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Full Length Research Paper

Vol. 5 (1), pp.1 - 7, January, 2017

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Evaluation of anti-hypertensive and analgesic activities of *Musanga cecropioides in rodents*

Salah Balla and M. Ahmed

Tai Solarin College of Education, Omu, Ijebu-Ode, Ogun State, Nigeria.

Abstract

A study was carried out to screen *Musanga cecropioides* R. Br ex Teddlie (Moraceae) for anti-hypertensive and analgesic properties using smooth and skeletal muscles in rodents in an attempt to evaluate the efficacy of medicinal plants and further search for novel structure. *M. cecropioides* locally known as "umbrella tree", Aga (Yoruba), Agar Umbrella (English), Parasolier (French) has been screened for anti-hypertensive and analgesic properties. The aqueous extract of *M. cecropioides* used in this investigation was prepared using the smooth and skeletal muscles in rodents. Aqueous extract of *M. cecropioides* was found to contain ingredients that were active as analgesic, anti-hypertensive and spaspogenic.

Keywords: *Musanga cecropioides* (Moraceae), analgesic, anti-hypertensive.

INTRODUCTION

The increasing rate in the widespread of endemic diseases which had drastically reduced the lifespan of Nigerian citizens is a major concern to medical practitioners. Despite the rich and vast medicinal plants endowed by nature in Africa, much has not been done through scientific research findings in exploring and establishing their phyto-constituents for the curing of prevalent diseases in the environment as obtained in China and India, where indigenous medicine and pharmacopoeia have greatly stabilized the healthy living of the people thereby enhancing and prolonging their life spans.

These prevalent infectious diseases that have jeopardized the safety of the people could be attributed to lack of complete committed interest in developing the available resources embedded in indigenous plants and herbs as well as lack of research facilities and funding. This has facilitated the high rate of dependence on the exorbitant orthodox medicines which are beyond the means of average people.

Although herbs are generally valued for their virtue as foods, and medicine (Oliver, 1960, 1982), yet most of their discoveries and usage had been premised/ based on trial and error. Treatments of diseases have always been discovered with administration of medicine which used parts of plants, animal to concoct "healing" portions in order to eliminate pains and control suffering and counteract disease.

The use of medicinal plants for the treatment of many diseases is associated with folk medicine from different parts of the world (Araujo, 2001). There is a great variety of compounds that can be extracted and characterized from plants. One good example is the harmaline, one of the indole alkaloids found in *Peganum harmala* (Zygophyllaceae) which is used in the treatment of dermatitis (Iwu et al., 1994). Another substance that can be found in plants is the morphine from the opium poppy, which has highly analgesic action and is still used. Its molecule as reported by Phillipson (1994) and affirmed by Araujo (2001) is used as a model for design to reach new drugs. The isolation of artemisinin showed the real importance to investigate plants that can be sources of new compounds with clinical activities. Based on these facts, we can conclude that plants produce a large number of substances, which can provide a wide spectrum of biological properties. One of such plants is

Musanga cecropioides which belong to the family Moraceae. It is commonly called “Umbrella” tree (English) and “Igi aga” (Yoruba). *M. cecropioides* is a forest tree that provides shade for hunters and farmer thus the name “umbrella” tree. The bark infusion is gargled to allay toothache. The root bark is eating with cola nut to cure cough, and the bark from callouses is tied on wounds where it is supposed to effect a cure (Adejuwon, 2001). This research aims at investigating the anti-hypertensive and analgesic activities of *M. cecropioides*.

MATERIALS AND METHODS

Collection of plant material

The plant material was collected along Ago-Iwoye / Sagamu road about half (½) km from the Olabisi Onabanjo University (formerly Ogun State University) permanent site situated in South Western Nigeria. The identification was confirmed by Prof. Z. O. Gbile, of Biological Science Department of the same institution in 1997.

Extraction protocol / preparation of extract

Leaf sample of *M. cecropioides* was rinsed after collection with water and teased into pieces. 50 g of the fresh pieces were packed into the Muslim cloth to allow for proper extraction using the Soxhlet extraction method.

