Neuroleptic-Like Properties of the Chloroform Extract of Maytenus obtusifolia Mart. Roots

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The effects of the chloroform extract of Maytenus obtusifolia Mart. roots on locomotor activity, catalepsy test, amphetamine-induced toxicity and active-avoidance test were studied. The results revealed that the extract caused a decrease in spontaneous activity and induced catalepsy in mice up to 240 min. The extract significantly protected the mice against amphetamine-induced toxicity and decreased the conditioned response in rats, in a dose-related manner. The results suggest that the chloroform extract of Maytenus obtusifolia Mart. possesses neuroleptic-like properties.

Key words Maytenus obtusifolia; neuroleptic activity; catalepsy

The species of Maytenus (Celastraceae) are effective against several kind of sickness including cancer, gastric ulcers, dyspepsia and also useful as an antibacterial and anti-inflammatory.1–3) Sesquiterpenes, triterpenes, quinone-methide and sesquiterpene pyridine alkaloids have been identified in these species.1,4) Maytenus obtusifolia Mart. is a plant found in many states of the Northeast and South-east of Brazil, which is used in traditional medicine for the treatment of ulcer.5) A chemical study of chloroform extract (CE) of this plant showed the presence of triterpenes of the series friedelan, oleanane, ursane and one pyranquinoline alkaloid.6) It is known that terpenes have actions pharmacological on animal behavior.7) Therefore it was made a preliminary screening which showed that the CE possesses a CNS depressant effect. In the present study, we report the neuroleptic activity of the CE of Maytenus obtusifolia Mart. roots.

MATERIALS AND METHODS

Plant Material Maytenus obtusifolia roots were collected in João Pessoa, Paraíba, Brazil, in February 1995. The plant was identified by Dr. Maria de Fátima Agra and a voucher specimen (3230) was deposited in the Herbarium of the JPB/Paraíba University.

Extraction Procedure The dried and powdered roots (2950 g) were extracted with 95% ethanol (12.0 l) in a soxhlet extraction apparatus. The ethanolic extract obtained was suspended in the mixture ethanol–water (7 : 3; 0.6 l) and then partitioned with hexane (2.0 l) and chloroform (2.0 l), respectively. The CE obtained (0.85% w/w) was stored under refrigeration at 4 °C.

Animals Male Wistar rats (150—250 g) and Swiss mice (25—35 g) obtained from the animal house of the laboratory were used. The animals were maintained under standard environmental conditions (temperature of 27±2 °C with an alternating 12 h light–dark cycle) with food and water ad libitum. All behavioral observations took place between 8:00 and 13:00 h.

Drug Administration Control animals received vehicle (cremophor and saline) while treated animals received either CE suspended in cremophor or reference drugs. Administration was by intraperitoneal (i.p.) route.

Toxicity Study The toxicity study was performed with different doses of CE to groups of 10 mice and rats administered i.p., and mortality was recorded for 48 h for the determination of LD50.8) Locomotor Activity Mice were divided into 2 groups of 10 each. Vehicle (control) and CE (125 mg/kg) were i.p. injected. The spontaneous motor activity of the animals was assessed in cages measuring 30×48×48 cm lined with floor demarcated in square measuring 12×12 cm. Sixty minutes after treatment, the number of squares traveled was recorded cumulatively in every 5 min.9) Catalepsy Test Three groups of 10 mice each received i.p. 0.9% saline, CE (125 mg/kg) and haloperidol (5 mg/kg), respectively. To measure cataleptic reaction the animals were placed in an uncomfortable position (stretched between two horizontal metal wires spaced apart at different levels) and observed at 60, 120, 180 and 240 min after administration of the drugs.10) Amphetamine-Induced Toxicity Test Two groups of 10 mice each were treated by via i.p. with vehicle and CE (125 mg/kg), respectively. After 60 min was administered amphetamine (12 mg/kg), i.p. and the mortality was recorded for 24 h.11) Active-Avoidance Test The rats were trained in an active-avoidance paradigm in a 24×24×56 cm shuttle-box with a buzzer located at the midline on the lid of the box and a floor consisting of stainless steel grid bars. The box was divided into two equal compartments by a wood panel with a 7.5×7.5 cm hole in the middle. A sound (conditioned stimulus) was presented during 20 s. The unconditioned stimulus was a 0.4 mA scrambled shock for a maximum of 40 s or until the rat escaped to the other compartment of the cage. The rats which had shown at least 90% avoidance responses during trials were selected for the experiment. The CE was injected i.p. at doses of 62.5, 125 and 250 mg/kg in groups of 13 rats. The animals were assessed individually 60 min after pre-treatment with the extract or vehicle.10) Statistical Analysis The data were analysed as mean± S.E.M. using ANOVA followed by Dunnet’s paired and unpaired test or Student’s t-test. The Fisher’s test was used for the amphetamine-induced toxicity. Results were considered significant with a probability level of 0.05.

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RESULTS AND DISCUSSION

The CE did not induce mortality in animals up to a dose of 500 mg/kg during the 48 h period after injection. Treatment of mice with CE (125 mg/kg) caused a significant decrease in spontaneous motor activity (Table 1), indicating a central depressant effect. To study the neuroleptic activity, 3 methods were used. Firstly, CE (125 mg/kg) induced catalepsy in mice up to 240 min (Fig. 1), with smaller activity than that recorded for the reference drug haloperidol (5 mg/kg). The Table 2 shows that the CE was effective in the amphetamine-induced toxicity test. The protection against action of amphetamine was observed with the dose of 125 mg/kg. The protective effect of CE suggests a possible interference with the central neurotransmission of dopamine, since amphetamine induces the release of dopamine from presynaptic dopaminergic nerve terminals.12) The neuroleptic potential of CE (62.5—250 mg/kg) was confirmed by a significant dose-related decrease of the conditioned avoidance response in rats without affecting the escape response to electric shock (Fig. 2). This behaviour differentiates neuroleptics from non-selective depressants, which inhibit both responses.10)

From the overall results we can conclude that the CE of Maytenus obtusifolia present central depressant action as shown by spontaneous motor activity assay. The neuroleptic-like effect was evidenced in mice and rats in the catalepsy, amphetamine-induced toxicity and active-avoidance tests. The mechanism of CE might be via a possible central dopaminergic action.

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REFERENCES


Table 1. Effect of CE on Spontaneous Motor Activity

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose (mg/kg)</th>
<th>Number of steps recorded mean±S.E.M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle</td>
<td>—</td>
<td>67.3±6.4</td>
</tr>
<tr>
<td>CE</td>
<td>125</td>
<td>29.2±5.5*</td>
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</tbody>
</table>

*p<0.05, n=10.

Table 2. Effect of CE on Amphetamine-Induced Toxicity

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose (mg/kg)</th>
<th>Number of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle</td>
<td>—</td>
<td>7</td>
</tr>
<tr>
<td>CE</td>
<td>125</td>
<td>0*</td>
</tr>
</tbody>
</table>

*p<0.05, n=10.

Fig. 1. Effect of CE, Haloperidol or Saline on Time of Catalepsy
Each bar represents the mean time of catatonia the animals. *p<0.05: **p<0.01: n=10.

Fig. 2. Effect of CE on Active-Avoidance Test in Rats
Each bar represents the percentage of avoidance or escape responses of animals after the stimulus. *p<0.05: **p<0.01: n=10.