Original

Nephroprotective Effects of *Beta vulgaris* Against Cimetidine-induced Renal Toxicity: Histological and Biochemical Evidence in a Rat Model.

[1]Mufutau Oladele Oladimeji, [2]Tolulope Adefola Edward, [3]Ugochukwu Umeaku, [4]Sylvester Sunday Edward, [2]Adepoju Luqman Hassan, [2]Samuel Olawafemi Olaniyi, [2]Foluso Olamide Ojo, [5]Babatunde Elijah Arayombo, [4]Asisat Bola Tijani, [6]Rukayat Adesewa Farinde, [5]Mokolade Samson Ige

[1]Department of Morbid Anatomy and, Forensic Medicine, Obafemi Awolowo University Teaching Hospital Ile-Ife, Osun State, Nigeria.
[2]Department of Anatomy, University of Ilesa, Osun State, Nigeria
[3]Department of Anatomy, Delta State University, Delta State. Nigeria.
[4]Department of Physiology, Obafemi Awolowo University (OAU), Ile-Ife, Osun State, Nigeria
[5]Department of Anatomy and Cell Biology, Obafemi Awolowo University Ile-Ife, Osun State, Nigeria.
[6]Department of Anatomy, Elizade University, Ondo State, Nigeria.

Corresponding author: Edward Tolulope Adefola, Department of Anatomy, University of Ilesa, Osun State, Nigeria. tolulope_edward@unilesa.edu.ng: +234 8068395639

Article history: Received 18 February 2026, Reviewed 07 March 2026, Accepted for publication 17 March 2026

ABSTRACT

Background: Renal toxicity remains a significant challenge in clinical pharmacology, often resulting from adverse drug effects such as those caused by cimetidine, a commonly used H_2 receptor antagonist. While effective in managing gastrointestinal conditions, prolonged or high-dose cimetidine administration has been linked to renal impairment, characterized by histopathological damage and alterations in biochemical markers. This study investigates the potential nephro-protective effects of beetroot (*Beta vulgaris* L.), a nutrient-rich plant known for its antioxidant properties, against cimetidine-induced renal injury.

Methods: Thirty-five male Wistar rats were allocated into seven groups to receive various treatments, including cimetidine alone, beetroot extract at different doses, and combinations thereof, over a seven-week period.

Results: Histological examinations revealed that cimetidine caused significant renal damage, including hemorrhage, necrosis, and fibrosis, which were notably ameliorated by beetroot supplementation, especially at higher doses. Biochemical analyses demonstrated that beetroot significantly mitigated oxidative stress markers such as malondialdehyde (MDA) relative to the untreated group (p-value 0.001); it also significantly preserved functional parameters including serum creatinine (p value 0.001) and lactate dehydrogenase (LDH) (p-value 0.003) compared to the untreated rats.

Conclusion: The findings suggest that beetroot exerts protective effects through its anti-oxidative and anti-fibrotic properties, attenuating cimetidine-induced nephrotoxicity. These results highlight the potential of natural bioactive compounds like beetroot as adjuncts to prevent or reduce drug-induced renal injury, warranting further molecular investigations and clinical validation.

Keywords: Nephro-protective, V*ulgaris*, Cimetidine, Renal, Rats

How to cite this article

Oladimeji MO, Edward TA, Umeaku U, Edward SS, Hassan AL, Olaniyi SO, Ojo FO, Arayombo BE, Tijani AB, Farinde RA, Ige MS. Nephroprotective Effects of *Beta vulgaris* Against Cimetidine-induced Renal Toxicity: Histological and Biochemical Evidence in a Rat Model. The Nigerian Health Journal 2026; 26(1): 432 – 440. https://doi.org/10.71637/tnhj.v26i1.1344

INTRODUCTION

Renal toxicity remains a significant concern in clinical pharmacology, often resulting from the adverse effects of certain medications, including cimetidine, a widely used histamine H_2 receptor antagonist.[1] While cimetidine effectively manages gastrointestinal disorders, its prolonged or high-dose usage has been associated with renal impairment, manifesting through alterations in renal function markers and histopathological changes.[2] The underlying mechanisms of its induced nephrotoxicity are multifactorial, involving oxidative stress, inflammation, and cellular apoptosis, which collectively compromise renal integrity in line with Zhang *et al.,* 2023,[3] El Gamal *et al*., 2014,[4] Nna *et al*., 2020.[5]

