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Antioxidants and Antiulcer Activity of Aqueous Unripe Fruits Extract of Musa Acuminata in Indomethacin-Induced Ulcer in Rats

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Abstract

Ulcer remains a public health problem associated with high incidence and mortality rate worldwide. *Musa acuminata* is widely available plant used in local management of many diseases including gastrointestinal disorders, constipation, piles, and hemorrhoids. The aim of this study was to evaluate the antioxidants and antiulcer activity of aqueous unripe fruits extract of *Musa acuminata* in indomethacin-induced ulcer in rats. The gastric ulcer was induced by intra-peritoneal injection of indomethacin (60 mg/kg, i.p.). Ulcer index and percentage ulcer inhibition was calculated using standard equations. The Lipid Peroxidation (Malondialdehyde) marker was determined using Thiobarbituric acid Reactive Substances (TBARS) method. The superoxide dismutase activity (SOD) and catalase (CAT) level was determined using standard ELISA kits. The antioxidant vitamins (Vit A, C, and E) were assayed by spectrophotometric technique. The extract (100 mg/kg, 200 mg/kg) demonstrated significant ($p < 0.05$) gastroprotective effect with high ulcer inhibition (95.49 %) at 200 mg/dL more than the reference standard drug, omeprazole (91.67 %). The extract (100 mg/kg, 200 mg/kg) demonstrated significant ($p < 0.05$) decrease in the level of lipid peroxidation marker (MDA) coupled with the significant ($p < 0.05$) increase in the level of SOD and CAT comparable to the reference standard drug, omeprazole. The results also showed a significant ($p < 0.05$) increase in vitamins A and E level significant ($p < 0.05$) decrease in vitamins C level in the gastric tissue homogenates of the rats treated with 100 mg/kg and 200 mg/kg of the extract. The aqueous unripe fruits extract of *Musa acuminata* demonstrated gastroprotective effect in indomethacin-induced ulcer in rats and might be attributed to increase in prostaglandins synthesis and cellular antioxidant activity.

Keywords: *Musa acuminate*, Ulcer, Antioxidant enzymes, Antioxidant vitamins.

INTRODUCTION

Ulcer is a chronic disease associated with many complications including gastrointestinal obstruction, haemorrhages, bleeding, perforations and gastric outlet obstruction (Silva and Sousa, 2021; Abubakar *et al.*, 2021). Ulcer is a gastro-intestinal disorder characterized by damage of mucosal integrity of the stomach, duodenum or lower esophagus (Abubakar *et al.*, 2020a; Kumar *et al.*, 2011). About 20% of the proportion of people in the world are affected by peptic ulcer disease (Beiranvand and Bahramikia, 2020; Ahmad *et al.*, 2019). It has been reported that four million people are affected by ulcer annually worldwide (Abbasi-Kangevari *et al.*, 2022; Abubakar *et al.*, 2020a). The global prevalence of peptic ulcer disease increased up to 25.82% between 1990 and 2019 (Xie *et al.*, 2022; Lanas and Chan 2017). In high income countries, the prevalence rate of ulcer was about 40% whereas the prevalence rate was almost 80% in low and middle income countries (Abubakar *et al.*, 2020b; Shristi *et al.*, 2012). The etiology of ulcer is multifactorial but the main causes are Helicobacter pylori infection and non-steroidal anti-inflammatory drugs (NSAIDs) such as indomethacin (Silva and Sousa, 2021; Abubakar *et al.*, 2021). Other causes of ulcer and its complications include excessive alcoholism, smoking, dietary factors, genetic factors, toxic substances, acid-pepsin secretions, gastritis, psychological factors, hormonal factors, and diseases factors (Silva and Sousa, 2021; Abubakar *et al.*, 2020a).

Ulcer is conventionally treated using categories of drugs including proton pump inhibitors (PPIs), antacids, histamine H2 receptor antagonists,

prostaglandin analogues, sucralfate, bismuth salts, and potassium-competitive acid blockers (Kuna *et al.*, 2019). These drugs produced many adverse effects such as hypergastrinemia, increased risk of bone fractures, Vitamin B12 deficiency, hypomagnesemia, abdominal pains (Sánchez-Mendoza *et al.*, 2024), gynecomastia (Iqbal *et al.*, 2025), impotence and galactorrhoea (Jenkins *et al.*, 2017). Other side effects of these drugs include increases toxicity by inhibiting Cytochrome P450 activity (Strand *et al.*, 2017). However, certain drugs are expensive to purchase by majority of people especially in local areas. More number of people in the world particularly in local communities has depending on plants and herbs for therapies. Medicinal plants are widely available and easy to access by local communities. Also, medicinal plants have no or few side effects than synthetic drugs. Plants and herbs have been used in traditional treatment of various diseases including ulcer and it's complications (Abubakar *et al.*, 2024; Hamedi *et al.*, 2015). The medicinal properties of plants and herbs could be attributed to their bioactive compounds that demonstrate pharmacological activities (Abubakar *et al.*, 2024; Abubakar *et al.*, 2022).

