement alongside standard RA treatment. However, 10 g of rosehip powder per day for a month showed no anti-inflammatory effect in those with RA. The rosehip ethanol extract was fractionated using different polarity solvents; the butanol and ethyl acetate fractions inhibited PGE1 and had anti-inflammatory effects in mice during the delayed phase of the inflammation process. Because n-hexane and dichloromethane extracts of fruit have a downregulatory effect on COXs and LTB4, these fractions are high in unsaturated fatty acids. Galactolipid, found in rosehip powder, has been demonstrated to have NO-inhibiting activities in laboratory and in vitro studies. [28]

### **Rosmarinus officinalis (Lamiaceae)**

In an open-label trial, the effects of rosemary (*Rosmarinus officinalis*) extract were evaluated in patients with OA, RA, and fibromyalgia for 4 weeks; C-reactive protein (hs-CRP) (an index for inflammation) was reduced noticeably in patients who had shown intensification in this index; thus, lessening in inflammation-related pain score was scrutinized during the treatment but not during the placebo period. There is evidence that *R. officinalis* possesses anti-inflammatory effects at the molecular level; as a result, rosmarinic acid may easily disrupt complement system activation by preventing C3b attachment; the dose required to have this effect is quite low (34  $\mu$ M). Additionally, rosemary extract has been shown to be more effective than omeprazole in avoiding stomach ulcers; this advantage is attributed to rosemary's capacity to limit neutrophil infiltration and diminish pro-inflammatory mediators like TNF- $\alpha$  and IL-1. In a preclinical study, however, a high dose of rosemary extract (500 mg/kg) reduced testosterone and spermatogenesis in rats, resulting in sterility. This plant helped mice heal wounds by acting as a topical anti-inflammatory. One of the primary components, carnosic acid (Figure 1), interacts with CYP-3A4 and CYP-2B6 substrates in human hepatocytes, generating toxicity with an EC50 value close to that of the conventional medication tamoxifen. [29]

### **Salvia officinalis (Lamiaceae)**

Anti-inflammatory phenolic diterpenescarnosic acid and carnosol are phenolic diterpenes. Two components may mask PGE2 production by blocking microsomal PGE2 synthase-1. The anti-inflammatory effect of a chloroform extract of sage leaves on atopic inflammation in mice was discovered. In mice that had been treated to cyclophosphamide-induced immunosuppression, however, sage essential oil showed no immunomodulatory effect. It's also worth mentioning that a baby and a young child had generalized tonic-clonic seizures after being accidentally exposed to sage oil, according to researchers. [30]

### **Sesbaniasesban (Fabaceae)**

The *Sesbania* genus has around 50 species, the majority of which are annuals. With 33 species, Africa has the largest diversity. Despite the fact that annual species have received a lot of attention, there have been a number of new researches on perennial species recently. One of the perennial species, *Sesbaniasesban*, has showed potential. Woody branches, yellow flowers, and linear pods characterize this low-growing perennial. According to the literature, phytochemical examination of crude saponin extract revealed the presence of several anti-inflammatory components such as terpenoidal and steroidal saponins, tannins, and flavonoids. This was confirmed by the fact that crude saponins extract suppressed carrageenan edema. The crude saponin extract was able to minimize the increase in paw edema in the early and late hours by limiting prostaglandin release. As a consequence, crude saponin extract's present anti-inflammatory activity might be due to its effects in the early and late phases of inflammation. [31]

### **Sidacordifolia (Malvaceae)**

*Sidacordifolia* is a Malvaceae family perennial mallow subshrub. After naturalizing all over the world, it has become a weed in Africa, Australia, the Hawaiian Islands, New Guinea, and French Polynesia. It is used to treat asthmatic bronchitis, nasal congestion, oral mucosa irritation, and blenorrhoea in traditional medicine. It's being looked at as an anti-inflammatory, a means to inhibit cell growth, and a technique to help the liver develop. [32]