Recent advancements in complementary and alternative medicine have shifted focus toward natural bioactive compounds with potential nephron-protective properties. Beetroot (Beta vulgaris), nutrient-dense root vegetable rich in antioxidants, nitrates, and phytochemicals, has garnered attention for its therapeutic benefits, including anti-inflammatory and anti-oxidative effects as reported by Stoica *et al.,* 2023[6]; Alshehri *et al*., 2024.[7] Several studies suggest that beetroot intake may mitigate oxidative stress-induced tissue damage, thereby offering a protective effect against various forms of organ toxicity.[7-8]

This study aims to elucidate the histological and biochemical impacts of beetroot administration on cimetidine-induced renal toxicity. By investigating the potential ameliorative effects of beetroot, this research seeks to contribute to the growing body of evidence supporting natural interventions in preventing or reducing drug-induced nephrotoxicity, ultimately fostering safer therapeutic strategies.

METHODOLOGY

Animal Procurement and Use: For this study, thirty-five (35) mature male Wistar rats aged 10-12 weeks, with weights ranging from 150 to 200g, were used for the study. The rats were procured from the animal holding section of the College of Health Sciences at Obafemi Awolowo University in Ile-Ife, Nigeria. Housed in plastic rat cages with standard environmental conditions and ample ventilation, the rats had unrestricted access to water and regular pellets. Before commencing the experiment, the rats were acclimatized to the research environment for a week.

Plant Material: The whole plants of *Beta vulgaris L*. were harvested from Mide farmland in Jos and authenticated in the Obafemi Awolowo University, Ile-Ife, Department of Botany. A voucher number (IFE-18073) was acquired, and the specimen was placed in the herbarium for future reference. The bulb was thoroughly washed in water, chopped into small pieces, air dried and grounded into powder using warring blender. The powder was soaked in distilled water for 24 hours. The resulting mixtures were filtered using whatman No 1 filter paper (0.2mm). The filtrates were lyophilized to produce a gelatinous substance. The obtained extract was stored in a refrigerator at 4^{o} C. The extract yield was 14.89 % as shown below

$$\% \text{ Yield} = \frac{\text{B.V.L fruit Extract (g)}}{\text{Powdered B.V.L (g)}} \times 100$$

$$\% \text{ Yield} = \frac{38.39 \text{ g}}{257.83 \text{ g}} \times 100$$

$$\% \text{ Yield} = 14.89\%$$

Determination of Cimetidine Dosage: Cimetidine was administered at a dose of 120mg/kg/b.w which was adopted from the study by Scheinfeld *et al.*[9]

***Determination of Extract Dosage*:** The dosage regimen utilized in this study for administering the extract (*Beta Vulgaris* L.) at 200mg/kg, 400mg/kg was adopted from previous work by El Gamal *et al.*[3]

Ethical Clearance: Ethical clearance for this study was obtained from the Health Research Ethics Committee (HREC) of the Institute of Public Health, College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Osun State Nigeria. (IPH; Assigned Number: IPH/OAU/12/2322).

Preparation of Stock Solution of Cimetidine: Cimetidine was supplied by the May and Baker Company in Sango-Ota, Ogun State, Nigeria, with the registration number A4-8541 from NAFDAC. An 800 mg quantity of cimetidine was mixed with 10 milliliters distilled water to make a stock solution of 120 mg. The calculation for the cimetidine volume took into consideration the body weight of the subjects. The solutions were consumed within three days after being stored at room temperature and protected from light.

Print ISSN: 0189-9287 Online ISSN: 2992-345X

Experimental Design

Table 1 Showing the Dosage Regimen Administered to the Rat

Grp	Number of rats	Administration	Duration
A	5	1ml\kg of distilled water	7weeks
B	5	120mg\kg of Cimetidine only	7weeks
C	5	120mg\kg of Cimetidine + 300mg\kg Vitamin C	7weeks
D	5	200mg\kg of B.V.L fruit extract only	7weeks
E	5	400mg\kg of B.V.L fruit extract only	7weeks
F	5	120mg\kg of Cimetidine + 200mg\kg of B.V.L fruit extract	7 weeks
G	5	120mg\kg of Cimetidine + 400mg\kg of B.V.L fruit extract	7 weeks

Cimetidine was administered orally BVL= beta Vulgaris L. were administered orally via oral cannula

Parameter Measured

Determination of Relative Organ Weight: Relative weight of the kidneys was calculated at sacrifice as follows:

$$\text{Relative organ weight} = \frac{\text{Organ Weight}}{\text{Body weight at sacrifice}} \times 100$$