Animal and treatment

Male rats of the Wistar strain with a body weight of 200 to 210 g were kept in animal room at an ambient temperature of 25 ± 1°C. They had free access to water and commercial food. In some other experiments, mice and rabbit were used under the same experimental condition mentioned above. Food pellets were purchased from Ladokun Feeds, Ibadan in Oyo State, Nigeria.

Pharmacological tests

Measurement of isometric tension

Male rats were killed by exsanguinations. The stomach strip (smooth) was dissected out and cut into strips according to the method of Vane (1975) while the isolated rat diaphragm of the same rat was disserted out of the skeletal diaphragm preparation, a model to study effect of *M. cecropioides* on neuro muscular junction and were placed in Tyrode solution gases with 95% O_2: 5% CO_2 and maintained at 37°C. The stomach strip was connected through a transducer model FT.03 to a polygraph recorded model 7PD for the isometric measurement. Tension, was maintained at 500 mg. The phrenic nerve preparation was connected by a fine platinum wire which attached the preparation to a light string lever adjusted for position on a slow moving drum. Continuous stimulation at the rate of 4 to 8 shocks / min using sub-maximal stimulus was used.

Blood pressure experiment

A rat was anaesthetized with sodium pentobarbital and was prepared for blood pressure recording. The arterial cannular was inserted in the carotid artery and connected through a mercury manometer to record on a dynamometer. Drugs were introduced through a cannular placed either in the external lugular or femoral veins. Some experimental rats were fed with animal feed mixed with 8% sodium chloride to induce hypertension, while other rats were left out of this experiment, before examining the effect of *M. cecropioides* on both normal and hypertensive rats.

Analgesic study

Analgesic activity was tested as antinociceptive effect against chemical stimuli.

Chemical method

In view of the postulated role of prostaglandin with indication of pain (Piper and Vane, 1971), Musanga extract was tested for analgesic activity, an acetic acid induced squirming method was used. In this experiment, squirming was taken to represent one or more of the following:

(i) Repeated abdominal contraction.
(ii) Stretching of the trunk and hind limbs
(iii) Tension of the body at the hips with inward rotation of one hind limb.

Rabbit Ileum preparation

The method employed was according to a modified method of Finkleman in Senjobi (1997), 2 to 3 cm length of intestine from fleshly killed rabbit was isolated with its mesenteric blood vessels attached. The end of the mesenteric attachment away from the segment of intestine was tied with the cotton string and threaded through a pair of electrodes. The preparation was then set up in model for recording pendulum movements. The nerve was stimulated by 10 V at 30 pulses per second. The high voltage of stimulation was necessary because of the insulation provided by the set in which the nerve was embedded.

RESULTS

Effect of *M. cecropioides* on blood pressure

In this experiment, the normal heart rhythm was recorded on the polygraph dynometer paper, while doses of aqueous extraction (0.6 M) were ingested through the femoral vein. As doses of extract increases, the heart blood lowering effect increases (Figure 1). The depression observed was watched with known vasodilator to compare efficacy.

Effect of *M. cecropioides* on ach-induced stomach strip contraction

Aqueous extract of *M. cecropioides* effect on Ach-induced contraction was examined on rat stomach strip preparation. A dose response effect was established (canticol) with 0.2 to 0.8 × 10^{-5} M after which the muscle was bathed in half dilusion of plant extract for 10 min (Figure 2).

