

# DEPRESSANT ACTION OF AN EXTRACT OF VERNONIA CINEREA

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## SUMMARY

*The effect of an aqueous extract of Vernonia cinerea (VX) on mice was determined. It is suggested that VX contains a depressant agent whose primary effect is that of analgesia.*

## INTRODUCTION

In Malaysia, Vernonia cinerea is a commonly found weed. It is reported to have sedative actions and as such is included in several traditional herbal preparations used for insomnia and related ailments (Majallah Tamat Latehan Sinsch China, 1976). Most preparations of Vernonia cinerea are concoctions where the plant is boiled in water. Any active ingredient is therefore presumably water soluble and heat stable. This paper describes an attempt to determine whether an aqueous extract of Vernonia cinerea contains any pharmacologically active depressant agent.

## MATERIALS AND METHODS

Freshly picked Vernonia cinerea leaves were blended in water using approximately 400 ml water

per 100g wet weight leaves. After aqueous insoluble residues were removed, saturated lead acetate solution was added to the filtrate to precipitate tannins. Saturated ammonium sulphate was next added to the clear solution which was warmed to coagulate proteins and precipitate excess lead as lead acetate. After filtration, the aqueous solution was evaporated to dryness under partial vacuum. The residues were extracted with methanol and then filtered. This methanol extract was distilled to dryness under partial vacuum leaving a syrupy dark brown liquid (VX). Appropriate dilutions of VX with normal saline were prepared for pharmacological testing.

VX was administered intraperitoneally (IP) to male albino mice weighing 25-35 g.

The effect of VX on barbiturate-induced sleeping time was determined according to the method of Winter (1948). Either VX or saline control was administered IP 10 minutes before 40 mg/kg pentobarbitone sodium IP or VX or saline control was administered at the same time in a single injection with 35 mg/kg pentobarbitone sodium. The duration of loss of righting reflex (sleeping time) was recorded.

Gross locomotor activity of groups of four mice was recorded using an Animex activity meter, type DSE. All experiments on activity were carried out between 8.00 a.m. and 10.00 a.m. Recordings began immediately after IP administration of VX saline control.

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Response to 'painful stimuli' was measured using the hot plate method of Wolfe and MacDonald (1944). Mice were individually placed on a hot plate at 50°C, 5, 15 and 25 minutes after IP administration of VX or saline control. The reaction time was taken as the time between first contact with the hot plate and when the mice licked their paws or jumped. Animals were removed from the hot plate if they had not responded within 30 seconds, this time therefore being the maximum.

To determine the lethal dose 50 (LD50) doses of 1000, 1200, 1400, 1700, 2000 or 2500 mg/kg VX were administered IP to groups of 10 mice. One hour after VX administration the percentage mortality at each dose was recorded. All animals which survived for more than one hour remained alive for the next 24 hours. The LD50 was determined by carrying out probit analysis followed by regression analysis of the log dose to percent mortality relationship (Fisher and Yates, 1963).

## RESULTS

**Gross observations:** Lethal doses (above 2500 mg/kg) of VX caused reduction in motor activity followed by signs of progressively increasing depression. Approximately 4 minutes after VX injection such doses caused convulsions, but did not appear to cause unconsciousness, followed by death. The effect of just sublethal doses (approximately 1200 mg/kg) followed a similar course with initial reduction in activity, followed by minor convulsions. Approximately 10 minutes after VX injection some, but not all, animals lost their righting reflex. Doses of 500 mg/kg or less produced no obvious gross alteration in mouse behaviour. Mice given 500 mg/kg remained alert and active, did not exhibit ataxia and did not show any increased tendency to group together.

**Barbiturate-induced sleeping time:** As shown in Fig. 1, when 1000 mg/kg VX was administered 10 minutes before 40 mg/kg pentobarbitone sodium there was no significant increase in sleeping time. However the animals treated with VX appeared to be more deeply anaesthetized during the initial few minutes of unconsciousness as compared to saline-

treated control animals. When animals received VX at the same time as 35 mg/kg pentobarbitone sodium, 500 mg/kg VX had no significant effect but 1000 mg/kg VX produced a significant increase ( $P < 0.05$ ) in sleeping time as compared to controls.

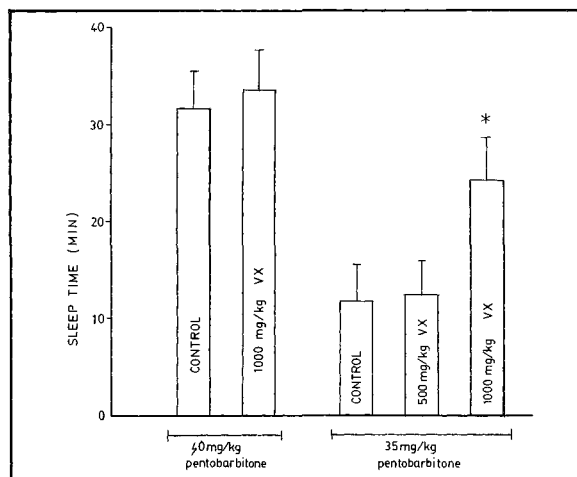


Fig. 1: The effect of Vernonia extract on mice sleeping time induced by pentobarbitone sodium. Vertical bars = s.e.,  $n = 12$ . Star indicates significant difference from control ( $P < 0.05$ ).