Musa acuminata is one of the most important and widely available plants worldwide. *Musa acuminata* is a tropical plant commonly called Banana and belongs to the family *Musaceae* (Takeuchi *et al.*, 2017). *Musa acuminata* has several nutritional values, medicinal properties, antioxidants and pharmacological activities due to its various phytoconstituents (Hont *et al.*, 2019; Pihan *et al.*, 2019; Ames *et al.*, 2018). Musa acuminata is highly nutrious plant rich in carbohydrates, fibre, proteins, minerals, and vitamins (Okoye, 2022). The plant has been used in treatment of various diseases including gastrointestinal disorders, constipation, piles, and hemorrhoids (Cheesman, 2019). Unripe fruits of *Musa acuminata* contain several phytochemicals including flavonoids, alkaloids, saponins, cardiac glycosides, tannins anthraquinines, volatile oils, steroids, balsams, and glycosides (Hawkey, 2016). The plant also possesses certain bioactive compounds such as myricetin that have potent antioxidant properties (Goswami *et al.*, 2018). *Musa acuminata* is commonly found in almost every place in Nigeria and is locally called ayaba (Hausa), unele (Igbo), and ogede wewe (Yoruba). In Nigeria, several parts of *Musa acuminata* have been used for the treatment of many diseases such as diabetes, hypertension, cancer, ulcers, diarrhoea, urolithiasis, Alzheimer's and infections (Okoye, 2022). Local communities and traditional herbalists have been claiming the use of *Musa acuminata* in treatment of ulcer. Scientific researches to validate these claims remain inadequate. This study aims at evaluating the antioxidants and antiulcer activity of aqueous unripe fruits extract of *Musa acuminata* in indomethacin-induced ulcer in rats.

MATERIALS AND METHODS

Drugs and Chemicals

Indomethacin and omeparazole manufactured by Salud Care (I) Pvt Ltd, India were purchased from Baiwa medicine store, Sir Yahaya Memorial Hospital, Birnin Kebbi, Kebbi, Nigeria. All the chemicals used were of analytical grade.

Experimental Animals

Twenty five albino rats weighing 180 – 200 g of either sex were obtained from Animal House, Faculty of Life Science, Usmanu Danfodiyo University, Sokoto, Nigeria. The animals were housed in polycarbonate cages five rats per cage. The rats were acclimatized to standard conditions (Temperature 23±2^{o}C, relative humidity 30-70% and 14 hours light-10 hours dark cycle) for two weeks prior to experiment. The animals were fed with commercial rat pellets and water *ad libitum.*

Plant Material

Fresh unripe *Musa acuminata* fruits were collected from garden of Professor Attahiru Jega, in Birnin Kebbi Local Government, Kebbi State, Nigeria. The plant sample was identified and authenticated by a taxonomist in the Department of Plant Science and Biotechnology, Kebbi State University of Science and Technology, Aliero, Kebbi, Nigeria. The voucher specimen (KSUSTA/PSB/VOUCHER51) was deposited in the herbarium.

Preparation of Plant Extract

The aqueous fruits extract of Musa acuminate was prepared according to the method described by Abubakar *et al*. (2024) with little modification. The fresh unripe *Musa acuminata* fruits were washed thoroughly and shade-dried at room temperature (25 ± 2 ^{o}C) for two weeks. The dried fruits were pulverized into fine powder using an electric blender. The powder sample (638 g) was soaked in 1.5 L of distilled water with intermittent stirring for three days. The mixture was filtered using Whatman No1 filter paper and the filtrate was concentrated using a rotary evaporator at 40 ^{o}C under reduced pressure for 180 minutes. The weight (33 g) and percentage yield (5.1 %) of the extract was obtained.

Antiulcer Activity Test

The antiulcer effect of the aqueous fruits extract of Musa acuminate was evaluated using indomethacin-induced ulcer model according to the method described by Abubakar *et al.*, (2020b).

Experimental Design

Twenty five Wistar rats (180 – 200 g) were randomly distributed into five groups each of 5 rats. Group 1 received normal saline (10 ml/kg bwt/day) and served as normal control.

Group 2 served as ulcer control in which ulcer was induced and no treatment was given. Group 3 was

induced with ulcer and then treated with omeprazole (20 mg/kg b.wt/day p.o) (MFDS, 2014). Group 4 and 5 were induced with ulcer and then treated with 100 and 200 mg/kg b.wt of the aqueous fruits extract of Musa acuminate, respectively.

