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Full Length Research Paper

Effects of the aqueous extract of *Ficus capensis* Thunb. (Moraceae) leaf on gastrointestinal motility

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Medicinal plants have always played a great role in preventing, controlling and alleviating various disease conditions. *Ficus capensis* Thunb. (Moraceae) leaves have been reported in literatures to possess anti-diarrhea properties and have been used as such by herbal practitioners in some parts of Benue State, Nigeria. This work examined the preliminary phytochemical constituents of the plant part using standard procedures and also the anti-diarrhea effects of the leaves of the plant in adult mice and albino rats using three models. Preliminary phytochemical screening of the powdered leaves revealed the presence of saponins, steroidal glycosides, flavonoids and tannins. In mice, between 100 - 400 mg/kg (orally administered), the crude aqueous extract of the leaves exhibited a dose-related reduction in the gastrointestinal tract motility as indicated by the distance moved by the charcoal meal. In albino rats, the aqueous extract also displayed significant delay in the onset of stooling, and produced remarkable decrease in the number and weight of stools produced with 100 - 400 mg/kg of the aqueous extract. In the organ bath model, the aqueous extract at concentrations of 50, 100 and 200 mg/ml was observed to have relaxant effects on the isolated rat ileum as it remarkably reduced the ileal contractions occasioned by administration of acetylcholine. The activities of the extract were comparable with that of atropine (0.1 mg/kg). The results of this work validated the claimed use of the leaves of *F. capensis* in controlling diarrhea among the Igede people of Benue State, Nigeria.

Key words: *Ficus capensis*, aqueous extract, gastrointestinal motility.

INTRODUCTION

In various parts of the world, medicinal plants constitute alternative sources of drugs for majority of populations that experience inadequate contacts with orthodox health care facilities. The non-availability of synthetic drugs to combat common ailments like diarrhea has indeed made many communities to continue beaming their searchlight on medicinal plants that can alleviate the condition or permanently put the secretary process leading to diarrhea under control.

Diarrhea is a disease condition characterized by frequent discharge of semi-solid or fluid fecal matter occasioned by uncontrolled peristalsis of the intestines. It may be acute or chronic. It can be very serious in infants and elderly people because of the risk of severe, potentially fatal dehydration. It ranges from a mild and socially inconvenient illness to a major cause of death probably due to additional effects of malnutrition among children in less developed countries (Bern et al., 1992). Drugs have a place in its management, but the first priority of therapy is to preserve fluid and electrolyte balance. The condition is often assumed to be microbial, but it may also be caused by anxiety, food, drugs or other toxins (Laurence et al., 1997). Although, quite a number of synthetic drugs have emerged over the years as found in literature, none has formed a place in the routine management of diarrhea (Farthing, 2002). The use of medicinal plants that possess potent anti-diarrhea activity could be of benefit in combating widespread diarrhea infections especially in third world countries (Adeyemi et al., 2003) where there is precarious distribution of drugs particularly to people in the rural areas.

Among the Igede people of Benue State, Nigeria, Igoli et al. (2005) reported the ethnomedicinal use of the leaves of

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Ficus capensis Thunb. (Moraceae) in treating diarrhea using decoction method. Earlier, Gill (1992) reported the use of the plant leaves in treating dysentery, oedema, epilepsy and rickets in infants among some tribes in Edo-Delta areas. The plant is known as *Uwaryara* in Hausa, *Opoto* in Yoruba, *Rima bichehi* in Fulani and *Obada* in Edo language.

Keay (1989) described *F.capensis* as having ovate to elongated elliptic leaves, about 7.5 - 15 cm long and 5 - 10 cm wide. The leaves have acute or blunt apex with a slightly cordate, sometimes rounded, occasionally cuneate or slightly unequal asymmetrical base. They are some what leathery, dark green with glabrous surfaces with no epidermal hairs. The margin could be dentate, wavy or at times, entire. The fruits are usually densely clustered along short branched shoots on the main stem and older branches. Solitary or paired figs may be found among the leaves. The individual figs have short stalks 2.5 - 3 cm long.

There are reports on the antimalarial, antibacterial and anti ulcer activities of the leaves (Muregia et al., 2007; Emeje, 2004; Atindehou, 2000). This work was carried out to examine the preliminary phytochemical constituents of the *F. capensis* leaves and to investigate the ethnomedicinal claim of the aqueous leaf extract in treating diarrhea using laboratory animals.