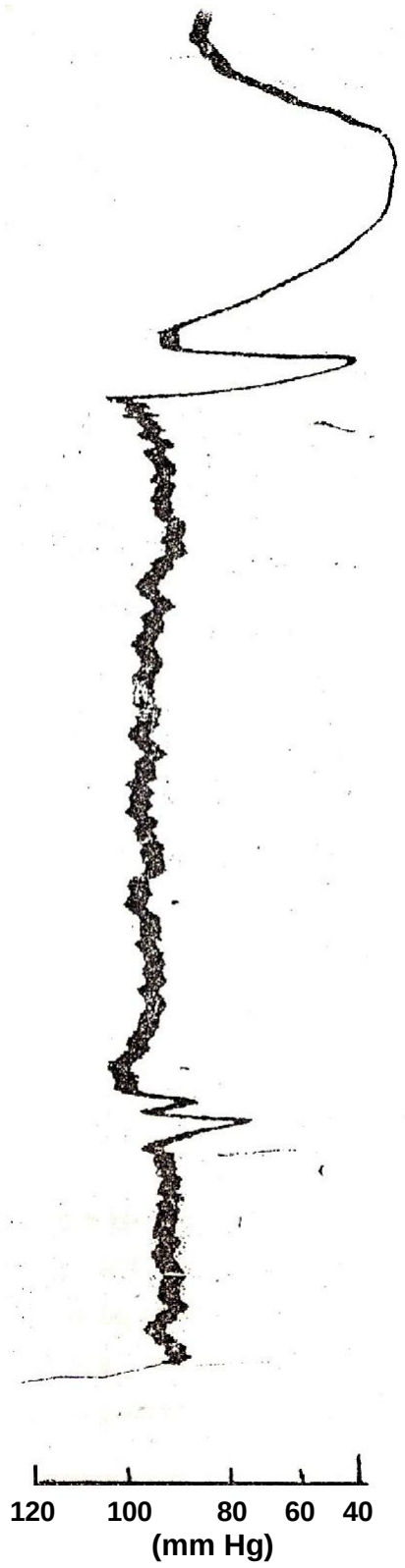

Figure 1. Effect of *M. cecropioides* on the blood pressure recording of the rat. Blood pressure lowering effect 16 to 64 mg/kg of the extract in spontaneously hypertensive rat.

Effect of aqueous extract on skeletal muscle preparation

The rat phrenic nerve muscle preparation was used to study transmission at the neuro muscular junction, aqueous extract of Musanga potentiated electrical stimulation when tissue was bottled in 20 min treatment with the extract. An increase in height of twitch responses was indication of modulatory role for the release of Ach at the neuromuscular junction (Figure 3).

Effect of extract on the rabbit ileum

The rabbit ileum preparation is a model for the study of nature of inhibition of the catecholamine effect of *M. cecropioides* (0.5 to 1.5 ml). As concentration increases, the nature of inhibition of the pendular movement decreases (Figure 4 and Table 1). The mice treated with *M. cecropioides* extract under twenty minutes observation did not show any of the signs of squirming, while in the control, the count of squirming per 20 min were between 28 to 30 counts, its inhibitory effect in this experiment was noted as the squirming effect was reduced as indicated in the count result ranging between 15 to 20 for extract /acetic acid.

DISCUSSION

This study revealed various pharmacological actions of aqueous extract of *M. cecropioides* on the smooth, skeletal muscles, blood pressure and analgesic activity of the compound. The result in which the extract did show significant effect of Ach-induced contraction suggests cholinonic properties, although atropine did not alter the effect of aqueous extract thereby excluding the possibility of muscarinic reception blockage. This is when the tissue was equilibrated in the presence of known muscarinic receptor blocker (Atropine).

The inhibiting action of the extract on the spontaneous or pendular movement of the rabbit ileum is indicative of its anti-adrenergic effect, because this model of experiment is one method of assessing the nature of inhibition of adrenergic neuron. Result involving the action of aqueous extract on the skeletal muscle showed that the extract significantly potentraned twitch responses in this experiment.

This finding could be interpreted as an indirect action, since at the neuromuscular junction, the transmitter released in Ach-Musanga could be Ach, Modulator. The result on blood pressure only confirmed earlier reports by Adjanohoun et al. (1988) and Bouquet (1979). It is possible that the extract might be producing its blood pressure lowering effect by vasodilatation and possibly stimulating catecholamine stores as confirmed by Ebiegbe et al. (1976). In the experiment in which

