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Analgesic , Anti-Inflammatory and CNS Depressant Activity of *Capparis decidua Edgew* Flowers

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ABSTRACT

The aim of the present study was to evaluate the analgesic, anti-inflammatory and CNS depressant property of flowers of *Capparis decidua Edgew*. in experimental animals. The analgesic activity of aqueous extract was evaluated by Eddy's hot-plate method and acetic acid induced writhing test. The depressant activity was evaluated by using digital actophotometer. The anti-inflammatory activity was evaluated by using digital plethysmometer (UGO Basile, Italy 7140). The study was carried out by using two different doses (50mg/Kg and 100mg/Kg i.p.) of the aqueous extract of *Capparis decidua Edgew*. flowers. The preliminary pharmacological screening of the extract showed significant dose dependant analgesic, CNS depressant activity with good anti-inflammatory profile

Keywords: Analgesic; CNS depressant; anti-inflammatory; *Capparis decidua Edgew*.

INTRODUCTION

Inflammation is a response of living mammalian tissues to injury. It is a body defense reaction in order to eliminate or limit the spread of injurious agent. There are various components of an inflammatory reaction that can contribute to the associated symptoms and tissue injury. Edema formation, leukocyte infiltration and granuloma formation represent such components of inflammation[16]. Edema formation in the paw is the result of a reaction between various inflammatory mediators that increase vascular permeability and/or the mediators that increase blood flow[14]. Several experimental models of paw edema have been described. Carrageenan-induced paw edema is widely used for determining the acute phase of inflammation. Histamine, 5-hydroxytryptamine and bradykinin are the first detectable mediators in the early phase of carrageenan-induced inflammation[4], whereas prostaglandins are detectable in the late phase of inflammation[21].

A large number of Indian medicinal plants are attributed with various pharmacological activities. Because it contains diversified class of phytochemicals. It is believed that current analgesics such as opioids and non-steroidal anti-inflammatory drugs are not useful in all cases, because of their side-effects and potency[1].

Morphine produces acute poisoning, hypotension, drug dependence, etc. As a result, a search for other alternatives seems necessary and beneficial. Medicinal plants having a wide variety of chemicals from which novel analgesic agents could therefore be discovered.

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Capparis decidua also called karir or kair, is a small much branched tree or shrub of Thar desert with a mass of slender, leafless branches, the small caducous leaves being found only on young shoots. It rarely exceeds a height of 15 feet. New flush of leaves appears in November-January. Red conspicuous flowers appear in March to April and August-September and ripe by May- October. It coppices well and produces root suckers freely. It is extremely drought resistant and frost hardy. The fruits are used for preparing vegetables, curry and fine pickles. It has got medicinal values[9]. It is traditionally used for toothache, arthritis, asthma, boil, cough, inflammation, laxative, malaria, rheumatism, swelling and as an astringent and vermifuge[10].

The fruit of plant is reported to have sharp taste, astringent to the bowels, destroys foul breath, biliousness, and urinary purulent discharges. It is found to be a good remedy in cardiac troubles. Recently antiatherosclerotic effect of Capparis decidua fruit extract in cholesterol fed rabbits has been reported.[12]

In the present study, we investigated the analgesic anti-inflammatory and CNS depressant activity of aqueous extract of *Capparis decidua Edgew*. flowers (AECDF) in experimental animals.

MATERIALS AND METHODS:

Plant Material:

The flowers of *Capparis decidua* Edgew. were collected in the month of August from local area of Sangli region, Maharashtra India. The plant material was taxonomically identified by Prof. V. B. Awale, Head of Department of Botany, Dr. Patangrao Kadam Mahavidyalya, Sangli, India.

Herbarium specimen number :Voucher No. 1/180.

