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Preliminary Study of Nephroprotective Potentials of Ethanolic Leaf Extract of *Euphorbia Kamerunica* Against Aluminum Chloride-Induced Nephrotoxicity in Wistar Rats

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ABSTRACT

Aluminium chloride ($AlCl_3$) is a widely used industrial reagent with well-documented nephrotoxic properties, capable of inducing significant oxidative stress, inflammation, and structural renal damage. This study evaluated the nephroprotective potential of the ethanolic leaf extract of *Euphorbia kamerunica* (EEEUK) in a Wistar rat model of $AlCl_3$-induced kidney injury, with emphasis on histoarchitectural and biochemical outcomes. Forty-two adult male Wistar rats (120–180 g) were randomized into six groups (n = 7): Control, $AlCl_3$ (200 mg/kg), EEEUK only (100 mg/kg), $AlCl_3$ + EEEUK (100 mg/kg), $AlCl_3$ + EEEUK (200 mg/kg), and $AlCl_3$ + donepezil (5 mg/kg) for 28 days (Oral administration of $AlCl_3$ for 14 days followed by oral administration of extract at varying doses for 14 days). At the end of the experiment, renal histomorphology, biochemical parameters, oxidative stress markers, and inflammatory indices were assessed. Phytochemical screening revealed abundant terpenoids and steroids, conferring significant antioxidant potency. Data obtained were analysed using statistical software (GraphPad Prism, 9.0). $AlCl_3$ administration induced severe renal pathology, including glomerular hypertrophy, tubular necrosis, vascular congestion, elevated serum creatinine, and heightened oxidative stress markers. EEEUK treatment dose-dependently reduced myeloperoxidase activity, superoxide anion formation, and peroxynitrite/hydroxyl radical generation, while restoring renal architecture and normalizing biochemical indices, with the 200 mg/kg dose demonstrating the most significant protective effect. EEEUK conferred significant nephroprotection against $AlCl_3$-induced renal toxicity through antioxidant, anti-inflammatory, and histomorphological preservation mechanisms, supporting its potential application in mitigating heavy-metal-related renal injury and warranting further investigation for therapeutic development.

Keywords: Aluminum chloride, *Euphorbia kamerunica*, nephrotoxicity, nephroprotection, oxidative stress

INTRODUCTION

Nephrotoxicity embodies a substantial clinical concern, delineated by the propensity of specific substances to inflict renal tissue injury and compromise normative kidney function [1]. Organs that are especially susceptible to toxic insult because of their increased metabolic rate and concentrating properties include the kidneys, which are indispensable organs responsible for filtration, excretion, maintenance of electrolyte balance, and regulation of blood pressure [2].

Aluminum (Al), which is the third most common constituent in the crust of the earth, has become a major environmental and occupational health problem as it can be explained by the fact that it is extensively utilized in industry and that human beings are most likely to come into contact with it [3] as it is commonly used in a variety of industrial reactions including catalysis, water purification, and production [4]. Although useful, aluminium chloride poses significant health impacts, especially on the renal system, through mechanisms including oxidative stress, inflammatory pathways, and cellular damage [5]. Nephrotoxic effects of aluminium substances have been well documented both in experimental and clinical studies. The build-up of aluminium in the tissues of the kidney can trigger tubular cell death, necrosis of glomeruli, and worsening of renal function via the generation of reactive oxygen species (ROS) and disruptions in cellular homeostasis [6]. The vulnerability of the kidney to the effects of aluminium toxicity can be explained by the fact that the latter is involved not only in

aluminium excretion but also by the fact that the said metal tends to concentrate in the renal tissues [7].

Modern treatment options in nephrotoxicity induced by heavy metals mainly rely on chelation therapy combined with supportive treatment, which has a poor potential and often leads to detrimental side effects [8]. This has led to a growing interest in the search for natural compounds that possess nephroprotective properties, especially those compounds that can be obtained from medicinal plants that have undergone proven safety and antioxidant activity [9].

Euphorbiaceae-type *Euphorbes*, such as *Euphorbia kamerunica* (commonly called cactus plant), are widespread succulent plants that occur throughout tropical and subtropical Africa [10]. Traditional medicinal systems have recognized the potential of different Euphorbia species in the treatment of a range of disorders, including kidney diseases, inflammatory diseases, and oxidative stress-related diseases [11]. The plant contains a myriad of phytochemical products, which include diterpenoids, flavonoids, alkaloids, and phenolic compounds, all of which play a part in the therapeutic properties of the plant [12]. Recent phytochemical studies have revealed that *Euphoria kamerunica* possesses high antioxidant, anti-inflammatory, and cytoprotective properties [13]. Its bioactive compounds, more specifically terpenoids and steroids, have shown the ability to counteract free radicals and tame inflammatory signaling, as well as protect cellular bodies against oxidative injury [14]. These properties highlight the possible therapeutic value of the plant in preventing and treating nephrotoxicity caused by heavy metals and other toxic agents.

Despite the documented biological activities of *Euphorbia kamerunica*, including antioxidant and anti-inflammatory properties, its nephroprotective potential against aluminium chloride-induced renal toxicity has not been investigated previously. The current study aimed to evaluate the nephroprotective properties of *Euphorbia kamerunica* ethanolic extract on the $AlCl_3$-induced nephrotoxicity in Wistar rats with special focus on histomorphological changes, renal functional biochemical parameters, and variables of oxidative stress. Explaining the protective response mechanisms that exist in this medicinal plant can help add to the arsenal of knowledge on the design of innovative approaches to reverse renal injury caused by heavy metals.

