Sahel Journal of Life Sciences FUDMA (SAJOLS)
September 2024 Vol. 2(3): 122-127
ISSN: 3027-0456 (Print)
ISSN: 1595-5915(Online)
DOI: https://doi.org/10.33003/sajols-2024-0203-16

Research Article

Renal Protective Effects of *Dialium guineense* Fruit Pulp on Serum Creatinine and Urea Levels in Ethanol-Induced Peptic Ulcers in Albino Rats

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ABSTRACT
Ethanol-induced peptic impacts various systems, such as renal function, with serum creatinine and urea as indicators of kidney dysfunction. Despite its known antioxidant and anti-inflammatory properties, *Dialium guineense* has not been explored for its potential to protect renal function against ulcerated conditions. This study evaluated its impact on renal function in albino rats with ethanol-induced peptic ulcers. Albino rats were divided into six groups (n=5): normal control, ulcer control, a reference group treated with omeprazole (20 mg/kg), and groups treated with *Dialium guineense* extract at 250 mg/kg, 500 mg/kg, and 1000 mg/kg. Additionally, five *Dialium guineense* fractions were administered at 250 mg/kg and 500 mg/kg Ulcer was induced using ethanol (5 ml/kg), followed by a 21-day treatment with *Dialium guineense* extract and omeprazole as the standard drug. Serum creatinine and urea levels were assayed biochemically. Ethanol significantly raised the serum creatinine and urea levels in the ulcer control group compared to the normal control ($p < 0.05$). *Dialium guineense* treatment led to a dose-dependent reduction, most notably at 1000 mg/kg ($p < 0.05$). The reduction in renal markers with *Dialium guineense* was comparable to omeprazole. Findings suggest that *Dialium guineense* fruit pulp may mitigate ethanol-induced renal dysfunction, indicating its potential renoprotective properties and highlighting a foundation for further research into its therapeutic uses for renal dysfunction associated with gastrointestinal disorders.

Keywords: *Dialium guineense*; Peptic ulcer; Renal; Serum creatinine; Serum urea; Ethanol-induced ulcer

Citation: Elekwa, E.A., Aloh, G.S., Agu, K.A., Okoro-Akapndu, E., & Ogwo, B. (2024). Renal Protective Effects of *Dialium guineense* Fruit Pulp on Serum Creatinine and Urea Levels in Ethanol-Induced Peptic Ulcers in Albino Rats. *Sahel Journal of Life Sciences FUDMA,* 2(3): 122-127. DOI: https://doi.org/10.33003/sajols-2024-0203-16

INTRODUCTION

Peptic ulcer disease still constitutes one of the most important health problems worldwide, especially when induced by ethanol. Ethanol, being among the most commonly used ulcerogenic agents in experimental models of gastric ulcers, exerts a harmful effect on the disruption of the gastric mucosal barrier, an inducing effect on ulcer formation, and an enhancing effect on gastric acid secretion (Beiranvand, 2022). Besides its localized toxic effect on the gastrointestinal tract, ethanol intake has been found to induce systemic oxidative stress that can provoke renal dysfunction (Hernández *et al*., 2016).

The kidneys are highly susceptible to oxidative stress and inflammation; hence, there is often an elevation in serum creatinine and urea levels, which are indicators

of glomerular filtration rate (GFR) and overall kidney functions, respectively (Gounden *et al.*, 2024). Renal dysfunction, as manifested by increased creatinine and urea levels, is a critical concern in patients with peptic ulcer disease (PUD), since this enhances the overall health burden and complicates treatment modalities (Kim *et al*.,2019. Conventional anti-ulcer medications, such as omeprazole, target gastric ulcers effectively but are limited in their protective scope for renal function (Kuna, 2019; Perico *et al*., 2020).

