

Preliminary Evaluation of Anti-ulcer Potential of Aqueous Extract of Fermented Unripe *Musa paradisiaca* in Wistar Rats

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Abstract *Musa paradisiaca* Linn. belonging to the family Musaceae is a common medicinal plants use in herbal medicine for the treatment of diseases like diabetics, hypertension and ulcer. This study evaluated the antiulcerogenic potentials of aqueous extract of fermented unripe *M. paradisiaca* fruits using acetic acid, aspirin, ethanol, indomethacin and pyloric ligation-induced ulcer models at the doses of 400 and 800 mg/kg body weight. Omeprazole at 5 mg/kg was used as a standard reference drug. The result of the acute toxicity test showed that up to 5,000 mg/kg body weight of the extract did not cause any mortality of the wistar rats. The different doses of the extract and the reference drug significantly ($p < 0.05$) decreased all the ulcer parameters (ulcer score and ulcer index) in a dose dependent manner in all the ulcer models. The degree of ulcer index is in the order: Pyloric-ligation (11.33 ± 0.12) < Indomethacin (12.03 ± 0.14) < Acetic acid (12.17 ± 0.23) < Aspirin (13.20 ± 0.10) < Ethanol (15.60 ± 0.40). Similarly, the percentage gastro-protective activity increased from 0% in the negative control up to 23.56% at the dose of 800mg/kg body weight of the extract. The degree of percentage gastro-protection is in the order: Pyloric-ligation (7.93%) < Indomethacin (10.51%) < Acetic acid (13.51%) < Ethanol (22.19%) < Aspirin (23.56%). The enhanced cessation of gastric erosions could be attributed to the synergistic role of probiotics and phytochemicals in the plant extract. In conclusion, fermented unripe *M. paradisiaca* fruit extract is a good candidate for screening of new antiulcer drugs.

Keywords: fermented extract, *Musa paradisiaca*, antiulcerogenic, gastro-protective activity

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1. Introduction

Peptic ulcer is one of the most prevalent gastrointestinal disorders in clinical practice. It is defined as a breach or lesion along the mucosal membrane of the gastrointestinal tract. In the world today, the exact pathogenesis of peptic ulcer has continued to elude medical and traditional practitioners; but a common ground has been elucidated. Peptic ulcer occurs due to an imbalance between the aggressive factors (acid, pepsin, *Helicobacter pylori*, and bile salts, NSAIDs) and defensive factors (mucin secretion, prostaglandins, cellular mucus, bicarbonate secretion, mucosal blood flow and cell turnover) resulting to an interruption in mucosal integrity [1,2]. The symptoms of peptic ulcer vary depending on the age of the persons or animals. Abdominal pain, bloating and abdominal fullness, water-brash, nausea, copious vomiting, loss of appetite and weight, hematemesis and melaena are commonly observed clinical symptoms [3]. To regain the balance and restore the integrity of the mucosal membrane, different therapeutic agents (conventional drugs and complementary or alternative medicine) have been used over years to

reduce gastric acid secretion. These conventional drugs such as: antacids (magnesium hydroxide, aluminum hydroxide); H₂-receptor blockers (ranitidine, cimetidine, famotidine); anticholinergics (pirenzepine, telenzepine) and proton pump blockers (omeprazole, lansoprazole) show limited efficacy against gastric erosions and are often associated with severe side effects [4,5]. In the medical field today, medicinal plants have contributed immensely in the management of diseases including ulcers. Sofowora [6] suggested that the essentiality of these plants is due to the accumulation of secondary metabolites. These phytoconstituents like flavonoids, coumarin, alkaloids, terpenoids, tannins, phenolic acids, antioxidants, and micronutrients [7,8] possess numerous ethnomedicinal benefits.

Many medicinal plants, including *Musa paradisiaca*, have been reported to have antiulcer activities. *Musa paradisiaca*, commonly known as plantain, belongs to the family Musaceae in the order Zingiberales. Many researchers have reported antitumor [9], hypoglycemic [10], antihelminthic [11] and anti-ulcerogenic [8] potentials of *Musa paradisiaca*. No information has been published on the antiulcer activity of aqueous extract of fermented unripe *M. paradisiaca* fruit, hence the novelty of this

study. Nonetheless, the thrust of the present study was to evaluate the efficacy of the extract of fermented unripe *Musa paradisiaca* fruits as a remedy against peptic ulcer using various experimentally-induced ulcer models in wistar rats.

