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ORIGINAL PAPER

Sedative and anticonvulsant effects of an alcoholic extract of *Capparis decidua*

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Abstract *Capparis decidua* (frock) Edgew (family Capparidaceae) is a xerophytic shrub, commonly known as karrel or ker, whose bark and shoot are used as analgesic, anti-inflammatory, hypolipidemic, and antidiabetic agents. The plant contains generous quantities of alkaloids. An alcoholic extract of aerial parts of *C. decidua*, including flowers and fruits, was screened for central nervous system (CNS) activity using conventional behavioral animal models. In the open field test all doses of *C. decidua* extract tested decreased the number of rearings, grooming, and fecal bolus ($P < 0.001$) when compared with control. In the barbiturate-induced sleeping test a significant ($P < 0.001$) a decrease in latency of sleeping and increase in sleeping time were observed at all doses (100, 200, and 300 mg/kg). *C. decidua* extract increased the percentage of animals exhibiting motor deficit in the rotarod test. In the pentylenetetrazole-induced seizures test the *C. decidua* extract dose-dependently decreased ($P < 0.05$) the number of animals with convulsions and increased convulsion latency ($P < 0.001$); none of the animals treated with extract died in the test. *C. decidua* extract decreased the duration of tonic hind leg extension in maximal electroshock-induced seizures ($P < 0.001$) when compared with control. The findings of the present animal study suggested that *C. decidua* has CNS depressant and anticonvulsant activities.

Keywords *Capparis decidua* · CNS depressant · Anticonvulsant

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Introduction

Capparis decidua (frock) Edgew (family Capparidaceae) is a xerophytic shrub, commonly known as karrel or ker. It is an extremely useful plant, all parts of which are used for medicinal purposes, and the fruit, which is a rich source of β-carotene, vitamin C, and minerals, is a nutritional supplement [1]. The plant is used for treatment of inflammatory and painful conditions, such as fracture, toothache, and boils, and in cardiovascular disorders [2]. In addition *C. decidua* has been reported to be an antioxidant, antidiabetic [3], and hypolipidemic agent [4, 5]. Ample phytochemical work has been done so far on *C. decidua*, which has been reported to contain β-sitosterols, indoles, aliphatic constituents, oxygenated heterocyclic compounds, isocodonocarpine, diterpene alcohol, tannins, β-carotene, vitamin C, minerals, and generous quantities of alkaloids, e.g., spermidine alkaloids and stachydrine [6–8]. Such alkaloids have central nervous system (CNS) depressant activity [9]. The aim of present work was to investigate the CNS activity of an alcoholic extract of aerial parts of *C. decidua*, including flowers and fruits, by using conventional behavioral animal models, specifically the open field test, rotarod test, barbiturate-induced sleeping time, pentylenetetrazole (PTZ)-induced convulsions test, maximal electroshock-induced seizures (MES) test, and the elevated plus maze (EPM) test.

Materials and methods

The experimental protocol and procedures used in this study were approved by the Institutional Animal Ethics Committee of the BIT Mesra, Ranchi, India. The approval number is BIT/PH/IAEC/01/2004.

Plant material

C. decidua is commonly grown in Rajasthan. The aerial parts of *C. decidua*, including flowers and fruits, were collected in April and May 2003 and identified by Prof. S. Jha, Department of Pharmacognosy, BIT Mesra. A voucher specimen (MG1584) was deposited in the Department of Pharmaceutical Sciences, BIT Mesra, in 2003.

Preparation of the plant extract

One kilogram of air-dried aerial parts of *C. decidua*, including flowers and fruits, was reduced into small pieces and homogenized. The powdered material was Soxhlet-extracted with ethanol until it become free of alkaloids. Alcohol was removed from the extract under vacuum to obtain semisolid residue (yield 7% w/w). The residue was dissolved in normal saline for use in experiments.

Animal material

Male Wistar rats weighing 180–220 g and male Swiss mice weighing 20–24 g were used. The animals had free access to a standard commercial diet and water ad libitum and were kept in rooms maintained at 25°C with a 12-h light/dark cycle. The experiments were performed during the light portion (0800–1600 h).

Drugs

Diazepam (Ranbaxy, India), pentobarbital sodium (Abbot Lab., Brazil), pentylenetetrazole (Sigma, St. Louis, MO, USA), phenobarbitone (Intas, India), and phenytoin (Sun Pharma., India) were used in the present study.