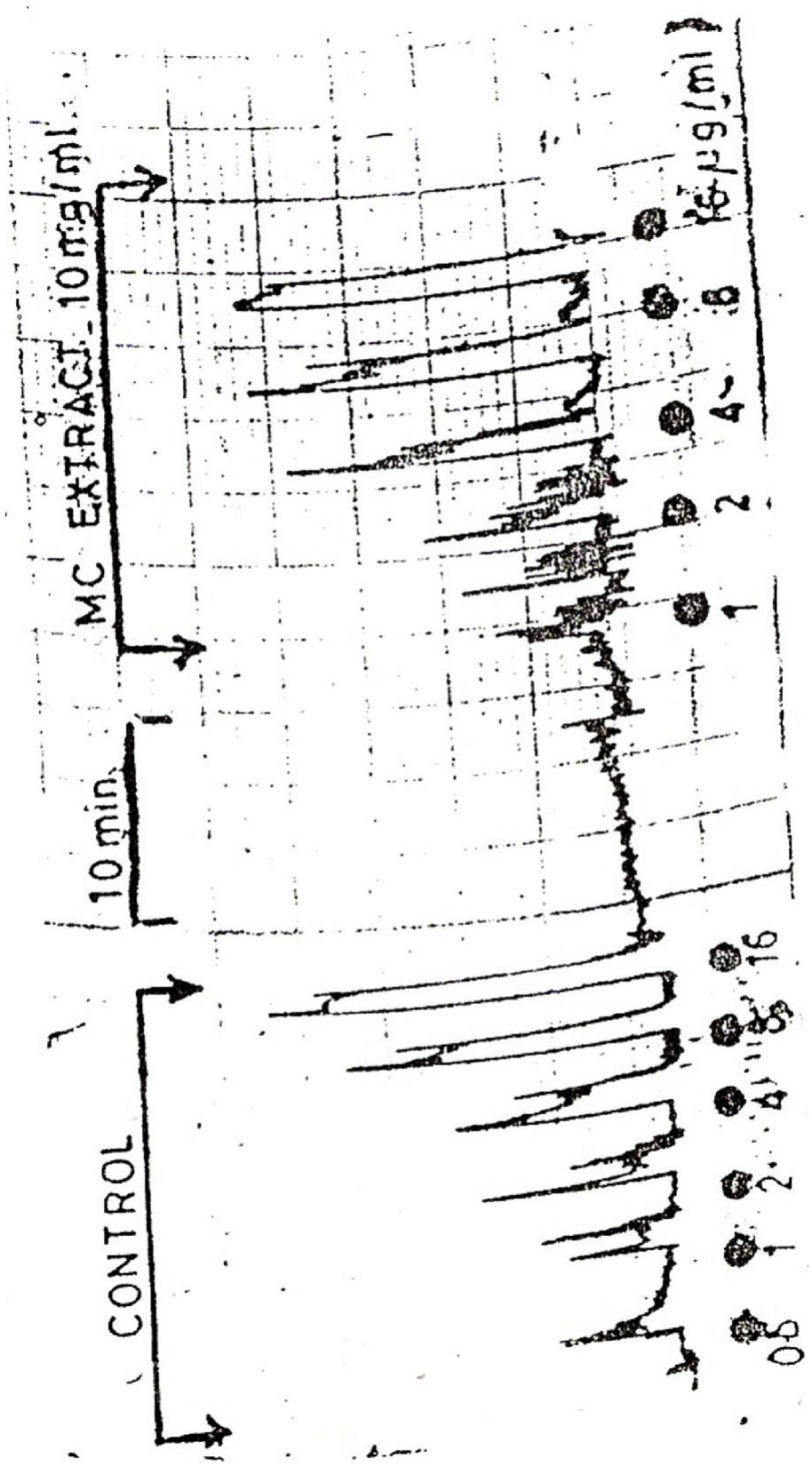

Figure 2. Effect of *M. cecropioides* on Ach-induced contraction of the rat stomach strip (.) indicates the concentration of agonist used, while arrow indicate point of addition of drugs in panel A and B respectively.