Herbal medicine has become a complementary and alternative treatment in managing peptic ulcers that may extend to offering renal protection (Kumadoh, 2021). *Dialium guineense*, also known as velvet tamarind, is a plant used in traditional medicine because of its various therapeutic properties, including antioxidant, anti-inflammatory, and gastroprotective effects [Abu, 2022; Airadion, 2021; Besong, 2016). However, few studies have been conducted on the use of the plant regarding renal protection, especially in conditions relating to ethanol-induced peptic ulcer medication.

This study, therefore, investigated the effect *of Dialium guineense* fruit pulp on serum urea and creatinine levels in ethanol-induced peptic ulcers in albino rats and explored its potential as a nephroprotective agent.

MATERIALS AND METHODS

Chemicals and Reagents

The chemicals and reagents used in the study included urea reagent and creatinine reagent, both obtained from Randox Diagnostics. Additionally, omeprazole, which was used as a reference drug, was sourced from Emzor.

Extraction [Crude extract]

Five hundred gram Fi of the pulverized pulp of *Dialium guineense* was soaked in 1.5 litres of ethanol for 48 hours. The mixture was filtered on Whatman No. 1 filter paper and the filtrate concentrated to a solid residue using a rotary evaporator.

Fractionation of the extract

A semi-solid ethanol extract (20 g) was fractionated on a glass column (150 cm × 15 cm) packed with 200 g of silica gel (30-90 mesh slurry). The elution with chloroform: petroleum ether followed by successive elution with ethanol and methanol gave the chloroform pet ether (PEF), ethanol (EF) and methanol (MF) fractions, respectively.

Chromatographic isolation and purification techniques

Five grams of methanol fraction was chromatographed in a glass column (1.5 cm diameter, 150 cm length) packed with silica gel, particle size between 30 and 60 microns, 90 mesh, at a stationary phase bed height of 100 cm. Gradient elution was performed using mixtures of hexane-chloroform, 1:3 (400 mL), followed by chloroform-ethyl acetate, 1:1 (400 mL each). Finally, increasing chloroform: ethyl acetate ratios of 1:3, 1:5 and 1:7 (400 mL each) were applied. Fractions were collected in 20 mL portions and combined based on having identical Rf values.

Experimental Animals

Adult albino rats weighing (150-200) were used for the study. The animals were housed under standard conditions, 12/12h light-dark cycle starting at 7:00 am at the temperature of 25±2^{o}C. The animals underwent seven days of acclimatization before the experiments. The rats were fed with standard grower pellets (Grand Cereals Ltd, Abia State) and had access to clean drinking water *ad libitum*.

Experimental Design

The study comprised an acute phase using the crude extract and a sub-acute phase for both the crude extract and fractions. In phase one (1), sixty (60) adult albino rats were used for the experiment, and thirty (30) were used for the acute and sub-acute of the crude extract respectively following the methodology of Raeesi *et al.* (2019). The animals were randomly assigned into six groups of five (5) animals each. Group 1 was the normal control that received feed and water alone (no treatment), and Group 2 was the negative control (ethanol-induced without treatment). Group 3 received 20 mg/kg body weight of omeprazole Group 4, 5, and received 250 mg/kg, 500 mg/kg and 1000 mg/kg body weight of *Dialium guineense* fruit pulp extract. In phase two (2), sixty – five (65) animals in thirteen experimental groups were used. Groups 1-3 were the same as in Phase 1. Groups 4-13 orally treated with 250 and 500 mg/kg body weight of *Dialium guineense* bioactive fractions. Gastric ulcer was induced via oral administration of ethanol (5 mL/kg body weight, 80% v/v) following a 24-hour fasting period for 30 minutes after treatment. Two hours post-ethanol induction, the animals were sacrificed, and Blood samples were collected for the analyses.

