



REGULAR ARTICLE

INFLAMMATION AND MEDICINAL PLANTS-AN ETHNOMEDICINAL APPROACH

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SUMMARY

There is an increasing demand for the medicinal plants in developing countries like India. Attention need to be given to assess the medicinal value of such plants to explore the potential drugs out of it. Inflammation is the condition associated with many of the disease states and this review elaborate the medicinal plants, their parts used in the effective management of Inflammation and its associated conditions.

Keywords: Inflammation, Medicinal plants.

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1. Introduction

Inflammation is a response to any damage in the body and can be caused by infection, trauma, chemicals, heat or foreign, unrecognized particles. Inflammation is defined as redness, heat, pain and loss of function, and there are several stages to the process of inflammation that explain these. The body tries to get as much blood as is possible to the damaged area. This is because there are lots of different substances in the blood that can help both to stop any further damage and also try and destroy the cause. This increased blood flow is the reason that inflamed areas are hotter and redder than the surrounding area. After increasing the blood flow to the area, the body needs to get the chemicals and the immune cells out of the blood vessels and into the tissues. To do this, the cells that make up the blood vessels start to pull apart and create tiny holes in their walls. This allows very small molecules like water and some chemicals to escape into the tissues, while keeping larger molecules and cells on the inside. The fluid that leaks out, as well as the

increased blood flow, is why the inflamed area appears swollen.

These substances that are 'leaking' into the tissue from the blood vessels start to wall off the damaged area because it contains a substance called fibrin. Fibrin is a substance that makes up part of a scab, and can become hard. This helps in keeping the damaging substance isolated and stops it from spreading. Other chemicals that leak out into the tissues mean that the nerve fibres that transmit pain signals can become activated far more easily, inflamed areas are painful and leaking the fluid.

The blood flowing through this area starts to become thicker and moves more slowly through the area. This slowing down of blood makes the blood cells move differently, and they start traveling closer to the vessel walls that before. White blood cells from the immune system then make their way into the damaged tissue by attaching to the blood vessel walls. To help with this, the vessel walls

in the inflamed area start to change the molecules on their surface meaning the white blood cells are more likely to attach.

Causes of Inflammation^{2,3,4}

The most common cause of a relatively short period of inflammation is an infection, and almost all infections with bacteria, fungus or virus will cause inflammation. The red, sore throat of a cold is an example of inflammation secondary to a virus. As mentioned previously though, things such as physical trauma, toxins, heat, cold and allergic reactions also cause inflammation.

Causes of Chronic Inflammation

Persistent Infections: Syphilis, Certain fungi.

Prolonged Exposure to Potentially Toxic Agents: Silicosis Breathing in a lot of carbon (eg. coal miners) Atherosclerosis (plaque build-up on blood vessel walls).

Autoimmunity: Rheumatoid arthritis. Systemic lupus erythematosus (SLE). Most other auto-immune conditions.

Tests for Inflammation^{5,6}

CRP (C-Reactive Protein): CRP is a chemical, the levels of which rise dramatically when inflammation is occurring in the body. Measuring CRP can aid in determining disease progress and the effectiveness of treatment. CRP increases in hours of inflammation starting and falls within two to three days of recovery.

ESR (Erythrocyte Sedimentation Rate): ESR is a non-specific indicator of the presence of disease. This is slower to show changes than CRP.

FBP (Full Blood Picture): A Full Blood Picture can give the doctor an idea of the level of white blood cells that are in the blood. If there are more white blood cells than usual then this indicates infection.

Types of Inflammation

There are two basic types of inflammation - acute and chronic. Acute inflammation is of short duration, which could be anything from a few minutes to a few days. Such inflammation is caused by foreign substances entering the body, or by physical damage. A viral infection may also precipitate acute inflammation. Chronic inflammation, on the other hand, is long lasting. It may persist for weeks, months or even years. Chronic inflammation may be brought on by acute inflammation or it may be the result of an auto immune disease. Two other, less common types of inflammation are sub-acute inflammation and granulomatous chronic inflammation. Sub-acute inflammation has clinical features of both acute and chronic inflammation - it is an intermediary stage between the two. Granulomatous chronic inflammation is a special type of chronic inflammation that is associated with tuberculosis and some lesser known diseases.

Types of acute inflammation⁷

1. **Catarrhal type-** Mild inflammation in mucous membrane and is characterized by copious outpouring of mucus along with desquamated epithelial cells and a few leucocytes. Example: Common cold, catarrhal appendicitis etc.

