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PLANTS HAVE ANTI-INFLAMMATORY EFFECTS TO RESTORE AND REJUVENATION OF LIFE- AN ANALYSIS

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ABSTRACT

Inflammation is the body's attempt at self-protection to remove harmful stimuli and begin the healing process. Inflammation is characterized by some sign e.g. redness, pain, swelling and heat. Different reasons are responsible for inflammation like microbial infections, some irritan and corrosive agents or tissue necrosis due to hypoxia and hypersensitivity reactions of immune systems. Various endogenous chemical mediators may be defined as acts on blood vessels, inflammatory cells to contribute to an inflammatory response like serotonin, histamine, nitric oxide, prostaglandins, bradykinin, thromboxane, leukotrienes, etc. Plants have specific anti- inflammatory action and have been using traditionally to treat inflammation e.g. Olibanum, Borage seed oil, Turmeric, Evening primrose oil, Ginger, Rosehip, Flaxseed and Blackcurrant etc. Medicinal plants may be used against inflammation due to cost effective, available and fewer side effects. In this review paper, some basic scientific research and clinical trial have been arranged to understanding the efficacy of anti-inflammatory actions of herbal plants. This article is focused on the potential role of herbs in treating inflammation and prospects for healthy, balance and normal life.

KEYWORDS: Inflammation, Redness, Pain, Swelling, Heat, Endogenous Chemical Mediators, Medicinal Plants.

INTRODUCTION

An inflammatory disease of the synovium, it results in pain, stiffness, swelling, deformity and, eventually, loss of function in the joints. Because there is currently no known cure or means of preventing RA, the American College of Rheumatology recommends the earliest possible diagnosis and treatment with disease modifying anti-rheumatic agents to limit the degree of irreversible joint damage.[1]

Herbal medicines offer one appealing way to reduce the use of anti-inflammatory drugs. The factors in favor of using herbs include long histories of use, extensive research on a number of agents, relative ease of administration, relatively low cost, and excellent safety records. It is unfortunate that some herbs have been given the moniker “anti-inflammatories,” however, because almost none of these herbs appear to act like the pharmaceutical versions of anti-inflammatories, either pharmacodynamically or clinically. Therefore, we propose that these agents should be referred to by a more descriptive—and correct—phrase: inflammation modulators.[2]

Inflammation is an adaptive physiological response induced by deleterious circumstances including infection and tissue injuries. Observational studies have revealed that inflammation is the product of complex series of responses triggered by the immune system. Inflammation also causes a wide range of physiological and pathological morbidities [3]. Curcumin shows strong anti-oxidation and anti-inflammatory activities. In the past two decades over 7000 articles have been discussed the molecular basis of curcumin’s attributed antioxidant, anti-inflammatory, antibacterial, antiapoptosis, anticancer and related activities. Over 100 clinical trials have focused on the role of curcumin in various chronic diseases, including diabetes and cancers, as well as autoimmune, cardiovascular, neurological and psychological diseases.[4]

Inflammation

Inflammation is a protective strategy evolved in higher organisms in response to detrimental insults such as microbial infection, tissue injury and other noxious conditions. It is an essential immune response by the host that enables the removal of harmful stimuli as well as the healing of damaged tissue. Acute inflammation has therefore been considered as a part of innate immunity,

the first line of host defense against foreign invaders and danger molecules. Mankind has known the classical symptoms of inflammation for hundreds of years, which include redness, pain, swelling and heat.[5]

Inflammation is characterized by (1) vasodilation of the local blood vessels, with consequent excess local blood flow; (2) increased permeability of the capillaries, allowing leakage of large quantities of fluid into the interstitial spaces; (3) often clotting of the fluid in the interstitial spaces because of excessive amounts of fibrinogen and other proteins leaking from the capillaries; (4) migration of large numbers of granulocytes and monocytes into the tissue; and (5) swelling of the tissue cells.[6]

Cardinal signs of Inflammation[7]

The four principal effects of inflammation (rubor, tumor, calor & dolor) were described nearly 2,000 years ago by the Roman Aulus Cornelius Celsus, more commonly known as Celsus. However, the addition of this fifth sign (functio laesa) has also been ascribed to Thomas Sydenham and Virchow.

Sign of normal inflammation

- Redness (rubor)
- Heat (calor)
- Swelling (tumor)
- Pain (dolor)
- Loss of function (functio laesa)

Redness (rubor): The inflamed tissue appears red, for example sunburn, cellulitis due to bacterial infection or acute conjunctivitis due to dilation of small blood vessels within the damaged tissues.

Heat (calor): The increase in temperature is look only in peripheral parts of the body, such as the skin due to increased blood flow (hyperaemia) due to vascular dilatation and the delivery of warm blood to the inflamed area.

Swelling (tumor): The swelling produce the edema the buildup of fluid in the extravascular space as part of the fluid exudates and to a much extent, by the inflammatory cells migrating into the area.