### **Thespesiapopulnea (Malvaceae)**

The bark and leaves of *Thespesiapopulnea* are used to create oil for healing fracture wounds and as an anti-inflammatory treatment for ulcers and boils in Sri Lanka and southern India. In both acute and chronic conditions, the ethanolic extract possesses anti-inflammatory properties. According to phytochemical analyses, alkaloids, carbohydrates, proteins, phenols, tannins, gums, flavonoids, saponins, mucilage, and terpenes were discovered in the ethanolic extract of bark. [33]

### **Uncariatomentosa (Rubiaceae)**

The efficacy and safety of *Uncariatomentosa* (cat's claw) in treating OA of the knee were studied in 45 patients who were divided into two groups (active and placebo). The active group exhibited some evidence of remission after four weeks by inhibiting TNF- $\alpha$  and reducing PGE2 production. This extract was given alongside sulfasalazine or hydroxychloroquine in a 24-week double-blind placebo-controlled trial to assess the effect of high purified extract of *U. tomentosain* RA patients; the treatment group showed a modest benefit in terms of pain, swelling, and joint tenderness when compared to the placebo group. It was investigated a



report on the production of remarkable remission in enteritis in rats. An edible extract of cat's claw prevented respiratory inflammation in mice by suppressing iNOS and NF- $\kappa$ B expression, which led in downregulation of TNF- $\alpha$ , IL-1, IL-1, IL-10, and IL-17 in that order. In addition, an in vivo study demonstrated that both COX-1 and COX-2 had a minor inactivation effect. The bark of this plant demonstrated anti-inflammatory efficacy similar to that of dexamethasone in an animal model, and it lowered IL-4 by around 40%, but dexamethasone did not. [34]

### **Urticadioica (Urticaceae)**

The anti-inflammatory activities of Urticadioica (nettle leaf) were investigated in a pilot study. A 50 mg daily dose of Diclofenac was administered to patients with acute arthritis, combined with a 50 mg oral infusion of U. dioica. This medication significantly reduced hs-CRP levels and some patients' complaints about diclofenac 200 mg/24 hours; based on these data, extract combined with NSAIDs has a remarkable synergistic effect. The topical effectiveness of nettle leaf was investigated in osteoarthritis of the thumb in a randomized controlled experiment; significant decreases in stiffness, pain, analgesic, and anti-inflammatory treatment requirements were reported. A combination of nettle leaf, rosehip, and willow bark inhibited IL-1 and COX-2 in chondrocytes. The anti-inflammatory and chondroprotective properties of these extracts were shown in this in vitro study. The leaf extract has been shown to inhibit the pro-inflammatory transcription factor NF- $\kappa$ B (scientific studies have shown an increase in NF- $\kappa$ B in RA patients' synovial fluid). In allergic rhinitis, antagonizing H1-receptors, reducing PGD2 production (allergy-specific prostaglandin), and suppressing mast cell tryptase have all been shown to have anti-inflammatory properties. [35]

### **Vacciniummyrtillus (Ericaceae)**

The following outcomes were published in a randomized clinical trial involving 27 patients with metabolic syndrome who were given 400 g fresh Vacciniummyrtillus (bilberry) daily: reductions in hs-CRP, IL-6, and IL-12, as well as circulating LPS levels in the active group. Bilberry caused remission in 63.4 percent of 13 ulcerative colitis patients after 6 weeks, with significant improvements in Mayo score and fecal protection level. After consuming one capsule of concentrated bilberry extract (36 percent w/w anthocyanins) every day, anti-inflammatory peptides (monocytes chemotactic protein-1) in diabetes individuals did not change. [36]

### **Zingiberofficinale (Zingiberaceae)**

Variable and inconsistent effects have been seen depending on the quantity of Zingiberofficinale extract eaten. Although administering mice ginger extract once or twice enhanced

tumor necrosis factor (TNF- $\alpha$ ) levels in peritoneal cells, long-term administration of the extract increased serum corticosterone and lowered pro-inflammatory markers. After two months of treatment with Z. officinale, TNF-alpha and high-sensitivity hs-CRP levels in type-2 diabetes patients with low-grade inflammation were considerably lowered. Ginger not only had the same pain-relieving efficiency as Diclofenac 100 mg in those with osteoarthritis, but it also had no side effects. In OA patients, ginger extract was compared to indomethacin and ibuprofen, with the findings revealing that indomethacin, ibuprofen, and ginger extract all decreased pain in the same manner. Ginger powder has been demonstrated to benefit musculoskeletal and rheumatism patients by inhibiting the COX and LOX pathways in synovial fluid. [37]