2. **Serous type-** Mild inflammation in serous surface such as pleural cavity joint cavity etc with accumulation of low protein containing fluid (effusion). Example: Tuberculosis pleurisy. It is also seen due to repeated mild trauma. Example: Common blisters.

3. **Fibrinous type-** Characterized by outpouring of exudates with high protein and less volume. Commonly seen in serous surface such as pleura, peritoneum, pericardium. Two contiguous surfaces covered in fibrin tend to stick together and if not lysed scar tissue is formed with permanent loss of function - Example: Adhesive and constrictive

pericarditis. **Lobar Pneumonia** due to *Streptococcus pneumoniae* is associated with massive fibrinous exudates in the lung alveoli.

4. **Membranous type-** Fibrinous inflammation in which network of fibrin entangling inflammatory cells and bacteria forms pseudo-membrane. Example: **Diphtheria**, Bacillary dysentery.

5. **Suppurative or purulent type-** Usually caused by pyogenic bacteria and is characterized by pus formation Example: Abscess.

Phlegmonous type- (Phlegmon means fire): Characterized by woody hardness of the inflamed area due to low resistance of the body and high virulence of the bacteria - Example: Erysipelas, pelvic cellulites etc.

Chronic Inflammation:⁷

Inflammation that has a slow onset and persists for weeks or more is classified as being chronic. The symptoms are not as severe as with acute inflammation, but the condition is insidious and persistent. Chronic inflammation may follow on from acute inflammation or exist by itself. An acute inflammation will become chronic if the immune system is unable to rid the body of the offending foreign agent or if the agent is constantly able to re-enter the body. In the case of persistent infections, such as tuberculosis, and autoimmune diseases chronic fatigue will arise without the person first going through the acute inflammation stage. The main cells involved in chronic infection are macrophages and lymphocytes. Because both these cells have a single nuclei, they are known as mononuclear cells. With the aid of chemical mediators such as lymphokines, macrophages do an excellent job of engulfing and neutralizing or killing foreign antigens.

Lymphocytes are the predominant cell in chronic inflammation. There are two types, labeled T and B. T-lymphocytes are produced in the thymus gland. They ensure cell based immunity from infection. B-lymphocytes

originate in the bone marrow and ensure humoral (bodily fluid) immunity. The activation of B-lymphocytes produces plasma cells, which manufacture and secrete antibodies to fight specific types of antigens. Macrophages and lymphocytes are interdependent in that the activation of one stimulates the actions of the other.

Certain chronic infections cells known as eosinophils accumulate. Within their cytoplasm are bright red granules. These granules contain a substance called 'major basic protein' which has the ability to destroy certain antigens. In cases of chronic inflammation involving foreign particulate matter, such as splinters, macrophages cells can fuse together to form multinucleated giant cells. Tuberculosis may also cause macrophage cells to unite in this manner. A key feature of chronic inflammation is collagen production. If too much collagen is formed, this can lead to the condition known as fibrosis. Connective tissue cells known as fibroblasts enter the area of tissue injury and then go to work to produce collagen which is necessary to replace the tissue lost during long term inflammation. The dilated blood vessels which are characteristic of acute inflammation are not evident in cases of chronic inflammation.

The two major complications associated with chronic infection are fibrosis leading to scarring and persistence. The overabundance of collagen production over time can lead to scarring that can cause permanent distortion of the tissue, interfering with its function. Chronic inflammation can be continually stimulated by substances with low antigenic properties or by auto-immunity.

Path ways^{8,9,10,11}

Inflammation is the response of an organism to external stressful stimuli or pathogen and is intended to eradicate the stimulus or pathogen from the organism. There are many key processes in the inflammatory response, including increasing

vascular permeabilization, releasing of eicosanoids, and the production of cytokines, chemokines, and amines (histamine) by immune cells. Cyclooxygenase (COX) and nitric oxide synthase (NOS) produce prostaglandins (eicosanoids) and nitric oxide, respectively elicited by inflammatory pathways.

