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# Evaluation of anti-inflammatory activity of *Ficus carica* Linn. leaves

Vikas V Patil* and Vijay R Patil

Department of Pharmaceutical Chemistry and Pharmacognosy

TVES's H'ble Loksevak Madhukarrao Chaudhari College of Pharmacy

Faizpur, Maharashtra, India

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The aim of the present study was to explore the probable anti-inflammatory effect of petroleum ether (PEE), chloroform (CE) and ethanol (EE) extracts obtained from the leaves of *Ficus carica* Linn. Anti-inflammatory activity was studied by carrageenan-induced rat paw edema and cotton pellet granuloma methods. The extracts were administered orally in doses of 300 and 600 mg/kg/day of body weight to healthy animals. The ethanolic extract (EEFC-II) 600 mg/kg exhibited maximum anti-inflammatory effect, which is 75.90% in acute inflammation and in chronic study showed 71.66% reduction in granuloma weight. The petroleum ether (PEE), chloroform (CE) and ethanol (EE) extracts significantly reduced carrageenan-induced paw edema and cotton pellet granuloma method in rats. These extracts showed a greater anti-inflammatory effect comparative to standard drug Indomethacin.

**Keywords:** Leaves, *Ficus carica*, Moraceae, Anti-inflammatory, Indomethacin

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## Introduction

The Fig tree, *Ficus carica* Linn. (Family-Moraceae) is one of the unique *Ficus* species widely spread in tropical and subtropical countries. It has edible fruits with high commercial value. Commercial fig production is either located around the Mediterranean Sea or is realized in countries possessing Mediterranean climate as in the case of California, Australia or South America[1, 2]. It is a small or moderate-sized deciduous tree, 3-10 m high with broad ovate or nearly orbicular leaves, more or less deeply 3-5 lobed, rough above and pubescent below; fruits axillary, usually peer shaped, variable in size and colour. The fruit of *F. carica*, like those of other species of *Ficus*, is a syconium a fleshy hollow receptacle with a narrow aperture at the tip. The bark is a cylindrical and pale grey coloured[3] (Plate 1). Previous reports concerning the nutrient composition of dried figs have indicated that it has the best nutrient score among the dried fruit, being an important source of minerals and vitamins[4]. Its fruit, root and leaves are used in the native system of medicine in different disorders such as gastrointestinal (colic, indigestion, loss of appetite and diarrhoea), respiratory (sore throats, coughs and bronchial problems), inflammatory and cardiovascular disorders[5, 6]. Fig has been traditionally used for its medicinal benefits as metabolic, cardiovascular, respiratory, antispasmodic and anti-inflammatory remedy[7, 8]. The root is tonic, useful in leucoderma and ringworm. The fruit is sweet, antipyretic, tonic, purgative useful in inflammation, weakness, paralysis, thirst "*Vatta* diseases" of head, diseases of liver and spleen, pain in

Plate 1—*Ficus carica* Linn.

*Correspondent author
Address: Opp. Jai Bhole Shankar Market, Kranti Chowk
SAVDA, Tal-Raver, Dist.- Jalgaon- 425502
E-mail: vikas312@rediff.com
Phone: 09423938637

chest, cures piles, stimulate hair growth. The milky juice is expectorant, diuretic and dangerous for eye. Fig latex is used as an anthelmintic and the leaves have been reported to be hypoglycaemic, hepatoprotective, immunodulatory, antipyretic, anthelmintic[9-15].

However, the plant has not been studied for anti-inflammatory activity. This study was aimed at providing pharmacologic basis for its folkloric use in inflammation and other species of *Ficus,* viz. *F. glomerata* Roxb. syn. *F. racemosa*[17], *F. bengalensis* Linn.[18, 19], *F. inspida* Willd. , *F. religiosa* Linn., *F. elastica* Roxb. and *F. indica* Linn.[20] were found to have anti-inflammatory activity. Based on this, an attempt has been made to evaluate the inflammation potency of *F. carica* leaves.