Acute study with Crude extract

Group 1: Normal control (non-ulcerated rats)
Group 2: Ulcer control (ethanol-induced, untreated)
Group 3: Ulcer-induced rats treated with omeprazole.
Group 4: Ulcer-induced rats treated with 250 mg/kg of *Dialium guineense* crude extract
Group 5: Ulcer-induced rats treated with 500 mg/kg of *Dialium guineense* crude extract
Group 6: Ulcer-induced rats treated with 1000 mg/kg of *Dialium guineense* crude extract

Subacute study with Crude extract

Group 1: Normal control (non-ulcerated rats).
Group 2: Ulcer control (ethanol-induced, untreated)
Group 3: Ulcer-induced rats treated with omeprazole.

Groups 4: Ulcer-induced rats treated with 250 mg/kg of *Dialium guineense* crude extract
Group 5: Ulcer-induced rats treated with 500 mg/kg of *Dialium guineense* crude extract
Group 6: Ulcer-induced rats treated with 1000 mg/kg of *Dialium guineense* crude extract

Subacute study with Fractions

Group 1: Normal control (non-ulcerated rats).
Group 2: Ulcer control (ethanol-induced, untreated).
Group 3: Ulcer-induced rats treated with omeprazole.
Groups 4-13: Ulcer-induced rats treated with 250 and 500 mg/kg of *Dialium guineense* fractions.

Methods

Macroscopic evaluation of the stomach (ulcer index)

The stomachs were excised and carefully opened along the line of greater curvature to expose the walls. The stomach contents were then washed off and viewed with the aid of a light microscope (x 100) to determine the ulcer scores using the method of Zatorski (2017). The ulcerative lesions were counted and scored as follows: a normal stomach was scored as 0, the presence of pinhole lesions was scored as 1.0, spot ulceration was given a score of 1.5, haemorrhagic streaks were assigned 2.0, small erosions were scored as 2.5, large erosions were rated 3.0, and perforations were scored as 3.5.

The mean ulcer score for each animal was used to express the ulcer index. The ulcer index (U.I) was calculated by using the formula:

$$U: I = \frac{1x\ (\text{No.of lesions of grades } 1) + 2\ x\ (\text{No.of lesions of grade } 2) + 3\ x\ (\text{No.of lesions of grades } 3)}{10}$$

The percentage of ulcer protection was determined using the formula

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

Determination of serum urea and serum creatinine concentration

Serum urea concentration was determined using the Berthelot method while the serum creatinine was determined by the Jaffe slot alkaline picric acid method. Both analyses were performed by using reagent kits from Randox Laboratories, UK. (Ochei and Kolhalkar, 2008; Cheesbrough, 2006).

Data Analysis

All values were expressed as mean and standard deviation. Data was analyzed by one-way ANOVA, followed by Turkey's post-hoc test and significant differences between groups were determined using SPSS software version.

RESULTS

Table 1 shows the effect of the acute study of *Dialium guineense* fruit pulp extract on the levels of serum urea and creatinine in experimental rats. There were remarkable variations between the groups, especially for normal control, ulcer control, and treatment groups. A dose-response trend in urea level reduction was observed at 250, 500, and 1000 mg/kg of *Dialium guineense* treatment. The 1000 mg/kg dose reduced the urea level within values comparable to the normal control group. *Dialium guineense* treatments at different doses resulted in significantly lower ($p< 0.05$) creatinine levels, closer to the values obtained in the normal control group. Compared with omeprazole, both urea and creatinine levels were lower compared to the ulcer control group but higher compared to the normal control and *Dialium guineense*-treated groups.

Table 1: The effect of crude extract of *Dialium guineense fruit pulp* on serum urea and creatinine concentration in ethanol-induced ulcer in albino rats (acute study)

Groups	Urea (mg/dl)	Creatinine (mg/dl)
Normal control	16.69 ± 1.16^{a}	0.72 ± 0.05^{a}
Ulcer control	19.69 ± 0.79^{c}	0.95 ± 0.03^{c}
Omeprazole (20 mg/kg)	18.89 ± 0.64^{bc}	0.82 ± 0.02^{b}
Dialium guineense (250 mg/kg)	17.56 ± 0.34^{ab}	0.76 ± 0.07^{ab}
Dialium guineense (500 mg/kg)	16.9 ± 0.87^{a}	0.76 ± 0.03^{ab}
Dialium guineense (1000 mg/kg)	16.55 ± 0.79^{a}	0.74 ± 0.03^{ab}

