International Journal of Research in Medical Sciences
Olukiran OS et al. Int J Res Med Sci. 2025 Oct;13(10):3940-3949
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20253128

Original Research Article

Effects of *Curcuma Aeruginosa* Roxb. on selected biomarkers of renal and liver function following gentamicin-induced nephrotoxicity and hepatic damage in male Wistar rats

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Received: 02 July 2025
Revised: 05 August 2025
Accepted: 25 August 2025

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ABSTRACT

Background: This study investigated whether *Curcuma aeruginosa* Roxb. (CAE) could improve kidney and liver function in rats with gentamicin (GM)-induced injury.
Methods: Thirty animals were divided into five groups. All groups received 100 mg/kg of GM for seven days. One group served as a positive control, another received the standard drug metformin, and the remaining three groups received different doses of CAE (100, 200, and 300 mg/kg). Metformin and CAE were administered orally for 28 days. After the treatment period, blood and tissue samples (kidney and liver) were collected for the assessment of liver and renal function markers. Histological examinations were also performed using H and E stains. The data was analyzed using one-way ANOVA, with a $p<0.05$ considered significant.
Results: Both metformin and a low dose of CAE significantly reduced plasma levels of cystatin-C (Cys C) and urea compared to the control group. However, the moderate and high doses of CAE did not significantly affect Cys C levels. The low dose of CAE significantly lowered ALT and AST in both plasma and liver tissue compared to all other groups. Histological examinations showed significant improvement in the kidney and liver tissues of rats treated with the low dose of CAE.
Conclusions: In contrast, the tissues of rats treated with metformin and the moderate and high doses of CAE showed no significant recovery from the GM-induced injury. The results suggest that the protective effects of this plant on the liver and kidneys are not dose-dependent, as the lower dose was more effective.

Keywords: *Curcuma aeruginosa*, Gentamicin, Kidney, Liver, Rats

INTRODUCTION

Gentamicin (GM), an aminoglycoside antibiotic, is a common treatment for serious and lethal infections by Gram-negative bacteria like bone infections and sepsis among others. However, its clinical application is constrained by undesirable adverse effects such as nephrotoxicity and hepatotoxicity.[1,3] The incidence of nephrotoxicity symptoms has been demonstrated to be as high as 30% in individuals receiving GM treatment.[4]

The proximal tubule serves as the primary region of GM accumulation, although it also collects in the final segment of the kidney tubule and urinary collecting tubule which activates tubular necrosis and glomerular congestion, which in turn lead to glomeruli and renal dysfunction by the production of free radicals, reduction in antioxidant

defense, mesangial cell contraction, with reductions in renal blood flow, leukocyte infiltration and cellular damages.[5] Furthermore, evidence suggests that GM triggers nephrotoxicity by elevating concentrations of various pro-inflammatory immune messengers, such as TNF-alpha and adhesion molecule ICAM-1.[6,7]

A host of problems arise when the kidneys fail, and advanced (end-stage) kidney failure is commonly managed with kidney transplantation and dialysis. Preventing GM-induced nephrotoxicity and hepatic damage would not only reduce morbidity and complications and decrease hospitalization costs but also potentially enable the use of higher dosages of this effective antibiotic, thereby enhancing its therapeutic potential. The substantial costs of care further emphasize the need for a cheaper alternative especially in the aspect of medications for liver and kidney diseases such as those induced by drug abuse of antibiotics. Phytochemicals exhibit a great potential in the treatment of pathological conditions due to their wide array of biological effects, including anti-oxidative, anti-mutagenesis, anti-inflammatory, myeloprotection, and immunomodulatory properties.[8] Naturally occurring substances with the ability to inhibit mutagenesis, oxidative damage, or inflammatory processes have been observed in drug-treated animals, positioning dietary constituents as highly encouraging candidates for preventing chemical and drug-induced organ damage.[9]

The genus *Curcuma*, in the *Zingiberaceae* family, includes perennial herbs with rhizomes and is naturally found in tropical and subtropical areas. There are nearly 93-100 species of curcuma.[10] CAE also belongs to the *Zingiberaceae* family. In Indonesia, this herbaceous plant is recognized for the distinct aroma of its rhizomes and has a rich history of traditional use for various ailments, including hypertension.[11] CAE is native to Indo-China and West Malesia. It's popular in Malaysia and Indonesia.[12] It grows best in a warm and moist atmosphere, either in the exposed or in semi-shade. It grows best in soils that are loose in structure, have a good texture, drain well, and are rich in nutrients.[13] CAE rhizome essential oils are medicinally valuable for their antiandrogenic, pain-relieving (antinociceptive), fever-reducing (antipyretic), anti-inflammatory, antioxidant, and antimicrobial effects, alongside their capacity to relax uterine muscles and suppress nitric oxide.[14]

According to the available published works, empirical evidence showing the ameliorative potential of CAE on chemical and drug induced liver and kidney damage is sparsely reported. Moreover, based on the reported antioxidant, antimicrobial, analgesic/anti-nociceptive function of CAE, and since oxidative stress triggered by free radicals' generation and inflammatory responses are the two main contributing factors to GM-related kidney toxicity and hepatic damage, the assumption is made that CAE could lessen kidney and liver damage induced by GM in rats.

