NEUROPHARMACOLOGICAL ACTIVITIES OF FICUS PLATYPHYLLA STEM BARK IN MICE

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Methanol Extract Ficus platyphylla stem bark in dosages (17, 40 and 75, 150mg/kg) was found to produce a profound decrease in exploratory activity in mice, the extract indicated peripheral and central analgesic effects as shown by significant inhibition of acetic acid-induced writhing, and delayed onset in leptazol induced-convulsion (seizures) in mice respectively. It also decreases the rate of leptazol induced mortality in mice. The totality of these effects showed that the extract possesses depressant action on the central nervous system.

Keywords: Neuropharmacology, Ficus platyphylla, stem bark, mice

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INTRODUCTION

Ficus platyphylla known as ‘Epo-Obo’ among Yoruba’s in south west Nigeria is used in traditional, medicine for the treatment of convulsive disorder. The use of the bioactive substances of the extract has great potential in combating diseases of microbial origin (Gandidaza and Gaza, 1993). It also constitute important sources of raw material for industrial processing and preparation of various chemical compounds (Penzo, 1980)

MATERIALS AND METHODS

Plant Material
F. Platypylla stem barks were collected from Mushin market in Lagos (south west Nigeria). The plant was identified by Professor J.D Olowokudejo of the department of Botany, University of Lagos and a voucher specimen has been deposited at the Departmental herbarium.

Extraction
The powdered bark were soxhlet extracted with methanol (MeOH). The extract on removal of solvent in vacuum, gave a yellow greenish residue yield (9.5% w/w). The preliminary photochemistry screening, of the extract showed positive results for flavonoids coumarins and saponin (Sayed et al, 1991). The dried extract was insoluble in saline solution, hence it was re-suspended using 0.5%carboxyl methyl cellulose which was stored at -4 °C according to Naik et al (2000).

Animals
Male albino mice weighing 20-25g were maintained under standard nutritional and environmental conditions throughout the experiment. The animals had access to water and food ad libitum. The animals were deprived of food 12h before experimentation.

Acute toxicity test
Acute toxicity of the extract was estimated using male mice. They were distributed into
six groups consisting of 10 mice per group. The animals were administered intraperitonealy with graded doses (15-150mg/kg) of the extract, and left for observation. The numbers of death in each group within 24h were recorded. The LD50 was estimated from the graph of probit against log dose of the extract.

**Exploratory behaviour**

The method used according (File and Wardril, 1975) using a white printed wooden board (40cm x 40cm) with four equidistant holes (1cm diameter x 2cm depth). The mice were placed at the centre of the board and moved freely in the box. A head dip into holes was used to indicate exploratory behaviour. The number of dip was observed for 10 minutes. The test was carried out 30 minutes after pretreatment of the animal with 15, 40 and 75 mg/kg i.p. Chlorpromazine hydrochloride (1mg/kg i.p) was used as standard control drug.

**Dose activity**

The method of Whittle (1964) was used, 30 minute after oral administration of the methanol extract stem bark 15, 40, 75 mg/kg and control aspirin 200 mg/kg i.p.) was given 30 minutes before mice were injected 0.6ml solution acetic acid intraperitoneally. A reduction in the writhing numbers as compared to the control group was considered evidence for analgesia.

% inhibition = Number of writhes in test group / mean number of writhes in control group x 100

**Tail flick test**

The mouse tail withdrawal from 55°C water bath was used to evaluate central analgesic effect of the extract. The animals 10 in group were treated with the extract 15, 40, 75 mg/kg i.p. or with control vehicle and 30 minutes later the tail were dipped in water bath maintained at 55°C. Time taken by the animal to withdraw tail out of the water indicated reaction time to pain (Turner, 1965).

**Hexobarbitone induced sleeping time**

The sedative - hypnotic effect of the extract was assessed using 85mg/kg i.p.) induced sleeping time in mice (Zia,1995) male mice were divided into four groups with 10 animals per group and later treated with the extract 15, 40, 75mg/kg and the control, 30 minutes later animals were given hexobarbitone (85mg/kg i.p). Sleeping time was measured as a time interval between loss and regain of righting reflex.

**Leptazol Induced Convulsion**

Animals were divided into four groups containing six animals each. Intraperitoneal pre-treatment with the extract or control vehicle 15, 40 and 75, (150mg/kg). The animals were later treated with leptazol (100mg/kg i.p.). The latency for convulsive episodes was evaluated in minutes.

**RESULTS**

The methanol extract of *F. platyphylla* stem bark produced a dose related fatalities in mice, its toxic activities was manifested in lethargy, convulsion and death, the lethal dose at 50% (LD was 150mg/kg. The exploratory activity of the extract decreased in dose dependent manner significantly at 75mg/kg see (Table 1). The extract produced 16.3, 44.4, 88.9% inhibition dose dependently (see Table 2) significantly inhibited tail flick response.

