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Research article

Anti-inflammatory perspectives of diverse natural resources

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ABSTRACT

Inflammation is a part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells, or irritants. It is characterized by redness, swollen joints, joint pain, stiffness, and loss of joint function. Inflammation is currently treated by NSAIDs. Unfortunately, these drugs cause an increased risk of blood clots resulting in heart attacks and strokes. Therefore, the developments of potent anti-inflammatory drugs from natural products are now under consideration. Natural products are a rich source for the discovery of new drugs because of their chemical diversity. A natural product from medicinal plants plays a major role to cure many diseases associated with inflammation. The conventional drug available in the market to treat inflammation produces various side effects. Due to these side effects, there is a need for the search for newer drugs with fewer or no side effects. There are hundreds of phytoconstituents reported to have many pharmacological activities although most of these reports are of academic interest and very few find an entry in clinical trials. The present review is directed towards the compilation of data on promising phytochemicals from herbal plants that have been tested in inflammatory models using modern scientific systems.

Keywords: Herbal Medicine, Inflammation, Natural Resources, Medicinal Plants, Cyclooxygenase, Anti-inflammatory

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INTRODUCTION

Inflammation is our body's defense response to potentially harmful stimuli such as allergens and/or tissue injury; however, an uncontrolled inflammatory response is the root cause of a wide range of disorders, including allergies, cardiovascular dysfunctions, metabolic syndrome, cancer, and autoimmune diseases, all of which place a significant financial burden on individuals and, as a result, on society. The major enzymes in the production of prostaglandins, prostacyclins, and thromboxanes, which are implicated in inflammation, pain, and platelet aggregation, are cycloxygenases (COXs), referred to as cycloxygenase-1 (COX-1) and cycloxygenase-2 (COX-2). Despite their unfavorable renal and gastric side effects, steroidal and non-steroidal anti-inflammatory medications (SAIDs and NSAIDs, respectively) are now the most extensively utilized medications in the treatment of acute inflammatory illnesses. COX-1 and COX-2 enzyme activities are inhibited by these medications. NSAIDs have been used in humans for a long time. As a consequence, long-term use of these medications causes negative side effects (gastric lesions, cardiovascular, renal, and gastrointestinal damage) and damages human biological systems such as the liver and gastrointestinal tract [1].

Process of Inflammation

Inflammation is the body's localized defensive response to allergic or chemical irritation, damage, and/or infection. Pain, heat, redness, swelling, and loss of function are all signs of inflammation, which are caused by dilatation of blood vessels, which increases blood flow, and enlarged intracellular spaces, which allows leukocytes, protein, and fluids to enter the inflamed areas. Understanding the function of chemical mediators of inflammation is critical. These mediators are plasma proteins or compounds produced by cells such as mast cells, platelets, neutrophils, and monocytes/macrophages. Irritation from allergies or chemicals, as well as injuries and diseases, may set them off. These mediators, which are referred to as pro-inflammatory basic factors influence the intensity of inflammation depending on the degree of the damage. These chemicals may enhance vascular permeability, enhance neutrophil chemotaxis, stimulate smooth muscle contraction, boost direct enzymatic activity, produce discomfort, and/or mediate oxidative damage by binding to particular target receptors on cells. Nitric oxide (NO), prostaglandins, leukotrienes, vasoactive amines (histamine, serotonin), and cytokines are examples of chemical

mediators. Some of the cytokines produced (IL-3, IL-4, IL-5, IL-6, IL-10, and IL-13) are helpful because they serve as anti-inflammatory mediators inside the cells [2].

Mechanism of inflammation

The inflammatory process involves a number of mechanisms, including prostaglandin synthesis, interleukin or other chemo toxin production, adhesive protein receptor activity, and platelet-activating factors (PAFs). All of them have the ability to serve as chemotactic agonists. Any stress on the membrane, or other triggers or stimuli, cause phospholipase A to hydrolyze membrane phospholipids into arachidonic acid, which then serves as a substrate for cyclooxygenase and lipooxygenase enzymes, producing prostaglandins PGE2, PGH2, and leukotrienes such as LTC4, LTB4, and others. Several cytokines, particularly interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-α) play important roles in directing the inflammatory process. The physiologic reactions to bacterial lipopolysaccharide are thought to be mediated by IL-1 and TNF (LPS, also called endotoxin). Monocytes and macrophages, as well as adipocytes and other cells, produce them. They mediate and enhance inflammation by inducing gene expression and protein synthesis in a range of cells in collaboration with each other and numerous cytokines and growth factors (including IL-8 and granulocyte-macrophage colony-stimulating factor). The production of prostaglandin (PGE2) or prostacyclin (PGI2) increases blood flow and blood vessel permeability by helping in the production of nitric oxide from endothelium-derived releasing factor, which causes vasodilation and aids in the adhesion of platelets and other chemo toxins (bradykinin, histamine). LTB4 is a powerful chemotactic agent for polymorphonuclear leukocytes, eosinophils, and monocytes, despite the fact that LTs are normally pro-inflammatory. LTB4 induces the aggregation of polymorphonuclear leukocytes, as well as degranulation and superoxide production, at greater doses. LTB4 enhances neutrophil adherence to vascular endothelial cells and trans-endothelial migration, as well as macrophage and lymphocyte generation of pro-inflammatory cytokines [3].