Values are presented as mean ± standard deviation (n = 5). Means with different superscripts along the rows are statistically significantly different $p<0.05$(n=5)

Table 2 shows the effect of sub- acute study of *Dialium guineense* fruit pulp extract on the levels of serum urea and creatinine in experimental rats. Administration of *Dialium guineense* extract at 250, 500, and 1000 mg/kg resulted in a return of urea levels close to the normal control. Creatinine levels were significantly higher ($p<0.05$) in the ulcer control group compared to the normal control which remained lower. However,

treatment with *Dialium guineense* significantly reversed this trend, as the dose of 1000 mg/kg was able to bring creatinine levels down near-normal control. Omeprazole administration gave levels of urea and creatinine that were significantly lower ($p<0.05$) than that of the ulcer control group but higher than that produced by the *Dialium guineense* treatment groups, especially at higher doses.

Table 3 shows the effect of sub-acute study of the fractions of the *Dialium guineense* fruit pulp on the serum urea and creatinine level in the experimental rats Urea levels were significantly higher ($p<0.05$) in the ulcer control group when compared with the normal control. All fractions of *Dialium guineense* resulted in a decrease in urea levels. The lowest urea value was recorded for Fraction III 250 mg/kg. Creatinine levels were also similar to those of urea in that the highest value was obtained in the ulcer control group. Treatment with Dialium guineense fractions reduced creatinine levels across the groups, though Fraction IV at 500 mg/kg showed creatinine levels that closely resembled the normal control. The levels of urea and creatinine were higher in the omeprazole-treated group than in most of the groups treated with *Dialium guineense* extracts.

Table 2: The effect of crude extract of *Dialium guineense* on serum urea and creatinine concentration in ethanol-induced ulcer in albino rats (sub-acute study)

Groups	Urea (mg/dl)	Creatinine (mg/dl)
Normal control	18.17±0.79^{a}	0.61±0.03^{a}
Ulcer control	21.71±1.78^{b}	0.90±0.06c
Omeprazole (20 mg/kg)	19.02±0.3^{a}	0.83±0.04^{c}
Dialium guineense (250 mg/kg)	18.35±0.25^{a}	0.74±0.03^{b}
Dialium guineense (500 mg/kg)	18.42±0.40^{a}	0.73±0.02^{b}
Dialium guineense (1000 mg/kg)	18.45±0.40^{a}	0.66±0.02^{a}

Values are presented as mean ± standard deviation (n = 5). Means with different superscripts along the rows are statistically significantly different $p<0.05$(n=5)

Table 3: The effect of the fractions of *Dialium guineense* on serum urea and creatinine concentration in ethanol-induced ulcer in albino rats (sub-acute study)

Groups	Urea (mg/dl)	Creatinine (mg/dl)
1	17.6±0.55^{a}	0.614±0.03^{a}
2	24.8±1.10^{c}	0.84±0.04^{d}
3	20.2±1.64^{ab}	0.76±0.04^{cd}
4	19.8±0.84^{ab}	0.754±0.07^{bcd}
5	19±1.23^{ab}	0.75±0.03^{bcd}
6	20±1.23^{ab}	0.69±0.04^{abc}
7	19.4±1.67^{ab}	0.72±0.04^{bc}
8	18.4±0.89ab	0.726±0.03^{bc}
9	19.6±1.52^{ab}	0.70±0.04^{abc}
10	19.6±0.55^{ab}	0.68±0.03^{abc}
11	19.4±1.3^{4ab}	0.67±0.04^{ab}
12	20.8±0.45^{b}	0.74±0.05^{bc}
13	20.4±0.55^{b}	0.76±0.03^{cd}

