The Journal of Phytopharmacology 2026; 15(4):190-198
Online at: www.phytopharmajournal.com

Research Article

ISSN 2320-480X
JPHYTO 2026; 15(4): 190-198
July- August
Received: 18-04-2026
Accepted: 07-07-2026
Published: 31-07-2026
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doi: 10.31254/phyto.2026.15401

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Antioxidant-mediated nephroprotective effects of the aqueous extract of *Desmodium adscendens* (Sw.) DC. against gentamicin-induced renal injury in Wistar rats

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ABSTRACT

Background: Gentamicin is an effective aminoglycoside antibiotic whose clinical use is limited by nephrotoxicity mainly associated with oxidative stress and tubular damage. **Objective:** This study investigated the nephroprotective effect of the aqueous extract of *Desmodium adscendens* (Sw.) DC. (Fabaceae) against gentamicin-induced renal injury in Wistar rats. **Materials and Methods:** The *in vitro* antioxidant effect of plant extract was evaluated on 2,2-diphenyl-1-picrylhydrazyl (DPPH), Nitric oxide (NO) and Ferric reducing antioxidant power (FRAP), at the concentration range from 1 to 1000 µg/mL. Nephrotoxicity was induced by intraperitoneal administration of gentamicin (80 mg/kg/day) for 14 days. The extract (100, 200, and 400 mg/kg, p.o.) was administered concomitantly. Renal function biomarkers (serum creatinine, urea, uric acid), urinary parameters, oxidative stress markers (malondialdehyde, superoxide dismutase, catalase), and histopathological changes were evaluated. **Results:** *In vitro* antioxidant effect of the aqueous extract showed half-maximal inhibitory concentrations of 108.30 and 226.10 µg/mL for DPPH and NO assay respectively. Gentamicin significantly increased serum creatinine, urea, uric acid, and malondialdehyde levels while decreasing antioxidant enzyme activities ($p < 0.001$). Treatment with the extract markedly attenuated these biochemical disturbances, restored antioxidant enzyme activities, and improved renal histoarchitecture by reducing tubular necrosis and glomerular alterations. **Conclusion:** The findings demonstrate that the aqueous extract of *D. adscendens* confers significant protection against gentamicin-induced renal damage, likely through antioxidant mechanisms, supporting its traditional use in renal disorders.

Keywords: *D. adscendens*, Nephroprotective, Gentamicin, Oxidative stress, Nephrotoxicity, Antioxidant.

INTRODUCTION

Nephrotoxicity is characterized by a rapid loss of kidney function due to toxic substances including drugs and chemicals [1]. Approximately, 20% of nephrotoxicity cases are attributable to drugs [2]. In older populations, this percentage grows owing to both increased longevity and the use of multiple medications [1]. The most frequent are acetaminophen [3], aminoglycosides [4], and methotrexate (anti-cancer drugs) [5]. Among nephrotoxic agents, gentamicin, a widely prescribed aminoglycoside antibiotic, is extensively used for the treatment of severe Gram-negative infections [6]. However, its therapeutic efficacy is limited by dose-dependent renal toxicity, which occurs in approximately 10–20% of treated patients [7].

Gentamicin preferentially accumulates in proximal tubular epithelial cells, leading to mitochondrial dysfunction, excessive generation of reactive oxygen species (ROS), lipid peroxidation, inflammation, and ultimately tubular necrosis [8,9]. The exact mechanisms underlying GM-induced toxicity are poorly understood [10]. However, oxidative stress is recognized as a central mechanism in gentamicin-induced renal injury. The imbalance between ROS production and antioxidant defense systems results in structural and functional alterations of renal tissue [11]. Consequently, natural products with antioxidant properties have attracted considerable attention as potential nephroprotective agents, based on their ability to neutralize free radicals [12].

Several antioxidants such as silymarin, N-acetyl systeine, ascorbic acid and several natural plants have showed a nephroprotective effect against gentamicin toxicity. However, new treatments approaches in cases of gentamicin poisoning are still interesting.

D. adscendens (Sw.) DC. (Fabaceae) is a plant widely used in traditional medicine for the management of inflammatory disorders, liver diseases, allergic conditions, malaria, gastric ulcer, hemorrhoids, infectious diseases, venereal diseases, asthma and detoxification [13]. Phytochemical investigations have revealed the presence of flavonoids, saponins, alkaloids, and polyphenolic compounds [13], many of which possess antioxidant [14] and cytoprotective activities [15]. Despite its traditional use, limited scientific evidence is available regarding its protective effects against drug-induced nephrotoxicity.

Therefore, the present study aimed to evaluate the nephroprotective effects of the aqueous extract of *D. adscendens* against gentamicin-induced renal injury in Wistar rats and to investigate the possible involvement of antioxidant mechanisms.

MATERIAL AND METHODS

Chemicals and reagents

All chemicals and reagents utilized in this study were of analytical grade. Gentamicin was purchased from Panpharma, while Silymarin was acquired from Quality pharmaceuticals industries. The following substances were purchased from Sigma-Aldrich (Germany): 2,2-diphenyl-1-picrylhydrazyl, thiobarbituric acid, Griess reagent, sodium nitroprusside (SNP), hydrogen phosphate, phosphoric acid, ferric chloride, Hydrogen peroxide and ascorbic acid. Creatinine, urea, alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) kits were obtained from SGM Italia (Roma).