## Materials and Methods

### Plant material

The plant material was collected from the Nashik district (MS) in the month of June 2008 and identified and authenticated by joint director of Botanical Survey of India, Pune dated 13/08/2008 and letter No.BSI/WC/Tech/2008/355. The leaves were separated, dried, coarsely powdered passed through sieve no 40 and stored in a closed container for successive extraction.

### Preparation of extracts

The powdered plant material (450 g) was repeatedly extracted in a 5000 ml round bottomed flask with 2000 ml solvents starting with petroleum ether, chloroform and ethanol. The reflux time for each solvent was 40 cycles. The extracts were cooled at room temperature and evaporated to dryness under reduced pressure in rotary evaporator[16].

### Acute toxicity study

Doses of 30, 100, 300, 1000, 2000 and 5000 mg/kg[21] of extracts were administered orally to mice. The extracts were given at the doses of 300 and 600 mg/kg/day of body weight. All the animals (albino mice of either sex) found to be safe at dose of 5000 mg/kg. Mice were then observed for incidence of mortality or any sign of toxicity up to 24 h. The dosing schedule was followed as per OECD (Guideline 425)[22].

### Animals

Wistar albino rats (120-200 g) of either sex supplied from Yash Farms, Pune India were used. The animals housed under standard laboratory conditions maintained at 25 ± 1°C and under 12/12 h light/dark cycle and fed with standard pellet diet (Gold Mohur Brand, Lipton India Ltd) and water *ad libitum*. The experimental protocol has been approved by the institutional animal ethics committee and by the animal regulatory body of the Indian Government (Registration No.652/02/a/ CPCSEA, dated 25/01/1999).

### Drugs and chemicals

Indomethacin (Micro labs, Bengaluru), Carrageenan (Sigma Chemicals), Ethanol AR (Thomas Baker Chemical Pvt. Ltd.), Petroleum ether AR (60-80°C, MCC) were used during the experimental protocol.

### Evaluation of anti-inflammatory activity

#### *Carrageenan-Induced Paw Edema*

The albino rats of either sex were divided into six groups of six animals each. Group I received 0.2 ml of 2% w/v carboxy methyl cellulose suspension orally for seven days as a control group, Group II received 300 mg/kg body weight of petroleum ether extract (PEEFC-I) orally for seven days, Group III received 600 mg/kg body weight of petroleum ether extract (PEEFC-II) orally for seven days, Group IV received 300 mg/kg body weight of chloroform extract (CEEFC-I) orally for seven days, Group V received 600 mg/kg body weight of chloroform extract (CEEFC-II) orally for seven days, Group VI received 300 mg/kg body weight of ethanolic extract (EEFC-I) orally for seven days, Group VII received 600 mg/kg body weight of ethanolic extract (EEFC-II) orally for seven days and Group VIII received 10 mg/kg of body weight of Indomethacin intraperitoneally for seven days as a standard drug[23,24]. Acute inflammation was induced in all groups by injecting 0.1 ml of 1%w/v carrageenan in to the sub-plantar region of the right hind paw of rats. On the seventh day, paw volume was measured 1 h prior to carrageenan injection using plethysmometer and at 0 and 3 h after the carrageenan injection[25, 26]. Mean increase in the paw volume was measured and percentage inhibition was calculated.

Percentage of inhibition =100 (1-Vt/Vc); where, Vc= edema volume in control and Vt= edema volume in test/standard compound.

