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Analgesic and anti –inflammatory activity of A. squamosa stems

T. Rahul * , K. Pavani
Department of pharmacy practice.
*Corresponding Authore: T. Rahul, Department of pharmacy practice.
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Abstract

This observational study was conducted to assess the risk factors, treatment of uterine fibroids. The data was collected from the hospitals for 3 months. The data collected was studied and results were interpreted. The collected information suggests that among all the risk factors, Age is the major risk factor in which 60-70% of 45-55 age group people are majorly affected. Also comorbidities like heavy menstrual bleeding and Anaemia are majorly observed in the subjects. Some of the complications like Pelvic pressure, growth of stomach and frequent periods are observed in many of the subjects. In women who present with acute uterine bleeding associated with uterine fibroids, conservative management with estrogens, selective progesterone receptor modulators, but hysterectomy may become necessary in some cases. We came to know that the cause of uterine fibroids are unknown, but there is evidence that multiple factors may increase the risk of developing uterine fibroids

Key words: anaemia ; chronic inflammation

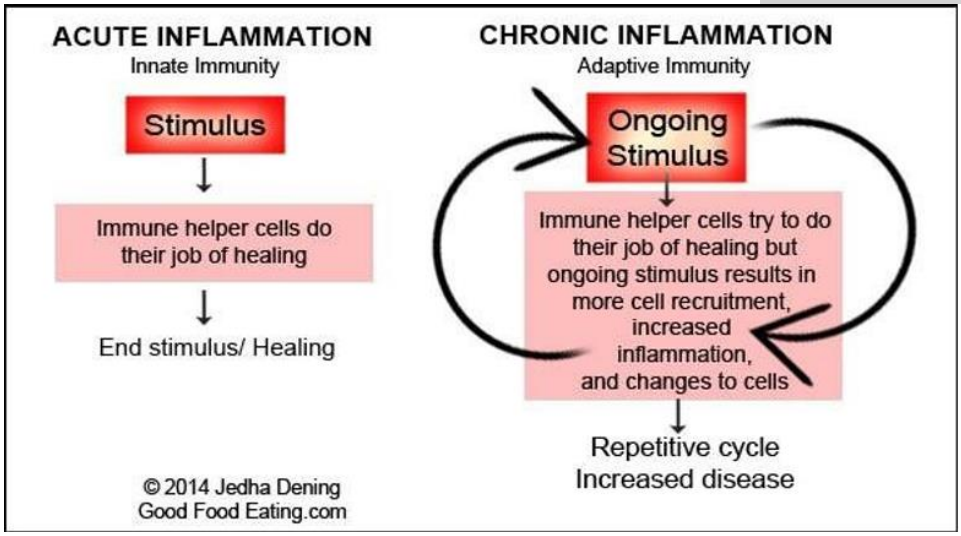
Introduction:
Inflammation is part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells, or irritants. Inflammation is a protective attempt by the organism to remove the injurious stimuli and to irritate the healing process, Inflammation is not a synonym for infection, even in cases where inflammation is caused by infection. Although infection is caused by a microorganism, inflammation is one of the responses of the organism to the pathogen. However, inflammation is a stereotype response, and therefore it is considered as a mechanism of innate immunity, as compared to adaptive immunity, which is specific for each pathogen.
Without inflammation, wounds and infections would never heal, similarly, progressive destruction of the tissue would compromise the survival of the organism. However, chronic inflammation can also lead to a host of disease, such as hay fever, periodontitis, artherosclerosis, rheumatoid arthritis, and even cancer (e.g., gallbladder carcinoma). It is for that reason that inflammation is normally closely regulated by the body.

Classification of Inflammation
Inflammation can be classified as two types

- Acute inflammation
- Chronic inflammation

Acute Inflammation

Acute inflammation is the initial response of the body to harmful stimuli and is achieved by the increased movement of plasma and leukocytes (especially granulocytes) from the blood into the injured tissues. A cascade of biochemical
events propagates and matures the inflammatory response, involving the local vascular system, and various calls within the injured tissue.