Hematoxylin and Eosin Staining Procedure: Sections of the slide were treated with dropping grades of alcohol and de-waxed in a solvent as follows: ethanol, ninety percent alcohol, seventy percent alcohol, fifty percent alcohol for five minutes each. To get rid of excess dye from the tissue, sections were differentiated using an acid-alcohol solution (1% acid in 70% alcohol). After section washing, the nucleic were blue. Sections were again stained using fluorescence and then washed with water. After a short rinse in water, parts quickly became dehydrated in increasing alcohol grades as follows: Alcohol content: 50%, 70%, 80%, and 90%. Mounted DPX (Distyrene Plasticizer and Xylene) with a cover slip after being cleared in solvent according to Awoniran and Adeyemi.[10]

Masson's Trichrome Staining: This technique distinguished muscle fibers, collagen, and nuclei. Tissue sections underwent deparaffinization, staining with Weigert's iron hematoxylin for nuclei, followed by phosphomolybdic acid, acetic acid, and Masson's trichrome reagents to differentiate tissue components. Slides were dehydrated, cleared, and mounted.

Photomicrography: The slides were scanned using Motic Easyscan scope Pro N6 in Virtual Slides format (SVS). The slides were loaded on the slide tray then inserted into the Motic machine. The slides were previewed and scanned at standard setting. The manufacturer guild was followed. The photomicrographs were taken at 400 magnifications.

Statistical analysis: Data were analyzed using one-way analysis of variance (ANOVA) and post hoc analysis was carried out using Student Neuman-Keuls test on Graph Pad 8 (Graph Pad Software Inc., CA, USA). Results were expressed as mean ±S.E.M, alpha values were set at less than 0.05 was taken as accepted level of significant difference.

RESULTS

Plate 1 showed sections of group A, D and E with normal histological features of renal tubules, glomerulus and interstitial space compared to group B that showed hemorrhage, mild necrosis, inflammatory cells, dilated glomerular space, distorted glomerulus, plague within the hemorrhage and cystic formation. However, group C, F and G (which were treated with 300mg/kg of vitamin C, 200mg/kg of beetroot and 400mg/kg of beetroot) respectively, showed a better preserved histo-architectural features when compared to group B; these features were similar to the findings in group A. In groups F and G, which had graded dosage of beetroot, the treatment ameliorated the histo-architectural effects in a dose dependent manner when compared to group A.

In this study, plate 2 demonstrated Masson trichrome (MT) staining showing evidence of fibrosis in group B resulting from loss of elastic fiber and accumulation of collagen fiber when compared to group A, D and E. The effect was ameliorated in the treated groups C and G (which were treated with 300mg/kg of vitamin C and 400mg/kg of beetroot) respectively, when compared to group A. Groups D and E revealed abundant elastic fiber and moderate collagen fiber similar to group A.