### Chronic inflammation study

#### *Cotton pellet granuloma in rats*

This study was carried out by cotton pellet implantation method in rats[27]. This method used here

Table 1—Effect of *Ficus carica* leaves extracts on carrageenan-induced paw edema in rats[a]

| Treatment | Dose mg/kg | Mean paw volume in ml | | | | | | Percent inhibition Vt |
|---|---|---|---|---|---|---|---|---|
| | | 0 min | 15 min | 30 min | 60 min | 120 min | 180 min | |
| Control | 2%CMC | 0.46±0.008 | 0.59±0.007 | 0.78±0.01 | 0.79±0.01 | 0.87±0.005 | 0.95±0.005 | Vc 0.74 |
| EEFC-I | 300 | 0.4±0.01* | 0.34±0.007* | 0.46±0.01* | 0.48±0.01* | 0.50±0.008* | 0.54±0.008* | 38.73 |
| EEFC-II | 600 | 0.42±0.008* | 0.19±0.01 | 0.13±0.007* | 0.12±0.01 | 0.11±0.008* | 0.10±0.008* | 75.90 |
| CEFC-I | 300 | 0.48±0.008* | 0.50±0.01 | 0.55±0.007 | 0.59±0.01 | 0.64±0.008* | 0.72±0.009* | 21.62 |
| CEFC-II | 600 | 0.43±0.01 | 0.36±0.009* | 0.35±0.005* | 0.34±0.008* | 0.32±0.01 | 0.36±0.007* | 51.35 |
| PEEFC-I | 300 | 0.45±0.009* | 0.52±0.01 | 0.57±0.007* | 0.63±0.008 | 0.68±0.009* | 0.75±0.01* | 18.91 |
| PEEFC-II | 600 | 0.41±0.009* | 0.45±0.007* | 0.40±0.01 | 0.39±0.007 | 0.38±0.007* | 0.37±0.008* | 45.94 |
| Indomethacin | 10 | 0.48±0.007 | 0.44±0.007 | 0.42±0.01 | 0.40±0.008 | 0.37±0.007 | 0.35±0.009 | 79.72 |

[a]Figures in parenthesis indicate oedema inhibition percentage, *N*=6 animals per group
**P*<0.001 by Student's t-test; *P*<0.05 by Student's t-test

was adopted from[28] under light ether anesthesia; sterile cotton pellets (10 mg) were implanted subcutaneously in the axilla and groin regions of the rats. The animals were treated orally with various extracts at different doses (300 and 600 mg/kg) daily for 7 consecutive days. Animals in the control group received either normal saline or the vehicle gum acacia. Indomethacin (10 mg/kg, orally) was given to animals in the reference groups. They were sacrificed on day 8, the cotton pellet removed, freed from extraneous tissue and dried overnight at 60°C and weighed. The percent inhibition of the dry weight of the granuloma were calculated and compared.

**Statistical analysis**

Statistical analysis was carried out using Graph Pad Prism 4.0 (Graph Pad software San Diego, CA). Results were expressed as Mean±SEM, statistical significance was calculated by applying by Student's t-test. *P*<0.001 was considered as significant.

## Results and Discussion

The results of carrageenan-induced paw edema method are given in Table 1. Extract of *F. carica* at 300 mg/kg body weight per day (EEFC-I) when given orally as a suspension the paw volume were reduced by 38.73% whereas in case of ethanolic extract of at 600 mg/kg body weight per day (EEFC-II) shows 75.90% inhibition after 3 h which indicate that effect of ethanolic extract is reflected in dose dependent manner. Both EEFC-I and EEFC-II showed inhibitory effect on carrageenan-induced paw edema thus, exhibiting anti-inflammatory effect against acute inflammation.

In case of chloroform (CEFC-I) and petroleum ether extract (PEEFC-I) at 300 mg/kg body weight per day reduced the paw volume 21.62 and 18.91%. Chloroform (CEFC-II) and petroleum ether extract (PEEFC-II) at 600 mg/kg body weight per day exhibited 51.35 and 45.94% reduction in paw volume after 3 h so chloroform and petroleum ether extracts do not possess significant anti-inflammatory activity when compared with control and Indomethacin treated animals (Table 1).