Types of inflammation

Acute inflammation develops within minutes or hours following tissue damage and is marked by the characteristic signs of redness, heat, and edema. It is a quick procedure. The exudation of fluids and plasma proteins, as well as the migration of leukocytes, particularly neutrophils, into the wounded region, define it. This initial inflammatory reaction is beneficial to the defense mechanism's goal of eradicating germs, viruses, and parasites while allowing wound healing to proceed. Chronic inflammation lasts longer and is characterized by the presence of lymphocytes and macrophages in the histology, leading to fibrosis and tissue necrosis. Chronic inflammation promotes the onset of degenerative diseases such as rheumatoid arthritis, atherosclerosis, heart disease, Alzheimer's disease, asthma, acquired immunodeficiency syndrome (AIDS), cancer, congestive heart failure, multiple sclerosis, diabetes, infections, gout, IBD-inflammatory bowel disease, aging, and other neurodegenerative CNS depressions. Chronic inflammation has also been linked to the loss of muscle mass that happens as people age. All of them are linked to immunopathological factors that seem to have a role in the genesis of the disease [4].

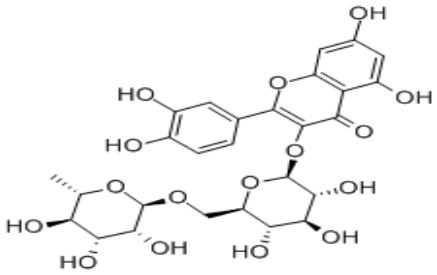
Approaches for treatment

There is a wide range of medications for regulating and inhibiting inflammatory crises, including SAIDs, NSAIDs, and immunosuppressant's, all of which have adverse effects, whereas our main objective in practice is to use the lowest effective dose with the highest efficacy and fewest side effects. As a consequence, natural anti-inflammatory components must be included in medication therapy to enhance pharmacological efficacy while limiting undesirable side effects. Herbal medicines are developing medical issues, and we must understand more about them. Herbal prescription recommendations are mostly derived from complementary, alternative, and traditional medicine; nevertheless, modern medicine must validate these prescriptions via scientific methods before using them in practice [5]. In this review, we sought to investigate the plants and the most clinical proof of their anti-inflammatory properties.

