Pacific Journal of Medical and Health Sciences
ISSN: 2456-7450 | Volume 2, Issue 1, January to March 2026, pp - 37 - 49

PJMHS
PACIFIC JOURNAL OF MEDICAL AND HEALTH SCIENCES

Research Paper

Dose-Dependent Effects of Aidan Fruit *(Tetrapleura tetraptera)* on Aluminum Chloride (AlCl3)-Induced Kidney Toxicity in Adult Male Wistar Rats

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Received : 21 August 2025
Revised : 30 September 2025
Accepted : 11 October 2025

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ABSTRACT

***Background**:*

Aluminum chloride ($AlCl_3$) is widely recognized for its nephrotoxic potential, primarily due to its ability to induce oxidative stress and inflammation in renal tissues. The search for natural agents with protective properties has led to increased interest in Tetrapleura tetraptera (Aidan fruit), a plant known for its rich phenolic and antioxidant content.

***Aim**:*

The study aimed to evaluate the dose-dependent effects of Tetrapleura tetraptera (Aidan fruit) on kidney function in adult male Wistar rats exposed to aluminum chloride.

Methods:

Thirty-five rats were randomly assigned into five groups (n=7): Group 1 received distilled water (control), Group 2 was administered $AlCl_3$ (100 mg/kg), Group 3 received $AlCl_3$ + low-dose extract (250 mg/kg), Group 4 received $AlCl_3$ + high-dose extract (500 mg/kg), and Group 5 received $AlCl_3$ + donepezil (10 mg/kg).Toxicity were induced for 28 days and treatments lasted 14 days, after which animals were sacrificed following IACUC guidelines. The right of the kidney was homogenized in (5xW/V) of phosphate buffer solution, PH 7.4 for biochemical analysis and the left was fixed in 10% formalin for histology analysis.

Results:

Aluminum chloride administration induced marked alterations in renal biochemical indices and oxidative stress markers. One-way ANOVA revealed significant differences in serum sodium ($F = 18.18$, $p = 0.00014$), chloride ($F = 27.45$, $p = 0.0000226$), and creatinine levels ($F = 9.39$, $p = 0.0020$) among the experimental groups. In contrast, potassium ($F = 2.46$, $p = 0.113$) and blood urea nitrogen (BUN) ($F = 1.485$, $p = 0.278$) did not differ significantly between groups. Treatment with Tetrapleura tetraptera extract produced dose-dependent improvements in electrolyte balance and renal function, with the high-dose group showing marked restoration of chloride levels and preservation of renal histoarchitecture. Furthermore, oxidative stress analysis revealed significant differences in malondialdehyde (MDA) ($F = 18.645$, $p = 0.0001$) and superoxide dismutase (SOD) ($F = 9.206$, $p = 0.0025$) levels among the experimental groups, while reduced glutathione (GSH) levels showed no statistically significant difference ($F = 2.400$, $p = 0.1193$). Treatment with Tetrapleura tetraptera extract attenuated oxidative stress and improved antioxidant status in a dose-dependent manner. Histological examination revealed severe glomerular and tubular degeneration in the toxic group, while treated groups, particularly the high-dose extract group, demonstrated substantial recovery and preservation of renal tissue integrity.

Conclusion:

Aidan fruit preserved glomerular structure, reduced tubular necrosis, particularly at higher doses. The effectiveness of Tetraptera tetrapluera was comparable to that of donepezil, a known neuroprotective and antioxidative properties and may serve as a potential therapeutic agent in prevent or reversing aluminum-induced kidney toxicity.

KEYWORDS: *Tetrapleura tetraptera,* Aluminum chloride, Kidney toxicity, Wistar rats, Nephroprotection, Oxidative stress, Donepezil

BACKGROUND

The kidney is bean-shaped located in the lower back region and weighs approximately 120-170 grams in adults, responsible for filtering blood, removing waste, balancing fluids and electrolytes, regulating blood pressure, hormonal functions such as producing erythropoietin and converting vitamin D to its active form and contributing to red blood cell production[1]. The kidney consists of several anatomical parts, including the renal capsule, renal cortex, renal medulla, renal pelvis, and nephrons which receives blood through the renal arteries and filter approximately 120-150 liters of blood daily to produce urine in three main steps: glomerular filtration, tubular reabsorption, and tubular secretion[2]. Nephrotoxicity, or toxic damage to the kidneys, can arise from exposure to chemicals, heavy metals, and drugs, given their high perfusion rate and exposure to various endogenous and exogenous is a major cause of acute kidney injury globally[3].

Aluminum (Al), the third most abundant chemical element after silicon and oxygen, is thought to be the most prevalent metal in the Earth's crust[4]. Industrialization has further raised the levels of Al in the environment significantly[5]. Humans are exposed to Al from a variety of sources, such as food additives found in baking powder, self-rising flour, cake mixes and some processed cheeses and contaminated water[6]. Naturally occurring aluminum in soil and rock can leach into groundwater and surface water leading to elevated aluminum levels in drinking water, also aluminum-based coagulants such as aluminum sulfate are used in water treatment which overtime potentially pose health concerns[7]. Aluminum hydroxide is a common ingredient in antacids and other over-the counter medication[8] and cosmetics[9].

Occupational exposure to Al can also arise from involvement in the Al processing industry (Skalny *et al.,* 2018). Previous research showed that vaccinations may be a source of aluminum exposure since they contain aluminum adjuvants, which are presently not commonly used and lower the risk of exposure to aluminum from vaccines[10].

One of the mechanisms behind aluminum-induced kidney damage is oxidative stress. Aluminum increases the production of reactive oxygen species (ROS), which in turn causes lipid peroxidation, protein damage, DNA fragmentation, and ultimately cell death[11]. Research using rodent models has confirmed that exposure to $AlCl_3$ causes nephrotoxicity and is characterized by histopathological changes in kidney tissues, elevation of serum urea and creatinine levels, oxidative damage to renal cells and compromised renal functions[12].

In search for novel nephroprotective agents with safer treatment and cost-effective options, researchers are increasingly turning to natural products[13]. One plant of interest is ***Tetrapleura tetraptera***, commonly called Aidan fruit, commonly used in traditional African medicine[14]. It contains a variety of bioactive compounds, including polyphenols, flavonoids, tannins, and saponins known for their antioxidant, anti-inflammatory, and neuroprotective properties all of which have demonstrated protective effects against oxidative stress and inflammation in preclinical studies[14,15].

Additionally, polyphenolic compounds, in particular, have been shown to scavenge free radicals, chelate metal ions, and upregulate endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT)[15]. These mechanisms make polyphenol-rich plant extracts promising agents for the mitigation of nephrotoxic damage[16].

