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# SOME PHARMACOLOGICAL STUDIES ON CARDIOSPERMUM HALICACABUM LINN

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***ABSTRACT:*** *Cardiospermum halicacabum used in Ayurveda has been investigated for various pharmacological actions in a number of experimental animal models. On central nervous system the decoction of the plant showed sedative effect. It exhibited significant analgesic and anti-inflammatory activities. The drug also showed vasadepressant activity which is considered to be transcient in nature. In vitro studies also revealed its antispasmodic effect. These findigns are in support of its use in Ayurvedic medicine.*

## INTRODUCTION

C. halicacabum (Jyotishmati) has been described in Ayurveda as a remedy in the treatment of rheumatism, piles, bronchitis and nervous diseases. Decoction of the plant is considered as diuretic, diaphoretic and laxative[1]. Recently, diuretic activity of the plant in experimental animals has already been reported[2]. However, there are not much reports on the other pharmacological effects of this medicinal plant and hence the present study was initiated to probe into its medicinal value using the aqueous extract (decoction) of the whole plant.

## MATERIALS AND METHODS

Pharmacognostically identified, shade dried whole plant was used to prepare the decoction as described by Nadkarni (1954)[3]. Albion rats, mice, g. pigs and dogs were used in the experiments and the drug decoction was given orally to them as otherwise indicated. Drug dose levels were calculated in terms of crude drug / kg body weight.

*i. Acute toxicity and general behaviour:*

Groups of 6 mice were used for each dose level with a control group receiving distilled water only. Overnight fasted albino mice were used for this study as described by Irwin (1963)[4]. Test drug decoction was given orally in dose levels of 1,5,10,20,30 and 50g/kg body wt. Behavioural changes were observed at 15,30,60, 120 and 240 min afer drug and for tonic effects and mortality up to 72 hrs.

*ii. Effect on pentobarbitone hypnosis:*

Test drug decoction was given to overnight fasted mice in dose levels of 1 to 20 g / kg and 30 min later pentobarbitone sodium was injected (50 mg/kg i.p) to all of them. Control group received distilled water orally

instead of the decoction. The period between the loss and the return of righting reflex was taken as the sleeping time and compared this with that of control.

*iii. Anticonvulsant activity:*

The effect of various doses of decoction of C. halicacabum (1, 5, 10,15 and 20 g / kg) was studied against maximal electroshock seizure test (150 mA, 0.2 sec) in male rats according to the method of Holland *et al* (1961)[5]. Percentage protection from convulsions was noted. Dilantin sodium (100 mg/kg p.o) was used as reference standard for comparison.

*iv. Analgesic activity:*

This was studied by the rat tail flick method using hotwire analgesiometer[6]. Drug decoction was administered orally (1,5,10 & 20g/kg) and acetylsalicylic acid (500 mg/kg p.o) was used as the standard drug.

*v. Anti – inflammatory activity:*

Drug decoction was screened against both acute and chronic types of inflammation.

a) Mouse ear oedema test; Method of Brown and Robson (1964)[7] with some modifications was adopted to study the effect of drug decoction (1,2,5 & 10g/kg ) in this acute inflammatory process. The difference between the mean oedema of the drug treated group and the control was calculated and expressed as percent inhibition. Phenylbutazone (100 mg/kg) was used as the standard drug for comparison.

b) Croton oil induced granuloma in rats: Method of Selye (1953)[8] with modification was followed. Test drug decoction was administered in two dose levels of 10 and 20 g/kg with a control group receiving distilled water and another group receiving phenylbutazone (100 mg/kg) as standard drug. The inhibitory effect on the granuloma formation was assessed by measuring the fluid accumulation and noting the weight of the pouch wall.

