

## Antihypertensive effect of *Cecropia obtusifolia* (Moraceae) leaf extract on rats

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**Abstract:** A lyophilized aqueous leaf extract of *Cecropia obtusifolia* proved to be antihypertensive when intravenously administered to conscious spontaneous hypertensive rats. Forty-five minutes after injection, the maximum fall in arterial pressure (-23.5% relative to preinjection values) was seen and recovery was not complete by the end of the 180 min observation period. The extract was also given to pre-hypertensive SHR and normotensive rats. The fall in blood pressure was more conspicuous in the two SHR groups and was not accompanied by changes in cardiac frequency in any group. This would appear to rule out either a direct or indirect involvement of the heart in regard to the observed hypotension.

Folklore medicine in Costa Rica is fairly common (Núñez, 1978), in spite of universal medical social security services and an outstanding literacy level of more than 90%. Until recently, no serious attempts have been made locally to corroborate in the laboratory the putative beneficial effects of plant extracts.

In previous reports (Salas, 1985; Salas & Morales, 1986), the hypotensive effect of a lyophilized aqueous leaf extract of *Cecropia obtusifolia* Bertol (Moraceae) was studied in dogs.

In a short communication, Vidrio (1982) reported a hypotensive effect for a *C. obtusifolia* extract using normotensive rats. However, a hypertensive animal model would appear to be mandatory to prove the suspected antihypertensive utility of this plant as used in the folk medicine of Costa Rica and tropical America (Guzmán, 1974). The present study tested the effect of a leaf extract on consciously hypertensive rats (SHR) relative to pre-hypertensive and normotensive rats.

## MATERIAL AND METHODS

**Plant extracts:** Specimens of *C. obtusifolia* were collected at the main campus of the University of Costa Rica in San José City (1,200 m above sea level) in November of 1984, at the end of the rainy season, and determined at the herbarium of the University.

The fresh leaves were finely minced and enough distilled water was added to cover the material in a Pyrex jar after stepping at room temperature for two days; the solution was filtered through Whatman paper No. 42 and prepared for the lyophilization process. The percent yield was 3.75% relative to fresh leaf material.

**Animal preparation:** The rats were housed at room temperature (22°C-26°C) in individual cages and anaesthetized with ether for implantation of catheters (PE-50) in the left carotid artery and in the right jugular vein. Both catheters were tunneled subcutaneously and ex-

TABLE 1

*Antihypertensive effect of C. obtusifolia extract on unanaesthetized spontaneously hypertensive rats*

Mean arterial pressure  $\pm$  SEM (mmHg)

Group <sup>1</sup>	N	Preinjection						
		Control	+15	+30	+45	+60	+120	+180 min
SHR	10	161.5 $\pm$ 3.3	146.5 $\pm$ 9.6	130.5 $\pm$ 7.7	123.5 $\pm$ 8.4	128.0 $\pm$ 10.0	132.5 $\pm$ 7.7	140.0 $\pm$ 6.1
P-SHR	8	128.1 $\pm$ 4.2	115.6 $\pm$ 5.2	113.8 $\pm$ 4.4	113.6 $\pm$ 5.9	104.4 $\pm$ 5.0	103.1 $\pm$ 6.3	122.5 $\pm$ 5.1
NOR	10	119.5 $\pm$ 5.3	118.4 $\pm$ 7.9	120.0 $\pm$ 4.7	113.5 $\pm$ 5.1	111.0 $\pm$ 5.1	116.0 $\pm$ 3.9	118.0 $\pm$ 4.3

<sup>1</sup> SHR: Spontaneously hypertensive rats. P-SHR: Pre-Spontaneously hypertensive rats; and NOR: Normal rats. All animals received a single bolus i.v. injection (50 mg/kg) of the extract.

teriorized in the back of the animal. Mean and pulsatile arterial pressure were continuously monitored by use of a pressure transducer (model RP-1500i), connected to a Hewlett-Packard polygraph (Model 7754A). Heart rate was measured from the peak pulse pressure of the recording.