Aidan fruit, is renowned for its significant nutritional and therapeutic value, making it a prominent candidate in managing toxin-induced organ damage. The fruit contains a variety of essential nutrients and bioactive compounds that contribute to its medicinal properties. It contains a rich array of macronutrients and micronutrients essential for physiological functioning[14].

Moreover, beyond its nutritional content, T. tetraptera is exceptionally rich in phytochemicals, including flavonoids, saponins, tannins, alkaloids, and particularly phenolic compounds. According to Ajayi *et al*.[16], these phytochemicals contribute to the plant's strong antioxidant and anti-inflammatory potential, further adding to its therapeutic arsenal. Hence the need to study the scavenge free radicals' potentials of Aidan fruit in aluminum chloride mediated kidney damage in adult male Wistar rats.

MATERIALS AND METHODS

Experimental Plant

Aidan fruit (*Tetrapleura tetraptera*): 1000g of Aidan fruit was obtained from mandate daily market Ilorin, Kwara State where it was powdered and the seed were removed and was taken to the Industrial Chemistry, Faculty of Physical Science, University of Ilorin, and Kwara State where it was extracted.

Experimental Chemical

Aluminum Chloride ($AlCl_3$): The Aluminum chloride ($AlCl_3$) produced by Span Chemie Company, India and was gotten from Dennis and Dennis Store Ilorin, Kwara State. Donepezil was bought from One-Step Pharmacy Ilorin, Kwara State.

Other Experimental Materials

Distilled water was obtained from the Department of Biochemistry, Faculty of Natural and Applied Science, AL-Hikmah University Ilorin, Kwara State. Dissecting kits, Syringes, Gloves and Sample Bottles: The syringes, gloves, sample bottles were bought from One-Step Pharmacy Ilorin, Kwara State.

Experimental Animals

This study utilized 35 male Wister rats, sourced from Al-Hikmah University's Department of Human Anatomy. The rats were kept in a controlled environment with a 12-hour day-night cycle and standard temperature, and fed purified water and a standard pellet diet. The rats underwent a two-week adaptation period before the experiment commenced.

Experimental Protocol

Group A, the Control group consisting of seven (7) Wister rats, where administered distilled water only for 28 days. Group B which was the Toxic group consisting of seven (7) Wister rats, were given $AlCl_3$ only for 28 days. Group C which was the Treated group consisting of seven (7) Wister rats, were administered $AlCl_3$ for 28 days and low dose of PT-T for 14 days. Group D which was the treated group consisting of seven (7) Wister rats, were administered $AlCl_3$ for 28 days and high dose of PT-T for 14 days. Group E which was the treated group consisting of seven (7) Wister rats, were administered $AlCl_3$ for 28 days and donepezil for 14 days. All administration was done using the oral cannula. The rats acclimatized for 14 days prior to administration and were maintained under standard atmosphere under dark/day circle. The rats were fed with standard rats feed and water *Adlibitum.* All administration were carried out through oral canula. After the last day the animal were fasted overnight and their final body weight were taken. The rats were **euthanasia** through cervical dislocation and midline incision was done to harvest the kidneys. The right of the kidney was homogenized in (5xW/V) of phosphate buffer solution, PH 7.4 for biochemical analysis and the left was fixed in 10% formalin for histology analysis.

Histopathology Examination

At the conclusion of the study (Day 29 and Day 43), the rats were humanely euthanized using cervical dislocation. The kidney was harvested and fixed in 10% formalin for 48 hours, after fixation, the kidney tissues were embedded in paraffin and sectioned into thin slices (5 μm). These sections were then stained with Hematoxylin and Eosin (H&E) to examine any

histological changes, including signs of tubular epithelial cell degeneration, glomerular atrophy, vascular congestion, and interstitial inflammation. Microscopic analysis was performed to identify and structural changes.

Biochemical Analysis

Renal Function Tests

Urea was measured using a Randox Urea assay kit while using the enzymatic Urease-glutamate dehydrogenase method[17]. Creatinine was measured using the Randox creatinine kit for Jaffe's colorimetric method, in which creatinine reacts with alkaline picrate to form a colored complex with maximum absorbance at 520nm[18]. Electrolytes were measured using the Ion-selective electrode (ISE) method using an ISE-based electrolyte analyzer to display the concentration of sodium, potassium and chloride, the electrolyte imbalance was used to infer tubular dysfunction or damage caused by aluminum toxicity or protective effects from treatments. Disruption in their levels often reflects underlying renal tubular damage[19].

Oxidative Stress Markers

Malondialdehyde (MDA) were measured using a lipid peroxidation assay kit specific to rats, in accordance with the manufacturer's instructions. An increase in MDA concentration within the kidney suggests elevated oxidative injury, which may disrupt cellular integrity[20]. The activity of superoxide dismutase (SOD) in kidney tissue was assessed using a rat-specific colorimetric assay kit, based on the manufacturer's protocol**.** Alterations in SOD activity are often indicative of oxidative stress levels and may reflect the kidney response to toxic insults or therapeutic interventions[21]. **The concentration of reduced glutathione (GSH) in kidney tissue was measured using a rat-specific colorimetric assay kit, in accordance with the manufacturer's instructions.** GSH is a crucial intracellular antioxidant that defends nephrons against oxidative damage by neutralizing free radicals and detoxifying harmful compounds[22].

Ethical Approval

In accordance with the Institutional Animal Care and Use Committee (IACUC), the Faculty of Basic Medical Science, College of Health Science, Ilorin review committee at Al-Hikmah University approved this research project on the Faculty of Basic Medical Science's recommendation.

Euthanasia

At the conclusion of the experimental period, all animals were humanely sacrificed following the determination of their final body weights. Euthanasia was carried out through cervical dislocation, adhering to established ethical standards for the care and use of laboratory animals. After euthanasia, a midline incision was made from the thoracic cavity to the abdominal cavity to expose the kidneys. Blood samples were collected directly from the heart using a sterile 2 ml syringe and transferred into ethylene diamine-tetra acetic acid (EDTA) bottles to prevent coagulation. The blood samples were immediately centrifuged and stored in an ice-filled container for further biochemical analyses. The kidneys were then carefully excised to preserve tissue morphology. Each kidney was rinsed in normal saline to remove excess blood and then placed in labeled sample containers filled with 10% buffered formaldehyde for fixation. The fixed tissues were subsequently processed, embedded in paraffin wax, and sectioned at 5 µm thickness using a rotary microtome. The sections were mounted on glass slides for histological and immunohistochemically evaluation. Following organ collection, the carcasses of the Wister rats were disposed through burial in an approved sanitary site, in line with institutional ethical guidelines.

