International Scholars Journals

International Journal of Biochemistry and Biotechnology ISSN 2169-3048 Vol. 13 (8), pp. 001-005, August, 2024. Available online at www.internationalscholarsjournals.org © International Scholars Journals

Full Length Research Paper

Oxytocic Activity of *Musanga cecropioides* R. Brown Stem Bark: A Water Extract Study

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Accepted 10 May, 2024

Musanga cecropioides **(Umbrella tree) is one of the medicinal plants used in tropical parts of Africa for its oxytocic, hypotensive and antidiabetic activities. This work examined the effect of the water extract of the stem bark on rat uterus pre-treated with 1 mg/kg stilboesterol for 24 h. The effects of oxytocin-a uterine contraction agonist, antagonists like atropine (1-2 mg) and salbutamol (2 µg) on the uterine contractile effect of the water extract as well as its acute toxic effect were investigated. The water extract of *M. cecropioides* produced a dose related increase in the force of uterine contraction. An equivalent force of uterine contraction of 1.10 ± 0.15 g produced by 12.5 mg of the extract was increased to 2.53 ± 0.6 g when 1600 mg of the extract was administered. Oxytocin at 0.08 i.u. was observed to elicit a similar force of contraction with 400 mg of the water extract. The drug was observed to potentiate the uterine contractile activity of the extract while pre-treating the tissue with either atropine or salbutamol before administering the water extract showed the inhibitory effects of the drugs on the activity of the extract. The inhibition effect showed by atropine suggests the probable stimulation of the muscarinic receptors of the uterus by the extract. Between doses of 1-4 g/kg, the water extract of *M. cecropioides* was observed to be well tolerated in mice as no obvious signs of toxicity were observed on the animals.**

Key words: *Musanga cecropioides*, stem bark, oxytocic effect.

INTRODUCTION

Musanga cecropioides is found mostly in the tropical forests of Africa stretching from Guinea to Congo. Traditionally, the plant is used to induce labour, reduce elevated blood pressure and also to reduce high blood sugar (Irvine, 1961). In some parts of Edo and Delta States of Nigeria, the plant is used as anthelmintic and antidysentric (Gill, 1994).

Available literature reports revealed the scientifically established uterotonic effects of the leaf in rats (Kamanyi et al., 1992), the hypotensive effects of the water extracts of the leaf and stem bark (Kamanyi et al., 1991,1996; Dongmo et al., 1996; Ayinde et al., 2003) as well as antihyperglycaemic activities of the leaf extract (Kamanyi et al., 2000) in laboratory animals. Also, Lacaille-Dubois et al. (2001) reported the isolation of isovitexin, vitexin, cholorogenic acid, catechin and procyanidins from the leaf. According to the authors, the compounds are responsible for the hypotensive effect of the leaf extract via inhibition of angiotensin converting enzyme. Phytochemical studies reported the presence of kalaic acid in the stem bark and some other triterpenoid acids in the leaves, stem bark and the root wood **(** Lontsi et al., 1989, 1990, 1991,1992,1998).

In the present study, the probable effect of the water extract of the stem bark on rat uterus in the presence of standard antagonists like salbutamol and atropine and a uterine stimulant like oxytocin were examined.

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MATERIALS AND METHODS

Plant material

The stem bark was collected (between May- August) from the tree growing in the fields of the University of Benin, Ugbowo Campus, Benin City. The plant was identified by Mr. A. Abukakar of Department of Pharmacognosy, Faculty of Pharmacy, University of Benin while it was authenticated at Forest Research Institute of Nigeria (F.R.I.N., Ibadan) where an herbarium specimen No FHT106428 was deposited.

Processing of the plant material

After removing the debris, pieces of the bark were cut into smaller pieces and spread on the laboratory table to dry over a period of 4 – 5 days. Thereafter, they were transferred into a plant oven maintained at 50^{o}C for another one day before being reduced to powder using an electric mill. The powdered material was preserved in airtight containers.

Phytochemical screening

Qualitative tests for the presence of plant secondary metabolites such as alkaloids, tannins, flavonoids and saponin glycosides were carried out on the leaf powder using standard procedures (Trease and Evans, 1989).