Print ISSN: 0189-9287 Online ISSN: 2992-345X

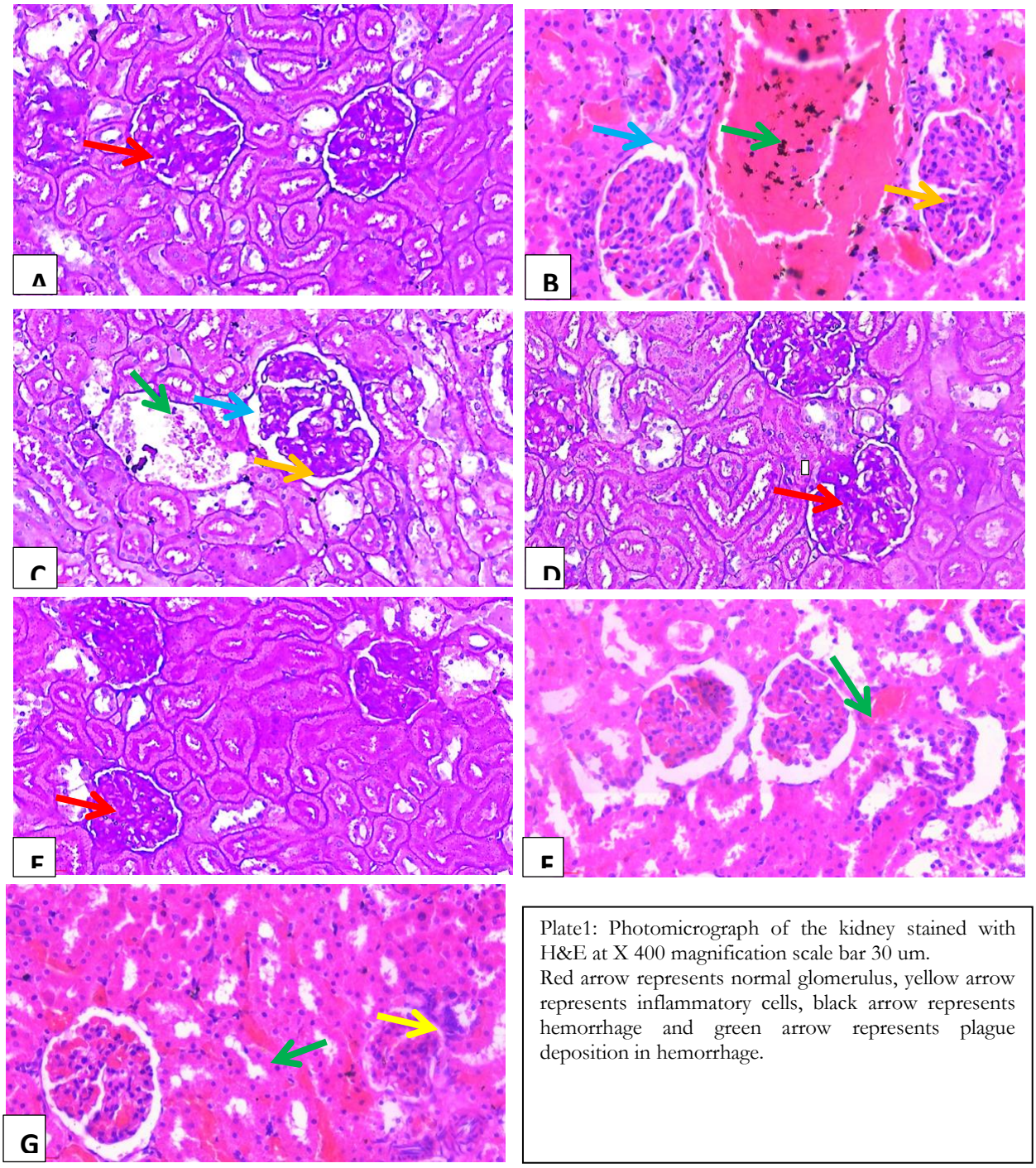

Plate1: Photomicrograph of the kidney stained with H&E at X 400 magnification scale bar 30 um.
Red arrow represents normal glomerulus, yellow arrow represents inflammatory cells, black arrow represents hemorrhage and green arrow represents plague deposition in hemorrhage.

