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Ulcer and Score Indices of Unripe Plantain Peels Extract Match that of Omeprazole as Antiulcerogenic Agent

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ABSTRACT

Comparative study of antiulcerogenic properties of unripe plantain peels of Musa *paradisciaca* plant and omeprazole was carried out in 50 animals (26 male and female albino rats and 24 male and female albino mice). The acute toxicity test carried out had the LD_{50} of 18070.87 mg/kg. There was significant different ($P<0.05$) in the reduction of ulcer index and ulcer number in the rats treated with low, medium and high dosages of the ethanolic extract of the plantain peel as compared with omeprazole. However, a more drastic decrease in ulcer number and index was observed with omeprazole administration alone and was very significant ($P<0.05$). But most drastic reduction in ulcer number and index was observed in combination dosages of the extract and omeprazole and was highly significant ($P<0.05$). There was a significant reduction in gastric acid output in the rats treated with high dose of extract than with low and medium dosages and the difference was significant, ($P<0.05$). Also, the gastric acid output was significantly reduced with high dosage of the extract than omeprazole. A combination of medium dosage with omeprazole showed decrease in gastric acid output than with medial dose alone. It is shown in the study that unripe plantain peel extract could be used as herbal remedy in the treatment of gastric.

Keywords: Unripe plantain peels, Gastric acid, Ulcer omeprazole, Ulcer

INTRODUCTION

Peptic ulcer results from physiological imbalance between certain profiles; gastrin, histamine, prostaglandin, hydrochloric acid, pepsin refluxed bile's reactive oxygen species (Ros) mucosa blood flow, cell renewal and migration, gastric barrier [1]. But specifically, the roles of the diet, coffee, lipton tea, are very critical factors in the pathogenesis of the disease [2]. Peptic ulcer which is the generic name for all types of ulceration in the gastrointestinal tract, e.g gastric, duodenal and esophageal ulcer is a sore form in the lining of the duodenum or stomach and the colon [3]. It is characterized by the discontinuity in the thickness of the gastric mucosa that is, there is reduction in the capacity of the mucosa due to the effect of the hydrochloric acid and that of pepsin metabolic activities. It is caused mainly by the disruption of the gastric barrier which can be the result of infection as in *Helicobacter pylori* which is also a normal flora of the gastrointestinal system, to cigarette smoking, non-steroidal anti-inflammatory drugs, alcohol etc. The pathophysiology of peptic ulcer is that of the disruption of the balance between the digestive acids and the protective mucosa layer. The disruption will lead to ulceration of the mucosa leading to ulcer. In gastric ulcer for instance the stomach lining is affected due to the imbalance between gastric acid and gastric mucosa. It is documented that duodenal ulcer is more prevalent than gastric ulcer. This may not really be so this is because many researchers have not been keen on the investigation concerning gastric ulcer and the gastric ulcer prevalent is rather salient, but many are affected [2]. The high prevalent rates of gastric ulcer is associated with *Helicobacter pylori*, characterized by inflammation, erosion of antral portion of the mucosa and cellular interactions [4]. The activities of the bacteria involve penetration and disruption of the mucous lawyer, inflammation and gastritis which affects the regulation of gastrin secretion and hydrochloric acid release. This imbalance will lead to gastric ulceration [2]. *Helicobacter pylori*'s action in increase gastric production can erode the mucosal lining of the stomach and results in ulcer [5]. Prostaglandin, (E_2) as mediators for the healing in ulcer by its mucous production properties are often inhibited by non-steroidal anti-inflammatory drugs which inhibit COX-1&2, pathways. The common signs and symptoms of peptic ulcer are burning aspect of the abdominal pain and is peculiar with gastric ulcer. This pain could be felt from the naval to the sternum affecting also the thoracic region of the spine [6]. The

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pain is the result of tissue ulceration, which has exposed the nerve fibers and also the effect of gastric acid in contact with ulceration. The pains may be worst when the stomach is without food, eating of spicy and acidic foods.

