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Costus Afer Ker Gawl Leaves Against Gentamicin-induced Nephrotoxicity in Rats

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Introduction. The nephroprotective effect of the aqueous extract of *Costus afer* leaves was evaluated in male albino Wistar rats with gentamicin-induced kidney injury.
Materials and Methods. In a 2-phase study, 30 weight-matched male Albino Wistar rats were divided into 6 groups of 5 animals to receive gentamicin, 90 mg/kg/d (except for the control group) for 7 days in the first phase to induce kidney injury. The second phase was treatment of rats with 375 mg/kg, 750 mg/kg, and 1125 mg/kg of aqueous extract of *Costus afer* leaves. One group received Silymarin only. Body weight, daily fluid and feed intakes, and serum levels of creatinine, urea, and electrolytes were monitored on a weekly basis, and renal histology was evaluated at the end of the study.
Results. The aqueous extract of *Costus afer* significantly increased the feed intake and fluid intake in a dose dependent manner when compared with the gentamicin-treated group. Low and medium doses of the extract reversed the deleterious effect of gentamicin on the kidney. The extract also significantly decreased the absolute kidney weight and relative kidney weight when compared with the corresponding weights in the gentamicin-treated group. *Costus afer* significantly decreased serum sodium, blood urea, and serum creatinine levels and significantly increased serum potassium level in gentamicin-induced nephrotoxic rats.
Conclusions. Aqueous extract of *Costus afer* leaves may attenuate gentamicin-induced nephrotoxicity in rats.

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INTRODUCTION

Nephrotoxicity is one of the most common kidney problems and occurs when body is exposed to a drug or toxin.[1] The nephrotoxic mechanism of gentamicin is well known. Gentamicin-induced nephrotoxicity model is mostly used to evaluate in vivo nephroprotective activity of natural compounds.[2,3]

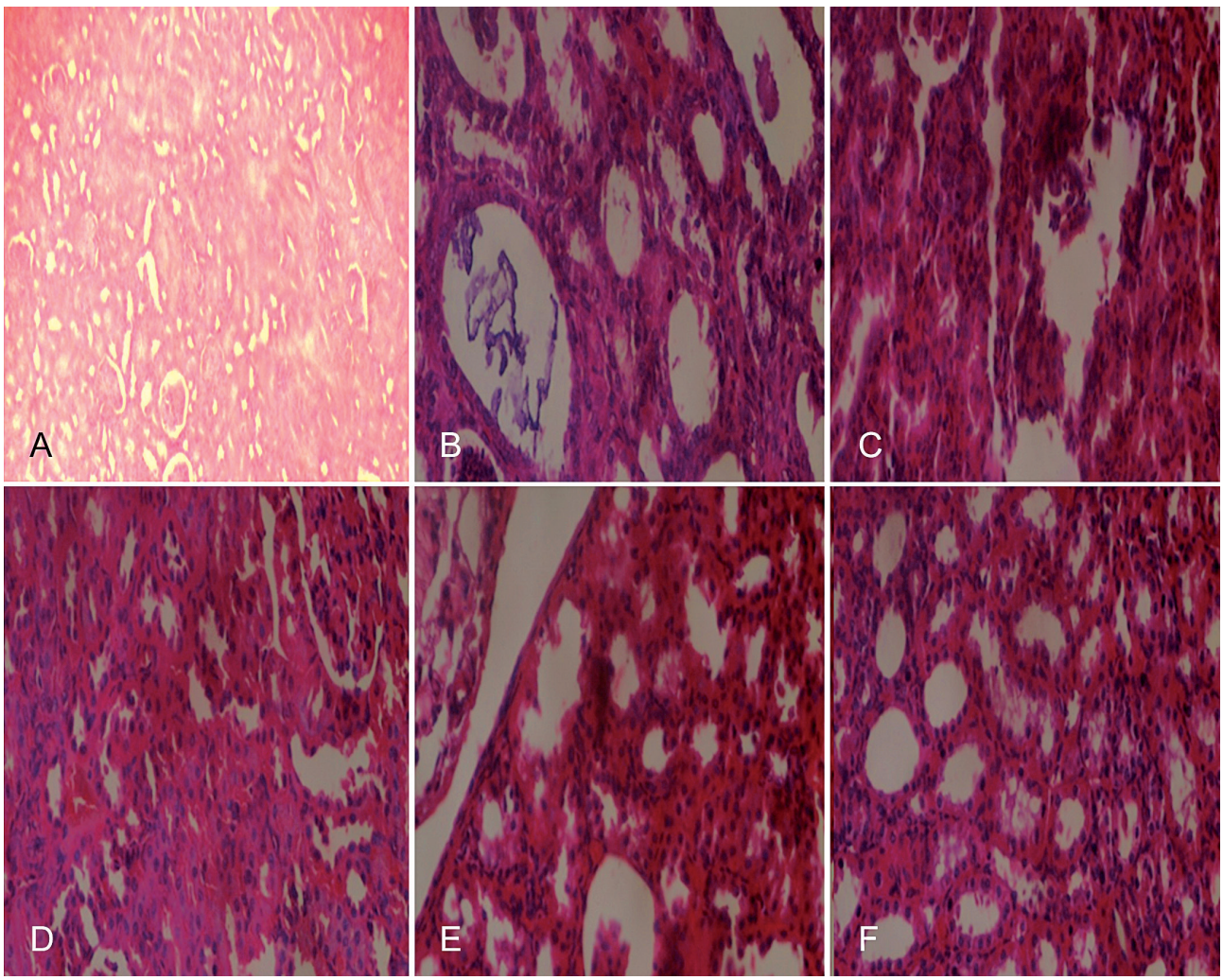
The plant *Costus afer* Ker-Gawl (*Costaceae*) is among 150 species of stout, perennial, and rhizomatous herbs of the genus *Costus*.[4] It can be found in the forest belt of Senegal, South Africa, Guinea, Niger, Sierra Leone, Ghana, Cameroon, and Nigeria.[4] *Costus afer* appears to have the potential as a renoprotective agent against nephrotoxic medications through its antioxidant, anti-inflammatory, and anti-apoptotic actions.[5] Hence, the present study aimed to assess the antinephrotoxic effect of the aqueous extract of *Costus afer* Ker Gawl leaves against gentamicin-induced nephrotoxicity in male albino Wistar rats.