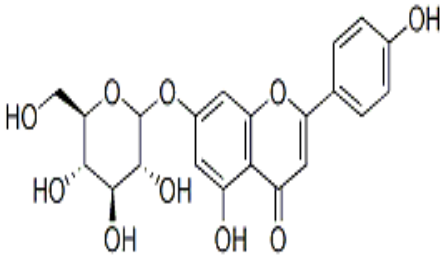
NATURAL RESOURCES WITH ANTI-INFLAMMATORY POTENTIALS

Figure 1. Phyto-constituents mediating prominent anti-inflammatory activity

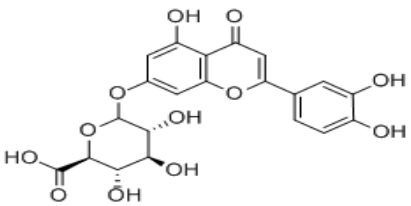
Rutin



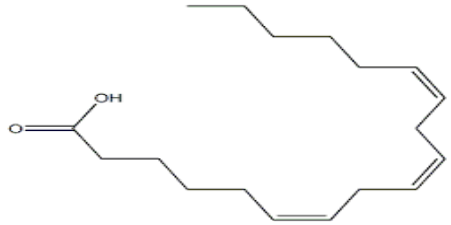
Aspigenin-7-O-Glucoside



Luteolin-7-O-Glucoside

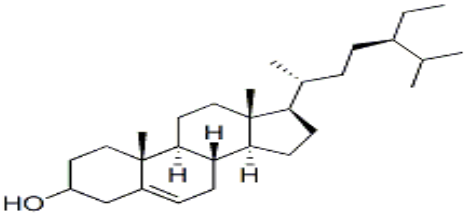


Gamma Linoleic Acid

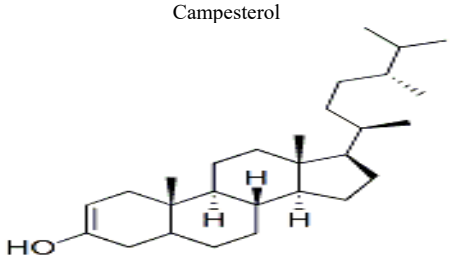


Tetracosanol

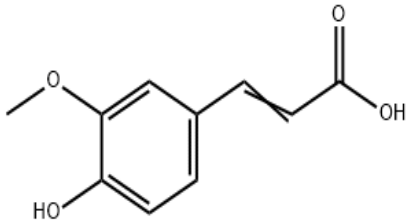
Beta-Sitosterol



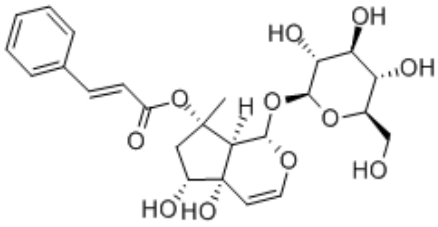
Campesterol



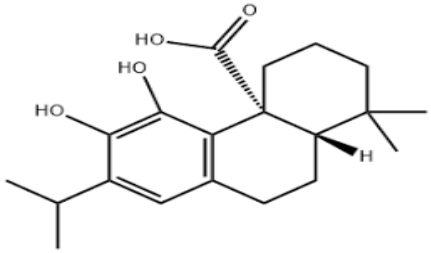
Ferulic Acid



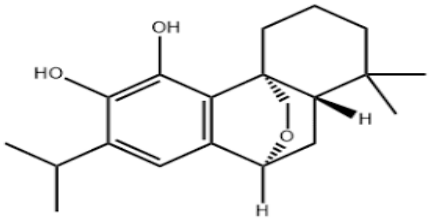
Harpagoside



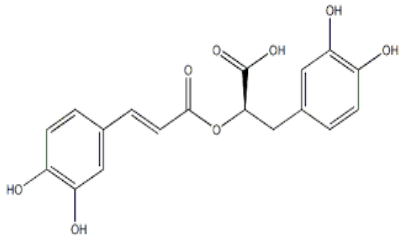
Carnosic Acid



Carnosol



Rosmarinic Acid



Achillea millefolium (Asteraceae)

Achillea millefolium L. is a perennial plant native to Europe that is well-known for its anti-inflammatory qualities in traditional medicine. Externally, the herb has long been used to heal wounds, burns, swelling, and irritated skin. Isoprenoids and phenolics, two types of secondary metabolites, have been shown to have a major role in anti-inflammatory activities in studies. Internally, aqueous and alcoholic extracts of A. millefolium are used in traditional medicine to treat gastrointestinal, hepatobiliary, and antiphlogistic illnesses. Sesquiterpenes' topical anti-inflammatory action is due to the suppression of arachidonic acid metabolism. Rutin, aspigenin-7-O-glucoside, and luteolin-7-O-glucoside are the three flavonoids found in the crude extract and concentrated in the flavonoid fraction. In vitro investigations show that the crude plant extract and two fractions enriched in dicaffeoyquinic acids and flavonoids inhibit human neutrophil elastase and matrix metalloproteinases (MMPs), which are linked to anti-inflammatory processes [6].

Aconitum heterophyllum (Ranunculaceae)

Aconitum heterophyllum, also known as 'Ativisha' or 'Patis' in Ayurveda, is a plant. It is used to treat the nervous system, digestive system, fever, and rheumatism illnesses. Alkaloids, glycosides, flavonoids, and sterols are found in the ethanolic extract of A. heterophyllum root. Plants having these chemical classes of chemicals have been shown to have powerful anti-inflammatory properties by inhibiting prostaglandin pathways. Cotton pellet-induced granuloma is a common method for determining the transudative and proliferative components of chronic inflammation. The quantity of granulomatous tissue is proportional to the weight of the wet cotton pellets. The weight of wet cotton pellets was shown to be inhibited by the administration of A. heterophyllum extract in a dosage-dependent manner, with the higher dosage of this extract exhibiting inflammatory inhibition that was very similar to that of

diclofenac sodium. The ethanolic root extract has been shown in the literature to have the capacity to prevent subacute inflammation by disrupting arachidonic acid metabolism [7].

Adhatoda vasica (Acanthaceae)

Adhatoda vasica L. is a native plant that belongs to the Acanthaceae family. The plant has been used as herbal cure for treating colds, coughs, whooping cough, chronic bronchitis, asthma, sedative expectorant, antispasmodic, anthelmintic, rheumatism, and rheumatic painful inflammatory swellings in indigenous systems of medicine all over the globe. The medication comes in a variety of forms, including fresh juice, decoction, infusion, and powder. It's also available in the form of an alcoholic extract, a liquid extract, or syrup. Alkaloids, tannins, flavonoids, terpenes, sugars, and glycosides are all found in this plant. Carrageenan-induced paw edema test and formalin-induced paw edema test in albino rats were used to test the anti-inflammatory properties of ethanolic extract. The ethanolic extract of A. vasica inhibited carrageenan and formalin-induced paw edema in a dose-dependent manner [8].

Bacopa monnieri (Scrophulariaceae)

Bacopa monnieri is a creeping, glabrous, succulent plant that roots at nodes and prefers marshes and muddy coastlines as its environment. It was historically used as a brain tonic to help with memory, learning, and attention. The herb is also used as a cardiac tonic, digestive aid, and to enhance respiratory function in situations of bronchoconstriction in India and Pakistan. When compared to indomethacin, the plant shows an anti-inflammatory effect in carrageenan-induced rat paw edema, inhibiting edema by 82 percent. The activity of 5-lipoxygenase (5-LOX), 15-lipoxygenase (15-LOX), and COX-2 were likewise dramatically decreased by B. monnieri. The plant extract has anti-inflammatory properties (due to the presence of triterpenoid and bacoside by reducing TNF-α and IL-6 levels), which might explain its usefulness in the treatment of numerous inflammatory disorders in traditional medicine. Lipopolysaccharide-activated peripheral blood mononuclear cells and peritoneal exudate cells were used to investigate this in vitro. As a result, B. monnieri has the capacity to reduce inflammation by modulating the release of pro-inflammatory mediators [9].

