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Effects of Ethanol Extract of *Musa Paradisiaca* on Kidney Biomarkers in Aspirin-Induced Ulcerated Wistar Rats

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ABSTRACT: The effect of ethanol extract of unripe *M. paradisiaca* on kidney biomarkers was investigated in an ulcerated rat model. A total of twenty-four (24) rats, randomly divided into six (6) groups, were acclimatized for 14 days and subsequently subjected to ulcer induction using aspirin (225 mg/200 g b. wt). The groups included a normal control, negative control, three groups treated with 200, 40 and 800 mg/kg b. wt. of *M. paradisiaca*, respectively and a positive control group administered omeprazole (5 mg/kg b. wt.). Extract administration lasted for 5 days and some kidney function parameters were evaluated. Results show that administration of the ethanol extract significantly enhanced the relative weight of the kidney comparable to the group administered the standard as there was no significant differences between these groups ($p > 0.05$). There were no significant differences in the total protein, creatinine and electrolyte levels in the ulcerated rats compared to the normal control ($p > 0.05$) and administration of the extract had no effect on the concentrations of these parameters. Furthermore, there was a significant decrease in the urea levels compared to the normal control ($p < 0.05$) and treatment with the extract (200 mg/kg b. wt.) reversed the ulcer-induced increase in urea levels. The result buttresses the safety of the extract as it did not alter the electrolyte and kidney biomarker concentration.

Keywords: *Musa paradisiaca*, Omeprazole, Gastric ulcers, HCO_3^{2-}, Ca^{2+}, PO_4^{3-} and K^+

Introduction

Gastric ulceration, a widespread gastrointestinal ailment, remains a significant global health challenge. Epidemiological evaluations indicate that gastric and peptic ulcers are high ranking global health challenges, affecting ~ 8 to 10 % of the population (Kelly *et al.*, 2009). Its multifaceted etiology includes stress, infections and the chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs) (Jones and Brown, 2020). *Helicobacter pylori* infections and certain drugs stimulate the secretion of gastric acid and pepsin (Bandyopadhyay *et al.*, 2001). There are a wide range of anti-ulcer agents commonly employed in the treatment of ulcer such as H_2-blockers (Cimetidine, ranitidine), M_1 -blockers (telenzepine, pirenzepine) and proton pump antagonists (omeprazole, lansoprazole), which decrease gastric acid secretion in the stomach (Ezekwesili *et al.*, 2014). Although, conventional treatments provide symptomatic relief, they often fail to address the underlying causes of ulcers, prompting the exploration of alternative and complementary therapies, particularly those derived from natural sources.

Medicinal plants have been used for centuries to contribute tremendously in the management of diseases and maintenance of health. This probably could be due to its availability and affordability. There have been several herbal preparations with *Musa paradisiaca*, commonly known as the plantain tree, employed in ulcer treatments. It is a perennial herbaceous plant within the *Musa* genus, known for its medicinal properties. Its leaves contain compounds like tannins and flavonoids, which have been traditionally employed to alleviate ulcers and related digestive issues (Lee and Kim, 2021). Analysis of plantain revealed a proximate composition of 15 % moisture, 9 % ash, 19 % crude protein, 27 % crude fiber and 39 % carbohydrate. This plant has been reported to contain some mineral elements like zinc, calcium, iron, potassium, phosphorus, magnesium, sodium and copper. (Obose *et al.*, 2018). This study aims to investigate the effect of the plant extract on kidney biomarkers in the Wistar rats.

