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**Review Article**

# Anti Inflammatory and Analgesic Activity of Medicinal Plants - A Review

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The various plants have a potential medicinal implication. Medicinal plants are considered as imperative therapeutic aid. Therapy of classical NSAIDs and the opoids in the management of inflammatory and pain stipulation are major problems. The conservative drug available in the marketplace treat inflammation and analgesia produces various side effects. For conquer this problems medicinal plants play a major role to alleviate many diseases related with inflammation and analgesia. These reviews try to make accessible an overview of reported analgesic and anti-inflammatory activities of plants with various screening models like Carrageenan induced paw edema, Cotton pellet granuloma method, Formaldehyde-induced paw edema models, Eddy's hot plate method, Formalin test, Acetic acid induced writhing test, Tail flick method, etc and inducing agents.

**KEYWORDS -** Inflammation, Analgesia, Medicinal plant.

## INTRODUCTION

Inflammation is a contained defensive reaction of cells/tissues of the body to allergic or chemical irritation, injury etc. The symptoms that produced inflammation are pain, redness, heat, swelling and failure of function that result from dilation of the blood vessels leading to an increased supply of blood and increased intercellular spaces resulting in the movement of leukocytes, protein and fluids into the inflamed regions.[1]

### Inflammatory Phase

Inflammation may have beneficial effects such as the destruction of invading micro-organisms and the walling-off of an abscess cavity to prevent spread of disease. Though, it may also produce disease; for example, an abscess in the brain. would act as a space-occupying lesion compressing vital surrounding structures or fibrosis resulting from chronic inflammation may distort tissues and permanently alter their function.

Inflammation is typically classified according to its time course as:

- Acute inflammation -The initial and often transient series of tissue reactions to injury.
- Chronic inflammation-The successive and regularly prolonged tissue reactions following the initial response.[2]

The two main types of inflammation are also characterized by differences in the cell types taking part in the inflammatory response.

### 1. Acute Inflammation

Acute inflammation is the preliminary tissue reaction to a wide range of injuries

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or insults and may last from a few hours to a a small number of days. The acute inflammatory reaction is similar whatever the causative agent.

The major causes of acute inflammation are:

- Microbial infections- e.g. viruses, pyogenic bacteria
- Hypersensitivity reactions- e.g.Tubercle bacilli, parasites
- Physical agents- e.g. trauma, ionizing irradiation, heat, cold
- Chemicals- e.g. reducing agent, alkali, corrosives, acids, bacterial toxins
- Tissue necrosis- e.g. ischemic infarction.

- **Microbial infections** - One of the commonest causes of inflammation is microbial infection. Viruses escort to death of individual cells by intracellular multiplication. Bacteria release specific exotoxins (chemicals synthesized by them which specifically initiate inflammation) or endotoxins (which are associated with their cell walls). Additionally, a few organisms cause immunologically-mediated inflammation through hypersensitivity reactions.

- **Hypersensitivity reactions** - A hypersensitivity reaction occurs when an altered state of immunological reaction causes unsuitable or excessive immune reaction which damages the tissues. The types of reaction are classify as Types I, II, III, & IV, other than all have chemical mediators related to those involved in inflammation.

- **Physical agents** - Tissue damage leading to inflammation may occur through physical trauma, uv & other ionizing radiation, burns, or excessive cooling ('frostbite').

- **Irritant and corrosive chemicals** - Corrosive chemicals (acids, alkalis, oxidizing agents) provoke inflammation through gross tissue spoil. Though, infecting agents may liberate specific chemical irritants which produce inflammation.

- **Tissue necrosis** - Death of tissues from lack of oxygen or nutrients resulting from inadequate blood flow is a potent inflammatory incentive. The boundary of a recent infarct often shows an acute inflammatory response.

- **Redness** – An acutely inflamed tissue appears red, for example- sunburn, cellulites due to bacterial infection or acute conjunctivitis. This is caused by dilation of tiny blood vessels within the damaged tissues.

