



Anti-inflammatory Activities of Plant Extracts



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Abstract

Inflammatory diseases are common in the aging society of developed and developing countries. These include rheumatoid arthritis. Drugs such as NSAID and corticosteroids have been used over the years. However, these drugs have side effects and in some cases they are irreversible. In addition the cost of manufacturing drugs is an expensive endeavours and before its use in human is approved, the drug has to be subjected to clinical trials, which may take several years. With an increase in inflammatory diseases around the globe, mankind has resorted to the use of traditional or phytomedicine. Tropical countries because of their rich biodiversity are of significant advantage in this regards, because their unique flora and fauna are a source of these therapeutic anti-inflammatory drugs. Plants can be administered as their crude extracts to fight inflammatory diseases or anti-inflammatory natural products can be isolated from them and used to combat inflammation. Amongst, natural products isolated from plants that have significant anti-inflammatory uses, include, curcumin, resveratrol, baicalein, boswellic acid, betulinic acid, ursolic acid and oleanolic acid.

Keywords: Inflammatory diseases; Rheumatoid arthritis; NSAID; Corticosteroids; Phytomedicine

Introduction

Inflammation is the immune system's response to harmful stimuli, such as pathogens, damaged cells, toxic compounds or ultraviolet irradiation. It acts by removing injurious stimuli and initiating the healing process [1,2]. Inflammation is the major and complex reaction of the body against infection upon tissue injury. Inflammation plays a significant role in the healing and restorative process. In some cases, chronic inflammation may develop that lasts throughout the lifetime of an individual. These inflammatory diseases include, rheumatoid arthritis, osteoarthritis, inflammatory bowel diseases, retinitis, multiple sclerosis, psoriasis and atherosclerosis. There are four primary indicators of inflammation. These are pain, redness, heat or warmth and swelling. The redness involves an increase of blood supply to the affected region by means of vasodilation [3]. In addition, there can be swollen joints and joint pain, stiffness and loss of joint function. Whenever there is an injury to any part of the human body, the arterioles in the encircling tissue dilate. This results in an increase in blood circulation towards the area, resulting in redness [4]. There are two forms of inflammation. These are acute inflammation and chronic inflammation. Acute inflammation is characterized by the exudation of fluids and plasma proteins and the migration of leukocytes, most notably neutrophils into the injured area. Acute inflammatory response is a defense mechanism, aimed at killing bacteria, virus and parasites, in

addition to still facilitating wound repairs. Chronic inflammation is prolonged and persistent inflammation, which is marked mainly by new connective tissue formation. It may be the continuation of an acute form or a prolonged low-grade form [5]. 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. It has also been responsible for muscle loss that occurs with aging [6]. Inflammation processes can be categorized into four distinct groups: Changes in the blood flow supply to the affected area induce changes in smooth muscles cell function, causing vasodilation. Secondly, there is contraction of cytoskeleton in endothelial cells, causing alterations in vascular permeability. Thirdly, there is passage of phagocytic leukocytes from capillary vessels into the surrounding interstitial spaces to the site of injury or inflammation. Fourthly, Phagocytosis is involved in the inflammation process [7].

Inflammation is a healthy process of the body, resulting from diseases. However, negative effects of the inflammatory process can occur, resulting in inflammatory disorders such as rheumatoid arthritis, osteoarthritis, inflammatory bowel diseases, retinitis, multiple sclerosis, psoriasis and atherosclerosis and asthma.

Figure 1 shows the synthesis of Eicosanoids that are necessary for the inflammation process. As is shown, the synthesis can be inhibited by anti-inflammatory agents such as aspirin (NSAIDs) and corticosteroids.