Extraction of the plant material

2.0 kg of the powdered stem bark of *M. cecropioides* was step-wise extracted with aliquots of distilled water using the decoction method for 40 min. The extract obtained was concentrated under vacuum. The yield was 10.64 ± 0.86% of the original weight. It was preserved in the refrigerator at 4^{o}C until needed.

Drugs and chemicals

Atropine (Indus Pharma), Salbutamol, Oxytocin (G. Richter), D-glucose, potassium hydrogen phosphate, magnesium sulphate heptahydrate, calcium chloride dihydrate (Merck), sodium chloride, (BDH Chemicals), sodium hydrogen carbonate (T.G.I.Ltd) and potassium chloride (Cambian Chemicals) were used in the experiments.

Preparation of the animals

Wister albino virgin rats were obtained from the Animal House of the Department of Pharmacology and Toxicology, University of Benin, Benin-City where they were maintained on normal animal pellets (Livestock, Benin) and water *ad labitum*. They were pre-treated with 1 mg/kg stilboesterol 24 h before the experiment. The rats were sacrificed by a blow on the head followed by exsanguinations**.** After opening the peritoneal cavity, approximately 1.5 cm of the uterine horns were removed and cleaned free from fatty and connective tissues. Each uterine strip was suspended in 50 ml organ baths containing De Jalon's physiological solution (composed of, in g/litre: NaCl, 9.0; $NaHCO_3$, 0.5; glucose, 0.5; KCl, 0.42, $MgCl_2$, 0.006; $CaCl_2$. $2H_2O$, 0.08) maintained at 36±1^{o}C and aerated with 5% CO_2 in O_2.

The uterine strips were connected to Ugo Basile isometric force-displacement transducer connected to Ugo Basile (7050) unirecorder which measured the mechanic responses. The transducer was previously calibrated to establish a relationship between the force applied to the transducer and gauge deflection with a 500 mg corresponding weight. The preparations were allowed to equilibrate for at least 30 min before the administration of the extract or drugs.

Effects of the water extract and other drugs on the uterus

The effects of the extract was tested between 12.5 –1600 mg/ml and compared with the effects of oxytocin 0.02 – 0.16 i.u. Probable synergies between the extract and oxytocin were investigated while the effects of pre-treating the tissue with atropine (1-2 mg) or salbutamol (2 µg) on the activities of the water extract were also tested. The organs were washed thrice and allowed to rest for 20 min after each of extract or oxytocin administration.

Acute toxicity test

20 mice (20-22 g) of either sex were obtained from the Animal House of the Department of Pharmacology and Toxicology, University of Benin, Benin-City. The animals were randomly divided into four (4) groups of five (5) mice each. Prior to testing, the animals were fed with mice pellets and had free access to drinking water but starved for 12 h prior to testing. The first three groups were orally administered with 1, 2 and 4 g/kg of water extract, respectively. The fourth group was given distilled water (0.5 ml). General symptoms of toxicity and mortality were first observed for 24 h after which the animals were left for further 14 days for any sign of delayed toxicity.

Statistical analysis

Where applicable, the data obtained were analysed statistically by Students' t-test and Analyses of Variance (ANOVA). The level of significance was $P < 0.05$.

RESULTS

The stem bark was observed to contain saponins, tannins, flavonoids with no traces of alkaloids, anthraquinones and cyanogenetic glycosides.

Both oxytocin and the water extract of *M. cecropioides* stem bark induced a dose-related increase in force of contraction of the rat-isolated uterus. Addition of varying concentrations of oxytocin to the tissue elicited a dose-dependent uterine contraction. While 0.02 i.u produced a force of contraction of 1.45 ± 0.22 g, maximum contraction was obtained with the administration of 0.16 i.u. which produced a force of 1.9 ± 0.08 g although the variations in the responses to each concentration were observed not to be significantly different ($P > 0.05$). While 12.5 mg of the extract elicited a mean force of contraction of 1.10 ± 0.15 g, administration of 1600 mg produced a corresponding maximum uterine force of contraction equivalent to 2.53 ± 0.6 g (Figure 1). The variations in the force of contractions were observed to be significant after administration of 800 mg of the extract. The uterine contractile effect produced by 400 mg of the water extract was observed to be similar to that produced by 0.16 i.u.oxytocin.

