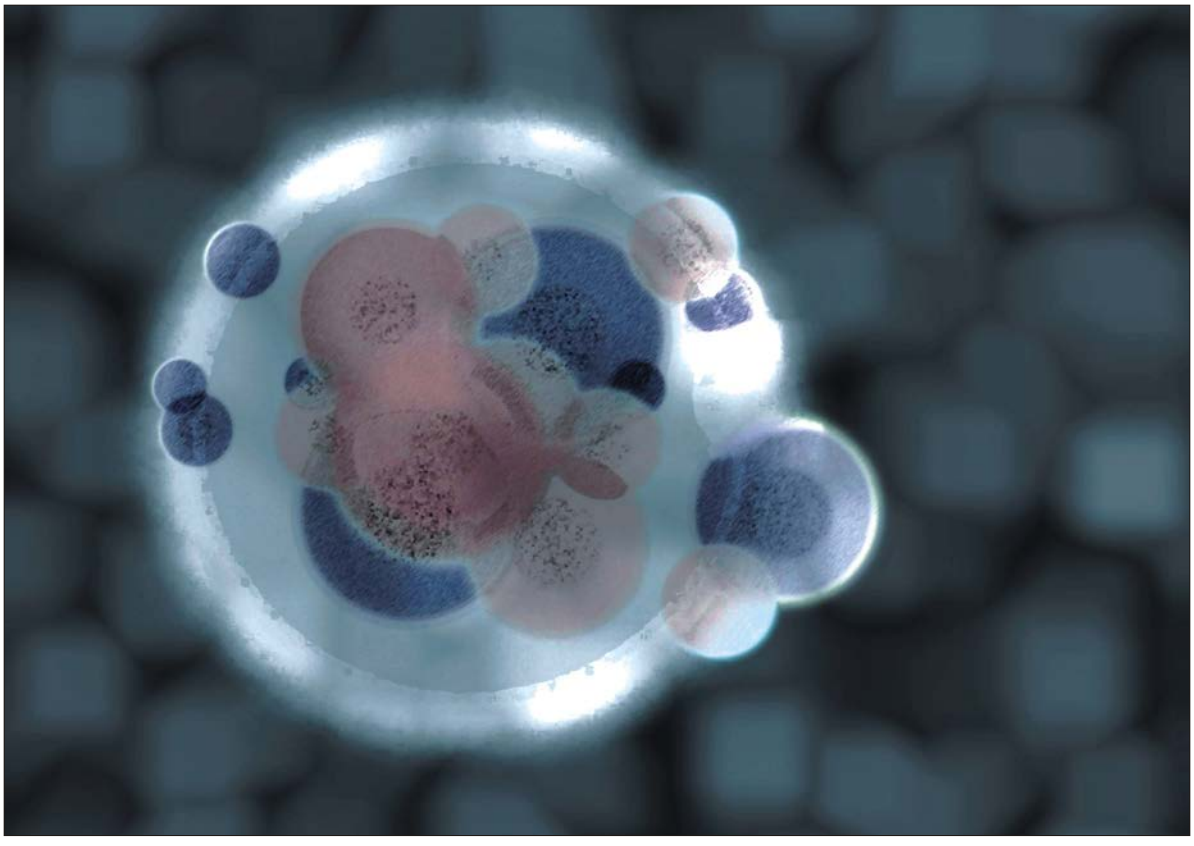

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Antiulcer Activity of Methanolic Extract of *Bryophyllum pinnatum* in Rats

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Abstract: The effect of *Bryophyllum pinnatum* leaves extract on indomethacin induced gastric ulceration was determined using 25 male albino rats. Animals were divided into 5 groups of 5 animals each. The control group received 0.5 mL of distilled water and varying doses of the extract were used for the remaining groups (10-40 mg kg^{-1} body weight). The result showed a significant reduction ($p<0.05$) in incidence of ulceration and mean basal and histamine (1 mg kg^{-1}) stimulated gastric acid secretion in a dose dependent manner thus justifying the use of *Bryophyllum pinnatum* as an anti-ulcer agent in folklore medicine.