Plant collection and extraction

The aerial fresh parts (leaves and stems) of *D. adscendens* were collected in Douala (Littoral Region of Cameroon) and authenticated at the National Herbarium of Cameroon, referencing Lowe J 3080 specimen N°-39615 SRF/Cam. The plant material was washed in distilled water, cut into small pieces, shade-dried and ground into fine powder. A total of one hundred grams (100 g) of *D. adscendens* powder was introduced into 3 L of distilled water and boiled for 45 min. After cooling, the mixture was filtered with wathman n°4 filter paper. The resulting filtrate was dried in an oven at 40 °C, yielding sixteen grams (16 g) of dried extract. This extraction procedure resulted in a yield of 16%. The extract was stored at 4 °C until use.

Animals

Both males and females Wistar rats (3-3.5 months; 190-230 g) were used in this study. Animals were randomly selected from the local breeding colonies and housed in the Laboratory of Animal Biology and Physiology, Faculty of Science of the University of Douala Cameroon. They were maintained in cages under room temperature conditions with free access to food and water. All experimental procedures complied with the guidelines of the Institutional Research Ethics Committee for Human Health of the University of Douala (CEI-UDo) for the use of laboratory animals for scientific research (Ref. n°3095 CEI-Udo/05/2022/M).

In vitro Antioxidant Activity

DPPH Radical Scavenging Test

The radical scavenging activity of the aqueous extract of *D. adscendens* was assayed using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay, following the method described by Nono *et al* [16]. A stock solution (1000 µg/mL) of extract and vitamin C was obtained by solubilizing *D. adscendens* extract or ascorbic acid in methanol. Serial dilutions of these solutions were made to obtain different concentrations of 700, 300, 100, 30, 10, 3 and 1 µg/mL by adding one volume of methanol. For each solution, 150 µL was taken and introduced into the cell pot and then completed with 850 µL of methanol. The first optical density (OD1) was measured at 517 nm against a blank consisting of 1000 µL of methanol. Subsequently, 500 µL of a DPPH solution (0.063 mg/mL) was added to each cell pot. After incubation (20 min at room temperature in the dark) the second optical density (OD2) was measured at the same wavelength. This experiment was performed in triplicate. The percentage of DPPH radical inhibition was calculated as follows:

$$\%\ \text{of inhibition} = \frac{(\text{OD2} - \text{OD1})\text{blank} - (\text{OD2} - \text{OD1})\text{sample}}{(\text{OD2} - \text{OD1})\text{blank}} \times 100$$

Nitric oxide scavenging test

The nitric oxide (NO) scavenging activity of *D. ascendens* was evaluated according to the method of Marcocci *et al* [17] using Griess reaction. Brefly, 50 µL of sodium nitroprusside (10 mM), prepared in phosphate buffer (200 mM, pH= 6.6) was introduced into the different test tubes containing 450 µL of the aqueous extract of *D. adscendens* or ascorbic acid solution at various concentrations (1, 3, 10, 30, 100, 300, 700 and 1000 µg/mL). The mixture was incubated for 3 h at room temperature, after which 250 µL of Griess reagent was added to each test tubes. The resulting solution was incubated in the dark, and the absorbance of the formed chromatophore was measured at 540 nm against a blank (sodium nitroprusside + Griess reagent + distilled water). The experiment was repeated 3 times. The nitric oxide (NO) radical scavenging activity was calculated using the following formula:

$$\text{NO radical scavenging activity (\%)} = \frac{\text{absorbance(blank)} - \text{absorbance(sample)}}{\text{absorbance(blank)}} \times 100$$

Reducing power of the aqueous extract of D. adscendens

The reducing power of the aqueous extract of *D. adscendens* was determined according to a method described by Benzie and Strain [18]. Half mL (0.5 mL) of plant extract or ascorbic acid (1, 3, 10, 30, 100, 300, 700 and 1000 µg/mL) was mixed with 1.25 mL of phosphate buffer solution (200 mM; pH= 6.6), and 1.25 mL of potassium ferricyanide solution (1%). The resulting solution was incubated at 50 °C for 20 min, after which 1.25 mL of trichloroacetic acid (10%) was added. The tubes were then centrifuged at 3000 rpm for 10 min. The supernatant obtained (1.25 mL) was combined to 1.25 mL of distilled water and 0.25 mL of $FeCl_3$ (0.1%) followed by incubation at 37 °C for 10 min. Absorbance was read in triplicate at 700 nm against the blank prepared by replacing the plant extract with distilled water.

Experimental study design and treatment

Animals were randomly divided into 6 groups of 6 rats each:

- Group 1 (normal control group), received distilled water (10 mL/kg, *per os*) and saline (0.9%);
- Group 2 (negative control), was treated with distilled water (10 mL/kg, *po*) and gentamicin (80 mg/kg, *ip*)
- Group 3 (positive control) received silymarin (100 mg/kg, *po*) and gentamicin (80 mg/kg, *ip*)
- Groups 4, 5 and 6 (test groups), received the aqueous leaves extract of *D. adscendens* at doses of 100, 200 and 400 mg/kg (*po*) respectively with gentamicin (80 mg/kg, *ip*)

One hour (1h) after administration of distilled water, silymarin or AEDA, all groups received gentamicin (80 mg/kg, ip) except the control group which received 0.9% saline solution (1 mL/kg, ip). The extract doses (100, 200 and 400 mg/kg) were obtained based on the toxicity studies reported by Quaye *et al* [19,20]. All substances were

administered daily during 14 days. Body weight of the animals was recorded at baseline and then every day throughout the experimental period.