*vi. Effect on arterial – blood pressure of anesthetized dog:*

Mongrel dogs of either sex (10 – 15 kg) were anesthetized with pentobarbitone sodium (35 mg / kg i.p). The drug decoction was injected intravenously by cannulating femoral vein and carotid pressure was monitored through a mercury manometer. Since the drug decoction elicited vasodepressor response the mode of action was evaluated in β-blocker (propranolol – 5 mg/kg) antihistamine (anthisan – 10 mg/kg) or anticholinersic agent (atropine – 2 mg/kg) pretreated animals. The effect of decoction on normal responses of adrenaline, Ach and nicotine was also studied.

*vii. Effect on perfused frog heart (in – situ):*

Contractions of the perfused frog heart was recorded on the smoked paper in a slow moving drum using starling heart lever. Decoction in varying dose levels was injected into the perfusing fluid in a constant volume and changes in the rate and force of contractions were recorded[9].

*viii. Antifertility activity:*

A preliminary study to detect the effect of drug decoction (1,2,5 & 10 g/kg) on implantation activity in mated Holtzman female rats (D1 – D5) was carried out. On D10 of pregnancy they were leparatomised and uterine horns examined for the number and size of implants[10].

*ix. Autonomic pharmacology (in – vitro tests):*

*a) On isolated ileum of guinea pig:*

Longitudinal contractions of ileum to alternate doses of acetylcholine and histmine (1 – 2 µg/ml) were recorded as described by Burn (1952)[9]. The tissue was suspended in Krebs' solution (37°C) and 3 min dose cycle was used. Test drug in various doses (in terms of crude drug) was added to the bath in a constant volume and the effect of Acetylcholine and histamine was noted.

*b) On rabbit jegunum:*

Effect of Acetylcholine, adrenaline (0.1 to 1 µg/ml) and test drug (up to 500 mg/ml) on the contractions of rabbit jejunum suspended in tyrode solution (37°C) was noted. Effect of decoction pretreatment on the spasmogenic effect of Acetylcholine and relaxation effect of adrenaline was also studied in a number of tissue preparations.

*c) On the rectus abdominis muscle of frog:*

The test was carried out as described by Burn (1952)[9]. Effect of decoction (10 mg to 100 mg) on the Acetylcholine induced spasm was studied.

**TABLE – I**
**Effect of C. Halicacabum on xylol induced acute mouse ear oedema**

| | Drug | Dose g/mg/kg (p.o.) | n | Oedema (mg) Mean ± S. E. | % inhibition of Oedema |
|---|---|---|---|---|---|
| i. | C. halicacabum (decoction) | 1g | 6 | 38.57 ± 6.99 | 20.73 |
| ii. | C. halicacabum (decoction) | 2g | 6 | 42.33 ± 6.31 | 13.00 |
| iii. | C. halicacabum (decoction) | 5g | 8 | 33.00 ± 10.24 | 32.18 |
| iv. | C. halicacabum (decoction) | 10g | 12 | 14.33 ±[a] 2.07 | 70.55 |
| v. | Controls Dist. Water | - | 6 | 48.66 ± 7.60 | - |
| vi. | Phenylbutazone | 100 mg | 8 | 25.85 ±[b] 2.80 | 46.87 |

n = number of mice in the group
p values – a <0.001, b <0.01

**TABLE – II**

**Effect of C. halicacabum on croton oil induced granuloma in rats**

| | Treatment (g/mg/kg) (p.o.) | n | Volume of inflammatory exudates (ml ± S. E.) | Weight of the Pouch g ± S. E. | Weight of adrenals g ± S. E. |
|---|---|---|---|---|---|
| i. | Controls – Dist. Water | 6 | 3.05 ± 0.06 | 3.71 ± 0.51 | 0.036 ± 0.003 |
| ii. | Phenylbutazone – 100 mg | 6 | 1.31 ± [c] 0.01 | 2.01 ± [a] 0.06 | 0.044 ± 0.002 |
| iii. | C. Halicacabum – 10 g | 6 | 1.86 ± [c] 0.02 | 3.02 ± 0.02 | 0.046 ± 0.002 |
| iv. | C. Halicacabum – 20 g | 6 | 1.42 ± [c] 0.04 | 2.12 ± [b] 0.01 | 0.047 ± 0.002 |

n = number of rats in the group
p values – a <0.005, b- <0.02, c - <0.001

## RESULTS AND DISCUSSION

*Acute toxicity and general behaviour:*

*C. halicacabum* decoction did note exhibit any toxic symptoms or mortality in mice upto 50 g/ kg dose level.

