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Anti-Stress Activity of Root of *Capparis decidua* Linn. on Experimental Rats

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ABSTRACT

The present study was undertaken to evaluate the anti-stress effect of ethanolic extract of root of *Capparis decidua*. *Capparis decidua* was investigated on a 14 day mild, unpredictable and inescapable foot shock stress induced suppression of sexual behavior, perturbation in behavior and cognitive dysfunction in experimental rats. Gastric ulceration and adrenal and spleen weight were also used to assess the stress intensity. All these chronic stress induced perturbation were attenuated dose dependently by Capparis deciduas (100, 200 and 400mg/kg, po) and compared with *Panax ginseng* (100 mg/kg, po) which was used as standard adaptogenic agent. The ethanolic extract of root of *Capparis decidua* at doses of 100, 200 and 400 mg/kg, possess good anti-stress activity.

Keywords: *Capparis decidua*, Ethanolic extract, Anti-stress activity

INTRODUCTION

Stress can be described as the sum total of all reaction of the body, which disturb the normal physiological equilibrium and result in a state of threatened homeostasis. Stress is a common phenomenon that is experienced by every individual. When stress becomes extreme, it is harmful for the body and, hence, need to be treated. Stress is involved in pathogenesis of variety of diseases that include psychiatric disorders such as depression and anxiety, immunosuppression, endocrine disorders including diabetes mellitus, male impotence, cognitive dysfunction, hypertension and ulcerative colitis [1].

Stress is a condition which is known to alter the physiological homeostasis of the organism and elicits various endocrinal and visceral changes such as changes in plasma cortisone and gastric mucosal integrity. Stress also increases brain serotonin (5-HT) level. The ascending 5-HT neurons from raphe nuclei innervates hypothalamic and limbic sites and have an overall role in regulating secretions of adrenocorticotrophic hormone (ACTH) during stress [2].

Capparaceae is a family related to the Cleomaceae and as well as to the Cruciferae family. It is place in the order Brassicales and is commonly known as the caper family [3]. The plant is used in folk medicine as insecticidal and is well known for curing a variety of aliment such as toothache, cough, asthma, intermittent fever and rheumatism. The seeds of *C. decidua* have antibacterial activity against *Vibrio cholerae*, *Vibrio inaba* and *Vibrio ettor*, while the fruit has anti-atherosclerotic, anti-diabetic, antihypertensive and anti-hyperlipidemic activity. The shoot and young leaves have rubifacient and hypocholesterolemic activity. Isocodonocarpin found in the root of plant was found to be responsible for anti-inflammatory and anti-asthmatic activity. The alcoholic extract of fruit pulp and root bark possesses anthelmintic activity.

Since *Capparis decidua* has a number of medicinal properties, the present study was undertaken to evaluate the anti-stress effect on experimental animals. The anti-stress effect of *Capparis decidua* was compared with *Panax ginseng* (PG). The PG was selected as a standard adaptogenic agent for comparison.

MATERIAL AND METHODS

Drug treatments

The fresh specimen sample of root of *Capparis decidua* was collected from Botanical garden, Banaras Hindu University; which where the authentication as well as identification of the *Capparis decidua* was done by Prof. SD Dubey, Department of Dravyaguna, Faculty of Ayurveda, Institute of Medical Science, Banaras Hindu University, Varanasi. A specimen of the plant including the sample root is deposited

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in the department of Pharmacy, Rameshwaram Institute of Technology and Management, Lucknow for future reference. Standardized extract of *Capparis decidua* was orally administered as 0.3% carboxymethyl cellulose (CMC) suspension, in the doses of 100, 200 and 400 mg/kg, once daily for 14 consecutive days, 1 h before the induction of stress. Experiments were conducted on day 14, 1 h after the last stress procedure and 2 h after the drug or vehicle administration. *Panax ginseng* (PG) was used as the standard adaptogenic agent for comparison. Control animals were treated with the vehicle (0.3% CMC suspension).