Borago officinalis (Boraginaceae)

This plant (also known as borage) is high in gamma-linoleic acid (GLA) (~25%). The component raises the prostaglandin-E (PGE) levels, which increases cyclic adenosine monophosphate (cAMP); and thereby GLA acts as a powerful TNF-suppressor. In this route, borage is contraindicated during pregnancy due to the risk of miscarriage. Anti-rheumatoid arthritis (RA) potential of borage seed oil was evaluated in two RCTs: in the first, 1.4 g/day borage seed oil was compared to placebo in RA patients; at the end of 6-month therapy, the treatment group showed 36.8% improvement. In the second research, patients were given 2.8 g of borage seed oil per day for six months; at the end of therapy, there was a significant improvement in RA manifestation: 64 percent in the treatment group compared to 21 percent in the control group. Similarly, the anti-inflammatory properties of borage oil were investigated in atopic dermatitis patients. A total of 12 clinical studies were conducted to determine the efficacy of this plant in treating atopic dermatitis. Five of them have shown an anti-inflammatory impact, and two of them have seen some patients improve, while there has been no evidence of remission in the other five studies [10].

Boswellia serrata (Burseraceae)

The efficacy of Boswellia serrata extract in patients with osteoarthritis has been shown; at the conclusion of the treatment period, there was a significant reduction in the frequency of joint swelling and discomfort, as well as an increase in joint flexibility and walking distance. Another clinical study found a substantial decrease in erythrocyte sedimentation rate (ESR), morning stiffness, and NSAID administration required during treatment in rheumatoid arthritis patients. After 12 weeks of treatment with this extract, no substantial remission in patient symptoms was reported in one pilot research on patients with chronic polyarthritis; only a slight reduction in the need for NSAIDs was reported. Collagenous colitis is an inflammatory bowel disease (IBD), and B. serrata has been shown to be clinically beneficial in the treatment of this condition when compared to a placebo. The combination of B. serrata, Curcuma longa, and Glycyrrhiza glabra has been shown to relieve asthmatic patient symptoms; also, after 4 weeks, the therapy group showed a substantial decrease in plasma levels of leukotriene C4 (LTC4), NO, and malondialdehyde. In vivo and in vitro investigations have shown that B. serrata extract may modulate inflammatory mediators (TNF-α, IL-1, IL-6, IFN-α, and PGE2). The major component of this gum is boswellic acid, which inhibits C3 convertase and suppresses the traditional complement pathway. It also has anti-inflammatory benefits on the skin as well as systemic effects [11].

Cassia fistula (Caesalpiniaceae)

The Cassia fistula tree is one of the most common in India's woods. The whole plant has therapeutic characteristics that may be used to treat skin conditions, inflammatory conditions, rheumatism, anorexia, and jaundice. In the acute and chronic anti-inflammatory models of inflammation in rats, the bark extracts have a substantial anti-inflammatory impact. Endogenous and exogenous reactive oxygen species (ROS) have been linked to the pathophysiology of illnesses such as atherosclerosis, diabetes, cancer, arthritis, and the aging process. Inflammatory disorders are complicated by the presence of ROS. Flavonoids and bio-flavonoids are the major components of C. fistula that have anti-inflammatory properties [12].

Curcuma longa (Zingiberaceae)

Curcumin, the main component of Curcuma longa has been shown to demonstrate anti-inflammatory properties in several clinical

research. In contrast to phenylbutazone, which was employed as a positive control, their findings imply that curcumin may be useful in lowering RA inflammation and clinical manifestations such as joint swelling and morning stiffness. Curcumin was also evaluated in individuals with anterior uveitis, and after two weeks, they had complete remission. Another clinical experiment demonstrated the efficacy of curcumin in patients with dyspepsia and/or stomach ulcer. After 12 weeks, the patients in this trial obtained remission (maximum). Curcumin is effective in the treatment of irritable bowel syndrome (IBS) and in the prevention of delayed graft rejection (DGR) following kidney transplant surgery. Curcumin also aids in the prevention of IBD and the lowering of the sedimentation rate in people with IBD. It has also been shown to help sustain ulcerative colitis and psoriasis improvement (by the selective prohibition of phosphorylase kinase) [13].

Daphne pontica (Thymelaeaceae)

Since the 2nd century AD, Daphne species have been thought to offer anti-cancer properties. Daphnodorins, a flavonoid component, were isolated from the roots of Daphne pontica, a plant with anti-tumor action. Several Daphne species have been utilized in the treatment of inflammation (Rheumatic pain and inflammatory conditions) over time by inhibiting PGE2 and IL-1β production [14].

Elaeagnus angustifolia (Elaeagnaceae)

An RCT involving 28 participants looked at the efficacy of Elaeagnus angustifolia in the treatment of oral lichen planus (OLP) lesions. In the case group, there was a 75% reduction in pain and a 50%-75% reduction in lesion size, respectively. In another randomized clinical study including 90 female patients with knee osteoarthritis (OA), the active treatment group showed a substantial reduction in pro-inflammatory mediators such as TNF-α and MMP-1 and an increase in IL-10 (an anti-inflammatory cytokine). In an animal model, E. angustifolia extract had an anti-inflammatory effect, although this effect was not significant when compared to sodium salicylate. This fruit's aqueous extract has been demonstrated to have anti-inflammatory characteristics in mice by inhibiting COX-1 and COX-2; however, there is no indication of a link between corticosterone levels and anti-inflammatory activity [15].