MATERIALS AND METHODS

The leaves of *Costus afer* (Voucher Number, INTERCEDD/033) were collected from Pharmacognosy Garden of Faculty of Pharmaceutical Science, University of Port Harcourt, Rivers State, Nigeria, in November 2012. Acute toxicity study and phytochemical analysis of the aqueous extract of *Costus afer* Ker Gawl leaves was investigated according to standard protocols.[6] Adult male Albino Wistar rats weighing between 113 g and 212 g obtained from the Department of Pharmacology's animal house, Nnamdi Azikiwe University, Awka, Nigeria, were used in the study. They were kept under standard laboratory conditions with ambient temperature (25 ± 2°C), relative humidity (55% to 64%), and 12-hour light-dark condition cycles. The rats were acclimatized for 2 weeks adhering to the ethics of research on animals and fed with standard rat chow (Sander Nigeria Ltd) with water *ad libitum*.

Body weight-matched rats were divided into 6 group of 5 rats each as follows: group 1, no induction of kidney injury and no treatment (negative control); group 2, gentamicin and 2 mL of distilled water for 7 days (positive control); group 3, gentamicin and 375 mg/kg (25% LD_{50}) of *Costus afer* for 7 days; group 4, gentamicin and 750 mg/kg (50% LD_{50}) of *Costus afer* for 7 days; group 5, gentamicin and 1125 mg/kg (75% LD_{50}) of *Costus afer* for 7 days; and group 6, gentamicin and 100 mg/kg of Silymarin for 7 days (reference group).

Body weight and feed and fluid intake of these rats were monitored for 14 days. Thereafter, the rats were anesthetized with ether and blood



Nephroprotective effect of aqueous extract of *Costus afer* Ker Gawl leaves against gentamicin-induced nephrotoxicity in albino Wistar rats (hematoxylin-eosin). **A**, Control (normal); **B**, Gentamicin alone; **C**, Gentamicin and *Costus afer*, 375 mg/kg; **D**, Gentamicin and *Costus afer*, 750 mg/kg; **E**, Gentamicin and *Costus afer*, 1125 mg/kg; **F**, Gentamicin and Silymarin, 100 mg/kg.

samples and kidneys were collected. The kidney weight was taken and the kidney was fixed in 10% formalin for histopathological examination. Biochemical parameters were measured according to the standard protocols, including serum sodium, serum potassium, blood urea, and serum creatinine levels.[7]

All data were represented as mean ± standard error of mean. Comparisons were made using the Mann-Whitney test. Groups were considered to be significantly different when *P* values were less than .05.

RESULTS

The phytochemisty of aqueous extract of *Costus afer* leaves revealed the presence of alkaloids, saponins, flavonoids, tannins, phenols, glycosides and terpenoids. Administration of gentamicin reduced feed and fluid intake. The aqueous extract of *Costus afer* significantly increased the feed intake (from 58.86 ± 1.87 g to 62.21 ± 2.16 g) and fluid intake (from 73.29 ± 1.28 mL to 75.36 ± 1.53 mL) in a dose dependent manner when compared with the gentamicin-treated group. Low and medium doses of the aqueous leaves extract of *Costus afer* (25 50% LD_{50} and 50% LD_{50} or 375 mg/kg and 750 mg/kg, respectively) reversed the deleterious effect of gentamicin on the kidney (Figure). The extract also significantly decreased the absolute kidney weight (from 1.52 ± 0.12 g to 1.16 ± 0.09 g; $P < .001$) and relative kidney weight from 1.21% to 0.61% when compared with the corresponding weights in the gentamicin-treated group. However, *Costus afer* did not reverse the decrease in body weight observed following the administration of gentamicin (Table 1).

