Evaluation of methanolic extract of *Ficus platyphylla* on gastrointestinal activity

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Methanolic extract of *Ficus platyphylla* was tested on isolated rabbit jejunum, rat duodenum and gastrointestinal motility in mice. The extract showed a biphasic effect on isolated smooth muscle. Lower concentration of extract caused contraction, while higher concentrations produced relaxation. The contractile phase was attenuated by atropine, while relaxant phase attenuated histamine induced contraction of guinea pig ileum. The extract also exhibited a dose-dependent inhibition of gastrointestinal motility. Acute toxicity test in mice established LD$_{50}$ value (ip) of the extract to be 2000 mg/kg. Preliminary phytochemical screening of the extract gave positive test for flavonoids, tannins and saponins.

Majority of the population in developing countries remains dependent on medicinal plants for health care. Based on this fact, scientists and WHO are focussing attention on medicinal plants, because of great potential that these plants carry in combating various diseases. *Ficus platyphylla* (Moraceae) is a tree commonly found in Savannah region, West Africa. In northern Nigeria, where it is commonly known as gamji, the latex heated or chewed is used as a birdlime. Our previous studies revealed that the plant possesses analgesic and anti-inflammatory effects and has behavioural effects in rodents. To the best of our knowledge, no report has been made on its activity on the gastrointestinal tract. This study was carried out to evaluate the effects of the methanolic extract of *F. platyphylla* on gastrointestinal tract.

**Materials and Methods**

*Plant collection and identification*—The plant material was collected from Hong, Adamawa State, Nigeria in September 1998. Botanical identity was confirmed by Messers. A Ohaeri and I. Muazzam, Department of Pharmacognosy and Alternative Medicine, NIPRD, Abuja, Nigeria. A voucher specimen of the plant has been deposited in NIPRD herbarium for future reference.

*Extraction of plant material*—The stem bark was cleaned, air-dried for 7 days and then reduced to coarse powder by grinding. The powder (80 g) was extracted with 1 L of methanol using a soxhlet extractor. The extract was subsequently concentrated to dryness in vacuo using a rotary evaporator and it gave a mean yield of 8.2% (w/w). This was stored at 4°C until used for the study.

*Animals*—Swiss albino mice (20-25 g), rats (180-220 g), guinea pigs (250-400 g) and rabbits (1.5-3 kg) bred in the Animal Facility Centre, NIPRD were used in these studies. The animals were kept under standard conditions of temperature, relative humidity and light/dark cycle. The animals were fed with Ladokun animal feeds and water ad libitum.

*Acute toxicity determination*—Eight groups, each consisting of 5 mice of both sexes were used for the test. Groups 1-7 were injected intraperitoneally (ip) with varying doses (100-4000 mg/kg) of the extract in normal saline, while group 8 which served as control received equivalent volume of normal saline. After treatment, the animals were observed for clinical signs and symptoms of toxicity over a period of 24 hr. Death within this period were recorded. LD$_{50}$ (with 95% confidence limits) was estimated using probit analysis.

*Phytochemical test*—Phytochemical analysis of the extract was performed according to the methods of Clarke, Odebiyi & Sofowora, and Trease & Evans. Test for alkaloids, saponins, tannins, flavonoids, etc. were carried out.

*Studies on rat duodenum*—The method of Schlemper et al. was followed and in brief, Wistar rats weighing 180-220 g of either sex were killed by a blow on the head and exsanguinated. The abdominal
cavity was exposed and the intestine removed. After discarding a part of 10 cm nearest the gastrointestinal junction, the duodenum was removed and placed in a petri dish containing Tyrode’s solution. The intestinal content was removed by flushing with Tyrode’s containing (mM) NaCl, 136.8; KCl, 2.7; CaCl$_2$, 1.3; NaHCO$_3$, 12; MgCl$_2$, 0.5; Na$_2$PO$_4$, 0.14; glucose, 5.5. The duodenum was cut into segments (3 cm) and each segment was mounted in a 20 mL organ bath containing Tyrode’s solution at 37° ± 1°C and aerated with air. An initial tension of 1.0 g was applied to the tissue for 60 min. During that time the physiological solution was changed every 15 min, after which the effect of the extract at final bath concentration of 0.05-3.2 mg/mL and acetylcholine (2.75 × 10$^{-10}$, 8.8 × 10$^{-7}$ M) were evaluated. Effects of the extract and acetylcholine on the tissue incubated with atropine (5×10$^{-9}$ M) were evaluated. Responses were recorded isometrically on Ugo Basile Unirecorder 7050. 