**2.Chronic Inflammation**

The word 'chronic' applied to any process implies that the process has extended over a long interlude of time. This is generally in the case of chronic inflammation, but here the term 'chronic' takes on a much more precise meaning, in this type of cellular reaction differ from that seen in acute inflammation. Chronic inflammation

possibly distinct as an inflammatory process in which plasma cells, lymphocytes and macrophages preponderate, and which is usually accompanied by the formation of granulated tissue, consequential in fibrosis. Chronic inflammation is generally primary, but does sporadically follow acute inflammation. The commonest appearance of chronic inflammation are:

- Chronic ulcer, such as a chronic peptic ulcer of the stomach with breach of the mucosa, a base lined by granulation tissue and with fibrous tissue extending through the muscle layers of the wall.
- Chronic swelling cavity- for example osteomyelitis
- Thickening of the wall of a hollow structure by fibrous tissue in the presence of a chronic inflammatory cell infiltrate.
- Granulomatous inflammation, possibly with caseous necrosis as in chronic fibrocaseous tuberculosis of the lung.
- Fibrosis, which may become the most prominent feature of the chronic inflammatory reaction when most of the chronic inflammatory cell infiltrate has subsided.[3]

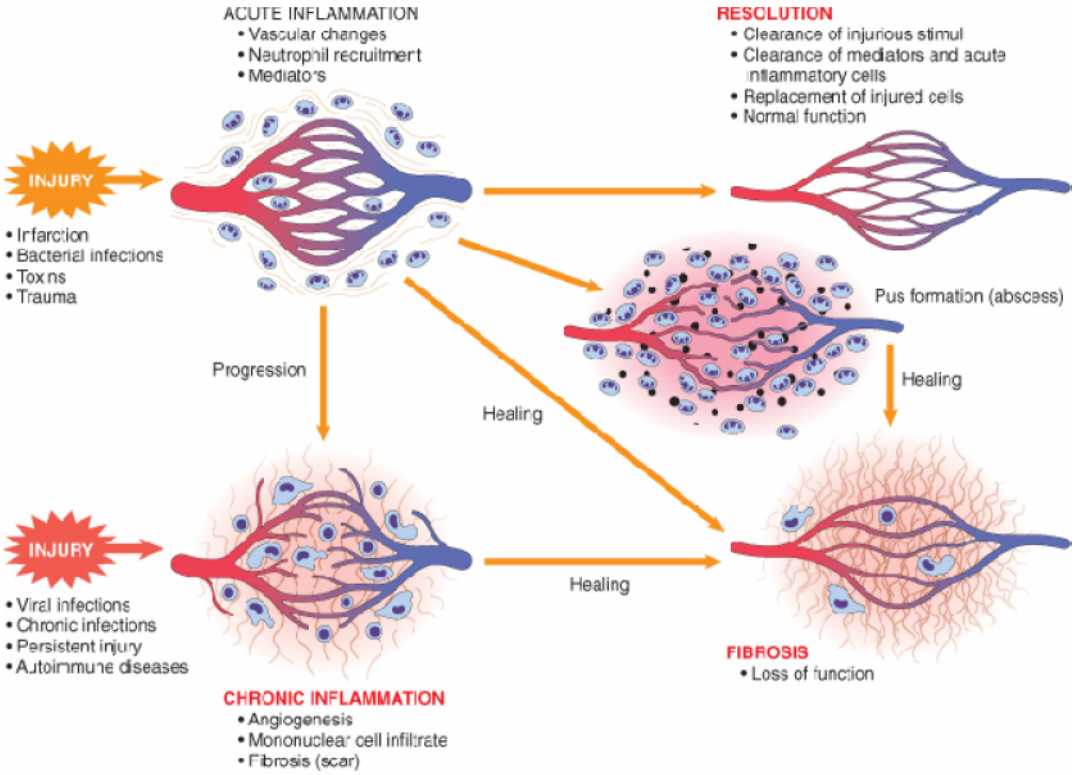


**Fig.1 : Pathway of Acute and Chronic Inflammation[3]**

**Analgesia**

Analgesia is a survival mechanism that serves as a warning sign of ongoing or impending tissue damage. Pain is an unpleasant sensory and produced by the excitation of particular receptors. Pain can classified as chronic or acute. The difference between acute & chronic pain is not based on its duration of feeling, other than the nature of the pain itself. Acute pain is symptom of pain. But chronic pain was the " disease of pain''. The generation of pain in response to tissue injury involves four basic elements:

- Transduction: A occupation of nociceptors that convert noxious stimulation to nociceptive signals
- Transmission: a process to sends nociceptive signals along nerve fibers from the site of injury to the central nervous system (CNS)
- Transformation or plasticity: a mechanism that modulates nociceptive signals at synaptic sites and at the level of the CNS through ascending, descending, or regional facilitation and inhibition
- Perception: Important component of the clinical pain experience that integrates cognitive and affective (emotional) responses.[4]

**Models for Anti-Inflammatory Activity Screening**

**1. Carrageenan-induced paw edema-**

In this model study the acute and sub acute phases of inflammation in rodents ( rat and mice). Carrageenan is a widely used irritant or inflammogen or a phlogistic agent. First of all the rats were divided into three groups of six animals. Acute inflammation was inducing by intraplantar administration of 0.1 ml of carrageenan (1% solution in normal salt). The level of paw was calculated prior to inj. of phlogistic agent (0 h) and then at a predetermined interval of 60 min up to 3 h after carrageenan injection. Volume of paw was calculated using Digital Plethysmometer. Change in the paw volume was measured and anti-inflammatory activity was calculated as follows:

$$\%\text{Inhibition of inflammation} = 1 - \frac{Vt}{Vc} \times 100$$

Where

Vt represent the change in the paw volume in drug treated group.

Vc represent the change in the volume of paw in the corresponding vehicle-treated control group.

**2. Serotonin-induced paw edema-**

In serotonin-induced model, the same process was carried out but 0.1 ml of serotonin (1%) was injected instead of carrageenan.[5]

**3. Histamine induced paw edema-**

In this model animals were divided as in the previous experiment and inflammation was induced by subcutaneous inoculation of 0.1ml of recently prepared solutions of histamine (1mg/ml) into the hind paws of the mice The percent inhibition of paw edema induced by each test sample was calculated as described as the same as the carrageenan induced paw test.[6]

**4. Cotton pellet granuloma method-**

In this model the rats were divided into 5 groups containing 6 rats. Below light ether anesthesia the hair in the auxiliary and groin region were cut and sterile cotton pellets of 15 mg each were fixed in the s.c. tissue on either sides of axilla and sterile grass pith (25x2mm) in the groin region. Wounds were subsequently sutured and animals were caged individually after recovery from anesthesia. The rats then received treatments. The list of drug administration was started on the day of implantation and repeated every 24 hours regularly for 7 days, any change in food intake, motor activity and diarrhea if any were noted. On the next day the rats were forfeit and cotton pellets and grass pith detached. The pellets free from tissue, were dried all night at 60° C to their dry weight.

Net granuloma weight was calculated by subtracting initial weight of cotton pellet (15mg) from weight noted and % protection by the drug can be calculated using the formula:

$$\%\text{Inhibition} = Wc - \frac{Wc}{Wt} \times 100$$

where Wc - mean dry weight of pellet granuloma for control group .

Wt- mean dry weight of pellet granuloma of test group.[7,8]

**5. Formaldehyde-induced paw edema-**

In this method the experimental rats in group 1 and groups 3 - 6 orally received 5ml/kg body weight of distilled water and graded levels of the extract (50, 100, 200 and 400 mg/kg body weight) correspondingly, for 7 repeated days. Rats in group 2 were administered with reference drug s.c. (sub-cutaneous). After one hour on the first and the third day of the experimental period the rats were injected with 0.1 ml of 2% formaldehyde into the footpad of the left hind paw on the first day, paw edema was measured using a micrometer screw gauge an hour before and 4 h after formaldehyde injection. On day 2 - 7 paw edema was measured daily an hour after the treatment with the extracts. The entitlement inhibition of inflammation was calculated as in the Carrageenan-induced rat paw oedema.[9]

**Various Models for Analgesic Activity Screening**

1. **Acetic acid induced writhing test-**

In this model mice of either sex (n = 6)

weighing 18–22g be used. All animals were solitary from groceries 2h before the start of experiment and were divided in five groups. Group I were injected with normal saline as control Group II received standard reference drug while the residual groups III, IV and V were injected with 100, 200 and 300 mg/kg i.p.of extract respectively. After 30min of saline, drug and plant extract injection, the animals were treated i.p. with 1% acetic acid. The numbers of abdominal constrictions (writhes) were counted after 5min of acetic acid injection for the period of 10 min.[10]