Statistical Analysis

Data were expressed as mean ± standard error of the mean (SEM). Statistical comparisons between groups were performed using one-way analysis of variance (ANOVA) followed by Turkey's post-hoc test to determine significant differences. A p-value of <0.05 was considered statically significant. All statistically analysis was performed using Graph-Pad Prism 8 software.

RESULTS

Physical Observation

Physical observations were carried out daily throughout the experiment to monitor the health status, behavioral changes, and overall physical response of the rats in each group.

Group 1 (Control – Distilled Water)

Rats in this group remained physically stable and active throughout the 28-Day period. They showed no signs of abnormal behavior, bleeding, or death. Feeding and grooming remained normal.

Group 2 (Toxic – Aluminum Chloride)

From day 2, rats in this group began showing signs of distress such as excessive calmness and hiccups. By day 4, nasal bleeding was observed. Mortality began by day 15, with two deaths occurring. Aggressiveness, reduced feed intake, and signs of meningitis were also noted. The group was sacrificed on Day 28.

Group 3 (Aluminum Chloride + Low Dose PPT)

Initial signs of distress (mucous secretion, spinning, walking sideways) were observed during the aluminum chloride phase. After the introduction of Aidan fruit extract on Day 29, gradual behavioral improvement and signs of healing were recorded.

However, some rats died on Day 32, 33, and 35. By Day 41, the remaining rats were visibly active with reduced signs of complication.

Group 4 (Aluminum Chloride + High Dose PPT)

This group exhibited significant distress, including nose bleeding and feed refusal, starting from the aluminum chloride phase. One death occurred early (Day 5), followed by progressive improvement after high-dose Aidan extract administration. However, one death was also recorded on Day 21. Signs of recovery (reduced swelling, improved feeding, and activity) became prominent by Day 30.

Group 5 (Aluminum Chloride + Donepezil)

Early signs included mucous secretion, limb paralysis, and aggressiveness. Mortality two occurred on Day 5 and 6. After donepezil administration began, improvement in motor function and healing of visible injuries (e.g., swollen limb, cleft palate) was recorded. By Day 30, healing was evident, and rats remained active up to Day 41.

Body Weight of the Rats

In this study, there was no significant difference in the weight changes across the groups. However, an increase was observed in the mean final body weight of the rats across the groups when compared with the initials [Figure 1].

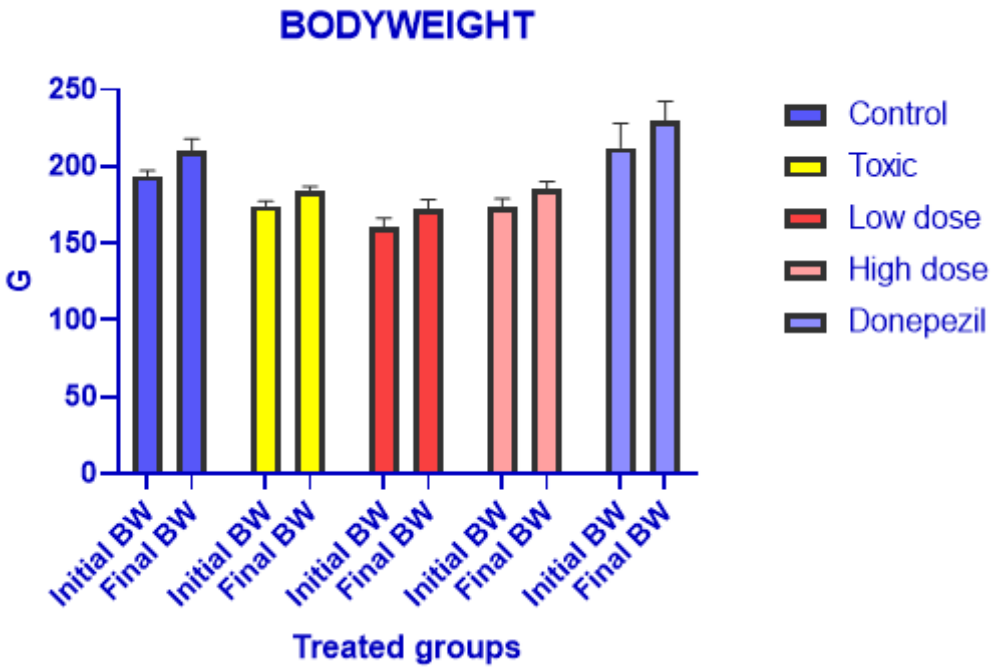

Figure 1: Initial and Final Body Weights of Rats in the Experimental Groups

Data are presented as mean ± SEM. Groups comprised control (distilled water, 100 mg/kg BW), toxic (Aluminum chloride 100 mg/kg BW), low-dose treatment (Aluminum chloride 100 mg/kg BW + Aidan 250 mg/kg BW), high-dose treatment (Aluminum chloride 100 mg/kg BW + Aidan 500 mg/kg BW), and donepezil (Donepezil 10 mg/kg BW + $AlCl_3$ 100 mg/kg BW). No statistically significant differences were observed among the experimental groups ($p > 0.05$)

Biochemical Analysis

Kidney Function Test

Serum electrolyte concentrations and renal function biomarkers were evaluated following aluminum chloride exposure and subsequent treatment with *Tetrapleura tetraptera* extract or donepezil. Analysis of serum sodium levels demonstrated a statistically significant difference among the experimental groups (F (4,10) =18.18, p=0.00014). The high-dose *Tetrapleura tetraptera* group exhibited the highest sodium concentration (186.61 ± 1.13 mmol/L), whereas the control and donepezil groups showed comparatively lower values (111.07 ± 10.72 mmol/L and 112.14 ± 0.41 mmol/L, respectively). These findings suggest significant modulation of sodium homeostasis following treatment. Potassium concentrations did not differ significantly among the groups (F (4,10) =2.46, p=0.113), although the toxic group recorded the highest potassium level (7.85 ± 0.11 mmol/L), while the donepezil-treated group showed the lowest value (5.00 ± 0.03 mmol/L). Chloride levels differed significantly across groups (F (4,10) =27.45, p=0.0000226). The high-dose *Tetrapleura tetraptera* group exhibited markedly elevated chloride concentrations (152.60 ± 0.38 mmol/L), whereas the toxic group recorded the lowest value (36.66 ± 4.00 mmol/L). Post-hoc analysis revealed significant differences between the high-dose treatment group and the other experimental groups, indicating a strong treatment effect on chloride regulation. Blood urea nitrogen (BUN) concentrations showed no statistically significant difference among the groups (F (4,10) =1.485, p=0.278), despite slight numerical increases in the treatment groups. Serum creatinine levels differed significantly among the experimental groups (F (4,10) =9.39, p=0.0020). Elevated creatinine concentrations observed in the aluminum chloride-treated rats indicated impaired renal function, whereas treatment with *Tetrapleura tetraptera* extract and donepezil modulated creatinine levels, reflecting varying degrees of renal protection and recovery.