There is relief after eating, but milk intake may re-initiate the pains. This is because milk intake and any food with protein content leads to the release of gastric which will stimulate histamine release and the release from the parietal cells consequently which leads to release of gastric acid [1]. Other signs and symptoms include passing of dark stool due to bleeding from the gastrin ulcer spots, it can also lead to vomiting of coffee like blood or fresh blood. The foul smell of the blood is due to oxidized iron of the hemoglobin. Other symptoms include heartburn indigestion, bloating, belching, loss of appetite and weight. Peptic ulcer can lead to anemia, peritonitis due to loss of blood and tissue perforation. It can be life- threatening if the ulcer affects one of the blood vessels e.g. gastroduodenal artery [7]. Also, stomach cancer can develop from stomach ulcer also stomach ulcer can be caused by stomach cancer or malignant tumour [6]. Peptic ulcer is treated with both H_2 blockers; cimetidine and ranitidine and proton pump inhibitors, omeprazole [8]. Such treatment needs a combination e.g. with antibiotics and bismuth salicylate. Cimetidine use is associated with drug toxicity, hypotension, gynecomastia in males and loss of libido and impotency [9]. Ranitidine use has been linked with irreversible hepaticyte damage [10] but with less adverse effect with long - lasting action. All these drugs can still lead to specific side effect that is hypochlorhydria which is the effect in the production of less acid for protein metabolism.

The plantain plant also known as Musa *paradisciaca* is very popular as tropical plant and all parts of it seems to be very important medicinally. The fruit is used in the treatment of diarrhoea, dysentery, ulcerative colitis, diabetes, spruce, uraemia, nephritis, gout, hypertension. The leaves are used for the treatment of gastric ulcer [2] and has granted potent license for this author. The plant is rich in potassium necessary in regulating heart rate and blood pressure against sodium [11]. It contains iron, magnesium, and phospurus and vitamin B_6. The aim of the study was to establish the antiulcerogenic potentials of the peels of the unripe plantain since such potential have been established with the leaves [12].

MATERIALS & METHODS

Animal stock and care

Twenty-six (26) and twenty-four (24) male and female Swiss albino rats and mice weighing 127-2329 and 18-209 respectively were used for the study. The animals were kept in a ventilated animal house of the College of Health Sciences, University of Uyo. The animals were fed with sterilized water and food pellets daily. They were used according to the regulation of institute of animal and ethical committee (IAEC) of Helsinki, 1964.

Plant collection and extraction

Four (4) bunches of unripe plantain, Musa *paradisciaca*) fruits were obtained from a private farm in Ikot Ekpene Local Government Area of Akwa Ibom State, Nigeria. The plant was identified by Prof. Mrs. Margaret Bassey a taxonomist in the Department of Botany and Ecological Studies, University of Uyo.

Extraction

The method of Trease and Evans 1996 was used for the extraction Fresh peels of the plantain fruits were removed from the four (4) bunches plantain peels preparation. The peels were chopped into pieces and dried in the sun for 14 days to get rid of the moistures. It was pulverized and weighed, it was 750 g. It was then macerated and extracted with 50% ethanol. It was left for 72 hours for derivation of active ingredient in the extract. It was filtered and the residue discarded. The filtrate was then concentrated using evaporator in the water bath at 45°C. The resulting extract was 68.3 g in weight. It was kept at 4°C in refrigerator for use in LD_{50} and other studies.

Acute toxicity test (LD50)

The method of Lorke [13] was used. A total of 24 Swiss albino mice were used and was carried out in two phases. In phase 1, the albino mice were grouped into 2 groups with 3 in each group. The first group was given 5000 mg/kg of the extract and the second group, 3000 mg/kg of the extract after 24 h fasting. The animals were observed for physical signs of toxicity within 24 h after administration e.g. restlessness, urination, excretion, death. The mortality rate was 100% in both groups administered with 3000 mg/kg and 5000 mg/kg. In phase 2, the animals having submitted to 24 h fasting were grouped into 6 groups with 3 in each group and administered the following extract concentration, 500 mg/kg 1000 mg/kg, 1500 mg/kg, 1750 mg/kg, 2000 mg/kg, 2500 mg/kg respectively. After administration 0% mortality was observed with the group administered with 500mg/kg and 17500 mg/kg of the extract. But 100% mortality with the group administered with 2000 and 2500mg/kg and the LD_{50} calculated based on this.

That is $LD_{50} = \sqrt{A \times B} = \sqrt{1750 \times 2000} = 1870.83$mg/kg

LD_{50} = 1870.83mg/kg

For 10% as low dose, it was 1877.03 mg/kg.

20% (medium dose) it was 374.17 mg/kg.

30% (high dose) it was 561.25 mg/kg.