At the end of the treatment period, animals were placed in metabolic cages for 24 h to collect urine. This urine was centrifuged at 3000 rpm for 15 min, aliquoted and stored at -20 °C for the evaluation of creatinine level. Subsequently, all animals were sacrificed under anesthesia. Blood was collected into dry tubes via abdominal aorta and centrifuged at 3000 rpm for 15 min to obtain serum. The serum was stored at -20 °C for biochemical assays.

Following blood collection, the two kidneys and the liver were carefully removed, cleaned of adipose tissue, rinsed with 0.9% NaCl solution and weighed. Relative organs mass was calculated using tibia length as:

Relative mass = (organ mass (g) / tibia length (mm)) × 100

The left kidney was homogenized in Tris buffer (50 mM; pH 7.4) to obtain 20% homogenate used to evaluate oxidative stress markers including malondialdehyde (MDA), nitrites (NO), reduced glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT). The right kidney was fixed in 10% buffered formalin (pH 7.4) for histological evaluation using hematoxylin and eosin staining.

***In vivo* biochemical essays on kidney and hepatic function and oxidative stress**

Kidney and hepatic function assessment

Kidney function parameters including ALT, AST, ALP, creatinine, urea, uric acid, and total protein were measured using commercial assay kits (SGM Italia) according to the manufacturer's instructions.

Diuresis (D) in mL/min/kg was calculated using the formula:

$$D = V \times 100 / M$$

Where V = urine volume (mL/min); M = mass of the animal (kg).

The glomerular filtration rate (GFR) was calculated from the creatinine clearance using the following equation:

$$GRF = U \times D / P$$

Where U = urinary creatinine (mg/dL); D = urine output (mL/min/kg) and P = creatinemia (mg/dL).

Determination of oxidative stress parameters

The tissue levels of oxidative stress markers including MDA, NO, GSH, SOD and catalase were quantified using colorimetric methods based on established protocols: Uchiyama and Mihara [21] for MDA, Ikeda *et al* [22] for NO, Ellman [23] for GSH, Misra and Fridovich [24] for SOD, and Sinha [25] for catalase.

Histological analysis

The kidney was fixed in 10% buffered formalin, dehydrated through a graded ethanol series, cleared in xylene, embedded in paraffin, sectioned, and stained with hematoxylin and eosin for microscopic examination.

Statistical analysis

Statistical analysis was performed using GraphPad Prism® software version 8.01. Results were expressed as mean ± standard error of the mean. IC_{50} value was determined using the nonlinear regression curve following logarithmic transformation. One way ANOVA followed by Turkey's post hoc test was used for single time point data collection, and two way ANOVA followed by Bonferroni's post hoc test for repeated measures (body weight). A value of $p < 0.05$ was considered statistically significant.

RESULTS

In vitro* antioxidant activities of the aqueous extract of *D. adscendens

The antioxidant properties of AEDA on the scavenging activity on DPPH radical are showed in Figure 1a. The results showed that the *D. adscendens* as well as ascorbic acid displayed a robust radical scavenging activity against DPPH, however this activity was notably lower to that of ascorbic acid. The inhibitory concentration 50 (IC_{50}) was 7.04 µg/mL and 108.30 µg/mL for ascorbic acid and the plant extract respectively (Figure 1A).

The analysis of Figure 1B showed that the aqueous extract of *D. adscendens* induced a concentration-dependent scavenging activity against NO radical. The IC_{50} was 226.10 µg/mL, versus 9.52 µg/mL for ascorbic acid.

The reducing power of ferric ions (Fe^{3+}) to ferrous ions (Fe^{2+}) by the aqueous extract of *D. adscendens* is showed in Figure 1C. The aqueous extract of *D. adscendens* had a concentration-dependent reducing power, although lower than ascorbic acid.

Effects of the aqueous extract of *D. adscendens* on gentamicin-induced nephrotoxicity in rats

Effects of the aqueous extract of D. adscendens on body weight and relative kidney and liver mass

Figure 2 showed that, administration of the plant extract at different doses tested as well as silymarin and gentamicin induced no significant change in body weight (Figure 2A) and relative liver mass (Figure 2C) compared to the control group. As showed on Figure 2B, gentamicin induced a significant ($p < 0.0001$) increase in relative kidney mass in the negative control group compared to the normal control. Administration of *D. adscendens* extract at doses of 200 and 400 mg/kg significantly ($p < 0.05$) inhibited the increase of the kidneys mass by 19.06% and 25.78%, respectively compared to the negative control group.

Effects of the aqueous extract of D. adscendens on serum transaminases, alkaline phosphatase and total proteins

Results presented in Table 1 showed that, administration of gentamicin significantly increased serum ALT ($p < 0.001$), AST ($p < 0.0001$), and ALP ($p < 0.0001$) levels and significantly decreased ($p < 0.01$) total protein levels compared to the control group.

