



AN OVERVIEW ON INFLAMMATION AND PLANT HAVING ANTI-INFLAMMATORY ACTIVITY

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ABSTRACT

Herbal medicines are promoting subjects in medicine and of course, we have to increase our knowledge about them. Complementary, alternative, and traditional medicines are the pivotal source of herbal medication guidance, but surely modern medicine must prove these guidelines through scientific methods before using them in practice. In this review, we have endeavored to assess the plants and the most clinical evidence of their anti-inflammatory effects. Chronic inflammation releases lymphocytes and macrophages into the affected tissue, and it is closely associated with allergies, atherosclerosis, cancer, arthritis, and Alzheimer's disease, as well as autoimmune diseases.

Keywords: Atherosclerosis, Anti-inflammatory, Complementary, Traditional medicines.

INTRODUCTION

Inflammation is a defense response of our body to hazardous stimuli such as allergens and/or injury to the tissues; on the other hand, uncontrolled inflammatory response is the main cause of a vast continuum of disorders including allergies, cardiovascular dysfunctions, metabolic syndrome, cancer, and autoimmune diseases imposing a huge economic burden on individuals and consequently on the society [1]. There are various medicines for controlling and suppressing inflammatory crisis; steroids, non-steroid anti-inflammatory drugs, and immunosuppressant are the practical examples of these medications which are associated with adverse effects while in practice our goal is to apply minimum effective dose by the highest efficacy with the least adverse effects. Thus, we need to apply natural anti-inflammatory factors within medication therapy to achieve increased pharmacological response and the lowest degree of unwanted side effects [1, 2].

Inflammation

A localized reaction that produce redness, warmth, swelling, and pain as a result of infection, irritation, or injury. Inflammation can be external or internal in fig 1 and 2 [3].

Infections caused by Group-A Streptococcus is a human pathogen which is responsible for many diseases, ranging from streptococcal pharyngitis to impetigo.

Infections which were caused by GAS have been documented as far back as 6500 BC. In the late 17th century, *Thomas Sydenham* clinically distinguished scarlet fever from measles. Records of holistic medicine go back to the Egyptian god of medicine. The origins of Egyptian medicine lie in religion and spirituality, and it was believed that the gods intervened in matters of health and disease. At that time it was recognized that blood was the nutritive and regulatory substance and the heart was the center of the circulatory system. It was widely recognized that respiratory patterns influenced blood circulation [4].

The Role of Inflammation

As part of the immune response, inflammation plays an important role in defending the body against pathogens such as viruses, bacteria, fungi, and other parasites. Acute inflammation releases leukocytes, erythrocytes and components of plasma into the affected tissue. If the inflammation is not corrected it can lead to chronic inflammation [5].

Biochemical influences, such as the imbalance of dietary fats, absence of specific substances that adversely affect the production of anti-inflammatory cells, as well as specific nutrient problems, result in chronic inflammation [6].

Functions of inflammation

- Inflammation is the first step in the healing or repair

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- Process after some physical or chemical injury or stress. It is a normal bodily function and it is a healthy action when it is controlled. If there no inflammation even a small cut on the finger could lead to death.
- Inflammation prevents the spread of damaged cells to other areas of the body that could cause secondary problems. A local infection, for example, can be contained due to the inflammatory response, instead of causing a body-wide infection.
- Inflammation rids the body of damaged and dead cells.

Benefits of inflammation

- Destruction of microbes, thereby eradicating infection
- Detoxification of toxins
- Clears infections
- Facilitates in the healing process
- Repairs damages tissues

Drawbacks of inflammation

Inflammatory responses may be harmful, such as in an anaphylactic shock. Inflammation of the peritoneum, leads to fibrous bands that cause intestinal obstruction. Pericardial inflammation results in the formation of dense pericardium that impairs the functioning of the heart [7-12].

Mechanism of inflammation

The inflammatory process is a combination of many pathways like a synthesis of prostaglandin, interleukin or other chemo toxin, adhesive protein receptor action, platelet-activating factors. All can act as chemotactic agonists. Inflammation initiates with any stress on the membrane or by other trigger or stimuli, these activate hydrolysis of membrane phospholipid by phospholipase A into arachidonic acid, which further substrate for cyclooxygenase and lipoxygenase enzyme and byproduct of these are prostaglandins PGE₂, PGH₂ and leukotrienes like LTC₄, LTB₄ etc [12-15].