These molecules then play critical roles in the development of inflammation and are attractive targets for drug discovery. Cyclooxygenase is a bifunctional enzyme consisting of both cyclooxygenase and peroxidase activities. Cyclooxygenase converts arachidonic acid to prostaglandin G₂, and the peroxidase converts prostaglandin G₂ to prostaglandin H₂. The prostaglandin H₂ is then further converted to other prostaglandins by cell specific enzymes. There are three forms of COX: COX-1, COX-2, and COX-3. COX-1 is constitutively expressed, while COX-2 is induced after cell stress induced by injury, bacterial, viral, or harmful stimuli. Prostaglandin synthesis mediates vasodilation, vasoconstriction, pain, and fever associated with the inflammatory response. Non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin, target COX inhibition. More recent drugs targeting COX include Celebrex and Vioxx. Nitric Oxide synthase is responsible for generation of nitric oxide (NO.) through oxidizing L-arginine to L-citrulline. NO. Serves as a signaling molecule in the cardiovascular system. It can react with other species to form more potent radicals such as peroxynitrite and lipid peroxides. There are three forms of NOS, eNOS expressed in endothelial cells, nNOS, expressed in neuronal cells, and iNOS, expressed in macrophages. Induction of iNOS through inflammatory mediators results in protein nitration, induction of apoptosis, oxidative stress, DNA damage, and inhibition of respiration. Glucocorticoids inhibit iNOS, and arginine analogs, such as L-NAME and L-NMMA inhibit both constitutive and inducible NOS. Some of these drugs show promise in septic shock models and in early clinical studies. iNOS and COX-2 kits were developed

using lipopolysaccharide (LPS) and interferon gamma (IFN γ) as the principle stimuli in macrophages and have been developed as singleplex assays. After stimulation, both iNOS and COX-2 are induced resulting in an increase in total cytoplasmic intensity in the cell. Prior to HCS, these enzymes have been measured by western, or by ELISA of their respective products, NO (iNOS), and PGE-2 (COX-2). The Singleplex iNOS and COX-2 Cellomics HCS Reagent Kits along with the Cellomics ArrayScan[®] HCS Reader and the Compartmental Analysis BioApplication Software Module enable the quantitative monitoring of COX-2 and iNOS induction. These kits also expand the number of targets in the inflammatory pathway offered by Thermo Fisher Scientific, and increase the capabilities of multiplexing targets in this pathway.

Role of Medicinal plants in Inflammation

The plants mentioned below are highly recommended for the management of inflammation as per the literature. *Eucomis autumnalis*, *Ocotea bullata*, *Siphonochilus aethiopicus*, ¹²*Forsythia suspense*, *Lonicera japonica*, *Isatis indigotica*, *Strobilanthes cusia*, *O. Kuntze*, *Astragalus membranaceus*, *Hedysarum polybotrys*, *Andrographis paniculata*, *Glycyrrhiza uralensis*, *Ligusticum wallichii*, *Lonicera japonica*, *Isatis indigotica*, *Astragalus membranaceus*, *Hedysarum polybotrys*¹³, *Anacyclus pyrethrum*, *Armeria alliacea*, *Asphodelus ramosus*, *Capparis spinosa*, *haponticum acaule*¹⁴, *Acanthus ebracteatus*, *Oroxylum indicum*, *Ryptolepis buchanani*, *Derris scandens*¹⁵, *Cimicifuga racemosa*, *Caulophyllum thalictroides*, *Sambucus* species, *Juniperus communis*, *Taxus brevifolia*, *Podophyllum peltatum*¹⁶, *Garcinia mangostana*, *Houttuynia cordata*, *Eupatorium odoratum*, *Senna alata*¹⁷, *Bidens pilosa*, *Eucomis autumnalis*, *Harpephyllum caffrum*, *Helichrysum nudifolium*, *Leonotis intermedia*, *L. leonorus*, *Ocotea bullata*, *Rumex saggitatus*, *Solanum mauritianum*, *Synadenium cupulare*, *Trichilia dregeana*¹⁸, *Calluna vulgaris*, *Corylus avellana*, *Geum urbanum*, *Juniperus communis*, *Polygonum aviculare*, *Potentilla erecta*, *Salix caprea*, *Geum rivale*, *Geum urbanum*, *Solanum dulcamara*, *Symphytum uplandicum*, *Vaccinium vitis-idaea*¹⁹, *Abrus*

*precatorius*²⁰, *Acorus calamus*²¹, *Alpinia galanga*²², *Andrographis paniculata*²³, *Aloe barbadensis*²⁴, *Achyranthes aspera*²⁵, *Aconitum napellus*²⁶, *Acacia catechu*²⁷, *Bambusa arundinacea*²⁸, *Boerhavia diffusa*²⁹, *Blumea lacera*³⁰, *Carica papaya*³¹, *Zingiber officinale*³², *Tamarindus indica*³³, *Pipernigrum*³⁴. *Andrographis paniculata*: ²³*Andrographolide* - the major active principle isolated from the plant *Andrographis paniculata*, has been shown to possess a strong anti-inflammatory activity. The possibility that the drug may affect asthmatic inflammation, through inhibition of the relevant inflammatory cytokines, has not been explored. The purpose of this study was, firstly, to investigate the ability of andrographolide to inhibit the release of inflammatory cytokines in vitro in a model of non-specific inflammation and subsequently *Acacia cornigera* bark, *Byrsonima crassifolia* bark, *Sphagneticola trilobata* leaves and *Sweetia panamensis* bark²⁷ These Four herbal drugs used in the folk medicine of Central America to treat inflammatory skin affections were evaluated for their topical anti-inflammatory activity.