Oxidative Stress Markers

Renal oxidative stress biomarkers were evaluated by measuring malondialdehyde (MDA), superoxide dismutase (SOD), and reduced glutathione (GSH) levels. MDA levels differed significantly among the experimental groups (F (4,10) = 18.645, p = 0.0001). The high-dose *Tetrapleura tetraptera* group exhibited the highest MDA level (5.10 ± 0.14), whereas the toxic group recorded the lowest value (2.43 ± 0.06). Significant differences among treatment groups indicate that administration of *Tetrapleura tetraptera* extract markedly influenced lipid peroxidation status. SOD activity also differed significantly among groups (F (4,10) = 9.206, p = 0.0025).

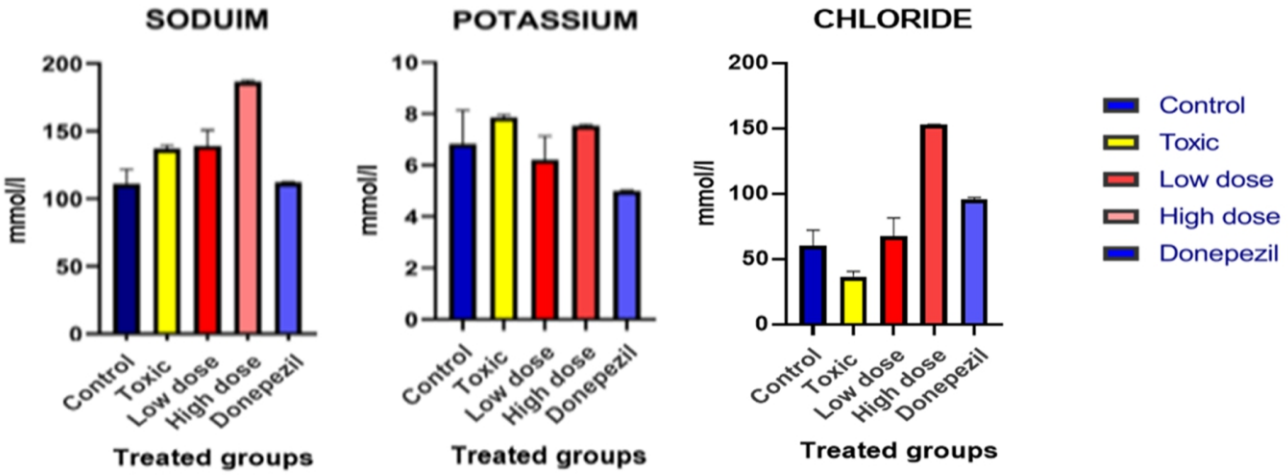

Figure 2: Effects of *Tetrapleura tetraptera* Extract and Donepezil on Serum Electrolyte Concentrations in Aluminum chloride-induced Nephrotoxicity

Values are expressed as mean ± SEM (n = 7 per group). Groups comprised control (distilled water, 100 mg/kg BW), toxic (Aluminum chloride 100 mg/kg BW), low-dose treatment (Aluminum chloride 100 mg/kg BW + Aidan 250 mg/kg BW), high-dose treatment (Aluminum chloride 100 mg/kg BW + Aidan 500 mg/kg BW), and donepezil (Donepezil 10 mg/kg BW + $AlCl_3$ 100 mg/kg BW). One-way ANOVA demonstrated a general significant difference in serum sodium (F = 18.18, p = 0.00014) and chloride (F = 27.45, p = 0.0000226) concentrations among groups, whereas serum potassium levels did not differ significantly (F = 2.46, p = 0.113)

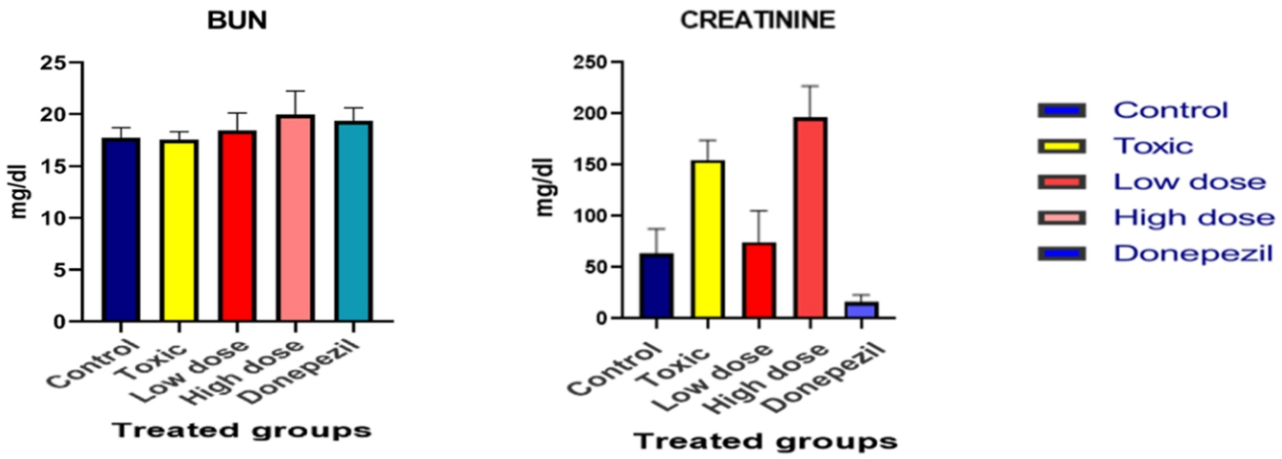

Figure 3: Effects of Aluminum chloride and Aidan Extract Treatment on Renal Function Biomarkers