Induction of Gastric Ulcer

The aqueous fruits extract of Musa acuminate (100 and 200 mg/kg b.wt) was orally administered to the rats for two weeks. After the extract administration, the rats were fasted for one day after which the last administration was done. The gastric ulcer was induced after 30 minutes of the last administration by intra-peritoneal injection of indomethacin (60 mg/kg, i.p.) (Abubakar *et al.*, 2020b). Four hours post-indomethacin administration, the rats were anaesthetized and then sacrificed by cervical dislocation.

Examination of Ulcers

The stomachs were removed and the gastric contents were drained into the test tubes. The stomach tissues were then dissected and rinsed with deionized water to remove blood clots. The stomachs were mount on a glass slide and examined for detection of gastric ulcers using 10× magnification lens and microscope. The number and the length of gastric lesions were determined (Abubakar *et al.*, 2020a). The ulcers were scored according to their severity into normal appearance of stomach (0), red appearance of stomach (0.5), spot ulcer (1), hemorrhagic streaks (1.5), ulcer ≥ 3 mm^2 but ≤ 5 mm^2 (2), and ulcer >5 mm^2 (3) (Kulkarni, 2002).

Determination of Ulcer Index and Percentage Ulcer Inhibition

Ulcer index was obtained using the following equation:

$UI = UN + US + UP \times 10^{-1}$ (Jyoti *et al.*, 2012)

Where; UI = Ulcer Index; UN = Mean of number of ulcer per animal; US = Mean of severity score; UP = Percentage of the ulcerative rats

The percentage ulcer inhibition was calculated using the formula below:

$$\% \text{ Ulcer Inhibition} = \frac{UIC - UTT}{UIC} X\ 100$$ (Jyoti *et al.*, 2012)

Where; UIC = Ulcer Index of Control; UIT = Ulcer Index of Test

Determination of Volume and pH of Gastric Contents

The gastric contents were drained into the graduated tubes and then the volume of gastric contents was obtained from the tubes. The distilled water (5 mL) was added into the tubes and then centrifuged at 10000 rpm for 5 minutes. The pH of gastric contents was measured from the clear supernatant obtained using pH meter (Nwinyl and Kwanashie, 2013).

Determination of Free and Total Acidity

The gastric juice (1 mL) was transferred into 100 mL conical flask followed by addition of 2 – 3 drops of topfer's reagent (Dimethyl-aminoazo-benzene, phenolphthalein). The solution was titrated against 0.01 N NaOH until a yellowish orange colour observed after which the volume of NaOH added (free acidity) was obtained. The end-point was again titrated until the pink color reappeared, then the volume of NaOH added (total acidity) was obtained. The acidity (free and total) expressed as mEq/1L/100gm was calculated using the following equation:

$$\text{Acidity (mEq/1L/100gm)} = \frac{\text{Volume of NaOH x 0.01N}}{0.1} X\ 100$$

(Shay *et al.*, 1954)

Preparation of Gastric Tissue Homogenate

The gastric tissues were cut to small pieces and then homogenized in 5 ml of PBS (ice-cold, 0.05M, pH 7.4) using tissue homogenizer. The cell membrane in the tissue homogenates was further broken by freezethaw cycles. The homogenates were centrifuged at 4000 ×g for 10 minutes and the supernatant was separated (Abubakar *et al.*, 2021). The supernatant was used for the analysis of the malondialdehyde (MDA) and levels of antioxidant enzymes (CAT, SOD) and antioxidant vitamins (Vit A, C, and E).

Determination of Antioxidant Activity

Determination of Lipid Peroxidation (Malondialdehyde) Level

The level of malondialdehyde (MDA) in the gastric tissue homogenates was estimated using Thiobarbituric acid Reactive Substances (TBARS) method as described by Varshney and Kale (1990). The tissue homogenate (0.1 mL) was mixed with 0.5 mL of 10% TCA and 0.5 mL of 75% TBA. The contents were incubated at 80 ºC for 45 minutes using water bath and then centrifuged at 4000 rpm to obtain clear supernatant. The absorbance of the solution was read at 530 nm. The test was calibrated using MDA as the standard and the results were expressed as the amount of free MDA produced. The malondialdehyde (MDA) level of the sample was calculated from the absorbance using molar extinction coefficient of 1.56×10^5 $M^{-1}cm^{-1}$ (Ádám-Vizi and Seregi, 1982).

MDA level = Absorbance of sample ÷ Molar extinction (Abubakar *et al.*, 2021)

Determination of Anti-oxidant Enzymes

The level of superoxide dismutase activity (SOD) and catalase (CAT) in the stomach tissue homogenate was estimated using standard ELISA kits manufactured by PARS BIOCHEM (Nanjing Pars Biochem CO., Ltd, China) in accordance to the manufacturer's instruction.