Print ISSN: 0189-9287 Online ISSN: 2992-345X

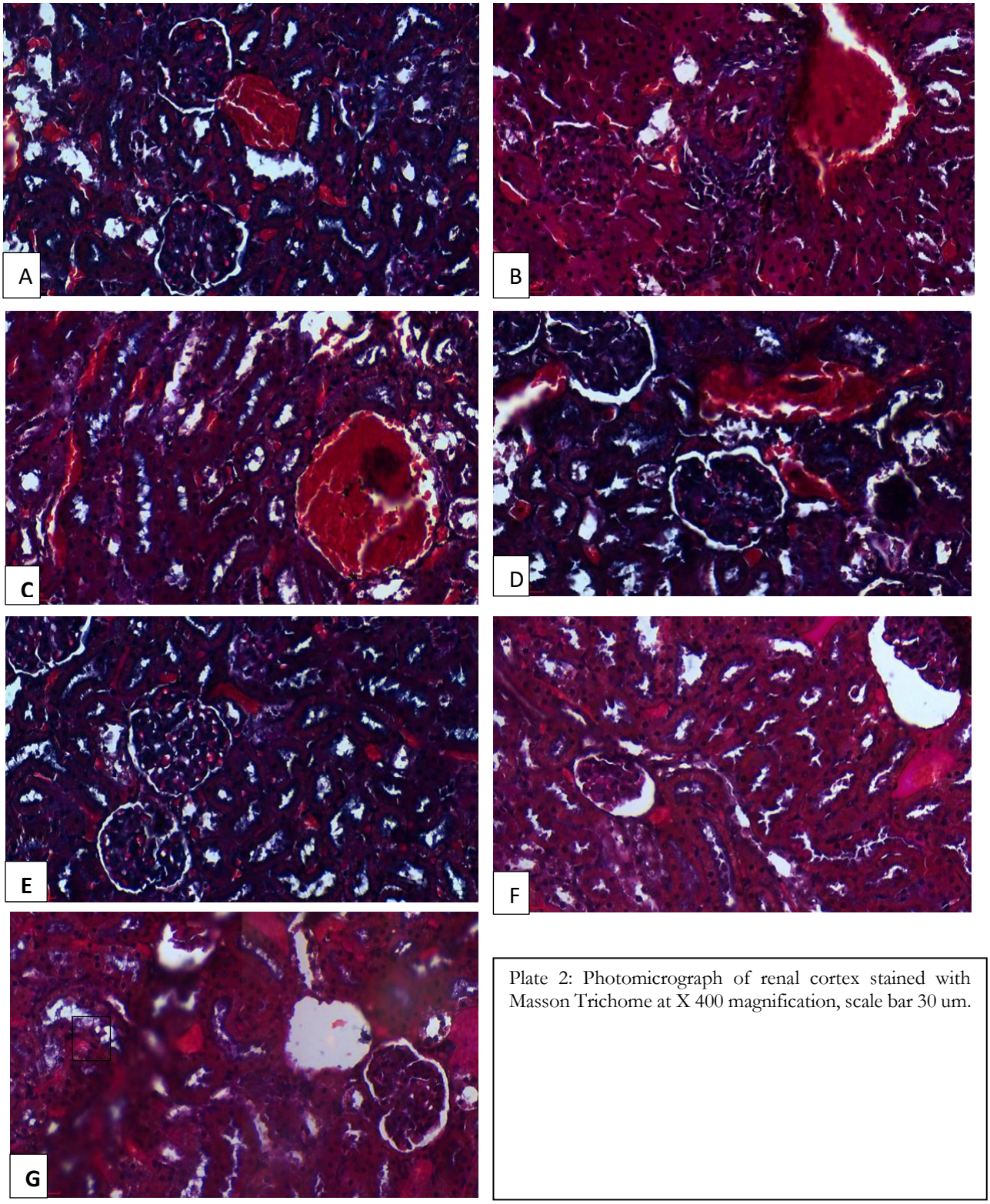

Plate 2: Photomicrograph of renal cortex stained with Masson Trichome at X 400 magnification, scale bar 30 um.

Print ISSN: 0189-9287 Online ISSN: 2992-345X

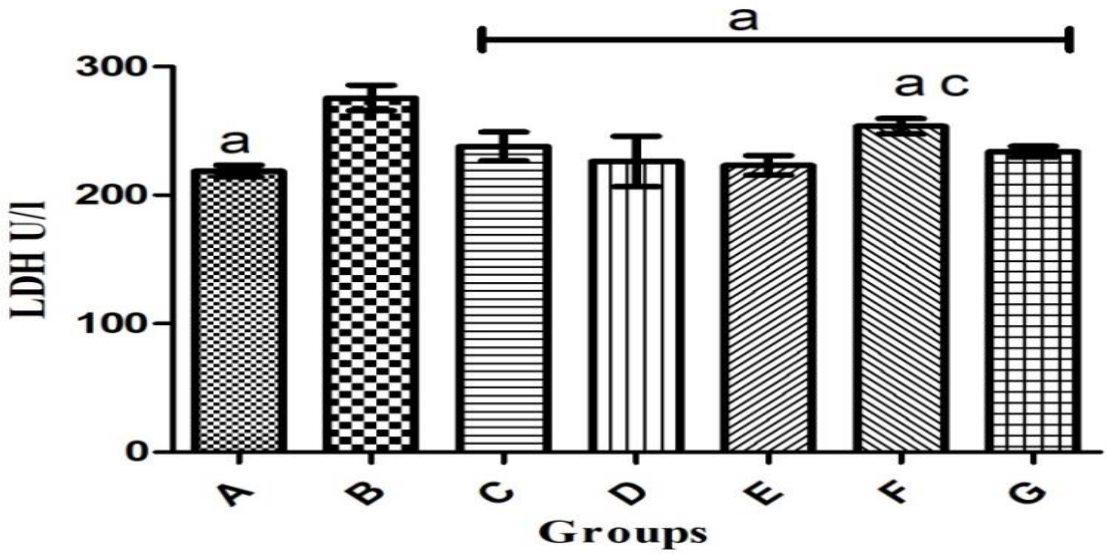

Fig. 1: Effect of ethanol extract *beet root* on LDH activity on cimetidine-induced renal toxicity in adult Wistar rats. Alpha level was set at less than 0.05
a: indicates significant difference compared to B,
b: indicates significant difference compared A.
c: indicates significant difference compared F.