Values are presented as mean ± SEM for serum blood urea nitrogen (BUN) and creatinine concentrations in the control group (distilled water), toxic group (100 mg/kg BW $AlCl_3$), low-dose Aidan extract group (100 mg/kg BW $AlCl_3$ + 250 mg/kg BW Aidan extract), high-dose Aidan extract group (100 mg/kg BW $AlCl_3$ + 500 mg/kg BW Aidan extract), and donepezil-treated group (100 mg/kg BW $AlCl_3$ + 10 mg/kg BW donepezil). One-way ANOVA revealed a general significant difference in serum creatinine levels (F = 9.39, p = 0.0020), while blood urea nitrogen (BUN) levels did not differ significantly among groups (F = 1.485, p = 0.278)

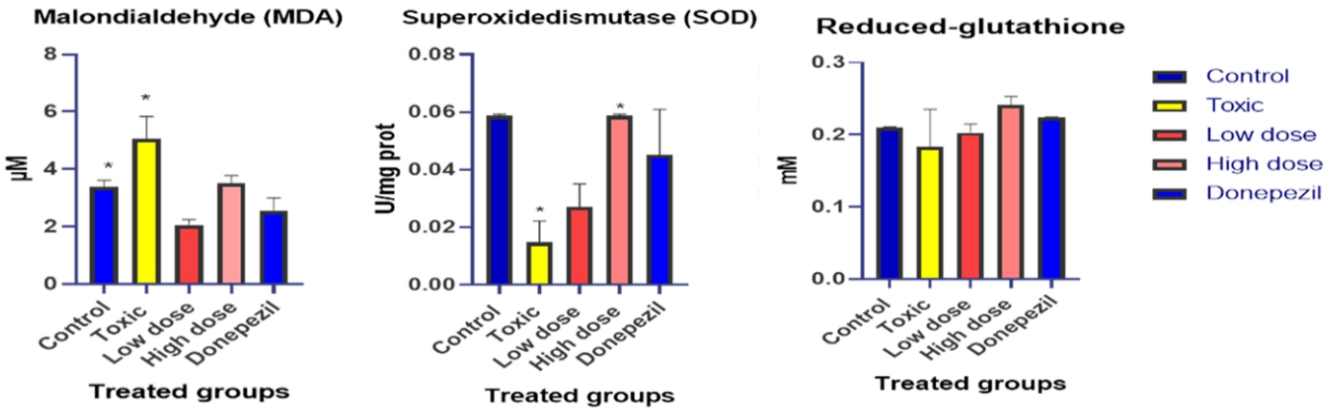

Figure 4: Effects of Treatment on Oxidative Stress and Antioxidant Biomarkers in Experimental Groups

*Bar charts showing the levels of malondialdehyde (MDA), superoxide dismutase (SOD), and reduced glutathione (GSH) across the control, toxic, low-dose, high-dose, and donepezil-treated groups. the control group (distilled water), toxic group (100 mg/kg BW $AlCl_3$), low-dose Aidan extract group (100 mg/kg BW $AlCl_3$ + 250 mg/kg BW Aidan extract), high-dose Aidan extract group (100 mg/kg BW $AlCl_3$ + 500 mg/kg BW Aidan extract), and donepezil-treated group (100 mg/kg BW $AlCl_3$ + 10 mg/kg BW donepezil). Data are presented as mean ± SEM. One-way ANOVA revealed significant differences in MDA (F = 18.645, p = 0.0001) and SOD (F = 9.206, p = 0.0025) among the experimental groups, whereas GSH levels did not differ significantly (F = 2.400, p = 0.1193). Statistical significance was accepted at *p < 0.05*

Treatment with *Tetrapleura tetraptera* extract and donepezil modulated antioxidant enzyme activity relative to the toxic group, with the high-dose treatment group demonstrating the greatest improvement in antioxidant defense. In contrast, GSH levels showed no statistically significant difference among groups (F (4,10) = 2.400, p = 0.1193), although numerical variations were observed across treatments. These findings suggest that while *Tetrapleura tetraptera* significantly influenced lipid peroxidation and SOD activity, its effect on GSH concentration was not statistically significant under the conditions of the present study.

Histological Investigations

The photomicrographs of the kidney tissue obtained from the control group shows a Histomorphological architecture including normal renal tubules, glomerulus, bowman's capsule, glomerulus, urinary pool, vascular pool; H&E stain 100x magnification**,** [as shown in Plate 1]. However, the toxic group photomicrograph of the histopathology architecture of the kidney tissues sections [showing in Plate 2] the disrupted renal tubules, spaced bowman's capsule, atrophy of the glomerulus, disrupted urinary pool, detached vascular pool; H&E stain 100x magnification**.** Furthermore, the photomicrograph of the histopathology architecture of the kidney tissues in the low dose group (100mg/kgBW $AlCl_3$ + 250mg/kgBW PT-T) [showing in Plate 3]. Tissue sections show partial repair renal tubules, reduced spaced bowman's capsule, mild atrophy of the glomerulus, repaired urinary pool, repaired vascular pool; H&E stain 100x magnification. Photomicrograph of the histopathology architecture of the kidney tissues in the high dose group (100mg/kgBW $AlCl_3$ + 500mg/kgBW PT-T) [shown in Plate 4]. Tissue sections showing repaired renal tubules, reduced spaced Bowman's capsule, minimal atrophy of the glomerulus, repaired urinary pool, repaired vascular pool; H&E stain 100x magnification. Additionally, photomicrograph of the histopathology architecture of the kidney tissues in the Donepezil group (100mg/kgBW $AlCl_3$ + 10mg/kgBW Donepezil) [showing in Plate 5]. Tissue sections showing repaired renal tubules, reduced spaced Bowman's capsule, normal glomerulus, repaired urinary pool, repaired vascular pool; H&E stain 100x magnification.

