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Gastroprotective Effects of Ethanolic Leaf Extract of *Musa Paradisiaca L.*(Musaceae) in Rats

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ABSTRACT

The preliminary screening of the gasroprotective effects of Musa paradisiacal L leaf extracts was investigated through bioactivity guided gradient extraction. Experimentally induced gastric ulceration was effected using indomethacin, ethanol, and aspirin models in rats. Preliminary phytochemical screening and lethality tests (LD $_{50}$) were carried out using standard methods. The acute toxicity showed the median lethal dose to be 1995.0mg/kg. The Phytochemical analysis showed the presence of alkaloids, terpenes, cardiac glycosides, and phlobatannin. The result showed that there was a significant ($p<0.05$) and dose dependent mucosal protection in all the models when compared to the control. Percentage ulcer inhibitions of extract at 1000mg/kg for ethanol, aspirin and indomethacin induced ulcers were 76 %, 85.91% and 60 % respectively In all the experimentally induced ulcer models studied, Musa paradisiacal L could be exploited in the treatment of peptic ulcer in man.

Key words: LD $_{50}$, gradient, ulcerogens, gastric ulcers, model.

INTRODUCTION

Natural products like plants present promise of cure, as they have been the raw materials for the synthesis of drugs and as an important source of new therapeutic agents [1]. Diverse chemical compounds have been isolated from medicinal plants with antiulcer activity [2]. Several factors

known to increase the incidences of peptic ulcer diseases (PUD) are smoking, nutritional deficiencies, alcohol consumption and frequent ingestion of non-steroidal anti-inflammatory drugs (NSAIDs) [3,4].

The plant, *musa paradisiacal L.* is a member of the banana family Musaceae closely related to common banana, *Musa sapientum.*

Sanyal *et al*, have reported the anti-ulcerogenic activity of dried powder of banana pulp (DRBP) against ulcers induced by histamine in guinea pigs and, phenylbutazone, restraint stress and prednisolone in rats [5-8]. Other workers like Elliott and Heward [9] and Best, *et al* [10] have also confirmed the anti-ulcerogenic activity of banana against histamine induced gastric ulcers in mice and aspirin-induced gastric ulcers in rats respectively.

Whereas much work has been done on other parts of the plant, no research has revealed the potential gastroprotective properties of the leaves of *Musa paradisiacal L.* This research, therefore,aims to investigate the ulcerogenic activity of the leaf

EXPERIMENTAL ANIMALS

Healthy Wistar albino rats of (150-200 g) and Swiss albino mice (17 - 25 g) were used throughout the experiments. The animals were procured from the Animal House of University of Uyo, Nigeria. Before initiation of experiment, the animals were acclimatized for a period of 7 days. Standard environmental conditions such as temperature (26-±2ºC), relative humidity (45-55%) and 12 hrs dark/light cycles were maintained in the quarantine. All the animals were fed with rodent pellet diet (Guinea® feeds, Ewu, Edo State) and water was allowed *ad-libitum* under strict hygienic conditions. Ethical clearance for performing the experiments on animals was obtained from Institutional Animal Ethics Committee (IAEC).

Drugs and chemicals

Mistoprostol, indomethacin, Aspirin, ethanol, chloroform and Acetic acid were purchased from Sigma Aldrich, U.S.A. Ferric chloride, acetic anhydride, Conc.H_2S0_4, 1% aqueous Hcl, Dragendoff's reagent were products of BDH Chemicals, England.Omeprazole was a gift from CIPLA. All the other chemicals used were of analytical grade.

Methods

Collection and authentication of the plant

The fresh leaves of Musa paradisiacal L. was collected in the morning of June 9, 2010 from Itak Ikot Akap, Ikono Local Government Area of Akwa Ibom State, Nigeria. The leaves were identified and authenticated by a taxonomist in the department of botany and ecological studies, University of Uyo, Nigeria.