Emblica officinalis (Euphorbiaceae)

Emblica officinalis is a subtropical and tropical tree found in China, India, Indonesia, and the Malay Peninsula. In these locations, it has been utilized for anti-inflammatory and anti-pyretic properties. The water fraction of methanol extract of plant leaves was revealed to have anti-inflammatory effects in recent research. The effects of the fraction on the generation of inflammatory mediators including leukotriene B4, PAF, and thromboxane were investigated. Human PMN migration was reduced by the water portion of methanol extract at low doses [16].

Garcinia mangostana (Guttiferae)

Garcinia mangostana fruit rinds have been used as a traditional medication to heal injuries and skin problems. The bioactive compounds xanthones and mangostins are discovered in the mangosteen fruit hulls. The biological effects of xanthones are shown through inhibiting inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2). Two mangostins have been shown to reduce PGE2 levels by inhibiting COX-2 activity and NO generation. It has been found that mangostin inhibits PGE2 release more effectively than either histamine or serotonin [17].

Harpagophytum procumbens (Pedaliaceae)

Harpagoside, one of the many metabolites of Harpagophytum procumbens, has been shown to be an anti-inflammatory component. Devil's claw root extract has been shown to reduce NO, inflammatory cytokines (IL-6, IL-1, and TNF-α), and PGE2, as well as block arachidonic acid metabolism and eicosanoid production, resulting in COX-2 suppression and inflammation reduction. Another preclinical investigation found that devil's claw had no effect on carrageenan-induced edema in the rat's hind foot. The efficacy of Devil's claw in osteoarthritis remission has been studied in an RCT. Anti-inflammatory effects of this plant were detected at the conclusion of the therapy period. In contrast, researchers found no remission or subjective or objective improvement with 410 mg TDS of H. procumbens liquid extract after 12 weeks in a pilot investigation on patients with arthritic illness (RA and psoriatic arthropathy). The most common adverse effect of this plant is gastrointestinal discomfort, which makes it contraindicated in people with gastric or duodenal ulcers, gallstones, or diabetes [18].

Lantana camara (Verbenaceae)

Many varieties of Lantana have aerial portions that are commonly utilized in folk treatments for cancer and tumors. Fever, influenza, and stomachaches were treated with tea made from leaves and flowers. Other plant applications include antimalarial, antibacterial, and anti-diarrhoeal properties. The aqueous extract of Lantana camara leaves has been shown in trials to be very effective and safe for the treatment of hemorrhoids, Also, the extracts demonstrate analgesic, anti-inflammatory, and anti-hemorrhoidal properties [19].

Lycopodium clavatum (Lycopodiaceae)

Lycopodium clavatum, often known as club moss, has been shown to have wound-healing properties. Only the chloroform extract and the alkaloid fraction from the aerial portions showed significant anti-inflammatory activity when compared to Indomethacin [20].

Mangifera indica (Anacardiaceae)

Mangifera indica is a tropical and subtropical plant whose components are widely used in traditional medicine to treat a number of ailments. The herb has been used for a variety of therapeutic purposes in traditional medicine, including monorrhagia, leucorrhoea, bleeding piles, and pulmonary hemorrhage. Warts on the eyelids are

removed using calcined idibs of the leaves. In diabetes, dried powdered leaves are employed. In diarrhea, chronic dysentery, and gleet, dried flowers in decoction or powder are beneficial. When compared to conventional medicine Ethyl acetate and ethanol extracts of the roots of M. indica have been shown to have significant anti-inflammatory action, as compared to Diclofenac. Flavonoids were discovered in the phytochemical investigations which suppress prostaglandin production, which have anti-inflammatory properties [21].

Oenothera biennis (Onagraceae)

Evening primrose (Oenothera biennis) oil contains GLA, linear aliphatic alcohols (e.g., tetracosanol), and a phenolic substance (ferulic acid) that have been shown to protect against pro-inflammatory indicators. This oil contains sterols such β-sitosterol and campesterol, which have modulator effects on NO, TNF-α, IL-1, and thromboxane B2 (TXB2), reducing COX-2 gene expression; as a result, primrose oil has a stronger anti-inflammatory impact than borage oil. In multiple sclerosis (MS), a chronic inflammatory disease, the efficacy of evening primrose oil combined with hemp seed oil has been scientifically tested. Patients with MS were given hemp seed/evening primrose oil or a placebo at random. In the therapy group, there was a significant drop in IFN-α and IL-17. The treatment group's illness recurrence rate was also reduced; this investigation demonstrated the immunomodulatory effects of these oils and their components. Researchers found subjective improvement and a decrease in the use of NSAIDs in an RCT on RA, but no change in clinical measures. Patients have also reported a reduction in morning stiffness with no changes in their articular index or pain. A clinical investigation on 18 individuals with RA after 12 weeks found no meaningful improvement in the target treatment group [22].

Olea europaea (Oleaceae)

Extra virgin olive oil (EVOO) or Olea europaea has been shown to have a favorable influence on postprandial plasma lipopolysaccharide, pro-inflammatory cytokines, TXB2 and LTB4, as well as reduced risk of coronary heart disease in healthy people and metabolic syndrome patients. In comparison to sunflower oil, oral olive oil has hastened wound healing and reduced hospitalization time in patients with profound second-degree and greater burn wounds (SFO). In addition, EVOO enriched food intake reduced disease activity index, tumor incidence of ulcerative colitis-associated colorectal cancer, and pro-inflammatory cytokines in mice when compared to SFO-fed animals [23].