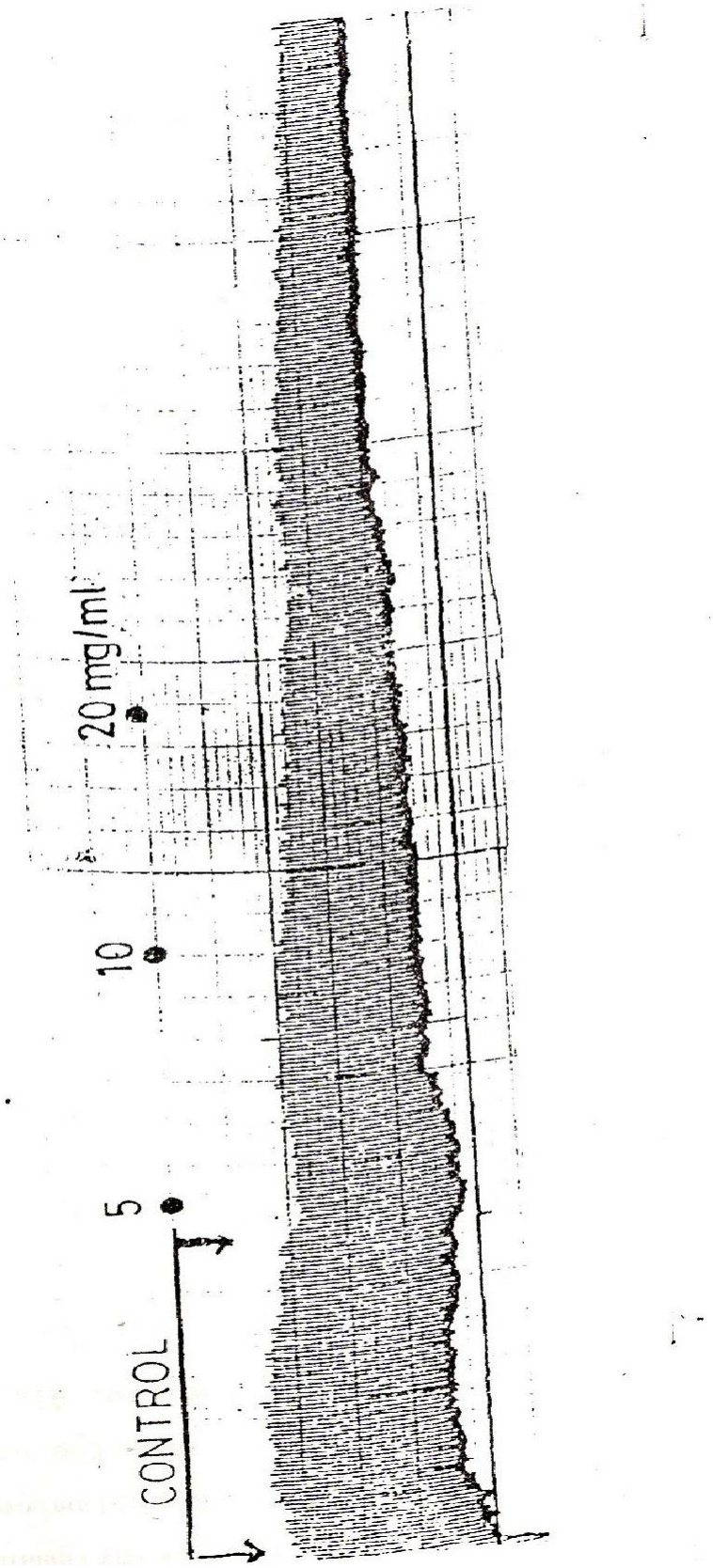

Figure 3. Effect of *M. cecropioides* on rat diaphragm nerve-muscle preparation. Arrows indicate control before the addition of the extracts and in the presence of extract.