Extraction of the Plant

The leaves were then finely powdered using electrical blender. The fine powder (250 g) was soaked in 500 ml ethanol (95%) in conical flask for 6 days. After 6 days the mixture was filtered, using a fine muslin cloth followed by filter paper (Whatman No. 1) and distilled under reduced pressure in an Eyela rotary evaporator (Sigma-Aldrich, USA).

Acute toxicity and lethality tests: Lorke's [11] method was used to ascertain the acute toxicity of the aqueous extract. 2 groups of 3 mice each were administered 312.5, 625 and 1000 mg/kg of the aqueous extract orally. The mice were observed for 24 h for effects of toxicity and the number dying in each group within the period noted. When no deaths were recorded, another five groups of 3 mice each were administered 1250, 1500, 2000, 2500 and 5000 mg/kg of the extract orally. The animals were observed for 48 h for effects of toxicity and the number dying in each group within the period was recorded.

Anti-ulcer activity: Three models (Ethanol, Aspirin, and Indomethacin) with effective induction of ulcer experimentally in rats were employed to evaluate the anti-ulcer activity of the aqueous extract of *Musa paradisiaca.* All the rats used were fasted for sixteen hours but were given water *ad libitum* till the start of the experiment.

Ethanol-induced ulcer: Thirty fasted animals were used in five groups of six animals each. Groups A and B received 2 ml/kg distilled water (negative control) and 50 mcg/kg p.o. Misoprostol (positive control) while rats in groups C, D and E were given 100, 250 and 500 mg/kg of *Musa paradisiaca* orally (p.o) respectively. After one hour all animals received 1 ml/kg of 80% ethanol orally. The rats were sacrificed with chloroform anesthesia after one hour. The stomachs were isolated, washed gently under clean flowing water and cut open along the greater curvature. The stomachs were then fixed in 10% formalin and craters observed and ulcer scores were recorded using the method by Aguwa and Ukwe [12]

Aspirin-induced ulcer: Thirty fasted rats were also used this model as five groups of six rats each. Groups A and B of this model received distilled water (2 ml/kg) and omeprazole 20 mg/kg p.o respectively, while groups C, D and E received 100 mg/kg, 250 mg/kg and 500 mg/kg p.o of the extract. After one hour, 200 mg/kg p.o of aspirin was given to each rat, and was scarified 4 h later [13] as described above. Stomachs were isolated, fixed and ulcers counted using the above mentioned method.

Indomethacin-induced ulcer: Animals (five groups of six rats each) in groups A, B, C, D and E received distilled water 2 ml/kg p.o., omeprazole 20 mg/kg p.o, 100, 250 and 500 mg/kg p.o of extract respectively. After 30 min, indomethacin 40 mg/kg p.o was administered to each rat. After 8 h of drug treatment [14], stomachs were isolated, cut and ulcers counted as before.

Statistical analysis: Ulcer indices were shown as the mean±standard error of mean and level of ulcer protection presented as percentage inhibition. The significance of the differences in mean ulcer indices between extract and negative control was calculated at 95% confidence interval using Student's t-test on Microsoft Excel 2003.

RESULTS

Phytochemical screening showed that the extract contains alkaloids, glycosides, saponins, tannins, flavonoids and resins. Acute toxicity results showed that the LD_{50} was greater than 5000 mg/kg.

Ethanol-induced ulcer: Ulcer inhibition was evident in all treatment of the aqueous extract of *Musa paradisiaca* compared to the negative control (Table 1,). However, statistically significant ulcer inhibition (60 and 76 %, $p<0.05$) could be seen only at doses of 500 and 1000 mg/kg of the aqueous extract. The protection from ulcer was dose dependent.

Aspirin-induced ulcer: The aqueous extract at all the doses provided dose dependent protection from ulcer. The aqueous extract at doses of 500 mg/kg and 1000 mg/kg provided statistically significant protection (74.65 % and 85.91 %, $p<0.05$) when compared with the negative control (Table 2).

Indomethacin-induced ulcer: The aqueous extract protected the rats from experimentally-induced ulcers at all dose levels but the lesions produced in this model were more severe than the aspirin model (Table 3). However, the percentage ulcer inhibition was the least when compared to values obtained in the other two models. The dose of 1000 mg/kg was the only dose with statistically significant protection (60 %, $p<0.05$).