MATERIALS AND METHODS

Collection and preparation of plant material

After proper identification by Professor M. Idu, Taxonomist, Department of Botany, University of Benin, the fresh leaves of *Ficus capensis* were collected within the University of Benin Ugbowo Campus. The leaves were air dried in the laboratory five (5) days after which they were oven dried at 40°C. The dried leaves were then reduced to powder using the electric grinding machine. The powdered material was kept in air-tight containers before use. A voucher specimen of the sample was deposited in the department of Pharmacognosy, University of Benin, Benin-City.

Drugs and chemicals

These included acetylcholine, chloroform (Sigma-Aldrich), sodium chloride NaCl, sodium hydrogen carbonate $NaHCO_3$, d-glucose, sodium dihydrogen phosphate NaH_2PO_4, potassium chloride KCl, magnesium chloride $MgCl_2$, calcium chloride $CaCl_2$ (BDH Chemicals).

Preliminary phytochemical analyses of the plant

The powdered sample of the plant material was subjected to phytochemical screening to test for the presence or otherwise of alkaloids, tannins, flavonoids, saponins, anthraquinones, cyano-genic and cardiac glycosides using standard procedures (Evans, 2002; Sofowora, 2008).

Extraction of the plant material

About 500 g of the powdered leaves was extracted with distilled water (4l) by decoction method. After filtration and concentration using on a rotatory evaporator, the extract obtained (43.9 g which constituted 8.78% of the plant material) was kept in a refrigerator maintained at 4°C until required.

Animals

Adult mice and albino rats weighing (20 - 25 g and 145 - 160 g respectively) were purchased from the Animal house, Ambrose Ali University, Ekpoma and maintained for four weeks in the Animal house, Department of Pharmacology and Toxicology, University of Benin, where they had access to feed (Livestock feeds, Benin) and water *ad libitum*. Approval for use of the laboratory animals was obtained from the Faculty of Pharmacy Ethical Committee on the use of Animals for Experiments.

Experiments

Determination of anti-diarrheal activity

Measurement of intestinal transit using activated charcoal: Adult mice of both sexes weighing between 20 and 25 g were divided into five groups of five mice each. Group one which was the control group was administered 0.1 ml of normal saline. The aqueous extract was administered to groups 2, 3 and 4 at doses of 100, 200 and 400 mg/kg respectively. Group 5 received atropine at a dose of 0.1 mg/kg (from a stock concentration of 100 ug/ml). All the administrations were carried out through the intraperitoneal route.

After 30 min of the administration, 0.2 ml charcoal meal was given orally to the mice in each group. About 30 min after the administration of the charcoal meal, the animals were sacrificed by placing them in a chloroform gas chamber. After opening each animal, the length of the small intestine was measured. The distance moved by the charcoal meal in the intestine of each animal was measured and expressed as a percentage of the actual length of the intestine.

The percentage inhibition of charcoal movement was calculated as;

$D_1 - D_2 / D_2$

Where D_1 is the percentage distance moved by the charcoal meal in the mice administered normal saline and D_2 is the percentage distance moved in those administered the extract.

Castor oil model

Adult mice were divided into five groups of five each. Group one was administered 0.1 ml of normal saline while groups 2, 3 and 4 were given 100, 200 and 400 mg/kg (i.p) of the aqueous extract respectively. The fifth group was administered 0.1 mg/kg of atropine (i.p).

After 30 min, each mouse in each group was given orally 0.3 ml castor oil with the aid of an orogastric tube. The animals were placed in separate cages and observed over a period of 4 h. The time it took each mouse to pass the first stool, the total number of fecal droppings, and the weight of stool at the end of the 4 h period were determined. For each group, the mean ± SEM was obtained for each of these parameters.

Effects of the extract on isolated rat ileum

Albino rats weighing (145 -160g) were anaesthetized via chloroform inhalation in a gas chamber and were afterwards sacrificed. After opening the abdomen using a dissecting set, the ileum was

Table 1. Summary of the preliminary phytochemical constituents of *F.capensis* leaf powder.

Phytochemical constituents	Results
Tannins	++
Saponins	++
Cardiac glycosides	++
Cynanogenic glycosides	-
Alkaloids	-
Anthracene derivatives	-
Flavonoids	++

harvested and carefully and transferred into a Petri dish containing Tyrode's solution with the following composition: sodium chloride 40 g, sodium hydrogen bicarbonate 5 g, d-glucose 5 g, sodium dihydrogen phosphate 0.25 g, potassium chloride 1 g, magnesium chloride 0.5 g, and calcium chloride 1.32 g in 5 L of distilled water. The lumen of the ileum was flushed with a 5 ml syringe and freed of the mesenteries by careful cutting with a scissors. Rat ileum (1 - 2 cm long) was cut and suspended in the organ bath containing the physiological salt solution with the aid of a tissue holder which was connected to a unirecorder (7050) via an isometric transducer. The equipment was set with a tension of 700 mg, sensitivity of 6, and speed of 5 mm/min. The organ bath was adequately aerated with 95% O_2 and 5% CO_2 with the temperature maintained at 36.0 ± 1°C. The tissue was allowed to equilibrate for 45 min.