Persea Americana (Lauraceae)

In a prospective multicenter, 3-month randomized control study, 153 OA patients were recruited and treated with soybean unsaponifiables (SU) of Persea Americana and NSAIDs; after 45 days of treatment, the need for NSAIDs decreased, but there were no significant improvements in patients' pain levels. The efficacy of ASU has been tested in three clinical studies on OA patients. Two of them showed reductions in Lequesne's functional index (LFI), pain, and disability; likewise, 71 percent of patients in the case group versus 36 percent in the control group had a 50 percent reduction in NSAID requirement; however, no intergroup changes in joint space width (JSW), which was considered the primary endpoint, were reported in the last trial. During three years of hip follow-up in OA patients using SU, no improvement in JSW was seen, however, a 20% reduction in JSW aggravation was seen. SU has also been given to 100 individuals with linear scleroderma and morphea; this research found that if SU is given early enough in the condition, it may help avoid atrophy, deformity, and contracture. Soybean extract has been tested as topical and nutritional treatment in individuals with mild to severe vulvar lichen sclerosus (VLS). The primary signs and symptoms of illness were greatly reduced at the conclusion of the 24-week therapy period [24].

Phyllanthus polyphyllus (Euphorbiaceae)

Phyllanthus polyphyllus is a tiny plant that is employed in anti-inflammatory folk medicine in India and Sri Lanka's tropical and subtropical areas. Four substances isolated from the entire plant, one benzenoid and three arylnaphalide lignans, inhibited the generation of NO and cytokines; TNF-α and IL-12), the principal pro-inflammatory cytokines released during the early stages of acute and chronic inflammatory disorders such as asthma, rheumatoid arthritis, and septic shock. These chemicals may be responsible for the usage of P. polyphyllus as an anti-inflammatory treatment in traditional medicine [25].

Ribes nigrum (Grossulariaceae)

Researchers evaluated the impact of Ribes nigrum or blackcurrant oil (BCO) on RA patients in a 6-week clinical study; the results were as follows: decrease in morning stiffness in the experimental group and decrease in pro-inflammatory mediators such as IL-1 and TNF-α in peripheral blood monocytes. The RA patients' disease activity symptoms were decreased after a 24-week therapy period with BC seed oil. In general, there were no significant changes in clinical signs and symptoms between the placebo and case groups. In 40 healthy volunteers over the age of 65, BC seed oil has a mild reinforcing impact on the immune response and an inhibitory impact on PGE2 production. A decrease in LTB4 production through polymorphonuclear neutrophil (PMN) and an increase in dihomolinoleic acid in PMN phospholipids were seen in another clinical trial in which 12 healthy participants ingested BC oil. In rats exposed to diethylnitrosamine (a hepatocarcinogen), the plant skin extract reduced heat shock protein (HSP-70 and HSP-90), COX-2, and NF-κB expression [26].

Ricinus communis (Euphorbiaceae)

Ricinus communis Linn. May be found practically

wherever in the world's tropical and subtropical areas. Researchers investigated the anti-inflammatory and free radical scavenging properties of a methanolic extract of the root in Wistar albino rats. In a carrageenan-indexed hind paw edema model, the methanolic extract showed considerable anti-inflammatory action. By reducing lipid peroxidation, the methanolic extract demonstrated considerable free radical scavenging activity. The presence of phytochemicals such as flavonoids, alkaloids, and tannins in the plant extract might explain the observed pharmacological action [27].

Rosa canina (Rosaceae)

Rosa canina or Rosehip's efficacy has been tested in patients with OA and RA. The following were the findings of these studies: individuals with OA received pain relief, reduced rescue medicine use, and stiffness, as well as a substantial drop in CRP after therapy with this plant. It's worth noting that the anti-inflammatory properties of rosehip pertain to the seed, not the shell. Two clinical trials on OA patients have validated the latter assertion. Rosehip powder has also been shown to lower ESR and enhance the quality of life in RA patients, suggesting that it might be used as a supplement in addition to traditional RA therapy. In individuals with RA, however, 10 g of rosehip powder/day for a month had no anti-inflammatory impact. The ethanol extract of rosehip was fractioned using various polarity solvents; the ethyl acetate and butanol fractions demonstrated anti-inflammatory effects in mice during the delayed phase of the inflammation process by inhibiting PGE1. These fractions are rich in unsaturated fatty acids because n-hexane and dichloromethane extracts of this plant's fruit have a downregulatory impact on COX-1, COX-2, and LTB4. Rosehip powder contains galactolipid, which has been shown to have NO inhibiting properties in laboratory and in vitro investigations [28].

Rosmarinus officinalis (Lamiaceae)

The effects of rosemary (Rosmarinus officinalis) extract were evaluated in patients with OA, RA, and fibromyalgia for 4 weeks in an open-label trial; C-reactive protein (hs-CRP) (an index for inflammation) was reduced noticeably in patients who had demonstrated augmentation in this index; by the way, reduction in inflammation related to pain score was observed during the treatment but not during the placebo period. There is evidence that R. officinalis has anti-inflammatory properties at the molecular level; according to this, rosmarinic acid may readily disrupt complement system activation by blocking C3b attachment; the dosage needed to have this effect is quite low (34 M). Furthermore, rosemary extract has been demonstrated to be more effective than omeprazole in preventing stomach ulcers; this benefit is due to rosemary's ability to suppress neutrophil infiltration and reduce pro-inflammatory mediators such as TNF-α and IL-1. Nonetheless, a high dosage of rosemary extract (500 mg/kg) lowered testosterone and spermatogenesis in rats in a preclinical investigation, resulting in sterility. In mice, this herb acted as a topical anti-inflammatory in wound healing. Carnosic acid (Figure 1), one of the main components, interacts with CYP-3A4 and CYP-2B6 substrates, causing toxicity in human hepatocytes with an EC50 value that is similar to the standard drug tamoxifen [29].