<table>
<thead>
<tr>
<th>Pre-Treatment</th>
<th>Dose (Mg/Kg)</th>
<th>Number of Head Dip ± Sem</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Vehicle</td>
<td>0.2ml</td>
<td>25.1 ± 0.72</td>
<td>10</td>
</tr>
<tr>
<td>Extract</td>
<td>15</td>
<td>24.3±2.20</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>14.7±1.51*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>5.3 ± 1.50*</td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>1</td>
<td>7.2 ± 0.36*</td>
<td>10</td>
</tr>
</tbody>
</table>

Statistical analysis was evaluated by students t-test Vs control (n=10); *P < 0.05.

Table 2 similarly acetic-acid induced writhing was inhibited close- dependently 87.4, 88.9 and 91.3%. However aspirin (200mg/kg i.p.) produced 85.8% see Table 3. The result of leptazol-induced mortality was significantly produced by administration of the extract at
33.3, 58.1 and 66.7% against seizures on doses used in the study (see Table 4).

Table 2:
Effect of Extract of F. platyphylla stem barks in tail flick response in mice after immersion in 55°C water bath

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg/Kg)</th>
<th>Mean Reaction Time ± SEM (mm)</th>
<th>% Increase In Reaction Time (Mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.2ml</td>
<td>1.8 ± 0.72</td>
<td>0</td>
</tr>
<tr>
<td>Extract</td>
<td>15</td>
<td>2.1 ± 0.14</td>
<td>16.3</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>2.6 ± 0.51</td>
<td>44.4</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>3.4 ± 0.73</td>
<td>88.9</td>
</tr>
</tbody>
</table>

Statistical analysis was evaluated by students t-test Vs control (n=10); *P < 0.05.

Table 3:
Effect of extract of F. platyphylla stem bark on acetic acid induced writhing in mice

<table>
<thead>
<tr>
<th>Pre Treatment</th>
<th>Dose (mg/Kg)</th>
<th>Mean Number of Writhing ± SEM</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control vehicle</td>
<td>0.2ml</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>0.2ml</td>
<td>36.6 ± 0.50</td>
<td>0</td>
</tr>
<tr>
<td>Extract</td>
<td>15</td>
<td>4.6 ± 0.52</td>
<td>87.4</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>4.0 ± 1.0</td>
<td>88.9</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>0.51*</td>
<td>91.3</td>
</tr>
<tr>
<td>Aspirin</td>
<td>200</td>
<td>5.2 ± 0.33*</td>
<td>85.8</td>
</tr>
</tbody>
</table>

*P < 0.05 Students t-test, compared to control (n=10)

DISCUSSION
The study has examined some neuropharmacological activities of Ficus platyphylla stem bark. The plant extract possessed central nervous system depressant activity as indicated by the decrease in exploratory behaviour in mice, it also showed a marked sedative effect as indicated by the reduction in gross behaviour and potentiation of hexobarbitone induced sleeping time. It is generally accepted that the sedative effect of drugs can be evaluated by measurement of spontaneous motor activity and hexobarbitone induced sleeping time in laboratory animal model (Ming-chin, 1998). This result corroborate those of Fujimori (1995) who proposed that the enhancement of barbital hypnosis is a good index of CNS depressant activity. Our result in analgesic activity are similar to those reported for morphine and aspirin (Distasi et al, 1988)

It is of interest to note that aspirin at 200mg/kg could not increase reaction time, but the plant extract showed a significant increase comparable to that of Morphine. This method of analgesic testing is usually considered suitable for centrally acting analgesic though no clear cut dose response relationship was observed unlike the dose-dependent inhibition of acetic acid induced writhing in this study which showed a peripheral affect, which was more potent than aspirin

Furthermore, the extract blocked leptazol induced convulsion, the blockade of convulsion induced by Glycine antagonist is indicative of facilitation of Glycine inhibiting effect on the CNS. Further studies are going on on the mechanism of action of Ficus platyphylla.

Table 4:
Effect of methanolic extract of Ficus platyphylla stem bark on leptazol-induced convulsion

<table>
<thead>
<tr>
<th>Pre-treatment</th>
<th>Dose (mg/kg)</th>
<th>Duration</th>
<th>% mortality</th>
<th>% protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control vehicle</td>
<td>0.2ml</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Leptazol</td>
<td>100</td>
<td>6 ± 0.73</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Extract</td>
<td>15</td>
<td>3.9 ± 0.33</td>
<td>80</td>
<td>33.3</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>2.6 ± 0.43*</td>
<td>40</td>
<td>58.1</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>2.2 ± 0.26*</td>
<td>40</td>
<td>66.7</td>
</tr>
</tbody>
</table>

Statistical analysis was evaluated by students t-test Vs control (n=10); *P < 0.05.
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