*Achyranthes aspera*²⁵ The anti-inflammatory activity of an alcohol extract of *Achyranthes aspera* was tested on carrageenin-induced hind paw edema and cotton pellet granuloma models in albino male rats. *Zingiber officinale*³² The effects of the crude hydralcoholic extract of ginger rhizomes on the classical models of rat paw and skin edema. The carrageenan-, compound 48/80- or serotonin-induced rat paw edema were inhibited significantly by the intraperitoneal administration of alcoholic ginger extract. *Bambusa arundinacea*²⁸. The anti-inflammatory effect of the methanol extract of the leaves of *Bambusa arundinacea* against carrageenin-induced as well as immunologically induced paw edema and also its antiulcer activity in albino rats have been studied and found to be significant when compared to the standard drugs. The combination of methanol extract and phenylbutazone (Non-Steroidal Anti-inflammatory Agent, NSAIA) has been studied and found to be the most potent anti-inflammatory activity experimentally with least toxic (no ulcerogenic) activity.

Table 1. Anti inflammatory medicinal plants

S.no	Botanical name	Part used	Actions
01	<i>Abrus precatorius</i>	Root,leaves	Eye inflammation
02	<i>Acorus calamus</i>	rhizomes	Rheumatoid arthritis
03	<i>Alpinia galanga</i>	rhizomes	Rheumatoid arthritis
04	<i>Andrographis paniculata</i>	Whole plant	Diminishing inflammation
05	<i>Aloe barbadensis mill</i>	Elio	Rheumatoid arthritis
06	<i>Achyranthes aspera</i>	Whole plant	Inflammation of blader stones
07	<i>Aconitum napellus</i>	Root	Eye inflammation
08	<i>Acacia catechu</i>	Heart wood	Chronic mucous membrane inflammation
09	<i>Bambusa arundinacea</i>	Sprouts	Rheumatoid arthritis
10	<i>Boerhavia diffusa</i>	Whole plant	Inflammation of gall bladder
11	<i>Blumea lacera</i>	Whole plant	Skin inflammation
12	<i>Carica papaya</i>	Fruits	Inflammation of liver
13	<i>Zingiber officinale</i>	rhizomes	Lungs inflammation
14	<i>Tamarindus indica</i>	Leaves	Ear oedema
15	<i>Piper nigrum</i>	fruits	Inflammatory response of nasal mucosal membrane

*Boerhaavia diffusa*²⁹ Effect of *Boerhaavia diffusa* extract on the Cell Mediated Immune (CMI) response in metastatic condition was studied using C57BL/6 mice model.

Administration of *Boerhaavia diffusa* enhanced Natural Killer (NK) cell activity, antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent complement

mediated cytotoxicity (ACC) and the activity was observed in treated group much earlier compared to the metastatic tumor bearing control. *Carica papaya*³¹ The anti-inflammatory activity of an ethanolic extract of *Carica papaya* leaves was investigated in rats using carrageenan induced paw oedema, cotton pellet granuloma and formaldehyde induced arthritis models. *Corrigiola telephiifolia*, *Echinops spinosus*, *Kundmannia sicula*, *Tamarindus indica* and *Zygophyllum gaetulum*³³ Aqueous, ethanol and chloroform extracts from *Corrigiola telephiifolia*, *Echinops spinosus*, *Kundmannia sicula*, *Tamarindus indica* and *Zygophyllum gaetulum* were evaluated for antiinflammatory properties in mice (ear oedema induced by arachidonic acid) and rats (subplantar oedema induced by carrageenan) after topical or i.p. administration, respectively. Our results showed that all the plants exhibit antiinflammatory activity,

Discussion

This review article detailed the study of inflammation and medicinal herbs in an ethano medicinal approach. Pathways of inflammation and action basis of the selected medicinal herbs are discussed here and it will be highly useful to the researchers who are working in this field.

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