2. Materials and Methods

2.1. Sample Collection and Identification

Freshly cut bunches of unripe *Musa paradisiaca* fruits were purchased from Eke Okigwe, Okigwe Local Government Area of Imo State, Nigeria. Eke Okigwe lies between latitude $5^{\circ}50'0.9''N$ and $5^{\circ}49'55''N$ and longitude $7^{\circ}21'32.6''E$ and $7^{\circ}23'17''E$. The plant was identified in the Department of Plant Science and Biotechnology, Abia State University, Uturu.

2.2. Sample Preparation

The fruits of unripe *Musa paradisiaca* were sorted to remove rotten fruits, dust and extraneous materials and washed with clean water. Exactly two (2) fingers of *Musa paradisiaca* were peeled and washed thoroughly. The fruits were cut into smaller sizes. With the aid of G & G® Electronic Scale, 200g of plantain was weighed into a beaker containing 270ml of distilled water. The beaker was covered with foiled and allowed to stand for 15 hours. Upon overnight fermentation, the extract was filtered using cheese cloth and the membrane filter paper of 47.0mm diameter and the pore size approximately $0.45\mu m$, with the aid of a suction pump. The filtrate was used immediately.

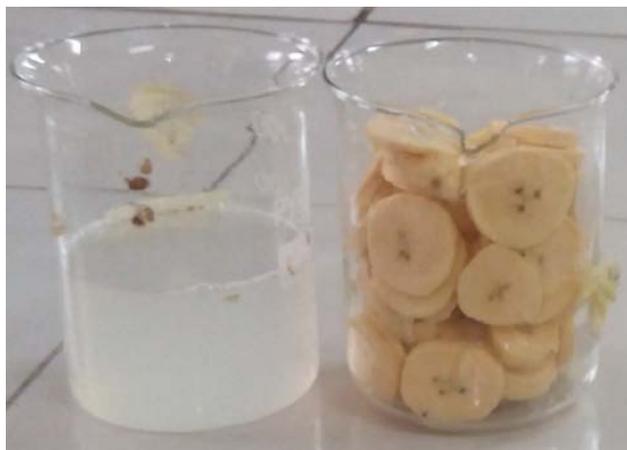


Figure 1. Diagram of *Musa paradisiaca* extract

2.3. Acute Toxicity Study

Lorke [12] method was adopted for the determination of median lethal dose of fermented aqueous extracts of *Musa paradisiaca* (Linn.) fruits. In the pilot study, twelve rats weighing between 150-200g were randomly divided into three groups (A, B, C and D) of three rats each and were administered *M. paradisiaca* 500, 1000, 2000 and 5000mg/kg body weight respectively. The animals were then observed for behavioural changes and mortality for 24 hours. The LD_{50} is usually calculated as the geographic

mean of the least lethal dose that killed a rat and the highest dose that did not kill a rat.

2.4. Experimental Animals

The male albino rats were obtained from the Department of Pharmacology and Toxicology, University of Nigeria, Nsukka, and were allowed to acclimatize for two (2) weeks in the Animal House of the Department of Biochemistry, Abia State University, Uturu. These animals were fed on grower mash. All the animals used had free access to clean water. They were kept in well ventilated rooms with 12/12 h light/dark condition and ambient room temperature. The experimental procedures used in this study conform to the United States National Institutes of Health Guidelines for Care and Use of Laboratory Animals in Biomedical Research [13].

2.5. Experimental Design

Acetic acid-induced ulcer study

The anti-ulcerogenic potentials of fermented aqueous extract of unripe *Musa paradisiaca* (Linn.) fruits on acetic acid-induced ulcer model in wistar rats was investigated using modified method of Hiruma-Lima *et al.* [14]. A total of fifteen wistar rats (150- 200g body weight) was starved for 24 hours and grouped into five groups (Group I and V) of three rats each based on their body weights. Each administration in the various groups was done according to the specification below:

Group I: Normal Control (n=3) given orally distilled water (5ml/kg) body weight.

Group II: Negative control (n=3) given orally acetic acid (0.5ml of 80%) body weight

Group III: Reference drug (n=3) given orally omeprazole (5mg/kg) body weight.

Group IV: Plant extract (n=3) given orally plantain extract (400mg/kg) body weight.

Group V: Plant extract (n=3) given orally plantain extract (800mg/kg) body weight.