Oral administration of the plant extract reduced the elevation of these parameters. ALT activity was significantly ($p < 0.001$) inhibited by 58.39%, 50.35%, and 70.29% at doses of 100, 200, and 400 mg/kg, respectively, compared to negative control animals. A significant inhibition of the increased AST activity was also observed at 100 mg/kg (46.13%; $p < 0.01$), 200 mg/kg (52.67%; $p < 0.001$), and 400 mg/kg (36.18%; $p < 0.05$) compared to the negative control group.

Similarly, the extract at 100, 200, and 400 mg/kg prevented the increase in serum ALP levels, with inhibition percentages of 56.74% ($p < 0.0001$), 29.50% ($p < 0.05$), and 74.49% ($p < 0.0001$), respectively, compared to the negative control group.

Regarding total protein levels, no significant difference was observed between the groups treated with the plant extract and the normal control group (Table 1).

Effects of the aqueous extract of D. adscendens on serum and urinary creatinine, urea, uric acid, urine output and glomerular filtration rate

Analysis of the results presented in Table 2 showed that intraperitoneal injection of gentamicin induced a significant increase ($p < 0.001$; $p < 0.0001$) in serum creatinine, urea, uric acid concentration, and diuresis, along with a significant decrease ($p < 0.001$; $p < 0.0001$) in urinary creatinine level and GFR compared to the control group. Treatment of rats with the aqueous extract of *D. adscendens* at all tested doses resulted in a significant ($p < 0.01$; $p < 0.0001$) attenuation of these parameters compared to rats receiving gentamicin alone (Table 2).

Effects of the aqueous extract of D. adscendens on some oxidative stress parameters

As observed in Figure 3, oxidative stress assessment revealed a significant increase in renal MDA (Figure 3A) and nitrites (Figure 3B) levels ($p < 0.001$; $p < 0.0001$) and a marked decrease in GSH level ($p < 0.0001$) (Figure 3C), SOD ($p < 0.001$) (Figure 3D) and catalase ($p < 0.05$) (Figure 3E) activities in the gentamicin group. Administration of AEDA significantly prevented ($p < 0.001$, $p < 0.000$, $p < 0.05$) prevented the increase of MDA and nitrites levels and decreased GSH level and SOD and Catalase activities compared to gentamicin group.

Effects of the aqueous extract of D. adscendens on kidney histology

Figure 4a showed the effect of AEDA on the microarchitecture of the kidney. In the control group (Figure 4A1), the kidney section showed normal glomerulus architecture with normal urinary space, proximal and distal convoluted tubule. Rats received gentamicin exhibited market pathological alterations as showed in Figure 4A2. The slides of these animals showed mesangial expansions, leukocytic infiltrations and ballooning of the tubular cells. Administration of the plant extract, induced a positive enhancement of the renal parenchyma, with more marked effects at the dose of 200 mg/kg (Figure 4A5). Compared to control group, administration of gentamicin only induced a significant ($p < 0,001$) increase of the number of mesangial expansions (Figure 4B), leukocytic cells (Figure 4C), and tubular ballooning (Figure 4D). The treatment with AEDA, as well as silymarin, reversed significantly ($p < 0,001$) the effects induced by gentamicin in the kidney (Figure 4B, C and D).

Table 1: Effects of the aqueous extract of *D. adscendens* on the activity of transaminases, alkaline phosphatase and total proteins in serum of rats

Parameters		Gentamicin 80 mg/kg +				
	Control	Distilled water	Silymarin 100 mg/kg	AEDA 100 mg/kg	AEDA 200 mg/kg	AEDA 300 mg/kg
ALT (IU/L)	160.34 ±19.91	389.19 ±26.29***	240.56 ±41.33^{b}	162.52 ±32.50^{c}	193.22 ±32.23^{c}	115.62 ±7.24^{c}
AST (IU/L)	82.06 ±6.56	217.96 ±28.03****	141.62 ±14.20^{b}	117.42 ±30.66^{b}	103.16 ±14.62^{c}	139.10 ±7.63^{a}
ALP (IU/L)	155.31 ±4.77	598.04 ±42.17****	431.93 ±44.35**	258.70 ±41.15^{d}	421.59 ±48.38**a	152.55 ±18.41^{d}
Total proteins (g/dL)	81.63 ±2.18	65.19 ±3.55**	63.20 ±0.93**	71.75 ±3.67	68.34 ±2.25	69.09 ±4.38

All values are expressed as mean ± SEM from 6 rats. **p < 0.01, ***p < 0.001, ****p < 0.0001 compared to control group and ^{a}p < 0.05, ^{b}p < 0.01, ^{c}p < 0.001, ^{d}p < 0.0001 compared to gentamicin group. AEDA: aqueous extract of *D. adscendens*. ALT = Alanine aminotransferase; AST = Aspartate aminotransferase; ALP = Alkaline phosphatase

Table 2: Effects of the aqueous extract of *D. adscendens* on serum and urine creatinine, urea, uric acid, urine output and glomerular filtration rate