**Studies on rabbit jejunum**—The rabbits were killed by a blow on the head, exsanguinated and abdomen opened. Segments of the jejunum (about 2-3 cm long) were removed and dissected free of adhering mesentery. The tissue was mounted in an organ bath (20 mL) containing Tyrode’s solution at 37° ± 1°C and aerated with air. A tension of 0.5 g was applied for 60 min (equilibration period) during which the physiological solution was changed every 15 min. At the end of the equilibration period, the effect of acetylcholine (ACh) and extract were evaluated.

**Studies on guinea pig ileum**—Adult guinea pigs (250-400 g) of either sex were starved overnight but had free access to water. Animals were killed by a blow on the head, exsanguinated and the abdomen opened. Ileum was removed and cut into segments of 2-3 cm long. The segments were dissected free of adhering mesentery and mounted in an organ bath (20 mL) containing Tyrode’s solution, gassed with air and maintained at 37°C. The tissue was equilibrated for 60 min during which the bathing solution was replaced every 10 min. At the end of the equilibration period, the effect of increasing concentration of the extract on histamine induced contraction of guinea pig ileum was evaluated. Responses were recorded on Ugo Basile Unirecorder 7050. Determinations were done in quadruplicates.

**Studies on gastrointestinal motility in mice**—To test the effects of the extract on gastrointestinal motility adult Swiss albino mice (20-25 g) were randomly divided into 5 groups of 5 mice each. The animals were starved for 24 hr prior to the experiments, but were allowed access to water. One group of animals was given 20 mL/kg of normal saline, while the remaining other 3 groups received ip the extract at doses of 25, 50 and 100 mg/kg. The last group received atropine (0.1 mg/kg; ip). After 5 min of drug administration, 0.5 mL of charcoal suspension (5%) in aqueous solution of tragacanth powder (10%) was administered to each animal orally. The animals were killed 30 min later and the abdomen was opened. Percentage distance of the small intestine (from pylorus to caecum) travelled by the charcoal plug in both the extract and the normal saline treated groups were determined

**Studies on castor oil induced diarrhoea**—Swiss albino mice of either sex (18-22 g) were used for the experiment. The mice were fasted for 18 hr prior to commencement of the experiment and were randomly divided into 4 groups of 5 mice each. The animals in group 1 received normal saline (30 mL/kg; ip), while those animals in groups II, III and IV received the extract (doses of 25, 50 and 100 mg/kg; ip). The last group received loperamide (5 mg/kg ip). After 30 min of drug pre-treatment, castor oil (0.2 mL/mouse) was administered intragastrically. The animals were placed in individual cages over clean filter paper. After 3 hr of oil challenge, mouse cages were inspected (by an observer unaware of the particular treatment) for the presence of characteristic diarrhoea droppings; their absence was recorded as a protection from diarrhoea$^{11,12}$ and the percentage protection was calculated

**Drugs**—Acetylcholine chloride, histamine, atropine (all from Sigma Chemical Company, USA), mepyramine (M & B) were used. All drugs were freshly prepared to desired concentrations with distilled water just before use. The extract was also freshly prepared using distilled water. Parallel control experiments were also carried out in order to correct possible effects caused by vehicle alone.

**Statistical analysis**—Results were expressed as mean ± SEM. The significance of difference between the means was determined by Student’s t test and results were regarded as significant at $P < 0.05$ (Ref. 14).

**Results**

Fresh extract of *F. platypylla* gave positive reactions for saponins, tannins and flavonoids. In the preliminary acute toxicity test in mice, LD$_{50}$ values of the extract given ip was 2000 mg/kg.

**Effect on rabbit jejunum**—Extract of *F. platypylla* exhibited biphasic effect on rabbit jejunum with lower
concentrations (0.05-0.4 mg/mL) producing contraction and higher concentrations (0.8-1.6 mg/mL) producing relaxation (Fig. 1).