Salvia officinalis (Lamiaceae)

Carnosic acid and carnosol are phenolic diterpenes that have anti-inflammatory properties. PGE2 synthesis might have been suppressed by these two components by inhibiting microsomal PGE2 synthase-1. In mice, a chloroform extract of sage leaves had an anti-inflammatory impact on atopic inflammation. Sage essential oil, on the other hand, exhibited no immunomodulatory impact on mice that had been subjected to cyclophosphamide-induced immunosuppression. It is also worth noting that researchers documented generalized tonic-clonic seizures in a newborn and a youngster after they were accidentally exposed to sage oil [30].

Sesbania sesban (Fabaceae)

There are roughly 50 species in the Sesbania genus, the majority of which are annuals. Africa has the most species variety, with 33 species. Although annual species have gotten a lot of attention, there have been a lot of recent studies on perpetual species. Sesbania sesban, one of the perennial species, has shown promise. It is a low-growing perennial with woody stems, yellow blooms, and linear pods. Phytochemical analysis of crude saponin extract indicated the presence of numerous elements such as terpenoidal and steroidal saponins, tannins, and flavonoids that have been shown to have anti-inflammatory action, according to literature. The suppression of carrageenan edema by crude saponins extract verified this. Because of the restriction of prostaglandin release, the crude saponin extract was able to reduce the rise in paw edema in the early and late hours. As a result, it is possible that crude saponin extract's current anti-inflammatory efficacy is attributable to its effect in the early and late stages of inflammation [31].

Sida cordifolia (Malvaceae)

Sida cordifolia is a perennial mallow subshrub in the Malvaceae family. It has become a weed in Africa, Australia, the Hawaiian Islands, New Guinea, and French Polynesia after naturalizing around the globe. In folk medicine, it is used to treat inflammation of the oral mucosa, blenorrhea, asthmatic bronchitis, and nasal congestion. It is been studied as an anti-inflammatory, a way to stop cell proliferation, and a way to promote liver development [32].

Thespesia populnea (Malvaceae)

In southern India and Sri Lanka, the leaves and bark of Thespesia populnea are used to make oil for treating fracture wounds and as an anti-inflammatory poultice for ulcers and boils. The ethanolic extract has anti-inflammatory effects in both acute and

chronic settings. Alkaloids, carbohydrates, proteins, tannins, phenols, flavonoids, gums and mucilage, saponins, and terpenes were found in the ethanolic extract of bark, according to phytochemical investigations [33].

Uncaria tomentosa (Rubiaceae)

The effectiveness and safety of Uncaria tomentosa (cat's claw) in treating OA of the knee were investigated in 45 patients who were separated into two groups (placebo and active); the active group showed some signs of remission after 4-weeks by blocking TNF-α and decreasing PGE2 production. This extract was administered along with sulfasalazine or hydroxychloroquine in a 24-week double-blind placebo-controlled trial to evaluate the effect of high purified extract of U. tomentosa in RA patients; the modest benefit of this herb in alleviating pain, swelling, and tenderness of joint was shown in the treatment group compared to the placebo group. There has been a report regarding the induction of remarkable remission in enteritis in rats. In mice, an edible extract of cat's claw exhibited a preventive effect against respiratory inflammation by suppression of iNOS and NF-κB expression, which has resulted in downregulation of TNF-α, IL-1, IL-1, IL-10, and IL-17 in that order. In addition, an in vivo investigation revealed that minimal inactivation impact over both COX-1 and COX-2. In an animal model, the bark of this plant had anti-inflammatory activity identical to that of dexamethasone, and it reduced roughly 40% of IL-4, but dexamethasone did not [34].

Urtica dioica (Urticaceae)

In pilot research, the anti-inflammatory properties of Urtica dioica (nettle leaf) were studied. Patients with acute arthritis were given 50 mg of Diclofenac each day, along with a 50 mg oral infusion of U. dioica. This treatment has resulted in a significant decrease in hs-CRP levels and some patients' complaints about 200 mg Diclofenac per day; based on these findings, extract mixed with NSAIDs has an amazing synergistic impact. In a randomized controlled trial, the topical efficacy of nettle leaf was evaluated in osteoarthritis of the thumb; substantial reductions in pain, stiffness, and anti-inflammatory and analgesic therapeutic needs were noted. In chondrocytes, a combination of nettle leaf, rosehip, and willow bark reduced IL-1 and COX-2. The chondroprotective and anti-inflammatory properties of this botanical extract were shown in this in vitro investigation. The leaf extract has been demonstrated to block the pro-inflammatory transcription factor NF-κB (scientific investigations have indicated an increase in NF-κB in the synovial fluid of RA patients). Antagonizing H1-receptors, lowering PGD2 synthesis (allergy-specific prostaglandin), and inhibiting mast cell tryptase have all been shown to have anti-inflammatory properties in allergic rhinitis [35].