Table 2—Effect of leaves extracts of *Ficus carica* on cotton pellet granuloma in rats[a]

| Treatments | Dose | Weight of cotton-pellet (mean±S.E.M.) mg | Inhibition (%) |
|---|---|---|---|
| Control | 2%CMC | 42.7±0.5 | - |
| EEFC-I | 300 mg/kg | 23.1±0.4** | 45.90 |
| EEFC-II | 600 mg/kg | 12.1±0.6* | 71.66 |
| CEFC-I | 300 mg/kg | 32.2±0.5 | 24.59 |
| CEFC-II | 600 mg/kg | 24.3±0.5 | 43.09 |
| PEEFC-I | 300 mg/kg | 33.6±0.6 | 21.31 |
| PEEFC-II | 600 mg/kg | 27.5±0.6 | 35.59 |
| Indomethacin | 10 mg/kg | 10.4 ±0.5* | 75.64 |

[a]*N*=6 animals per group ; **P*<0.001 by Student's t-test; ***P*<0.05 by Student's t-test

Cotton pellet granuloma method showed the result given in Table 2. Ethanolic extract at 300 mg/kg body weight per day (EEFC-I) when given orally as a suspension the weight of cotton pellet were reduced by 45.90% whereas in case of ethanolic extract given at 600 mg/kg body weight per day (EEFC-II) showed 71.66% inhibition after 3 h which indicate that effect of ethanolic extract of *F. carica* is reflected in dose dependent manner. Both EEFC-I and EEFC-II showed inhibitory effect on cotton pellet granuloma thus, exhibiting anti-inflammatory effect against chronic inflammation.

In case of chloroform (CEFC-I) and petroleum ether extract (PEEFC-I) at 300 mg/kg body weight per day the weight of cotton pellet 24.59 and 21.31%. Chloroform (CEFC-II) and petroleum ether extracts

(PEEFC-II) at 600 mg/kg body weight per day exhibited 43.09 and 35.59% reduction in the weight of cotton pellet after 7 days so chloroform and petroleum ether extracts do not possess significant anti-inflammatory activity when compared with control and Indomethacin treated animals (Table 2).

Inflammation has different phases, the first phase is caused by an increase in vascular permeability, the second one by infiltrate of leucocytes and the third one by granuloma formation. We determined anti-inflammatory activity by using inhibition of carrageenan induced inflammation which is one of the most feasible methods to screen anti-inflammatory agents. The development of carrageenan induced edema is bi-phasic; the first phase is attributed to the release of histamine, serotonin and kinins and the second phase is related to the release of prostaglandins and bradykinins[29-33]. We observed that EEFC-I and EEFC-II showed significant inhibition against carrageenan-induced paw edema in the dose dependent manner but in case of chloroform and petroleum ether extract failed to possess the anti-inflammatory effect may be due to absence of flavonoid[34]. This response tendency of the extract in carrageenan-induced paw edema revealed good peripheral anti-inflammatory properties of the ethanolic extract. This anti-inflammatory effect of EEFC-I and EEFC-II may be due to the presence of flavonoids. It has been reported that a number of flavonoids possess anti-inflammatory activity[35]. The presence of flavonoid identified might be responsible for the anti-inflammatory activity in ethanolic extract. Thus, it is concluded that the ethanolic extract of bark of *Ficus carica* produces significant anti-inflammatory activity in dose dependent manner.

The screening of extracts was first done by carrageenan rat paw edema. This is a suitable test for evaluating anti-inflammatory drugs which have been frequently used to assess the anti-edematous effect of natural products[36]. The second method employed for the screening was the cotton pellet granuloma, which has certain advantages for natural product testing. First, the response is local and involves the skin thus the topical application avoids drug metabolism and excretion. Secondly, this model uses very small amounts of drugs. Like wise, the granulomatous tissue formation is related to the chronic inflammatory process, which is characterized by several phases[37].

## Conclusion

From these investigations it may be concluded that the various extracts of leaves of *Ficus carica* showed anti-inflammatory effects, similar to those observed for non-steroidal drug such as Indomethacin. It is important to point out that the phytochemical analysis showed the presence of flavonoids and this might be responsible for anti-inflammatory activity. Further investigations are under process in our laboratory to isolate and characterize the specific active components of the plant extracts which is responsible for observed pharmacological actions.

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