Parameters		Gentamicin 80 mg/kg +				
	Control	**Distilled water**	**Silymarin 100 mg/kg**	**AEDA 100 mg/kg**	**AEDA 200 mg/kg**	**AEDA 300 mg/kg**
Serum creatinine(mg/dL)	0.45 ± 0.06	4.60 ± 0.36****	0.91 ± 0.33^{d}	0.58 ± 0.11^{d}	0,65 ± 0,15^{d}	0.39 ± 0.07^{d}
Urine creatinine (mg/dL)	15.32 ± 2.01	3.33 ± 1.00****	7.29 ± 1.00**	7.54 ± 1.00**	8.90 ± 1.33*^{a}	9.36 ± 1.13*^{a}
Urea (mg/dL)	48.42 ± 5.43	366.67 ± 42.49****^{a}	249.41 ± 31****^{a}	133.33 ± 9.62^{d}	137.50 ± 10.48^{d}	225.00 ± 25***^{b}
uric acid (mg/dL)	0.78 ± 0.08	3.34 ± 0.35***	2.16 ± 0.19**^{b}	2.05 ± 0.13**^{b}	1.38 ± 0.25^{d}	1.06 ± 0.10^{d}
Diuresis (mL/min/kg)	0.54 ± 0.14	5.66 ± 0.42****	3.01 ± 0.28****^{c}	2.19 ± 0.17**^{d}	2.33 ± 0.35**^{d}	2.59 ± 0.57**^{d}
GFR (mL/min/kg)	17.67 ± 1.94	2.68 ± 0.92***	8.84 ± 2.45	9.34 ± 1.03	12.14 ± 2.14^{a}	25.26 ± 0.67^{d}

All values are expressed as mean ± SEM from 6 rats. *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001 compared to control group and ap < 0.05, bp < 0.01, cp < 0.001, dp < 0.0001 compared to gentamicin group. AEDA: aqueous extract of *D. adscendens*. GFR: glomerular filtration rate.

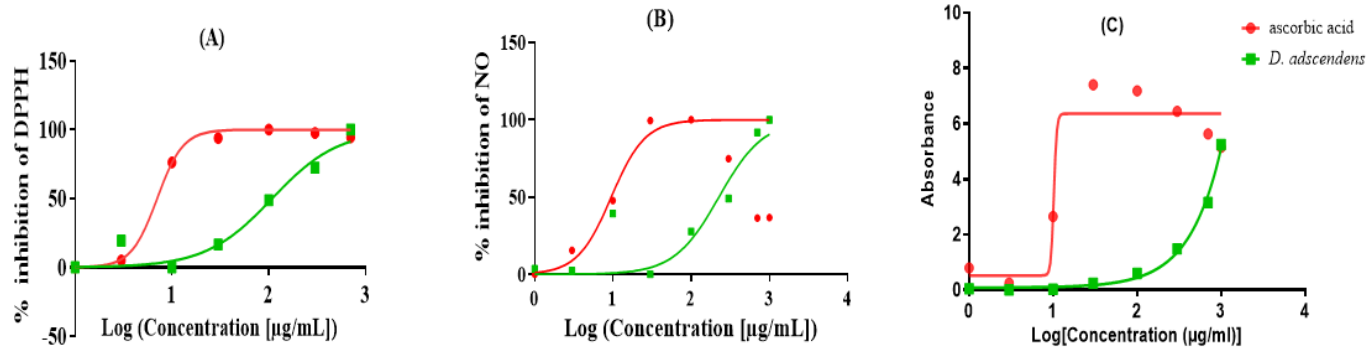

Figure 1: Effects of the aqueous extract of *D. adscendens* on DPPH radical scavenging (A), Nitric oxide radical scavenging (B) and Ferric reducing antioxidant power (C)

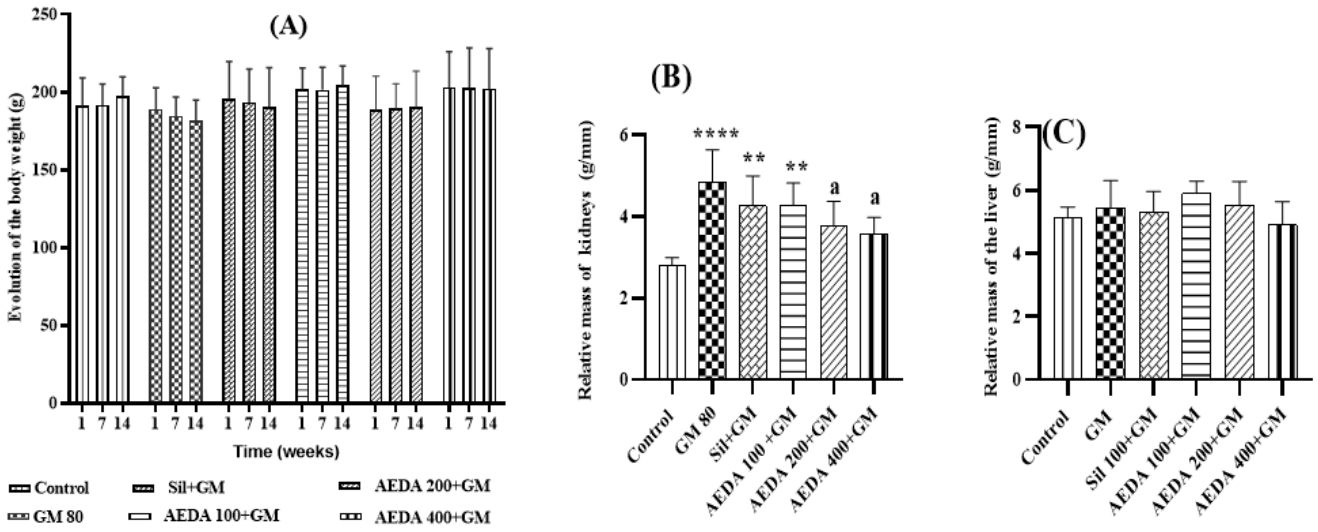

Figure 2: Effects of the aqueous extract of *D. adscendens* on body weight (A) and relative mass of kidney (B) and liver (C)
Each bar represents mean ± SEM, n = 6. **p < 0.01, ****p < 0.0001 compared to control group; [a]p < 0.05 compared to negative control group. GM: gentamicin; Sil: silymarin; AEDA: aqueous extract of *D. adscendens*