The five cardinal signs of acute inflammation are

1. Redness (rubor) which is due to dilation of small blood vessels within damaged tissue as it occurs in cellulitis.
2. Heat (calor) which results from increased blood flow (hyperemia) due to regional vascular dilation
3. Swelling (tumor) which is due to accumulation of fluid in the extravascular space which, in turn, is due to increased vascular permeability.
4. Pain (dolor), which partly results from the stretching & destruction of tissues due to inflammatory edema and in part from pus under pressure in, as abscess cavity. Some chemicals of acute inflammation, including bradykinins, prostaglandins and serotonin are also known to induce pain.
5. Loss of function: The inflamed area is inhibited by pain while severe swelling may also physically immobilize the tissue.

Chronic Inflammation

Prolonged inflammation known as chronic inflammation, lead to a progressive shift in the type of cells present at the site of inflammation and is characterized by simultaneous destruction and healing of the tissue from the inflammatory process.

Causes of chronic inflammation:

1.Persistent infections - Certain microorganisms associated with intracellular infection such as tuberculosis, leprosy, certain fungi etc characteristically cause chronic inflammation. These organisms are of low toxicity and evoke delayed hypersensitivity reactions.

2.Prolonged exposure to non-degradable but partially toxic substances: either endogenous lipid components which result in atherosclerosis or exogenous substances such as silica and asbestos.

3.Progression from acute inflammation:

Acute inflammation almost always progresses to chronic inflammation following:

Persistent suppuration as a result of un-collapsed abscess cavities, foreign body materials (dirt, cloth, wool, etc), or a sinus/fistula from chronic abscesses.

4.Autoimmunity:

Autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosis are chronic inflammations from the outset.

Chronic inflammation can be classified into the following two types based on histologic features:

1.Nonspecific chronic inflammation:

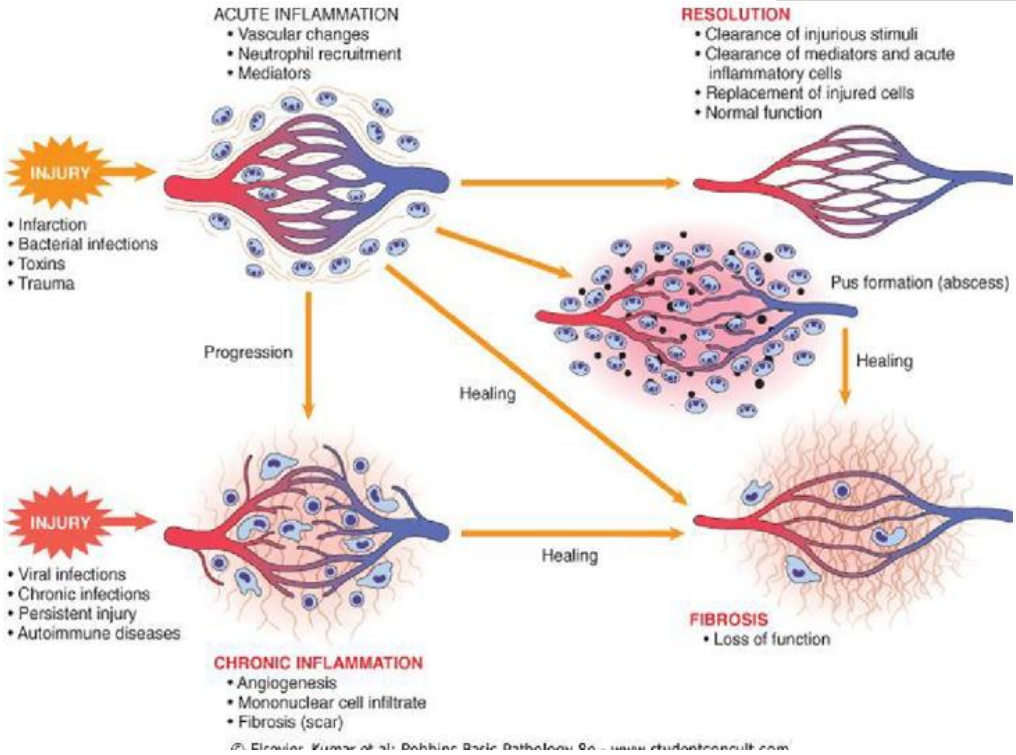
This involves a diffuse accumulation of macrophages and lymphocytes at site of injury that is usually productive with new fibrous tissue formations.