Animals

Foster albino rats (150 ± 10 g) were used in the study. Animals were obtained from central animal house of Institute of Medical Sciences, Banaras Hindu University, Varanasi. The animals were housed in groups of six in polypropylene cages at an ambient temperature of 25 ± 1°C and 45-55% relative humidity, with a 12:12 h light/dark cycle. Rats were provided with commercial food pellets and water *ad libitum*, unless stated otherwise. Rats were acclimatized to laboratory conditions for at least one week before using them for experiments. Body weight of rats was measured periodically. Principles of laboratory animal care guidelines (NIH publication number 85-23, revised 1985) were followed.

Induction of chronic stress

The method of Armando was used. The stressed rats were subjected daily to 1 h of foot shock through a grid floor in a shock chamber for 14 consecutive days. The duration of each shock (2 mA) and the interval between the shocks was randomly programmed between 3 and 5 s and 10 and 110 s, respectively (in order to make the shocks unpredictable). Animals were sacrificed on day 14, 1 h after the last shock procedure and on completion of other test procedure involved [4].

Techniques used for assessment of stress intensity

The following parameters were used to assess the intensity of stress-induced effects:

Gastric ulceration: The change in body weight of rats was observed during the experimental period. In order to observe ulcerogenic effect of stress and protective effects of CD and PG, stomach was removed and split open along the greater curvature. The numbers of discrete ulcers was noted by the help of a magnifying glass. The severity of the ulcers was scored after histological confirmations, 0=no ulcers, 1=changes limited to superficial layers of the mucosa with no congestion, 2=half the mucosal thickness showing necrotic changes and congestion, 3=more than two-third of mucosal thickness showing necrotic changes and congestion and 4=complete destruction of the mucosa with marked hemorrhage. Thereafter, the period ulcer severity score was calculated [5].

Adrenal gland and spleen weights: The adrenal gland and spleen were removed and weighed [6].

Methods used to assess stress-induced perturbations

Stress-induced 'behavioral depression: The following methods were used to assess behavioral depression:

(a) Stress-induced 'behavioral despair' test: Rats were forced to swim individually in a polypropylene vessel (45 × 40 × 30 cm) with a water level of 20 cm, which ensured that the rat's feet does not touch the floor of the vessel and that it could not climb out of it. The rat was allowed to swim for 10 min. Thereafter, during the next 5 min, the total period of immobility, characterized by complete cessation of swimming with the head floating above water level, was noted. This immobility period, after initial frenzied attempts to escape, is postulated to represent 'behavioral despair' as an experimental model of endogenous depression [7].

(b) Learned helplessness test: On day 12 of the investigation, rats were subjected to foot shock (60 scrambled shocks, 15 s duration, 0.8 mA, every min) in a two compartment jumping box (Techno) with the escape door to the adjoining un-electrified compartment closed. The exercise continued for 1 h. On day 14, 48 h later, the rats were subjected to avoidance training, using the same apparatus but keeping the escape route to the un-electrified chamber open. During this avoidance training the rats were placed in the electrified chamber and allowed to acclimatize for 5 min before being subjected to 30 avoidance trials, with an inter-trial interval of 30 s. During the first 3 s of the trial, a buzzer stimulus (conditioned stimulus, CS) was presented followed by electroshock (unconditioned stimulus, UCS) (0.8 mA) delivered via the grid floor for the next 3 s. The avoidance response was characterized by escape to the adjoining 'safe' chamber during CS. Failure to escape during UCS within 15 s was assessed as 'escape' failure which is postulated to indicate despair or depression [8].

Stress-induced suppression of sexual behavior in male rats: A male rat was placed in a cage in a dimly room for 10 min with 2 estrinised (sequentially treated with estradiol valerate 5 µg/rat, followed 48 h later by hydroxyprogesterone 1.5 mg/rat, s.c.) female rats. The total numbers of mounts were counted [9].

Stress-induced cognitive dysfunction: The following parameters were used to assess the effect of stress on retention of a learned task as memory:

(a) **Active avoidance test:** Rats were trained for an active avoidance task before subjecting them to stress. During training, the rat was placed in the right electrified compartment of a shuttle box (Techno) and allowed to acclimatize for 5 min. Thereafter, the animal was

subjected to 15 s of a buzzer stimulus (conditioned stimulus) which was followed by electric shock (1 mA, 50 Hz) given through the grid floor (unconditioned stimulus). The rats were given at least 10 trials, with an inter-trial interval of 60 min, until they reached the criterion of 100% avoidance response of jumping to the un-electrified left chamber of the shuttle box during conditioned stimulus. The test was repeated on day 14 in order to assess the retention of the active avoidance learning [10].

