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Cardiovascular effects of the aqueous extract of *Chrysanthellum indicum*

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Abstract

Objective: To study the effects of the aqueous extract of *Chrysanthellum indicum* on cat blood pressure and isolated rat atria. Materials and methods: Cardiovascular activity was evaluated directly on anaesthetised cat, isolated rat atria and isolated rabbit jejunum. Safety assessments were carried out in mice and preliminary phytochemical screening was also carried out on the extract. Results: The aqueous extract of *Chrysanthellum indicum* (2 - 32 mg /kg i.v.) were found to cause a dose dependent decrease in blood pressure. The fall in blood pressure was attenuated by atropine. The extract also exhibited a concentration - dependent decrease in the force of contraction of the spontaneously beating atria. The extract evoked a concentration - dependent contraction of the isolated rabbit jejunum, which was abolished by atropine. The intraperitoneal LD_{50} of the extract was found to be 282.2 ± 5.2 mg/kg and the extract gave positive reactions to flavonoids, tannins, glycosides and alkaloids. Conclusion: The aqueous extract of *C. indicum* may contain some biologically active principle(s), which may be relevant in the management of cardiovascular disorders, thereby agreeing with some aspects of the traditional use of this plant as a remedy for heart troubles.

Key words: *C. indicum*, Cardiovascular activity, Blood pressure, Rat atria, Rabbit jejunum

1. Introduction

Medicinal plants represent a great deal of untapped reservoir of drugs and the structural diversity of their component molecules makes them a valuable source of novel lead compounds against newly discovered therapeutic targets [1, 2]. *Chrysanthellum indicum* Linn. Vatke (Compositae), is a faintly aromatic herb that is widely distributed in the tropics. A decoction of the plant is used in the treatment of jaundice and urinary complications. It has also been used in the treatment of gonorrhea, fever, heart trouble and as poultice for maturing boils [3]. The anti-oxidant properties of the flavanoid isolated from the plant has been reported [4].

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Recently, Amos, *et al,* [5,6] reported on some of the pharmacological activities of the aqueous extract of this plant. In those studies the extract caused a dose-dependent contraction of the gastrointestinal smooth muscle, which was blocked by atropine, suggesting muscarinic receptor involvement. In addition, the extract of *Chrysanthelellum indicum* possess significant and dose-dependent anti-inflammatory activity in rats induced by egg albumin.

The extract of *Chrysanthellum indicum* possess significant and dose-dependent anti-inflammatory activity in rats induced by egg albumin. It was also found to inhibit abdominal constriction caused by acetic acid in mice dose-dependently. There are no reports in the literature on the cardiovascular activity of the aqueous extract of *C. indicum.* The present study was designed to investigate the effect of the extract on the cardiovascular system in rodents.

2. Materials and methods

2.1 Collection and preparation of plant material

The plant material was collected at Idu, Abuja, Nigeria. The plant was identified and authenticated by the late A. Ohaeri and I. Muazzam of the Herbarium Unit, Department of Medicinal Plant Research and Traditional Medicine, National Institute for Pharmaceutical Research and Development (NIPRD), Abuja. A voucher specimen was deposited for future reference at the Herbarium.

The whole shoot of *C. indicum* were cleaned, air-dried and crushed into coarse powder with a pestle and mortar. 100 g of the powdered plant material was cold-macerated with 1 litre of distilled water for 36 h with occasional shaking using the ASH Shaker model 3017. The resulting filtrate was freeze-dried and it gave a mean yield of 20% w/w.

2.2 Phytochemical Test

Phytochemical analysis of the extract was performed using standard methods [7 - 9]. Tests for alkaloids, saponins, tannins, flavonoids and glycosides were carried out.

2.3 Drugs

Acetylcholine, histamine, atropine, propranolol, isoprenaline (all from Sigma Chemical Company, USA), Mepyramine (M & B, USA). All drugs were freshly prepared to desired concentration with distilled water just before use. The extract was also freshly prepared using distilled water. Parallel control experiments were carried out in order to correct possible effects due to vehicle alone.