MATERIALS AND METHODS

Plant material and extract preparation

Fresh leaves of *Euphorbia kamerunica* were obtained at the Okun-Owa village, Ijebu, Ogun State, Nigeria. Identification and authentication of the given specimen were done at the Ife Herbarium, Department of Botany, Obafemi Awolowo University, Ile-Ife, Nigeria, and a voucher specimen was deposited. The obtained leaves were washed and dried at ambient temperature and finally crushed in a mechanical blender (Kenwood BL237, Kenwood, UK). The resulting powder (500g) was mixed with 80% and stirred with it over 24 hours at room temperature. The extract was then filtered on Whatman No.1 filter paper and concentrated with a rotary evaporator, which was operated at 40°C to produce the crude ethanolic extract of *Euphorbia kamerunica* (EEEUK) [15].

Experimental animals and ethics

The animal housing facility of Babcock University supplied forty-two male adult Wistar rats (body weight range of 120-180 g). Rats were housed in plastic cages under normal room conditions. Standard water and pellet feed were given *ad libitum*. This experiment was approved by the Babcock University Health Research and Ethics Committee (reference BUHREC 439/24) and conducted in accordance with the ethical standards of animal research[16]. All procedures followed the Animal Research Reporting of In Vivo Experiments (ARRIVE) guidelines for reporting animal research [17].

Experimental design

After a period of one week of acclimatization in their plastic cages, the rats were randomly divided into six groups of seven animals each. Group A (Control) was treated with oral normal saline (2ml/kg) for 28 days. Group B ($AlCl_3$ alone) was orally administered 14 days of $AlCl_3$ (200mg/kg) for 14 days and normal saline. The ethanolic extract (EEEUK) at 100mg/kg was orally administered to Group C (EEEUK only) over 28 days. $AlCl_3$ (200 mg/kg) was added to Group D ($AlCl_3$ + EEEUK LD) for 14 days, followed by EEEUK (100 mg/kg) for 14 days. Group E ($AlCl_3$+ EEEUK HD) was treated with the addition of $AlCl_3$ (200 mg/kg) for 14 days, followed by EEEUK (200 mg/kg) for 14 days. Group F ($AlCl_3$+ Donepezil) was treated with 14 days of $AlCl_3$ (200 mg/kg) followed by 14 days of donepezil (5 mg/kg), thus used as the positive control. All therapies were administered orally through an oral cannula. The weights of the body were measured weekly during the time of the experiment [20].

Sample collection and analysis

At the end (final day of administration) of the experimental period, animals were fasted overnight and sacrificed by cervical dislocation to minimize gastrointestinal content interference with tissue biochemistry, reduce anesthesia-related metabolic confounders, and ensure that cervical dislocation, a rapid, humane method causing immediate loss of consciousness through spinal cord severance, yields tissues with minimal stress-induced hormonal or metabolic artifacts, thereby preserving the histological and biochemical integrity of harvested organs. Blood samples were collected via cardiac puncture for biochemical analysis. Both kidneys were carefully dissected, excised, removed, weighed, and processed for histological and biochemical analyses.

Phytochemical analysis

Qualitative phytochemical screening was carried out according to the guidelines in an attempt to identify the existence of saponins, tannins, flavonoids, cardiac glycosides, terpenoids, steroids, phenols, alkaloids, and anthraquinones [18]. Antioxidant action of the ethanolic extract of the plant (EEEUK) was evaluated using 2,2-diphenyl-1 -picrylhydrazyl (DPPH) radical scavenging assay, using ascorbic acid as reference antioxidant [19].

Evaluation of myeloperoxidase (MPO), reactive nitrogen species and superoxide dismutase (SOD) levels

Renal inflammation was assessed by measuring myeloperoxidase (MPO) activity, a well-established marker of neutrophil infiltration and oxidative-mediated tissue inflammation [20]. Intracellular concentrations of reactive oxygen species (ROS) and reactive nitrogen species (RNS) were quantified via flow cytometry using the FACSCanto II system (Becton Dickinson, USA), following established fluorometric protocols [21, 22]. Superoxide dismutase (SOD) activity was determined using the nitroblue tetrazolium (NBT) reduction method [23], which measures the enzyme's capacity to inhibit NBT reduction by superoxide radicals. Together, these complementary methodologies provided a comprehensive, multi-dimensional evaluation of the oxidative stress burden, antioxidant defense capacity, and inflammatory milieu within renal tissue, enabling robust interpretation of nephroprotective outcomes.

Histological analysis

Kidney tissues were fixed in 10% neutral buffered formalin and processed using the standard paraffin embedding technique. Sections of 5µm thickness were cut and stained with hematoxylin and eosin (H&E) for general histological examination, periodic acid-Schiff (PAS) for glycogen and basement membrane demonstration, and Masson's trichrome for collagen fiber visualization [24].