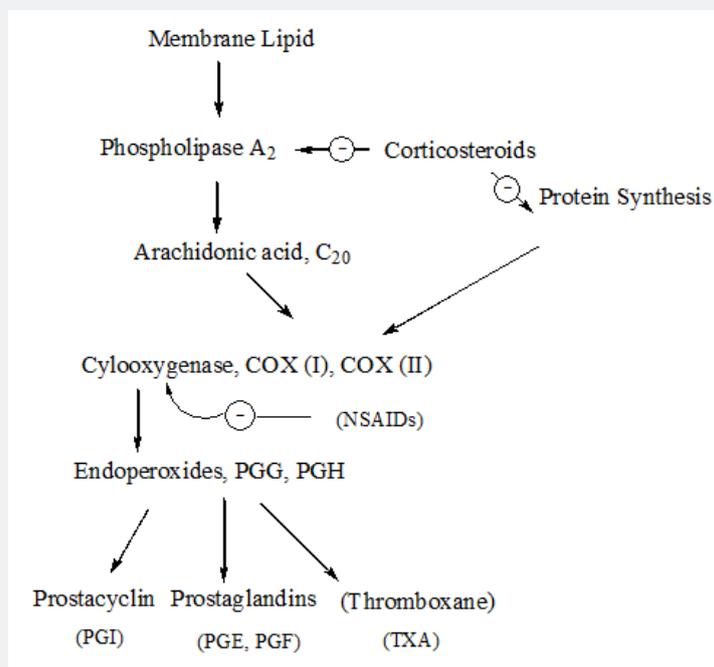


Figure 1:

Synthetic drugs have been used against the inflammation process. These include aspirin, indomethacin, non-steroidal anti-inflammatories (NSAIDs). In addition, other anti-inflammatory drugs are under development. However, due to their adverse side effects such as kidney problems, bleeding risks and ulcers, plant extracts and isolated natural products have been used as anti-inflammatory agents [8-14]. Table 1 gives a list of plant extracts being used as anti-inflammatory agents.

There are many articles in the literature that report the use of plant extracts as anti-inflammatory agents. Only five are reported in this mini-review. The anti-inflammatory activities of aqueous extracts derived from holy basil leaf, sesame seed, long pepper and cubeb pepper on monocyte-derived macrophages (MDMs) have been reported. After exposing MDMs to these extracts for two hours, they subjected the cells to lipopolysaccharide (LPS) stimulation for 24 hours, then the expression of pro-inflammatory genes were analysed. The effects of the extracts on the oxidation of low-density lipoprotein (LDL) by enzymatic (myeloperoxidase) and non-enzymatic (copper) reactions, were also investigated. It was found that all four extracts reduced LPS-induced inflammation and inhibited LDL oxidation. This study could serve as a guide for future studies on natural medicines that will be useful for consumers and producers, as well as industries that make use of bioactive compounds [15].

Six medicinal plant extracts used in traditional medicine, were investigated for their anti-inflammatory potential against adjuvant-carrageenan-induced inflammation (ACII). All doses expressed here are equivalents of dried starting plant materials (1.50g dry plant/kg body wt.). Plant extracts from *Synedrella nodiflora*, and the hexane leaf extract of *Bursera simaruba*, showed interesting results. In ACII, orally administered extracts (at doses 40 and 80mg/kg, respectively), inhibited both the acute and chronic phases of this experimental model of inflammation, mainly the chronic phase. These extracts exhibited potent anti-inflammatory activity daily throughout the experiment, and were effective as reference drugs, phenylbutazone (80mg/kg) and indomethacin (3mg/kg) [16].

The anti-inflammatory activity of various fruits, herbs and spices in a lipopolysaccharide-stimulated macrophage model have been reported. These compounds acted by reduction of pro-inflammatory interleukin (IL)-6 or tumour necrosis factor (TNF)-alpha production, enhancement of anti-inflammatory IL-10 production, or reduction of cyclooxygenase-2 or inducible nitric oxide synthase expression. The highest anti-inflammatory potential was detected with chili pepper. Amongst the plants that improved the secreted cytokine profile were allspice, basil, bay leaves, black pepper, licorice, nutmeg, oregano, sage and thyme. The compounds apigenin, capsaicin, chrysin, diosmetin, kämpferol,

luteolin, naringenin, quercetin and resveratrol moderately rich in fruits, herbs and spices may contribute to the reduction of reduced IL-6 and TNF-alpha secretion. Resveratrol and rosmarinic acid increased secretion of IL-10. Our findings indicate that a diet the inflammatory response and related diseases [17].