Thus, the goal of this study is to evaluate the effects of CAE on GM-induced renal and liver damage in rats with a view to intending to scientifically document the plant's potential benefits as hepato and renoprotection in GM-treated patients.

METHODS

Drugs

GM sulphate (manufactured by Jiangsu Huayang Pharmaceutical Co., Ltd, China) is marketed as an antibacterial agent effective against diverse pathogenic Gram-negative and Gram-positive bacteria. Each ampoule contained 2 mL and 100 mg/kg was given to rats. Metformin hydrochloride used in this study is a product of Inventia Healthcare Pvt. Ltd in India. The rats received a 100 mg/kg dose of a 1000 mg tablet dissolved in distilled water. All remaining chemicals employed in this study were of analytical purity.

Plant extraction

Methanol extract of CAE rhizome

CAE was identified and authenticated at the Botany department, Bowen University, Iwo, Nigeria. The rhizomes were washed, cut into small, thin pieces, and rinsed. After being soaked in methanol for a few minutes, they were spread on a clean surface and left to dry for 28 days. After the time period had elapsed, they were crushed by an electric grinder to give a powdered substance. The powdered substance was then soaked in methanol and was placed in an electric shaker for three days. After 72 hr. of shaking, filtration was performed using Whatmann paper. Then, the liquid was placed in a vacuum evaporator to obtain the plant extraction yield. This was then dissolved in Tween-20. Graded doses of the extract were prepared so that each rat received 0.08 mL/100g. For rats receiving 100 mg/kg of CAE, a stock solution was prepared by the dissolution of 2.75 g of CAE in 17.6 mL of distilled water mixed with 4.4 mL of Tween 20.

Animal welfare and management

A total of thirty male Wistar rats, weighing between 120 and 150 g, were procured from the animal house facility at the college of health sciences, Bowen university, in Iwo, Osun State. The study was conducted there from January to April, 2025. The rats were kept in sanitary plastic cages and housed in the same location where the experiment was carried out. The rats were allowed two weeks to acclimatize under a natural 12-hour light/dark cycle, and they had unrestricted access to standard rat chow and water before drug administration and extracts commenced. This study adhered to the guide for the care and use of laboratory animals (NIH guide).[15] Ethical approval for the study was granted by the institutional review board of Bowen university, Iwo, Nigeria, under approval number BUTH/REC/2357.

Experimental design

Rats were divided into five groups, with six rats in each group. Over a period of four weeks, the rats received different treatments as follows:

Group 1 (Positive control): received a solution of Tween 20 and distilled water, which served as the vehicle for the extract.

Group 2 (Standard group): received 100 mg/kg of metformin orally.

Group 3: received 100 mg/kg of CAE rhizome extract orally.

Group 4: received 200 mg/kg of CAE rhizome extract orally.

Group 5: received 300 mg/kg of CAE rhizome extract orally.

After treatment period, rats were euthanized with ketamine hydrochloride and blood samples were drawn by puncturing the heart, and transferred into lithium heparin tubes, and immediately centrifuged at 3000 rpm for five minutes to isolate the blood's plasma. The plasma was stored frozen at 4° C until needed.

The kidneys were then removed, cleaned, and weighed using a Camry sensitive weighing balance (Camry, Zhejiang, China). Portions of the renal and hepatic tissues were blended in phosphate buffer solution using a glass homogenizer while on ice.

The homogenate was later centrifuged at 5000× gm for 5 minutes to obtain the supernatant, which was collected into plain bottles and stored frozen for later use.

Assessment of biochemical parameters

Biochemical kits sourced from Fortress Diagnostics (Antrim, UK) were used to determine the liver and renal markers in both plasma and renal tissue following standard colorimetric method while cystatin C was quantified using rat-specific ELISA kits (Elabscience Biotechnology Inc., Wuhan, China), following the manufacturer's sandwich ELISA principle.

Phytochemical analysis

Plant extract underwent qualitative phytochemical analysis to determine the presence or absence of alkaloid, phenols, saponins, terpenoids, glycosides, reducing sugars, tannins, flavonoids, and polyphenols.

Histological examination

The fixed kidney tissue was dehydrated through ascending grades of alcohol, cleared in xylene, and subsequently mounted in dibutyl phthalate polystyrene xylene (DPX). Slides were examined using an olympus CH light imaging system (Olympus, Tokyo, Japan), and photomicrographs were captured at 400× magnification with a Leica DM 750 camera.

Statistical analysis

All data represent the mean±standard error of mean. ANOVA was used to assess statistical differences, followed by Tukey's Kramer multiple comparison test (GraphPad Prism, GraphPad Software Inc., San Diego, California). For statistical significance, a threshold of $p<0.05$ was used.

RESULTS

Phytochemical screening result of methanol extract of CAE

The qualitative phytochemical assessment of CAE confirm the existent of saponins, flavonoid, tannins, terpenoids, alkaloids, glycosides, reducing sugars but polyphenols were absent (Table 1).

Table 1: Phytochemical screening result of methanol extract of CAE.

Test performed	Results
Saponins	+
Flavonoid	+++
Tannins	++
Terpenoids	+
Alkaloids	+
Glycosides	+
Polyphenols	-
Reducing sugars	+

"+" denotes present; "-" denotes absent

Plasma and renal tissue creatinine concentration (µmol/l) in rats treated with CAE following GM induced nephrotoxicity.

