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Short report

## Inhibitory Effects of *Musanga cecropioides* on Noradrenaline and Potassium-Induced Contractions in Rat Thoracic Aorta

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The pharmacological effects of *Musanga cecropioides* on rat thoracic aorta were examined in high K<sup>+</sup> medium (55mM), Ca<sup>2+</sup> 3mM) induced vasoconstriction was inhibited by *Musanga cecropioides* in a concentration-dependent manner. The tonic contractions elicited by KCl 55mM were relaxed by *Musanga* and were more marked in 0.45mM Ca<sup>2+</sup> than 1.8mM Ca<sup>2+</sup> medium. NA -induced responses were antagonized non competitively by *Musanga*. NA- sustained contraction was relaxed, the relaxing effect of *Musanga* was not antagonized by indomethacin or methylene blue. It is concluded that *Musanga* relaxation of the rat aorta does not involve cyclo-oxygenase, nor cAMP pathway, but unique, unlike those of known classical vasodilators.

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**Keywords:**

*Musanga cecropioides*, contraction, inhibition, Potassium, thoracic aorta

### INTRODUCTION

Medicinal plants have been used as traditional remedies in Africa. In our previous studies, we reported that *Musanga cecropioides* did not affect Ach-induced contractile response but produced significant inhibition of the movement of the rat and rabbit gut smooth muscles, Aziba *et al* (2000). It is also reported to have a blood pressure lowering effect and it is used to procure painless childbirth, Adjanohoun *et al* (1989). These actions prompted us to investigate in the present study, the effects of the aqueous extract of the leaves on the rat aorta on contractions — induced NA and K on receptor and voltage mediated responses respectively.

### MATERIALS AND METHODS

Male Wistar rats (200-350g) were killed by a blow on the head. The thoracic aorta was located, while excess fat and connective tissue was removed. The vessels were cut into strips according to Furchgott and Bhadrakom (1953). The contractile responses were recorded isometrically using a force displacement transducer (FT-03, Grass) and the signals amplified with a polygraph (Grass, model

7D). The preparations were equilibrated for 1hr in the organ bath containing 10ml modified Krebs solution of the following composition (mM): NaCl 118, KCl 1.2, CaCl<sub>2</sub> 1.8, MgCl<sub>2</sub> 1.2, KH<sub>2</sub>PO<sub>4</sub> 1.2, NaHCO<sub>3</sub> 25, and glucose 11.7. The tissue bath solution was bubbled with a 95% O<sub>2</sub>, 5% CO<sub>2</sub> gas mixture which maintained the solution at pH of between 7.2-7.4. In some preparation, K Krebs solution was prepared by replacing NaCl with KCl. The Krebs solution with high potassium concentration was prepared by mixing the K Krebs. The calcium free Krebs solution was prepared by deleting Ca<sup>2+</sup> during preparation of the Krebs solution. Drugs used were Noradrenaline hydrochloride (Sigma, St. Louis, MO USA) methylene blue (laboratory I-HBL reagent).

### Animals

The adult albino rat (>6 weeks old, Sprague Dawley strain) used in the experiment were supplied by the National Institute of Medical Research, Yaba, Lagos, Nigeria. The animals were maintained in the Preclinical House in a well ventilated condition, under constant temperature (30°C) and humidity 50% and exposed to 12hr light-dark cycle for 2 weeks before use. The animals were fed on

standard livestock pellets (Pfizer, Nigeria Ltd), with free access to water and were treated ethically according to the guidelines for the treatment of experimental animal as determined by the animal council.

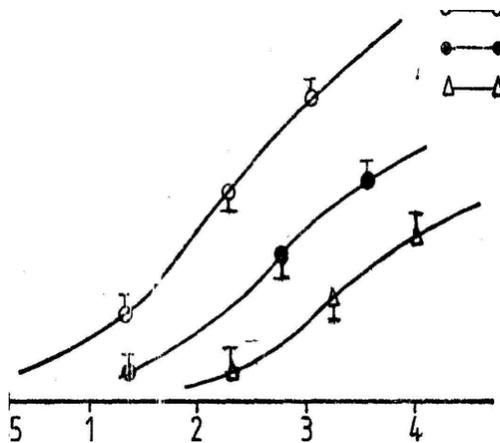
### Statistical Analysis

The data obtained from this experiment were expressed as the mean (S.E.M) for nobobservation. The value obtained in different groups were compared using test and probabilities of les than 5% ( $P < 0.05$ ) were considered to indicate a significant difference.