Other causes of inflammation include

Chronic low-grade food allergies food sensitivities that may cause few symptoms. An imbalance of bacteria and fungi in your gastrointestinal tract also known as dysbiosis. This causes your immune system to overreact to bacteria in your gut and can be without notable symptoms.

Stress Constant psychological, emotional or physical stress raises the level of cortisol, creating inflammation. For more on the effects of stress on your body, read How Stress Creates a Double-Whammy Threat to Your Health.

Environmental toxicity from our air, water, food pollutants and toxic metals like mercury and lead all contribute to inflammation and have been linked to diseases as varied as endometriosis and cancer [15-19].

TYPES OF INFLAMMATION

Acute Inflammation

Acute inflammation usually has becoming within minutes or at most hours after tissue injury, and may be

characterized by the classical symptoms of redness, heat, oedema. It's a short term process. It is characterized by the exudation of fluids and plasma proteins and the migration of leukocytes, most importantly neutrophils into the injured area. This acute inflammatory response is useful to the defense mechanism aimed at killing of bacteria, virus and parasites while still facilitating wound repairs in fig 3 [20, 21].

Chronic Inflammation

Chronic inflammation is of a more prolonged duration and histologically by the presence of lymphocytes and macrophages, resulting in fibrosis and tissue necrosis. The chronic inflammation increases the development of the degenerative diseases such as rheumatoid arthritis, atherosclerosis, heart disease, Alzheimer, asthma, acquired immunodeficiency disorder (AIDS), cancer, congestive heart failure, multiple sclerosis, diabetes, infections, gout, IBD-inflammatory bowel disease, aging and other neurodegenerative CNS depression, Chronic inflammation also has been implicated as part of the cause of the muscle loss that occurs with aging in fig 4 [22, 23].

SECONDARY METABOLITES USED AS ANTI-INFLAMMATORY

Phenolic compounds

Phenolic compounds are of important pharmacological value, some having anti-inflammatory properties. Different types of phenolic compounds such as flavonoids, condensed tannins, and Gallo tannins are known to inhibit some molecular targets of pro-inflammatory mediators in inflammatory responses.

Condensed tannins

Condensed tannins (proanthocyanidins) are essentially derived from (+) gallocatechin, (-) epicatechin, (+)catechin and epigallocatechin, and their derivatives via carbon to carbon (C-C)links. Proanthocyanidins are naturally occurring plant metabolites, widely available in fruits, vegetables, nuts, seeds, flowers and bark.

Proanthocyanidins play important roles at the nutritional and physiological level and in pharmacology for their antioxidant properties. Proanthocyanidins are also associated with a number of biological activities, such as anti-inflammatory, anti-asthmatic, anticancer, antimicrobial, anti-allergy, antihypertensive and Cardio protective. The beneficial effects of proanthocyanidins on human health have been attributed mainly to their strong free radical-scavenging and antioxidant activities. These compounds are antagonists of particular hormone receptors or inhibitors of particular enzymes such as COX enzymes.

Gallotannins

Gallotannins exert various biological effects ranging from anti-inflammatory to anticancer and antiviral properties. The mechanisms underlying the anti-inflammatory effect of tannins includes the scavenging of radicals and inhibition of the expression of inflammatory mediators, such as some cytokines, inducible nitric-oxide

synthase (iNOS) and COX-2. The high amount of the guillotine was detected in *protea simplex* leaf.

Flavonoids

Flavonoids are polyphenolic compounds that occur ubiquitously in foods of plant origin. Over 4000 different flavonoids have been described, and they are categorized into flavonols, flavones, catechins, flavanones, anthocyanin's and isoflavonoids. Flavonoids have a variety of biological effects in numerous mammalian cell systems, in vitro as well as invivo. They have been shown to exert antimicrobial, antiviral, antiulcerogenic, cytotoxic, anti-neoplastic, mutagenic, anti-inflammatory, antioxidant, anti-hepatotoxic, antihypertensive, hypolipidemic and antiplatelet activities. Flavonoids are known to act on the inflammatory response via many routes and block molecules like, COX cytokines; nuclear factor- κ B and matrix metalloproteinases. Flavonoids were investigated in models of inflammation in rats and were found to possess significant activity in both proliferative and exudative phases of inflammation. Flavonoids showed anti-inflammatory activity and inhibited the development of the induced granuloma.

Coumarins

Coumarins represent a vast family of compounds which were naturally found in plants. It has been already reported that several coumarin derivatives have significantly anti-inflammatory and antioxidant activities. Thus, coumarin derivatives could be particularly effective in the treatment of high protein edemas. It was reported that some coumarins possessed the antioxidant capacity scavenging superoxide anion radicals and some coumarins could inhibit both the lipoxygenase and cyclooxygenase pathways of arachidonic acid metabolism.