Preparation of extract:

The flowers were extracted by Maceration process. The extract was filtered and evaporated to dryness. The dark brownish semi-

Table I: Effect of aqueous extract of flowers of *Capparis deciduas Edgew*. on locomotor activity

Treatment	Before Administration of drug	After administration of drug 30min	% Activity	60min	% Activity	90min	% Activity	120min	% Activit
Control	422.2 ± 1.6	423.2 ± 1.6	—	424.2 ± 1.5	—	425.2 ± 1.5	—	423.2 ± 1.6	—
Chlorpromazine (3mg/kg i.p.)	230.0 ± 1.5	02.0 ± 0.2*	99.52	002.0 ± 0.2*	99.52	02.0 ± 0.2*	99.52	03.0 ± 0.2*	99.28
Aqueous Extract (50mg/kg i.p.)	422.2 ± 1.6	323.2 ± 1.6*	23.44	295.0 ± 8.1*	30.12	209.6 ± 5.2 *	50.35	336.0 ± 1.0*	46.47
Aqueous Extract (100mg/kg i.p.)	422.2 ± 1.6	270 ± 1.8*	36.00	210 ± 2.1*	50.26	182 ± 1.9*	56.89	363.6 ± 5.4*	52.72

*Values are mean ± SEM.(n=5), *p<0.01*

Table II: Effect of aqueous extract of flowers of *Capparis deciduas Edgew*. on latency to hot plate test

Time after administration (min)	Vehicle Distilled.Water (10 ml/kg, i.p.)	% protection	Aqueous extract (50 mg/kg i.p.)	% protection	Aqueous extract (100 mg/kg, i.p.)	% protection	Pentazocine (5 mg/kg i.p.)	% protection
0	7.93 ± 0.3	—	8.2 ± 0.5	03.20	8.26 ± 0.5	03.99	8.90 ± 0.4	10.89
30	7.62 ±1.3	—	11 ± 0.4*	30.72	12.4 ± 0.3*	38.54	15.2 ±1.9*	49.86
60	6.92 ± 0.3	—	13.8 ±0.7*	49.85	14.9 ± 0.4*	53.83	16.82 ±0.3*	58.85

*Values are mean ± SEM.(n=5), *p<0.01.*

Table III: Effect of aqueous extract of flowers of *Capparis deciduas Edgew*. On latency to acetic acid induced writhing test

Time after administration (min)	Vehicle (10 ml/kg, i.p.)	Aqueous extract (50 mg/kg, .p.)	% Inhibition	Aqueous extract (100mg/kg, i.p.)	% Inhibition	Pentazocine (5mg/kg i.p.)	% Inhibition
0	72.01±0.32	66.6±0.060	07.50	65.4±1.66	09.16	67.0±1.02	06.90
30	67.8±3.3	16.4±0.010*	75.37	10.4±1.00*	84.09	2.80±0.58*	95.82
60	62.4±1.12	13.70±1.04*	79.43	8.2±0.910*	87.46	4.50±0.89*	93.28

*Values are mean ± SEM.(n=5), *p<0.01*

Table IV: Anti-inflammatory activity of aqueous extract of flowers of *Capparis deciduas Edgew*. on carrageenan induced paw oedema in rats

Treatment	Dose (mg/kg)	Mean Paw Volume (ml) ± S.E.M 0 hr EV (ml)	EI (%)	1 hr EV (ml)	EI (%)	2 hr EV (ml)	EI (%)	3 hr EV (ml)	EI (%)
Control	—	1.846 ± 0.04	-	1.890 ± 0.01	-	1.990 ± 1.03	-	1.870 ± 0.04	-
Aceclofenac sodium	10 mg/kg	1.232 ± 0.03*	33.26	1.034 ± 0.04*	45.29	0.960 ± 0.04*	51.75	0.910 ± .05*	51.33
Aqueous extract	100mg/kg	1.424 ± 0.04*	22.86	1.218 ± 0.05*	35.55	1.124 ± .05*	37.68	1.366 ± .06*	26.95

*Values are mean ± SEM.(n=5), *p<0.01*

solid mass obtained was stored in a well-closed airtight light resistant container.

