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Anti-Inflammatory Activity of Aqueous Extract of *Carica papaya* Seeds in Albino Rats

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ABSTRACT

To study the anti-inflammatory effect of aqueous extract of *Carica papaya* seeds in acute, sub-acute and chronic experimental models in albino rats. The aqueous extrac tof air-dried seeds of *Carica papaya* was studied in arrangement-induced paw oedema in rats and the paw volume was measured plethysmometrically at 0 and 3 h after injection and compared with control and standard drug, diclofenac. The drug was subjected to cotton pellet-induced granuloma test in rats. The implanted pallets, removed 8th day were cleaned, dried and weighed. The percentage inhibition of granuloma formation was calculated in comparison to control. The drug was also investigated in formalinduced oedema model in rats. Degree of inflamation was measured plethysmometrically on day 1 and 0 and compared with control and standard drug, diclofenac. All the drug were administered orally. The aqueous extract of *Carica papaya* significantly (p>0.01) reduced carrageenam-induced pedal oedema (83.5%) and formalininduced pedal oedema (79.06) in rats. It also decreased formation of granulation tissue (52.55) in cotton pellet-induced granuloma in rats in comparasion to control. The aqueous extract of *Carica papaya* seeds showed significant anti-inflammatory action in acute, sub-acute and chronic experimental models in rats.

Key words: *Carica papaya* inflammation, oedema granuloma diclofenac.

INTRODUCTION

Carica papaya Linn belonging to family Caricaceac is commonly known as papaya, Paw paw, Melon tree. It is a medicinal plant originated from Central America, which has spread to different parts of the world, Africa and Nigeria in particular. It is known for its plethora folkloric used and pharmacological activities. It contains two major bioactive compounds, Papain and Chymopapain, which are sued in brewing, wine making, textile and tanning industries[1]. It also contains alkaloids, flavonoids and other phenolic compounds. It is used by the negatives in treating malarial fever, diabetes mellitus, bacterial infections, as de-wormer and as an ecbolic agent[2-4]. The dry seeds of *Carica papaya* are chewed to alleviate nagging headache and in reducing swollen wounds and reducing high blood pressure. The central nervous and cardiovascular effects of the methanol leaf extract of *Carica papaya* have been documented[5]. The fruits can be directly applied topically to skin sours[6]. Papaya seeds extract is being currently marketed as a nutritional supplement with purported ability to rejuvenate the body condition and to increase energy. The product claims to improve immunity against common infections and body functioning. The provides the evidence for its immunomodulatory and its anti-inflammatory actions. Recently, the methanol extract of *Carica papaya* seeds has been reported to have anti-nociceptive and anti-inflamatory activity in mice and rats[7].

The present study is undertaken to evaluate the anti-inflammatory activity of aqueous extract of *Carica papaya* seeds (CPE) in acute, sub-acute and chronic inflammatory models in albino rats.

MATERIAL AND METHODS

Plant material and drug preparation

Six mature, unripe fruits of *Carica papaya* were collected from local market, Raichur and authenticated. The papaya fruits were cut in to piece and the wet seeds were separated out. These were then gently but thoroughly rinsed in tap water two times and completely air-dried at room temperature for 4 weeks. The dried seeds were pulverized in to fine powder using a domestic mixer grinder. 40 g of powdered seeds was boiled in 500 ml of distilled water for 30 minutes after which it was filtered using a piece of clean white cotton gauze. The filtrate was evaporated to complete dryness at 40°C, producing a fine sweet smelling and chocolate color solid residue (yield : 22.5%, w/w). The extraction process was repeated 4 times and the solid residue was weighed and pooled together in air and water proof container kept in a refrigerator at 4°C. From this fresh preparations were made whenever required.

Experimental procedure

The anti-inflammatory (acute, sub-acute and chronic) effect of CPE was assessed using adult albino rats of either sex (n=54) weighing 150 to 200g. The animals were maintained with standard pellet diet and water ad libitum. They were further divided in to three groups (n=6) in each model : Group I rats were given 0.1 ml of 4% gum acacia suspension, which served as the control. Group II rats were treated with CPE, 400 mg/kg and Group III rats were treated with standard drug, Diclofenace, 10 mg/kg. All the drugs were administered orally. All the experiments were conducted as per the norms approved by Institutional Animal Ethics Committee.

Carragenan-induced paw oedema in rat

The anti-inflammatory effect of CPE was evaluated using carrageenan-induced paw oedema in rats[8]. Animals were divided in to three groups of 6 animals in each group. In all groups, acute inflammation was produced by sub-plantar injection of 0.1 ml of freshly prepared 1% suspension of carrageenan in normal saline in the right hind paw of the rat and paw volume was measured plethysmometrically at 0 and 3 h after carrangeenam injection. Animals were premedicated either with vehicle (4% gum acacia) or CPE (400 mg/kg) or diclofenac (10 mg/kg) orally one hour before injection of carrageenam. Mean increase in paw volume was measured and percentage inhibition was calculated.

Cotton pellet-induced granuloma in rat

The method is based on measuring the amount of granulation tissue formed around at implanted foreign body like cotton pellet. Albino rats were divided in to 3 groups of six animals in each group. After shaving of the fur, the animals were anesthetized. Sterile pre-weighed cotton pellets were implanted in the axilla region of each rat through a single needle incision[9]. Animals were treated either with vehicle (4% gum acacia suspension) or CPE, 400 mg/kg of diclofenac, 10 mg/kg orally for seven consecutive days from the day of cotton pellet implantation. On the eight day, the animals were anesthetized; the cotton pellets were removed surgically and made free from extraneous tissues. The pellets were incubated at 37° C for 24 h and dried at 60°C to constant weight. The increment in the dry weight of the pellets was regarded as measure of granuloma formation.