Two coumarin derivatives, columbianetin (A) and libanoridin (B) were isolated from *Corydalis heterocarpa* [18], and coumarins isolated from *Torreseacearensis*, *Justicia pectoralis*, *Eclipta alba*, *Pterodonpolygaliflorus* and *Hybanthus ipecacuanha* showed significant anti-inflammatory activity.

Alkaloids

Some alkaloids such as isoquinoline, indole and diterpene are known to have good anti-inflammatory activity. Three types of isoquinoline alkaloids were detected in the roots, barks and branches of Turkish *Berberis* species: protoberberine, bisbenzylisoquinoline and aporphine.

Saponins

Saponins are steroid or triterpene glycosides widely distributed in the plant kingdom that include a large number of biologically active compounds. Saponins isolated from about 50 plants showed anti-inflammatory activity against several experimental models of inflammation in mice and rats.

Three triterpenoid saponins with significant anti-inflammatory activity were isolated from *Polygala*

japonica. There are a number of reports of saponins with anti-inflammatory properties. Frutescensaponin B, a bidesmosidic saponin with an unbranched saccharide

Moiety isolated from *Bupleurum frutescens* L was shown to have the highest anti-inflammatory activity of the all the saponins tested in them oedema assays. In vivo studies on saponins isolated from *Bupleurum rotundifolium* L. (Apiaceae) were reported to have anti-inflammatory activity against both 12-O-tetradecanoylphorbol-13-acetate (TPA) induced ear oedema and chronic skin inflammation.

Sterols

Phytosterols and their derivatives are essential components of plant bio membranes and they are biogenetic precursors of numerous metabolites such as plant steroid hormones. Plant sterols have been investigated as an alternative for lowering plasma cholesterol levels, and several studies have shown that they significantly reduce plasma total and LDL cholesterol. Anti-atherosclerotic effects of plant sterols are well documented. The anti-atherogenic effects may be due, not only to their cholesterol-lowering activities, but also to other properties, such as effects on the coagulation system, an antioxidant system, and hepatic and lipoprotein lipase activities. Moreover, plant sterols have been shown to have other metabolic effects. For example, several epidemiological and animal studies suggest that phytosterols suppress the growth of colon tumors.

Terpenoids and Essential oils

Essential oils are volatile, natural, complex compounds characterized by a strong odour and are formed by aromatic plants as secondary metabolites. Essential oils are highly enriched in compounds based on an isoprene structure. They are called terpenes, their general chemical structure is C₁₀H₁₆, and they occur as diterpenes, triterpenes, and tetraterpenes (C₂₀, C₃₀, and C₄₀), as well as hemiterpenes (C₅) and sesquiterpenes (C₁₅). When the compounds contain additional elements, usually oxygen, they are termed terpenoids. Examples of common terpenoids are menthol and camphor (monoterpenes) and farnesol and artemisin. Artemisin and its derivative α -arteether, also known by the name qinghaosu, find current use as antimalarials [24].

CURRENT INVESTIGATION OF PLANTS SHOWING ANTI INFLAMMATORY EFFECT

Cassia occidentalis

Whole plant of *Cassia occidentalis* using ethanolic extract. For investigation of anti-inflammatory potential dose taken 250 mg/kg and using carrageenan induced paw edema model. The result revealed that significant reduction in malondialdehyde levels of murine hepatic microsomes and significantly reduced carrageenan induced inflammation in mice at a dose of 250 mg/kg in fig 5 [25, 26].

Hedera rhombea

The leaves of *Hedera rhombea* Bean were investigated and using methanol and butanol fractions and evaluated by carrageenan induced edema method showed considerable analgesic activity, anti-inflammatory activity was found in the methanol, butanol and ether fractions by carrageenan induced edema test in fig 6 [27].

Bryophyllum pinnatum

The *Bryophyllum pinnatum* was investigated by ojewole *et al.* The study was undertaken to investigate anti-inflammatory and of the plant leaf aqueous extract in experimental animal models. In this experiment using fresh egg albumin-induced pedal (paw) oedema model and drug taken Diclofenac 100 mg/kg. The results revealed of this experimental animal study suggest that *Bryophyllum pinnatum* leaf aqueous extract possessed anti-inflammatory. The different flavonoids, polyphenols chemical constituents of the herb are speculated to account for the observed anti-inflammatory of the plant in fig 7 [28].

