

## Effects of Anti-Inflammatory and Analgesic Activity of Bark of Crataeva Religiosa

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### Abstract:

The *Crataeva religiosa* (Hook and Frost) is one of the herbal drug, belongs to the family capparidaceae. The name *Crataeva* is given in the honor of *Crataevus*, a Greek botanist, who was living in the time of Hippocrates and the name *religiosa* indicates its growth near the places of worship. The drug is well known for its various pharmacological properties like diuretic, antiinflammatory, laxative, antioxidant, antioxaluric, hepatoprotectant, lithonotriptic, antirehumatic, antiperiodic, antimycotic, contraceptive, antipyretic, antilithitic, antihelminthic, rubifacient and vasicant properties.

The bark of the *Crataeva religiosa* is useful in the urinary disorders and kidney stone remover. The coarse powder of *Crataeva religiosa* bark was subjected to extraction with petroluem ether, chloroform, ethanol in soxhlet extractor and aqueous extract by macceration process. The preliminary phytochemical investigation showed the presence of sterols, triterpenoids, phenolic compounds glycosides and alkaloids. The various pharmacognostical studies such as microscopy, ash value and extractive values reveals that the identity of genuine drug source

.In this work, the analgesic and antiinflammatory activities of the various extracts of bark of the *Crataeva religiosa* was studied by using acetic acid induced writhing and carrageenan induced paw edema in mice and rat respectively. The ethanolic and aqueous extract shows significant activity in analgesic and antiinflammatory models at the dose level 400mg / kg. The findings of this experimental animal study indicate that crude extracts of *Crataeva religiosa* possesses antinociceptive properties and thus lend pharmacological support to folkloric information of painful, inflammatory conditions.

### Key words:

*Crataeva religiosa*, analgesic, antiinflammatory.

### I.INTRODUCTION:

Inflammation is a pathophysiological response to injury leading to the accumulation of various mediators like Prostaglandins, Histamines, 5-HT, Leukotrienes etc at the site of injury. Though it is a defense mechanism of the body, different events and complex mechanisms involve in it are responsible to maintain and aggravate many type of inflammatory disorders including Rheumatoid arthritis (RA)[1]. Inflammatory diseases are currently treated with steroidal and nonsteroidal anti-inflammatory drugs (NSAIDs) [2].. Unfortunately, both of these widely prescribed drug classes have significant negative side effects, reducing their use in certain segments of the population [3]. Hence, there is a need to develop new drugs with new modes of action that do not produce considerable side effects. The use of traditional medicine and medicinal plants in most developing countries, as a normative basis for the maintenance of good health, has been widely observed [3].. Natural product-based on anti-inflammatory agents with a transcriptional mode of action, good efficacy, and lower risk of side effects offer promising treatment and prevention of inflammation-related conditions. *Crataeva religiosa* hook & frost belonging to family capparidaceae (cappaceae) is a tree usually found in the vicinity of temples of central and eastern India[4][5].

It is known as pasugandha in sanskrit, three legs in capper in English, Varuna in hindi. *Crataeva religiosa* is globally distributed in India, Myanmar, Sri Lanka, Malaysia, Indonesia and China. In India, it is found in Peninsular India, Western India, Gangetic Plains, and Eastern India, up to Tripura and Manipur [6]. The plant part used for the medicinal purpose includes Leaves, stem bark and Root bark [5][7]. Plant is used ethnopharmacologically as diuretic, laxative, lithonotriptic, antirehumatic, antiperiodic, bitter tonic, rubifacient and counterirritant [5][7]. The bark is used in the urinary disorders including kidney and bladder stones, antiemetic, and calculous affections and as an antidote in snake bite [5]. Scanty literature is available on bactericidal properties of bark of this plant

and hence the plant is screened for the bactericidal potential.

## 2. MATERIALS AND METHODS

### 2.1. Collection and processing of the plant material:

Bark samples of *Crataeva religiosa* were collected from Nagamalai Hills, Arachalur, Erode district.