A dose response curve was obtained with 0.001 - 1 mg/ml acetylcholine with a contact time of 30 s and resting time of 1 min 30 s (2 min time cycle). The effects of the crude extract on the contractions produced by the various concentrations of acetylcholine were tested at 50, 100 and 200 mg/ml.

Statistical analysis

All data were expressed as mean ± SEM (standard error of mean) and n represents the number of animals used. Where applicable, the data were compared using one way analysis of variance (ANOVA), Graph pad Instant^R version 2.05a software (UK). The level of significance was from $P < 0.05$.

RESULTS AND DISCUSSION

The preliminary phytochemical tests carried out on the leaf powder of *F. capensis* revealed the presence of tannins, saponins, flavonoids, and cardiac glycosides. The plant material was observed to lack alkaloids, cyanogenic glycosides and anthracene derivatives (Table 1).

The aqueous extract of the plant was observed to produce a dose-related increase in percentage inhibition of the movement of the charcoal meal in the small intestine of the mice. At a dose of 100 mg/kg, the extract showed a percentage inhibition of 23.52% relative to the distance moved by the charcoal in the mice administered normal saline. The inhibition was further increased to 31.41 and 48.95% at doses of 200 mg/kg and 400 mg/kg respectively. Atropine at a dose of 0.1 mg/kg showed a percentage inhibition of 44.02%. The results were observed to be statistically significant at $P < 0.05$ (Figure 1).

In the castor oil model also used to test the effect of the extract on gastrointestinal motility, there was a dose dependent increase in the average onset of stooling in the animals treated with the aqueous extract. While the onset observed in the animals treated with for normal saline treated animals was 12.3 ± 8 min., those of 100, 200 and 400 mg/kg were 22 ± 5.7, 23.3 ± 3 and 29 ± 0 min respectively. The onset of stooling in atropine treated animals was 19 ± 0 min.

The crude extract exhibited a significant dose-dependent decrease in the number and weight of stool produced by the mice. At a dose of 100mg/kg of the extract, 3 ± 0.5 stools produced weighed 93.3 ± 9.7 mg compared to 11.5 ± 3.5 stools with average weight of 222.5 ± 8.8 produced by normal saline treated (control) animals. At 200 and 400 mg/kg, the animals produced 3 ± 1.2 and 2.25 ± 0.5 stools with average weights of 82.5 ± 2.2 and 75 ± 5.8 mg respectively. With atropine, the mice passed 3 ± 1 stools weighing 57 ± 2.8 mg (Table 2).

On the isolated ileum, acetylcholine was observed to produce a dose-dependent contraction of the ileum. At a concentration of 4ng/ml, a contraction of 27 ± 3.1 was observed. This continued to increase until a maximum contraction was obtained at 4000 ng/ml of acetylcholine. Simultaneous administration of the acetylcholine concentrations with 1 ml of the crude extract at 50, 100, and 200 mg/ml produced corresponding decreases in contractions earlier observed with acetylcholine alone. For example, 4 µg/ml concentration of ACH which earlier produced 27 ± 3.1 mm was reduced to 6.2 ± 2.1 with 100mg/ml of the crude extract (Figure 2). The ACH alone (used as the control) gave an EC50 of 50.2 while in the presence of the aqueous extract concentrations of 50,100 and 200, the EC50 was observed to be 109.8, 109.8 and 143.3 respectively. The observed pharmacological activities of medicinal plants in animals are due to various phytochemical constituents they contain. The gastrointestinal motility inhibition the aqueous extract of *F. exasperata* showed on the animals may be due to the presence of the saponins, tannins and flavonoids. However, further work would be necessary to ascertain the exact group of constituents that could responsible for observed antispasmolytic effect. The fact that the extract significantly reduced the distanced moved by activated charcoal in the intestines of the treated animals showed that it had a potent relaxant effect on the intestine. This observation was further established in the animals treated with castor oil along with the aqueous extract of the plant. The precise mechanism of action of castor oil remains elusive, partly because of its multiple effects on the gut. Its induction of diarrhoea is attributed to its active constituent ricinoleic acid (Phillips and Gaginella, 1977) which stimulates the production of several mediator substances that include prostaglandins, nitric oxide, platelet activating factor, and tachykinins (Gaginella et al.,1977 and Izzo et al., 1999). This phenomenon of secretions may be responsible for early production of stools in the normal saline treated animals. The aqueous extract of *F.capensis* may be said to inhibit the effects of the castor oil on the