Open field test

The open field test was used to evaluate the exploratory activity and emotional response of the animals. The apparatus consists of an arena of white wood (150-cm diameter) enclosed by stainless steel walls and divided in 19 squares by black lines. The open field was placed inside a light and sound-attenuated room. Rats were divided into four groups of six. All animals in a group received intraperitoneal (i.p.) injection of saline or extract at a dose of 100, 200, or 300 mg/kg. After 30 min each animal was placed in the center of the arena and during the following 5 min was observed for the number of squares crossed (with four paws), rearing, latency for the crossing of first square (as measures of exploratory activity), and numbers of grooming and fecal bolus (as measures of emotionality) [10].

Rotarod test

Mice were divided into five groups of six. Mice were placed with the four paws on a 7-cm-diameter bar revolving at 12 rpm, 24 cm above the floor. All animals were trained to remain on the bar for three consecutive trials of 1 min each. On the next day all animals in a group received saline, diazepam 2 mg/kg, or extract at a dose of 100, 200, or 300 mg/kg (i.p.). After 30 min each animal was placed on the bar for three consecutive trials of 1 min. Percentage of animals exhibiting motor deficit and the average duration of stay on rotating bar were calculated [11].

Barbiturate-induced sleeping time

Mice were divided into five groups of six. All groups were treated with pentobarbital 40 mg/kg (i.p.). Forty-five minutes before pentobarbital administration all animals in a group received saline, diazepam 2 mg/kg, or extract at a dose of 100, 200, or 300 mg/kg (i.p.). Sleep latency time (time to loss of the righting reflex) and sleeping time (duration of loss of the righting reflex) were recorded [12].

Elevated plus maze (EPM) test

The elevated plus maze apparatus was made of wood and consisted of two opposite open arms of 50 × 10 cm (surrounded by 1-cm-high Plexiglas) and two enclosed arms 50 × 10 × 40 cm, elevated to a height of 50 cm above the floor. The junction area of the four arms (central platform) measured 10 × 10 cm. The maze was placed inside a light and sound-attenuated room. Rats were divided into five groups of six. All animals in a group received saline, diazepam 1 mg/kg, or extract at a dose of 100, 200, or 300 mg/kg (i.p.). After 30 min each animal was placed on the center platform of the maze facing the enclosed arm for 3 min. Time spent in the both open and enclosed arms and the number of entries into the open arms were recorded [13].

Pentylenetetrazole-induced seizures test

Mice were divided into five groups of ten. All animals in a group received saline, phenobarbitone 10 mg/kg, or extract at a dose of 100, 200, or 300 mg/kg (i.p.). Thirty minutes later seizures were induced by the administration of pentylenetetrazole 60 mg/kg (i.p.). The animals were observed during the first 30 min for number of animals with convulsions, latency of the first convulsion, and death latency [14].

Table 1 Effect of alcoholic extract of *C. decidua* in open field test

Group	Number of animals	Dose	Squares crossed (counts)	Rearing (counts)	First crossing latency (s)	Grooming (counts)	Fecal bolus (counts)
Control	6	2 (ml/kg)	59 ± 0.24[b]	6.2 ± 0.11	6.6 ± 0.26[b]	4.0 ± 0.17	5.0 ± 0.02
C. decidua I	6	100 (mg/kg)	32 ± 0.31[a,b]	0.5 ± 0.09[a]	12.4 ± 0.27[a,b]	1.0 ± 0.20[a]	1.4 ± 0.03[a]
C. decidua II	6	200 (mg/kg)	21 ± 0.42[a,b]	0.4 ± 0.22[a]	18.4 ± 0.14[a,b]	0.9 ± 0.07[a]	1.2 ± 0.12[a]
C. decidua III	6	300 (mg/kg)	13 ± 0.11[a,b]	0.3 ± 0.10[a]	43.4 ± 0.26[a,b]	0.4 ± 0.02[a]	0.8 ± 0.08[a]

Values are expressed as the mean ± SEM of six observations

[a] $P < 0.001$; statistical comparisons are made between control versus groups I–III

[b] $P < 0.05$; pairwise multiple comparison between groups by Student–Newman–Keuls method

Maximal electroshock-induced seizures test

Mice were divided into five groups of ten. All animals in a group were treated with saline, phenytoin 70 mg/kg, or extract at a dose of 100, 200, or 300 mg/kg (i.p.). Thirty minutes later seizures were induced by a current stimulus (45 mA for 0.2 s) delivered by using ear electrodes. The percentage protection and duration of tonic hind leg extension was compared with the control group. Protection was defined as complete absence of tonic hind leg extension [15].

Statistical analysis

The percentage of deaths and percentage of animals developing seizures per group were analyzed by the Chi-square test and Fisher's exact test. The other parameters were analyzed by the parametric ANOVA test followed by the multiple comparison by Student–Newman–Keuls (SNK) method/Dunnett's test wherever necessary.