Table 1: Demonstrates a list of plants that have rich anti-inflammatory properties.

Plants (Scientific Name)	Common Name	Family
<i>Zingiber officinale</i>	Ginger	Zingiberaceae
<i>Aconitum heterophyllum</i>	atish	Ranunculaceae
<i>Aegle Marmelos</i>	bael bili or bhel also Bengal quince, golden apple. Japanese bitter orange, stone apple or wood apple,	Rutaceae
<i>Mirabilis jalapa</i>	The marvel of Peru or four o'clock flower	Nyctaginaceae
<i>Bryophyllum pinnatum</i>	Air plant, cathedral bells, life plant, miracle leaf, Goethe plant, Tamil: Malaikkalli, Runakkalli	Crassulaceae
<i>Solanum nigrum</i>	Black night shades	Solanaceae
<i>Piper ovatum</i>	joão burandi" or "anesthetic	Piperaceae
<i>Viola betonicifolia</i>	arrowhead violet, showy violet or mountain violet	Violaceae
<i>Azadirachta indica</i>	neem, nimtree or Indian lilac	Meliaceae
<i>Achillea Millefolium</i>	Yarrow or common yarrow	Asteraceae
<i>Boswellia Serrata</i>	It is also known as Indian oli-banum, Salai guggul, and Sallaki in Sanskri	
<i>Persicaria stagnina</i>	Bishkatali	Polygonaceae
<i>Scoparia dulcis</i>	Misridana	Seophulariaceae
<i>Cordyline terminalis</i>	Ti plant	Agavaceae
<i>Polygonium viscosum</i>	Athalo Bishkatali	Polygonaceae
<i>Lippia nodiflora</i>	Bakhan	Verbenaceae
<i>Imperata cylindrica</i>	Ulu	Poaceae
<i>Amoora cucullata</i>	Dhandul, Amar	Meliaceae
<i>Clerodendron viscosum</i>	Bhant	Verbanaceae
<i>Piper chaba</i>	Choi	Piperaceae
<i>Leonurus sibiricus</i>		Lamiaceae
<i>Polygonium lanatum</i>	Bara Bishkathali	Polygonaceae
<i>Desmodium triflorum</i>	Kulaliya	Fabeceae
<i>Hedychium coronarium</i>	Dolon Champa	Zingiberaceae
<i>Sida cordifolia</i>	Brela	Malvaceae
<i>Phyllanthus reticulatus</i>	Chitki, Panjuli	Euphorbiaceae
<i>Costus speciosus</i>	Keu, Kemak	Zingiberaceae
<i>Azadirachta indica</i>	Neem	Meliaceae
<i>Albizia lebbek</i>	Sirish, Koro	Fabaceae
<i>Xeromphis spinosa</i>	Monphal	Rubiaceae
<i>Mangifera indica</i>	Aam	Anacardiaceae
<i>Acalypha indica</i>	Muktajhuri	Euphorbiaceae
<i>Adenantha pavonina</i>	Rakta kombol	Fabaceae
<i>Polygonum stagninum</i>	Bara Bishkathali	Polygonaceae
<i>Argyreia argentea</i>	Bitarak	Convolvulaceae
<i>Brassica nigra</i>	Kalo Sarisha	Brassicaceae

The anti-inflammatory activity of the ethanolic extract of flowers of *Hymenocallis littoralis* (Amaryllidaceae) have been noteworthy of mentioned. Using inhibition of protein denaturation method, crude extract of its flowers were subjected to in vitro antiinflammatory activity. The ethanolic extract have shown potent anti-inflammatory activity by HRBC membrane stabilization method with 83.46% and 84.72% for 100 and 500µg/ml, respectively. Significant antiinflammatory activity by HRBC membrane stabilization was shown by crude ethanolic extract. All the concentrations prepared were paving dose dependent anti-inflammatory activity [18].

The anti-inflammatory activity of the methanolic extract of *Smithia sensitiva* (MESS) by both in vitro and in vivo methods have been investigated and reported. The plant is traditionally used as refrigerant, galactogogue and as lotion in headaches. In vitro method was estimated by bovine serum albumin denaturation (BSA) method and in vivo method was estimated by Cotton pellet-

induced granuloma method. Both approaches showed significant anti-inflammatory property of the methanolic extract. The MESS at a concentration of 400µg/ml showed potent activity on comparing with the standard drug [19].