(b) **Passive avoidance test:** The test apparatus was a rectangular box (45 × 30 × 40) with an electrified grid floor. An 8 cm high platform (17 × 12 cm) was fixed to the centre of the floor. A rat was placed on the platform and allowed to step down. 24 h later, on day 1 of the experiment, the rat was again placed on the platform and on stepping down, received foot shock (0.75 mA, 2 s) through the grid floor. The rat was given 3 more trials until the latency of step down had stabilized. The test was repeated on day 14 and retention of learning as memory, for each rat was recorded [11-14].

STATISTICAL ANALYSIS

The values are expressed as mean ± SEM. Statistical significance of the differences between control and treated groups was calculated using one way analysis of variance (ANOVA) followed by Dunnet test. $P<0.01$ was considered to be significant.

RESULTS AND DISCUSSION

Gastric ulceration

Chronic stress markedly increases the number and severity of gastric ulcers. The first doses of CD (100 mg/kg, po) show less significantly reduction in stress induced Gastric ulcer than the other dose of CD and PG, but CD (200 mg/kg and 400 mg/kg, po) and PG (100 mg/kg, po) significantly reduced this stress-induced gastric ulcer **(Table 1)**.

Table 1. Effect of CD and *Panax ginseng* compared to vehicle on chronic stress-induced gastric ulcerations in rats.

Treatment	Dose (mg/kg)	Number of ulcers	Severity of ulcers
Vehicle+Stress (VS) (10)	-	6.70 ± 1.70	9.60 ± 1.17
CD+VS (6)	100	4.33 ± 1.51[a]	7.33 ± 1.03[a]
CD+VS (6)	200	3.16 ± 1.16[a]	5.66 ± 1.03[a]
CD+VS (6)	400	2.50 ± 1.04[a]	4.33 ± 0.81[a]
Panax ginseng+VS (6)	100	2.33 ± 0.81[a]	3.83 ± 1.47[a]

Values in parentheses indicate number of animals; [a] indicates difference with VS (ANOVA followed by Dunnet-test)

Adrenal cortex and spleen weights

Chronic stress significantly increases adrenal gland weight and reduction of spleen weight. These stress induced changes were significantly ($P<0.05$) reduced by CD (100 mg/kg, 200mg/kg and 400mg/kg, po) and PG (100 mg/kg, po) **(Table 2)**.

Table 2. Effect of CD and *Panax ginseng* compared to vehicle on chronic stress-induced change in adrenal gland and spleen whites in rats.

Treatment	Dose (mg/kg)	Adrenal gland wt. (mg/100 g)	Spleen wt (mg/100 g)
Vehicle (10)	-	24.6 ± 2.46	195.3 ± 4.76
Vehicle+Stress (VS) (10)	-	39.8 ± 3.61[a]	128.1 ± 5.76[a]
CD+VS (6)	100	30.5 ± 2.17[b]	156.16 ± 4.02[b]
CD+VS (6)	200	29.3 ± 2.42[b]	172.83 ± 3.06[b]
CD+VS (6)	400	27.82 ± 2.93[b]	176.16 ± 2.79[b]
PG+VS (6)	100	27.5 ± 1.87[b]	177.33 ± 4.32[b]

Values in parentheses indicate number of animals; [a] indicates difference with vehicle treated group; [b] indicates difference with VS (ANOVA followed by Dunnet-test)

Stress induced behavioral despair test

Chronic stress increased the duration of immobility test, while increasing escape failure with concomitant decrease in avoidance response in learned helplessness test, features indicative of depression. CD (200 and 400 mg/kg, po) and

PG (100 mg/kg, po) tends to reverse the stress-induced behavioral changes **(Figure 1)**.