Swertia

The *Swertia chirata* was chosen for pharmacological screening of anti-inflammatory activities in animal models. The anti-inflammatory activity was using the carrageenan-induced rat paw edema model and taken rat paw edema model induced by carrageenan. The result revealed that the extract was found to reduce significantly ($p < 0.001$) the formation of edema at the 400 mg/kg dose level and showed 57.81% ($p < 0.001$) inhibition of edema volume at the end of 3 h, the ethanolic extract of *swertia chirata* reduced the inflammation in fig 8 [29].

Zingiber officinale

Shimoda *et al* 2010 was investigated the anti-inflammatory effect of *Zingiber officinale* and prepared 40% ethanolic extract from dried red ginger and evaluated its anti-inflammatory activity using acute and chronic inflammation models. The result possessed found a potent suppressive effect on acute and chronic inflammation, and inhibition of macrophage activation seems to be involved in this anti-inflammatory effect in fig 9 [30].

Sida cordifolias

The *Sida cordifolia* was evaluated by Franzotti (2000). The leaves of *Sida cordifolia* were taken for carrageenan-induced rat paw edema at a dose of 400 mg/kg administered orally, but did not block the edema induced by arachidonic acid in fig 10 [31].

Pluchea indica

The anti-inflammatory activity of the methanolic fraction of a chloroform extract of *Pluchea indica* roots was investigated and evaluated by Sen (1991). The extract showed significant inhibitory activity against carrageenan-, histamine-, serotonin-, hyaluronidase- and sodium urate-induced pedal inflammation and also inhibited carrageenan- and cotton pellet-induced granuloma. The anti-inflammatory activity of the methanolic fraction of a

chloroform extract of *Pluchea indica* roots was investigated and evaluated by Sen 1991 in fig 11 [31]

Ricinus Communis

The *Ricinus communis* (Euphorbiaceae) Linn. The root was studied in Wistar albino rats. The methanolic extract at doses 250 and 500 mg/kg of anti-inflammatory activity in carrageenan-induced hind paw edema model. The results of the study indicate that the methanolic extract of *Ricinus communis* root possesses significant anti-inflammatory activity in acute and chronic inflammatory models in rats in fig 12 [32].

Thespesia populnea

The *Thespesia populnea* leaves were evaluated in animal models for anti-inflammatory activity and established by Ilavarasan (2012). The extracts reduced paw oedema induced by carrageenan in rats. The results obtained in this study suggest that *Thespesia populnea* extracts have and anti-inflammatory properties in fig 13 [33].

Achillea millefolium

The *Achillea millefolium* was investigated and measured by the mouse paw edema test. The result revealed by the isolation of a material which reduces inflammation by 35 % in fig 14 [33].

Aconitum heterophyllum

The *Aconitum heterophyllum* has been evaluated in cotton pellet-induced granuloma in rats. The anti-inflammatory properties of the extract and the effects were compared to diclofenac sodium. The extract has reduced inflammation in fig 15 [34].

Aegle marmoles

The Bilwa was prepared and tested for anti-inflammatory activity in albino rats using Carrageenan induced paw edema model and cotton pellet induced granuloma and the standard drug was taken indomethacin and Bilwa. The result revealed that anti-inflammatory activity was expressed the inhibition in fig 16 [34].

Emblica officinalis

The *Emblica officinalis* using carrageenan and cotton pellet induced acute and chronic inflammatory animal model. The compounds were studied for their acute and chronic anti-inflammatory activity at a dose level of 20 and 40 mg/kg against standard drug diclofenac. The results indicated that in both acute and chronic reduction in the inflammation, but significant effects were observed only at high doses in fig 17 [34].

Annona squamosal

The *Annona squamosal* plant and studied for its anti-inflammatory activity and evaluated by Chavan (2009). The dose taken of Caryophyllene oxide of 12.5 and 25mg/kg body wt. and unsaponified petroleum ether extract at a dose of 50 mg/kg body wt. These activities of caryophyllene oxide were given significant effect against inflammation in fig 18 [35].