Pain (dolor): Pain is one of the best features of acute inflammation. It results from the stretching and distortion of tissues due to inflammatory edema and from pus under pressure in an inflamed cavity. Sometime of the chemical mediators produced acute inflammation, including prostaglandins, serotonin & bradykinin.

Loss of function (functio laesa): Loss of function was added by Rudolf Virchow ("father of modern pathology") (1821-1902) to the list of features written by Celsus. The Movement of the inflamed area is conscious inhibited by pain, while the swelling may physically immobilize the tissues.

Causes of Inflammation[8]

Microbial infections

One of the most common causes of inflammation is microbial infection. Microbes include viruses, bacteria, protozoa, fungi and various parasites. Viruses lead to death of individual cells by intracellular multiplication, and either cause the cell to stop functioning and die, or cause explosion of the cell (cytolytic), in which case it also dies. Bacteria release specific toxins – either exotoxins or endotoxins. Exotoxins are produced specifically for export (like anthrax toxins or tetanus toxins) whereas endotoxins are just part of the cell walls of Gram negative bacteria and they do terrible things to the body too but they aren't as specific in their actions as the exotoxins.

Hypersensitivity reactions

A hypersensitivity reaction occurs when an altered state of immunologic responsiveness causes an inappropriate or excessive immune reaction that damages the tissues.

Physical agents, irritant and corrosive chemicals

Tissue damage leading to inflammation may occur through physical trauma, ultraviolet or other ionizing radiation, burns or excessive cooling ('frostbite'). Corrosive chemicals (acids, alkalis, oxidizing agents) provoke inflammation through direct tissue damage. These chemical irritants cause tissue damage that leads directly to inflammation.

Tissue necrosis

Death of tissues from lack of oxygen or nutrients resulting from inadequate blood flow (infarction) is a potent inflammatory stimulus. The edge of a recent infarct often shows an acute inflammatory response.

Endogenous chemical mediators[9]

A variety of chemical mediators from circulation system, inflammatory cells, and injured tissue actively contribute to and adjust the inflammatory response. The released chemical mediators include (1) vasoactive amines such as histamine and serotonin, (2) peptide (e.g., bradykinin), and (3) eicosanoids (e.g., thromboxanes, leukotrienes, and prostaglandins).

Anti-inflammatory mechanisms of plants

Indian Olibanum (*boswellia serrata*)

B. serrata treated rats significantly decreased the paw edema and histopathological finding of cellular infiltrates and found to be greater at higher concentration i.e., 200 mg/kg/b/wt as compared to standard drug. The finding of the study proves that B. serrata has high anti-inflammatory activity and supports its usage in traditional medicine as herbal anti-inflammatory medicine.[10]

Pure compound from *Boswellia serrata* extract exhibits antiinflammatory property in human peripheral blood mononuclear cells (PBMCs) and mouse macrophages through inhibition of tumor necrosis factor-alpha (TNF-

alpha), interleukin-1beta (IL-1beta), NO and mitogen activated protein (MAP) kinases. Incensole acetate, a novel antiinflammatory compound isolated from *Boswellia* resin inhibits nuclear factor-kappa B activation.[11]

Borage seed oil *(Borago officinalis)*

Borage seed oil, first compared 1.4 g/day of GLA, administered as borage seed oil, with placebo capsules containing cottonseed oil. At the end of 6 months of treatment, patients treated with borage seed oil had significant improvement, compared with those in the placebo group, in joint tenderness counts and scores, joint swelling scores, physician global assessment, and pain.[12]

Borage seed oil is a rich source of gamma linoleic acid (GLA), 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 TNF-α. The mechanism mentioned above can clarify the anti-inflammatory effect of borage oil in rheumatoid arthritis (RA).[13]

Evening primrose oil (EPO) (*Oenothera blennis)*

A study of EPO involved 49 patients with mild RA, EPO capsules provided 540 mg GLA and EPO/fish oil capsules provided 450 mg GLA and 240 mg essential fatty acids. However, a significantly greater percentage of patients in the treatment groups reported subjective improvement compared with the placebo patients (94 vs 30%) and 73% of EPO and 80% of EPO/fish oil patients had reduced or stopped their non-steroidal anti-inflammatory drugs (NSAIDs) compared with only 33% of placebo patients ($P < 0.05$).[14]

Turmeric (*Curcuma longa)*

An artificially induced wound has been examined in twenty-five guinea pigs. Complete healing time of the artificially induced wound in various treatment groups vary with the effectiveness of the treated materials. All pastes seemed to be effective for wound healing. The paste of turmeric showed the best results where healing was complete in 12 days. The garlic paste and aloe showed the different results where healing were completed in 15 and 17 days respectively.[15]

Eighteen patients participated in a crossover study of 1200 mg/day of curcumin vs 300 mg/day of phenyl butazone. Patients in each group showed significant improvement from baseline in morning stiffness, walking time and joint swelling. Although the authors indicate 'convincing evidence of the anti-rheumatic activity of curcumin', no comparisons were reported between the curcumin and phenylbutazone groups.[16]