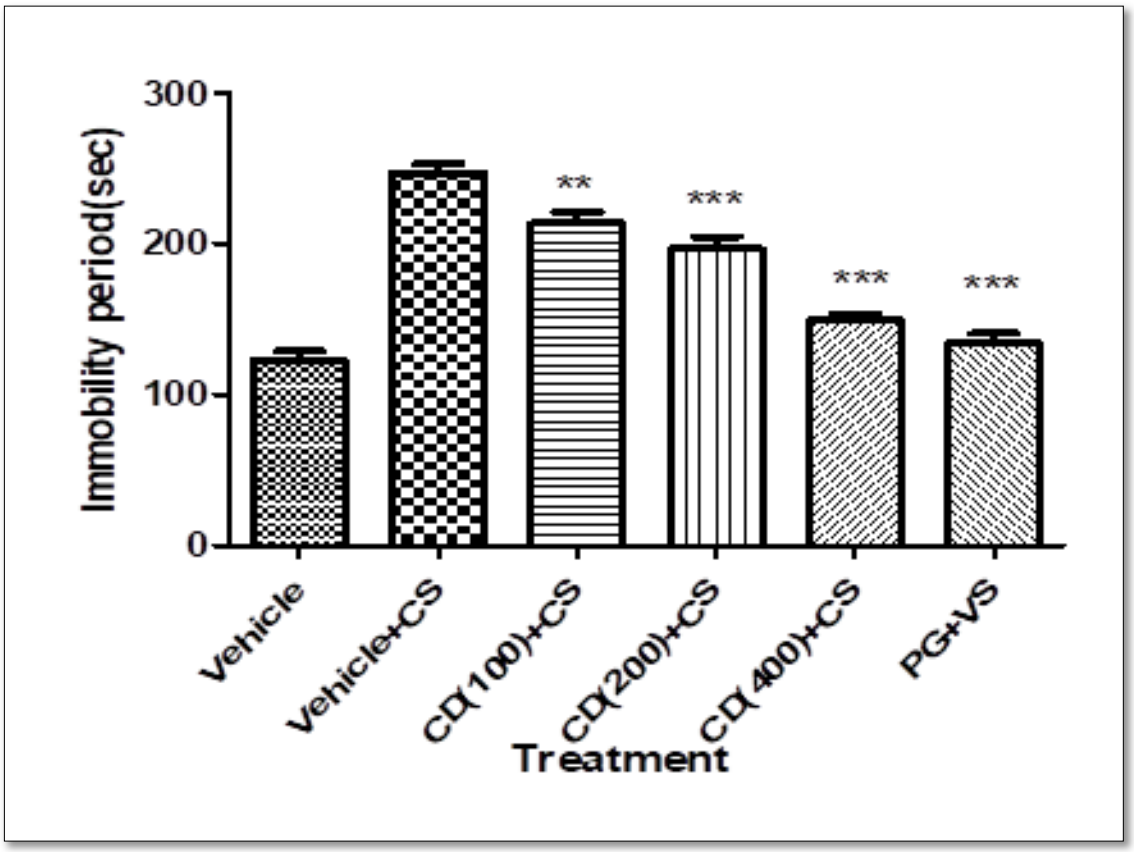

Figure 1. Effect of ethanolic extract of *Capparis decidua* on immobility time in stress induced behavioral despair test.
CD: Capparis deciduas; PG: Panax ginseng; CS: Chronic Stress; VS: Vehicle+Stress
N=10 for vehicle and vehicle+CS treated groups. N=6 for CD and PG treated groups. Value are given as mean ± SEM
**p<0.001, **p<0.05, ***p<0.01 as compared to control*

Stress-induced inhibition of male sexual behavior

The result indicates that male, unstressed rats showed more number of mounting when compared to stress rats. Chronic stress significantly decreases in the number of mounting. This stress effect was attenuated by CD (100, 200 and 400 mg/kg, po) and PG (100 mg/kg, po) **(Table 3 and Figure 2)**.

Table 3. Effect of CD and *Panax ginseng* compared to vehicle on chronic stress-induced increase in swim stress immobility and suppression of sexual behavior.

