

## Short Communication

# Smooth muscle relaxant activity of 3-carbomethoxypyridine from *Pyrenacantha staudtii* leaf on isolated rat uterus

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*Pyrenacantha staudtii* leaf (Icacinaceae) is a medicinal herb used in ethnomedicine for the treatment of threatened abortion and gastrointestinal disorders. Previous chemical work in our laboratory reported the isolation and characterization of 3-carbomethoxypyridine from the methanolic extract of this plant. The inhibitory effect of the crude extract on isolated rat uterus was also established. The objective of this study was to investigate the inhibitory activity of the isolated compound, 3-carbomethoxypyridine, on rat isolated uterine preparation. This was achieved by subjecting the compound to uterine preparation in an organ bath containing a physiological salt solution of De Jalon. The contractions were recorded with an FT03 transducer attached to an Ugo Basil recorder. The study has shown for the first time that 3-carbomethoxypyridine has a relaxant effect on the smooth muscle of the uterus promoting relaxation of the spontaneous and oxytocin-induced contractions.

**Key words:** 3-carbomethoxypyridine, smooth muscle, rat uterus, *Pyrenacantha staudtii*

## INTRODUCTION

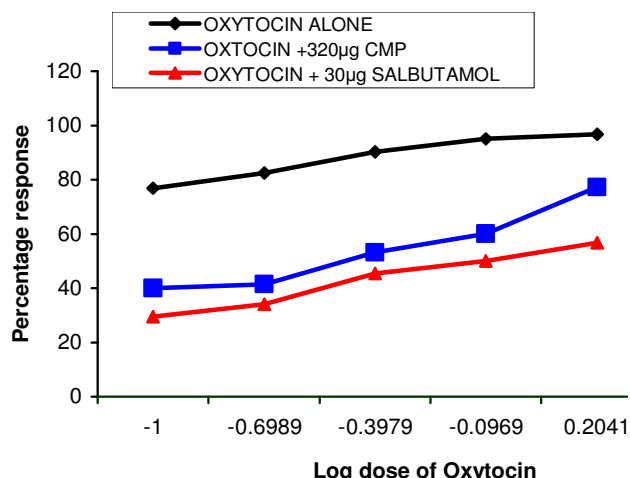
The use of herbal preparation by the populace in the treatment of diseases is assuming a wide dimension. In line with this, the World Health Organization (WHO) is strongly in support of traditional medicine (WHO, 1995). However, it will be scientifically useful if the active constituents are isolated and used in the treatment of ailments rather than the crude extract as it is currently being practiced. This will go along way in reducing the cumulative and harmful effects of other secondary metabolites in the crude extract to the vital organs and tissues of man.

*Pyrenacantha staudtii* is a woody climber found in the tropical forest and farm land. The leaves are intensively bitter. The plant is used in folk medicine for the treatment

of stomach colic, dysmenorrheal and threatened abortion (Hutchinson and Dalziel, 1966). The aqueous extract of the leaves have also been known to possess antimalarial activity (Mesia et al., 2005). It was also found to reduce gastric ulcer in experimental animals (Aguwa, 1983). Further research also showed that the crude methanolic extract showed inhibitory activity on the isolated rat uterus (Falodun et al., 2005).

This present study was undertaken to determine pharmacological activity (tocolytic effect) of 3-carbomethoxypyridine (CMP) isolated and characterized in our laboratory, using bioactivity guided principle (Falodun and Usifoh, 2006). The compound is reported to have a vasodilatation effect on the skin of humans (Leopold and Lippold, 1995). Recent study also showed that 3-carbomethoxypyridine (methyl nicotinate) is a useful pharmacological tool in inducing skin inflammation, using a new methodology based on laser-Doppler velocimetry (Duteil et al., 1990). A perusal of the literature revealed

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**Figure 1.** Effect of 3-carbomethoxypyridine, oxytocin and salbutamol on the isolated rat uterus.

no previous work has been executed on the uterine relaxation effect of 3- carbomethoxyl pyridine.