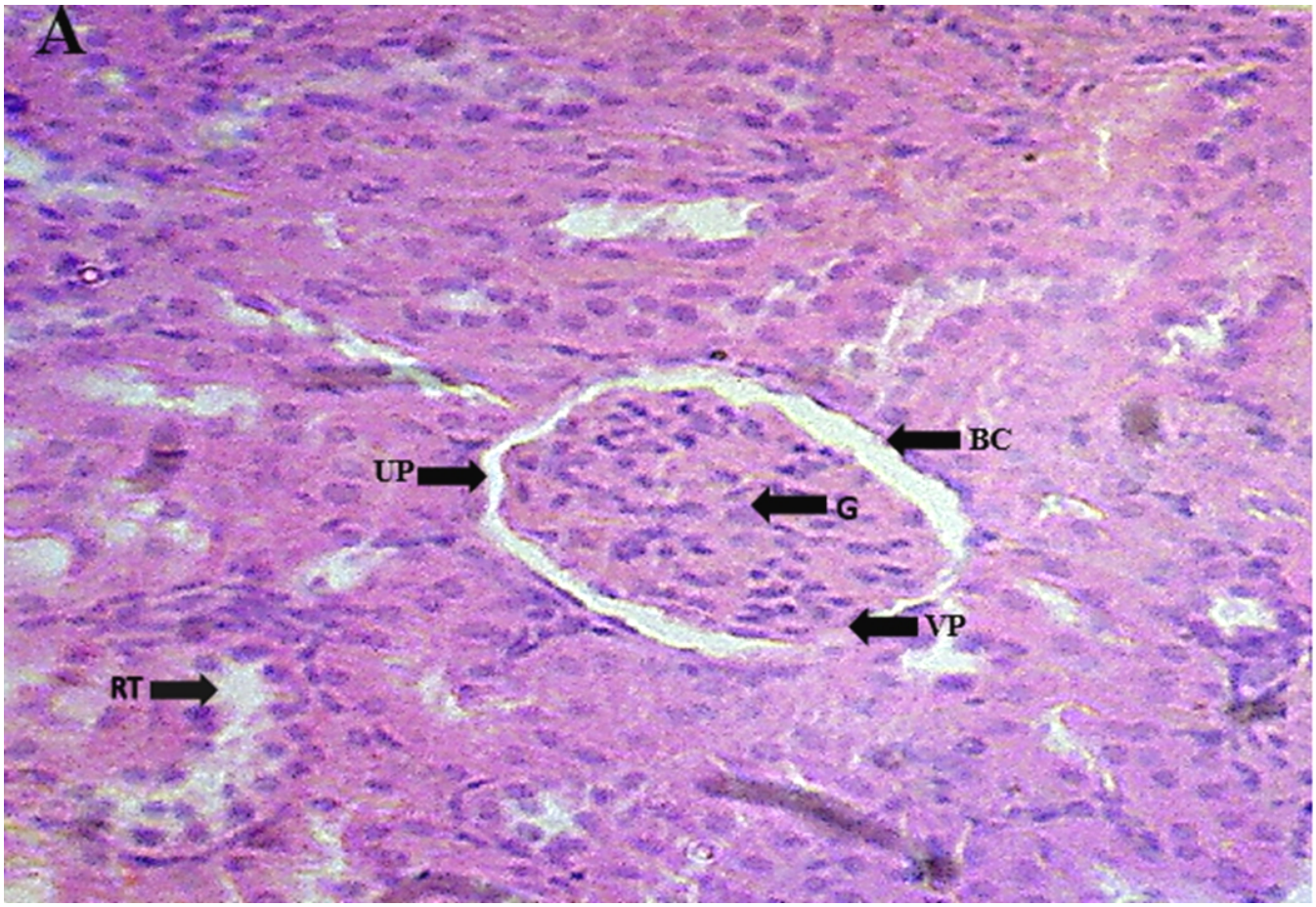

Plate 1: Photomicrograph of the Histomorphological Architecture of the Kidney Tissues in the Control Group. Tissue Section Showing Normal Morphology of Renal Tubules (RT), Bowman's Capsule (BC), Glomerulus (G), Urinary Pool (UP), Vascular Pool (VP); H&E Stain 100x Magnification

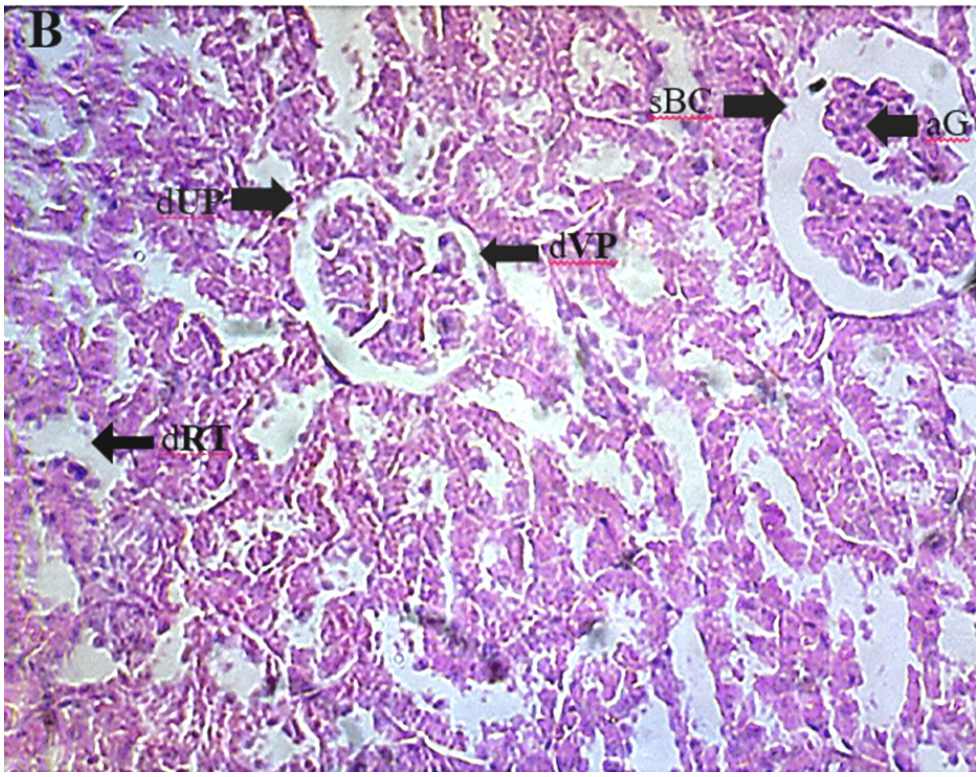

Plate 2: Photomicrograph of the Histopathology Architecture of the Kidney Tissues in the Toxic Group. Tissue Sections Showing Disrupted Renal Tubules (dRT), spaced Bowman's Capsule (sBC), Atrophy of the Glomerulus (aG), Disrupted Urinary Pool (dUP), Detached Vascular Pool (dVP); H&E Stain 100x Magnification