The bark samples were cut into pieces, sun-dried to reduce the moisture level. After the completion of drying, the plant material was pulverized to get coarser powder material, which was stored in air tight plastic container.

### 2.2 Procurement of Experimental Animals:

Swiss albino mice (20-25 g) and albino Wistar rats (150-200 g) of either sex and of approximate same age are used in the present studies were procured from Nandha College of pharmacy, Erode. The animals were fed with standard pellet diet (Hindustan lever Ltd. Bangalore) and water ad libitum. All the animals were housed in polypropylene cages. The animals were kept under alternate cycle of 12 hours of darkness and light. The animals were acclimatized to the laboratory condition for 1 week before starting the experiment. The animals were fasted for at least 12 hours before the onset of each activity.

### 2.3 Acute toxicity studies:

Oral acute toxicity studies were carried out with Albino mice weighing 20-25gm. The extracts were administered as per the staircase method. The mice were fed with alcoholic and aqueous extracts of *Crataeva religiosa* separately suspended in 5%w/v normal saline at dose 500, 1000, 1500, 2000, 2500 mg/kg bodyweight. The animals were observed continuously for 2 hours for the gross behavioral changes and then intermittently once in every 2 hours and finally at the end of 24 and 72 hours to note for any signs of toxicity including death[13].

### 2.4 Acute inflammatory model

#### Carrageenan induced paw edema in rats

Everyone has personal experience of inflammation and pain. The classic signs of inflammation have long been recognized; the tissues become red, swollen, tender, or painful, there is local heat and the patient may be febrile. Inflammations can be categorized mainly as Chronic and Acute inflammatory disease[10].

Acute and chronic inflammatory diseases are still one of the most important health problems in the world. Although several agents known to treat inflammatory disorders, their prolonged use often leads to gastric intolerance, bone marrow depression, water and salt retention. For this reason there is a need to find and develop new anti-inflammatory drugs with low side effects[11]. Formaldehyde, Dextran, Carrageenan, histamine, and other inflammatory induced inflammation models are frequently used in screening for the anti-inflammatory activity of new compounds, where implantation of foreign body under the skin is often used to investigate the effects of drugs on the proliferative phase of the chronic inflammation model. In the present study the attempt has been focused to evaluate the anti-inflammatory activity of various extracts of Bark of *Crataeva religiosa* using carrageenan induced paw edema in rats as a model. For comparison purpose, indomethacin was taken as a reference compound.

### Treatment Design

- \* Group I: - Normal control (Carrageenan 1%w/v)
- \* Group II: - Positive control (indomethacin 10mg/kg, i.p.)
- \* Group III: - Petroleum ether extract (400mg / kg)
- \* Group IV: - Chloroform extract (400mg / kg)
- \* Group V: - Ethanolic extract (400mg / kg)
- \* Group VI: - Aqueous extract (400mg / kg)

### Procedure:

1. Male albino Wistar rats weighing between 150-200 gm were selected and divided into 6 groups.
2. The different groups were treated as shown in design.
3. The paw volume measured at 0, 30, 60, 120, 180 mins after carrageenan injection using the plethysmometer.
4. The animals of group III, IV, were pre-treated with ethanolic extracts and V, VI with aqueous extracts, 60 minutes before the administration of Carrageenan.
5. Acute inflammation was produced by the sub plantar administration of 0.1% carrageenan in normal saline in the left paw of rats.
6. Inhibition of swelling is compared with that of control group[12].

The % inhibition of paw edema is calculated by:

$$\% \text{ inhibition of Paw-edema} = \frac{C - T}{C} \times 100$$

Where,

C = increase in paw-volume of control group

T = increase in paw-volume after administration of extracts.