The plasma creatinine concentration of animals given a low, moderate and large doses of CAE extract did not significantly vary ($F=28.01$; $p=0.264$) from rats treated with GM only. Similarly, metformin did not significantly lower the plasma creatinine in the rats. Furthermore, metformin was not able to significantly reduced creatinine concentration in plasma relative to CAE at the three doses used in this study (Figure 1A).

The changed level of creatinine in the kidney tissue of rats following GM administration was not significantly reversed ($F=1.706$; $p=0.149$) by metformin and CAE at low, moderate and high doses, respectively. Also, no significant difference was observed in the kidney tissue creatinine of the rats treated with metformin as opposed to CAE treated group (Figure 1B).

Plasma and renal tissue urea concentration (mg/dl) in rats treated with CAE following GM induced nephrotoxicity

The moderate and high doses of CAE were able to significantly lower the urea concentration in the rat's following GM induced renal damage in the rats (F=12.02; p=0.032). However, low dose of the extract was not able to significantly lower the plasma urea level in the rats. Furthermore, the urea level in rats' plasma after treatment with metformin was not significantly different from that of those treated with the low, moderate and high doses of CAE (Figure 1C).

In contrast to plasma urea, the renal tissue urea concentration of rats treated with low, moderate and high doses of CAE and metformin remains unchanged when compared with the GM treated rats. Though, rats treated with low dose of CAE had lower urea concentration. Also, rats treated with the three doses of CAE had in their renal tissue, urea concentration that did not significantly vary (F=2.156; p=0.340) from metformin treated rats. Similar result was obtained when the renal tissue urea concentration of CAE treated rats at the three doses was compared with each other (Figure 1D).

Plasma and renal tissue Cys C concentration (ng/dl) in rats treated with CAE following GM induced nephrotoxicity

The low dose of CAE and metformin were able to significantly reduced (F=4.270; p=0.02) Cys-C concentration in the plasma of the rats following GM induced renal damage. Nonetheless, the moderate and high doses of CAE did not reverse the altered Cys-C level in the plasma of the rats. Relative to the rats treated with varying CAE doses, metformin did not significantly lower the plasma Cys-C. Furthermore, the Cys -C level of the rats treated with the low, moderate and high doses of the CAE was not significantly different from each other (Figure 2A).

The alteration in renal tissue Cys-C caused by GM administration was considerably lessened in rats treated with CAE at the low dose and metformin. However, the medium and high doses of CAE were not able to attenuate the alteration in Cys C in the rats. Metformin treated rats had renal tissue Cys-C level that was not significantly different (F=19.76; p=0.312) from that of the rats treated with the low, medium and high dose of CAE. The low dose of CAE reduced the concentration of Cys-C in the renal tissue compared to the medium and high doses (Figure 2B).

Plasma and liver tissue alanine transaminase (µmol/l) in rats treated with CAE following GM induced hepatotoxicity

The low dose of CAE significantly attenuated the plasma ALT activity of the rats (F=3.000; p=0.043). However, treatment with metformin, medium and high doses of CAE could not reverse the alteration in plasma ALT activity resulting from GM assault in the rats. Moreso, no significant difference existed within the plasma ALT activity of the metformin treated group when compared with CAE at the low, medium and the high doses (Figure 3A).

GM treatment significantly increased ALT activity in the liver tissue of the rats compared to rats treated with CAE and metformin (F=21.86; p=0.0001). However, low dose of CAE lessened the increased ALT activity in the liver tissue compared to the other groups treated with CAE and metformin (Figure 3B).

Plasma and liver tissue aspartate transaminase (µmol/l) in rats treated with CAE following GM induced hepatotoxicity

The plasma AST activity of the rats treated with different doses of the CAE and metformin was noticeably reduced compared to the rats treated with GM only. Moreso, no significant difference was seen between the serum AST concentration of rats treated with the metformin when compared with those treated with the low, medium and high doses of CAE (F=1.311; p=0.29) (Figure 3C).

Administration of CAE at the three doses and metformin did not cause a significant reduction (F=3.51; p=0.031) in AST activity in the liver tissue compared to rats treated with GM only. Additionally, the liver tissue AST activity of rats treated with metformin was not significantly different from that of rats treated with the low, medium and high doses of CAE (Figure 3D).

Plasma and liver tissue albumin concentration (g/dl) in rats treated with CAE following GM induced hepatotoxicity

The alteration in serum albumin concentration caused by GM administration was not significantly reversed (F=2.462; p=0.079) by treatment with CAE at the low, medium and high dose. Also, metformin was not able to significantly lower the plasma albumin concentration of the rats following GM administration. Additionally, no significant difference was found between the serum albumin concentration in rats treated with metformin when compared with the low, medium and high doses of CAE (Figure 4A).

GM administration significantly raised the liver albumin concentration in the rats which was restored by treated with metformin and CAE at the low and high doses (F=1.457; p=0.02). However, the medium dose of CAE did not significantly reverse the elevated liver albumin concentration in the rats. No significant difference was observed between the liver albumin concentration in the rats treated with metformin when compared with the low, medium and high doses of the CAE (Figure 4B).