Statistical analysis

Data were expressed as mean ± standard error of mean (SEM). Statistical analysis was performed using GraphPad Prism 9.0. One-way analysis of variance (ANOVA) followed by Tukey's post-hoc test was used for multiple group comparisons. Statistical significance was set at $p<0.05$ [25]

RESULTS

Phytochemical screening of *Euphorbia kamerunica*

Table 1 shows the phytochemical constituents of ethanolic extract of *Euphorbia kamerunica* (EEEUK); saponins, tannins, flavonoids, phenol, alkaloids, and anthraquinones are present, while terpenoids and steroids are abundantly present. Cardiac glycosides are absent in EEEUK.

Organ weight changes

Kidney weight analysis revealed significant changes across groups. For the right kidney, there was a significant increase when control was compared with $AlCl_3$ only and EEEUK only groups. The $AlCl_3$ + EEEUK high dose groups showed a significant decrease compared to control. Left kidney weights showed similar patterns with significant differences across all groups. The EEEUK-only group had the highest kidney weight, while the $AlCl_3$ + EEEUK high dose group showed the lowest weight (Figure 1).

EEEUK mitigates renal inflammation damage by lowering myeloperoxidase function in $AlCl_3$-induced rats

Figure 3 illustrates a significant surge in MPO enzyme activities in the $AlCl_3$-induced group when compared with untreated animals. More importantly, the plant extract lowered the renal inflammatory response, as evidenced by a considerable decrease in MPO enzyme activity at 200 mg/kg when compared to the $AlCl_3$-induced group and the Donepezil-induced group (Figure 2).

Effect of EEEUK on superoxide dismutase activity

Superoxide dismutase (SOD) activity analysis revealed significant increases across all groups compared to control. The control group showed baseline SOD activity, while all experimental groups demonstrated elevated levels: $AlCl_3$ only, EEEUK only, $AlCl_3$ + EEEUK low dose, $AlCl_3$ + EEEUK high dose, and $AlCl_3$ + Donepezil. The progressive increase in SOD activity in treatment groups suggests enhanced antioxidant defense mechanisms (Figure 3).

Histological, histochemical and immunohistochemical examination of the kidney following $AlCl_3$ exposure

Histological examination of kidney sections across the four staining protocols revealed consistent patterns of $AlCl_3$-induced nephrotoxicity and dose-dependent EEEUK-mediated renoprotection. H&E staining demonstrated glomerular hypertrophy, vascular congestion, and tubular vacuolation in $AlCl_3$-treated rats, with progressive architectural recovery in EEEUK-treated groups (Figure 4). Masson Trichrome staining revealed marked interstitial fibrosis and collagen deposition following $AlCl_3$ administration, which was significantly attenuated by high-dose EEEUK treatment (Figure 5). PAS staining showed loss of brush borders and mesangial expansion in the $AlCl_3$ group, with marked restoration of PAS-positive reactivity in high-dose EEEUK-treated rats. Bcl-2 immunoreactivity was significantly diminished in

$AlCl_3$-treated kidneys, indicating increased apoptotic susceptibility (Figure 6), while EEEUK treatment dose-dependently upregulated Bcl-2 expression, confirming anti-apoptotic and renoprotective mechanisms (Figure 7). Donepezil-treated rats showed comparable protection across all staining protocols.

Table 1: Phytochemical screening of crude ethanolic extract

Test	Crude Ethanolic Extract
Saponins	+ve
Tanins	+ve
Flavonoids	+ve
Glycosides	-ve
Terpenoids	++ve
Steroids	++ve
Phenol	+ve
Alkaloids	+ve
Anthraquinones	+ve

NB; +ve: Present, ++ve: Abundantly present, -ve: Absent

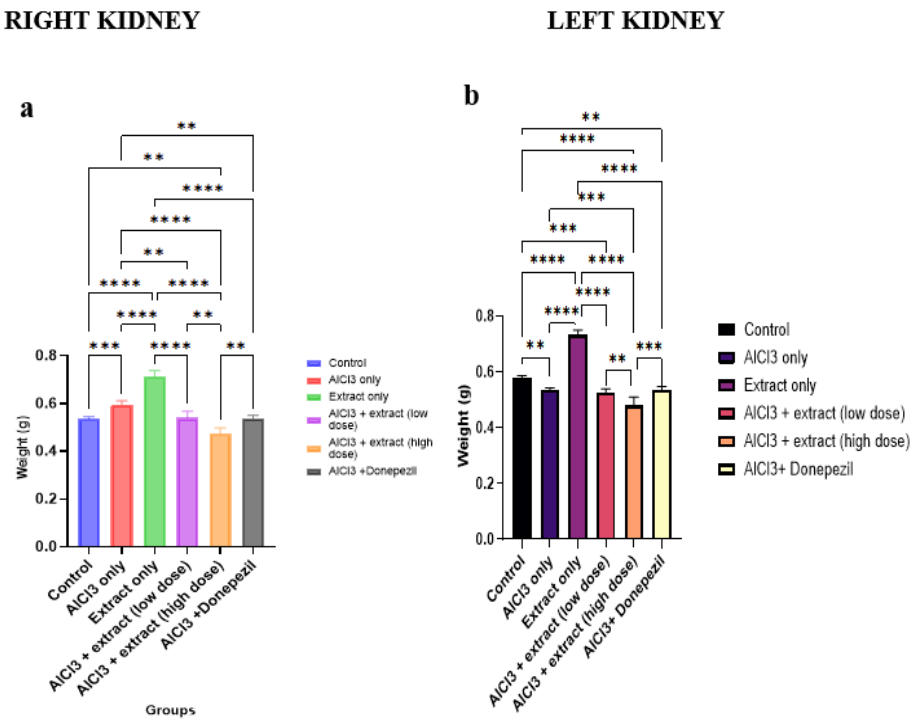

Figure **1 a and b:** Bar chart showing the right and left kidneys' weight across all groups. Data are expressed as Mean ± SEM. **p<0.01, ***p<0.001, ****p<0.0001