Treatment	Dose (mg/kg)	Duration of Immobility	Number of mountings (N)
Vehicle (10)	-	122.60 ± 5.94	5.70 ± 1.70
Vehicle+Stress (VS) (10)	-	246.90 ± 6.24[a]	1.20 ± 0.63[a]
CD+VS (6)	100	213.67 ± 7.45[b]	2.17 ± 0.75[b]
CD+VS (6)	200	196.50 ± 8.26[b]	2.50 ± 1.04[b]
CD+VS (6)	400	149.50 ± 3.94[b]	3.83 ± 0.98[b]
Panax ginseng+VS (6)	100	134.33 ± 6.28[b]	4.50 ± 1.05[b]

Values in parentheses indicate number of animals; [a] indicates difference with vehicle treated group; [b] indicates difference with VS (ANOVA followed by Dunnet-test)

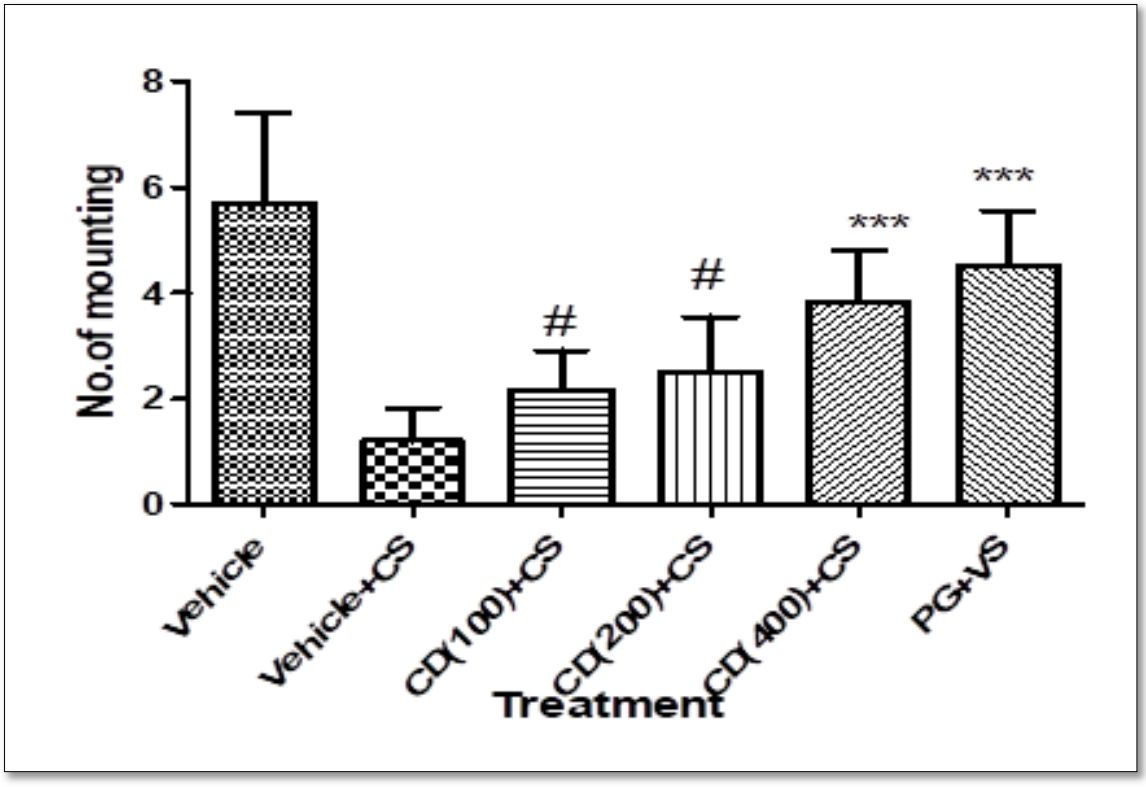

Figure 2. Effect of ethanolic extract of *Capparis decidua* in stress induced suppression of sexual behavior.
CD: Capparis deciduas; PG: Panax ginseng; CS: Chronic Stress; VS: Vehicle+Stress
N=10 for vehicle and vehicle+CS treated groups. N=6 for CD and PG treated groups. Value are given as mean ± SEM
**p<0.001, **p<0.05, ***p<0.01, #p>0.05 as compared to control*

Active and passive avoidance test

Chronic stress produced significant decrease in retention of acquired active and passive learning. These stress induced memory deficits were reduced by CD (200 and 400 mg/kg, po) and PG (100 mg/kg, po) (Table 4 and Figure 3).

Table 4. Effect of CD and *Panax ginseng* compared to vehicle on chronic stress-induced memory deficit in passive avoidance response in rats.