Ginger (*Zingiber officinale)*

Oral administration of *Z. officinale* extract has shown different and inconsistent effects, depending on the quantity of consumption. Although administration of squeezed ginger extract to mice one time or twice has elevated the tumor necrosis factor-α (TNF-α) in peritoneal cells, long-term consumption of the extract has increased the serum corticosterone level and has reduced proinflammatory markers.[17]

Z. officinale was also tested in type 2 diabetic patients with low-grade inflammation; after 2 months of treatment, serum level of TNF-α and high-sensitivity C-reactive protein (hs-CRP) were decreased definitely.[18]

Rosehip (*Rosa canina*)

Rosehip powder is extracted from the seeds and husks of the fruits have been shown to inhibit expression of iNOS, IL-1α and MMP-9, and IL-1β-induced ADAMTS-4, MMP-1, MMP-13, IL-1α, and IL-8 in chondrocytes. The likely mechanism of action is via the specific galactolipid constituent.[19]

A study involving 112 patients with osteoarthritis of the hip, knee, hand, shoulder or neck, found that compared to those receiving placebo, patients who received 5g/day of standardized rosehip powder for 3 months experienced significant reductions in pain ($p<0.0078$) and stiffness ($p<0.0025$). 66% of patients receiving active treatment reported improvement in pain compared to only 36% of placebo patients.[20]

Flax seed (*Linum usitatissimum*)

48 male mice were randomly designated into 6 groups of 8 each, including control, dexamethasone as positive control and experimental groups to conduct a study of the anti-inflammatory effect. For analgesic evaluation, 192 male Balb/c mice were randomly designated into 4 sets of 6 groups. The groups consisted of control group, which received 10 mL/kg normal saline, morphine (2.5 mg/kg) as positive control, morphine (2.5 mg/kg) plus naloxone, experimental groups (200 and 500 mg/kg extract), and extract (500 mg/kg) along with naloxone (4 mg/kg) groups. The analgesic activities were evaluated at 5, 15, 30, and 60 minutes, respectively, in each set.[21]

Blackcurrant (*Ribes nigrum*)

The major compounds isolated from *Ribes nigrum* leaves, on the proteoglycans (PGs), type II collagen (coll. II) and prostaglandin E2 (PGE2) production by differentiated human chondrocytes cultivated in long term (12 days) and in clusters as well as their inhibition potential on COX-1 and COX-2 in vitro. Gallocatechin trimer (GC–GC–GC) showed the higher stimulation of PGs and coll. II production (1 µg ml–1) and the synthesis of PGE2 were significantly reduced by gallocatechin dimer (GC–GC), gallocatechin-epigallocatechin (GC–EGC) and GC–GC–GC at 10 and 100 µg ml–1. The inhibition of PGE2 synthesis was confirmed by the in vitro test on purified COX enzymes, showing the selectivity of prodelphinidins on COX-2.[22]

In vitro experiments demonstrated that PACs were able to significantly inhibit ICAM-1 but not IL-8 and VEGF165 mRNA expression. Moreover, VEGF121 mRNA expression was dose-dependently enhanced. This study provides evidence to support the anti-inflammatory activity of proanthocyanidins is related to an inhibition of leukocyte infiltration.[23]

Olive oil (*olea europaea*)

Olea europaea increases nitric oxide (NO) production in macrophages challenged with lipopolysaccharide through induction of the inducible form of the enzyme nitric oxide synthase, thus increasing the functional activity of these immunocompetent cells. It is well known that oleuropein elicits anti-inflammatory effects by inhibiting lypoxygenase activity and the production of leukotriene B4.[24]

In order to evaluate the anti-nociceptive activities of the methanolic and aqueous extracts of defatted fruits of *Olea europaea*, formalin test was used and for evaluation of anti-inflammatory effects of the extract, the volume of paw edema was measured. The results of paw edema volume measurement indicated that the aqueous extract has anti-inflammatory effects at dose of 600 mg/Kg.[25]

Avocado (*Persea Americana)*

The aqueous leaf extract of *P. americana* (800 mg/kg) produced a significant inhibition of the swelling caused by carrageenan at 3 h. This effect was similar to that produced by indomethacin in the same duration.[26]

The analgesic activity was assessed using acetic acid stimuli to induce peripheral pain in mice. Results of this research showed that both all level doses of infusion and methanolic extract of avocado seeds have a significant reduction on the mice paw edema. All level doses of methanolic extract of avocado seeds have a significant reduction on the number of abdominal writhes induced by acetic acid, but only the lowest dose of infusion showed a significant reduction.[27]

CONCLUSIONS

Herbal medicine is being used for several ailments of body from the ancient time. Plants have specific phytochemicals and every chemical has its specific actions. In this article a brief discussion has been demonstrated for anti-inflammatory actions of herbal plants. Pharmacological properties and clinical studies have justified the positive influencing role of several herbal plants in treating inflammation. Further research and clinical trials of herbal plants may open the way for new potential therapeutic agent for inflammation.

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