After 30 minutes of treatment, each animal in Groups II- V received 0.5ml of 80% acetic acid orally. After 1 hour, all the animals were anaesthetized with chloroform and dissected. The stomachs were excised and carefully opened along the line of greater curvature to expose the walls. The stomachs' contents were then washed off and the stomach walls viewed with the aid of hand lens (x10) to determine the ulcer scores using the method of Raju *et al.* [1]. The ulcerative lesions were counted and scored as follows:

Normal stomach	-	-	-	0
Pinhole	-	-	-	1.0
Spot ulceration-	-	-	-	1.5
haemorrhagic streaks	-	-	-	2.0
Small erosion	-	-	-	2.5
Large erosion	-	-	-	3.0
Perforation	-	-	-	3.5.

2.6. Aspirin-induced Ulcer Study

The anti-ulcerogenic potentials of fermented aqueous extract of unripe *Musa paradisiaca* (Linn.) fruits on aspirin induced ulcer model in wistar rats was investigated

using modified method of Raju *et al.* [1]. A total of fifteen wistar rats (150-200g body weight) was starved for 24 hours and grouped into five groups (Group I and V) of three rats each based on their body weights. Each administration in the various groups was done according to the specification below:

Group I: Normal Control (n=3) given orally distilled water (5ml/kg) body weight.

Group II: Negative control (n=3) given orally aspirin (1000mg/kg) body weight.

Group III: Reference drug (n=3) given orally omeprazole (5mg/kg) body weight.

Group IV: Plant extract (n=3) given orally plantain extract (400mg/kg) body weight.

Group V: Plant extract (n=3) given orally plantain extract (800mg/kg) body weight.

After 30 minutes of treatment, each animal in Groups II- V received 1000mg/kg of aspirin orally. After 1 hour, all the animals were anaesthetized with chloroform and dissected. The stomachs were excised and carefully opened along the line of greater curvature to expose the walls. Their stomachs were removed and treated as mentioned and the ulcers scored.

2.7. Ethanol-induced Ulcer Study

The anti-ulcerogenic potentials of fermented aqueous extract of unripe *Musa paradisiaca* (Linn.) fruits on ethanol-induced ulcer model in wistar rats was investigated using the method of Mbagwu *et al.* [15]. A total of fifteen wistar rats (150-200g body weight) was starved for 24 hours and grouped into five groups (Group I and V) of three rats each based on their body weights. Each administration in the various groups was done according to the specification below:

Group I: Normal Control (n=3) given orally distilled water (5ml/kg) body weight.

Group II: Negative control (n=3) given orally ethanol (1.2ml absolute) body weight

Group III: Reference drug (n=3) given orally omeprazole (5mg/kg) body weight.

Group IV: Plant extract (n=3) given orally plantain extract (400mg/kg) body weight.

Group V: Plant extract (n=3) given orally plantain extract (800mg/kg) body weight.

After 30 minutes of treatment, each animal in Groups II- V received 1.2ml of absolute ethanol orally. After 1 hour, all the animals were anaesthetized with chloroform and dissected. Their stomachs were removed and treated as previously mentioned and the ulcer scores determined.

2.8. Indomethacin-induced Ulcer Study

The anti-ulcerogenic potentials of fermented aqueous extract of unripe *Musa paradisiaca* (Linn.) fruits on indomethacin-induced ulcer model in wistar rats was investigated using the method of Ubaka *et al.* [16]. A total of fifteen wistar rats (150-200g body weight) was starved for 24 hours and grouped into five groups (Group I and V) of three rats each based on their body weights. Each administration in the various groups was done according to the specification below:

Group I: Normal Control (n=3) given orally distilled water (5ml/kg) body weight.

Group II: Negative control (n=3) given orally indomethacin (100mg/kg) body weight

Group III: Reference drug (n=3) given orally omeprazole (5mg/kg) body weight.

Group IV: Plant extract (n=3) given orally plantain extract (400mg/kg) body weight.

Group V: Plant extract (n=3) given orally plantain extract (800mg/kg) body weight.

After 30 minutes of treatment, each animal in Groups II- V received 100mg/kg indomethacin orally. After 1 hour, all the animals were anaesthetized with chloroform and dissected. Their stomachs were removed and treated as previously mentioned and the ulcer scores determined.