Animals:

Adult male Albino mice (20-35 g) were used for evalution of analgesic and CNS activity. Animals were devided in to three group each contain five animals.Adult male wistar rats (150–200 g) were used to study the anti-inflammatory activity. The animals (five per cage) were maintained under standard laboratory conditions (light period of 12 hrs/day and temperature 27° C ± 4° C), with access to food and water ad libitum. The experimental procedures were carried out in strict compliance with the Institutional Animal Ethics Committee regulations. All experiments were performed in the morning according to the guidelines for the care of laboratory animals[28]. Institutional animal ethical committee having registration no.843/AC/04 CPCSEA has approved all animal experiments protocol.

Locomotor Activity [23]

Adult Albino Mice of either sex were randomly divided into three groups of 5 mice each. First group served as a control (received normal saline,i.p.), second group served as positive control (received chlorpromazine, 5mg/kg, i.p.) while the third group received aqueous extract of flowers of *Capparis decidua Edgew*. (ACDFE) at a dose of 50mg/kg and 100mg/kg (i.p.) body weight respectively. The locomotor activity was studied after half an hour of administration of the test and standard drugs with digital actophotometer, which operates on photoelectric cells connected with a counter. A count is recorded when the beam of light falling on the photocell of the actophotometer is cut off by animal. The percentage inhibition of locomotor activity shown by capparis deciduas edgew was calculated by using following formula.

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

Where, Vc= control reading
Vt= test reading

Hot plate test:

The method originally developed by Woolfe and MacDonald 1944. The paws of mice and rat are very sensitive to heat at temperature, which are not damaging the skin. The response is in the form of

jumping, withdrawal of the paws or licking of the paws[5, 13, 17, 22]. The hot plate test was performed to measure response latencies.[11] The hot-plate (Model KI 9514) was maintained at 55.0 ± 0.2° C and the animals were placed into the perspex cylinder on the heated surface and the time (sec) to discomfort reaction (licking paws or jumping) was recorded as response latency, prior to and 30, and 60 min after administration of the extract (50 and 100 mg/kg, i.p.). A latency period of 20 sec was defined as complete analgesia and the measurement was terminated if it exceeded the latency period in order to avoid injury.

Average reaction times were then calculated and the percentage variation calculated using the following ratio:

Acetic acid-induced writhing:

The antinociceptive activity of ACDFE was assessed using writhing test (abdominal constriction test)[3]. Acetic acid solution (10 ml/kg, 0.6% in normal saline) was injected intraperitonially, and the contraction of abdominal muscles together with stretching of the hind limbs was cumulatively counted over a period of 10 min beginning 5 min after acetic acid injection. The ACDFE (50 and 100 mg/kg, i.p.) was administered 30 min. before the acetic acid injection. Anti-nociceptive activity was expressed as the percentage inhibition of abdominal constrictions between control animals and mice pre-treated (n=5) with the extract. In an attempt to investigate the participation of the opioids separate groups of mice (n=5) were pretreated with non-specific opioids receptor antagonist, pentazocin (5 mg/kg, i.p.), injected 15 min before the administration of the acetic acid. The percentage inhibitions were calculated by using the formula.

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

Where, Vc= control reading
Vt= test reading

Anti-inflammatory activity:

ACDFE was evaluated for anti-inflammatory activity by carrageenan induced rat paw oedema method[23, 26]. Male Albino Wistar rats (150–200 g) were randomly distributed into 3 groups of 5 animals each. First group served as a control, second group served as the standard (received Aceclofenac sodium 10 mg/kg, i.p), while the third group received 100 mg/kg, body weight of ACDFE respectively. After 30 min 0.1 ml of 1 % w/v suspension of carrageenan was injected into the sub plantar region of right hind paw to all the three groups. The paw volumes were measured using plethysmometer (UGO Basile, 7140 Italy) every hour till 3 h after carrageenan injection, and mean increase in paw volumes were noted.