Materials and methods

Collection and identification of plant samples: Unripe *M. paradisiac*a fruit was obtained from New Benin Market, Benin City, Edo State, Nigeria. The plants were identified and authenticated at the Department of Plant Biology and Biotechnology University of Benin, Benin City, by Dr. H.A. Akinnibosun**.**
Preparation of the ethanol extract: The skin was peeled off to obtain the pulp of the fruit, which was diced in pieces then sundried for days until there was no moisture in it. The dried plantain fruit was blended into a powder and then soaked in ethanol. To facilitate the extraction of the plantain's active constituents, 2000 g of the powdered plantain was soaked for 72 h in 5 L of ethanol solvent with periodic stirring. The solution was filtered using a cheese net with tiny pores to get the filtrate, which was concentrated by exposing it to a rotating evaporator to obtain the plant extract required.
Aspirin-induced ulcer study: The effect of the extract on aspirin-induced ulcer model was studied according to the method of Ubaka *et al*. (2010). A single dose of aspirin (255 mg/200 g b.wt.) was administered to all the fasting rats groups except for the rats in the normal control group.
Experimental design: A total of twenty-four (24) healthy male adults Wistar rats (albino rats), weighing about 180-200 g were procured from the Animal House of the Department of Biochemistry, University of Benin, Edo State and were used for this study. The rats were housed in clean cages under normal temperature (27 – 30 °C) where they were fed standard diet (Guinea Feeds Ltd, Ibadan) and water *ad libitum*. The animals were acclimatized for 14 days before the induction of ulcer, followed subsequently by the administration of ethanol extract of unripe plantain that lasted for five (5) days. They were randomly allocated into six (6) groups consisting of four (4) animals each. The groups were designated as groups 1, 2, 3, 4, 5 and 6. Extract administration was done as follows:
Group 1 **–** Normal control (no induction; administered 2 mL/kg of distilled water)
Group 2 **–** Negative control (ulcer induction, no treatment).
Group 3 **–** Ulcer induction, treated with 800 mg ethanol extract of *M. paradisiaca* per kg b. wt. of rat
Group 4 **–** Ulcer induction, treated with 400 mg ethanol extract of *M. paradisiaca* per kg b. wt. of rat
Group 5 **–** Ulcer induction, treated with 200 mg ethanol extract of *M. paradisiaca* per kg b. wt. of rat
Group 6 **–** Ulcer induction, treated with Omeprazole (5 mg/kg b. wt. of rat).
The administration was given orally between the hours of 6 – 8 am daily and lasted for a period of 5 days. Each animal was anaesthetized by being placed in a chloroform chamber, 24 hours after the last administration and dissected.

Biochemical assays

Determination of serum urea concentration: Urea concentration was determined using commercially purchased Randox kits based on the method of Tietz (1983).
Determination of creatinine concentration: Kidney creatinine concentration was determined using the method of Bartels and Bohmer (1972) as described in the Randox kit.
Determination of serum total protein: Serum total protein was determined using the method of Tietz (1983) following the instructions described in the Randox kit.
Estimation of potassium (K^+) ions: The procedure described by Terri and Sesin (1958) was employed for determine the potassium levels.
Estimation of bicarbonate (HCO_3^-) ions: Bicarbonate was determined using the method of Norris *et al.* (1975).
Estimation of calcium (Ca^{2+}) and phosphate (PO_4^{3-}) ions: Concentrations of Ca^{2+} and PO_4^3were determined using commercially available diagnostic kits (Randox Lab., UK) following manufacturers instruction.
Statistical analysis: The results are presented as mean ± SEM. The SPSS software (v17) and GraphPad Prism software (v10.0) were used to perform the one-way Analysis of Variance test (ANOVA) and data visualization, respectively. The differences between the mean values between groups were compared by the Fisher's Least Significant Difference (LSD) post hoc test, with p values < 0.05 considered statistically significant.

Results

Effect of administration of ethanol extract on kidney weight and kidney to body weight ratio: Table 1 shows the effect of the ethanol extract of *M. paradisiaca* on the kidney weight of the animals and kidney wt. to final body wt. ratio. The kidney weight of the groups were all statistically similar ($p > 0.05$). However, induction of ulceration significantly reduced the relative weight of the kidney in Group 2 rats compared to the normal rats ($p < 0.05$). Administration of the ethanol extract significantly enhanced the relative weight of the kidney comparable to the group administered the standard as there was no significant differences between these groups ($p > 0.05$).

Table 1: Kidney weight/final body weight ratio of the experimental animals

Groups	Weight of kidney (g)	Final body weight (g)	Kidney/Body weight ratio
Group1	0.93±0.10	224.78±14.6	1:250
Group 2	0.99±0.13	147.11±10.17	1:148*
Group 3	1.19±0.07	220.11±9.96	1:185*#
Group 4	1.14±0.04	205.36±3.20	1:180*#
Group 5	1.04±0.10	197.57±6.23	1:190*#
Group 6	1.14±0.11	229.33±3.32	1:201*#

Values are presented as mean ± SEM, n = 4. * $P < 0.05$ compared to the control; # $p < 0.05$ compared to the untreated control.

Effect of M. paradisiaca on the total protein, urea and creatinine levels: The effect of the extract of *M. paradisiaca* on serum total protein, urea and creatinine levels are presented in Figure 1. There were no significant differences in the total protein and creatinine levels in the ulcerated rats compared to the normal control ($p > 0.05$). Administration of the extract had no effect on the concentrations of these parameters. On the other hand, induction of ulcer in Group 2 rats significantly decreased the urea levels compared to the normal control ($p < 0.05$. Ethanol extract of unripe plantain at 200 mg/kg body weight and omeprazole restored the urea levels to that of the normal control.