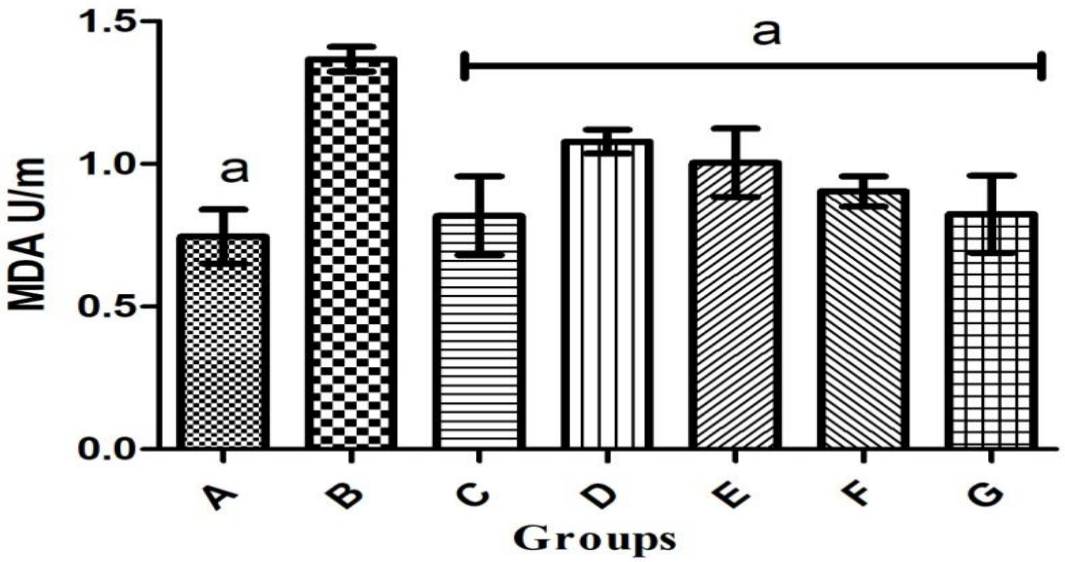

Fig. 2: Effect of ethanol extract *beet root* on MDA activity on cimetidine-induced renal toxicity in adult Wistar rats. Alpha level was set at less than 0.05.
a: indicates significant difference compared to group B.

Print ISSN: 0189-9287 Online ISSN: 2992-345X

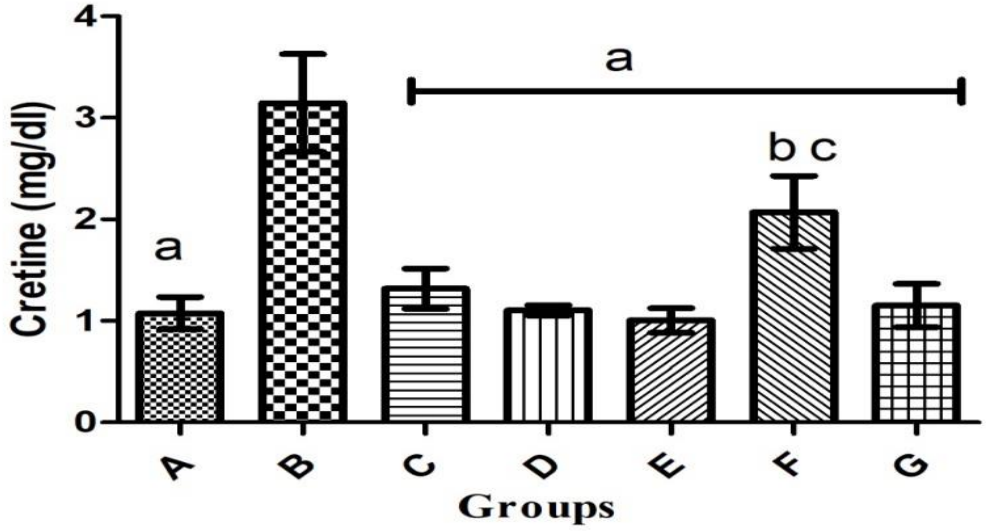

Fig. 3: Effect of ethanol extract *beet root* on creatinine activity on cimetidine-induced renal toxicity in adult Wistar rats. Alpha level was set at less than 0.05.
a: indicates significant difference compared to B
b: indicates significant difference compared A.
c: indicates significant difference compared F.