## 2.5 Analgesic Activity:

Analgesia is defined as a state of reduced awareness to pain, and analgesics are substances, which decrease pain sensation (pain - killers) by increasing threshold of painful stimuli. The commonly used analgesics are Aspirin, Paracetamol (Non - narcotic type) and Morphine (Narcotic type). Painful reaction in experimental animals can be produced by applying noxious (unpleasant) stimuli such as (i) thermal (radiant heat as a source of pain), (ii) chemical (irritants such as acetic acid and bradykinin) and (iii) physical pressure (tail compression) [12]. In the present study the attempt has been focused to evaluate the analgesic activity of various extracts of bark of *Crataeva religiosa* against acetic acid induced writhing response in mice.

## Treatment Design

- \* Group I :- Normal control (Acetic acid 3%v/v )
- \* Group II:- Positive control( Pentazocine 5mg / kg )
- \* Group III:- Ethanolic extract(300mg / kg)
- \* Group IV:- Ethanolic extract(600mg / kg)
- \* Group V:- Aqueous extract(300mg / kg)
- \* Group VI:- Aqueous extract(600mg / kg)

## Procedure:

1. Albino mice weighing between 150-200gm were selected and divided into 6 groups.
2. Acetic acid is administered in the dose of 30mg/kg or 0.3 ml to the first group (normal control) and number of writhing responses (constriction of abdomen, twisting of trunk and extension of hind limbs) are recorded for a period of 10 mins.
3. The animals of group III, IV, were pretreated with ethanolic extracts and V, VI with aqueous extracts 15 minutes before the administration of Acetic acid.
4. Reduction in number of writhes is taken as analgesic activity and compared with that of control group [12].

## 3.0 Results and Discussion:

The inflammatory process may be defined as a sequence of events that occurs in response to noxious stimuli, infection or trauma [14]. The classic signs of inflammation are local redness, swelling, pain, heat and loss of function.

The events of inflammation that underline these manifestations are induced and regulated by a large number of chemical mediators, including kinins, eicosanoids, complement proteins, histamine and monokines [15]. Due to the increase frequency of NSAID and their common side effects the use of medicinal herb in the treatment and prevention of diseases is attracting attention by scientists worldwide[16]. *Crataeva religiosa* is used as an anti inflammatory agent in folklore. To give a scientific validation to this plant an attempt was made to study the anti inflammatory activity. Sub planter injection of carrageenan in rats shows time dependent increase in paw thickness. Carrageenan induced rat hind paw edema has been widely used for the discovery and evaluation of many anti-inflammatory agents, since the relative potency estimates obtained from most drugs tend to reflect clinical experience[17]. Development of edema in the paw of the rat after injection of Carrageenan is a biphasic event [18]. The first phase is due to the release of histamine and serotonin and the second phase is due to the release of prostaglandins kinin like substances, protease and lysosomes[19].

It has been reported that second phase of edema is sensitive to most clinically effective anti-inflammatory drugs, which has been frequently used to access the anti-edematous effect of natural products [20]. The various extracts of bark of *Crataeva religiosa* was tested for Anti-inflammatory activity against carrageenan induce paw-edema in rats. All the extracts are having anti-inflammatory activity against the carrageenan induced paw oedema in rats. The reductions of paw oedema of rats are compared with the standard drug i.e. indomethacin. The ethanolic and aqueous extract shows significant activity as compared with standard drug indomethacin which was shown in the Table-1 and fig-1.

The leaves of medicinal plant '*Crataeva nurvala* Buch. Ham' was extracted in ethanol to evaluate the peripherally acting analgesic potential using acetic acid induced writhing and antidiarrhoeal activity using intestinal motility test both in mice. The crude extract showed significant ( $P < 0.01$ ) analgesic activity at oral doses of 200 and 400mg/kg body weight with an inhibition of writhing 68.4% and 76.3% compared to 67% for the positive control. In the motility test, the crude extract at same oral doses showed 31.16% and 35.31% inhibition of intestinal propulsion of charcoal marker where as positive control group exhibited 36.25% inhibition of propulsion of charcoal through the intestine[21].