Determination of Antioxidant Vitamins

Estimation of Vitamin A

The level of Vitamin A in the stomach tissue homogenate of the rats was determined using the method of Rutkowski *et al*. (2006). The normal saline (0.02 mL) was added to 5 mL of distilled water and 0.02 mL of whole blood (Hbss) and incubated in a test tube at 27^0C

for 1 hour. The absorbance of hemoglobin (Hb) and methyl hemoglobin (mHb) was determined spectrophotometrically at 630 nm and 540 nm, respectively. The concentration was expressed in mg/dL.

Estimation of Vitamin C

Vitamin C concentration in the stomach tissue homogenate of the rats was determined using the method described by Rutkowski and Grzegorczyk (1998). One 1 mL of the homogenate was pipetted into test-tube followed by addition of 1 mL of 95% ethanol. The contents were mixed and 1 mL of 1N KOH in 90 percent ethanol was added. The contents were mixed and placed in a 60^0C oven for 20 minutes. Two miles of petroleum ether was added and the tube was shaked for 10 minutes. The tubes were centrifuged for about 30 seconds. The petroleum ether (2 mL) was added and shaked for only 5 minutes. The absorbance of the sample was read at 440 nm.

Estimation of Vitamin E

The method described by Rutkowski *et al*. (2005) was employed for the determination of vitamin E level in the stomach tissue homogenate of the rats. The standard solution (1.5 mL) was then added to a test tubes containing 1.5 mL of the homogenate sample. The standard and blank test tubes were treated with 1.5 mL of distilled water. All the test tubes were treated with 1.5 mL of xylene. The contents were mixed and centrifuged for 10 minutes. One mile of xylene layers was treated with 1 mL of ∝-dipyridyl reagent. The contents were mixed and the absorbance of the sample and standard were read against the blank at 460 nm. After 5 minutes, all the test tubes were treated with 0.33 mL of ferric chloride solution. The contents were mixed and the absorbance was measured at 520 nm. The concentration of vitamin E in the sample was obtained using the equation below:

$$\text{Conc. of Vit E} = \frac{\text{Abs of sample at 520nm} - \text{Abs of sample at 460nm x Conc. of standard}}{\text{Abs of standard}}$$

Histopathological Examination of Stomach Tissue

The histopathological examination of gastric tissue was performed using the method of Drury *et al*. (1967). The stomach tissues of the experimental rats were fixed in 10% buffered formalin for 48 hours. The tissues were dehydrated using a graded ethanol series (70%, 80%, 90% and 100%), cleared in xylene and embedded in paraffin wax. The section (5µm thick) was prepared, mounted, and stained with hematoxylin and Eosin (H×E). The slides were examined for histopathological changes using microscope at of 40×, 100× and 400× magnification. The microsphotograph of histopathological features were captured using the microscope's camera.

Statistical Analysis

The results were statistically analyzed using Statistical Package for Social Sciences (SPSS) version 22 software and expressed as mean ± SEM. Significant differences between the treatment and control groups were computed at 95 % confidence level by One-way analysis of variance (ANOVA). Significance was considered by two-tailed ($p < 0.05$) values.

RESULTS

Effect of Aqueous Fruit Extract of *Musa acuminata* on Mean Ulcer Index in Rats

Table 1 shows the effect of aqueous fruit extract of *Musa acuminata* on mean ulcer index in rats. The extract (100 mg/kg, 200 mg/kg) demonstrated significant ($p < 0.05$) decreased in mean ulcer index compared with ulcer control. A high percentage ulcer inhibition was observed in the rats administered with the extract (100 mg/kg, 200 mg/kg). At 200 mg/dl, the exhibited maximum protective effect (95.49 %) more than the reference standard drug, omeprazole (91.67 %) (Table 1).

Table 1: Effect of aqueous fruit extract of *Musa acuminata* on mean ulcer index

Treatment	Mean Ulcer Index	% Ulcer Inhibition
Normal Control	0.00 ± 0.00	–
Ulcer Control	5.76 ± 0.78	–
OME (20 mg/kg)	0.48 ± 0.23*	91.67
Ma (100mg/kg)	1.36 ± 0.59*	76.38
Ma (200mg/kg)	0.26 ± 0.16*	95.49

Results are expressed as mean ± SEM (n=5 rats/group)

*$p < 0.05$ statistically significant when compared with ulcer control (One-way ANOVA) followed by Tukey's multiple comparison test. *Musa acuminata* (Ma), Omeprazole (OME).

Effect of Aqueous Fruit Extract of *Musa acuminata* on pH, Gastric Volume, Free and Total Acidity

The effect of aqueous fruit extract of *Musa acuminata* on pH, gastric volume, free and total acidity is shown in Table 2. In comparison with the ulcer control, a significant ($p < 0.05$) increased in pH value of gastric juice and significant ($p < 0.05$) decreased in volume of gastric juice, free and total acidity was found in the rats with the extract (Table 2).

