STUDIES ON THE PHARMACOLOGICAL ACTIONS OF CARDIOSPERMUM HELICACABUM

C. GOPALAKRISHNAN, R. DHANANJAYAN AND LALITHA KAMESWARAN,

Medicinal Chemistry Research Centre,
Department of Pharmacology,
Madras Medical College, Madras-600003

Summary: The leaves of the plant "Cardiospermum helicacabum" were extracted with different solvents and found to contain largely tannins, saponins and traces of alkaloids. The alcoholic extract was tested for its pharmacological effects on various intact and isolated biological preparations. On the CNS the extract produced depression in near lethal doses. On the CVS the extract produced fall of blood pressure and bradycardia. The fall of blood pressure was antagonised partially by atropine and anti-histamine. On guinea pig ileum the extract produced powerful contraction which was partially antagonised by atropine and anti-histamine. The extract produced mild analgesia as tested by the radiant heat method in rats. It appears to be a proconvulsant in nature as tested by the electroshock method in rats. The extract when administered orally produced significant anti-inflammatory effect in rats as tested by the granuloma puoch and cotton pellet implantation methods.

Key words: cardiospermum helicacabum, alcoholic extract, preliminary screening, analgesic, proconvulsant, anti-inflammatory

INTRODUCTION

Cardiospermum helicacabum, known in Tamil as "Mudakkattan" and in Hindi as "Kanphutti" belongs to the family Sapindaceae. A decoction of the plant (root) is considered to be a diuretic, diaphoretic and laxative. The whole plant has also been used both internally and externally in rheumatic disorders and lumbago (2 & 3). Leaves boiled in oil are applied over areas of rheumatic pain, swellings and tumours and the juice of the plant has been used as ear drops (10). Hopkins *et al.* have reported the isolation of Me 4,4 dimethoxy-3 (Methoxymethyl) butyrate, a volatile ester ($C_9H_{18}O_5$)from the seed oil of this plant (8). Since it has been widely used by practitioner of Indian systems of medicines in treating various painful conditions and rheumatic disorders, an attempt was made to analyse the pharmacological effects in animals.

MATERIALS AND METHODS

Preparation of extracts : The air-dried leaves of the plant were successively extracted with petroleum ether and 95% alcohol. The petroleum ether extract was found to contain mainly chlorophyll and plant waxes. The alcoholic extract was evaporated under vacuum and the residue was analysed for the presence of alkaloids and glycosides (6). The alkaloidal content of the plant was negligible when compared to the content of glycoside. A 10% suspension of

the alcoholic extract concentrate was prepared with 2% gum acacia and used for pharmacological studies.

Experimental procedures :

Preliminary screening : This was done according to Turner (13). 40 Swiss male albino mice of 20-25 g body weight were divided into two groups of 20 animals and were given the following intraperitoneally.

Group A—alcoholic extract (10-100 *mg*/100 *g*)

Group B—gum acacia suspension.

For acute toxicity 80 mice were used and the LD_{50} was calculated according to Read-Muench (11).

Analgesic activity : This was tested on 30 wistar albino rats, according to Gujral (7) using an analgesiometer and the tail flicking response to radiant heat was observed. The animals were divided into 3 groups and the following drugs were administered intraperitoneally.

Group A—alcoholic extract (100 *mg*/*kg*).

Group B (control)—gum acacia suspension.

Group C (positive control)—Morphine sulphate (10-20 *mg*/*kg*)

Anti-convulsant activity : This was studied according to Dikshit *et al.* (5), using 60 rats. The animals were divided into 3 groups and were given the following intraperitoneally.

Group A—alcoholic extract (100 *mg*/*kg*).

Group B (control)—gum acacia suspension.

Group C (positive control)—Phenobarbitone sodium (20 *mg*/*kg*).

The effects of drugs on the tonic spasm of the hind limbs induced by electro-shock were observed.

Effects on cardiovascular system :

1. The effect of the alcoholic extract on perfused heart was observed (1).
2. The effect of the alcoholic extract on frog's vascular perfusion was studied according to (1).
3. The effect on blood pressure and myocardiogram was studied on dogs anaesthetised with chloralose according to (4).

Effects on smooth muscles :

1. The effect of the alcoholic extract on guinea pig ileum was studied according to (12).
2. Effects of the extract on intestinal movements of dogs were studied according to (3).

Effects on experimental inflammation :

This was studied in albino rats by the granuloma pouch technique (13) and the cotton pellet implantation method (14). The effect of the alcoholic extract was compared with phenylbutazone (100 *mg/kg*) and cortisone (25 *mg/kg*).

RESULTS

Preliminary screening : Demonstrable CNS depressant activity was noted in near lethal doses (20 *mg*/25 *g*) characterised by ptosis, decreased motor activity, ataxia, loss of muscle tone, loss of righting reflex and urination within 20-30 minutes after administration of the alcoholic extract. The LD_{50} was 20 *mg*/25 *g* body weight in mice.