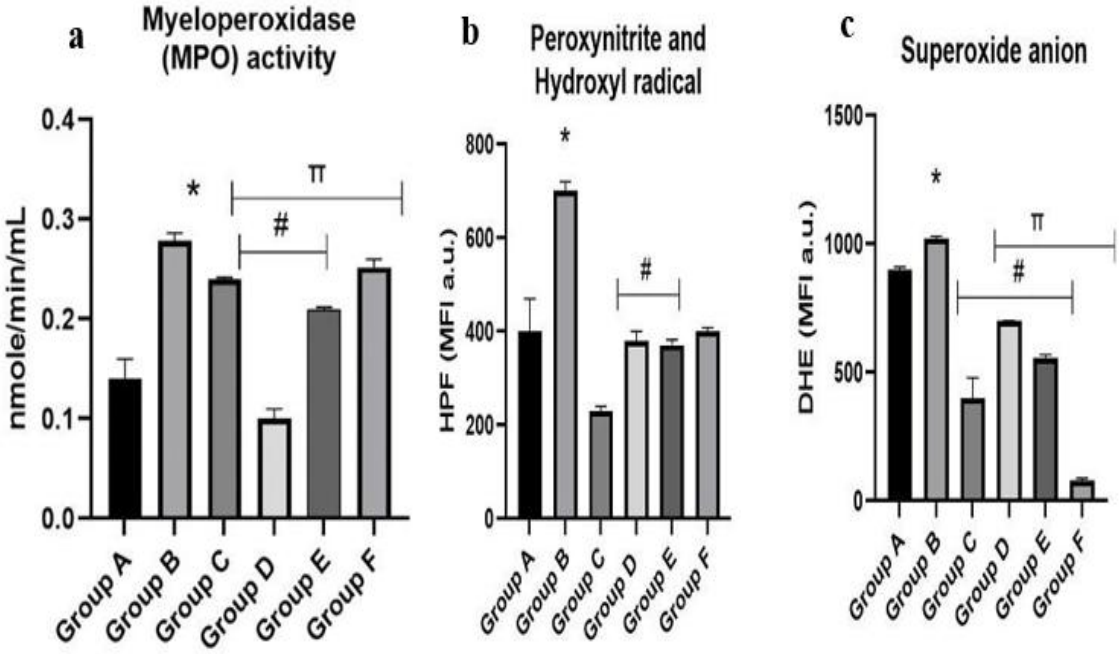

Figure 2 a-c: Bar charts showing EEUK mitigates renal inflammation by lowering (a) myeloperoxidase (MPO) (b) peroxynitrite and hydroxyl radical (c) superoxide anion production in $AlCl_3$-induced Rats. Data are expressed as Mean ± SEM. * -denotes a substantial difference between the $AlCl_3$ group and the control group. # -denotes a substantial difference between the EEUK treatment cohorts and the $AlCl_3$-induced group. While π-indicates a substantial difference between the positive control group and the EEUK treatment groups. Group A (Control): Administered normal saline orally; Group B ($AlCl_3$ only): Administered aluminium chloride (200 mg/kg body weight) orally; Group C (EEUK only): Administered EEUK (100 mg/kg body weight) orally; Group D ($AlCl_3$ + EEUK LD): Administered Aluminium chloride (200 mg/kg), followed by EEUK (100 mg/kg); Group E ($AlCl_3$ + EEUK HD): Administered aluminium chloride (200 mg/kg) for 14 days, followed by EEUK (200 mg/kg); Group F ($AlCl_3$ + Donepezil): Administered aluminium chloride (200 mg/kg) followed by donepezil (5 mg/kg) as a positive control.

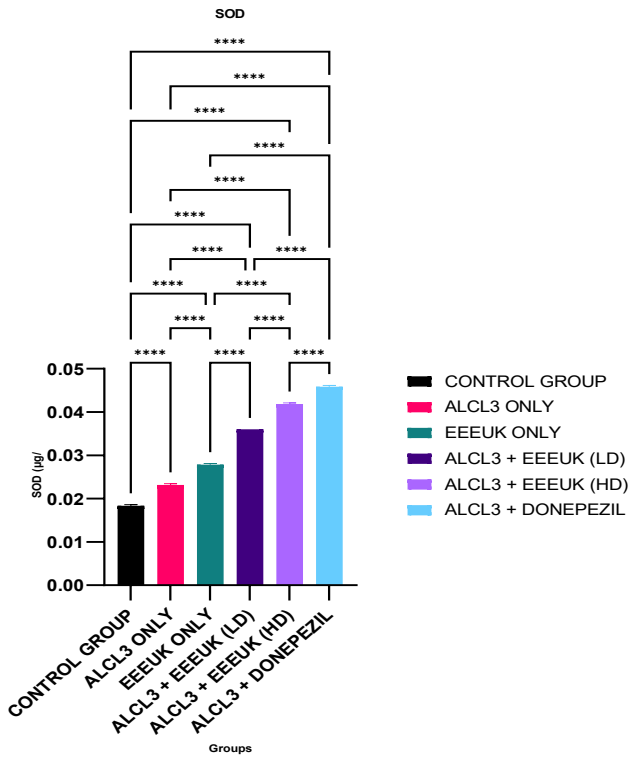

Figure 3: Bar charts showing superoxide dismutase (SOD) activity analysis revealed significant differences across all groups. Data are expressed as Mean ± SEM, ****-p<0.0001