2.9. Pyloric Ligation of Ethanol Induced Ulcer Study

The anti-ulcerogenic potentials of fermented aqueous extract of unripe *Musa paradisiaca* (Linn.) fruits were studied using the pyloric ligation method of Raju *et al.* [1]. A total of fifteen wistar rats (150-200g body weight) was starved for 24 hours and grouped into five groups (Groups I-V) of three rats each based on their body weights. Their abdomen was slightly opened under mild chloroform anesthesia, and their pylorus carefully lifted and ligated. The stomachs were quickly replaced and the abdomen sutured. Each administration in the various groups was done according to the specification below:

Group I: Normal Control (n=3) given orally distilled water (5ml/kg) body weight.

Group II: Negative control (n=3) given orally ethanol (1.2ml absolute) body weight

Group III: Reference drug (n=3) given orally omeprazole (5mg/kg) body weight.

Group IV: Plant extract (n=3) given orally plantain extract (400mg/kg) body weight.

Group V: Plant extract (n=3) given orally plantain extract (800mg/kg) body weight.

After 30 minutes of treatment, each animal in Groups II- V received 1.2ml of absolute ethanol orally. After 1 hour, all the animals were anaesthetized with chloroform and dissected. Their stomachs were removed and treated as previously mentioned and the ulcer scores determined.

Calculation of ulcer index and percentage inhibition

Ulcer Index (UI) = Mean of ulcer scores per rats

Percentage Ulcer inhibition:

The percentage ulcer protection was determined using the formula of Suzuki *et al.* [17].

Protection Index

$$= 1 - \frac{\text{Ulcer index with extract}}{\text{Ulcer index with distilled water}} \times 100.$$

2.10. Statistical Analysis

Results were expressed as mean \pm SD (standard deviation). Statistical analysis was performed by One-way analysis of variance (ANOVA) with the GraphPath Prism® Statistic software package, version 7.01. One-way ANOVA with a Turkey's multiple comparisons test was

used to identify statistical differences among groups. A p -value of ≤ 0.05 was considered statistically significant.

3. Results

The result of acute oral toxicity (LD_{50}) in experimental rats showed that doses of fermented aqueous extracts of unripe *Musa paradisiaca* fruits as high as 5,000mg/kg body weight did not cause any behavioural change or mortality in the animals.

As regard to ulcer parameters there was significant increase ($p < 0.05$) in ulcer score and ulcer index of the acetic acid group (negative control) than observed in omeprazole (reference drug) and *Musa paradisiaca* fruit extract groups. The results revealed that pretreatment of the animals with omeprazole (5mg/kg body weight) and 400mg/kg body weight of aqueous extract of *M. paradisiaca* fruit prior to acetic acid injection protected against ulcerogenesis by 8.76% and 7.11% respectively. Higher dose of the extract (800mg/kg body weight) inhibited ulceration by 13.51% (Table 1). The inhibition among these dose groups was statistically significant ($p < 0.05$).

The effect of orally administered aqueous extract of fermented unripe *Musa paradisiaca* fruit on gastric damage induced by aspirin (1000mg/kg body weight) in wistar rats after one hour is shown in Table 2. Oral injection of aspirin to the experimental animals in groups II to V produced mucosal lesions in the rat stomachs in the form of haemorrhagic streaks with ulcer index of 21.00 ± 1.00 , 13.00 ± 1.00 , 11.00 ± 1.00 and 9.00 ± 1.00 respectively. Omeprazole and 800mg/kg body weight of the extract

offered significant protection of 10.08% and 23.56% respectively. There was no significant difference ($p < 0.05$) in gastro-protective activity between omeprazole group and 400mg/kg and 800mg/kg of the extracts, but at higher dose of the extract, there gastro-protective activity was statistically significant ($p < 0.05$).

The gastro-protective effect of omeprazole and treatment at different doses of fermented *Musa paradisiaca* on ethanol induced ulcer in wistar rats after one hour is shown in Table 3. The oral administration of ethanol damages the mucosal lining resulting in gastrointestinal bleeding with ulcer index of 15.60 ± 0.40 , 12.87 ± 0.32 , 12.73 ± 0.38 and 12.13 ± 0.15 in groups II to V respectively. The results revealed that there was significant difference ($p < 0.05$) in ulcer index between the negative control and the treatment groups. The percentage gastro-protective activity was highest with 800mg/kg body weight of the extract than omeprazole pretreated group.