Analgesic activity : The alcoholic extract produced mild analgesia in rats. In the control group tail flicking was noted 8.82 ± 0.8 secs. In the alcoholic extract treated animals, it was seen at 12 ± 1.1 secs. No response was seen with morphine treated animals upto 30 secs.

Anticonvulsant activity : The extract did not show any anticonvulsant property. The extract increased the duration of the tonic extensor spasm from the control 12.5 ± 2.6 secs to 23.8 ± 7.6 secs.

Effects on cardio vascular system : i) Frog's perfused heart *in situ* : Administration of 2 *mg* of the extract produced myocardial depression. Heart rate and force of contraction were diminished by the drug. The myocardial stimulant effect of 10 *mcg* adrenaline was not antagonised by the extract. The myocardial depressant effect of the extract was antagonised by 10 *mcg* of atropine. The myocardial depressant effect appeared to be due to the parasympathomimetic action of the extract.

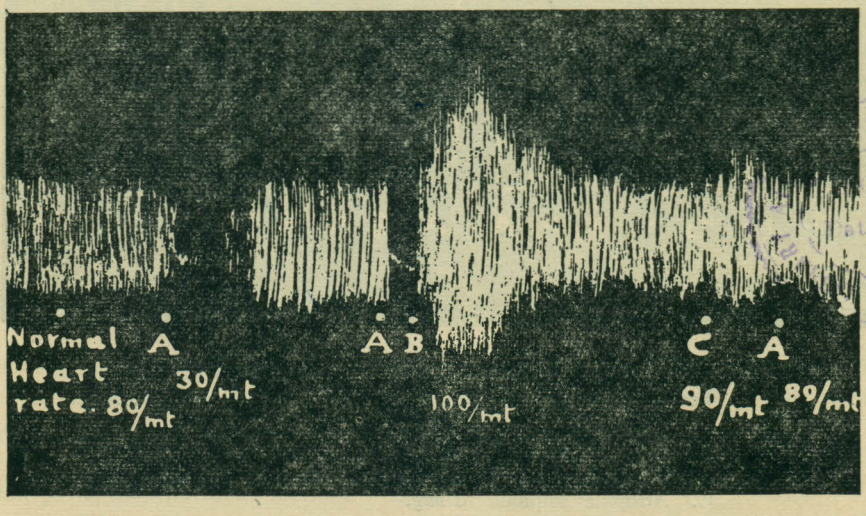

Fig. 1 : Effect of cardiospermum helicacabum on frog's heart *in situ*.
Perfusion fluid — Ringer.
A. C.h. extract, 2 *mg*.
B. Adrenaline, 10 *mcg*.
C. Atropine, 10 *mcg*.

(ii) *Frog's vascular perfusion* : 0.1 *mg%* of the extract significantly increased the perfusion rate which was comparable to that product by sodium nitrite (0.1 *mg%*). The normal perfusion rate in frogs was 1.4±0.1 *ml*/min. With sodium nitrite the rate increased upto 2.8±0.48 *ml* and with C.h. extract, it was 2.2±0.2 *ml.*

(iii) *Effects on anaesthetised dog's blood pressure and myocardiogram* : Intravenous administration of 50 *mg* of the extract produced significant fall in blood pressure and myocardial depression. It did not affect the "bracketing-norms". The effects on blood pressure and heart rate were antagonised by atropine (0.6 *mg*). Antihistamine, chlorpheniramine maleate also blocked the hypotensive effect of the extract partially.

Effect on smooth muscles :

1. *Guinea pig ileum :* 1 *mg* of the extract produced very powerful contraction. The contractile effect of the extract was partially antagonised by atropine (10 *mcg*) and chlorpheniramine maleate (10 *mcg*) when added to an isolated organ bath of 50 *ml* capacity. The contractile effect appeared to be due to mixture of parasymathomimetic and histamine like principles.

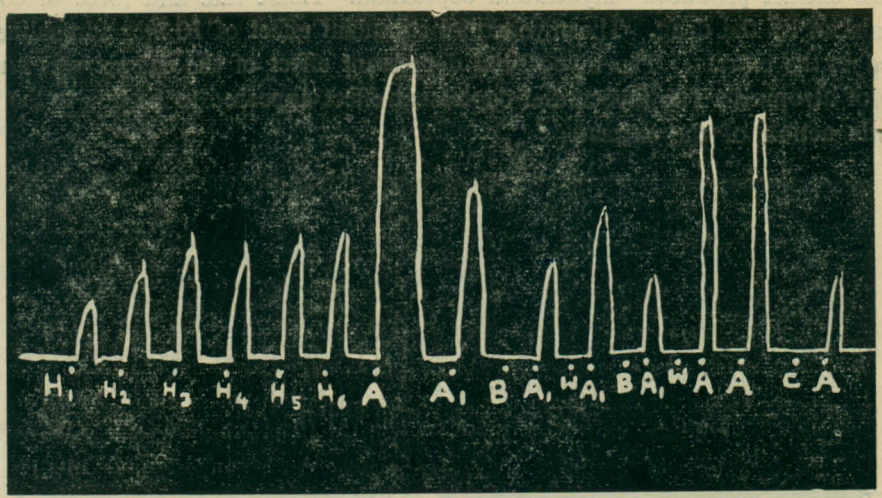

Fig. 2: Effect of cardiospermum helicacabum on guinea pig ileum.
Perfusion fluid-Tyrode, 95% O_2 5% CO_2 Bath volume : 50 *ml.*

