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# Influence of Atropine and Loperamide on Reduced Intestinal Transit Induced by *Calotropis procera* Latex in Rats

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## *ABSTRACT*

*The effects of Calotropis procera latex alone and in the presence of loperamide and atropine on intestinal transit in rats were determined to elucidate the action of C. procera on intestinal transit. Six groups of rats containing ten rats per group were used. Each rat in the control group (I) received 0.5 ml of normal saline. Each rat in groups II, III, and IV received 0.25 ml/100 g, 0.5 ml/100g and 1.0 ml/100g of C. procera latex respectively. Thirty minutes before the administration of 0.25 ml of latex of C. procera, each rat in groups V and VI received 0.4 mg/100g atropine sulfate and 0.1 mg/100g loperamide hydrochloride respectively. Intestinal transit was measured in all animals by charcoal meal test and was expressed as the percentage of the distance traveled relative to the entire length of the intestine from the pyloric junction to the anal orifice. The mean transit point of the dye in the control group was 85.19 ± 8.51%. For Calotropis procera treated rats, the mean transit points were 68.47 ± 6.37%, 54.49 ± 6.67% and 25.06 ± 4.79% for 0.25 ml/100g, 0.5 ml/100g and 1.0 ml/100g of the latex respectively. The mean transit points in the groups pretreated with 0.4 mg/100 g atropine (Group V) and 0.1 mg/100 g loperamide (Group VI) were 55.29 ± 5.09% and 66.87 ± 6.20% respectively. The results showed that the latex of Calotropis procera inhibited intestinal motility and its action was potentiated by atropine and loperamide. This inhibitory action is contradictory to the observation of diarrhea in fed animals* ***(Afr. J. Biomed. Res. 9: 125 - 128, May 2006)***

**Keywords:** *Calotropis latex, Intestinal transit, Atropine, Loperamide*

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## INTRODUCTION

The use of parts and products of *Calotropis procera* for the treatment of variety of ailments including fever, joint pain, muscular spasm, constipation, and gastric disorders (Diaziel, 1937; Derasari, 1965; Iwu, 1993) abound in literature. Diarrhea has been reported as one of the toxic signs of the latex of *C. procera* in animals (Mahmound *et al*., 1979; Dada *et al*., 2002). Diarrhea is a common and often dangerous problem especially in young animals. It was once thought that diarrhea was the result of excessive motility in the intestinal tract; that intestinal contents were rushed through prematurely in a sequence of muscular spasm. Drug usage has been popular in diarrhea. Atropine is sometimes included in diarrhea remedies and also employed in various forms of intestinal colic by virtue of its depressant effect on nerve-endings to smooth muscle (British Pharmacological Codex, 1911). Loperamide is an opioid used also in the treatment of diarrhea (Coupar, 1987; Kroma, 1988; Eghianruwa, 2002). These drugs have inhibitory effects on both the intestinal smooth muscle contraction and gland secretion through different mechanisms.

The effects of *C. procera* on several smooth muscles have been reported. It has been observed to stimulate the uterus (Saha *et al*., 1961; Chopra *et al*., 1965). The plant has also been described as abortifacient (Saha *et al*., 1961; Al-Robai et al., 1993). Since *C. procera* is used in traditional medicine for various gastrointestinal ailments, we thought it necessary to investigate the effect of the latex of *C. procera* on intestinal transit.

## MATERIALS AND METHODS

*Animals and Management*

Sixty (60) albino rats of both sexes weighing between 100-130g were used for this study. The rats were of different ages and obtained from the Department of Veterinary Physiology and Pharmacology, University of Ibadan. The animals were kept in metal cages in a well-ventilated animal house and fed with commercially formulated rat feed. Water was given *ad libitum*. The cages and feeding troughs were cleaned daily. The animals were allowed to acclimatize for one week before the commencement of experiment.