## RESULTS

### Effect of *M. Cecropioides* on $K^+$ Induced Contractions

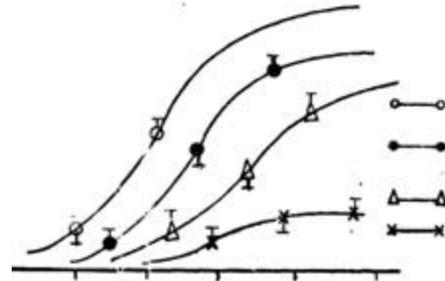
In high  $K^+$  (55mM)  $Ca^{2+}$  free medium. The cumulative addition of  $Ca^{2+} > 3mM$  to the aortic strip caused increase in contractile force. The maximum contraction  $> 3mM$  was  $1.2 \pm 0.25g$  ( $n = 10$ ). After incubating the strip in musanga (10 - 1000mg/ml) for 10 minutes, inhibited contraction in a concentration dependent manner (fig 1A), the  $IC_{50}$  value was calculated to be 1 5. increasing the incubation time did not cause any pronounced inhibitory action of Musanga.(fig 1B) low doses inhibited the high  $K^+$  induced  $Ca^{2+}$  dependent contraction, suggesting action on voltage operated  $Ca^{2+}$  channel effect.



### Effects of Musanga on Noradrenaline Induced Contraction

Cumulative addition of NA (5nM - 2nM), caused increase of contractions of rat aorta. The maximum contraction induced by 10nM noradrenaline was  $1.56 \pm 0.12g$  ( $n = 10$ ). Musanga produced a non competitive blockade of noradrenaline induced contraction. This relaxing action of Musanga was not blocked by either methylene blue 40nM or indomethacin 10nM. Pre-incubated aorta in Nifedipine for 10 minutes,  $K^+$  55mM induced contraction was

completely blocked while it had no effect on NA induced contractions (Fig 2).



## DISCUSSION

Rat aorta pre-treated with *Musanga cecropioides* in this study inhibited contractile responses to Noradrenaline and high  $Ca^{2+}$  55mM), it also caused the relaxation of the blood vessel when Musanga was added to NA induced sustained contractions. Contraction of Vascular smooth muscle requires increase in free cytosolic  $Ca^{2+}$  (Karaki and Weis 1979), the actions of Musanga was more enhanced in low medium  $Ca^{2+}$  0.45mM, then high  $Ca^{2+}$  medium 1.8mM in this study. The  $K^+$  induced contraction of the smooth muscle arise from increased  $Ca^{2+}$  influx through voltage dependent  $Ca^{2+}$  channels (Karaki and Weis 1979). Bay K 8044, a derivative of Nifedepine, a known  $Ca^{2+}$  entry facilitator did affect this action of Musanga. The inhibitory effect of musanga was much reduced in high  $Ca^{2+}$  medium 1.8mM. The tonic tension in response to Noradrenaline results from  $Ca^{2+}$  entry through receptor operated calcium channel (Bolton 1979). The inability of musanga to inhibit the actions of indomethacin and methylene blue, rules out, the possibility of the plant action involving cyclo-oxygenase nor cyclic AMP pathways. The totality of this result indicated that the inhibitory effects of *Musanga cecropioides* on the contractile responses caused by high  $K^+$  or NA are not due to increase in cyclic

nucleotide. Yang- Chong *et al* (1993) Musanga relaxes the rat aorta in a unique manner different from the known vasodilators and its actions on receptor is not specific since on receptor mediated responses, it suppressed maximum contractile response induced by Noradrenaline and high  $K^+$  in a non competitive manner.

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