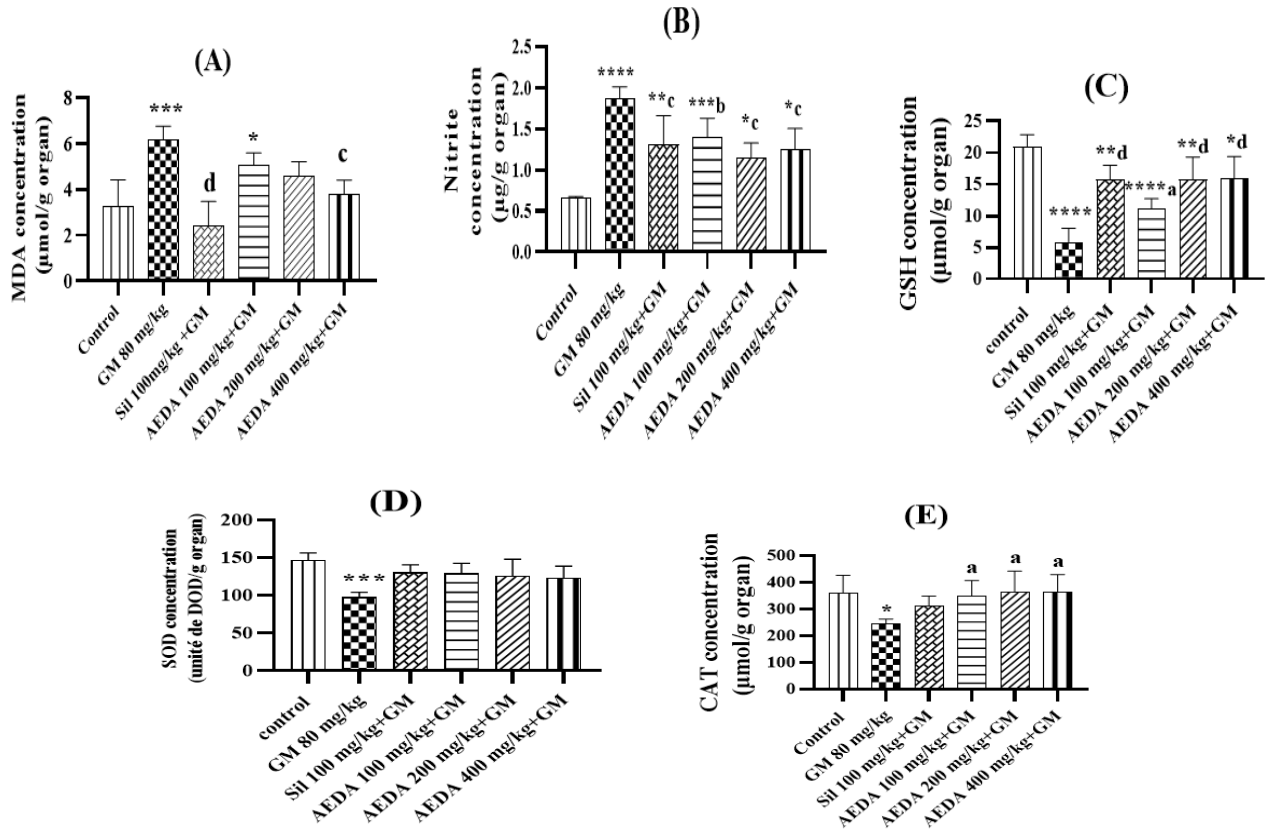

Figure 3: Effects of *D. adscendens* on Malondialdehyde (A), nitrites (B), reduced glutathione (C), superoxide dismutase (D) and Catalase (E) on the kidney
Each bar represents mean ± SEM, n = 6. *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001 compared to the control group; [a]p < 0.05, [b]p < 0.01, [c]p < 0.001, [d]p < 0.0001 compared to gentamicin group. GM: gentamicin; Sil: silymarin; AEDA: aqueous extract of *D. adscendens*