2.4 Acute toxicity studies (LD_{50})

LD_{50} determination was conducted using the method of Lorke (10). Male and female mice weighing between 18 - 22 g were divided into five groups of five mice each. After overnight fasting, they were treated with the extract as follows 1, 10, 100, 1000 and 2000 mg/kg i.p. Animals were observed for signs and symptoms of toxicity. The number of deaths in each group within 24 h was recorded.

2.5 Pharmacological investigations

2.5.1 Studies on cat blood pressure

Adult cats weighing between 2 - 3.5 kg were anaesthetized using sodium pentobarbital (40 mg/kg i.p.).

After the depth of anesthesia was achieved, the trachea was intubated to facilitate spontaneous respiration. The femoral vein was cannulated with heparinized polyethylene tubing (PE - 50) for intravenous injection of the plant extract, while the carotid artery was cannulated and connected to a Bentley trantec pressure transducer for blood pressure measurement on the Ugo Basile Microdynamometer. Temperature was maintained at 37 ± 1°C by

means of a thermostatically controlled dissecting table. Animals whose blood pressures fluctuate by more than 10% within the first 30 min of recording were discarded.

After a 30 min equilibration period intravenous administration of the extract (with a maximum volume of injection, 0.4 ml) was carried out slowly and it lasted not more than 30 s. Effects of mepyramine (1 mg/kg), propranolol (2 mg/kg) and atropine (2 mg/kg) were studied against the blood pressure lowering effects of the extract. The antagonist was allowed for a period of 5 min before the extract and the specific agonist was added. The effectiveness of receptor blockade was tested by injecting an agonist at an effective dose [11, 12].

2.5.2 Studies on isolated rat atria

Wistar rats of either sex weighing between 150 - 250 g were killed and exsanguinated. The thoracic region was opened, the heart was rapidly removed and placed in Lorke's solution of the following composition (mM) : NaCl 153.8, KCl 5.6, $CaCl_2$ 2.1, $NaHCO_3$ 5.9 and glucose 5.5. This was kept at a temperature of 30 ± 1°C and aerated with 100% O_2.

The atria were carefully dissected out and mounted in an organ bath containing 20 ml of Lorke's solution. A resting load of 0.5 g was applied and the tissue was allowed to equilibrate for a period of 60 min during which the physiological solution was changed every 15 min. Effects of the extract were recorded on the Ugo Basile Unirecorder 7050. The effects of isoprenaline, acetylcholine , propranolol and atropine on the rat atria were investigated.

The drug contact time for the extract was 1 min with an interval between successive doses of at least 5 min. The incubation period for drug interaction was 5 min. Determinations were done in quadruplicates.

2.5.3 Studies on the rabbit jejunum

Adult rabbits of either sex weighing between 1.5 - 2.5 kg were killed by a blow on the head, exsanguinated and the abdomen opened. Segments of the jejunum about 2 - 3 cm long were removed and dissected free of adhering mesentery. The tissue was mounted in a 20 ml organ bath containing Tyrode solution at 37 ± 1°C and aerated with air.

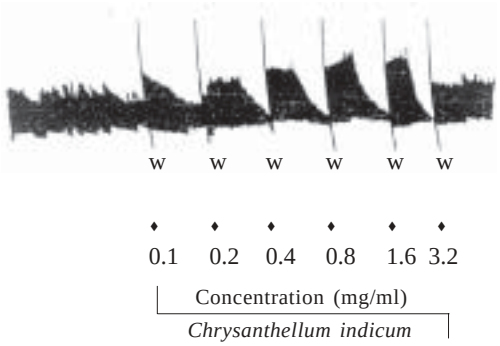

Figure 1. Effect of the aqueous extract of *Chrysanthellum indicum* on force of contraction of the spontaneously beating rat atria

Table 1.
Effect of *Chrysanthellum indicum* aqueous extract on cat blood pressure

Treatment	Dose (mg/kg)	Mean Arterial Pressure (mm/Hg)
Normal Saline	0.2 ml	110 ± 1.6
Chrysanthellum indicum	2	96 ± 2.1
	4	92 ± 1.7*
	8	87 ± 2.4*
	16	84 ± 1.8*
	32	79 ± 1.4*

Values are expressed as mean ± S.E.M.; Comparision between control and treated groups; *P<0.05

A resting load of 0.5 g was applied. A 60 min equilibration was allowed during which the physiological salt solution was changed every 15 min. The effect of the extract (0.05 - 3.2 mg/ml) and acetylcholine (2.5×10^{-9} - 1.0×10^{-7} M) were evaluated on the spontaneous contractions of the rabbit jejunum. The inhibitory effect of atropine (5.0×10^{-9} M) on extract and acetylcholine induced contractions of the rabbit jejunum was also investigated. Responses were recorded on Ugo Basile Unirecorder 7050 via an isometric transducer 7040.