Table 1: Effects of aqueous leaf extract of *Musa paradisiaca* on Ethanol induced Ulcers in Rats (n=6)

Treatments	Dose mg/kg p.o	Quantal ulcer incidence	Ulcer index	Ulcer inhibition (%)
Distilled water	2 ml/kg	6/6	2.0± 0.25	-
Misoprostol	50 mcg	6/6	1.45 ± 0.10	27.50
Extract	250	6/6	1.38 ± 0.19	31.00
Extract	500	5/6	0.80 ± 0.09*	60.00
Extract	1000	4/6	0.48 ± 0.09*	76.00

Ulcer indices are expressed as mean ±SEM: n number of animals in each group
**: p<0.05 vs negative control (Students t-test)*

Table 2: Effects of aqueous leaf extract of *Musa paradisiaca* on Aspirin induced Ulcers in Rats (n=6)

Treatments	Dose mg/kg p.o	Quantal ulcer incidence	Ulcer index	Ulcer inhibition (%)
Distilled water	2 ml/kg	6/6	0.71 ± 0.10	-
Omeprazole	20	5/6	0.14 ± 0.03	80.28
Extract	250	6/6	0.26± 0.06*	63.38
Extract	500	6/6	0.18 ± 0.02*	74.65
Extract	1000	2/6	0.10 ± 0.03*	85.91

*Values are mean ±SEM: n number of animals in each group. *: p<0.05 vs negative control (Students t-test)*

Table 3: Effects of aqueous leaf extract of *Musa paradisiaca* on Indomethacin induced Ulcers in Rats (n=6)

Treatments	Dose mg/kg p.o	Quantal ulcer incidence	Ulcer index	Ulcer inhibition (%)
Distilled water	2 ml/kg	6/6	3.50 ± 0.43	
Omeprazole	200	6/6	0.58 ± 0.12	83.43
Extract	250	6/6	2.20 ± 0.4	37.10
Extract	500	6/6	2.68 ± 0. 25	23.43
Extract	1000	6/6	1.40 ± 0.15*	60.00

*Values are mean ±SEM: n number of animals in each group. *: p<0.05 vs negative control (Students t-test)*

DISCUSSION

The anti-ulcer activity of the aqueous of *Musa paradisiaca* against ethanol-, aspirin- and indomethacin-induced ulcers was established in this study. Results of acute toxicity showed that the plant is safe as exemplified by its use as food in domestic and wild animals. The extract protected the stomach against ethanol's necrotic damage and its effect was more pronounced than misoprostol, a cytoprotective agent. Ethanol challenge induces gastric injury due to production of oxygen free radicals leading to increased lipid peroxidation, which causes damage to cell and cell membrane [15] presenting as red streaks of sores. The protection by the extract of this type may suggest a possible cytoprotective mechanism of action

An earlier study has suggested the plant's ability to protect against HCl/Ethanol challenge [16] by prostaglandin-like cytoprotection. However, an antisecretory effect might be indicated as the extract protected the stomach mucosa from NSAIDS (aspirin and indomethacin) induced damage. This damage is elicited by the inhibition of prostaglandin synthesis, which is essential for mucosal integrity and regeneration [17]. This results to a sustained reduction in mucosal blood flow and a subsequent generation of ulcer. misoprostol and omeprazole were employed in this study for the latter's cytoprotective but not anti-secretory effect and its effectiveness against experimentally induced ethanol ulcers [18] and omeprazole exhibits an anti-secretory and protective effect [19] against ulcers and agents providing ulcer healing against NSAID induced ulcers may provide similar effect.

The presence of saponins, tannins, glucosides and alkaloids in this extract as seen in this study has also been reported by earlier studies [20,21]. Ulcer protection may be attributed to any of these. This study has demonstrated that the aqueous leaf extract of *Musa paradisiaca* has an ulcer healing property against experimentally induced ulcers in rats and this study confirms folkloric claims of the benefits of the plant in treatment of ulcer.

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