The various extracts of bark of *Crataeva religiosa* was evaluated for analgesic activity against acetic acid-induced writhing in mice. All the extracts are having analgesic activity against the acetic acid induced writhing in mice but the activity of the ethanolic and aqueous extract shows significant activity than petroleum ether extract and chloroform extract. The reduction in writhing response are compared with the standard drug i.e. pentazocine and the result was shown in the Table -2 and fig-2. The pharmacological activity of *C. religiosa* are screened for anti-inflammatory and anti-analgesic activity shows that

the ethanolic and aqueous fractions are having more activity than petroleum ether and chloroform extracts. The pharmacological potency as in the case of anti-inflammatory and analgesic activity in *Crataeva religiosa* leads to the bioactivity graded fractionation of phytoconstituents paving way to the introduction of these herbal medicine as pharmaceutical products. The future research will be focused on the investigation of bioactivity graded separation and the formulation development may be beneficial to human kind.

**TABLE : 1 ANTI-INFLAMMATORY ACTIVITIES OF VARIOUS EXTRACTS OF BARK OF CRATAEVA RELIGIOSA**

Group	Treatment Design	Dose	Paw volume in ml as measured by mercury displacement at				
			0 min	30min	60 min	120 min	180 Min
I	Normal control (Carrageenan)	0.1ml	0.51 ± 0.018	0.562 ± 0.023	0.73 ± 0.023	0.86 ± 0.023	1.1 ± 0.084
II	Standard (Indomethacin)	10mg/kg	0.45 ± 0.024	0.48 ± 0.034	0.55 ± 0.024	0.55 ± 0.024	0.48 ± 0.018
III	Petroleum ether extract	400mg / kg	0.45 ± 0.024	0.57 ± 0.044	0.66* ± 0.024	0.68* ± 0.033	0.71 ± 0.065
IV	Chloroform extract	400mg / kg	0.42 ± 0.034	0.55 ± 0.023	0.64 ± 0.024	0.72 ± 0.036	0.69 ± 0.046
V	Ethanolic extract	400mg / kg	0.35 ± 0.034	0.46 ± 0.044	0.62* ± 0.042	0.64* ± 0.028	0.58* ± 0.052
VI	Aqueous extract	400mg / kg	0.36 ± 0.037	0.45 ± 0.024	0.62 ± 0.023	0.65 ± 0.046	0.60 ± 0.037

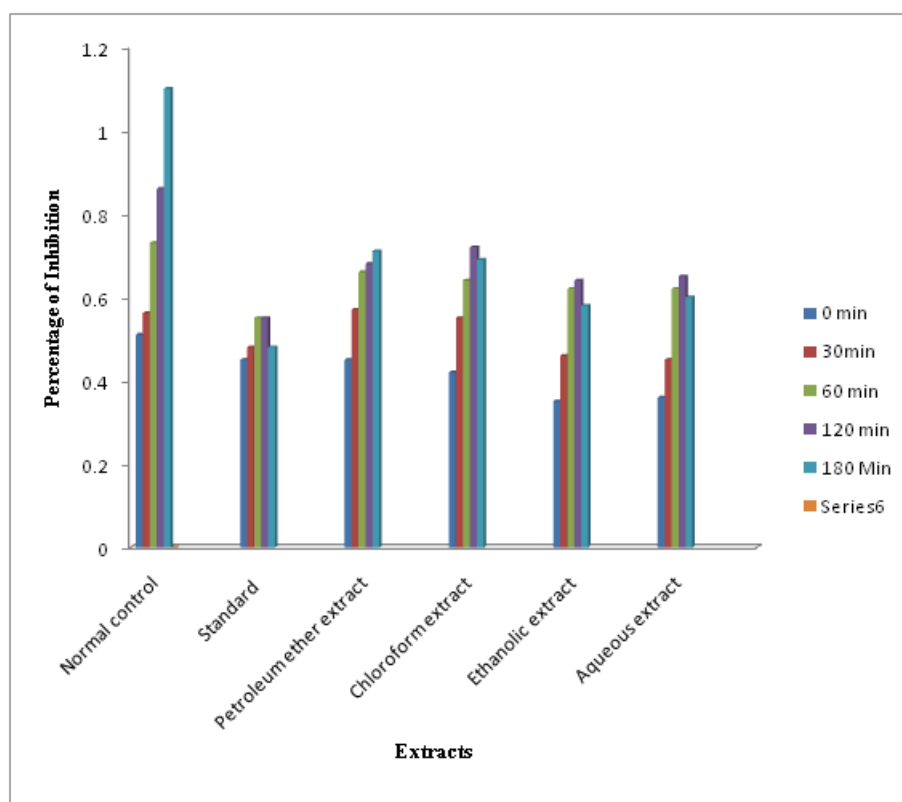
P values: \*\* P<0.01; \* P<0.05.