Three groups of rats were used, according to the following criteria: (i) adult (269  $\pm$  6.8 g; mean  $\pm$  SEM), spontaneous hypertensive (SHR) animals of the Okamoto-Aoki Strain with mean arterial blood pressure (MAP) higher than 150 mmHg; (ii) prehypertensive (P-SHR) rats as represented by younger (205  $\pm$  7.3 g) SHR animals with MAP less 150 mmHg; and (iii) normotensive (NOR) albino rats (243  $\pm$  6.4 g) of the Sprague-Dawley strain. All the animals were fed a locally produced rat chow (Cartago, Costa Rica) and tap water *ad libitum* and were reared at the biotery of the University of Costa Rica, with 13 hours light and 11 hours darkness cycles.

Surgery was performed in the morning and the control MAP recording was obtained in the afternoon of the same day. Fifty mg/kg of the extract was then administered intravenously in isotonic saline 0.9% (0.4 ml/min) by infusion using a Gilford pump (Model 105 S).

During the experiment the rats were conscious and allowed to rest freely in the cage. A dose of 50 mg/kg was chosen, because it gave a marked and yet non-lethal effect, according to previously documented dose response curve data. The MAP response was recorded for three hours. After pooling the data, the results were expressed as the mean value  $\pm$  the standard error of the mean ( $X \pm$  SEM). Significance of

means was tested using ANOVA followed by Tukey's analysis.

## RESULTS

The intravenous infusion of lyophilized extracts of *C. obtusifolia* on SHR caused a decrease in MAP of 23.5% (Table 1). The hypotensive response was apparent a few minutes after administration and reached maximum effect 45 minutes later. Three hours later, the MAP still had not returned to the pre-injection level (Fig. 1). At all times, except 15 minutes after the injection of the extract, the MAP showed significant differences as compared with the preinjection value ( $P < 0.01$ ). When the same dose was administered to the P-SHR group, the response followed the same trend as the SHR group, but the hypotension was less profound and the maximum fall was delayed in time (60-120 minutes). A nearly complete recovery was seen by the end of the recording period (Fig. 1). The response of the NOR rats was close to that of the P-SHR group, with no significant differences between them. It is interesting to note that the acute fall in the MAP appeared to be dependent upon the level of the preinjection pressure, i.e., the anti-hypertensive effect was more evident in the group with higher blood pressure.

With regard to the cardiac frequency, the control values in the three groups were statistically different. Nevertheless, the cardiac frequency after extract injection remained unchanged for all three groups when subjected to statistical analysis (Table 2).