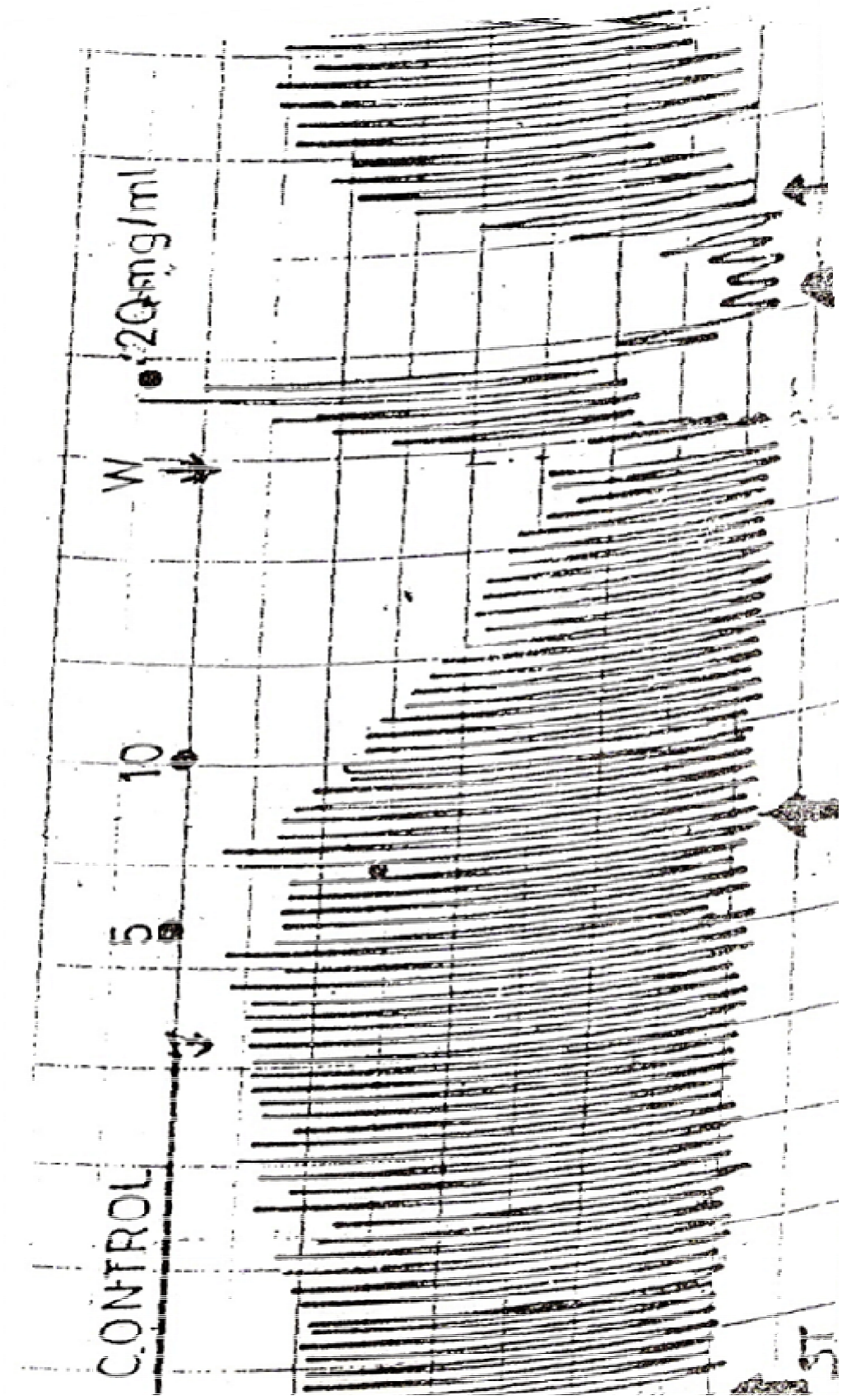

Figure 4. The inhibitory effect of *M. cecropioides* on isolated rabbit ileum preparation. Arrows indicate point before and addition of drugs.

Table 1. Squirming count per 20 min.

Test	Group I	Group II	Group III	Mean conc.
Normal	-	-	-	-
Acetic acid	32.0	28.0	30.0	30.0
Extract	-	-	-	-
Extract acetic acid	20.0	15.0	20.0	18.3

analgesic study was examined, the fact that all of the symptoms of pain such as forelimb torsion, abdominal pain, trunk stretching were lacking is indicative of the inhibiting effect of the extract. In conclusion this study revealed that aqueous extract of *M. cecropioides* contained ingredients that were active as analgesic, antihypertensive and saprogenic. Further studies on the plant phytochemical, isolation, identification and purification evaluation should be targeted with the aim of formulating chemotherapeutic agents from it.

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