*On pentobarbitone hypnosis:*

Drug decoction in dose level of 2g/ kg onwards showed potentiation of pentobarbitone hypnosis and at 8 and 20g / kg there was significant effect ($p<0.05$) indicating CNS sedative activity.

*Anticonvulsant activity:*

Up to 20 g / kg test drug did not afford any protection to rats exposed to electro shock seizures.

*Analgesic activity:*

At 10 and 20 g/kg doses drug exhibited significant analgesic activity in rats with maximum activity 60 min after drug administration similar to acetylsalicylic acid, the standard drug used for comparison. However acetysalycylic acid (500 mg/kg) was found to be superior in activity.

*Anti – inflammatory activity:*

Effects of C. Halicacabum on acute and chronic inflammatory process induced by xylol and croton oil are summarized in table 1 and 2, respectively. In acute inflammation in mouse, the test drug in 10 g / kg dose leve, afforded significant ($p < 0.001$)

protection from oedema. It showed 70% inhibition of oedema as compared to 46% of phenylbutazone. Similarly in chronic inflammatory process drug decoction 10 and 20 g / kg showed very significantly ($p < 0.001$) reduced the inflammatory exudate with reduction in weight of pouch wall. This activity was almost similar to that of phenylbutazone (100 mg/kg).

*On blood pressure in anesthetized dogs:*

Drug decoction up to 250 mg / kg did not exhibit any effect on blood pressure and respiration. But from 500 mg/kg onwards there was hypotensive effect and this did not modify the action of acetylcholine, adrenaline or histamine. However atropine partially blocked this hypotensive effect.

*On perfused frog hear (in-situ):*

Decoction from 100 mg onwards produced negative inotropic and chronotropic effect with a transcient arrest in diastole which lasted for 3 – 5 min depending upon the dose. This cardiac arrest was not blocked by atropine and drug did not potentiate the negative inotropic action of acetylcholine. At 2000 mg and above the drug exhibited complete cardiac arrest.

*Antifertility activity:*

Test drug up to 10 g/ kg did not exhibit any anti – implantation effect in female rats.

*On isolated G. pig ileum:*

Decoction in 200 mg/ml bath fluid completely blocked the sparmogenic effect of Acetylcholine and histamine (500 ng/ml).

*On rabit jejunum:*

Test drug from 100 mg/ml showed relaxation of smooth muscle of intestine and blocked the sparmogenic effect of acetylcholine completely.

*On frog recuts abdominis:*

At 100 mg/ml, test decoction exhibited marked curare like action by blocking the spasmogenic effect of acetylcholine.

Present preliminary investigations on the aqueous extract of *C. halicacabum*, it was observed that this plant possessed marked central nervous system (CNS) effects without any acute toxic effects up to 50 g/kg orally. From its significant analgesic effect as well as potentiation of pentobarbitone hypnosis the drug can be presumed as a CNS sedative. However it failed to show any anti-convulsant property. Test drug also showed significant anti – inflammatory effect in both acute and chronic experimental models. Cardiovascular studies exhibited myocardial depressant effect more or less similar to cholinergic agents and this hypotensive effect was partially blocked by anticholinergic drug, atropine, in anesthetized dogs. In-vitro tissue experiments showed the antispasmodic and curare like actions of the test drug.

From these experimental findings, the usefulness of *Cardiospernum halicacabum* decoction in rheumatism, nervous diseases, pain and as diuretic in Ayurveda is being substantiated.

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