Table 2: Effect of aqueous fruit extract of *Musa acuminata* on pH, gastric volume, free and total acidity

Treatment Group	Gastric pH	Gastric Volume (mL)	Free Acidity (mEq/L)	Total Acidity (mEq/L)
Normal Control	5.90 ± 0.27	2.66 ± 0.10	33.00 ± 0.71	97.20 ± 0.73
Ulcer Control	2.84 ± 0.18	4.53 ± 0.13	81.40 ± 0.92	131.80 ± 1.07
OME (20 mg/kg)	5.96 ± 0.17*	2.02 ± 0.08*	24.20 ± 1.96*	81.20 ± 0.86*
Ma (100mg/kg)	4.60 ± 0.19*	3.00 ± 0.10*	42.60 ± 0.93*	110.80 ± 1.06*
Ma (200mg/kg)	6.64 ± 0.21*	1.80 ± 0.07*	21.00 ± 0.70*	77.40 ± 0.92*

Values are mean ± SEM (n=5 rats/group)

*$p < 0.05$ statistically significant when compared with ulcer control (One-way ANOVA) followed by Tukey's multiple comparison test. *Musa acuminata* (Ma), Omeprazole (OME).

Effect of Aqueous Fruit Extract of *Musa acuminata* on Marker of Lipid Peroxidation

Figure 1 shows the effect of aqueous fruit extract of *Musa acuminata* on marker of lipid peroxidation. The extract (100 mg/kg, 200 mg/kg) demonstrated significant ($p < 0.05$) decrease in the level of MDA (marker of lipid peroxidation) in dose-dependent manner (Table 2). The extract (200 mg/kg) exhibited significant ($p < 0.05$) decrease in the MDA level more than the reference standard drug, omeprazole.

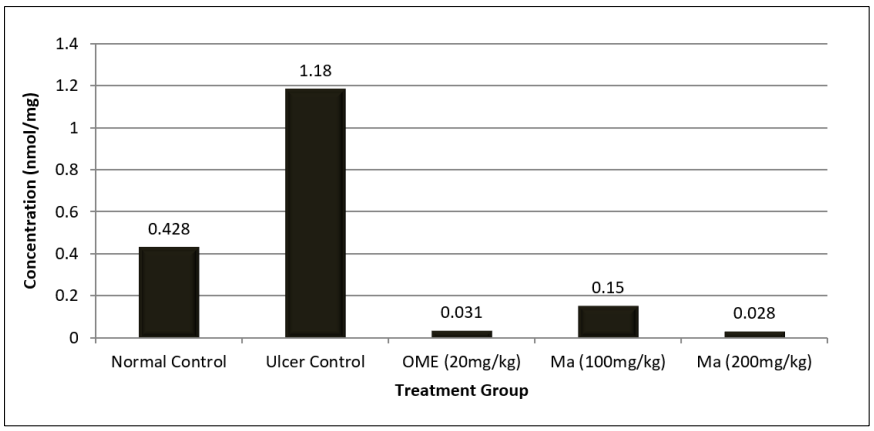


Figure 1: Effect of aqueous fruit extract of *Musa acuminata* on marker of lipid peroxidation

*$p < 0.05$ statistically significant when compared with ulcer control (One-way ANOVA) followed by Tukey's multiple comparison test. *Musa acuminata* (Ma), Omeprazole (OME).

Effect of Aqueous Fruit Extract of *Musa acuminata* on Anti-oxidant Enzymes Levels

The effect of aqueous fruit extract of *Musa acuminata* on anti-oxidant enzymes levels in the stomach homogenates of the rats is presented in Figure 2. The result showed that administration of the extract (100 mg/kg, 200 mg/kg) in the rats significantly ($p < 0.05$) increased the level SOD and CAT in the stomach homogenates of the rats compared with the ulcer control (Figure 2).

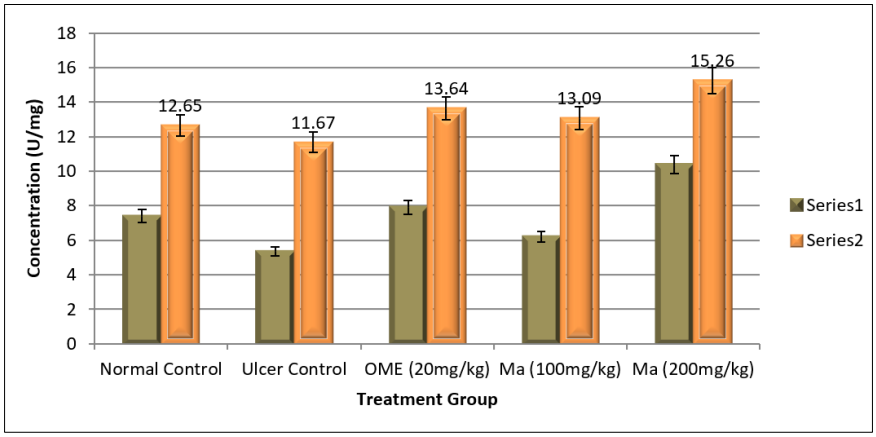


Figure 2: Effect of aqueous fruit extract of *Musa acuminata* on anti-oxidant enzymes levels