**Mouse locomotor activity:** As shown in Fig. 2, 1000 mg/kg VX caused a significant reduction in mouse locomotor activity as compared to saline-treated controls. The effect was significant only for 20 minutes.

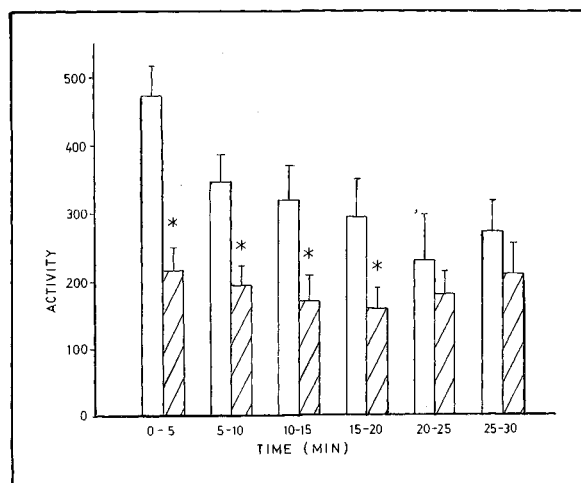


Fig. 2: The effect of Vernonia extract on gross locomotor activity of groups of four mice. Open columns = control, shaded columns = 1000 mg/kg VX. Vertical bars = s.e.,  $n = 5$ . Stars indicate significant difference from control ( $P < 0.05$ ).

Hot plate response: As shown in Fig. 3, VX caused a significant increase in reaction time to the hot plate. It is interesting to note that doses of 250 mg/kg were effective and significant effects were still apparent 25 minutes after VX administration.

Lethal dose 50: Calculated by probit and regression analysis (Fisher and Yates, 1963), the LD50 of VX was 1874 ( $\pm$  s.e. 122) mg/kg.

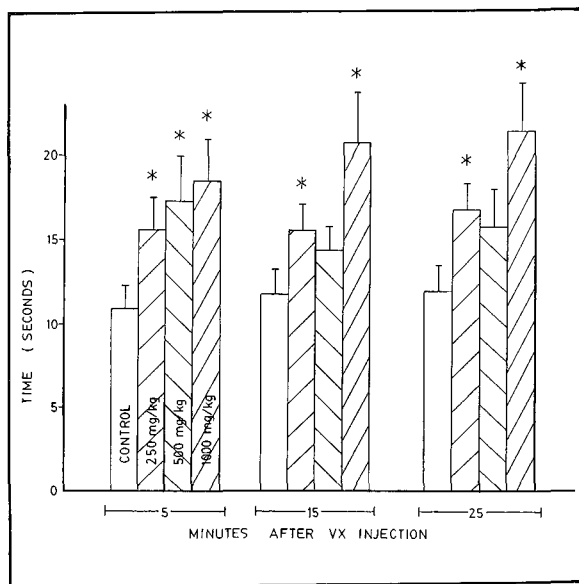


Fig. 3: The effect of 250, 500 and 1000 mg/kg Vernonia extract on mouse reaction time to a hot plate at 50°C. Vertical bars = s.e., n = 10. Stars indicate significant difference from control ( $P < 0.05$ )

## DISCUSSION

Conclusions drawn from the results have to take into account the LD50 of VX. Actions of drugs given in near lethal doses cannot be taken as a reliable guide to their true pharmacological action as the effects manifested could be only, or at least altered by, toxic manifestations (Mantegazza and Piccinini, 1966). For instance, near lethal doses of VX could sometimes cause the loss of righting reflex but doses of 1000 mg/kg could not. This suggests that VX probably does not contain a sedative agent.

The observation that 1000 mg/kg VX prolonged the sleeping time induced by 35 mg/kg but not by 40 mg/kg pentobarbitone sodium suggests that VX

does have a centrally acting depressant action but indicates that the duration of action is short. This is supported by the observation that VX caused a statistically significant reduction in gross locomotor activity and that the effect on activity was only apparent for a period of 20 minutes following administration of VX.

VX cause a significant increase in hot plate reaction time. Doses of 250 mg/kg produced a significant increase and this effect was still apparent (and statistically significantly different from controls) 25 minutes after VX administration. Thus the hot plate reaction time was increased by a dose of VX which had no observable effects on any other monitored mouse reaction.

Effects produced by VX at a dose of 1000 mg/kg might be considered to be in part toxic manifestations as this dose is over half the LD50 however 250 mg/kg is considerably less being about one seventh of the LD50. Thus the increase in hot plate reaction time can reasonably be considered a true pharmacological effect. It is therefore suggested that the active agent in VX may be an analgesic agent.

Though these results are preliminary in nature, they may suggest that the use of aqueous extracts of Vernonia cinerea for its sedative effect may entail hitherto unknown dangers since effective sedative actions in mice appear to occur only at relatively high doses but that the plant may contain an agent which might be of use at relatively lower (and therefore safer) doses for the control of pain.

## REFERENCES

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