Plasma and liver tissue total protein concentration (g/dl) in rats treated with CAE following GM induced hepatotoxicity

Total protein concentration in the plasma of rats treated with CAE at the three doses and metformin remains unaltered when compared with the rats treated with GM only. Moreso, no significant difference was noticed between the serum total protein concentration of the rats treated with metformin when compared with the low, moderate and high doses of the CAE (F=0.483; p=0.748) (Figure 4C).

GM induced significantly higher liver total protein in the rats was not reversed by the treatment with low and high doses of CAE and metformin (F=5.283; p=0.03). However, the medium dose of CAE reduced the liver total protein concentration, however, the value was not significantly different from the rats treated with GM only. The liver total protein concentration in rats treated with metformin was not significantly different from that of rats treated with the low, moderate and high doses of CAE (Figure 4D).

Photomicrographs of rats treated with CAE following GM induced nephrotoxicity

Light micrograph of the kidneys of rats administered with GM only demonstrated widened bowman space (yellow arrow) and severe distention of the renal tubules whereas the rats that were given metformin showed slight dilatation of the renal tubules and bowman's space (yellow arrow). The photomicrograph of the kidney tissue of the rats treated at the low dose (100 mg/kg) showed improved kidney histoarchitecture with the glomeruli, urinary capsule, proximal tubule and distal tubule all well-defined. However, the photomicrographs of those treated at the moderate and high doses (200 and 300 mg/kg) exhibited leukocytes infiltration, within the matrix around the glomerulus (black arrow) and inflammation and congestion of the renal corpuscle (blue arrow) respectively (Figure 5).

Photomicrographs of rats treated with CAE following GM induced hepatotoxicity

Light micrograph of the rats' liver treated with GM only indicated centrilobar necrosis with extensive vascular congestion (yellow arrow) while rats treated with metformin (Standard drug) revealed mild vacuolation (red arrow) and necrosis of the hepatocytes. The photomicrographs of the renal tissue of the rats treated at the low dose (100 mg/kg) indicated regular arrangement of the hepatocyte with clearly visible nucleus, arranged in plates round the central vein with sinusoids between the plates but the photomicrographs of rats treated with 200 mg/kg of CAE showed plates of hepatocyte radiating from central veins (black arrow) seen with mild congestion of the sinusoids. Also, the photomicrographs of rats treated with 300 mg/kg of CAE revealed severe congestion of the central vein and sinusoids as well as some necrotic hepatocytes (blue arrow) respectively (Figure 6).

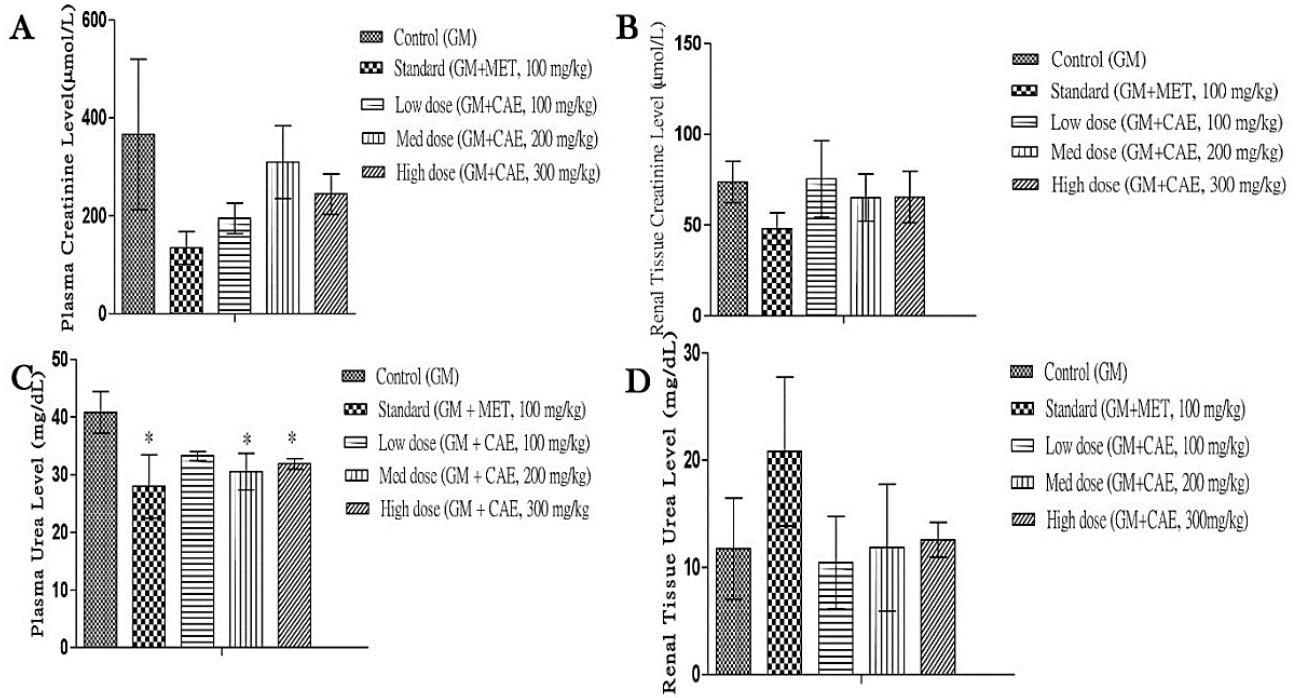

Figure 1 (A-D): Plasma and renal tissue creatinine and urea concentrations in rats treated with CAE following gentamicin induced nephrotoxicity.