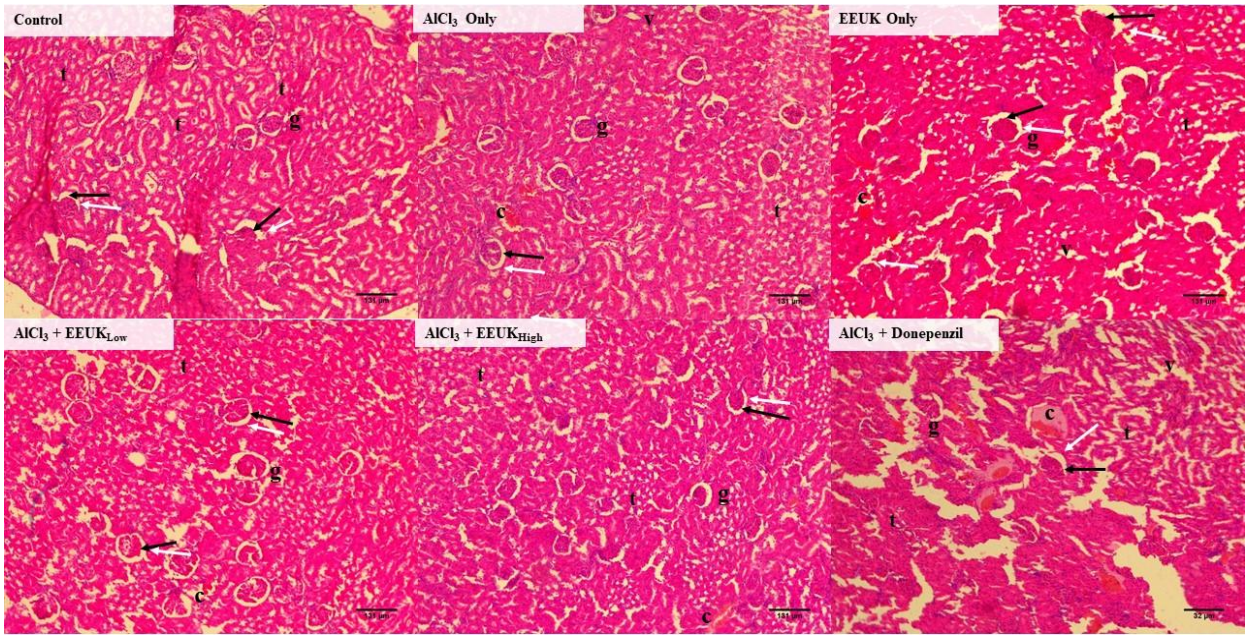

Figure 4: Photomicrograph of kidney section stained with H&E X400. The control group showed normal glomeruli (g), Bowman's capsule visceral (black arrow) and parietal (white arrow) layers, and proximal (p) and distal (d) convoluted tubules. AlCl3 nephrotoxicity revealed enlarged glomeruli (g), congested blood vessels (c), and vacant areas between tubular cells and basal lamina (blue arrow). EEUK only showed nearly normal glomeruli (g) with slight change in convoluted tubules (d & p) and vacuolation (v). AlCl3 +EEUK and AlCl3 + Donepenzil showed signs of recovery to normalcy in glomeruli (g), surrounding Bowman's capsule (black & white arrow), and tubules (d & p). Scale bar: 32 µm.