Natural products as anti-inflammatory agents

Numerous anti-inflammatory natural products are being derived from plant and marine sources. These include alkaloids, steroids, terpenoids, phenolics, fatty acids and lipids [20]. The structure of some of these are being shown below: These compounds are thought to be inhibitors of pro-inflammatory mediators and enzymes. Natural products can modulate various molecular pathways involved in the inflammation process. A disadvantage of the use of natural products is the amount isolated is of insufficient use for developments and clinical uses. Figure 2 shows the structure of some of these natural products that have been isolated from selected plants.

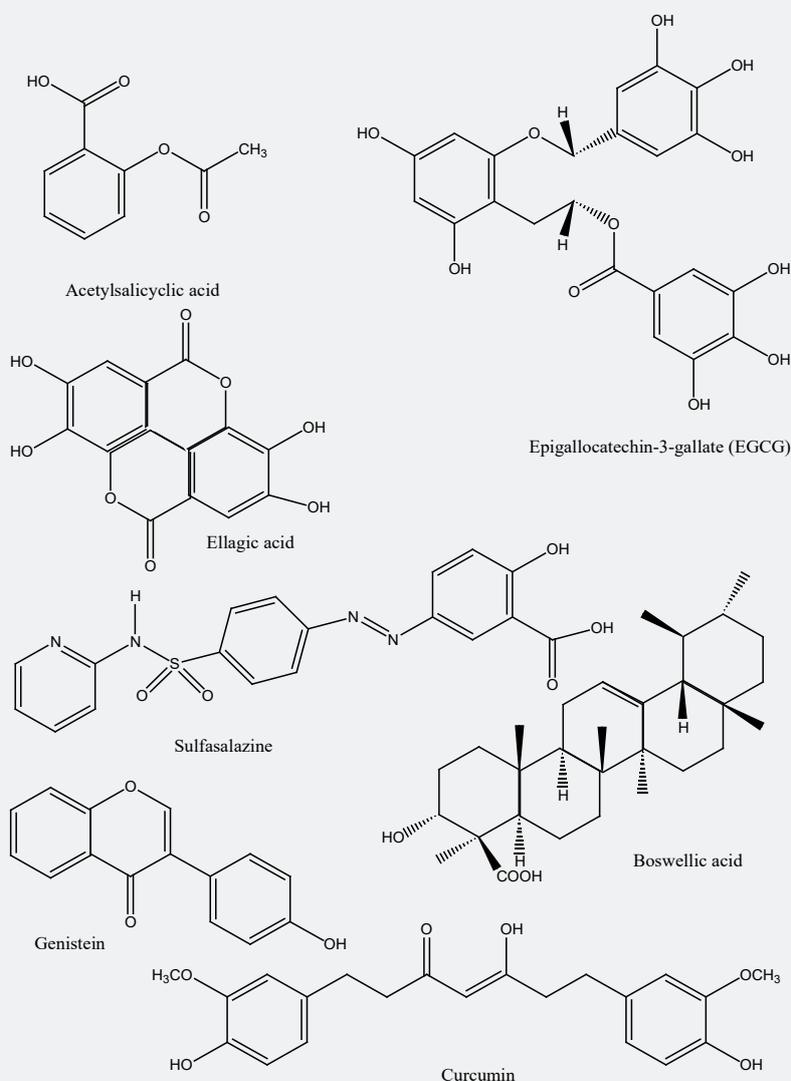


Figure 2:

Conclusion

There is an increasing need to use plant extracts or traditional medicine as a source of anti-inflammatory agents, compared to synthetic medicines. This stems from the side effects that synthetic anti-inflammatory agents impose to the health of mankind and the negative environmental impact. In addition, the cost of synthetic anti-inflammatory agents is an expensive endeavour and research in herbal plant extracts will further promote "green chemistry research" and lead to a safe world environment in addition to safe health to mankind.

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