Stock Preparation: 1 g of the extract was dissolved in 10 ml of distilled water i.e. 1g/10ml distilled water

= 1000 mg/10ml distilled water

= 100 mg/ml as stock solution

The amount to be given to the animal was based on the weight of the animal by g and by the concentration and the stock solution = $\frac{Weight\ of\ animal \times LD_{50}}{Stock\ solution\ (100\ mg/kg)}$

Ulcer Induction: The methods of Bary 1983 were used. The rats were starved for 24 h and after that, 0.5 ml of 99% ethanol was administered orally using canula, by-passing the esophagus and delivered into the stomach. The rats were observed for ulceration 4 h after the administration of ethanol. This was done by chloroform anesthesia and the incision of (removal) the rat stomach with scissors and opened along the greater curative to expose the mucosa. The ulcer was counted using hand lens and the ulceration spots counted according to Bary et al. [14] as follows:

Gastric Secretion: Baker 1983 [14].

Methods of Silverton and was used. Count of opened stomach was drained and diluted with 5 ml of distilled water and gastric acid output calculated as follows:

Ulcer Scoring and Index:

0 = No lesion
1 = Mucosal edema and petechiae
2 = 1-5 small lesion,
3 = more than 5 small lesion
4 = intermediate lesions
5 = Perforated ulcers

Ulcer index was calculated from the formula:

$$UI = \frac{Total\ ulcer\ score}{\frac{No.of\ animals\ ulcerated}{\frac{K.X\ mmol}{Y}}}$$

X = Average
K = Concentration
Y = Volume of diluted fluid (original volume)

Grouping and administration of extract and omeprazole

The following were the groupings and administration

Group A = Induced with ulcer without treatment

Group B = Normal without ulcer inducement

Group C = Given low dose of extract (187.03mg/kg) (ulcer induced)

Group D = Given medium dose of extract (374.17mg/kg) (ulcer induced)

Group E = Given High Dose of extract (561.25mg/kg) (ulcer induced)

Group F = Given medium dose of extract + omeprazole (ulcer induced)

Group G = Given omeprazole 20mg/kg (20mg/kg) (ulcer induced)

Preparation of omeprazole

Itals = 20 mg taken to average weight of man

= 20/70 g = 0.29 mg/kg

The administration was done orally using canula by-passing oesophagus and delivered into the stomach [15] for 14 days to observe for healing with extract and omeprazole.

RESULTS

The effects of extract of unripe peels of plantain are shown in this study **(Table 1 and Figure 1)**. The animals treated with ethanolic extract of *Musa paradsceaca* at low dose, 187.03 mg/kg, medium dose; 374.17 mg/kg and high dose 561.25 mg/kg respectively showed significant (P<0.05) reduction in the number of ulcer count and index (3.75±0.25, 3.25±0.25 and 2.00±0.00, UI = 3.6, 3.3, 2.0 respectively as against induced ulcer count and index of 3.35±0.25, ulcer index of 4.5 in group B).

The ulcer index was further significantly reduced (P<0.05) when the medium dose of the extract was administered in combination with omeprazole (0.29 mg/kg) (374.17 mg/kg) (0.75±0.48, (UI = 0.8) UI = ulcer index)). Administration of omeprazole alone also resulted in significant (P<0.05) decrease in ulcer score and ulcer index. (0.25±0.25, UI = 0.3 compared with control but the decrease was lower than that of combination of omeprazole and extract.

The acid output in group treated with low dose extract, 187.0.3 mg/kg was significantly higher (P<0.05), 4.63±0.09 than the medical and control groups group. Also, the acid output in group D with medium dose treatment (374.17 mg/kg) was significantly lower (P<0.05), 6.08±0.11 than the group with low dose. However, group treated with high dose of the extract, 571.25 mg/kg had low acid output significantly lower (P<0.05) (3.96±0.01) than acid output in low and medial dosages of the extract. And the animals treated with omeprazole and medium dose extract had very low acid output significantly lower (P<0.05) than other groups. And whereas a very drastic low acid output was observed in the administration of omeprazole, (P<0.05), 0.96±0.05 than any other group **(Table 2)**.

DISCUSSION

The study has unveiled the anticulcerogenic potentials of unripe peels *Musa paradisciaca* fruits. Such potentials have already been observed in the leaves of the same plant which is now a remedy for gastric ulcer treatment and has granted potent licence for the author [2]. The effects of plantain peels are both alkaline and antiulcerogemic. Dried peels of this plant are often used to cook bitter vegetable (Eritan) in the rural areas, people prefer this to limestone which according to them has anti-potency properties for males. The action of this peels is basically neutralizing which act on the acidic nature and

Table 1. Ulcer scores obtained following treatment with varied doses extract of *Musa paradisiacal* and omeprazole.