E.g. Chronic cholecystitis.

2.Specific inflammation (granulomatous inflammation:

Granulomatous inflammation is characterized by the presence of

Granuloma. A granuloma is a microscopic aggregate of epithelioid cells. Epithelioid cell is an activated macrophage, with a modified epithelial cell-like appearance (hence the name epithelioid). The epitheloid cells can fuse with each other & form multinucleated giant cells. So, even though, a granuloma is basically a collection of epithelioid cells, it also usually contains multinucleated giant cell & is usually surrounded by a cuff of lymphocytes and occasional plasma cells.



Methods and Reserch:

Process of Inflammation:

Inflammation is a generally localized defensive response of the body to various allergic or chemical irritation, infections and/or injury.When a microorganism infection is established within the body, the aim of the system is to manage or eradicate it. There may be several "triggers", which will spur the system into action. The cardinal signs of inflammation resulted by blood vessels dilation leading to an enhanced flow of blood and from augmented intracellular spaces results in the movement of various substances such as leukocytes, fluids and protein into the site of injury.

This is very important to understand the role of various chemical mediators of inflammation. These mediators products are those generally released as plasma proteins, or that originate from differentcells types like mast cells, neutrophils platelets, and monocytes/macrophages. These mediators are generally triggered by allergic or other chemical irritation, infections and injury. These modulators or mediators termed as pro- inflammatory fundamental factors, generally determine the severity of inflammation by depending on the duration of tissue or nerve injury.

Inflammation has a wide range of physiological and pathological response. Importantly it plays a role in the regulation of CNS. Major factors which mainly triggers inflammation in the brain include mainly, adhesion molecules expression such as intracellular adhesion molecule (ICAM-1) on WBCs capillary and endothelial cells which mainly facilitate the adhesion and trans endothelial migration of neutrophils and macrophages These complete process is tends to Diapedesis and development of various symptoms of inflammation including, swelling, heat, redness, and pain.

The released mediators mostly binds to specific receptors target on the cells surface and augment vascular permeability, stimulate smooth muscle contraction, promote neutrophil, chemotaxis, induce pain,increase direct enzymatic activity and/or mediate oxidative damage. Several examples of chemical mediators include: prostaglandins (PGs), leukotrienes (LT), nitric oxide, cytokines and vasoactive amines (serotonin, histamine). Although,released of several cytokines such as IL-3, 4,5,6,10 and 13 are beneficial since these act as anti- inflammatory mediator within the cells.

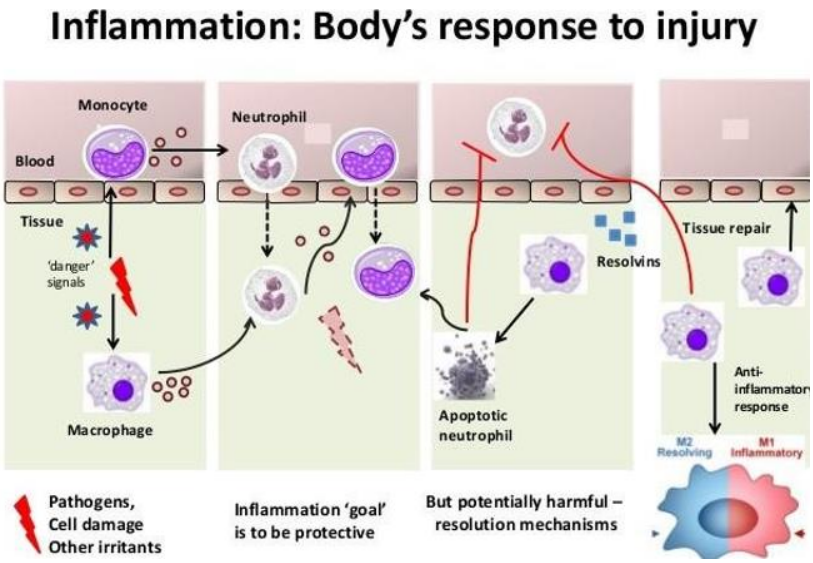


Figure 3 : Different Molecules in Inflammation

Pathogenesis of Inflammation:

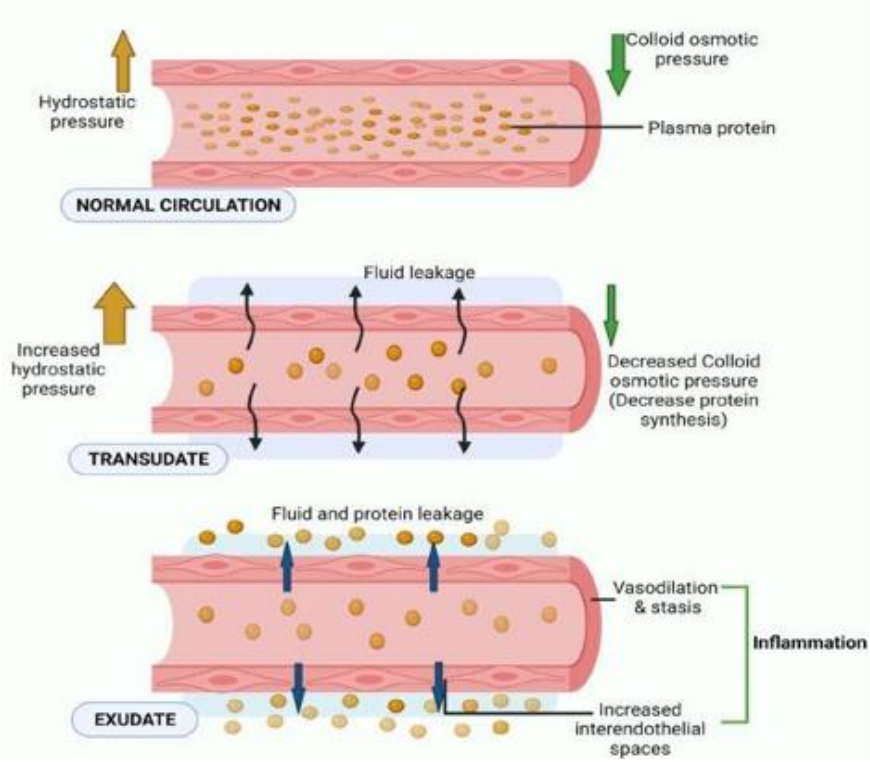


Figure 4:Pathogenesis of inflammation

Chronic inflammation is the root cause of so many diseases. The origin of all pain is due to inflammation and the inflammatory response. Pathogens (bacteria, viruses or fungi), external injuries (scrapes or damage through foreign objects), effects of chemicals or radiation, etc. are the causative factors of inflammation the initial inflammation phase consists of three subphases: acute, subacute, and chronic (or proliferative).

The special cells that take part in inflammation are called inflammatory cells and they are part of the body's immune system. The acute phase typically lasts 1–3 days and is characterized by the five classic clinical signs: heat, redness, swelling, pain, and loss of function. Inflammation results from activation of the immune system in response to a broad range of different stimuli. Shifts in the inflammatory response from short- to long-lived can cause a breakdown of immune tolerance and lead to major alterations in all tissues and organs, as well as normal cellular physiology, which can

increase the risk for various non-communicable diseases in both young and older individuals. When living with chronic inflammation, animal body's inflammatory response can eventually start damaging healthy cells, tissues, and organs. Over time, this can lead to DNA damage, tissue death, and internal scarring. Indeed, chronic inflammatory diseases are the most significant cause of death in the world today, with more than 50 percent of all deaths being attributable to inflammation-related diseases.

AIM:

Evaluation of Analgesic and anti-inflammatory activities using stem extracts of Annona squamosa Linn. Stem.

OBJECTIVES:

- Collection of plant material -Fresh stems of Annona squamosa.
- Extraction of the stems of Annona squamosa. Using Ethanol.
- Phytochemical screening of the Annona squamosa stem extract.
- Study of anti-inflammatory activity using ethanolic stem extracts of Annona squamosa L.
- Study of Anangesic activity using ethanolic stem extracts of Annona squamosa L. Stem

Discussion

The preliminary phytochemical analysis showed that the Ethanolic extract of Annona squamosa stem revealed the presence of alkaloids, Glycosides, Terpenoids, Saponins, Tannins and flavonoids.