## **FUTURE PERSPECTIVES**

Plants have played a significant role in human health care from the ancient age. In the creation of new pharmaceuticals, traditional botanicals play a crucial role. The great majority of the world's population is affected by inflammation-related diseases. Current analgesics, such as opiates and NSAIDs, are regarded to be inefficient in certain situations due to side effects such as liver failure, GIT irritation, and other problems. A number of immunosuppressive drugs have been developed based on their COX-1 inhibition mechanism, but long-term usage has serious side effects. Selective COX-2 inhibitors were developed to counteract the detrimental effects of COX-1 inhibitors. In contrast, one of these inhibitors has been related to a higher risk of myocardial infarction and atherothrombotic events. COX-2 inhibitors, as a consequence, are unlikely to be useful in the treatment of chronic inflammatory diseases like rheumatoid arthritis. The majority of rheumatoid arthritis medications on the market today are geared at managing pain or the inflammation associated with synovitis. Traditional or folk medicine has used a range of plant species to treat inflammatory disorders. Many of them have been studied and shown to be potent anti-inflammatory medicines in the lab. Despite the fact that plant medicines have a wide range of bioactivities against a wide range of diseases, the active components of most plant extracts have remained a mystery due to their complicated combinations. The chemical families of anti-inflammatory medications found in nature include polyphenols, terpenoids, flavonoids, anthraquinones, alkaloids, polysaccharides, lignans, peptides, and saponins. According to current studies, flavonoids are important anti-inflammatory agents. Some of them act as phospholipase inhibitors in inflammatory situations, while others have been discovered as TNF- $\alpha$  inhibitors. Flavonoids have also been shown to impede the COX and LOX arachidonic metabolic pathways, depending on their chemical structures. It has been documented the



anti-inflammatory activity of alkaloids of the purported skeletal type based on the pyridine ring system; for example, berberine from *Berberis* is a traditional arthritic therapy. Terpenoids have an important function in preventing chronic joint swelling. Terpenoids have the ability to change a number of inflammation-related pathways that develop as a consequence of diverse etiological events. Many herbal therapies for inflammation and rheumatism, on the other hand, have yet to be scientifically tested. As a consequence, all herbal drugs must investigate their pharmacological activities, isolate the single ingredient responsible for anti-inflammatory activity, and produce suitable formulations to address inflammatory disorders.

## CONCLUSION

The rise of allopathic medicine drew scientific and public focus away from traditional therapeutic approaches. However, in recent years, there has been a significant paradigm change. Traditional medicine has regained popularity due to the increased cost of contemporary pharmaceuticals, the time and money required to bring a treatment to market after extensive clinical trials, severe side-effects of a variety of contemporary treatments, and drug resistance growing in both microbes and parasites. As a consequence, researchers are now interested in indigenous peoples' plant-based traditional therapeutic compositions. In recent years, anti-inflammatory herbs have been the subject of research. Inflammatory illnesses are common in ageing cultures in both developed and developing countries, but therapies for them, such as rheumatoid arthritis, may have serious side effects. Several plant-derived chemicals, including rosmarinic acid, campesterol, rutin, ferulic acid, and carnosol, are now being studied as prospective anti-inflammatory drugs. This discovery will benefit present and future researchers by helping them to find anti-inflammatory medicinal plants from whose active components may be separated using various separation processes. These types of research might pave the way for the discovery of additional chemicals that could assist in the treatment of inflammatory diseases. According to the majority of research, the anti-inflammatory activity is linked to the reduction of the enzyme cyclooxygenase, which suppresses prostaglandin formation. A more complete research, on the other hand, may be required to determine the exact mechanism(s) of action.

## CONFLICT OF INTEREST

The author declares no conflict of interest.

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The author did the literature survey from standard databases, collected all essential elements, and wrote this manuscript.

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