Costus afer significantly decreased serum sodium level ($P < .05$), significantly increased serum potassium level ($P < .05$), significantly decreased blood urea level ($P < .05$), and significantly decreased serum creatinine level ($P < .05$) in gentamicin-induced nephrotoxic rats (Table 2).

DISCUSSION

This study assessed the nephroprotective effects of the aqueous extract of *Costus afer* Ker Gawl leaves in gentamicin-induced nephrotoxic rats. The phytochemisty of aqueous extract of *Costus afer* leaves revealed the presence of alkaloids, saponins, flavonoids, tannins, phenols, glycosides

Table 1. Feed and Fluid Intake and Kidney Weight (Mean Values) of Gentamicin-Induced Nephrotoxic Rats Treated With *Costus Afer* Extract and Silymarin

Parameter	Animal Groups					
	Control	Gentamicin	Gentamicin + 25% LD50 *Costus Afer*	Gentamicin + 50% LD50 *Costus Afer*	Gentamicin + 75% LD50 *Costus Afer*	Gentamicin + Silymarin
Feed intake, g	157.80 ± 13.73	57.86 ± 1.79	58.86 ± 1.87	61.43 ± 1.99*	62.21 ± 2.16*	157.80 ± 13.73*
Fluid intake, mL	155.90 ± 18.69	61.79 ± 1.45	73.29 ± 1.28*	70.71 ± 2.28*	75.36 ± 1.53*	82.79 ± 2.41*
Absolute kidney weight, g	1.00 ± 0.05	1.52 ± 0.12	0.90 ± 0.05*	0.90 ± 0.05*	1.16 ± 0.09*	0.82 ± 0.06*
Relative kidney weight, %	0.64	1.21	0.59	0.49	0.61	0.55
Initial body weight, g	113	165	174.7	212	192	165
Final body weight, g	156.8	126.0	151.0	183.3	191.7	148.3

*$P < .05$

Table 2. Kidney Function Parameters (Mean Values) in Gentamicin-Induced Nephrotoxic Rats Treated With *Costus Afer* Extract and Silymarin

Parameter	Animal Groups					
	Control	Gentamicin	Gentamicin + 25% LD50 *Costus Afer*	Gentamicin + 50% LD50 *Costus Afer*	Gentamicin + 75% LD50 *Costus Afer*	Gentamicin + Silymarin
Serum sodium, mmol/L	132.40 ± 1.25	138.60 ± 4.57	133.20 ± 3.51	102.80 ± 9.29*†	135.60 ± 2.62	141.80 ± 1.16
Serum potassium, mmol/L	5.36 ± 0.14	5.76 ± 0.24	4.42 ± 0.16*	7.32 ± 0.43*†	13.42 ± 0.53*†	4.50 ± 0.16*
Blood urea, mmol/L	3.96 ± 0.09	14.88 ± 1.48‡	1.74 ± 0.36*†	9.32 ± 0.63*†	3.94 ± 0.12*	5.26 ± 0.16*
Serum creatinine , µmol/L	34.89 ± 7.69	131.40 ± 1.03‡	96.40 ± 4.84*	101.60 ± 8.79*†	87.40 ± 3.09*	79.00 ± 4.83*

*$P < .05$ as compared with the positive control (gentamicin) group
†$P < .05$ as compared with the Silymarin group
‡$P < .05$ as compared with the control group

and terpenoids, which agrees with the previous studies.[8] Gentamicin-induced nephrotoxicity is characterized functionally by increased serum creatinine and increased blood urea nitrogen.[9] The aqueous extract of *Costus afer* leaves significantly decreased urea and creatinine levels in gentamicin-induced nephrotoxic rats. This observation is similar to the results of Tava and colleagues[10] who reported that increase of serum creatinine and urea were inhibited significantly in rats simultaneously treated with olive leaf extract and gentamicin in comparison with gentamicin-only treated animals. Also our results on *Costus afer* is in agreement with protective effect of grape seed extract on gentamicin-induced acute kidney injury reported by Safa and colleagues.[11]

Alkaloids are known to have anti-inflammatory chatracteristics.[12] Flavonoids, saponins, and phenols are potent water-soluble antioxidants which prevent oxidizing cell damage, suggesting anti-inflammatory properties. The therapeutic potential of antioxidants in controlling degenerative diseases with marked oxidative damage from reactive oxygen species or free radicals have been reported.[12] Low and medium doses of the extract reversed the deleterious effect of gentamicin on the kidney (Figure).

CONCLUSIONS

The aqueous extract of *Costus afer* may have nephroprotective activities at least in part attributable to flavonoids, saponins, and phenols.

CONFLICT OF INTEREST

None declared.

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