*$p < 0.05$ statistically significant when compared with ulcer control (One-way ANOVA) followed by Tukey's multiple comparison test. *Musa acuminata* (Ma), Omeprazole (OME).

Effect of Aqueous Fruit Extract of *Musa acuminata* on Anti-oxidant Vitamins Levels

Figure 3 shows the effect of aqueous fruit extract of *Musa acuminata* on anti-oxidant vitamins levels in the stomach homogenates of the rats. In comparison with the ulcer control, the extract (100 mg/kg, 200 mg/kg) exhibited significant ($p < 0.05$) increase in vitamins A and E level in the stomach tissue homogenates of the rats (Figure 3). However, a significant ($p < 0.05$) decrease in vitamins C level was observed in the gastric tissue homogenates of the rats treated with 100 mg/kg and 200 mg/kg of the extract (Figure 3).

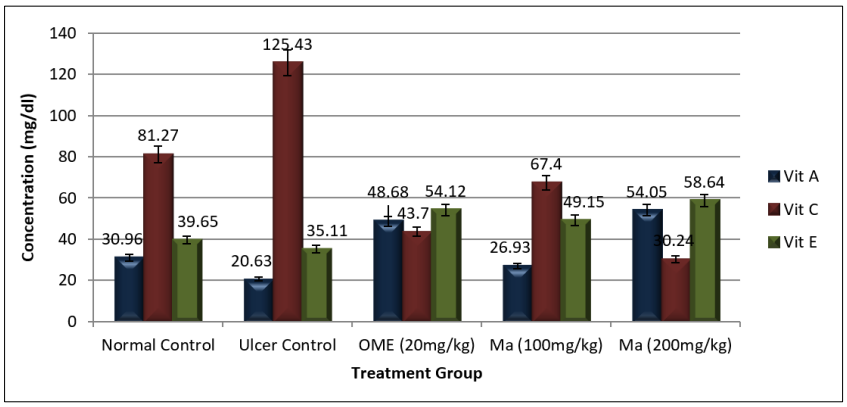
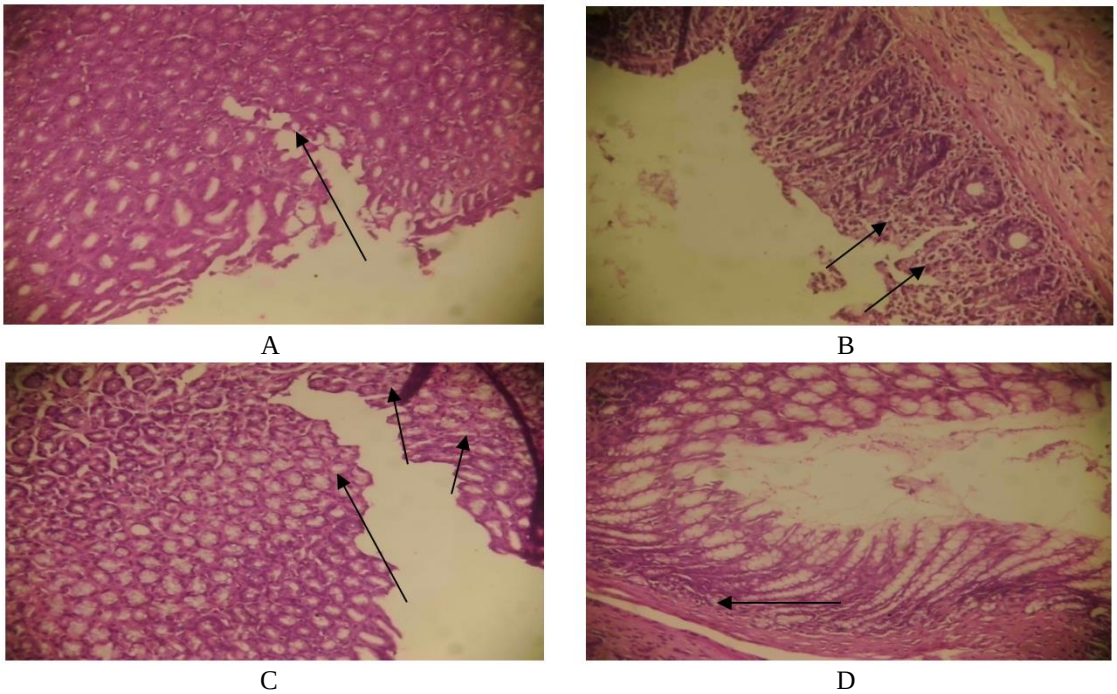


Figure 3: Effect of aqueous fruit extract of *Musa acuminata* on anti-oxidant vitamins levels

*$p < 0.05$ statistically significant when compared with ulcer control (One-way ANOVA) followed by Tukey's multiple comparison test. *Musa acuminata* (Ma), Omeprazole (OME), Vitamin (VIT).