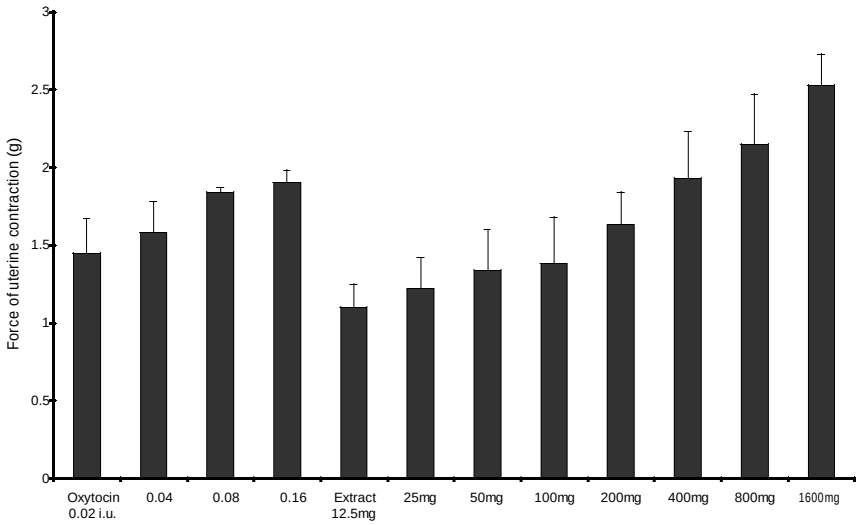

Figure 1. The contractile effects of oxytocin and the water extract of M. cecropioides on the rat uterus

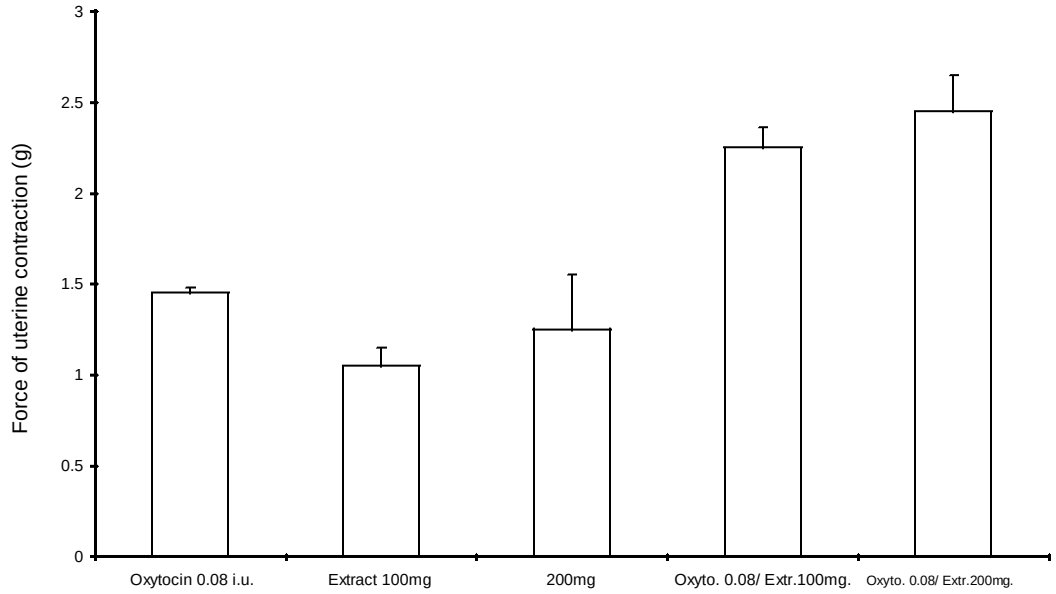

Figure 2. The effects of co-administration of oxytocin and the water extract of M.cecropioides stem bark.

Simultaneous administration of oxytocin and the water extract produced uterine force of contractions significantly higher than either oxytocin or water extract alone (Figure 2).