2.6 Statistical Analysis

Results were expressed as mean ± SEM. Statistical analysis of the data was done using Student's *t* - test and the difference between means were regarded as significant when $P < 0.05$.

3.0 Results and Discussion

The intraperitoneal LD_{50} of the extract in mice was found to be 282.2 mg/kg (261.2 - 294.6 mg/kg within 95% confidence limits). Intravenous administration of the aqueous extract of *Chrysanthellum indicum* (2 - 32 mg/kg) exerted a significant fall in blood pressure in anaesthetized cats (Figure 1). The fall in blood pressure was observed immediately after the administration of the plant extract suggesting a possible direct relaxing effect of the extract on vascular smooth muscles [13].

The extract induced fall in blood pressure was neither affected by propranolol (2 mg/kg) nor mepyramine (1 mg/kg) but was abolished by atropine (2 mg/kg). The data obtained suggests that β-adrenoceptors and histaminergic mechanisms may not be involved in the observed phenomenon [11, 12] since the blood pressure lowering effect of the extract was attenuated by atropine, It may be suggesting a role for cholinergic receptors may have a role to play in the activities of *C.indicum.*

The aqueous extract of *Chrysanthellum indicum* (0.1 - 3.2 mg/ml) produced a reduction in the force of contraction of the spontaneously beating atria, with no effects on the frequency of contraction. However, the extract did not attenuate isoprenaline-induced contraction of the atria, propranolol was found to inhibit the contraction induced by isoprenaline.

This means that β_1 adrenergic receptors may not be linked with the observed activity. The

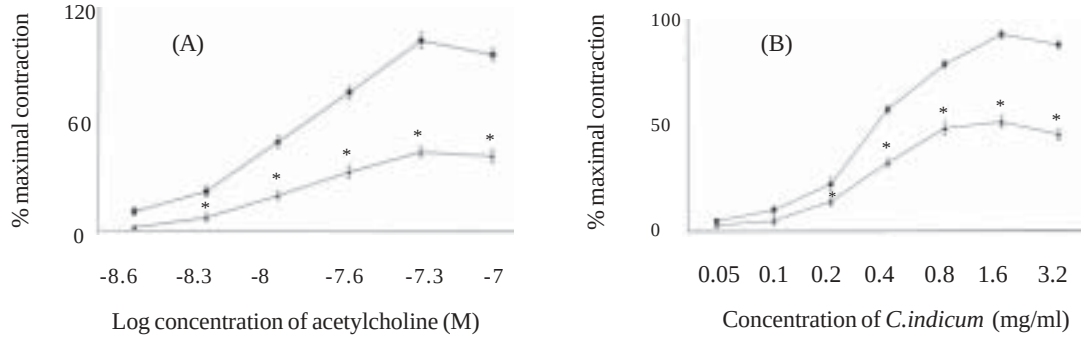

Figure 2. Effect of Atropine 5×10^{-9} M on (A) Acetylcholine (2.5×10^{-9} - 1.0×10^{-7} M) and (B) *Chrysanthellum indicum* (0.05- 3.2 mg/ml) induced contraction of the rabbit jejunum.

observed decrease in the force of contraction of the spontaneous beating atria by the extract may therefore involve peripheral stimulation of muscarinic receptors of the heart as suggested by Taesolikul *et al* [14].

This speculation is supported by the antagonism shown by atropine in this study. The extract (0.05 - 3.2 mg/ml) exhibited a concentration-dependent contraction of the rabbit jejunum, which was blocked by atropine (Figure 2A, B)

This further buttresses the like between cholinergic receptors and observed pharmacological effects due to *C.indicum* extract. These results give positive indication of the traditional use of *C.indicum* in the management of heart troubles.

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