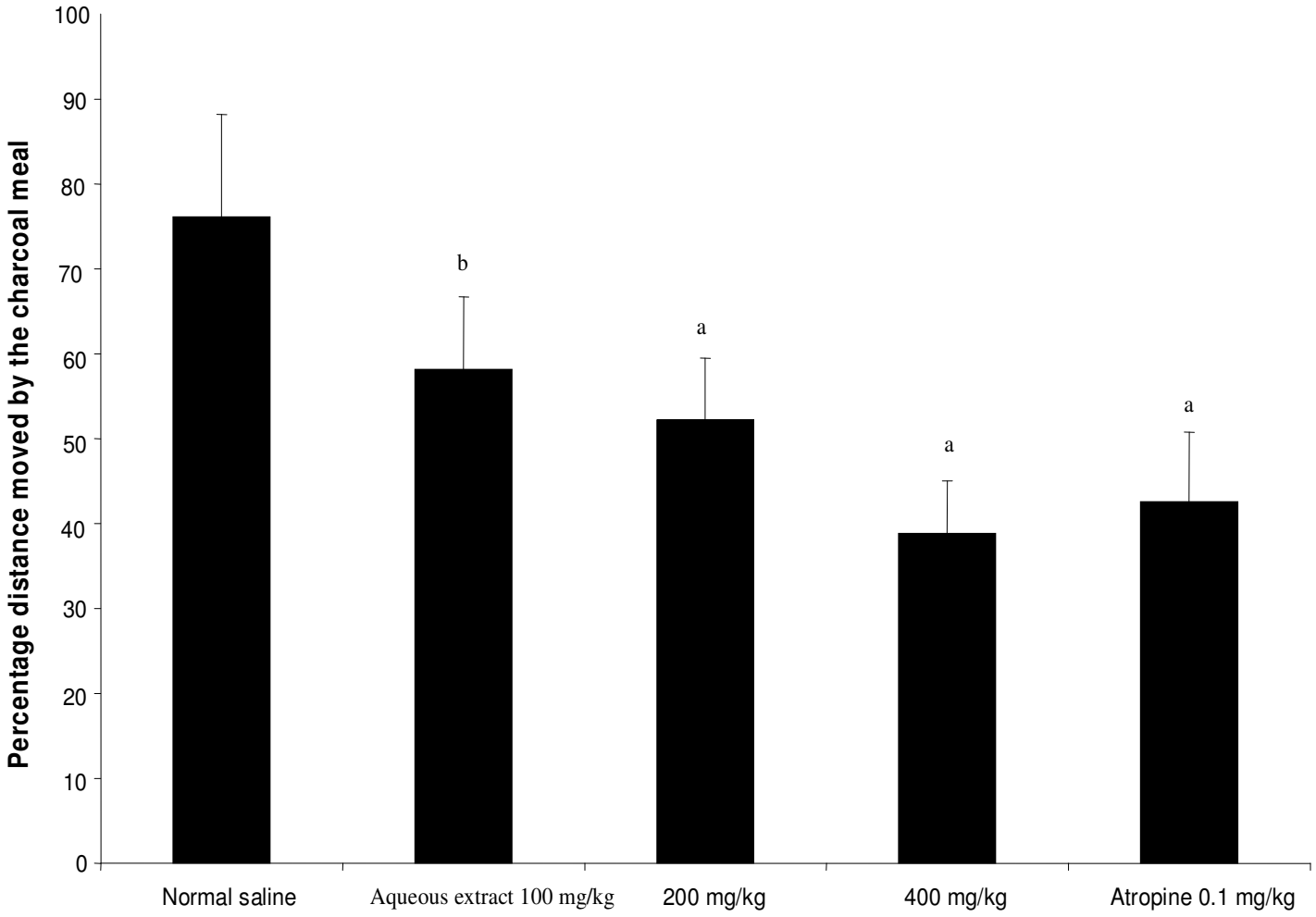

Figure 1. Effects of the aqueous extract of *F. capensis* leaf on the gastrointestinal motility of the mice. Values are mean ± SEM. (n = 5 per group). [a]P < 0.0001 and [b]P<0.05, significantly different from the control group.

Table 2. The effects of the aqueous extract of *Ficus capensis* on the stools produced by rats.