Treatment	Dose (mg/kg)	Latency (step-through) (s)	
Vehicle (10)	-	12.2 ± 2.78	18.7 ± 1.18
Vehicle+Stress (VS) (10)	-	11.7 ± 2.05[a]	6.6 ± 2.01[a]
CD+VS (6)	100	11.67 ± 1.75[b]	15.33 ± 2.25[b]
CD+VS (6)	200	12.17 ± 1.94[b]	15.67 ± 2.16[b]
CD+VS (6)	400	12.50 ± 1.87[b]	16.67 ± 3.61[b]
Panax ginseng+VS (6)	100	11.50 ± 2.07[b]	17.5 ± 1.87[b]

Values in parentheses indicate number of animals; [a] indicates difference with vehicle treated group; [b] indicates difference with VS (ANOVA followed by Dunnet-test)

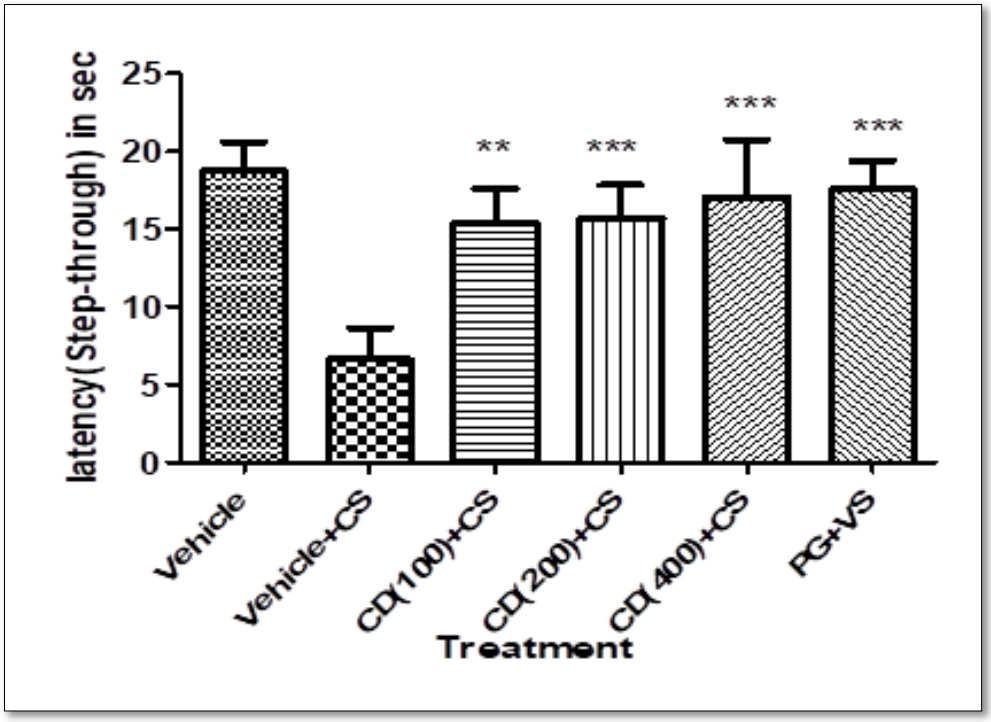

Figure 3. Effect of ethanolic extract of *Capparis decidua* in stress induced passive avoidance test.
CD: Capparis deciduas; PG: Panax ginseng; CS: Chronic Stress; VS: Vehicle+Stress
N=10 for vehicle and vehicle+CS treated groups. N=6 for CD and PG treated groups. Value are given as mean ± SEM
**p<0.001, **p<0.05, ***p<0.01 as compared to control*

CONCLUSION

From above study it was concluded that all the three doses of *Capparis decidua* extract showed good anti-stress effect in tested models. The *Capparis decidua* extract significantly reduce the stress induced gastric ulceration, change in adrenal cortex and spleen weight. Capparis decidua tended to reverse the stress-induced behavioural changes. Chronic stress significantly decrease the sexual behaviour of male rats, this stress effect was reversed by *Capparis decidua*. Stress induced memory deficits were reduced by *Capparis decidua* extract. The ethanolic extract of root of *Capparis decidua* at doses of 100, 200 and 400 mg/kg, possess good anti-stress activity.

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