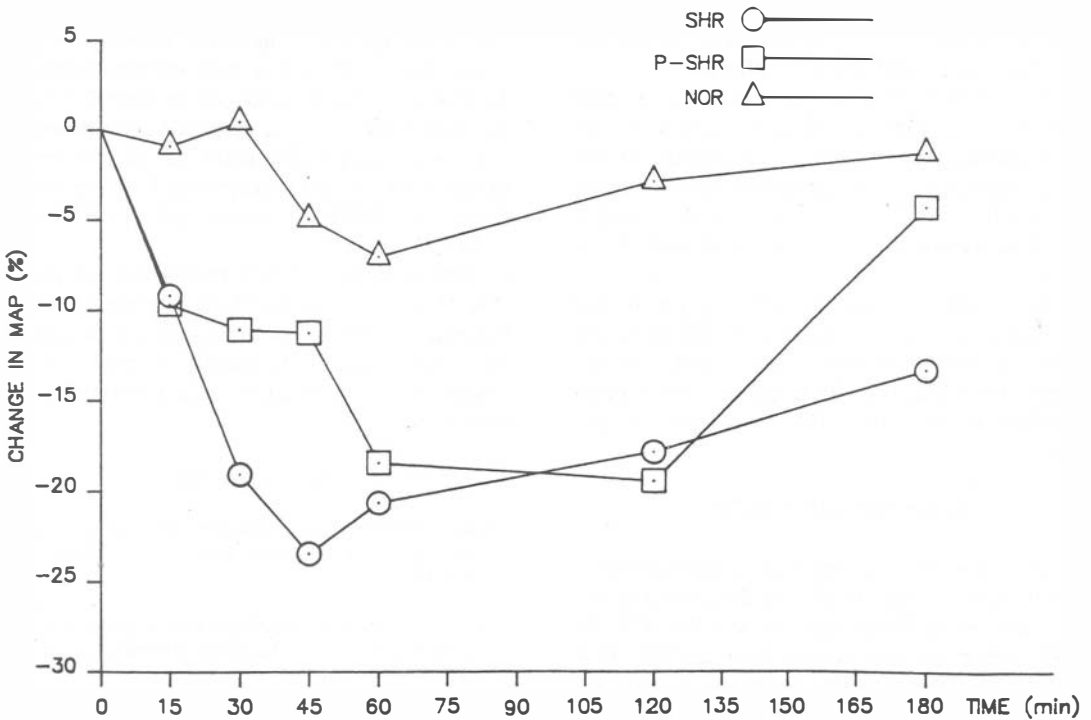


Fig. 1. Temporal evolution of the MAP on conscious hypertensive, pre-hypertensive and normotensive rats, acutely treated with i.v. extract of *C. obtusifolia*. SHR: spontaneous hypertensive rats; P-SHR: prehypertensive rats and, NOR: normotensive rats.

TABLE 2

*Effect of C. obtusifolia extract on cardiac frequency*

Cardiac frequency  $\pm$  SEM (beats/min)

Group <sup>1</sup>	N.	Preinjection						
		Control	15	30	45	60	120	180
SHR	6	360.0 $\pm$ 10.7	364.5 $\pm$ 8.6	358.0 $\pm$ 9.3	360.0 $\pm$ 9.9	366.0 $\pm$ 8.2	366.0 $\pm$ 7.2	364.5 $\pm$ 8.3
P-SHR	8	330.0 $\pm$ 16.5	332.7 $\pm$ 14.2	353.7 $\pm$ 22.9	344.0 $\pm$ 20.2	339.7 $\pm$ 22.4	323.2 $\pm$ 20.6	330.7 $\pm$ 15.6
NOR	10	292.6 $\pm$ 18.4	288.2 $\pm$ 22.5	296.6 $\pm$ 18.2	274.0 $\pm$ 17.3	279.0 $\pm$ 14.4	270.0 $\pm$ 18.9	285.1 $\pm$ 19.4

<sup>1</sup> SHR: Spontaneously hypertensive rats; -SHR: Pre spontaneously hypertensive rats; and NOR: Normal. All animals received a single i.v. injection of *C. obtusifolia* of 50 mg/kg.

## DISCUSSION

In recent reports of natural products research, plant extracts with hypotensive effects are rather common (Ojewole, 1981; Ammon, 1985). In our case, in two groups of experimental animals tested, an antihypertensive effect was found and the lowering of blood pressure appeared to be proportional to the pre-injection

pressure level. In the normotensive group, even though some hypotension was present, the fall was not significant. No attempts were made to clarify the site or mechanism of action of the extract, but the data suggest a possible blockade of the baroreceptor response. No change in cardiac frequency was observed in the three experimental groups at any time after injection. In dogs, three mechanisms for the hypotension

have been proposed in dogs: ganglionic blockade, decreased inotropism and bradycardia (Salas, 1985; Salas and Morales, 1986).

It is worthy to note that, contrary to other investigators (Vidrio, 1982), we could not detect significant changes in blood pressure or cardiac frequency in normotensive rats; however our methods were quite different with regard to the extract preparation, doses used and animal model.

The main contribution of this paper is that the active anti-hypertensive principle of *C. obtusifolia* exerts its maximum effect without bradycardia and that SHR animals seem more sensitive to its effects than normotensive animals.

#### ACKNOWLEDGEMENTS

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#### RESUMEN

El extracto crudo liofilizado de *Cecropia obtusifolia* administrado intravenosamente a ratas espontáneamente hipertensas (SHR), no anestesiadas (50 mg/kg de peso), mostró poseer propiedades antihipertensivas. La presión arterial disminuyó a un mínimo nivel (76.4%) del valor control (161.5 mmHg), 45 minutos después de

la inyección. El extracto se administró por infusión a tres grupos de animales: hipertensos, prehipertensos (SHR) y a normotensos (Sprague Dawley). La disminución de la presión arterial fue más evidente en el grupo de ratas hipertensas, siendo estadísticamente significativa en relación a los otros dos grupos ( $p, 0.05$ ) de acuerdo con el ANOVA y análisis por el método de Tukey.

Esta disminución de la presión arterial media (PAM) no fue acompañada por variaciones de la frecuencia cardíaca en ningún grupo, lo cual indica que no hay participación del nodo sinusal directa o indirectamente en la hipotensión observada.

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