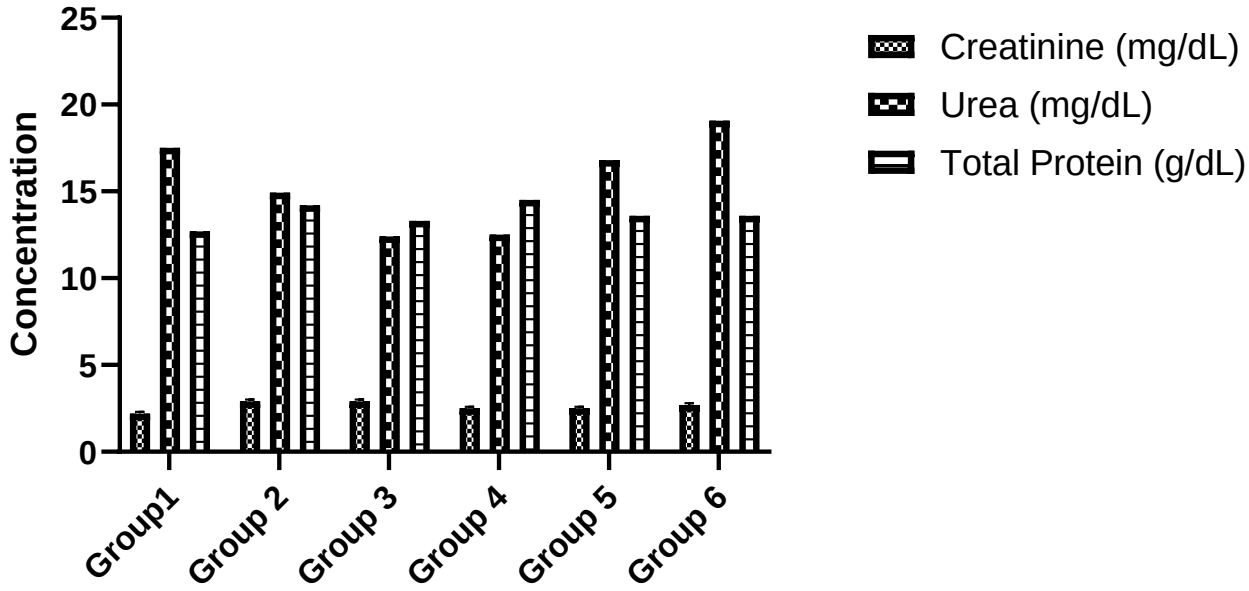

Figure 1: Effect of *M. paradisiaca* on total protein, urea and creatinine levels. Column height represents the mean

Effect of unripe plantain extract on serum electrolyte concentrations: The electrolyte levels of normal and ulcerated rat treated with or without the ethanol extract of *M. paradisiaca* are presented in Figure 2. The concentrations of bicarbonate (HCO^{3-}) and phosphate (PO_4^{3-}) were statistically similar ($p > 0.05$) between all groups (Figure A). Furthermore, there was no significant differences in the calcium (Ca^{2+}) and potassium (K^+) ion levels between the normal control and the paracetamol-induced ulcer groups ($p > 0.05$).