*Significantly different from the control (GM) ($p<0.05$) (One-way ANOVA followed by Newman-keuls' post-hoc), bars represent mean±SEM, (n=5).

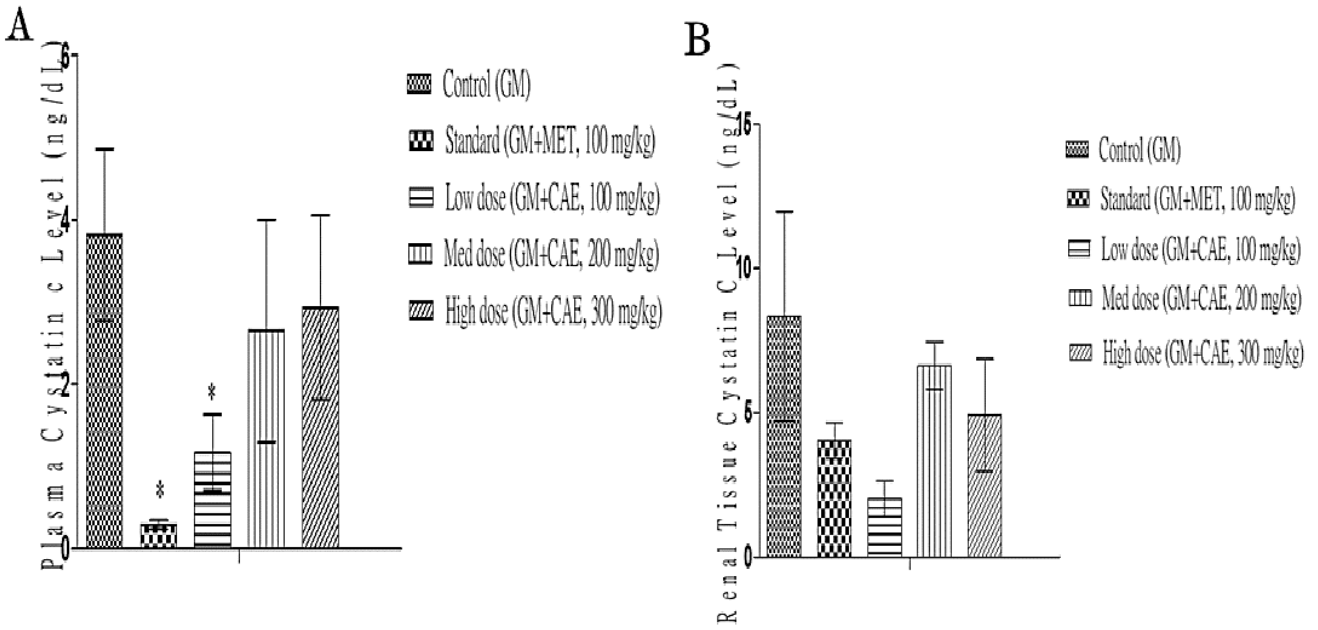

Figure 2 (A and B): Plasma and renal tissue cystatin C concentration in rats treated with CAE following gentamicin induced nephrotoxicity.

*Significantly different from the control (GM) ($p<0.05$). (One-way ANOVA followed by Newman-keuls' post-hoc), bars represent mean±SEM, (n=5).