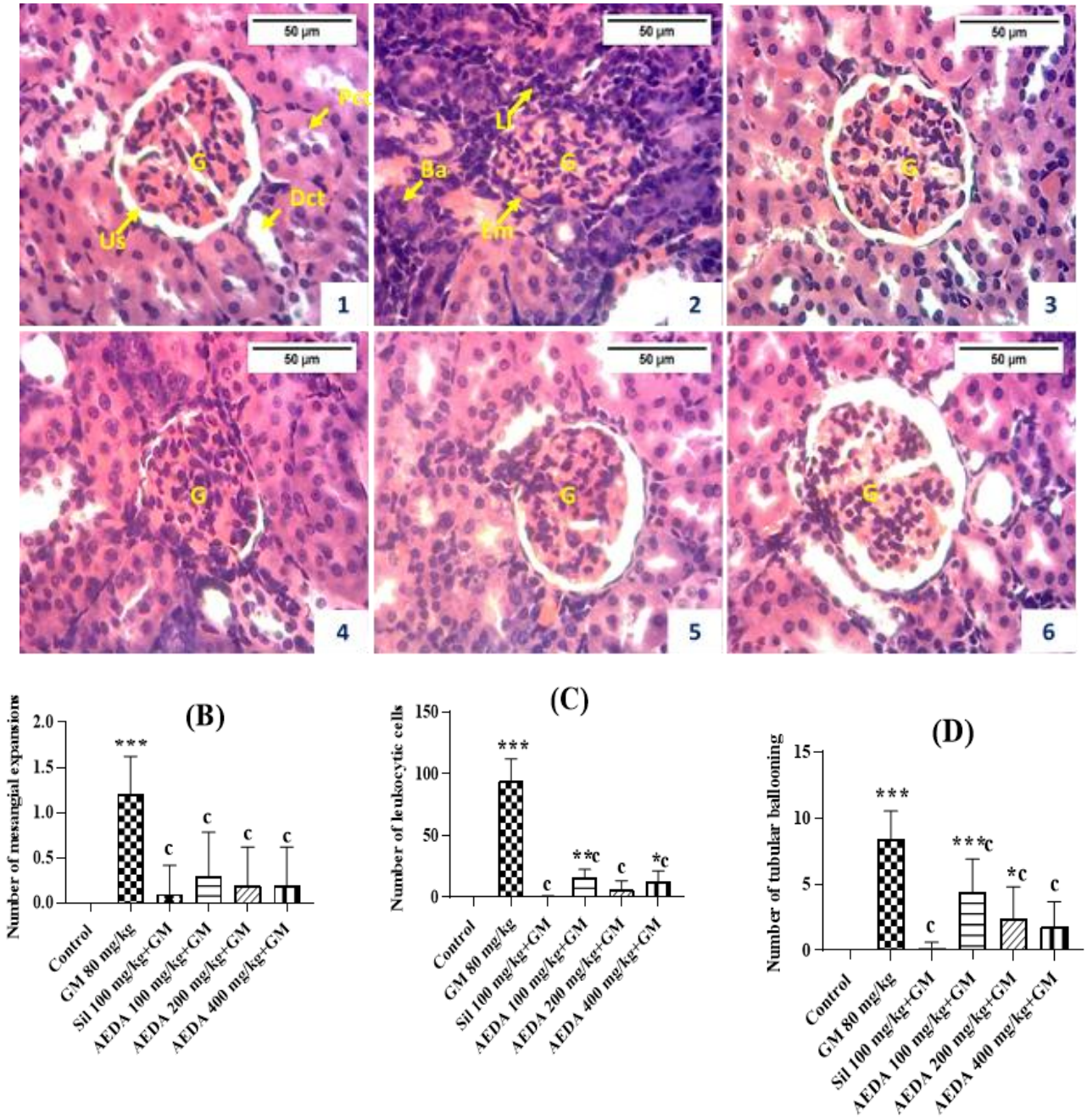

Figure 4: Microphotographs and histomorphometry showing the preventive effect of *D. adscendens* of the microarchitecture of the kidney in gentamicine treated rats (HE x250)

Each bar represents mean ± SEM, n = 6. *p < 0.05, **p < 0.01, ***p < 0.001 compared to control group; °p < 0.001 compared to Gentanicin group. The kidney was stained with Hematoxylin-eosin and observed at 250X. GM: gentamicin; Sil: silymarin; AEDA: aqueous extract of *D. adscendens*. G: Glomerulus; Us = Urinary space; Dct = Distal convoluted tubule; Pct = Proximal convoluted tubule; LI = Leukocyte infiltration; Ba = Tubular cell bloat; Em = Mesangial expansion

DISCUSSION

Gentamicin-induced nephrotoxicity is primarily attributed to its preferential accumulation in proximal tubular epithelial cells, leading to mitochondrial dysfunction, excessive generation of reactive oxygen species (ROS), lipid peroxidation, and subsequent tubular necrosis [8,9]. The present study aimed to evaluate the nephroprotective effects of the aqueous extract of *D. adscendens* against gentamicin-induced renal injury in Wistar rats and to investigate the possible involvement of antioxidant mechanisms. Oxidative stress is a key contributor to the development of gentamicin-induced renal injury [11]. In the literature, it is well known that substances that can inhibit oxidative stress and mediated damage may play an important role in preventing these adverse effects [8,26]. To support this hypothesis, the *in vitro* antioxidants capacities of AEDA were first assessed using DPPH and nitric oxide radical scavenging assays, as well as ferric reducing antioxidant power. Results obtain in this study showed that scavenging activities of injury could be of great importance for the prevention of these side effects. AEDA increased with concentration. These results suggest an increased ability of aqueous extract of *D. adscendens* to donate hydrogen ions and/or electrons to scavenge free radicals [27]. Results also showed that AEDA exhibit a concentration dependent strong reducing capacity. It is known that compounds with reducing power can reduced lipid peroxidation processes and convert them to more stable product. These antioxidant activities are likely associated with the phenolic compounds present in the plant, which are well known for their free radical scavenging properties [28]. Similar findings have been reported previously for the same plant species [14]. These antioxidant properties of *D. adscendens* could prevent gentamicin-induced nephrotoxicity, since gentamicin in its toxic mechanism of action leads to oxidative stress [29,30].