Effect of Aqueous Fruit Extract of *Musa acuminata* on Histological Features of the Gastric Tissue

The effect of aqueous fruit extract of *Musa acuminata* on histological features of gastric tissue is shown in Figure 4. The gastric tissue of the normal control rats showed normal goblet cells within the covering gastric mucosa i.e. complete gastric intergridity In comparison with the normal control, a marked decrease in mucous cells within the gastric mucosa due to severe gastric damage with perforation was observed in the gastric tissue of the ulcer control rats (Figure 4B). The stomach tissue of the rats treated with omeprazole (20 mg/kg) showed an increase in mucous cells within the covering gastric mucosa (Figure 4C). In comparison with the ulcer control, an increase in mucous cells within the gastric mucosa was observed in the rats treated with 100 mg/kg of the extract (Figure 4D). A marked increase in mucous cells within the gastric mucosa was observed in the gastric tissue of the rats treated with 200 mg/kg of the extract compared with the ulcer control (Figure 4E).



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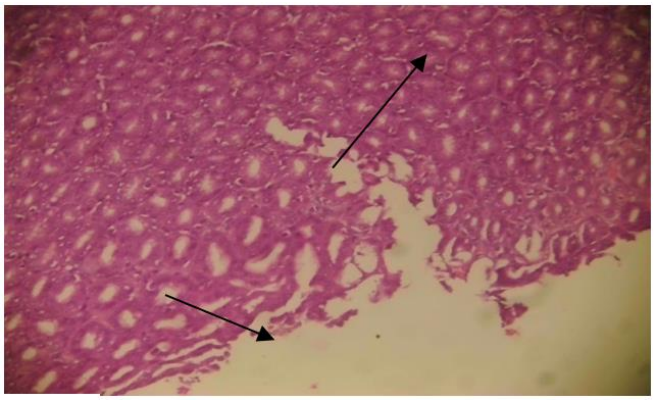

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Figure 4: Effect of aqueous fruit extract of *Musa acuminata* on histological features of the gastric tissue

(A) Norma control group showing normal goblet cells within the covering gastric mucosa i.e. complete gastric intergridity (arrows), (B) Ulcer control group showing marked decrease in mucous cells within the gastric mucosa (Severe gastric damages with penetration and perforation), (C) Omeprazole (20 mg/kg) treated group showing an increase in mucous cells within the covering gastric mucosa (arrows), (D) *Musa acuminata* (100 mg/kg) treated group showing increase in mucous cells within the gastric mucosa (arrows), (E) *Musa acuminata* (200 mg/kg) treated group showing marked increase in mucous cells within the gastric mucosa (arrows).

DISCUSSION

In this study, the aqueous unripe fruit extract of *Musa acuminata* demonstrated significant inhibition of indomethacin-induced gastric ulcer in rats. Nonsteroidal anti-inflammatory drugs (NSAIDs) have been documented as one of the major causes of peptic ulcer disease (Abubakar *et al.*, 2024; Lanas and Chan, 2017). Indomethacin demonstrates more significant potential to induce gastric damage than the other NSAIDs (Musumba *et al.*, 2013). NSAIDs inhibit cyclooxygenases (COX-1 and COX-2) which catalyze the synthesis of prostaglandins from arachidonic acid resulting to the damage of gastrointestinal mucosa (Ahmad *et al.*, 2019). Prostaglandins regulate gastric acid secretion, increase mucus and bicarbonate synthesis, and mucosal blood flow via prostaglandin receptors (EP) 1-4 (Mohamed *et al.*, 2021; Kuna *et al.*, 2019). Hence, inhibition of prostaglandin synthesis by NSAIDs decreases production of mucus and bicarbonate, impairs mucosal blood flow, and increases gastric acid secretion (Lu *et al.*, 2025).

