GASTROINTESTINAL EFFECTS OF CROTON TIGLIUM IN EXPERIMENTAL ANIMALS
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Abstract: Croton tiglium used as a cathartic in Ayurvedic system of indigenous medicine, was investigated for its effects in experimental animals. 50% EtOH extract of the dried nuts of the plant was used of the study. The extract exhibited a dose dependent cathartic effect in albino rats, the extract also showed an increase to gut movement with an increased contractile movement on rabbit jejunum, partially blocked by atropine these preliminary findings suggest tat the ethanol extract of the croton dried nuts elicit a purgative effect by increasing the gut motility, partially via muscarinic receptor activation.

INTRODUCTION

Croton tiglium Linn (Euphorbiaceae) is a medicinal plant seen throughout India, Burma and Ceylon. Seeds, leaves, bark ad root are said to be used in traditional medicine for various ailments. In ayurvedic system of medicine the expressed Croton seed oil has been used in minute doses in dropsy, obstinate constipation, intestinal obstruction, lead poisoning, cerebral affections like apoplexy convulsions insanity and in high blood pressure. Phytochemical studies reported earlier sow that the seeds contain a fatty fixed oil, the croton oil which is composed of (i) crotonoleic acid, the active principle, (ii) tiglic acid or methyl crotonic acid, (iii) Crotonal, a non-purgative fraction, (iv) several volatile acids and (v) fatty acids crotonoleic acid is a mixture of croton resin with inactive fatty acids. The activity of carton oil as a vesicant externally and purgative internally is attributed to the presence of crotonoleic acid which is said to occur in free state. It is freely soluble in alcohol and in combination as a glyceride this free acid is a powerful irritant to skin and intestine1.

In the present study an attempt as been made to evaluate scientifically the proposed action of croton seed as a purgative in traditional medicine and also to detect its possible toxicity, using suitable experimental conditions.

Material and Methods:

Plant Materials: Corton berries were collected by the survey of medicinal plants unit, Trivandrum (Kerala, India) from the forest area in Jan. 1995, were pharmacognostically identified and the voucher specimen was kept at the herbarium of the above institute.

Preparation of extract:

Berries were dried in shade for few days, then powdered coarsely before use, weighed quantity of this powder was successively
extracted with 50% EtOH in a Soxhlet apparatus for 48 h with slow leading. The hydro-alcohol extract thus obtained was concentrated by evaporation the solvents the residual mass thus obtained was weighed n a chemical balance and the yield was found to be 15.8 % (w/w). This crude alcohol extract was made soluble in dist. Water and used for experimental studies.

Animals: Albino mice (20-25g) and Holtzman rats (200-250g) of either sex maintained in standard conditions of temperature (20-32°C), relative humidity and light were used. They were fed on Hind lever feed pellets and water ad libitum.

Pharmacological tests:

a) Acute toxicity:

Mice of either sex in groups of 6 or more were used for each dose level. The extract was administered orally (p.o) or intraaperitoneally (i.p) in various dose levels form 10mg to 1000 mg/kg. The behavioural effects and mortality were observed for 24th LD50 was determined according to Miller and Tainter2.

b) Purgative active:

The rats of either sex were used for the study. They were fasted for 6h before the experiments and animals that produced semisolid motion within this period were removed. Thus elected animals were randomly allocated to 7groups of 5 animals or more each and animals in each group received respective drug or vehicle in various dose levels, C.tiglium extract was tested at doses form 100 to 500 mg/g. Bisacodyl i.p (Dulcolax German remedies Ltd, Goa) as a standard laxative was tested at the dose of 10 and 20 mg/kg while a control group received only saline (10 ml/kg. All treatments were give by gavage. Then, the animals were kept separately in individual cages lined with white blotting paper at the bottom. Te total number of wet faces produced by each was observed of 24. Moreover the onset and duration of purgative effects were noted3.

c) Gastro – intestinal motility (Charcoal meal test):

Forty adult mice of either sex were divided into 5 groups. They wee starved for 24 h prior to experiments but had free access to water. Animals treated with the test extract were dosed with 250 and 500 mg/kg while the other groups received Bisacodyl at 10 and 20 mg/kg. The control groups received saline (10ml/kg). All treatments were given b gavage. Five min. after drug administration 0.5 ml of a 5% charcoal suspension was administered to each animal orally. Min later the were sacrificed and the abdomen opened. The distance of the small intestine (from the pylorus to caecum) traveled b the charcoal plug was determined4.