The results on body weight changes in gentamicin induced nephrotoxicity are conflicting. Some authors showed that intoxication with gentamicin induced loss of body weight [31], but others authors showed that intoxication with gentamicin did not affect body weight [32]. In this study, daily administration of gentamicin (80 mg/kg) for 14 days had no significant effect on body weight changes between different experimental groups. However, a significant increase in relative kidney weight was observed in the negative control group, which likely reflects inflammation, edema, and oxidative stress following gentamicin exposure [33]. Treatment with AEDA at 200 and 400 mg/kg prevented this increase in relative kidney mass in rats when compared to negative control, suggesting that the aqueous extract of *D. adscendens* could exert an inhibitory activity on the release of chemical mediators during inflammatory reactions.

Gentamicin administration caused a significant elevation in serum creatinine, urea, and uric acid levels, consistent with its nephrotoxic profile [32,34]. Decreased creatinine excretion further confirmed impaired renal function, likely due to reduced glomerular filtration rate (GFR) [35]. The significant rise in diuresis and the decline in GFR in the gentamicin group support the notion that gentamicin accumulation in renal tissue impairs nephron viability and causes proximal tubular degeneration [36]. In contrast, AEDA treatment significantly improved serum renal biomarkers, reduced diuresis, and inhibited GFR, suggesting a beneficial effect of this extract on renal function.

Gentamicin also produced significant increases in serum AST, ALP, and ALT activities, in line with previous reports of its hepatorenal toxicity [37] and confirm the detrimental effect of gentamicin on the kidney and even the liver. Co-treatment with AEDA reversed these alterations. Additionally, gentamicin significantly reduced serum total protein levels, a finding consistent with earlier studies [37,38]. This reduction may reflect enhanced protein catabolism and/or impaired renal reabsorption [39]. Treatment with AEDA prevented this decline, suggesting a protective effect against gentamicin-induced protein degradation or a possible enhancement of protein synthesis.

Oxidative stress plays a central role in gentamicin-induced renal injury. The observed increase in malondialdehyde (MDA) levels indicates enhanced lipid peroxidation of cellular membranes [36], while the reduction in superoxide dismutase (SOD) and catalase (CAT) activities reflects depletion of endogenous antioxidant defenses. These alterations confirm that ROS overproduction contributes significantly to renal structural and functional impairment [30,40]. The elevated NO levels may promote peroxynitrite formation, a potent mediator of renal injury [41,42].

Treatment with AEDA significantly reversed these biochemical changes, decreasing MDA and NO levels and increasing GSH level and CAT and SOD activities. These results confirm the *in vitro* antioxidant potential of AEDA and suggest that the nephroprotective effect of the extract is mediated, at least in part, through its antioxidant properties. The plant is known to contain bioactive phytochemicals such as flavonoids, saponins, and polyphenolic compounds, which may scavenge free radicals, stabilize cellular membranes, and enhance endogenous antioxidant systems [13].

Histopathological observations further corroborated these findings, as extract-treated groups showed reduced tubular necrosis, preservation of glomerular structure, and improved renal architecture compared to the gentamicin group. This structural protection aligns with the biochemical improvements observed.

CONCLUSION

In conclusion, these results indicate that the aqueous extract of *D. adscendens* mitigates gentamicin-induced renal injury through antioxidant-mediated mechanisms and preservation of tubular integrity, supporting the potential therapeutic relevance of this plant in traditional medicine and pharmacological applications. However, further studies investigating molecular pathways, inflammatory mediators, and specific active compounds are warranted to elucidate the precise mechanisms involved.

Acknowledgements

The authors are sincerely grateful for the grand apparatus support of the Alexander von Humboldt Foundation to M. AB Dongmo which was used for this study.

Author Contributions

CSS: Investigation, Methodology, Data analysis, Writing original draft. DFNN: Investigation, Methodology, writing initial manuscript draft. MFMD: Methodology, Data analysis, Review and editing. CBZ: Data analysis and processing, writing original draft. JJKW: Methodology writing, Data analysis, review and editing. AKN: Investigation, Methodology, Writing initial manuscript. RCNT: Investigation, data analysis. FGZ: Data analysis, Writing initial manuscript, ADA: Conceptualization, Investigation, Methodology, Data analysis and processing, Writing original draft, Review and editing. ABD: Review and editing, Validation, Supervision. All authors reviewed and approved the final version of the manuscript.

Data Availability Statement

The data that support the findings of this study are available and will be made available upon request.

Use of AI in Drafting of Manuscript

The authors declare that they have not used any generative AI/AI-assisted technologies in the writing of this manuscript.

Conflict of interest

The authors declared no conflict of interest.

Financial Support

None declared.

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HOW TO CITE THIS ARTICLE
Sonfack CS, Nkwayep DFN, Donfack MFM, Zangueu CB, Kojom JJW, Nkonjap AK *et al*. Antioxidant-mediated nephroprotective effects of the aqueous extract of *D. adscendens* (Sw.) DC. against gentamicin-induced renal injury in Wistar rats. J Phytopharmacol 2026; 15(4):190-198. doi: 10.31254/phyto.2026.15401

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