Key words: Antiulcer; *Bryophyllum pinnatum*, gastric acid, rats

INTRODUCTION

Several plants and herbs are used in folkloric medicine to treat gastrointestinal disorders, including peptic ulcers. Recently, there is a growing interest in identifying new anti-ulcer agents from plant sources (Njar *et al*., 1995; Raji *et al*., 2000, 2004). *Bryophyllum pinnatum* (S. Kurz) is a fleshy shrub, which grows 2-4 feet tall. The plant, which belongs to the family Crassulaceae is widely grown in the region for ornamental and medicinal uses (Burkill, 1985). The English name is never die or resurrection plant. It is called abamoda by the Yoruba tribe of Southwestern Nigeria where it is used in traditional treatment of several ailments including stomach upset (Iwu, 1993). In Sierra Leone, a cough medicine is made from the roots while in Ivory Coast, the root sap is taken by the draught for attacks of epilepsy. In Congo, leaf sap is given to children to relief convulsion and epilepsy. The Shien of Ivory Coast take a decoction of the whole plant as a febrifuge and tranquillizer as well as for refractory cough. In Ghana the leaves of the plant are rubbed on the head and inserted in the nostrils to relief headache. Curative and analgesic actions are also claimed for the plant (Iwu, 1993). It has been reported that a decoction of the leaves is taken in West Indies for the treatment of arthritis and to clean the bladder (Seaforth *et al*., 1983). The plant is listed by Wong for the treatment of earache and in ophthalmic and the poultice used for sprains, dysmenorrhea and cold in the head (Wong, 1976). Topical application of the plant extract is used for the treatment of external ulcers and burns (Wong, 1976).

There is no information in the literature on the effect of *Bryophyllum pinnatum* on gastrointestinal activity. This study was therefore designed to investigate the effect of the methanolic extract of *Bryophyllum pinnatum* on indomethacin induced gastric ulceration and gastric acid secretion in rat.

MATERIALS AND METHODS

Acute toxicity study: Twenty-five mice were divided into 5 equal groups. Different doses of *Bryophyllum pinnatum* extract ranging from 10 to 200 mg kg^{-1} b.w. were administered orally to the mice each as a single dose. The mice were starved for 16 h prior to administration of the extract. The control group received 0.1 mL distilled water. All rats were observed for general behavior over a period of 24 h. The mortality rate was recorded daily.

Plant materials and extraction procedure: Fresh leaves of *Bryophyllum pinnatum* were collected, chopped, air-dried and pulverized. This was done to enable the sample enter the Soxhlet apparatus and also to provide a large surface area for the extraction. About 667 g of the powdered sample was extracted using methanol. A condenser and a round bottom flask were fitted at the top and bottom of the Soxhlet, respectively. The solvent was poured into the round bottom flask and the flask was placed in a water bath. There was a water pump circulator that provided water for cooling the condenser. As the extract was collected in the round bottom flask with the solvent, the water bath heated it and the solvent evaporated and condensed. The solvent was then re-used for more extraction. The cycle continued until the extract obtained from the sample was about 61 g (9.15% yield).

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Animals and chemicals: Adult male albino rats of Wistar strain, weighing between 150-220 g were used. They were obtained from the Animal House, College of Medicine, University of Ibadan, Ibadan, Nigeria. The animals were housed in separate cages where they were acclimated to laboratory conditions for 3 weeks. Indomethacin was prepared by dissolving it in 2% sodium carbonate.

Gastric ulceration experiment: This experiment was carried out as described by Njar *et al.* (1995). Male rats were randomly assigned into 5 experimental groups of 5 rats each. Food and water were withdrawn about 16 h before commencement of the experiment. Group 1(control) rats received 0.5 mL distilled water (vehicle for the extract). After 2 h 40 mg kg^{-1} b.w. of indomethacin dissolved in 2% sodium carbonate in water was administered intraperitoneally to the rats in this group. Groups 2, 3 and 4 rats received 10, 20 and 40 mg kg^{-1} b.w., respectively of *Bryophyllum pinnattum* extract dissolved in distilled water. Group 5 rats received 40 mg kg^{-1} b.w. propranolol intraperitoneally. In each group, 2 h after administration of the extract, 40 mg kg^{-1} b.w. indomethacin dissolved in 2% sodium carbonate in water was administered intraperitoneally to each rat. The rats were killed 4 h later by cervical dislocation. Scoring of gastric ulceration was done as earlier described by Alphin and Wards (1967). Ulceration in the stomach was accessed by means of a scoring technique whereby macroscopic examination of the stomach was made using a hand lens and ulcers were scored using the method and criteria of Elegbe and Bamgbose (1976). Normal gastric mucosa was scored 0, punctuate haemorrhage, pinpoint ulcer was scored 0.5, one or two small hemorrhages ulcer was scored 1.0 while ulcers greater than 3 mm in diameter were scored 2.0. Ulcer index and percentage inhibition of ulceration were calculated as earlier described (Njar *et al.*, 1995; Raji *et al.*, 2000, 2004) thus:

$$\text{Ulcer Index} = \frac{\text{Mean degree of ulceration} \times \% \text{ group of ulceration}}{100}$$

$$\% \text{ Inhibition of Ulceration} = \frac{\text{Ulcer Index in control - Ulcer Index in test} \times 100}{\text{Ulcer Index in Control}}$$

Gastric acid secretion experiment: This was done essentially as earlier described (Raji *et al.*, 2004). The effects of *Byrophyllum pinnatum* extract (10, 20 and 40 mg kg^{-1} b.w.) on basal and histamine-induced (1 mg kg^{-1}) gastric acid secretion in albino rats fasted for 24 h was studied. Briefly adult male rats (150-220 g) were anaesthetized with i.p. injection of 0.6 mL/100 g 25% ethyl carbamate. The femoral vein (route of drug administration), oesophagus and pyloro-duodenal junction were cannulated. The stomach was perfused with normal saline (37°C) via oesophageal cannula and gastric effluent was collected (via pyloro-duodenal cannula) at a constant rate of 1 mL min^{-1}. The effluent was titrated against M/400 NaOH solution as previously carried out (Njar *et al.*, 1995; Raji *et al.*, 2000, 2004). The effects of *Byrophyllum pinnatum* extract (10, 20 and 40 mg kg^{-1} b.w.) alone and in combination with histamine (1 mg kg^{-1}) on gastric acid secretion were also studied. The results were expressed as mEq L^{-1}.

Statistical analysis: Data were expressed as mean±SEM The differences between two or more values were compared using the students' t-test and ANOVA where appropriate. The significance of difference was accepted at $p<0.05$.

RESULTS AND DISCUSSION

The results showed that *Bryophyllum pinnatum* possess potent antiulcer properties. In the acute toxicity study carried out, a dose of 25 mg kg^{-1} given intraperitoneally caused neither death nor any observable adverse symptoms (Table 1). There was no significant change in daily body weight compared with untreated control during the next 3 weeks. However i.p. administration of 200 mg kg^{-1} of *Bryophyllum pinnatum* caused 100% mortality in rats. This result indicates that the extract has a sufficient margin of safety; consequently its administration as it is used in folk medicine may not have any immediate deleterious effect.

The result in Table 2 showed that extract of *Bryophyllum pinnatum* exhibited a dose dependent gastro-protective effect on indomethacin induced ulceration in rat. The cyto-protection offered by 40 mg kg^{-1} b.w. was greater than that produced by 40 mg kg^{-1} b.w. propranolol indicating that the extract could probably be more potent than propranolol in the measured variables. Table 3-5 show the results of gastric acid secretion of methanolic extract of *Bryophyllum pinnatum.* The study on effects of methanolic extract of *Bryophyllum pinnatum* on gastric acid secretion showed that the extract caused a decrease in both basal and histamine-induced gastric acid output. The decrease in gastric acidity was progressively duration and dose dependent (Table 3-5).