d) Effect on isolated Rabbit jejunum:

Segments of fresh rabbit jejunum were suspended in Tyrode solution in a 10ml organ bath. The solution was aerated and maintained at 37°C. The tissue was suspended in the solution and allowed 30 min as resting period. Histamine and acetyl choline were used as agonist in the concentration of 2/ug /ml bath fluid. The effect of the test extract in varying dose levels (100/ug/ml bath fluid) were recorded and compared with that of agonist. Atropine sulphate (2/ug/ml) and chlorphenaramine maleate (2ug/ml) were used as antagonists.
RESULTS:

Acute Toxicity: Acute toxicity test in mice sowed no toxicity and mortality up to 1000 mg/kg on intraperitoneal administration. The LD50 was found to be 89.12 ± 26.62 mg/kg (i.p).

Purgative activity:

The comparative cathartic efficacy of *C. tiglium* extract and bisacodyl in albino rats is sown in table I. A dose dependent effect was noticed with the onset of action at about 2h after treatment. The effect lasted for about 24h in the case of bisacodyl the onset of effect was at about 3h after treatment, while the effect lasted for 12h.

Gastrointestinal motility:

The results of the charcoal meal test are reported in Table 2. Croton extract at 250 mg/kg produced a significant increase in gut movement as compared to saline controls (p<0.01). Bisacodyl did not exhibit any significant effect on gut movement.

Effect on isolated rabbit jejunum:

Extract of *C. tiglium* exhibited dose dependent contractile movements up to 1mg/ml. This contractile effect was comparable to that of agonists. But atropine at 2 ug/ml partially lacked the spasmogenic effect of the extract at 1 mg/ml whereas the antihistamine, chlorphenaramine maleate at the above dose did not block the contractile effect of *Croton* extract.

DISCUSSION:

Above investigations clearly indicated that the test extract possessed significant purgative effect in experimental animals this activity may be due to the presence of the irritant active principle, the crotonoleic acid in the ethanol extract of croton seeds. Crotonoleic acid which is a mixture of croton resin with inactive fatty acids may act as a powerful irritant to the intestinal mucosa and thereby causing enteropooling effect. In vitro studies using the extract showed the presence of muscarinic activity. Hence it can be presumed that the stimulation of the gut caused by the extract may partly be due to the activation of muscarinic receptors present. However the present findings may be of support to the use of Groton seed oil as a drastic purgative in traditional medicine.

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Table 1: Cathartic effect or oral treatment with ethanolic extract of *C. tiglium* nuts in rats.

| Drug            | Dose (mg/kg p.c) | Mean distance travelled (%) ± SEM |
|-----------------|------------------|-----------------------------------|
| *C. tiglium* ext| 250 (8)          | 70.17 ± 7.14                      |
|                 | 500 (8)          | 43.11 ± 2.52                      |
| Bisacodyl       | 10 (8)           | 23.92 ± 3.64                      |
|                 | 20 (8)           | 30.30 ± 2.65                      |
| Saline          | 10 ml (8)        | 35.97 ± 4.33                      |
Figures in the parenthesis show number of rats in the group
*p<0.01

Table -2 Effect of oral treatment with ethanolic extract of *C. tiglium* nuts on intestinal movements in rats.

| Treatment      | Dose (mg/kg p.c) | Number of wet feces ± SEM | % of rats sowing cathartic effect |
|----------------|------------------|---------------------------|----------------------------------|
| *C. tiglium ext* |                  |                           |                                  |
| 100 (5)        |                  | 0.20 ± 0.20               | 20                               |
| 200 (5)        |                  | 2.40 ± 0.97*              | 60                               |
| 250 (10)       |                  | 2.90 ± 0.65**             | 70                               |
| 500 (10)       |                  | 3.20 ± 0.58**             | 90                               |
| Bisacodyl      | 10 (5)           | 1.40 ± 0.67               | 80                               |
|                | 20 (5)           | 1.40 ± 0.31**             | 90                               |
| Saline         | 10 ml (10)       | -                         | -                                |

Figures in the parenthesis show number of rats in the group.
*p<0.05      **p<0.01

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