## MATERIALS AND METHODS

### Animal preparation

Normal female Wistar rats weighing about 150-160 g were pretreated with 1 mg/kg of stilbesterol 48 h prior to the actual experiment. The rats was anesthetized and exsanguinated. The abdomen was opened and the two horns of the uterus carefully isolated, freed of mesenteric fat and a 1 cm piece was mounted in a 50 ml organ bath containing De Jalon solution with the following chemical composition: NaCl, 9 g/l; NaHCO<sub>3</sub>, 0.5 g/l; D-glucose, 0.5 g/l; KCl, 0.402 g/l; CaCl<sub>2</sub>·2H<sub>2</sub>O, 0.08 g/l. The tissue was aerated with 95% oxygen 5% carbon (IV) oxide at 37°C. The spontaneous contraction of the uterus was recorded with FT 03 transducer connected to an Ugo basile recorder (7075). The transducer was previously calibrated to establish a relationship between the force applied to the transducer and the gauge deflection (500 mg). The tissue was allowed to equilibrate for 30 min before the commencement of the experiment. The dose response curves of oxytocin induced contractions were obtained and the effect of 3- carbomethoxypyridine and that of the positive control (salbutamol) were determined.

### Statistical analysis

All results are expressed as the mean of five experiments ± SEM. The statistical package used was SAS, 1994 Users guide, Version 8.2. SAS Institute Inc., Cary, NC, USA. The statistical significance (P<0.05) of differences between means was assessed by an analysis of variance (ANOVA) followed by Duncan's multiple range test.

## RESULTS AND DISCUSSION

Evaluation of the data indicates that there was a significant (P<0.05) reduction in the contraction produced

by salbutamol and solution of 3-carbomethoxypyridine. The results show that various concentrations of oxytocin (0.1 to 1.6 ml of 1 IU) produced a significant contraction of the rat uterus, with maximum response been produced at 1.6 ml of 1 IU. There was also a significant decrease in the contraction produced by 0.32 mg/ml of 3- carbomethoxypyridine with a decrease in the spontaneous contraction of the uterine smooth muscle (Figure 1). The observed inhibition of the contractions of the rat uterus may be due to the reduction or abolition of the spontaneous contraction. The result in Figure 1 also showed a comparative inhibitory activity produced by the compound and salbutamol which is used clinically in the treatment of threatened abortion in gravid uterus.

However, the mechanism involved in the inhibition of the smooth muscle of the uterus is presently unclear. Further work will need to be carried out to establish the mechanism involved. Although direct extrapolation of results from animal models cannot be made to humans, results obtained are however indicative of the likely trend. The present study therefore suggests the inhibition of the rat uterine contractions produced by 3- carbomethoxypyridine at a dose of 0.32 mg/ml be further investigated.

In conclusion, 3- carbomethoxypyridine has a relaxant effect on uterine smooth muscle; this pharmacological activity is consistent with the popular use of this plant for the treatment of threatened abortion (misabortion). Most importantly it also lends support to vasorelaxant effect of 3- carbomethoxypyridine in the blood vessels of the skin. This study reveals for the first time the tocolytic property of 3- carbomethoxypyridine.

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## REFERENCES

- Aguwa CN, Mittal GC (1978). Study of Anti-ulcer Activity of Aqueous extract of the leaves of *Pyrenacantha staudtii* (Icacinaeae) using various models of experimental gastric Ulcer in rats. Eur. J. Pharmacol. 74: 215 -219.
- Duteil L, Queille C, Poncet M, Ortonne JP, Czernielewski J (1990). Objective assessment of topical corticosteroids and no -steroidal anti-inflammatory drugs in methyl- nicotine induced skin inflammation. Clin. Exp.Dermatol., 15 ( 3): 195-199.
- Falodun A, Usifoh CO, Nworgu ZAM (2005). Phytochemical and Active column fractions of *Pyrenacantha staudtii* on isolated rat uterus. Pak. J. Pharm. Sci. 18 (4): 31 – 33.
- Falodun A, Usifoh CO, Nworgu ZAM (2006). Isolation and characterization of 3-carbomethoxypyridine from the leaves of *Pyrenacantha staudtii* (Hutch and Dalz) Icacinaceae. Acta Polonia (in press).
- Hutchinson J, Dalziel JM (1966). Flora of West Trop. Afr. Crown Agents for Overseas governments and Administration , London 1 (1) : 72.
- Leopold CS, Lippold BC (1995). Enhancing effects of lipophilic vehicles on skin penetration of methyl nicotine invivo. J Pharm Sci. 84 (2) 195-198.

Mesia G K, Tona G L, Penge O, Lusakibanza M, Nanga T M, Cimanga R K, Apers S; Van Miert S, Totte J, Pieters L, Vlietinck AJ (2005). Antimalarial activities and toxicities of three plants used as traditional remedies for malaria in the Democratic Republic of Congo: *Croton*

*mubango*, *Nauclea pobeguinii* and *Pyrenacantha staudtii*. *Annals of Tropical Med. and Parasitol.* 99 (4) 345 – 57.  
World Health Organization (WHO) (1995). *The World Health Reports. Bridging the gap* WHO, Geneva; 1 118.