DISCUSSION

The histopathological examination of renal tissue demonstrated notable differences among the experimental groups. While groups A, D, and E exhibited normal renal histological features, the cimetidine-only group showed significant histopathological alterations, including hemorrhage, mild necrosis, infiltration by inflammatory cells, dilation of the glomerular space, distortion of the glomeruli, presence of plague within hemorrhagic areas, and cystic formations. These findings suggest that cimetidine administration induces substantial renal damage, consistent with its known nephrotoxic potential in line with previous reports by Adikwu *et al.* 2018, [11] Morimoto *et al.*, 2021,[12] and Border *et al.*[13]

In this study, the beetroot-treated groups demonstrated marked improvements in the histo-architecture of the distorted kidney; the extent of tissue restoration was more pronounced in groups receiving higher doses of beetroot, indicating a dose-dependent protective effect. The amelioration observed suggests that beetroot possesses nephroprotective properties, potentially attributable to its antioxidant constituents, which may mitigate oxidative stress and inflammatory responses induced by cimetidine in line with earlier studies by Abdu *et al.,* 2019,[14] and Albasher *et al.*, 2019.[15]

The cimetidine-induced group exhibited a significant loss of elastic fibers and an abnormal accumulation of collagen fibers, indicative of fibrosis and extracellular matrix remodeling due to injury. Conversely, groups treated with beetroot extract showed a notable reduction in collagen deposition and preservation of elastic fibers, signifying attenuation of fibrotic processes, in line with finding by Chen *et al.*[16] Group G demonstrated marked improvements similar to the control group, thereby underscoring the efficacy of higher beetroot doses in preventing fibrosis. The groups which received beetroot alone displayed elastic fibers and collagen levels similar to the control, suggesting that beetroot does not adversely affect normal renal architecture similar to the report by Chapman *et al.*[17]

Biochemical assessments revealed that cimetidine exposure led to increased LDH activity, reflecting enhanced cellular damage and membrane leakage. This increase was significantly higher in the cimetidine-treated group compared to the control.[18-19] Treatment with beetroot extract effectively reduced LDH activity in a dose-dependent manner, indicating cellular protection.[20] Similarly, markers of oxidative stress, such

Print ISSN: 0189-9287 Online ISSN: 2992-345X

as malondialdehyde (MDA), were elevated in the cimetidine group, signifying heightened lipid peroxidation. Beetroot administration mitigated this effect, with higher doses producing more substantial reductions, further emphasizing its antioxidant capacity similar to the findings by previous authors namely Farhana *et al.,* 2017, [21] and Sharma *et al.,* 2022[22] among others.

Serum creatinine, a renal function marker, was significantly elevated in the cimetidine-only group confirming impaired renal function in line with Singh et al.[19] The protective effect of beetroot was evidenced by the normalization of creatinine levels in treated groups, with a dose-dependent trend observed as previously reported by Kumar *et al*[20] and Sharma *et al.*[22] These findings collectively suggest that beetroot extract not only alleviates structural damage but also preserves renal functional integrity against cimetidine-induced toxicity.

The current data support the hypothesis that beetroot possesses protective effects against cimetidine-induced renal injury. Its ability to reduce oxidative stress, prevent fibrosis, and maintain renal function underscores its potential as a nephroprotective agent. Future studies should aim to elucidate the precise molecular mechanisms involved and evaluate the long-term benefits of beetroot supplementation in nephrotoxicity models.

CONCLUSION

The findings of this study underscore the nephroprotective potential of beetroot extract against cimetidine-induced renal toxicity. Histological analyses demonstrated that high dose of beetroot effectively mitigated tissue damage, including hemorrhage, inflammation, and fibrosis. Biochemically, beetroot attenuates oxidative stress markers such as MDA, reduces cellular damage indicators like LDH activity, and preserves renal function as evidenced by normalized serum creatinine levels. The protective effects highlight the therapeutic potentials of beetroot in safeguarding renal integrity and suggesting it as a complementary strategy to prevent or minimize drug-induced nephrotoxicity.