Formallin-induced paw oedema in rat

This method is also based on the plethysmometric measurement of oedema produced by injection of 0.1 ml of 2% formalin into the sub-plantar area of hind paw of rat. Albino rats were divided in to three groups of six animals in each and treated with either 0.1 ml of 4% gum acacia suspension or CPE, 400 mg/kg of diclofenac, 10 mg/kg. All the drugs were administered orally one hour prior to formalin injection and continued for 9 consecutive days. The second injection of formalin was given on the third day[10]. The paw volume was measured by plethysmometer on day 1 and day 9. The difference in paw volume of 1 and day 9 was considered as inflammatory edema. Volume changes in standard group and test group were compared with that of control group and the percentage inhibition of inflammation was calculated.

Statistical analysis

The results were presented as mean ± S.E.M. and subjected to one way ANOVA. P values of 0.05 or less were considered significant.

RESULTS

Carrageenam-induced pedal oedema

The anti-inflammatory effect of CPE in carrageenam-induced paw oedema at the end of 3 h is presented in table 1. CPE significantly reduced paw volume (P<0.01) at 3 h compared to the control (83.85). The reference drug, diclofenac inhibited the paw oedema by 53.64% (P<0.01). Thus the anti-inflammatory effect of CPE (400 mg/kg is higher than that of standard drug, diclofenac, 10 mg/kg.

Cotton pellet-induced granuloma

The results of CPE on cotton pellet-induced gramuloma are shown in Table 2. Animals treated with CPE signifcantly (P<0.01) inhibited granuloma formation (52.55%). Diclofenac also markedly inhibited granuloma formation (97.44%). In this model the anti-inflammatory effect of CPE is lower than that of standard drug, diclofenac.

Formalin-induced paw oedema

Table 3 shows the effect of CPE on formalin-induced paw oedema. The percentage inhibition of edema at the end of 9 days with CPE is 79.06% (P<0.01) as compared to the control rats. Diclofenac also exerted significant (P<0.01) inhibitory action on edema formation (60.45%). In this model also the effect of CPE is higher than the standard drug, diclofenace.

Table 1: Effect of CPE in carrageenam - induced rat hind paw oedema

Treatment	Dose (mg/kg P.O.)	Paw volume increase after 3 h (ml)	Percentage of inhibition
Control	-	1.49 ± 0.05	-
CPE	400	0.99 ± 0.01*	83.85
Diclofenac	10	1.05 ± 0.03*	53.64

Values are expressed as mean ± SEM, number of animals used are six each group,
*P <0.01.

Table 2: Effect of CPE in cotton pellet- induced granuloma formation in rat

Treatment	Dose (mg/kg P.O.)	Weight of cotton pellets on day 8 (mg)	Percentage of inhibition
Control	-	65.83 ± 0.90	-
CPE	400	47.00 ± 1.88*	52.55
Diclofenac	10	30.91 ± 0.45*	97.44

Values are expressed as mean ± SEM, number of animals used are six each group,
*P <0.01.

Table 3: Effect of CPE in formalin-induced rat hind paw oedema

Treatment	Dose (mg/kg P.O.)	Paw volume increase on day 9 (ml)	Percentage of inhibition
Control	-	1.503± 0.04	-
CPE	400	1.105 ± 0.03*	79.06
Diclofenac	10	1.262 ± 0.04*	60.46

Values are expressed as mean ± SEM, number of animals used are six each group,
*P <0.01.

DISCUSSION

The results of presently study show that the aqueous extract from seeds of *Carica papaya* possesses significant anti-inflammatory effect on acute, sub-acute and chronic inflammatory models in albino-rats.

Inhibition of carrageenan-induced inflammation in rats is one of the most suitable test procedures to screen anti-inflammatory agents. Inflammation induced by carrageenam involves three distinct phases of the release of mediators including serotonin and histamine in first phase, kinins in the second phase and prostaglandins in the third phase[11]. CPE showed significant anti-inflammatory activity in this model. However, this effect was more at the end of 3 hr. Therefore it is possible that CPE moght be reducing edema by decreasing kinins and Prostaglandins release.

Cotton pellet-induced granuloma represents the exudative phase of inflammation. Kinin is said to be the main mediator of granuloma as it both vasodilates and increases vascular permeability in the early stages of inflammation. CPE showed significant activity against granuloma formation. It might be acting by inhibiting kinin formation and also probably by inhibiting migration of eosinophils, neutrophils and platelets.

It is well known that inhibition of formalin-induced paw oedema in rat is one of the most suitable test procedures to screen anti-arthritic and anti-inflammatory agents as it closely resembles human arthiritis[12]. Injection of formation subcutaneously in to hind paw of rats produced localized inflammation and pain. The nociceptive effect of formalin is biphasic, an early neurogenic component followed by a later tissue mediated response[13]. Thus formalin-induced arthritis is a model used for the evaluation of an agent with probable anti-proliferative activity. Formalin-induced paw edema in rats represents the proliferative phase of inflammation. CPE showed significant activity in this model. Therefore it appears to activity. Formalin-induced paw edema in rats represents the proliferative phase of inflammation. CPE showed significant activity in this model. Therefore it appears to act by inhibiting proliferative phase and thus could be an effective anti-proliferative agent.

Carica papaya contains alkaloids, flavonoids and polyphenolic compounds[14], and alkaloids, flavonoids and saponins have been found in other natural products with analgesic and anti-inflammatory properties[15]. Therefore the anti-inflammatory activity of CPE may be due to the presence of alkaloids, flavonoids and other polyphenols.

In conclusion, this study has shown that, the aqueous extract of *Carica papaya* seeds showed significant anti-inflammatory effect, which may be responsible for its use in treating skin sours and swollen wounds.

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