2**. Hot plat test**

In this model mice of either sex (n = 6) weighing 18–22g were acclimatized to laboratory conditions one hour before the start of experiment with food and water available adlibitum. Animals were then subjected to pre-testing on hot plate (Harvard apparatus) maintained at 55 ± 0.1°C.Animals having latency time greater than 15 s on hotplate during pre-testing were rejected (latency time). All the animals were divided in eight groups each of six mice. Group I was treated with saline (10ml/kg), group II was treated with reference drug. Group III, IV and V were treated with 100, 200 and 300mg/kg correspondingly. After 30min of handling the animals were placed on hot plate and the latency time (time for which mouse remains on the hot plate (55 ± 0.1°C) without licking or flicking of hind limb or jumping) was considered in seconds. In order to avoid the tissue damage a cut-off time of 30 s were imposed for all animals. To find out the opioid agric mechanism in the analgesic activity of plant extract Groups VI and VII were treated with reference drug and after 10min these groups were treated with plant extract while group VIII was treated with reference drug after 10min of injection. The latency time for all groups was recorded at 0, 30, 60, 90 as well as 120 min. % analgesia was calculated using the following formula.[11]

% Analgesia = (Test latency – control latency) / (Cut – off time – control latency) × 100

**3. Tail immersion test**

In this method mice of either sex were divided into five groups each of six animals (18–22g). Saline (10ml/kg), plant extract and reference drug were administered intraperitoneal injection. The animal was kept in vertical position to hang up the tail, which was up to 5cm into a pan of warm water maintained at 55 ± 0.5°C. The time in seconds to withdraw the tail out of water was taken as the reaction time (Ta). The reading was taken later than 0, 30, 60, 90 and 120 min of supervision of the test drugs. The discontinue time, that is time of no

response was put at 30s, while (Tb) was consider their action time for control group.[12]

$$\%\text{Inhibition} = \frac{Ta - Tb}{Tb} \times 100$$

**4. Tail-flick test-**

The tail-flick test is widely and reliably used for revealing the potency of opioid analgesic. In this test heat is used as the noxious stimulus. The stimulus cause a simple nociceptive spinal reflex response in which the rat or mouse flick its tail away from the heat source. It is very useful test for discrimination between centrally acting drug like analgesics and non-opioid analgesics. In this method mice weigh (18-22g) are used and a light beam is focused (radiant heat) to the proximal third of the tail. The reaction time of movement is recorded. Then test drug and standard are administered either orally or sub-cutaneously. Same procedure is repeated and reaction time noted after 30, 60 and 120 min.

**5. Formalin test-**

In this model 10% formalin solution used as a chemical noxious stimulus. Male wistar rat weight between 180-300 g are used. In the dorsum of front paw of the animal 0.05 ml of 10% formalin is injected subcutaneously. Each animal is placed separate cage for observation of pain responses in early and late phase. Scoring of this pain response from pain scale. After administration of the test drug again scoring is done after 30, 60 min. comparison.[13]