Thus edema volumes in control (Vc) and in groups treated with test compounds (Vt) were calculated. The percentage inhibitions were calculated by using the formula [8].

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

Where, Vc = Edema volume of Control
Vt = Edema volume of Test

Statistical Analysis:

The statistical analysis of all the results was carried out using one-way ANOVA followed by Dunnet's multiple comparisons test and all the results obtained in the study were compared with the vehicle control group. p values < 0.01 were considered statistically significant.

RESULTS:

Locomotor Activity:

The effect of aqueous extract on spontaneous locomotor activity are summarized in Table I, it is indicates that the locomotor activity count in the aqueous extract treated group was significantly reduced when compared to normal saline control group.

Analgesic activity:

Plant extracts, when given in doses of 100 mg/kg, i.p. elicited a significant analgesic activity in the hot plate as evidenced by increase in latency time in seconds (Table II) as compared with vehicle control at the end of 30 min. The increase in latency time was dose dependent. The analgesic activity data (Hot plate method) are presented in table II. Latency time was noted at 30 and 60 min after the administration of the vehicle, standard, and plant extract. Plant extract at 100 mg/kg, i.p. showed significant increase in latency time. The results of ACDFE on acetic acid-induced writhing test indicated a significant increase ($p<0.01$) in reaction time, which is comparable to the reference drug pentazocin (Table IV).

Anti-inflammatory Activity:

The results of ACDFE against carrageenan-induced paw edema are depicted shown in (Table III). ACDFE (100 mg/kg, i.p.) showed the significant ($p<0.01$) reduction of rat paw edema at all assessment times. The aqueous extract showed maximum inhibition of 51.75% at the dose of 100 mg/kg after 2 hr of drug treatment in carrageenan induced paw oedema, whereas the standard drug showed 99.43 % of inhibition after 3 hr of drug treatment in carrageenan induced paw oedema.

DISCUSSION:

The thermal stimuli in hotplate test and the writhing response of the animals to an intra-peritoneal injection of noxious chemical are used to screen both centrally and peripherally acting analgesic activity respectively. Acetic acid causes algesia by liberating endogenous substances that excite the pain nerve endings[18]. From the results it is apparent that the AECDFE showed a significant antinociceptive effect in hot plate test and writhing response, which are comparable to that of the standard. Studies demonstrate that various flavonoids such as rutin, quercetin, luteolin, hesperidin and biflavonoids produced significant antinociceptive and anti-inflammatory activities[7,20]. There are also few reports on the role of tannins in antinociceptive and anti-inflammatory activitiesd[19]. NSAIDs can inhibit cyclo-oxygenase in peripheral tissues, thus interfering with the mechanism of transduction in primary afferent nociceptors[6]. The mechanisms of antinociceptive action of AECDFE could be due to the presence of flavonoids, mediated through central and peripheral mechanisms. Carrageenan induced paw oedema was taken as a prototype of exudative phase of acute inflammation. Inflammatory stimuli microbes, chemicals and necrosed cells activate the different mediator syflowers through a common trigger mechanism. The development of carrageenan induced oedema is believed to be biphasic. The early phase is attributed to the release of histamine and serotonin [15, 24] and the delayed phase is sustained by the leucotrienes and prostaglandin.2 From the above discussion, the aqueous extract of flowers of *Capparis decidua Edgew*.(AECDFE).exhibited significant analgesic and anti-inflammatory activity. Further detailed investigation is underway to

determine the exact phytoconstituents those are responsible for these activities.

The experimental findings from the study showed that the aqueous extract of *Capparis deciduas Edgew.* Significantly potentiated the depression time in mice at dose of 50mg/Kg and 100mg/Kg i.p. of body weight which suggests its central depressant activity. Moreover the extract produced a significant decrease in exploratory behavior pattern in mice. These results, therefore support the central sedative properties of the extract. The overall results tend to predict the central nervous system depressant action of the extract.

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