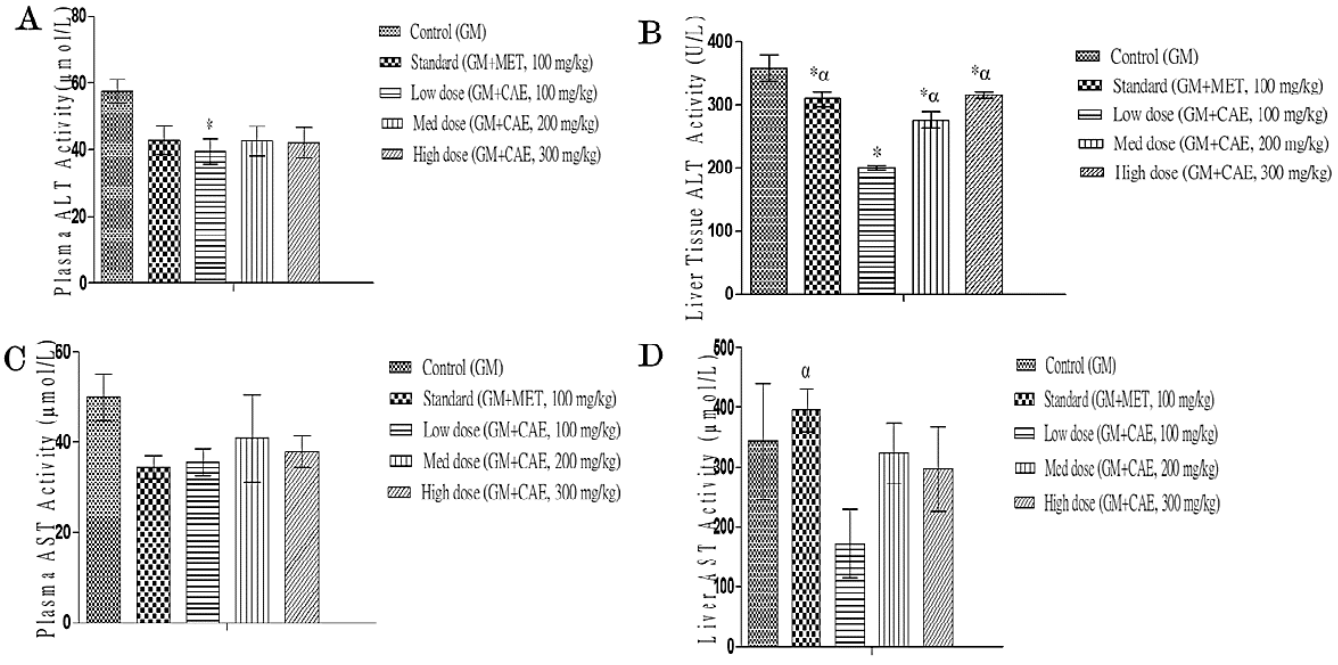

Figure 3 (A-D): Plasma and liver tissue alanine and aspartate transaminases in rats treated with CAE following gentamicin induced hepatotoxicity.

*Significantly different from the control (GM). $^{\alpha}$=significantly different from the low dose of extract (100 mg/kg) ($p<0.05$). (One-way ANOVA followed by Newman-keuls' post-hoc), bars represent mean±SEM, (n=5).

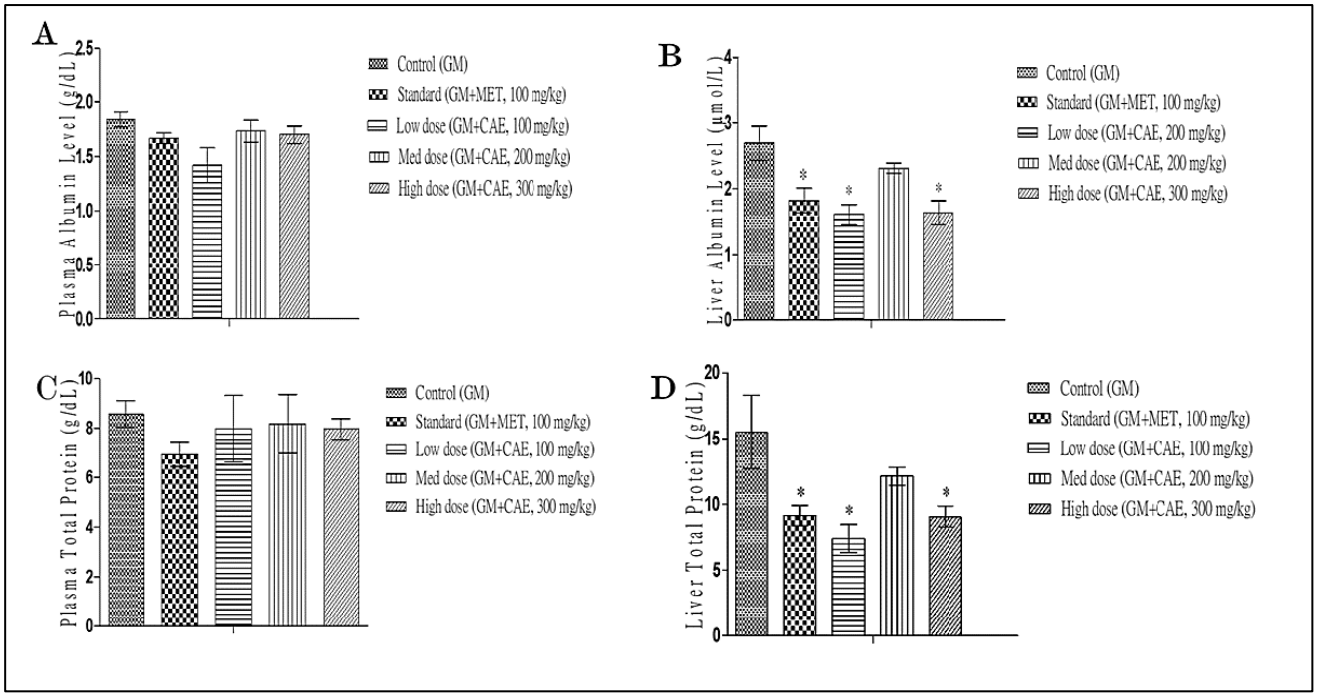

Figure 4 (A-D): Plasma and renal tissue albumin and protein concentrations in rats treated with CAE following gentamicin induced hepatotoxicity.

*Significantly different from the control (GM) ($p<0.05$)(One-way ANOVA followed by Newman-keuls' post-hoc), Bars represent mean±SEM, (n=5).