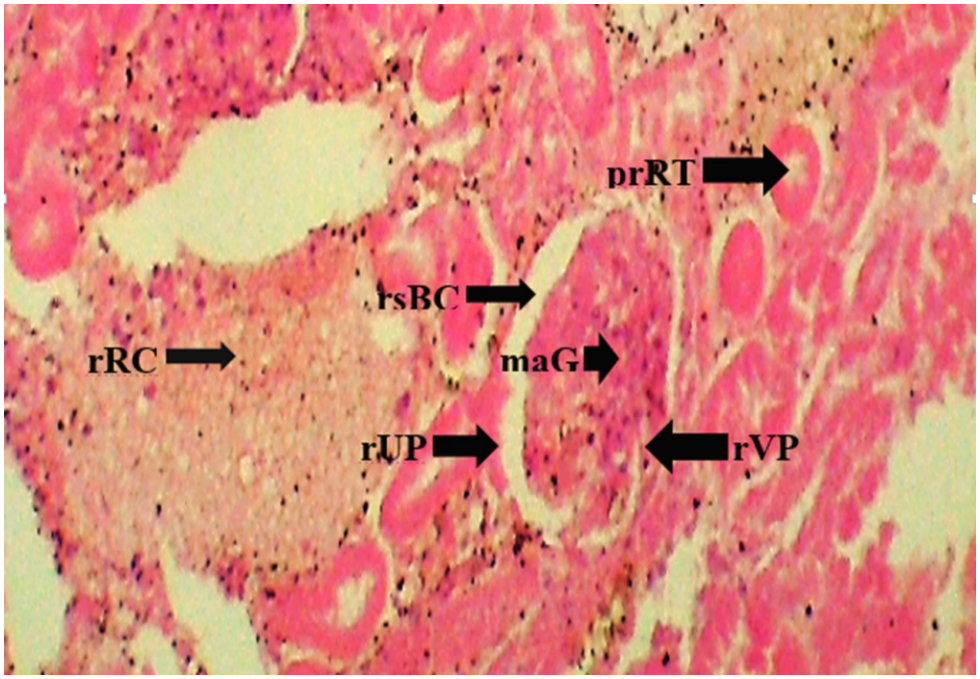

Plate 3: Photomicrograph of the Histopathology Architecture of the Kidney Tissues in the Low Dose Group (100mg/kgBW $AlCl_3$ + 250mg/kgBW PT-T). Tissue Sections Showing Partial Repair Renal Tubules (prRT), Reduced Spaced Bowman's Capsule (rsBC), Mild Atrophy of the Glomerulus (maG), Repaired Urinary Pool (rUP), Repaired Vascular Pool (rVP); H&E Stain 100x Magnification

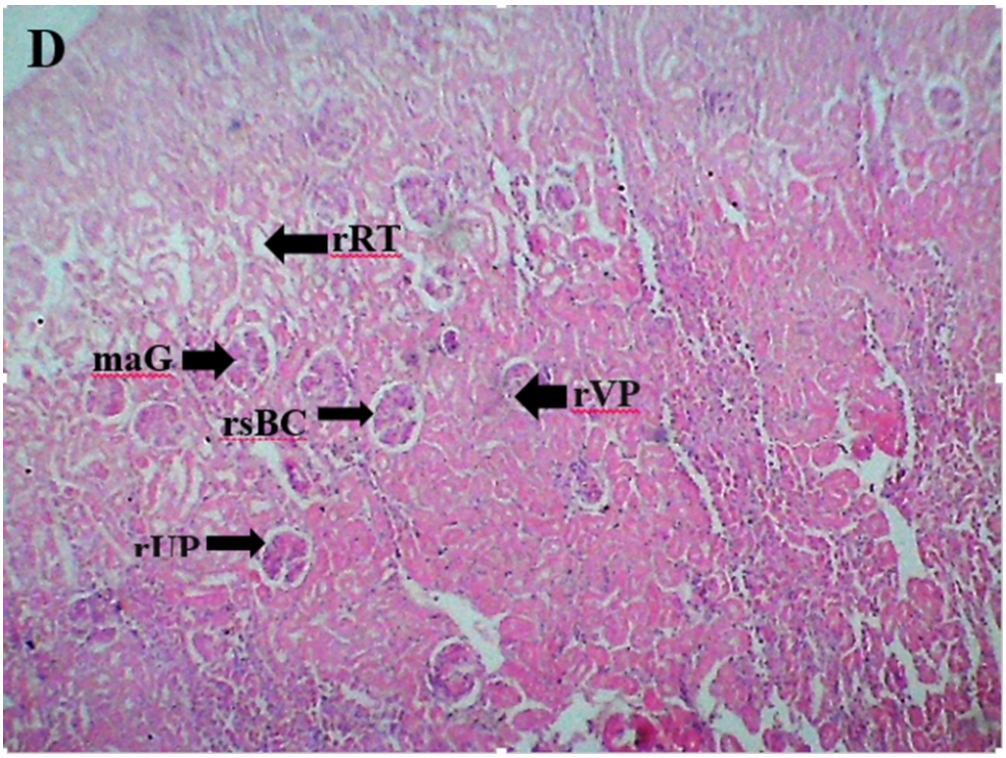

Plate 4: Photomicrograph of the Histopathology Architecture of the Kidney Tissues in the High Dose Group (100mg/kgBW $AlCl_3$ + 500mg/kgBW PT-T). Tissue Sections Showing Repaired Renal Tubules (rRT), Reduced Spaced Bowman's Capsule (rsBC), Minimal Atrophy of the Glomerulus (maG), Repaired Urinary Pool (rUP), Repaired Vascular Pool (rVP); H&E Stain 100x Magnification