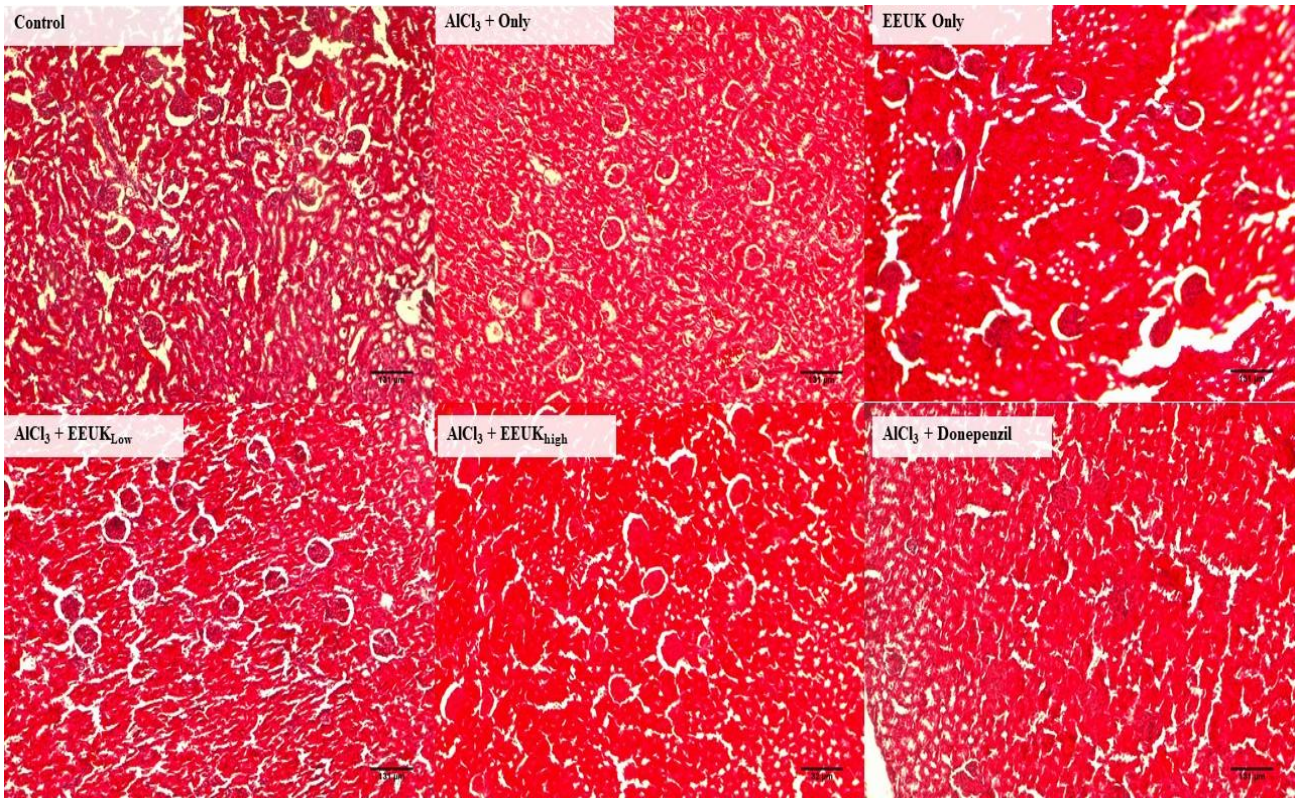

Figure 5: Photomicrographs of Masson Trichrome-stained kidney sections (×400); scale bar 32 µm) across groups: Control shows normal architecture; $AlCl_3$-only exhibits severe tubular necrosis, collagen deposition (blue), and interstitial fibrosis; $AlCl_3$+low-dose EEUK shows moderate improvement; $AlCl_3$+high-dose EEUK demonstrates significant restoration of tubular integrity and reduced fibrosis; EEUK-only maintains normal histology; $AlCl_3$+donepezil shows comparable renoprotection to high-dose EEUK treatment.

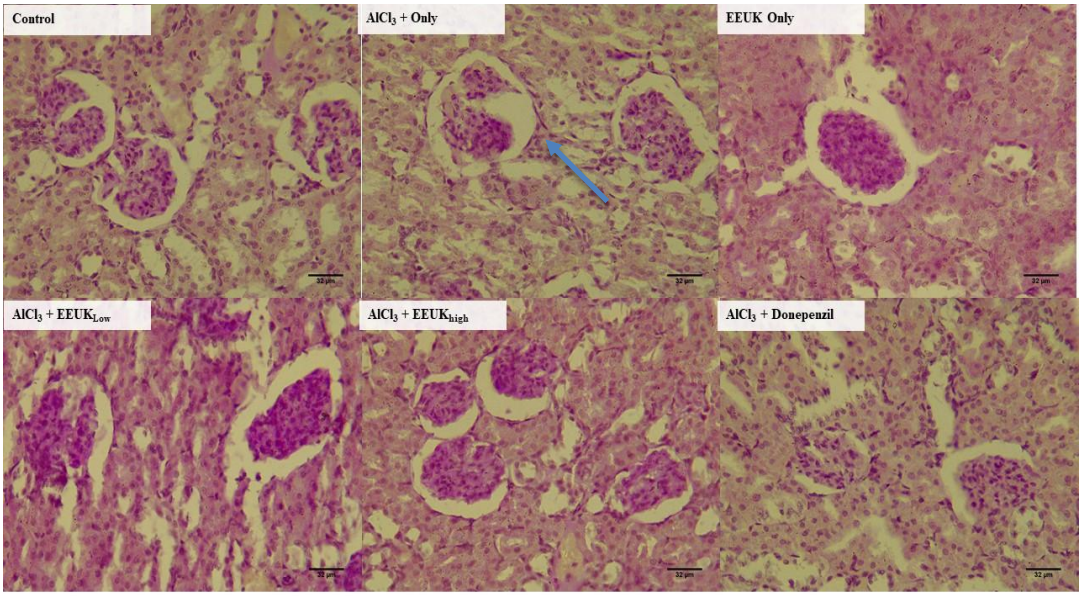

Figure 6: Photomicrographs of PAS-stained kidney sections (×400; scale bar 32 µm). Control has intact glomeruli and PAS-positive brush borders. $AlCl_3$-only: loss of brush borders, tubular degeneration, mesangial PAS expansion (blue arrow). $AlCl_3$+low-dose EEUK: partial restoration. $AlCl_3$+high-dose EEUK: marked recovery with preserved PAS reactivity. EEUK-only: normal histology. $AlCl_3$+donepezil: substantial improvement, comparable to high-dose EEUK, indicating protective effects.