*Extraction of the Latex*

The latex of *Calotropis procera* was obtained from several plants located at the University of Ibadan campus in February 2004. The plants were first identified and authenticated by the Department of Botany and Microbiology, University of Ibadan. Latex was obtained by breaking the leaf stock and allowing the latex to flow into a glass beaker. Fresh latex was obtained in the morning on the day of experiment.

*Preparation of Dye*

The dye was prepared by a modified method of Uwagboe and Orimilikwe [1995]. Ninety five ml of 10% aqueous suspension of charcoal [BDH, England] was mixed with 5 ml of giemsa stain [BDH, England].

*Experimental Procedure*

Twenty four hours before experiment, food was withdrawn from the animals in the group to be used; but water was allowed until the morning of experiment. The rats were randomly divided into six groups (I – VI) of ten rats per group. Each rat was weighed to determine the dose of the latex and drugs to be administered. To each animal in group I [control], 0.5 ml of normal saline was administered orally using an oral cannula. After a period of 30 minutes, 0.5 ml of dye was given orally. The rats were then kept in their cage for 1 hour after which they were euthanized with chloroform.

Each animal in group II received 0.25 ml/100g of the latex of *C procera* orally administered through an oral cannula. Thirty minutes later, each animal received 0.5 ml of dye, which was also administered orally using an oral cannula. The rats were then kept is their cage for 1 hour after which they were sacrificed with chloroform. Animals in groups III and IV received the same treatment as those in group II except for the dose of *C. procera* which in these cases were 0.5 ml/100g and 1.0 ml /100g for groups III and IV respectively.

Each animal in group V received 0.4 mg/100g of atropine sulfate. This doses of atropine and loperamide were chosen from pilot experiments. After a period of 30 minutes, 0.25 ml/100g of latex was administered to each rat. Thirty minutes following administration of latex, 0.5 ml of dye was administered. The animals were euthanized using chloroform after 1 hour following administration of the dye. Animals in group



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VI received 0.1 mgl/100g of loperamide hydrochloride followed in 30 minutes by 0.25 ml/100g of the latex of *C. procera* and then 0.5 ml each of dye after another 30 minutes. All administrations were made orally using an oral cannula. The animals were euthanized using chloroform after 1 hour following administration of the dye.

Following euthanasia, the peritoneum of each rat was opened and the whole length of the intestine from the pyloric junction to the anus was stretched out and measured using a piece of cotton thread and a tape rule. The point reached by the dye was also measured from the pyloric junction and recorded for each rat.

Analysis of Results

For each rat, the distance reached by the dye from the pyloric junction was calculated as a percentage of the entire length of the intestine. This was regarded as the transit point of the dye with each given dose of the latex, latex plus atropine, latex plus loperamide and saline. The means of the percentage transit points and the standard deviations were calculated for each group. The levels of significance were determined by using Student 'T' test and a P value of $< 0.05$ was taken as significant. Graphic representations of the data were obtained using the computer software, Microsoft Excel.

## RESULTS

The latex of *Calotropis procera* produced dose-dependent decrease in transit point. The mean transit point and standard deviation in control animals was 85.19 ± 8.51%. In the group that received 0.25 ml of *C. procera* latex, the mean transit point fell significantly ($P < 0.05$) from 85.19 ± 8.51% of control to 68.47 ± 6.37%. The mean transit points in the groups that received 0.5 ml and 1.0 ml *C. procera* latex were 54.49 ± 6.67(%) and 25.06 ± 4.79(%) respectively. These reductions in transit points were significant ($P < 0.05$). These data are represented in figure 1.

*Influence of Atropine and Loperamide pretreatment*

In the group pretreated with 0.4 mg/100g atropine (Group V), 0.25 ml *C. procera* latex produced a mean transit point of 55.29 ± 1.09(%). This value was significantly ($P < 0.05$) lower than that obtained in the group that received 0.25 ml of *C. procera* latex without pretreatment. In group (VI), which was pretreated with 0.1 mg/100g loperamide, 0.25 ml *Calotropis* procera latex produced a mean transit point of 66.87 ± 1.27%. This value was minimally but not significantly ($P < 0.05$) lower than that obtained in the group that received 0.25 ml of C. procera latex without pretreatment (Figure 2).