Administration of atropine did not evoke any effect on the activity of the uterus but significantly inhibited the contractile activity of the water extract in a competitive and dose-dependent manner. Pre-treating the tissue with 1 mg atropine decreased the uterine contraction of 1.22 ± 0.25 g elicited by the 25 mg of the water extract to 0.19 ± 0.01 g. Administration of 2 mg of atropine completely inhibited the contraction induced by the same concentration of the extract. Contractions induced by 100 and 400 mg of the extract were also significantly inhibited by 2 mg atropine (Figure 3).

Salbutamol was observed to show remarkable inhibition of uterine contraction elicited by both the oxytocin and water extract. While the contractile effect of 0.16 i.u. oxytocin was reduced by 63%, administration of 2 μg salbutamol before 25 mg/ml of the water extract produced no contraction. This inhibition was sustained with administration of 100 mg/ml of the extract. Also, 2 μg of the drug almost completely inhibited the uterine contractile effect of 400 mg/ml of the water extract (P <

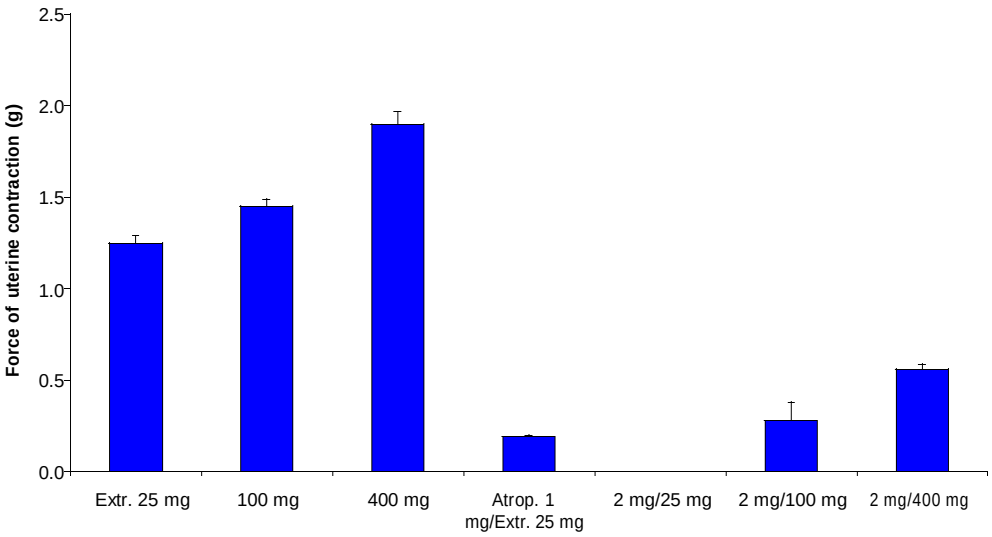

Figure 3. Inhibitory effect of atropine on the uterine contraction induced by the water extract of *M. cecropioides* stem bark. The force of uterine contractions produced by the water extract was significantly reduced when the tissue was pre-treated with atropine before administration of the extract.