Results of investigation of the effect of fermented unripe *M. paradisiaca* fruit extract on indomethacin-induced ulcer is presented in Table 4. The injection of indomethacin causes gastric lesions and haemorrhagic streaks with ulcer index of 12.03 ± 0.14 , 11.50 ± 0.09 , 10.90 ± 0.17 and 10.77 ± 0.06 in groups II to V respectively. The gastroprotective activity of the extract at different doses and that of the reference drug was statistically significant ($p < 0.05$). The percentage ulcer inhibition was highest with 800mg/kg body weight of the extract and lowest with omeprazole (the reference drug). The result further showed that the gastroprotective potentials at 400mg/kg and 800mg/kg body weight of the extract was not statistically significant at $p < 0.05$ level of significance.

Table 1. Gastroprotective effect of omeprazole and treatment at different doses of fermented *Musa paradisiaca* on acetic acid induced ulcer in wistar rats after one hour

Test	Group I (Normal Control)	Group II (Negative Control)	Group III (Omeprazole 5mg/kg)	Group IV (400 mg/kg)	Group V (800 mg/kg)
Ulcer Score	0.00±0.00 ^a	15.00±1.00 ^d	6.33±0.76 ^c	8.67±0.58 ^c	3.67±0.58 ^b
Ulcer Index	0.00±0.00 ^a	12.17±0.23 ^b	11.10±0.23 ^b	11.30±0.10 ^b	10.60±0.10 ^b
Inhibition (%)	-	-	8.76	7.11	13.51

Values represent the mean \pm SD for N=3. Values in the same row bearing the same letter of alphabets are not significantly different from each other ($P > 0.05$).

Table 2. Gastroprotective effect of omeprazole and treatment at different doses of fermented unripe *Musa paradisiaca* fruit extract on aspirin induced ulcer in wistar rats after one hour.

Test	Group I (Normal Control)	Group II (Negative Control)	Group III (Omeprazole 5mg/kg)	Group IV (400 mg/kg)	Group V (800 mg/kg)
Ulcer Score	0.00±0.00 ^a	21.00 \pm 1.00 ^c	13.00 \pm 1.00 ^b	11.00±1.00 ^b	9.00±1.00 ^b
Ulcer Index	0.00±0.00 ^a	13.20±0.10 ^b	11.87±0.15 ^b	11.87±0.15 ^b	10.09±1.83 ^b
Inhibition (%)	-	-	10.08	10.08	23.56

Values represent the mean \pm SD for N=3. Values in the same row bearing the same letter of alphabets are not significantly different from each other ($P > 0.05$).

Table 3. Gastroprotective effect of omeprazole and treatment at different doses of fermented *Musa paradisiaca* on ethanol induced ulcer in wistar rats after one hour.

Test	Group I (Normal Control)	Group II (Negative Control)	Group III (Omeprazole 5mg/kg)	Group IV (400 mg/kg)	Group V (800 mg/kg)
Ulcer Score	0.00±0.00 ^a	31.00±3.00 ^d	18.33±2.08 ^c	17.67±1.53 ^c	13.33±1.53 ^b
Ulcer Index	0.00±0.00 ^a	15.60±0.40 ^c	12.87±0.32 ^b	12.73±0.38 ^b	12.13±0.15 ^b
Inhibition (%)	-	-	17.46	18.30	22.19

Values represent the mean \pm SD for N=3. Values in the same row bearing the same letter of alphabets are not significantly different from each other ($P > 0.05$).

Table 4. Gastroprotective effect of omeprazole and treatment at different doses of fermented *Musa paradisiaca* on Indomethacin induced ulcer in wistar rats after one hour

Test	Group I (Normal Control)	Group II (Negative Control)	Group III (Omeprazole 5mg/kg)	Group IV (400 mg/kg)	Group V (800 mg/kg)
Ulcer Score	0.00±0.00 ^a	12.33±0.76 ^d	8.33±0.29 ^c	5.33±0.58 ^b	4.67±0.58 ^b
Ulcer Index	0.00±0.00 ^a	12.03±0.14 ^b	11.50±0.09 ^b	10.90±0.17 ^b	10.77±0.06 ^b
Inhibition (%)	–		4.43	9.42	10.51

Values represent the mean ± SD for N=3. Values in the same row bearing the same letter of alphabets are not significantly different from each other (P > 0.05).