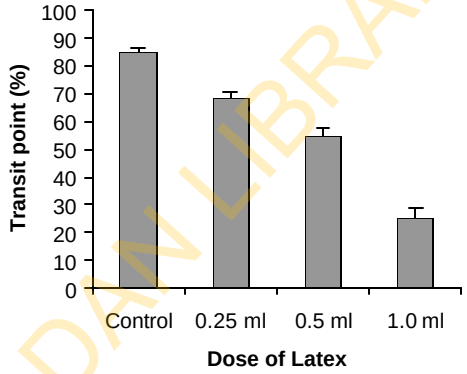


**Fig. 1**
**Effect of *C. procera* latex on Intestinal Transit in Rats**

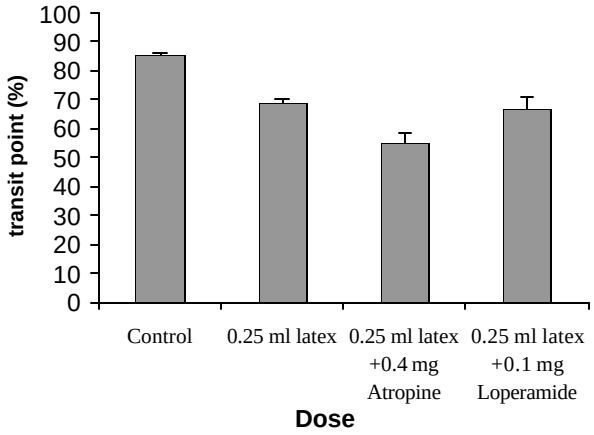


**Fig. 2**
**Influence of Atropine and Loperamide on action of *C. procera* latex**

## DISCUSSION

*Calotropis procera* latex caused a dose-dependent decrease in mean transit point thus, increasing transit time. This observation is associated with reduced intestinal motility or increased muscle tone. This result contradicts those of Dada *et al.*, (2002) in which

diarrhea was observed as one of the effects of *C. procera* latex in rats. Other studies have also reported diarrhea caused by *Calotropis procera* (Mahmound *et al*., 1979; Al-Robai *et al*., 1993). This apparent contradiction may be due to differences in methodology. In this study, rats were starved for 24 hours before the experiment, while in the study carried out by Dada *et al*., (2002) the rats were fed. It has been shown that feeding alters intestinal motility (Schemann and Ehrlein, 1986). The pattern of contraction has also been reported to vary with the type of meal (Schang et al., 1978; Schemann and Ehrlein, 1986).

Atropine and loperamide potentiated the action of *C. procera* latex on intestinal transit. Pretreatment with both drugs caused a further reduction in the mean transit points produced by *C. procera*. The level of potentiation was higher with atropine than loperamide. While loperamide has innate activity through opioid receptor stimulation, atropine is a pure competitive antagonist. Hence, loperamide may have reduced transit time as a direct result of its innate pharmacological action. The potentiating effect of atropine indicates that *C. procera* may be acting through cholinergic pathways. The rather contradictory reports of diarrhea on one hand, and reduced motility on another, may also indicate more than one mechanism. For instance many of the adverse effects such as tachycardia (Mahmound *et al*., 1979), reduction in urine flow are indications of direct anticholinergic activities while those like excessive salivation (Chopra *et al*., 1965), diarrhea (Chopra *et al*., 1965; Dada *et al*., 2002) are indications of cholinergic action resulting from spared acetylcholine or direct cholinergic receptor stimulation. Indirect cholinergic action resulting from spared acetylcholine may also be responsible for its insecticidal action (Watt and Breyer-Brandwilk, 1962; Iwu, 1993).

Results from this study in comparison with earlier reports indicate that the use of *C. procera* latex as a purgative may not produce required effects in all cases.

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