

Antinociceptive Action of the Seeds of *Carica Papaya* Linn Extracted in Aqueous Medium in Mice

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ABSTRACT

To study the antinociceptive action of the seeds of *carica papaya* linn extracted in aqueous medium (CPE) in mice. The *Carica Papaya* aqueous seed extract was evaluated for its antinociceptive effect in mice by producing writhing using acetic acid. One hour after administration of mice with the test, control and the standard drugs the mice were given 0.2 ml of acetic acid (3%) solution intraperitoneally to produce writhing. The number of constrictions of abdominal muscles induced along with extending and jerking of the hind limb were counted from 5 to 15 minutes. The response of the mice treated with the *carica papaya* aqueous seed extract and that of the standard drug treated groups were compared with those of the mice in the control group. Percentage inhibition of the writhing movements in mice was considered as an index of analgesic effect. The *Carica Papaya* aqueous seed extract reduced the number of writhing in test group 5 (CPE 400 mg/kg) significantly ($P < 0.05$) in comparison to the control group. Percentage inhibition in test group 5 (60.8%) was comparable to the percentage inhibition in the standard drug (diclofenac) group (70.3%). The *Carica Papaya* aqueous seed extract showed significant antinociceptive effect in mice.

Keywords: The Seeds of *carica papaya* linn extracted in aqueous medium (CPE), Nociception, acetic acid, writhing.

INTRODUCTION

Majority of the diseases or any damage to the human body produces an important symptom known as pain. Pain helps in reminding and facilitating the diagnosis of a disease. It is a guarding process for the body that would come into action whenever any part of the body is damaged¹. Most of the presently used drugs having analgesic action like Non-Steroidal Anti-inflammatory drugs (NSAIDs) & opioids are not helpful in all the cases either because of their adverse drug reactions or less potency². The

most common adverse effects produced by NSAIDs is gastric irritation. Gastric ulcers, perforation and bleeding are the other complications produced by the NSAIDs³. Hence it is necessary to look for other alternative drugs which have got lesser adverse effects as compared to the currently used analgesic drugs. The use of medicinal plants is very closely linked with the history of civilization. According to the world health organization, majority of the population in many countries still use medicinal plants for their health care needs either due to poverty or inability to access the modern medicine⁴. Considering the



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fact that the most important analgesic drugs such as salicylic acid and morphine have originally been obtained from plant sources, the study of plants which were used traditionally as pain killers would be an important research strategy in searching for the new drugs with analgesic effect⁵.

Carica papaya is an important plant with lot of medicinal properties which was first identified in Central America, and later it has been found to spread to other countries like Africa, Nigeria etc. It has been established that the plant *carica papaya* contains two important compounds namely papain and chymopapain and these compounds have found uses in different industries such as in textile industry, wine making, tanning industries and in brewing⁶. This plant is known to contain substances which have got uses in the treatment of various conditions such as in the treatment of ulcers, amoebiasis, fungal infections, and various other infections. It also has got lipid lowering action, free radical scavenging activity, diuretic activity, antifertility activity and also employed in the healing of wounds^{7,8}. The natives of Nsukka used to chew the dry seeds of *Carica papaya* which helped them in overcoming nagging headache (migraine), in reducing swollen wounds and reducing high blood pressure. It has been reported that the methanol seed extract of *Carica papaya* has got antinociceptive effect in mice and rats⁹.

Therefore, it was decided to explore the antinociceptive action of the seeds of *carica papaya* linn extracted in aqueous medium (CPE) in mice

MATERIALS and METHODOLOGY

Plant material & Extraction

four fresh fruits of *Carica papaya* which are mature and unripe were obtained from local market and authenticated. The papaya fruits were sliced opened and the wet seeds were taken out and separated. These were then washed in tap water thoroughly and left to dry completely at room temperature for 4 weeks. The dried seeds were crushed in to fine powder using a grinding machine. 50 grams of powdered seeds was added to 500 ml of distilled water in a container and it was boiled for half an hour after which it was filtered by using a clean cotton gauze. The filtrate was completely evaporated & dried at 40 °C, leading to formation of a chocolate

colour solid residue (yield: 22.5%, w/w). This process of extraction was repeated four times and the solid residue obtained was weighed and collected in a water and air proof container and it was placed in a refrigerator at 4 °C. Fresh preparations were made using this extract as and when required.

Experimental Animals

Mice weighing between 25-30 gm were selected and they were grouped into 5 groups, each group containing 6 mice. The mice were given standard pellets and adequate water and they were allowed to acclimatize to the new environment of the housing conditions for at least one week. All the procedures were followed as per the guidelines of the Institutional Animal Ethics Committee.