Values are presented as mean ± standard deviation (n = 5). Means with different superscripts along the rows are statistically significantly different $p<0.05$(n=5). Group1=Normal control, group 2=Ulcer control, group 3=Omeprazole, 20 mg/kg group,4=Fraction I, 250 mg/kg bw, group 5=Fraction I, 500 mg/kg bw group,6=Fraction II, 250 mg/kg bw, group 7=Fraction II, 500 mg/kg bw , group 8=Fraction III, 250 mg/kg bw, group 9=Fraction III, 500 mg/kg bw, group 10=Fraction IV, 250 mg/kg bw, group 11=Fraction IV, 500 mg/kg bw, group 12=Fraction V, 250 mg/kg bw, group 13=Fraction V, 500 mg/kg bw

DISCUSSION

Ethanol-induced peptic ulcers are mostly associated with systemic complications such as renal dysfunction, an indication that ethanol acts destructively on virtually every organ system. Ethanol induces disruption in the gastric mucosa, leading to gastrointestinal bleeding that may cause hypovolemia, reduced blood flow to the kidneys, and thus renal dysfunction (Golbabapour *et al*. 2013; Chan *et al*., 2014). Increased levels of creatinine

and urea in this context reflect impaired glomerular filtration and kidney damage (George and Gounden, 2019; Shahbaz, 2024). The treatment with *Dialium guineense* crude extract and its fractions demonstrated a clear nephroprotective effect, as evidenced by the dose-dependent reduction in these renal biomarkers.

This study revealed that the crude extract of *Dialium guineense* and fractions exerted nephroprotection through dose-dependent reductions in serum creatinine and urea levels. The antioxidant properties of *Dialium guineense*, which can be attributed to its high content of polyphenols, flavonoids, and tannins, may have played a crucial role in mitigating renal oxidative stress and preserving kidney function (Abu *et al*., 2020; Abu *et al*., 2022; Aja *et al.*, 2022). The restoration of urea and creatinine levels toward normal values implies that *Dialium guineense* protects the kidneys either by reducing oxidative stress or by inhibiting inflammatory pathways that contribute to renal damage (Tienda-Vázquez *et al*., 2022).

Most interestingly, Fraction III and Fraction IV also showed better renoprotective activity, indicating that some certain compounds could be present in these fractions with increased activity. This therefore means that further isolation and identification of active components may possibly present new avenues of therapy for the management of renal dysfunction in peptic ulcer conditions.

Compared to a standard anti-ulcer medication like omeprazole, *Dialium guineense* had comparable or even better effects in the reduction of renal dysfunction markers and might, therefore, represent an alternative or adjuvant therapy in the management of ethanol-induced renal damage (Karolin, 2011).

Several studies have highlighted the nephroprotective effects of plant-derived compound; *Aloe vera* and *Zingiber officinale* have demonstrated protective effects against renal damage induced by ethanol and other toxins through their antioxidant properties (Khodai *et al*., 2014; Fathi, *et al*., 2021). The present study corroborates these findings, as *Dialium guineense* was able to mitigate the oxidative stress caused by ethanol, leading to improvements in renal function parameters.

CONCLUSION

This present study has established that the fruit pulp of *Dialium guineense* exerts a protective effect on renal function in the context of ethanol-induced peptic ulcers by reducing the elevated levels of serum creatinine and urea. From these results, it is clear that *Dialium guineense* may be used therapeutically in the prevention or management of renal dysfunction associated with gastrointestinal disorders, particularly those involving oxidative stress. This will therefore require further research into the underlying mechanism and its clinical efficacy in establishing *Dialium guineense* for long-term.

Conflict Interest

Authors have no competing interest to declare.

Author contribution

EAE identified the research problem, designed the experiment, and wrote the manuscript. AGS supervised the experimental set-up, OE proofread the manuscript. EAE handled the data analysis, EB conducted the literature review, AGS designed the study while AKA assembled the methodology.

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