This influence was confirmed by the inhibitory effect of the different doses of the extract on histamine (1 mg kg^{-1} b.w.) induced gastric acid secretion indicating that the active agent in the methanolic extract of the

Table 1: Acute toxicity study of *Bryophyllum pinnatum* extract on mice

Dose (mg kg^{-1} b.w.)	Log dose	No. dead	No. alive	Mortality (%)
200.0	2.300	5	0	100
100.0	2.000	4	1	80
50.0	1.699	3	2	60
25.0	1.398	0	5	0
12.5	1.097	0	5	0
0.0	0.000	0	5	0

Table 2: Effect of *Bryophyllum pinnatum* extract on indomethacin-induced gastric ulceration in rats

Dose of *B. pinnatum* (N = 5)	Ulcer index Mean±SEM	Mean total acidity	Inhibition of ulceration (%)
Control	8.3±0.14	0.45±0.02	0.00
10 mg kg^{-1} b.w.	6.2±0.66	0.39±0.01	25.30
20 mg kg^{-1} b.w.	4.2±0.58	0.28±0.01	49.39
40 mg kg^{-1} b.w.	2.4±0.96	0.14±0.02	71.08
Propranolol (40 mg kg^{-1})	8.0±0.52	0.50±0.03	3.61

Table 3: Effect of 10 mg kg^{-1} b.w. of cmde extract of *Bryophyllum pinnatum* on gastric secretion

Time (min)	Basal output	Histamine stimulated	10 mg kg^{-1} b.w. *B. pinnatum*
10	0.036±0.009	0.052±0.002	0.054±0.008
20	0.045±0.007	0.064±0.003	0.058±0.002
30	0.043±0.001	0.082±0.005	0.041±0.005
40	0.038±0.008	0.084±0.003	0.036±0.006
50	0.039±0.004	0.083±0.006	0.031±0.001
60	0.035±0.005	0.082±0.008	0.050±0.003

Table 4: Effect of 20 mg kg^{-1} b.w. of cmde extract of *Bryophyllum pinnatum* on gastric secretion

Time (min)	Basal output	Histamine stimulated	20 mg kg^{-1} b.w. *B. pinnatum*
10	0.067±0.003	0.059±0.009	0.062±0.004
20	0.053±0.006	0.071±0.002	0.052±0.003
20	0.048±0.005	0.078±0.009	0.041±0.002
40	0.053±0.003	0.077±0.001	0.029±0.001
50	0.047±0.004	0.076±0.001	0.028±0.003
60	0.044±0.001	0.072±0.009	0.039±0.009

Table 5: Effect of 40 mg kg^{-1} b.w. of cmde extract of *Bryophyllum pinnatum* on gastric secretion

Time (min)	Basal output	Histamine stimulated	40 mg kg^{-1} b.w. *B. pinnatum*
10	0.052±0.007	0.054±0.004	0.053±0.001
20	0.050±0.008	0.056±0.009	0.039±0.007
30	0.046±0.005	0.057±0.002	0.041±0.001
40	0.045±0.003	0.061±0.004	0.027±0.005
50	0.044±0.002	0.060±0.002	0.027±0.006
60	0.044±0.001	0.064±0.007	0.028±0.003

Bryophyllum pinnatum probably competed with the histamine receptors. Previous phytochemical studies on this plant revealed the presence of xanthones, flavonoids, anthraquinones and traces of alkaloids. Potent cytotoxic bufadienolides, bryophyllin A and B have been isolated from the plant (Yamagishi, 1989). Cardiac glycosides, known as bryotoxins, are also present in the plant. The results suggest that extract of *Bryophyllum pinnatum* probably act by inhibiting gastric acid secretion. The gastric acid stimulatory action of histamine is mediated by H_2 receptor as demonstrated by several studies (Batzri and Dyeri, 1981; Berglindh, 1977; Bottcher *et al*., 1989; Dial *et al*., 1981). Histamine stimulation of acid secretion is inhibited competitively by selective H_2 receptor antagonists (Hirschowitz and Molina, 1983). Since endogenous histamine formation and release in the gastric mucosa have been implicated in the pathogenesis of gastric ulcers, antihistamine agents may be useful in the prevention of such lesions (Parmar and Gosh, 1981). It is possible that some of the chemical constituents of *Bryophyllum pinnatum* extract might act as antihistamine. It could be concluded that the extract of *Bryophyllum pinnatum* has a high tendency of being a good anti-ulcer agent. Further studies could therefore concentrate on the detailed mechanism by which the extract reduces the total gastric acidity of the stomach. The compound(s) responsible for this action could also be characterized. Furthermore, other solvents could be used to extract *Bryophyllum pinnatum* and the gastric antisecretory effect of different extracts could be monitored.

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