Results

Open field test

Table 1 shows the effects of the *C. decidua* extract in the open field test. At all doses tested the *C. decidua* extract decreased the numbers of rearings, grooming, and fecal bolus ($P < 0.001$) when compared with the control group, but the decrease was not dose dependent. Latency for the crossing of first squares was increased and number of squares crossed decreased ($P < 0.001$), and the difference was found to be dose dependent ($P < 0.05$) in pairwise multiple comparison between tested groups.

Rotarod test

In the rotarod test (Table 2) the *C. decidua* extract increased the percentage of animals exhibiting motor deficit and decreased the duration of stay on the rotating rod ($P < 0.001$) when compared with the control group. In comparisons with the diazepam-treated group the difference was found to be significant ($P < 0.05$) in groups administered with extract at 100 and 200 mg/kg.

Table 2 Effect of alcoholic extract of *C. decidua* and diazepam in the rotarod test

Group	Number of animals	Dose	Duration of stay on rotating rod (s)	Percentage of animals exhibiting motor deficit
Control	6	2 (ml/kg)	120 ± 2.20	0
Diazepam	6	2 (mg/kg)	51 ± 1.21[a]	83.3[a]
C. decidua I	6	100 (mg/kg)	66 ± 1.05[a,b]	50[a,b]
C. decidua II	6	200 (mg/kg)	61 ± 1.35[a,b]	66.6[a,b]
C. decidua III	6	300 (mg/kg)	53 ± 0.92[a]	66.6[a,b]

Values are expressed as the mean ± SEM of six observations

[a] $P < 0.001$; statistical comparisons are made between control versus diazepam and groups I–III

[b] $P < 0.05$; statistical comparisons are made between diazepam versus groups I–III

Barbiturate-induced sleeping time

A significant ($P < 0.001$) decrease in latency of sleeping and increase in sleeping time were observed at all doses (100, 200, and 300 mg/kg) when compared with the control group (Table 3). In comparison with the diazepam-treated group, a dose-dependent difference was found ($P < 0.05$) at all doses.

Elevated plus maze test

In the elevated plus maze test (Table 4) the number of open arm entries and time spent in open arms were decreased ($P < 0.001$) when compared with the control group. In comparison with the diazepam-treated group a significant difference was found ($P < 0.05$) at all doses tested.

The time spent in the enclosed arm was increased significant ($P > 0.05$) at doses of 200 and 300 mg/kg in

comparison with the control group; in the diazepam-treated group a decrease in time spent in the closed arm was observed ($P < 0.05$) when compared with the control group.

Pentylenetetrazole-induced seizures test

A significant dose-dependent decrease ($P < 0.05$) in number of animals with convulsions was produced when compared with the control group (Table 5); convulsion latency was found to be increased significantly ($P < 0.001$) when compared with the control group and none of the drug-treated animals died in the test.

Maximal electroshock-induced seizures test

In the MES test (Table 6) a significant decrease in duration of tonic hind leg extension was observed ($P < 0.001$) when compared with the control group; in comparison with the phenytoin-treated group a significant difference ($P < 0.05$) was found at a dose of 100 mg/kg, but for groups receiving extract at 200 and 300 mg/kg the difference was found to be insignificant ($P > 0.05$).

Table 3 Effect of alcoholic extract of *C. decidua* and diazepam on barbiturate-induced sleeping

Group	Number of animals	Dose	Sleep latency time (s)	Sleeping time (min)
Control	6	2 (ml/kg)	153 ± 2.31	98 ± 2.12
Diazepam	6	2 (mg/kg)	102 ± 1.92[a]	240 ± 4.56[a]
C. decidua I	6	100 (mg/kg)	131 ± 3.35[a,b]	150 ± 3.23[a,b]
C. decidua II	6	200 (mg/kg)	121 ± 2.74[a,b]	188 ± 3.69[a,b]
C. decidua III	6	300 (mg/kg)	110 ± 2.96[a,b]	225 ± 3.47[a,b]

Values are expressed as the mean ± SEM of six observations

[a] $P < 0.001$; statistical comparisons are made between control versus diazepam and groups I–III

[b] $P < 0.05$; statistical comparisons are made between diazepam versus groups I–III

Discussion

The present study was carried out to investigate the effect of an alcoholic extract of *C. decidua* on the central nervous system by using behavioral animal models. The acute treatment with the alcoholic extract of *C. decidua* did not show anxiolytic effects in animal models of anxiety but it seems to have a CNS depressant effect, the latter revealed by the reduced locomotor activity in the open field test and

Table 4 Effect of alcoholic extract of *C. decidua* and diazepam in elevated plus maze test