Fig 1. Foot Inflammation



Fig 2. Joint Inflammation



Fig 3. Acute inflammation

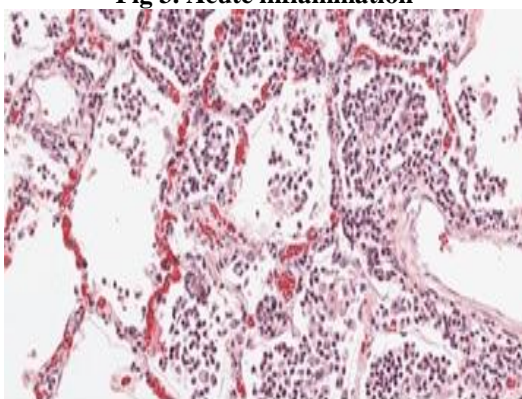


Fig 4. Chronic inflammation

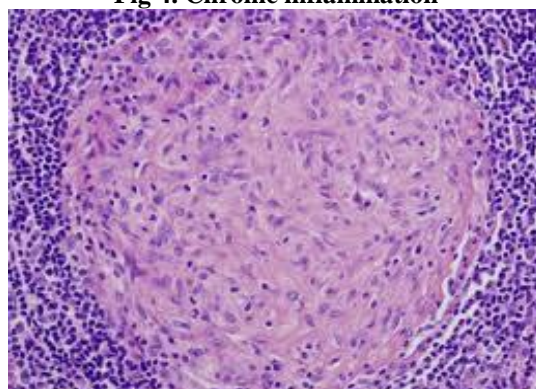


Fig 5. *Cassia occidentalis*



Fig 6. *Hedera rhombea*

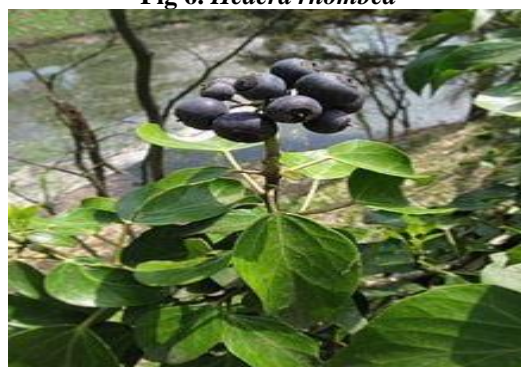


Fig 7. *Bryophyllum pinnatum*



Fig 8. *Swertia*



Fig 9. *Zingiber officinale*



Fig 10. *Sida cordifolias*



Fig 11. *Pluchea indica*

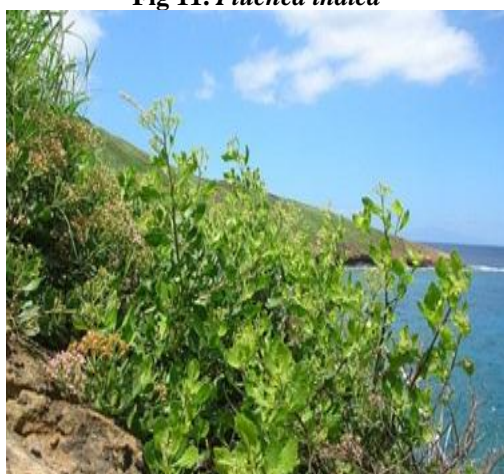


Fig 12. *Ricinus Communis*



Fig 13. *Thespesia populnea*



Fig 14. *Achillea millefolium*



Fig 15. *Aconitum heterophyllum*



Fig 16. *Aegle marmoles*



Fig 17. *Emblica officinalis*



Fig 18. *Annona squamosa*



SUMMARY AND CONCLUSION

Inflammation is a defense mechanism of the body and inflammation is a healthy process resulting from some disturbance or disease. But in some conditions when negative effect of the inflammatory process is produced example, these inflammatory disorders are rheumatoid arthritis, osteoarthritis, inflammatory bowel diseases, retinitis, multiple sclerosis, psoriasis and atherosclerosis.

To overcome this problem anti-inflammatory agents are very requiring. For this purpose variety of safe and effective anti-inflammatory agents are available, including aspirin and other nonsteroidal anti-inflammatories, with many more drugs under development. So these agents are very helpful to reduce the inflammatory response.

These agents are called anti-inflammatory agents. Plants have played an important role in human health care since the ancient times. Traditional plants play a very

important role in the discovery of new drugs. Now present days, inflammation is a very big challenge of mankind. So much of anti-inflammatory drugs are available, but it is believed that these drugs such as opioids and analgesia inducing drugs like NSAIDs are not useful in all cases and these drugs also produce side effects, so to overcome this problem new drugs are very requisite and in plants have many of phytoconstituents which are helpful in inflammation and have less side effects. So in this medicinal plants on behalf of their phytoconstituents which can be helpful in inflammation

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Nil

CONFLICT OF INTEREST

No interest

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