Groups	Initial Ulcer Scores	Final Ulcer Scores	Ulcer Index
A	0.00±0.00	0.00±0.00	0.0
B	4.00±0.00	3.50±0.29[a]	4.5
C	5.00±0.00	3.75±0.25[a]	3.6
D	5.00±0.00	3.25±0.25[a,b]	3.3
E	5.00±0.00	2.00±0.00[a,b,c,d]	2.0
F	5.00±0.00	0.75±0.48[a,b,c,d,e]	0.8
G	5.00±0.00	0.25±0.25[a,b,c,d,e,f]	0.3

Legend: *a, c, d, e and f = significantly different from groups A, B, C, D, E, and F respectively, (P <0.05)*
Group A: *Control induced with ulcer*
Group B: *Control without ulcer*
Group C: *Low dose extract*
Group D: *Medium dose extract*
Group E: *High dose extract*
Group F: *Medium dose + omeprazole*
Group G: *Omeprazole only*

Table 2. Gastric acid secretion: Acid output (mmol) following treatment with varied doses of extract of *Musa paradisaca* and omeprazole.

Groups	Treatment	Acid output (mmol)
A (Normal control)	10 ml distilled water	2.25 ± 0.22
B (Control induced)	10 ml distilled water	2.25 ± 0.27
C	Low dose Musa p.	4.63± 0.09 a, b
D	Medium dose Musa p.	4.08±0.11 a, b
E	High dose Musa p.	3.96± 0.01 a,b,c,d
F	Medium dose + Omeprazole	1.28±0.09 a,b,c,d,e
G	Omeprazole	0.96± 0.05 a,b,c,d,e,f

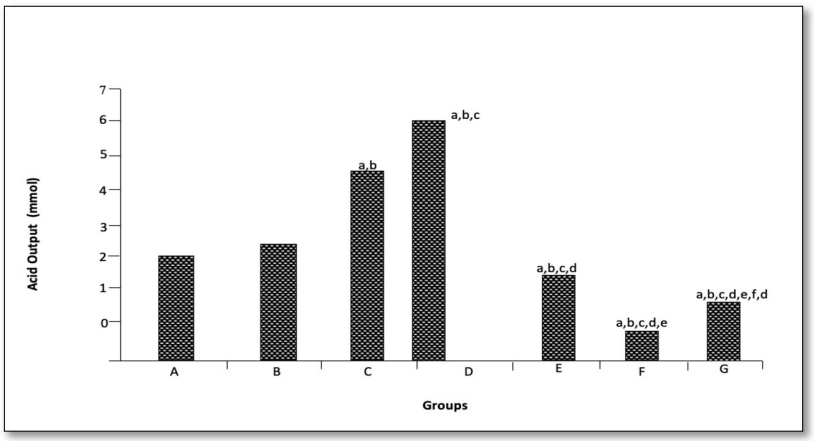

Figure 1. Comparing the acid output in m mol following treatment with varied doses of extract of *Musa paradisiaca* and omeprazole.

convert such to alkaline. The competitive action of the peels of plantain with omeprazole by its medial dose combination means it has same pathway of anti-acid activity which is the reduction of positive hydrogen and prevention of its combination with chloride ions [1]. The reduction of acid output with the peeled plantain extract is observed to be dose dependent as with high dosage of the extract a more acid output reduction was observed. The dosage comparatively was higher than that of omeprazole (0.29 mg/kg). But gives no worry to likely toxicity with this concentration as no death was recorded but certain degree of toxicity may happen as even omeprazole may have little toxicities associated with it. However, the dosage was within the safe dosage as confirmed by the acute toxicity test. The ulcer count and index were also found to be reduced with low medium and high dosages of the extract ulcer count and score indices are functions of direct effect of extract on ulceration. This implies that the extract has the healing potentials on ulcer, just as omeprazole has. It is also possible that certain phytochemical properties of the peels could ameliorate the healings. The pathway of such healing may also be like those of prostaglandin analogues e.g misoprostol which healing is done by mucosal growth, turnover and migration, inhibition of adenylate cydase, reducing cydic AMP production and reducing protein kinase activity necessary in generating hydrogen ion [16]. But importantly the study has shown that unripe plantain peels has antiulcerogenic potentials compared to omeprazole. It is an herbal plant which is now under growing purification steps for its utilization as herbal drug in the treatment of peptic ulcer.

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