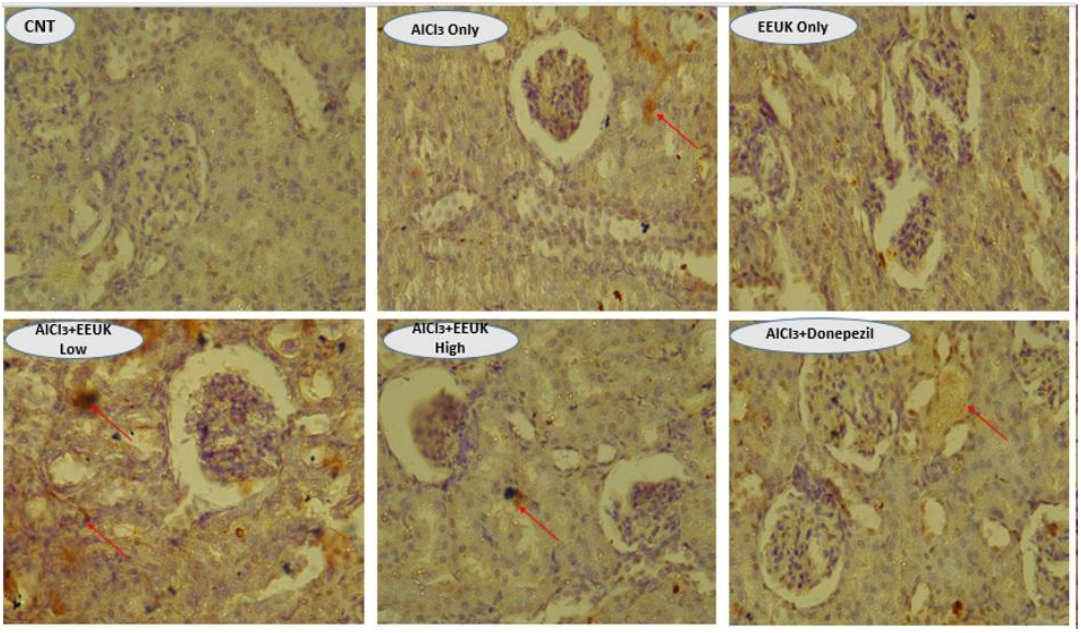

Figure 7: Photomicrographs showing BCl-2 immunoreactivity (brown staining) in kidney sections of Wistar rats (magnification ×400). Photomicrographs showing BCl-2 immunoreactivity (brown staining) in kidney sections of Wistar rats (magnification ×400). Control shows normal saline-treated rats displaying strong BCl-2 expression in renal tubular epithelial cells, indicating normal cellular homeostasis and anti-apoptotic activity. $AlCl_3$ only: Aluminum chloride (200 mg/kg) for 14 days followed by normal saline, showing significantly diminished BCl-2 immunoreactivity, suggesting aluminium-induced nephrotoxicity and increased apoptotic susceptibility. EEUK alone: EEEUK (100mg/kg) for 28 days, demonstrating robust BCl-2 expression similar to controls. $AlCl_3$ + EEUK LD: Aluminum chloride followed by low-dose EEUK (100 mg/kg), showing moderate restoration of BCl-2 expression. $AlCl_3$ + EEUK HD: High-dose EEEUK (200 mg/kg) treatment exhibiting marked BCl-2 upregulation and renoprotective effects. $AlCl_3$ + Donepezil: Positive control with donepezil (5 mg/kg) showing enhanced BCl-2 expression. Scale bar = 50µm. Arrows indicate BCl-2-positive tubular cells.

DISCUSSION

The current study establishes strong nephroprotective properties of an ethanolic extract of *Euphoria kamerunica* over $AlCl_3$-induced nephrotoxicity in Wistar rats. Such results offer good support to the therapeutic use of the medicinal plant in alleviating the effects of heavy metals on the kidneys by various protective mechanisms. EEEUK possesses a variety of bioactive compounds, as phytochemical analysis showed that the compound has a significant proportion of terpenoids and steroids, which also play a role in its therapeutic effects. The high antioxidant property over ascorbic acid implies effective free-radical scavenging of the antioxidant, which is essential in the prevention of oxidative-stress-related cellular loss [26]. These findings are in line with other literature that has shown the antioxidant effect of the species of the genus Euphorbia and its possible uses in therapy [27].

The administration of $AlCl_3$ was able to induce nephrotoxicity as observed in histopathological alterations and the modulation of markers of oxidative stress. The renal injury (enlarged glomeruli, congested blood vessels, and tubular degeneration) is consistent with known pathways of aluminum-induced nephrotoxicity characterized by oxidative stress, inflammation, and dysfunction of cells [28]. The effects of EEEUK on oxidative stress and inflammation were observed via the cellular concentrations of MPO and production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) [29]. Both inflammation and oxidative stress are reported as signs of renal diseases [30, 31]. The kidney, with its high metabolic needs and high level of mitochondrial density, is highly vulnerable to excessive ROS overproduction in stress situations [31]. According to Ebert *et al*. [30], acute inflammatory responses caused by the pathological stimuli increase the impact of oxidative stress and support the generation of ROS. The current research determined that the level of kidney myeloperoxidase activity and ROS were significantly elevated by $AlCl_3$. Similar to the findings provided in the past, tissue injury and inflammation have been directly linked to MPO activity increase that is mostly due to inflammation [33,34]. MPO enhances oxidative injury by promoting the conversion of hydrogen peroxide to

hypochlorite, thereby increasing cellular injury and the progression of inflammation [32-35].