**Table -1 : Medicine plants used for Analgesic and Anti Inflamatory activity**

| Sr. No | Plant Name | Family | Plant part used | Inflammation and analgesia inducing agent | Screening method | Ref. No. |
|---|---|---|---|---|---|---|
| 1. | *Dracaena cinnabari balf* | Agavaceae | Balf resin (ethanolic extract) | 1.Carrageenan 2.Acetic acid | 1.Winter test, Rie-sterer & jaques test 2. Koster test & Tail flick test | 14 |
| 2. | *Ageratum conyzoides* | Asteraceae | Leaves (ethanolic extract) | 1.Zymogen & dextran | 1.Zymogen & dextran induced paw edema | 15, 16 |
| 3. | *Melanthera scandens* | Compositae | Leaves (ethanolic extract) | 1.Carrageenan, Egg albumin 2.Acetic acid, Formalin, Thermally | 1.Carrageenan induced paw edema and Egg albumin induced paw edema test 2.Acetic acid induced writhing method, Formalin induced hind paw licking method | 17 |
| 4. | *Solanum trilobatum* | Solanaceae | Root (methanolic extract) | 1.Cotton pellets, Carrageenan 2.Themally, Acetic acid | 1.Carrageenan induced paw edema and Cotton pellet induced granuloma method 2.Hot plate and acetic acid induced writhing | 18 |
| 5. | *Zizyphus rugosa* | Rhamnaceae | Root bark (extract of water,chloro-form,ethyl acetate and methanol) | 1.Carrageenan 2.Acetic acid | 1.Carrageenan induced paw edema method 2.Acetic acid induced writhing method | 19 |
| 6. | *Anacardium occidentale* | Anacardiaceae | Bark | 1.Carrageenan, Cotton pellet, dextran 2. Acetic acid | 1.Carrageenan induced paw edema, dextran induced paw edema and | 20 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | Cotton pellet induced granuloma method 2.Acetic acid induced writhing method | |
| 7. | *Crossopteryx febrifuga* | Rubiaceae | Leaves (methanolic extract) | 1.Carrageenan 2.Acetic acid | 1.Carrageenan induced paw edema method 2.Acetic acid induced model and analgesyometer | 21 |
| 8. | *Microtrichia perotitii* | Asteraceae | Leaves (methanolic extract) | 1.Formaldehyde 2.Acetic acid | 1.Formaldehyde induced model 2.Acetic acid induced writhing method | 22 |
| 9. | *Anogeissus accuminata* | Combretaceae | Leaves (methanolic extract) | 1.Carrageenan,Formalin 2.Thermally | 1.Carrageenan induced paw edema and formalin induced paw method 2.Hot plate method | 23 |
| 10. | *Stereospermum kunthianum* | Bignoniaceae | Leaves | 1.Formalin | 1.Formalin induced pain test and Randall-selitto model | 24 |
| 11. | *Abutilon indicum* | Malvaceae | Leaves(extract of methanolic, ethanolic, aq. chloroform and petroleum ether | 1.Carrageenan 2.Acetic acid | 1.Carrageenan induced paw edema method 2.Tail flick method | 25 |
| 12. | *Oscillatoria willei* | Oscillatoriaceae | Leaves (methanolic extract) | 1.Cotton pellets, Carrageenan 2.Themally, Acetic acid | 1.Carrageenan induced paw edema and Cotton pellet induced granuloma method 2.Hot plate and acetic acid induced writhing method | 26 |
| 13. | *Phyllanthus emblica Linn* | Euphorbiaceae | Fruit (water extract) | 1.Arachidonic acid, Cotton pellets, Carrageenan 2. Formalin | 1.Arachidonic acid induced ear edema method, Carrageenan induced paw edema and Cotton pellet induced granuloma method 2.Formalin induced pain test | 27 |
| 14. | *Azadirachta indica* | Meliaceae | Leaves (neem oil) | 1.Carrageenan & Cotton pellet | 1.Carrageenan induced paw edema and Cotton pellet induced granuloma method | 28 |
| 15. | *Pinus roxburghii sarg* | Pinaceae | Bark (alcoholic extract) | 1.Carrageenan & Cotton pellet 2.Acetic acid | 1.Carrageenan induced paw edema and Cotton pellet induced granuloma method 2.Acetic acid induced writhing method | 29 |
| 16. | *Aloe ferox* | Aloaceae | Leaves (aqueous extract) | 1.Carrageenan,Formaldehyde & Histamine 2.Formalin & Acetic acid | 1. Carrageenan, Form-aldehyde & Histamine induced paw edema method 2. Formalin test & Acetic acid test | 30 |
| 17. | *Berberis aristata* | Berberidaceae | Root (aqueous & alcoholic extract) | 1.Carrageenan 2.Themally | 1.Carrageenan induced paw edema method 2.Hot plate method | 31 |
| 18. | *Allium cepa* | Alliaceae | Fresh onion juice | 1.Carrageenan 2.Formalin, Thermally | 1.Carrageenan induced paw edema method 2.Hot plate method & Formalin test | 32 |
| 19. | *Lippia multiflora mold* | Verbanaceae | Leaves (methanolic & ethyl acetate extract) | 1.Egg albumin 2.Acetic acid | 1.Egg albumin induced paw edema test 2. Acetic acid test | 33 |

**Conclusion**

Medicinal plants are the largest part imaginative source of medicinal substances natural supplements and

pharmaceutical compounds. In this review article the various extracts of plants are found to have momentous analgesic and anti-inflammatory activity unconcerned types of study models (screening method). In addition these medicinal plants will continue to serve as reservoir for improvement of potent drug with less serious and severe adverse effects. The occurrence of inflammation and analgesia (pain) is increasing now day by day due to present living condition. For this reason this review articles reported the advantageous effect of medicinal plant.

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