Acetic Acid – Induced Writhing in Mice

The method of Koster et al was used to produce writhing in mice¹⁰. The group 1 (control) was given normal saline orally in a dose of 0.2 ml. The group 2 (standard) was given 10 mg/kg body weight of diclofenac sodium orally. The *Carica papaya* aqueous seed extract was given orally in a dose of 100, 200 and 400 mg/kg body weight to the test groups 3, 4 and 5 respectively. The animals were kept on fasting for a period of 16 hours before the treatments. The mice were injected intraperitoneally one hour after treatment, with 0.2 ml of acetic acid (3%) solution to produce the writhing. After injecting acetic acid, the number of constrictions of abdominal muscles produced along with stretching & jerking of the hind limb were counted from 5 to 15 minutes. The abdominal constriction and extension of hind limb indicates a writhe. The response of the mice in test groups and standard group was compared with that of the control group. The reduction in the number of writhing movements was considered as an important index of analgesic activity.

Percentage protections against writhing movements was calculated as follows:

$$\% \text{ Inhibition} = \frac{W_m (\text{control}) - W_m (\text{test})}{W_m (\text{Control})} \times 100$$

Where W_m = Mean number of writhing.

Statistical Analysis

The results were presented as mean \pm S.E.M. One way ANOVA test was applied & $P < 0.05$ was considered significant.

RESULTS

Acetic Acid – Induced Writhing in Mice

The results of the antinociceptive action of the seeds of carica papaya linn extracted in aqueous medium (CPE) in mice in abdominal writhing induced by acetic acid is presented in Table 1. Diclofenac sodium (10 mg/kg) and CPE (400 mg/kg) reduced the number of abdominal writhing significantly ($p < 0.05$). Percentage inhibition of writhing produced by the CPE 400mg/kg (60.8%) was similar to that of standard drug diclofenac (70.3%). This percentage inhibition has been depicted with the help of Graph 1.

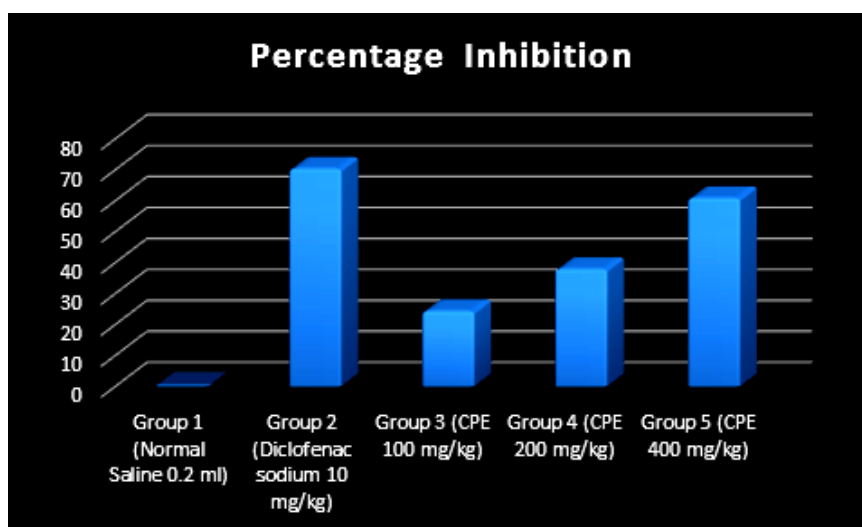
DISCUSSION

The standard drug (diclofenac) and the aqueous extract at 400 mg/kg had significant

difference with the control group. This means that the extract has effect on peripheral pains as the writhing test is used to test for peripheral analgesia. To evaluate the antinociceptive effect of the drugs on the visceral pain, writhing induced by acetic acid was used¹¹. This pain mechanism is believed to involve local peritoneal receptors¹². It has been reported that injection of acetic acid intraperitoneally releases prostaglandins like prostaglandin E2 (PGE2) and prostaglandin GF2á (PGF2á) and their levels are increased in the peritoneal fluid¹³. The abdominal constriction observed during the test is due to the stimulation of pain receptors by these prostaglandins. It may therefore be possible that the carica papaya aqueous seed extract have significant antinociceptive effect either by reducing the synthesis or by blocking the action of prostaglandins, thereby having inhibitory effects on peripheral pains.

Table 1: The action of the seeds of carica papaya linn extracted in aqueous medium (CPE) in mice on writhing induced by acetic acid in mice

Groups	Mean Writhing ± S.E.M	% Pain inhibition
Group 1 (Normal Saline 0.2 ml)	73.5 ± 0.76	0.0
Group 2 (Diclofenac sodium 10 mg/kg)	21.8 ± 0.94	70.3
Group 3 (CPE 100 mg/kg)	55.6 ± 0.71	24.3
Group 4 (CPE 200 mg/kg)	45.6 ± 1.02	37.9
Group 5 (CPE 400 mg/kg)	28.8 ± 0.47	60.8
N=6	Mean ± SEM	P < 0.05



Graph 1: Percentage inhibition of writhing in different groups

CONCLUSION

In conclusion, the carica papaya aqueous seed extract has got significant anti-nociceptive effects on mice and these effects are comparable to standard drug (diclofenac sodium). In order to substantiate these results additional research work is needed.

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