In addition to that, high levels of MPO have been shown to induce inducible nitric-oxide synthase (iNOS) and increase the production of nitric oxide (NO) [35]. NO, a crucial regulator of renal hemodynamics, is able to respond to ROS to form toxic peroxynitrite [35, 36]. Under conditions of reduced intracellular concentrations, NO acts as a signaling molecule, controlling a number of physiological systems, including the endocrine system [37]. However, high levels are widely known as one of the possible mediators of pro-inflammatory responses [31,32,34]. This study proposes a potential increase in the concentration of NO in the kidneys of AlCl3-treated rats, causing nitrosative stress because of the formation of peroxynitrite, having a potential to cause tissue damage [34,35]. However, previous studies suggest that the species of Euphorbia alleviate apoptotic activity caused by H_2O_2 [38]. The present research showed that EEEUK reduced the initial increase in inflammatory biomarkers produced by $AlCl_3$, and the effects were especially significant in lowering the level of MPO, ROS, and RNS in renal cells of experimental units. The results are consistent with the earlier studies that have indicated the antithrombotic and anti-inflammatory effects of methanolic leaf extracts of the plant species of the genus Euphorbia on the kidney [39]. The positive impact of the EEEUK could be attributed to its antioxidant capability that fights oxidative damage [40]. EEEUK can also include bioactive molecules, including alkanols and terpenoids, which react with the active site of MPO and counteract its actions [41].

The increase in SOD activity in $AlCl_3$-treated animals is a compensatory mechanism for oxidative stress. SOD is an essential antioxidant enzyme that counteracts superoxide radicals, and its up-regulation points to the efforts of the organism to overcome the effects of aluminum-related oxidative damage [42]. The incremental upsurge of SOD activity in EEEUK-treated groups indicates the improvement of the antioxidant defense systems, which favors the protective effects of the plant. EEEUK exhibited nephroprotective characteristics using several parameters. The dose-dependent improvement of renal architecture was observed by the histopathological examination, whereby the high dose group exhibited better restoration of glomerular architecture and less tubular damage. Basement-membrane integrity, which is evidenced by PAS staining, is a sign of protection against structural damage caused by aluminum. The decreased accumulation of collagen in the trichrome staining technique by Masson indicates the inhibition of the fibrotic alterations that come with chronic nephrotoxicity.

The pathways that have led to the described nephroprotective activity of EEEUK are probably multifarious. Antioxidant activity, anti-inflammatory effects, and cellular protection may be attributed to the high phytochemical content of the plant, with terpenoids and steroids being the main ones [43]. Flavonoids and phenolic compounds found in the extract are characterized by the power to eliminate free radicals, alter effects of inflammation, and protect the cell membranes against oxidative injury [44]. The dose-dependent effects observed in this study show that an increase in bioactive compound concentration offers greater protection. Histopathological preservation and antioxidant enzyme activity were also more favorable in the high-dose (200mg/kg) group than the low one, which shows that there is a therapeutic limit of nephroprotection. The therapeutic potential of this plant extract is justified by the similarity of its effectiveness to the clinically administered neuroprotective agent, donepezil. However, the natural origin of EEEUK could have benefits in safety profile and fewer adverse effects than synthetic drugs [45].

The aluminum chloride considerably decreased the expression of BCL -2 in the renal tubular cells, which implies an increase in the susceptibility to apoptosis and nephrotoxicity, as reported earlier. The anti-apoptotic protein BCL -2 is the one that preserves mitochondrial membrane integrity and inhibits cytochrome c leakage [46,47]. There was a dose-dependent restoration of BCL-2 immunoreactivity by EEEEUK treatment, which implicated Renoprotective pathways via apoptosis suppression. The high-dose EEEUK sample exhibited similar efficacy to donepezil, suggesting the presence of powerful anti-apoptotic activities that could be due to the presence of antioxidant phytochemicals [48]. The research results are consistent with those that indicate that natural compounds reduce organ damage caused by aluminum by increasing survival proteins [49]. BCL 2 replacement indicates a positive association with renal architecture, which is in favor of the therapeutic effect of EEEUK against metal-induced nephrotoxicity.

Limitations of the study are rather limited period of treatment and acute nephroprotective effects. Research in the future should focus on long-term preventive effects, dose route optimization and bioactive compounds that are causing a protective effect on the kidney. Also, mechanistic research on the molecular pathways of EEEUK protective actions would be informative to the development of a therapeutic intervention.

CONCLUSIONS

This study has established that an ethanolic extract of *Euphorbia kamerunica* has considerable nephroprotective properties in nephrotoxicity induced by $AlCl_3$ in Wistar rats. The therapeutic potential of *Euphorbia kamerunica* in the prevention and

treatment of nephrotoxicity in human beings will require a clinical trial to validate its therapeutic potential.

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