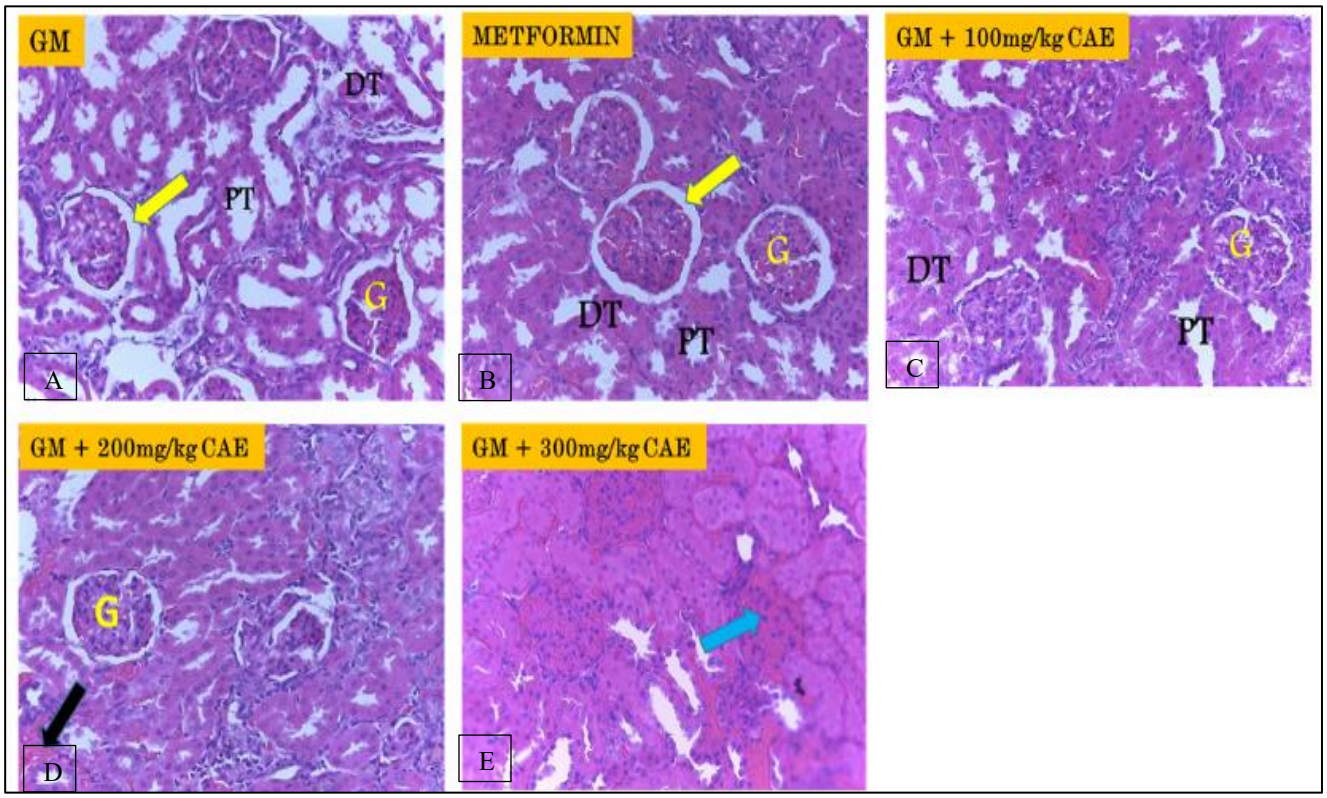

Figure 5 (A-E): Representative photomicrographs of rats treated with CAE following gentamicin induced nephrotoxicity.

Rats that received only gentamicin showed severe kidney damage, in contrast to those treated with metformin, who revealed mild damage. Low-dose treatment improved the kidney histoarchitecture in rats, whereas moderate and high doses were unable to significantly reverse the gentamicin-induced changes.