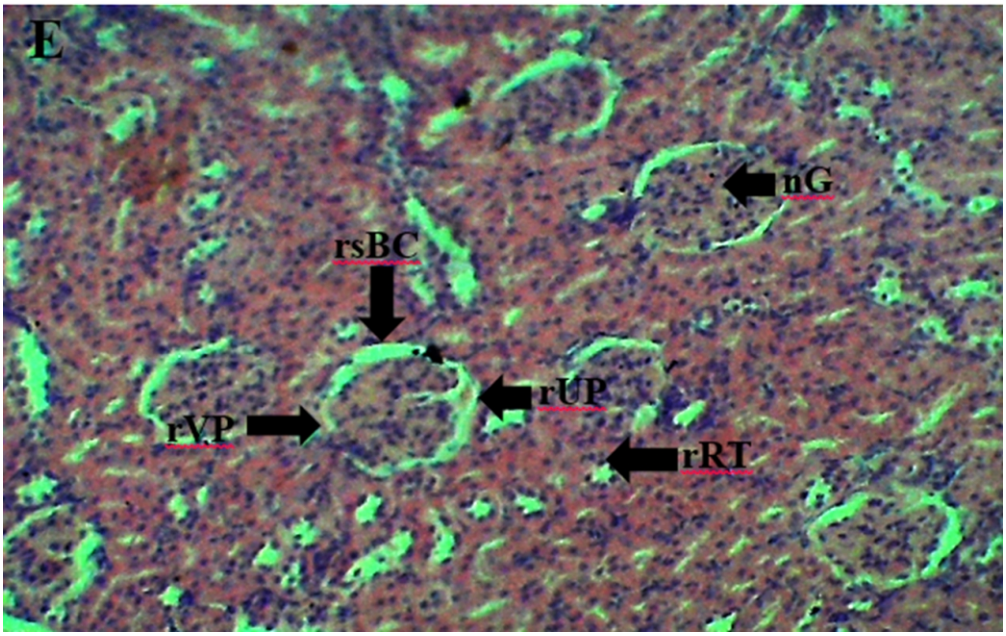

Plate 5: Photomicrograph of the Histopathology Architecture of the Kidney Tissues in the Donepezil Group (100mg/kgBW $AlCl_3$ + 10mg/kgBW Donepezil). Tissue Sections Showing Repaired Renal Tubules (rRT), Reduced Spaced Bowman's Capsule (rsBC), Normal Glomerulus (nG), Repaired Urinary Pool (rUP), Repaired Vascular Pool (rVP); H&E Stain 100x Magnification

DISCUSSION

Environmental toxicant exposure to aluminum remains a significant public health concern due to its accumulation in the kidneys. The toxic effect of aluminum on the kidneys leads to oxidative stress, functional impairment, and structural damage, contributing to the development of chronic kidney diseases. The observations of the rats' physical behavior added further insight into the effects of each treatment, rats in the aluminum-only group showed clear signs of sickness, including fatigue, nosebleeds, and reduced movement symptoms similar to those described by Igbekwe *et al.*[23], in aluminum toxicity studies. In contrast, rats treated with Aidan extract, especially at higher doses, appeared healthier and more active, with better appetite and general behavior. Rats treated with donepezil also showed improvements, such as restored energy levels and fewer signs of physical distress[24].

The biochemical evaluation of blood serum urea (BUN), creatinine, and antioxidant enzymes, particularly superoxide dismutase (SOD), revealed critical insights into renal function and oxidative stress mitigation across all treated groups. In the $AlCl_3$-exposed rats (toxic/ group two), significantly elevated levels of urea and creatinine confirmed impaired glomerular filtration, suggesting nephrotoxicity. These findings align with previous studies indicating that aluminum chloride disrupts renal tubular and glomerular integrity, thereby compromising excretory efficiency[5,8].

The rise in BUN and creatinine concentrations in the $AlCl_3$-exposed group suggests reduced glomerular filtration rate (GFR) and compromised excretory function. This aligns with reports by Ezejiofor *et al*.[20] and Kumar and Gill[12], who identified aluminum toxicity as a major disruptor in accumulation of nitrogenous wastes.

Interestingly, treatment with *tetrapluera tetraptera* led to significant improvements in these parameters. Rats administered low and high dose of the extract showed progressive normalization of BUN and creatinine levels, indicative of nephroprotection. The high-dose group demonstrated biochemical values close to those of the control group, suggesting superior efficacy. These findings support prior research showing that *T. tetraptera* possesses strong antioxidant and anti-inflammatory compounds such as polyphenols, tannins, and flavonoids, which mitigate tissue damage by scavenging ROS and restoring membrane integrity[16,25].

In terms of antioxidant activity, superoxide dismutase (SOD) levels were significantly depleted in the $AlCl_3$-only group, constituent with previous studies linking aluminum toxicity to oxidative stress-mediated enzyme depletion[12]. Treatment with Aidan fruit significantly restored SOD levels in a dose-dependent manner, likely due to enhanced free radical scavenging. Notably, high-dose Aidan fruit restored SOD activity close to baseline, further supporting its antioxidative therapeutic potential.

Another important antioxidant in the body is glutathione (GSH), which helps to maintain the balance between oxidants and antioxidants and also plays a key role in detoxifying harmful substances. In this study, GSH levels slightly decreased in the rats treated with aluminum chloride, indicating early signs of oxidative damage. This is consistent with findings from [26], who reported that aluminum exposure can decrease GSH reserves. Both low and high doses of Aidan extract caused slight increases in GSH, though the difference was not statistically significant. This may be due to a short treatment period or its rate of absorption. This finding agrees with the work of Lawal *et al*.[27] who found greater improvements in GSH activity using plant antioxidants. Donepezil also caused a small increase in GSH, supporting its role in enhancing the body's antioxidant capacity.

Histological examination further reinforced the biochemical observations, H&E-stained sections of the kidney from $AlCl_3$-only rats exhibited severe glomerular atrophy, tubular degeneration, and obliteration of urinary spaces. These structural disruptions corroborated biochemical indicators of renal dysfunction [28,29]. In contrast, kidneys of rats treated with high-doses of Aidan fruit showed largely preserved glomeruli and minimal tubular necrosis. The low-dose group showed partial architectural restoration, with reduced vacuolization and mild interstitial inflammation. These observations suggest a dose-dependent restoration of renal architecture due to *T. tetraptera's* phytochemicals, which may stabilize lysosomal membranes and inhibit lipid peroxidation, as supported by Rahman *et al*.[30]. The restoration seen in the high-dose group suggests that the plant extract (Aidan fruit) may exert a curative rather than merely preventive effect in the context of $AlCl_3$-induced renal injury.

Moreover, the group treated with donepezil; a well-known acetylcholinesterase inhibitor with anti-inflammatory and antioxidant properties, demonstrated comparable histological and biochemical outcomes to the high-dose *T. tetraptera* group. This aligns with findings by Lee *et al*.[31] who indicated cholinergic neuroprotection with reduced systemic oxidative stress and improve renal tissue perfusion. This trend reinforces the theory that the nephroprotective action of *T. terapluera* is strongly rooted in its antioxidant potential[32,33].

In conclusion, Aluminum chloride exposure induced marked renal dysfunction, evidenced by elevated levels of serum urea (BUN) and creatinine, decreased antioxidant enzyme activity (SOD), and severe histological alterations including glomerular atrophy and tubular necrosis.

However, treatment with *T. tetraptera* extract mitigated these effects in a concentration-dependent manner. The low-dose group showed partial improvements in biochemical parameters and kidney structure, while the high-dose group achieved near-complete restoration of renal function and histoarchitecture.

ACKNOWLEDGMENT

Special acknowledgment is extended to Co-author Aisha Abdulrauf for her critical assistance during the final review phase of this manuscript. Her timely intervention to rectify technical anomalies in the visual data and standardise the citations allowed this research to proceed to publication without delay. We commend her academic rigor and collaborative professionalism. - Editor

CONFLICT OF INTEREST: None

FINANCIAL SUPPORT: None

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