Gastric juice; hydrochloric acid and pepsin are mucosal aggressive factors (Al-Qaisi *et al.*, 2025). The current findings revealed that the extract exhibited significant increase in the pH of gastric juice and significant decrease in the volume of gastric secretions, free and total acidity of the gastric contents. The results of this study are in agreement with the results of the relevant studies on the anti-ulcer effects of other plant extracts which showed significant increase in the pH of gastric juice couple with significant decrease in the volume of gastric secretions, free and total acidity of the gastric juice (Albaayit *et al.*, 2016). A decrease in the volume of gastric secretions and total acidity of gastric contents is an indication of ulcer healing (Lu *et al.*, 2025). Gastric acid is a primary indicator (aggressive factor) of peptic ulcer disease due to its proteolytic and hydrolytic effects (Satoh *et al.*, 2025). Decrease in free and total acidity of gastric juice is a significant index of mucosal gastroprotective function (Gupta *et al.*, 2023). The increase in pH of gastric contents observed in this study might be due to inhibition of hydrochloric acid secretion by the parietal cell proton pumps similar the reference drug, Omeprazole function. The decrease in the volume of gastric juice could be due to decrease in gastric juice secretion.

NSAIDs disrupt mitochondrial transmembrane potential resulting to the release of reactive oxygen species such as superoxide and hydrogen peroxide which cause cellular membrane damage via lipid peroxidation leading to cell death (Matsui *et al.*, 2011). Prolong administration of NSAIDs induce aggregation of neutrophils in the gastric vascular endothelium resulting to production of ROS that mediate gastric mucosal damage (Suzuki *et al.*, 2010). High levels of ROS stimulate lipid peroxidation in the membranes of the gastric cells causing increase levels of malondialdehyde (MDA), reduce mucus secretion, and damage of DNA (Cheng *et al.*, 2013). Reactive oxygen species (ROS) are scavanged by the anti-oxidant defense enzymes, including catalase, superoxide dismutase, and glutathione peroxidase (Maity *et al.*, 2009). MDA is an important biomarker of lipid peroxidation (Abu-Baih *et al.*, 2024). Elevated level of malondialdehyde (MDA) is an indicator of excessive lipid peroxidation in gastric tissue (Kwiecien *et al.*, 2014). In the present study, decrease level of MDA and increase level of superoxide dismutase and catalase was observed in the gastric tissue homogenate of the rats treated with the extract. The primary function of SOD is conversion of superoxide anion to hydrogen peroxide, a more stable, less reactive, and less toxic compound (Paguigan *et al.*, 2014). Catalase catalyzes the conversion of hydrogen peroxide to water and oxygen (Salehi *et al.*, 2018). High activity

and/or elevated levels of the cellular antioxidant enzymes is an important cytoprotective role in gastric tissues (Sugano *et al.*, 2012).

This finding is in agreement with the results of similar studies in other plants extracts which showed significant decrease in MDA level and significant increase in SOD and CAT levels in gastric homogenate tissue of the rats administered with the extracts (Abu-Baih *et al.*, 2024; Abubakar *et al.*, 2021; Zanata *et al.*, 2021). Study showed that ulcer healing is attributed to an increase in the cellular antioxidant activity (Lu *et al.*, 2025). Study by Alkushi and Elsawy (2017) showed that quercetin, the most potent antioxidant flavonoid, exhibited anti-ulcer activity in rats by increasing the antioxidants enzymes activity (Catalase, SOD, and GSH). Vitamin E is an important lipid-soluble antioxidant exclusively derived from the diet (Volker-boham, 2018). The antioxidant activity of Vitamin E nourishes the gastric mucosa in animals (Kamisah *et al.*, 2014). Vvitamin E helps in preservation of gastric mucosal integrity by inhibition of lipid peroxidation and accumulation of activated neutrophils (Becker *et al.*, 2004). It was suggested that administered vitamin E defends gastric mucosal lesions in rats through its anti-oxidant activity (Kamisah *et al.*, 2014). Thus, the gastroprotective effect of the aqueous fruit extract of *Musa acuminata* could be attributed to increase in prostaglandins synthesis and cellular antioxidant activity.

CONCLUSION

The aqueous unripe fruits extract of *Musa acuminata* demonstrated gastroprotective effect against indomethacin-induced gastric damage in rats. The anti-ulcer activity of the extract could be attributed to increase in prostaglandins synthesis and cellular antioxidant activity. Further studies should be done to isolate and characterize the active compounds responsible for the gastroprotective effect of *Musa acuminata*.

Conflict of Interest: The authors declared that no conflict of interest.

Contribution of the Authors: The experimental design was done by Zayyanu Abdullahi. The plant extract was prepared by Shamsu Nasiru. Ulcer induction and ulcer examination was performed by Zayyanu Abdullahi with help of Shamsu Nasiru and Usman Abubakar. All the authors were participated in the analysis of biochemical parameters. The original draft of the manuscript was written by Zayyanu Abdullahi. Shamsu Nasiru and Usman Abubakar reviewed and edited the original draft. The approved version of the manuscript was revised and by all the authors.

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