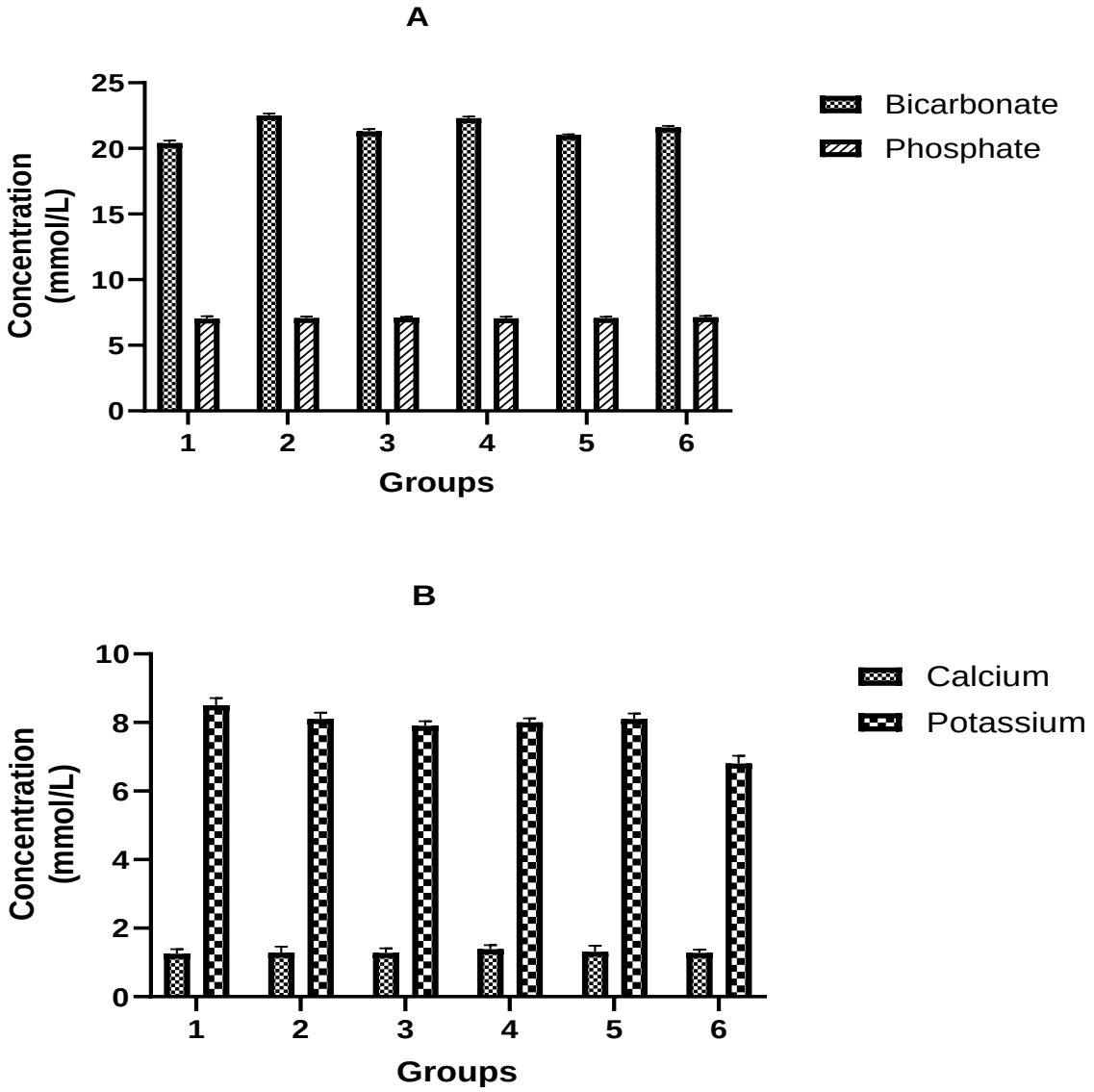

Figure 2: Serum electrolyte levels in normal and paracetamol-induced ulcerated rats treated with or without ethanol extract of *M. paradisiaca*. (A) Bicarbonate (HCO^{3-}) and phosphate (PO_4^{3-}) ions (B) Calcium (Ca^{2+}) and potassium (K^+) ions. Column height represents the mean

Discussion

This study presents the outcomes of treatment of paracetamol-induced gastric ulceration with *Musa paradisiaca* (plantain) on the renal health in a rat model. The result of the study shows that the kidney weight of the groups were all statistically similar ($p > 0.05$). However, in comparison to the body weight of the rats, the relative weight of the kidney in the ulcerated groups was significantly reduced compared to the normal rats ($p < 0.05$). Treatment with the extract improved the relative weight of the kidney which was comparable to the group administered the standard ($p > 0.05$). It is widely accepted that determination of the organ weight to body ratio is an indication of the toxicity of a treatment or chemical entity (Lazic *et al*., 2020). Therefore, ulcer induction with paracetamol is toxic to the kidney.

Also, the results show that administration of the extract had no effect on the total protein, creatinine and electrolyte levels in comparison to the normal control. This correlates with the studies of Focho *et al*. (2019), who observed that treatment with the ethanol extract (at various concentrations) did not cause any significant changes ($p > 0.05$) in serum creatinine levels. Furthermore, this study correlates with that of multiple studies showing that consuming plantain has negligible effects on serum protein levels (Abu- Lebdeh and Nair, 2016;

Hasan and Abdulsattar, 2015). However, the result negates the findings of Kawai and co-workers, which showed that treatment with the extract did not result in any significant changes in the serum urea levels. The extract (200 mg/kg body weight) of unripe plantain restored the urea levels to that of the normal control. Finally, the results indicate that the extract and standard drug did not exhibit any significant effect ($p > 0.05$) on the electrolyte concentration.

Conclusion

Musa paradisiaca ethanol extract improves the kidney health in ulcerated Wistar rat models. Furthermore, the result buttresses the safety of the extract as it did not alter the electrolyte and kidney biomarkers.

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