Values are expressed in mean ±SEM, n=6 animals in each group.

One way ANOVA followed by DUNNETT'S, multiple comparison tests

**GRAPH -1 ANTI-INFLAMMATORY ACTIVITIES OF VARIOUS EXTRACTS OF BARK OF CRATAEVA RELIGIOSA**



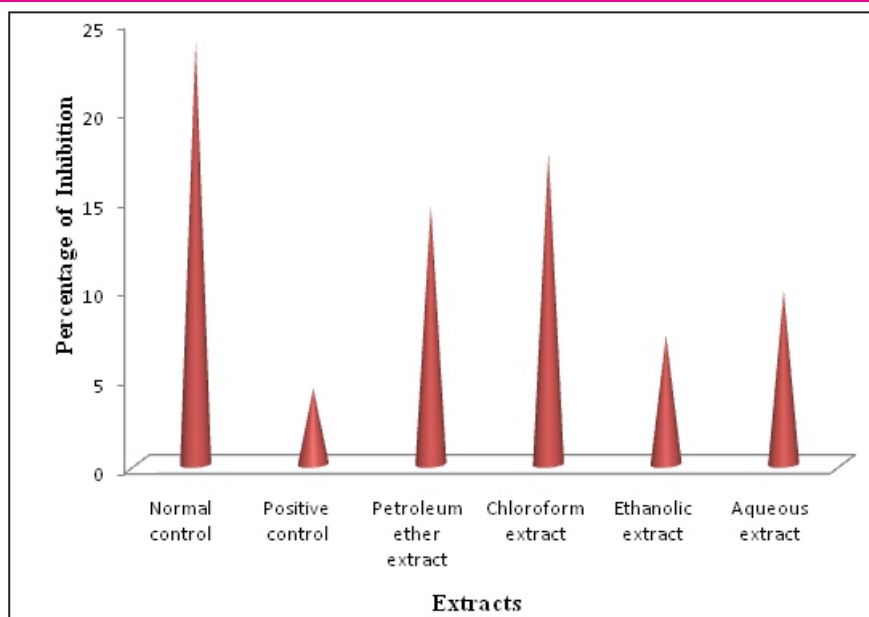


**TABLE :2 ANALGESIC ACTIVITY OF VARIOUS EXTRACTS OF BARK OF CRATAEVA RELIGIOSA**

Group	Treatment design	Dose	Mean No. of wriths (In 10 mins.)
I	Normal control (Acetic acid)	1%v/v	23.75±0.75
II	Positive control (Pentazocine)	5mg/kg	4.25 ± 0.25**
III	Petroleum ether extract	400mg / kg	14.5 ± 0.84*
IV	Chloroform extract	400mg / kg	17.5 ± 0.54*
V	Ethanolic extract	400mg / kg	7.25 ± 0.90**
VI	Aqueous extract	400mg / kg	9.75 ± 0.64**

P values: \*\* P< 0.01; \* P<0.05. Values are expressed in mean ±SEM, n=6 animals in each group. One way ANOVA followed by DUNNETT'S, multiple comparison tests.

**GRAPH -2 ANALGESIC ACTIVITY OF VARIOUS EXTRACTS OF BARK OF CRATAEVA RELIGIOSA**



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