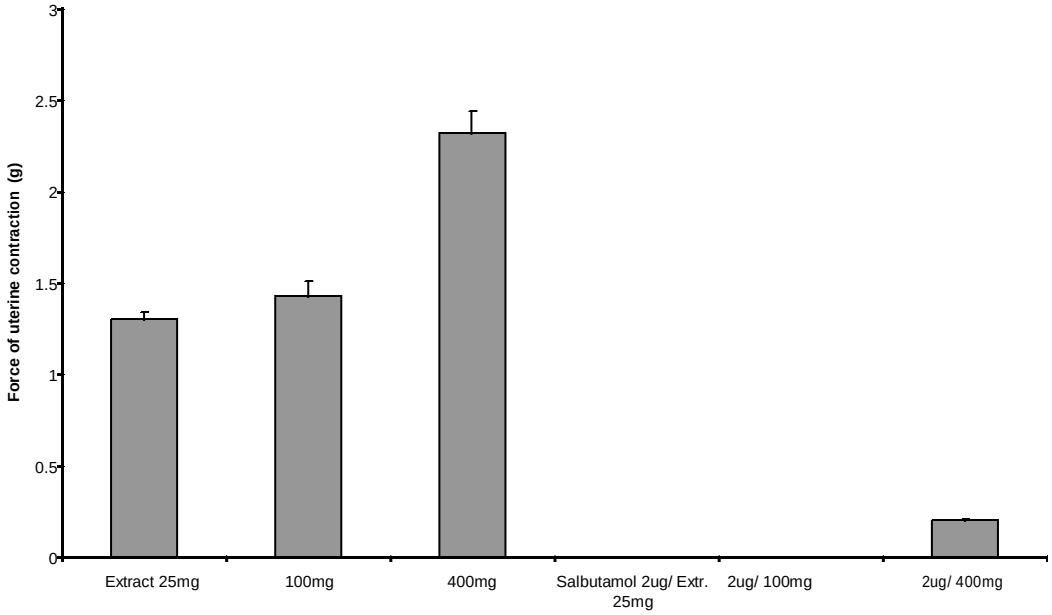

Figure 4. Inhibitory effects of salbutamol on the uterine contractile effect of the water extract of *M. cecropioides* stem bark. Pre-treating the tissue with salbutamol before administering the water extract resulted in almost complete inhibition of uterine contraction.

0.05) (Figure 4).

The water extract was well tolerated by the animals as no signs of acute toxic effects like restlessness, dizziness, excitation, food or water avoidance were observed after the administering the extract between 1-4 g/kg.

DISCUSSION

This work has established the oxytocic effects of the water extract of *M. cecropioides* stem bark. The fact that the contractile effect was dose-related showed the potency of the stem bark in contracting the uterus. In literature, the water extract of the leaf has been reported

to evoke uterine contraction in rats (Kamanyi et al., 1992).

The oxytocin exhibited higher potency than the water extract which may be attributed to the purity of drug while the extract in its crude and un-purified state contains different components, some of which may even have antagonistic effect. However, the contractile effect of 0.16 i.u. oxytocin was similar to the effect of 400 mg. The fact that the effects of oxytocin was augmented or potentiated by the presence of the extract suggests a probable synergism in the activities of the two. The extract may enhance the binding of oxytocin to the uterine tissues thereby causing a greater response or vice versa.

The use of medicinal plants to facilitate labour may be due to stimulation of muscarinic receptors in the uterine tissue or through the synthesis and release by prostaglandins well known to be myometrial stimulants reported to mediate the activity of most drugs that stimulate uterine contraction (Solloff, 1979). Although, this work could not establish the latter, the probable involvement of muscarinic receptors in the uterine contractile effect of the extract was supported by the significantly reduced contraction observed when the tissue was pre-treated with atropine before the water extract. Atropine is a well known antagonist of muscarinic receptors. Uterine contractile effects of the leaf extract of *M. cecropioides, Agapanthus africanus* and *Monechma ciliatum* were earlier reported to be significantly reduced in the presence of atropine (Kamanyi et al., 1992; Veale et al., 1999; Uguru et al., 1998).

The uterine contractile effect of the water extract of *M. cecropioides* stem bark was completely inhibited by salbutamol. The drug reduced the uterine contractile effect of oxytocin by 63% (result not shown); the inhibitory effect it showed on the extract was almost absolute. The higher inhibitory effect shown by salbutamol over atropine suggests probable higher concentration of salbutamol-sensitive receptors for the extract than atropine sensitive receptors. Salbutamol is known to be a $_2$ -receptor stimulating agent which has been reported to elicit marked decrease in uterine contractility even in dysmenorrheic women (Lalos and Joelsson, 1981).

Pharmacological activities observed in plant extracts are due to the presence of various chemical constituents they possess. The observed uterine contractile effect of the water extract of *M. cecropioides* stem bark are invariably due to the constituents it contains. The fact that the mice used in the acute toxicity test did not show any signs of toxicity indicates that the constituents of the water extract are well tolerated in the animals. More work is being carried out to ascertain and isolate the constituent(s) that may be responsible for the oxytocic effect of the stem bark.

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