**Effect on rat duodenum**—Extract of *F. platyphylla* exhibited a biphasic effect on rat duodenum. Lower concentrations (0.1-0.4 mg/mL) evoked a concentration dependent contraction of duodenum, while higher concentrations (0.8-1.6 mg/mL) showed relaxation on smooth muscle. The extract induced contraction was blocked by atropine and relaxant phase did not attenuate ACh induced contractions of duodenum (Fig. 2).

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**Fig. 1**—Biphasic effects of methanolic extract of *F. platyphylla* on the spontaneous activity of rabbit jejunum.

**Fig. 2**—Effect of methanolic extract of *F. platyphylla* (E; 0.1-1.6 mg/mL); acetylcholine (A); and atropine (Atr; 5×10⁻⁹ M) on the rat duodenum.
**Effect on guinea pig ileum**—Extract of *F. platyphylla* was devoid of contractile effect on guinea pig ileum. However, the extract inhibited histamine evoked responses of ileal segment in a concentration dependent manner (Fig. 3).

**Effect on gastrointestinal transit in mice**—The results of charcoal meal test showed that the extract of *F. platyphylla* caused a significant decrease in gut motility when compared with normal saline. Average percentage distance travelled by the charcoal plug has been shown in Table 1.

**Effect on castor oil induced diarrhoea**—The extract (25, 50 and 100 mg/kg) and loperamide (5 mg/kg) protected mice against diarrhoea induced by castor oil significantly as compared to control. (Table 2).

**Discussion**

The present study has provided a preliminary data, which suggested that methanolic extract of *F. platyphylla* contains biologically active components. The contractile response of the extract at lower concentrations was similar to those of acetylcholine on cholinergic receptors. Atropine a known cholinergic antagonist blocked the effect of this contractile phase of the extract, in a similar way it blocked Ach induced sub-maximal contractions of the smooth muscle. The contractions evoked by the

<table>
<thead>
<tr>
<th>Treatment (mg/kg)</th>
<th>Maximum distance travelled (%)</th>
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<tbody>
<tr>
<td>Normal Saline</td>
<td>71.2 ± 5.3</td>
</tr>
<tr>
<td>20 mL/kg</td>
<td></td>
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<tr>
<td><em>F. platyphylla</em></td>
<td></td>
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<tr>
<td>25</td>
<td>66 ± 2.4</td>
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<tr>
<td>50</td>
<td>44.7 ± 3.2*</td>
</tr>
<tr>
<td>100</td>
<td>40.5 ± 2.6*</td>
</tr>
<tr>
<td>Atropine 0.1</td>
<td>32.5 ± 6.5*</td>
</tr>
</tbody>
</table>

Significant at *P<0.05 treatment group vs normal saline.

<table>
<thead>
<tr>
<th>Treatment (mg/kg)</th>
<th>No. of mice with diarrhoea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Castor oil (0.2 mL/kg)</td>
<td>5/5</td>
</tr>
<tr>
<td><em>F. platyphylla</em> + Castor oil</td>
<td>5/5, 1/5, 0/5*</td>
</tr>
</tbody>
</table>

n = 5 significant at *P<0.05 treatment group vs normal saline.

![Fig. 3—Inhibitory effect of extract of *F. platyphylla* (E; 0.1-0.8 mg/mL) on histamine (H; 3.3×10⁻⁹ M) induced contraction of the guinea pig ileum.](image-url)
extract, therefore, might have resulted from activation of muscarinic receptors. On the other hand, relaxant phase of the extract on smooth muscle did not attenuate Ach induced contraction, but was found to inhibit histamine induced contractions in a concentration dependent manner. Activity of the extract in this regard was similar to that of mepyramine, a known H1 receptors blocker, which also blocks the contractile response evoked by histamine. Thus, it is proposed that the relaxant phase might be mediating its effects through blockade of histaminergic receptors.

The charcoal meal test, which allows for comparative evaluation of the degree of inhibition/stimulation of gastrointestinal motility in laboratory animals, the finding that F. platyphylla decreased peristaltic movement in the charcoal meal study corroborated with some of the results of in vitro studies. Phytochemical screening of the extract revealed the presence of flavonoids, tannins and saponins. These constituents are known to be bioactive principles. Flavonoids are known to inhibit contractions induced by spasmogens and inhibit small intestinal transit. Properties such as this may underlie the observed pharmacological effects. The results provided useful guide for isolation of active principles in this plant.

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References