Group	Number of animals	Dose	Open arm entries (counts)	Time spent in open arm (s)	Time spent in enclosed arm (s)
Control	6	2 (ml/kg)	6.6 ± 0.42	29.5 ± 0.52	149.2 ± 3.51
Diazepam	6	1.0 (mg/kg)	12 ± 1.02[a]	58.4 ± 1.24[a]	118.4 ± 2.36[a]
C. decidua I	6	100 (mg/kg)	5.0 ± 0.32[a,b]	25.4 ± 0.25[a,b]	150.3 ± 4.21[b]
C. decidua II	6	200 (mg/kg)	3.2 ± 0.25[a,b]	15.8 ± 0.35[a,b]	160.4 ± 3.72[a,b]
C. decidua III	6	300 (mg/kg)	2.2 ± 0.22[a,b]	12.2 ± 0.27[a,b]	162.5 ± 2.82[a,b]

Values are expressed as the mean ± SEM of six observations

[a] $P < 0.001$; statistical comparisons are made between control versus diazepam and groups I–III

[b] $P < 0.05$; statistical comparisons are made between diazepam versus groups I–III

Table 5 Effect of alcoholic extract of *C. decidua* and phenobarbitone on pentylenetetrazole-induced seizures

Group	Number of animals	Dose	Number of convulsed/number used	Convulsion latency (min)	Death latency (s)
Control	10	2 (ml/kg)	10/10	6.38 ± 0.88	1,651 ± 14
Phenobarbitone	10	10 (mg/kg)	1/10[a]	–	1,800 ± 0
C. decidua I	10	100 (mg/kg)	6/10[a,b]	9.61 ± 1.81[a]	1,800 ± 0
C. decidua II	10	200 (mg/kg)	5/10[a,b]	12.20 ± 2.73[a]	1,800 ± 0
C. decidua III	10	300 (mg/kg)	2/10[a]	16.00 ± 1.76[a]	1,800 ± 0

Values are expressed as the mean ± SEM of ten observations

[a] $P < 0.001$; statistical comparisons are made between control versus phenobarbitone and groups I–III

[b] $P < 0.05$; statistical comparisons are made between phenobarbitone versus groups I–III

Table 6 Effect of alcoholic extract of *C. decidua* and phenytoin on maximal electroshock-induced seizures

Group	Number of animals	Dose	% of protection	Duration of tonic hind leg extension (s)
Control	10	2 (ml/kg)	0	10.3 ± 0.23
Phenytoin	10	70 (mg/kg)	90[a]	2.2 ± 0.12[a]
C. decidua I	10	100 (mg/kg)	20[a,b]	7.5 ± 0.31[a,b]
C. decidua II	10	200 (mg/kg)	30[a,b]	3.5 ± 0.25[a]
C. decidua III	10	300 (mg/kg)	50[a,b]	2.9 ± 0.18[a]

Values are expressed as the mean ± SEM of ten observations

[a] $P < 0.001$; statistical comparisons are made between control versus phenytoin and groups I–III

[b] $P < 0.05$; statistical comparisons are made between phenytoin versus groups I–III

a decrease in grip strength and muscle incoordination in the rotarod test [16]. In the elevated plus maze test, the extract-treated animals do not increase the number of entries and time spent in the open arm, which indicates absence of anxiolytic activity [17].

The *C. decidua* extract potentiated pentobarbitone-induced sleep, since a decrease in sleep latency and increase in sleeping time were observed. These effects are classically related to central nervous system depressant drugs. However, this is not a specific test because compounds that interfere with biotransformation of pentobarbital by cytochrome P450 complex can also show the same effects [18]. The extract of *C. decidua* significantly inhibited the pentylenetetrazole-induced convulsions; increased latency of tonic convulsion and a decrease in the percentage of animals developing convulsions were seen in each group, which can be indicative of a more specific CNS effect due to action on the GABA system [19]. The decreased duration of tonic hind leg extension and decrease in number of animals developing convulsions in the MES test further confirms the involvement GABA by any of possible mechanism, e.g., GABA agonist action or decreased reuptake of GABA.

C. decidua has been reported to contain β-sitosterols, indoles, aliphatic constituents, oxygenated heterocyclic compounds, isocodonocarpine, diterpene alcohol, tannins, spermidine alkaloids, stachydrine, and inorganic substances. Our present knowledge of the chemical constituents of the extract is limited. It is therefore, impossible for us at this stage to pinpoint and identify with certainty the CNS depressant and anticonvulsant constituent/s of *C. decidua*. However, it is speculated that alkaloids present in *C. decidua* are responsible for the observed CNS depressant and anticonvulsant activities, although there are not sufficient scientific data or evidence to justify this speculation. In conclusion, the findings of the present laboratory animal studies suggest that *C. decidua* has CNS depressant and anticonvulsant activities.

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