H_1—H_6 Histamine dihydrogen phosphate
A and A_1 — Cardiospermum helicacabum, 1 *mg* and 0.5 *mg.*
B. Antihistamine (chlorpheniramine maleate) 10 *mcg.*
C. Atropine sulphate 10 *mcg.*

(iii) *Intestinal movements of aneasthetised dog :* Administration of 5 *mg/kg* of the alcoholic extract produced significant contraction of intestine. This contractile effect was blocked by antihistamine, chlorpheniramine maleate (5 *mg/kg*) and atropine (0.1 *mg/kg*) partially.

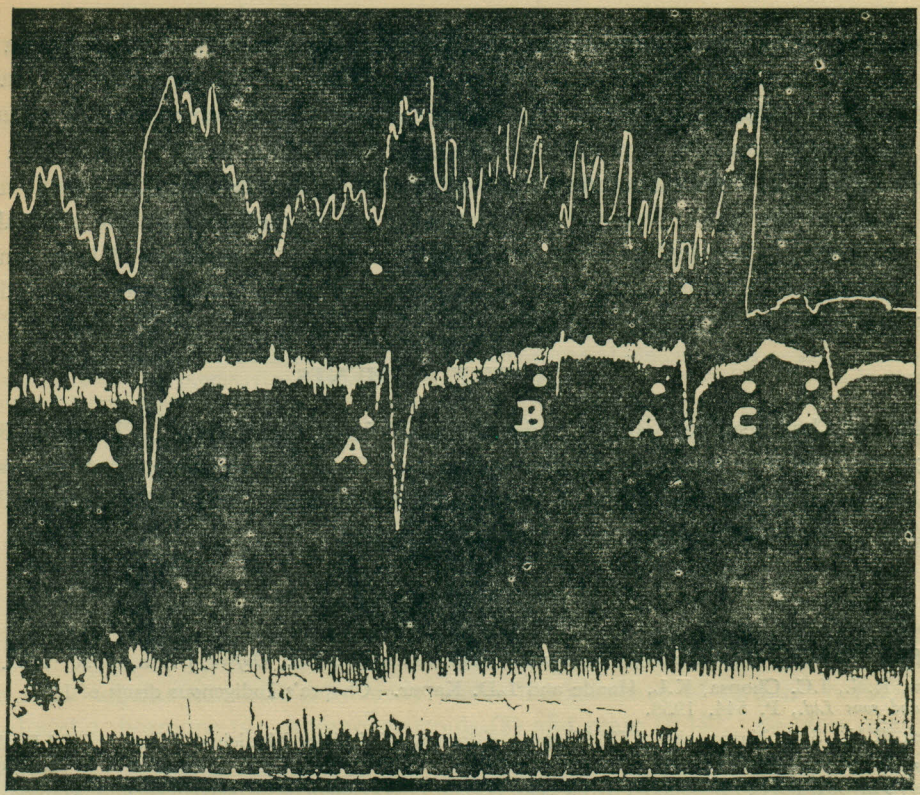

Fig. 3: Effect of cardiospermum helicacabum on dog's respiration, blood pressure and intestinal movements.
Anaesthesia: Chloralose, 100 *mg/kg*, i.v.,
A - Alcoholic extract, 2 *mg/kg* and 5 *mg/kg*.
B - chlorpheniramine maleate, 5 *mg/kg*.
C - atropine sulphate, 0.1 *mg/kg*.

Effect on experimental inflammation :

(i) *Granuloma pouch method :* In the control animals the volume of the exudate was 8.85±1.19 *ml*. In the phenylbutazone treated animals it was 5.34±1.22 *ml* and in the alcoholic extract treated animals it was 5.98±1.17 *ml*.

(ii) *Cotton pellet implantation method :* In the control animals the weight of the cotton pellet was 57±2.6 *mg*. In cortisone treated animals the weight of the pellet was 28.6±2.6 *mg* and in animals treated with the alcoholic extract it was 37.8±3.2 *mg* thereby showing that the extract produced a definite anti-inflammatory effect but was not as effective as cortisone.

DISCUSSION

The alcoholic extract of cardiospermum helicacabum has been found to possess a number of interesting pharmacological effects. The extract produces CNS depression in near lethal doses and analgesic effect in mice and rats. It appears to be a proconvulsant in nature. On the CVS and smooth muscles it produces cholinergic and histaminergic effects. The anti-inflammatory effect of the extract is comparable to phenylbutazone as tested by the granuloma pouch method. Whether the anti-inflammatory effect is direct or mediated by the adrenal glands needs further study. Chemical analysis of the plant revealed the presence of large amount of saponins and traces of alkaloids. Further studies using the individual components of the plant are under investigation.

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