Aqueous extract/ Drugs administered	Onset of stooling (min)	Number of stools produced	Weight of stool (mg)
Normal saline	12.3 ±8	11.5 ± 3.5	222.5 ±8.8
100 mg/kg	22 ± 5.7 [b]	3 ± 0.5 [a]	93.3 ± 9.7 [a]
200 mg/kg	23.3 ± 3 [b]	3 ± 1.2 [a]	82.5 ± 2.2 [a]
400 mg/kg	29 ± 0 [b]	2.25 ± 0.5 [a]	75 ± 5.8 [a]
Atropine (0.1 mg/kg)	19 ± 0 [b]	3 ± 1.0 [a]	57 ±2.8 [a]

Values are mean ± SEM. (n = 5 per group). [a]P < 0.0001 and [b]P<0.05, significantly different from the control group.

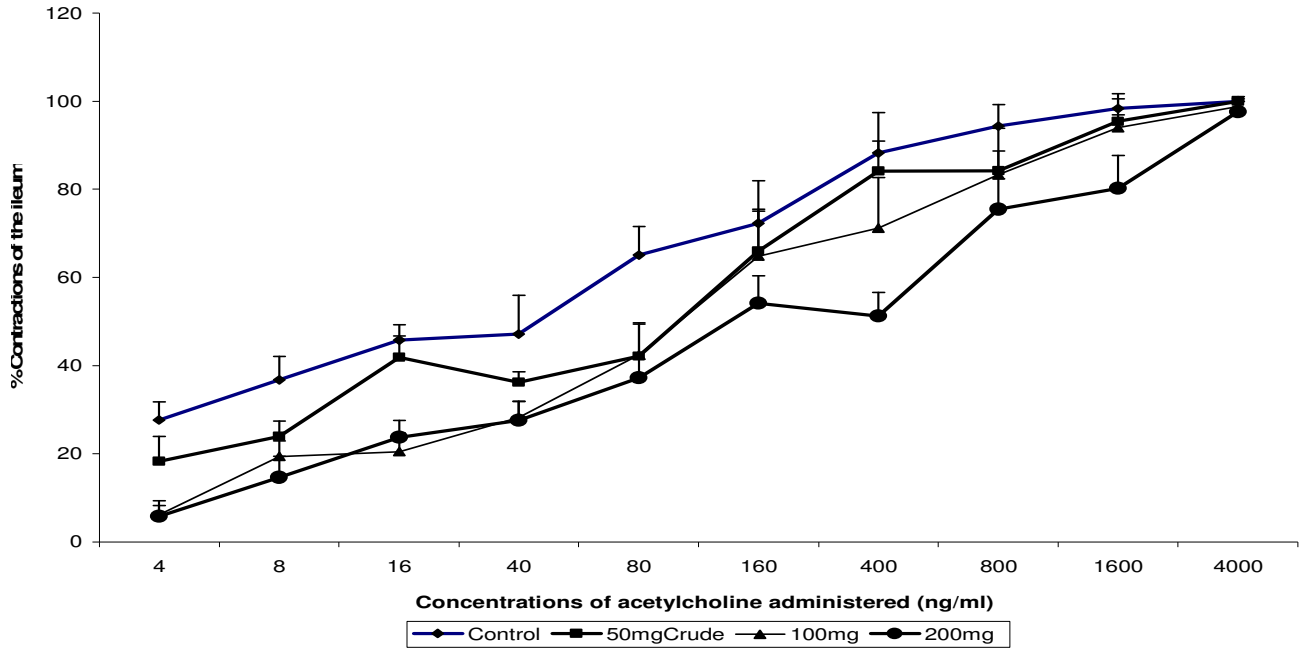

Figure 2. The effect of the aqueous extract of *F. capensis* leaves on the contraction of the rat ileum induced by acetylcholine. Values are mean ± SE. (n = 5 per experiment); $P < 0.05$, significantly different from the control group.

gastrointestinal tract by probably by mitigating the rate at which these secretions carried are out as indicated in the significant reduction in the number and weight of feacal matter produced. The wetness of the feacal matters produced was observed to reduce with increase in the doses of the extract and these may as well account for the progressive reduction in their weights. The extract can also be said to act as antimuscarinic agent like atropine by reducing the intestinal motility as well as inhibiting the ileum contraction caused by acetylcholine. The inhibitory effect of the extract was further established in the concentration of ACH required to effect intestinal contraction in the presence of the extract. The fact that the EC50 of 50.2 elicited by ACH alone increased to 143.3 in the presence of the 200 mg/ml of the extract implied that the extract inhibited the intestinal contractile effect of the ACH.

The results obtained from this work have validated the ethnomedicinal use of the leaves extract of *F. capensis* in controlling diarrhea.

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