Table 5. Gastroprotective effect of omeprazole and treatment at different doses of fermented *Musa paradisiaca* on pyloric-ligation of ethanol induced ulcer in wistar rats after one hour

Test	Group I (Normal Control)	Group II (Negative Control)	Group III (Omeprazole 5mg/kg)	Group IV (400 mg/kg)	Group V (800 mg/kg)
Ulcer Score	0.00±0.00 ^a	7.67±0.76 ^c	6.00±1.00 ^c	2.67±0.58 ^b	2.33±0.58 ^b
Ulcer Index	0.00±0.00 ^a	11.33±0.12 ^b	11.03±0.21 ^b	10.53±0.21 ^b	10.43±0.06 ^b
Inhibition (%)	–	–	2.65	7.05	7.93

Values represent the mean ± SD for N=3. Values in the same row bearing the same letter of alphabets are not significantly different from each other (P > 0.05).

The results of the pyloric-ligation of ethanol induced ulcer in wistar rats after one hour revealed the presence of gastric erosion and hemorrhagic streaks. However, the oral administration of the extract of fermented unripe *M. paradisiaca* fruit inhibited ulcer by 7.93% at higher dose (Table 5). The degree of gastro-protection was in the order Omeprazole < 400 mg/kg < 800 mg/kg of the extract.

4. Discussion

The use of conventional drugs in the management of peptic ulcer is currently declining. Medicinal plants have shown promising results. Fermented products of certain medicinal plants have been suggested to yield better promising results owing to the generation of live microorganisms called probiotics, which have a lot of gut benefits. Therefore, the present study was undertaken to evaluate the gastro-protective activity of the extract of fermented unripe *Musa paradisiaca* fruits on acetic acid, aspirin, ethanol, indomethacin and pyloric ligation of ethanol-induced ulcer models in wistar rats. The results from our studies indicate that the oral administration of acetic acid, aspirin, ethanol and indomethacin produced severe gastric lesions and haemorrhagic streaks on the experimental animals. The results revealed that the induction of ulcers by these models was statistically significant at p < 0.05. The manifestation of ulceration by these agents (acetic acid, aspirin, ethanol, indomethacin and pylorus ligation) could be due to inhibition of the enzyme cyclooxygenase, which catalyzes the rate limiting step in the conversion of arachidonic acid to prostaglandins [18] and also the expression of histamine, gastrin and acetylcholine receptors, which are responsible for gastric acid secretion [19].

Acetic acid, otherwise known as ethanolic acid, is a weak acid. The administration of acetic acid in experimental animals has indeed led to the ulceration of the gastric mucosa. However, the administration of the plant extracts and omeprazole inhibited ulcerogenesis due to acetic acid (Table 1). Acetic acid is able to induce ulceration of the gastric mucosa by increasing the acid content of the stomach, thus disturbing the natural balance.

This observation is in line with the works of Dharmanni *et al.* [20] who reported the anti-ulcerogenic and ulcer-healing properties of *Ocimum sanctum*.

Aspirin, otherwise known as acetylsalicylic acid (ASA) is a non-steroidal anti-inflammatory drug which adversely affects the gastro-duodenal mucosa causing ulcerative lesions on the mucus membrane [21]. The development of ulcer may result through several mechanisms including suppression of the synthesis of gastric gastro-protective prostaglandin (through blocking of cyclooxygenase) [18], decrease blood supply to gastric mucosa [22], increased gastric acid secretion and activation of the growth factors involved in mucosal defence and repair [23]. In this study, the aqueous extract of fermented unripe *M. paradisiaca* inhibited the manifestation of ulcerogenesis (Table 2). This means that the extract might have the tendency of cancelling the competitive inhibition at the active site of cyclooxygenase. This work is also not unconnected with the findings of Mbagwu *et al.* [15], Enemchuwku *et al.* [24], Ezekwesili *et al.* [8], who reported the protective effects of unripe plantain peel extracts against aspirin and ethanol induced ulcers in wistar rats.

The result of this study showed that the oral administration of ethanol induces ulcer in experimental animals (Table 3). Ethanol is a common aggressive factor in the pathogenesis of peptic ulcer. Ethanol induces ulcerogenesis by depletion of gastric mucus content, lowering of the concentration of non-protein sulphhydryl especially glutathione, damaged mucosal blood flow, mucosal cell injury, lowering of bicarbonate secretion, and activation of endothelin-1 [25]. Secondary metabolism of ethanol is also implicated in the development of ulceration by activation of tumor necrosis factor alpha (TNF- α), mitogen activated kinases (MAPK), generation of superoxide and hydroperoxy free radicals, which causes lipid peroxidation, and also lead to apoptosis. The manifestation of ulcerogenesis by ethanol was prevented to a very reasonable degree by pretreatment of the experimental animals with omeprazole (the reference drug) and the different doses of fermented unripe *Musa paradisiaca* fruit extract. This observation is not unconnected with the findings of Ezekwesili *et al.* [8] who