Vaccinium myrtillus (Ericaceae)

In a randomized clinical study including 27 patients with metabolic syndrome who were given 400 g fresh Vaccinium myrtillus (bilberry) daily, the following results were reported: decreases in hs-CRP, IL-6, and IL-12, as well as circulating LPS levels in the active group. After 6 weeks, bilberry produced remission in 63.4 percent of 13 ulcerative colitis patients, with substantial reductions in Mayo score and fecal protection level. Anti-inflammatory peptides (monocytes chemotactic protein-1) in diabetic patients did not alter after taking one capsule of concentrated bilberry extract (36 percent w/w anthocyanins) every day [36].

Zingiber officinale (Zingiberaceae)

Depending on the amount of Zingiber officinale extract consumed, varied and inconsistent effects have been observed. Although giving mice squeezed ginger extract once or twice raised tumor necrosis factor (TNF-α) levels in peritoneal cells, long-term use of the extract boosted serum corticosterone levels and decreased pro-inflammatory indicators. TNF-alpha and high-sensitivity hs-CRP levels in type-2 diabetes individuals with low-grade inflammation were significantly reduced following 2 months of therapy with Z. officinale. In individuals with osteoarthritis, ginger exhibited not only the same effectiveness as Diclofenac 100 mg in terms of pain relief, but it also had no adverse effects. In OA patients, ginger extract was compared to ibuprofen and indomethacin; the findings showed that ibuprofen, indomethacin, and ginger extract all improved pain scores similarly. By blocking the COX and LOX pathways in synovial fluid, ginger powder has been shown to help musculoskeletal and rheumatism sufferers [37].

FUTURE PERSPECTIVES

Since ancient times, plants have played an important part in human health care. Traditional plants play an important role in the development of novel medications. Inflammation-related illnesses impact the vast majority of the world's population. Current analgesics, such as opiates and NSAIDS, are thought to be ineffective in certain circumstances due to side effects such as GIT irritation, liver dysfunction, and other issues. A variety of immunosuppressive drugs have been developed based on their COX-1 inhibition mechanism, however, long-term use causes significant adverse effects. To prevent the negative effects of COX-1 inhibitors, selective COX-2 inhibitors were created. One of these inhibitors, on the other hand, has been linked to an increased risk of myocardial infarction and atherothrombotic events. As a result, COX-2 inhibitors are unlikely to be effective in the treatment of chronic inflammatory illnesses like rheumatoid arthritis. Currently, available medicines for rheumatoid arthritis are mostly aimed at controlling pain or the inflammation associated with synovitis. Inflammatory illnesses have been treated using a variety of herbal species in traditional or folk medicine. Many of them have been scientifically investigated and shown to be effective anti-inflammatory agents. Despite the fact that plant medicines have diverse bioactivities against many illnesses, the active components of most plant extracts have not been extensively

explained owing to their complex combinations. Polyphenols, flavonoids, terpenoids, alkaloids, anthraquinones, lignans, polysaccharides, saponins, and peptides are among the main chemical families of anti-inflammatory drugs found in nature. Flavonoids are key anti-inflammatory agents, according to the research done so far. In various inflammatory circumstances, some of them work as phospholipase inhibitors, while others have been identified as TNF inhibitors. Flavonoids have also been demonstrated to block both the COX and the LOX pathways of arachidonic metabolism, depending on their chemical structures. The anti-inflammatory action of alkaloids of the claimed skeletal type based on the pyridine ring system has been described; for example, berberine from Berberis is a traditional treatment for arthritis. Terpenoids have a key role in the prevention of chronic joint swelling. Terpenoids have the potential to alter a variety of mechanisms related to inflammation that arise as a result of various etiological events. Many herbal remedies for inflammation and rheumatism, however, have yet to be subjected to scientific testing. As a result, it is imperative that all such herbal medications explore determining their pharmacological actions, isolating the single item responsible for anti-inflammatory action, and developing appropriate formulations to combat inflammatory illnesses.

CONCLUSION

Allopathic medicine's growth diverted scientific and general public attention away from traditional therapeutic treatments. However, a dramatic paradigm shift has occurred in recent years. Because of the increased cost of contemporary pharmaceuticals, the time and money required bringing a treatment to market after thorough clinical trials, severe side-effects of a variety of contemporary treatments, and drug resistance growing in both microbes and parasites, traditional medicine has regained popularity. As a result, researchers are presently interested in plant-based traditional medicinal formulations used by indigenous peoples. Anti-inflammatory plants have been the focus of study in recent years. Inflammatory disorders are frequent in industrialized and developing nations' aging societies, yet the treatments used to treat them, such as rheumatoid arthritis, sometimes have major adverse effects. Several plant-derived compounds, such as rosmarinic acid, campesterol, rutin, ferulic acid, and carnosol, are presently being investigated as potential anti-inflammatory medications in the future. This study will aid current and future researchers in their study by allowing them to identify anti-inflammatory medicinal plants from whose active ingredients may be isolated using different separation procedures. These kinds of studies might lead to the discovery of novel compounds that may aid in the treatment of inflammatory illnesses. The anti-inflammatory action may be related to the suppression of the enzyme cyclooxygenase, which inhibits prostaglandin production, according to the majority of the studies. However, a more thorough investigation may be carried out to discover the actual mechanism(s) of action.

Conflict of interest

The author declares no conflict of interest.

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Author's contribution

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