The extract was examined for anti-inflammatory activity using formalin-induced paw oedema and carrageenan-induced paw oedema in rats, as well as analgesic activities using acetic acid- induced writhing and hot plate tests. For this experiment Rats 24 were selected and divided into 4 groups containing 6 each.

All the activities have been performed and came to know that the ethanolic extract from Annona squamosa stem exhibits anti-inflammatory and analgesic activities and the results suggests that the constituents present in the extract are having these activities. The results are calculated as per statistical methods to know the p-value and its significance, comparing the test drug and standard with the control group.

The flavonoids are known to possess Anti-inflammatory activity by inhibiting the cyclooxygenase responsible for synthesis of inflammatory prostaglandins. Acetic acid induced writhing in mice attributed visceral pain finds much attention of screening analgesic drugs. The extracts of the plant showed significant analgesic action compared to the reference drug indomethacin. Pain sensation in acetic acid induced writhing method is elicited by triggering localized inflammatory response resulting release of free arachidonic acid from tissue phospholipid via cyclooxygenase (COX), and prostaglandin biosynthesis. In other words, the acetic acid induced writhing has been associated with increased level of PGE2 and PGF2α in peritoneal fluids as well as lipoxygenase products. The agent reducing the number of writhing will render analgesic effect preferably by inhibition of prostaglandin synthesis, a peripheral mechanism of pain inhibition. The results obtained in the analgesic test experiments appear to suggest that Ethanolic extract possess centrally and peripherally mediated analgesic properties. The central analgesic action may be mediated via inhibition of central pain receptors, while the peripheral analgesic effect may be mediated through inhibition of cyclooxygenase and/or lipoxygenase (and other inflammatory mediators).

Carrageenan-induced oedema involves the synthesis or release of mediators at the injured site. These mediators include prostaglandins, especially the E series, histamine, bradykinins, leukotrienes and serotonin, all of which also cause pain and fever. Development of oedema induced by carrageenan is commonly correlated with early exudative stage of inflammation. Since carrageenan-induced and Formalin-induced inflammation model are significant predictive tests for anti-inflammatory agents acting by the mediators of acute inflammation. The results of this are an indication that Annona squamosa can be effective in acute inflammatory disorders.

The results of the present study show that the Ethanolic extract from Annona squamosa stem exhibit significant analgesic and anti-inflammatory activities.

Conclusion

These experimental results have established a pharmacological evidence of the drugs to be used as an analgesic and anti-inflammatory activity. The study showed that the plant is safe for use. The study has thus provided some justification for the folkloric use of the plant in several communities for conditions such as pain and inflammations. The study validates the use of stem of Annona squamosa for treatment of painful inflammatory conditions.

The results of the phytochemical screening showed that the ethanolic extract of Annona squamosa contains Alkaloids, glycosides, Terpenoids, Saponins, Carbohydrates, Tannins, Flavonoids.

The results of acetic acid induced writhing test with ethanol extract of Annona squamosa stems (100 mg/kg and 200mg/kg, p.o.) was able to reduce acetic acid-induced writhings compared with the control group and the reduction was statistically significant (***$p < 0.001$). The inhibition % of the doses of ethanolic extract was 48.1% and 52.59% respectively.

In Hot plate test, animals treated with diclofenac (10 mg/kg, i.p.) had an evident increase in the latency time 30, 60, 90 ,120, and 180 min (***$p < 0.001$). For the groups treated with Ethanolic extract (100 mg/kg and 200mg/kg p.o.), less effect was shown in the first 30 min. However, an increase in latency time was found in 60, 90 and 120 min and a reduction was evident in 180 min. The diclofenac proved to be a potent analgesic, increasing the latency time within the time evolution.

Effect of stem extract of Annona squamosa and Indomethacin on carrageenan induced paw edema was statistically significant (***$p < 0.001$). The mean paw size for indomethacin treated and both doses of extract showed statistically significance compared to control group.

The effect of the extract which was statistically significant ($p < 0.001$). The mean paw size for indomethacin treated and both doses of extract showed statistically significance compared to control group. The result of the study indicated that Ethanolic stem extract of Annona squamosa has significant anti-inflammatory activity.

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