in their investigations revealed that the peel of *M. paradisiaca* has antiulcerogenic activity in wistar rats. The outcomes of this study are also in agreement with the works of Mbagwu *et al.* [15] and Enemuchukwu *et al.* [24] who investigated the anti-ulcer activity of ethanolic leaf extract of *Musa paradisiaca* in rats and aqueous extract of unripe plantain in wistar (albino) rats respectively.

Indomethacin is also another class of non-steroidal anti-inflammatory drugs that induces ulcerogenesis. The result of the study revealed that the oral administration of indomethacin causes gastric lesions and haemorrhagic streaks. The gastro-protective activity of the extracts at measured doses showed a significant increase when compared to the reference drug (Table 4). The result revealed that omeprazole is not an effective therapeutic agent in the amelioration of indomethacin induced ulcer. This is because study has identified that omeprazole synergizes with indomethacin in causing mucosal impairment. This observation is similar to the findings of Ezekwesili *et al.* [8] who studied the comparison between omeprazole and the extract of *M. paradisiaca* peel in indomethacin-induced ulcer.

Another valuable parameter in the assessment of the integrity of the gastric mucosa is the pyloric ligation [26]. According to Brodie, [27], the digestive effects of accumulated gastric juice and interference with gastric blood circulation are responsible for induction of ulceration by pyloric ligation. Results of pyloric-ligation of ethanol induced ulcer revealed a significant decrease in ulcer index across the row (Table 5). The negative control group animals had the highest ulcer index while the group that was treated with 800mg/kg body weight of the extract had the least ulcer index. The results further revealed that the gastro-protective activity of the extract and the reference drug (omeprazole) was statistically significant ($p < 0.05$). The results of the study support early findings of Hiruma-Lima *et al.* [14] who investigated the antiulcer activity of *Qualae grandiflora*, a Brazilian “Cerrado” medicinal plant.

Also, the inhibition of ulcerogenesis by fermented unripe *Musa paradisiaca* fruit extract could be attributed to two major factors: the presence of bioactive compounds and the growth of lived microorganisms (probiotics) during the course of fermentation. Compounds found in plants which have shown anti-ulcer properties include flavonoids, saponins, tannins, and flavonoids [8] and phytochemical screening of unripe *M. paradisiaca* fruits revealed the presence of these compounds. Therefore, it is possible that the ulcer-protective activity of fermented unripe plantain fruits is, in part, due to their presence, and this study has confirmed the application of the plant in folk medicine for the management of peptic ulcer. Several studies have identified the role of flavonoids in the prevention of gastric ulcer. This may take place through an increase in the amounts of neutral glycoproteins and in prostaglandin concentrations, and inhibition of histamine secretion from mast cells by inhibition of histidine decarboxylase, thus reducing stimulation of H₂ receptors, or by secretion of prostaglandin-like compounds [28,29,30]. Saponins also reduce the risk of ulcers by increasing defensive factors of gastric mucosa and stopping the inflammatory process resulting from induction by aspirin (indicated by absence of ulceration

and severe haemorrhagic streaks in the gastric mucosa of experimental animals receiving aqueous extracts of fermented unripe *Musa paradisiaca* fruits [29]. Probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits on the host [31]. Traditionally, probiotics have been associated with gut health, and most clinical interest has focused on the prevention or treatment of gastrointestinal infections and diseases. Nonetheless, the enhanced cessation of gastric erosions as observed in this study could be attributed to the synergistic role of probiotics and the bioactive compounds present in aqueous extract of fermented unripe *Musa paradisiaca* fruit.

5. Conclusion

The present study was undertaken to ascertain whether the aqueous extracts of fermented unripe *Musa paradisiaca* fruits could confer antiulcerogenic activity on acetic acid, aspirin, ethanol, indomethacin and pyloric ligation-induced ulcer models in wistar rats. The results showed comparable antiulcer activity of omeprazole and the different doses of the extract against the different models of ulcer employed in the study. Aqueous extracts of fermented unripe *Musa paradisiaca* fruits is a good candidate for screening of new anti-ulcer drugs.

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