Declarations

Conflict of Interest: No conflict of interest
Funding: Self-funded

REFERENCES

1. Nugent CC, Falkson SR, Terrell JM. H2 Blockers. InStatPearls [Internet] 2024. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK525994/
2. Khan F, Saini A. Histamine H_2-receptor antagonists–induced nephrotoxicity: Review of case reports and mechanisms. Int J Clin Pharmacol Ther. 2016;54(5):367–78.
3. El Gamal AA, AlSaid MS, Raish M, Al-Sohaibani M, Al-Massarani SM, Ahmad A, Hefnawy M, Al-Yahya M, Basoudan OA, Rafatullah S. Beetroot (Beta vulgaris L.) extract ameliorates gentamicin-induced nephrotoxicity associated oxidative stress, inflammation, and apoptosis in rodent model. Mediators of inflammation. 2014;2014(1):983952.
4. Nna VU, Usman UZ, Ofutet EO, Obiandu C. Aqueous beetroot juice extract improves renal function and histopathological alterations in carbon tetrachloride-induced nephrotoxicity in rats. Ann Trop Pathol. 2020;11(2):108–14.
5. Zhang D, Luo G, Jin K, Bao X, Huang L, Ke J. The underlying mechanisms of cisplatin-induced nephrotoxicity and its therapeutic intervention using natural compounds. Naunyn-Schmiedeberg's archives of pharmacology. 2023; 396(11):2925-41.
6. Stoica F, Râpeanu G, Raţu RN, Stănciuc N, Croitoru C, Ţopa D, Jităreanu G. Red Beetroot and Its By-Products: A Comprehensive Review of Phytochemicals, Extraction Methods, Health Benefits, and Applications. Agriculture. 2025;15(3):270.
7. Alshehri MA, Felemban SG, Alotaibi AA, Aljuaid AE, Altamimi MA. *Beta vulgaris* juice exerts antioxidant and anti-inflammatory effects in type 2 diabetic rats. Saudi Pharm J. 2024;32(3):223–31.
8. Chaudhari AA, Raut SY. Nephroprotective potential of *Beta vulgaris* extract in experimental animal models: A review. J Tradit Complement Med. 2023;13(1):54–60.
9. Scheinfeld N. Cimetidine: A review of the recent developments and reports in cutaneous medicine. Dermatology online journal. 2003;9(2).
10. Awoniran PO, Adeyemi DO. Ethanol extract of Curcuma longa rhizome mitigates potassium bromate-induced liver changes in the Wistar rat: Histological, histochemical and immunohistochemical assessments. Morphologie. 2018;102(339):276-88.
11. Adikwu E, Bokolo B. Protective assessment of cimetidine against cyclophosphamide-induced kidney injury. Asian J Med Sci. 2018;9(6):25–30.

Print ISSN: 0189-9287 Online ISSN: 2992-345X

12. Morimoto K, Kanzaki G, Niikura T, et al. Acute tubulointerstitial nephritis associated with antineutrophil cytoplasmic antibody following cimetidine treatment: a case report. BMC Nephrol. 2021; 22:294.
13. Border SP, Tomaszewski JE, Yoshida T, Kopp JB, Hodgin JB, Clapp WL, Rosenberg AZ, Buyon JP, Sarder P. Investigating quantitative histological characteristics in renal pathology using HistoLens. Scientific reports. 2024;14(1):17528.
14. Albasher G, Almeer R, Alarifi S, Alkhtani S, Farhood M, Al-Otibi FO, Alkubaisi N, Rizwana H. Nephroprotective Role of Beta vulgaris L. Root Extract against Chlorpyrifos-Induced Renal Injury in Rats. Evidence-Based Complementary and Alternative Medicine. 2019;2019(1):3595761.
15. Abdu S, Salisu A, Alhassan AM, Musa B, Muhammad H, Sulaiman A. Nephroprotective effects of red beetroot-based beverages against gentamicin-induced renal stress. *J Food Biochem*. 2019;43(7):e12873. doi:10.1111/jfbc.12873
16. Chen L, Zhu Y, Hu Z, Wu S, Jin C. Beetroot as a functional food with huge health benefits: Antioxidant, antitumor, physical function, and chronic metabolomics activity. Food science & nutrition. 2021; 9(11):6406-20.
17. Chapman CL, Schlader ZJ, Reed EL, Worley ML, Johnson BD. Acute beetroot juice ingestion does not alter renal hemodynamics during normoxia and mild hypercapnia in healthy young adults. Nutrients. 2021;13(6):1986.
18. Al-Saadi HA, Al-Rawi SM, Al-Khafaji ZM. Protective effects of beetroot (Beta vulgaris) on cimetidine-induced hepatotoxicity in rats. *J Pharm Sci Res*. 2018;10(5):1025-1030.
19. Singh R, Sharma S, Gupta R. Ameliorative potential of beetroot extract against cimetidine-induced oxidative stress and renal dysfunction in rats. *Phytomedicine*. 2019; 62:152989.
20. Kumar S, Yadav A, Singh S. Antioxidant and nephroprotective effects of beetroot juice in cimetidine-induced nephrotoxicity in rats. *J Food Biochem*. 2020;44(3):e13152.
21. Farhana A, Lappin TR. The role of oxidative stress in drug-induced nephrotoxicity. *J Clin Pharmacol*. 2017;57(3):325-334.
22. Sharma S, Kaur G, Singh R. Protective effect of beetroot extract on cimetidine-induced oxidative stress and nephrotoxicity in rats. *J Pharmacol Pharmacother*. 2022;13(1):15-22.

Print ISSN: 0189-9287 Online ISSN: 2992-345X