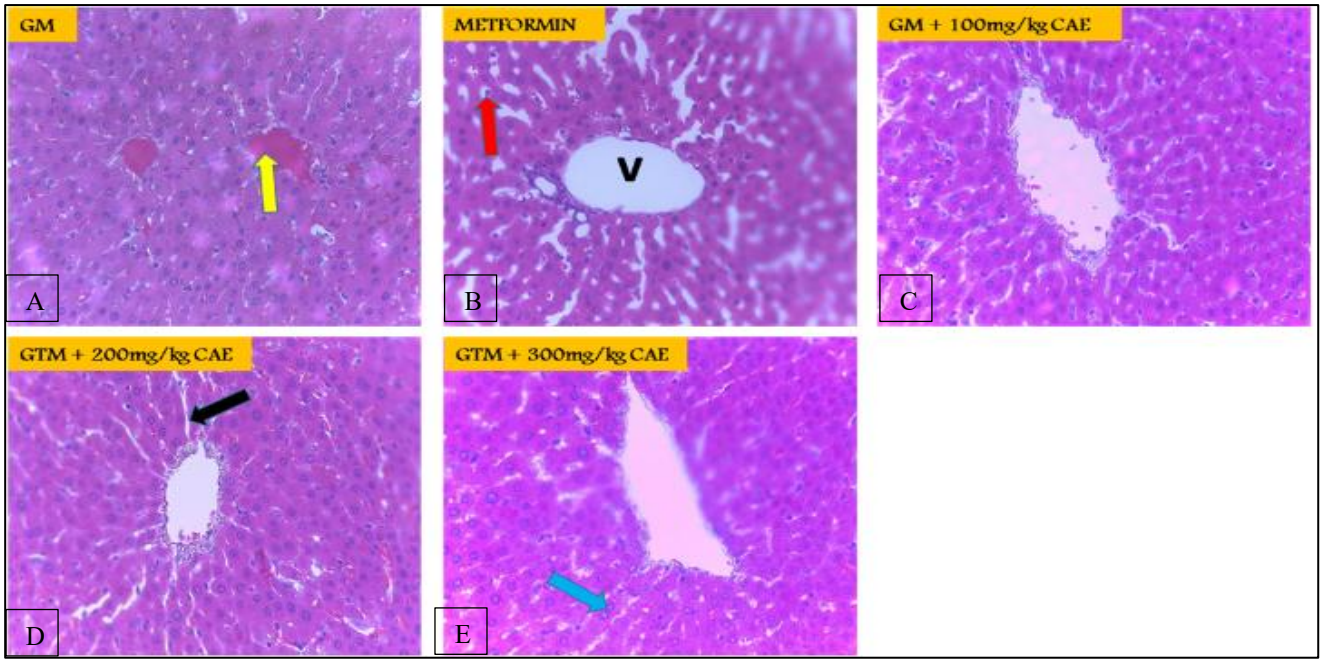

Figure 6 (A-E): Representative photomicrographs of rats treated with CAE following gentamicin induced hepatotoxicity.

Rats treated with gentamicin showed severe liver damage, while those given metformin had only mild damage. Low-dose treatment improved liver's histoarchitecture in rats, whereas moderate and high doses had no significant effect on alterations caused by gentamicin

DISCUSSION

The liver and kidneys are primarily linked by the urea cycle (also known as the ornithine cycle), a series of reactions in which the liver converts nitrogenous waste into less toxic urea. Urea is released from hepatocytes into the bloodstream and subsequently transported by the kidneys. Hence, chronic hepatic disease can lead to renal failure and vice versa as seen in this study, where drug induced nephrotoxicity leads to hepatic damage.

Creatinine, a constant byproduct of muscle creatine phosphate, is almost entirely cleared from the blood by the kidneys. A decline in kidney function results in reduced creatinine clearance by the kidneys, leading to higher blood creatinine.[16] As part of this research, it was noticed that the creatinine of rats treated with varying doses of CAE was not significantly difference from that of the control (GM). This observation supports the findings of Tomsa et al who reported significantly higher creatinine in curcumin-supplemented rats compared to control following GM induced nephrotoxicity.[17] In contrast, research carried out by Laorodphun et al showed that curcumin lowered BUN and creatinine in the serum of GM-nephrotoxic rats.[18] The kidney's photomicrograph of GM group, and rats treated with moderate and high doses of CAE showed distortions in the histoarchitecture of their kidneys. This should have elicited an elevation in their plasma creatinine concentrations since GM has been reported to increase renal vasoconstriction and tubular injury, and decrease glomeruli ultra-coefficient, thereby reducing rate of glomeruli filtration.[19] The fact that the creatinine of the treated rats was comparable to the control group as seen in this study could indicates that the dose of GM used and the duration of administration might not be sufficient enough to cause significant elevation in the plasma levels of creatinine by constricting or increasing renal vascular resistance. This is further supported by studies that revealed that male Sprague Dawley rats exposed to GM can develop extensive proximal tubule necrosis (up to 75%) before any detectable increases in BUN or sCr.[20]

Cys C is an endogenous biomarker of kidney function and it's consistently produced by all nucleus-containing cells, independent of muscle mass. It's cleared from the bloodstream solely by glomerular filtration, with full reabsorption and breakdown within the initial segment of the renal tubule, with negligible excretion in urine.[21] Urine Cys C has been validated as a suitable biomarker for detecting acute tubular and glomerular injury in rats, showing an increase when the proximal convoluted tubule (PCT) exhibits impaired re-absorptive function.[22] Plasma Cys C levels increase before creatinine levels in cases of acute kidney injury. Rats treated with the standard drug and low-dose extract had significantly lower plasma Cys C concentrations than the control (GM) group. Plasma Cys-C increase occurs earlier in cases of drug induced nephrotoxicity.[23] This indicates it's a more sensitive marker for early kidney impairment than creatinine. The decreased Cys C level that was seen in the plasma of the rats with CAE could be as a result of decreased vascular resistance and tubular necrosis resulting from reduced oxidative stress and cellular damage. This assertion is

substantiated by He et al study.[24] They found that curcumin ameliorate acute kidney injury caused by GM by preventing cellular stress from free radicals and cell death in the renal tubules. Blood urea nitrogen (BUN) is a nitrogenous compound synthesizes by the liver as the final product of protein metabolism and urea cycle. Elevated serum urea levels indicate diminished kidney clearance, as seen in short-term and long-term kidney failure and impairment.[16] The plasma concentration of urea is dependent on the rate of excretion by the kidney. The elevation of urea that was seen in rats treated with GM only may indicate renal injury associated with GM administration, leading to an impaired kidney filtering capacity with abnormal retention of urea. Its concentration significantly decreased in the rats administered with medium and large doses of the extract relative to the control (GEN). This finding appears to validate the earlier work of Bulboaca et al that curcumin administration decreased BUN levels in male Wistar-Bratislava rats.[25] The observed decrease in urea concentration in the experimental animals may have arisen from the ability of CAE to restore the structural integrity of the nephron following GM induced renal damage, since the photomicrographs of their renal tissues showed signs of leukocytes infiltration in the matrix around the glomerulus, inflammation and congestion of the renal corpuscle respectively but may be ascribed to the inhibition of the enzyme arginase that is required for the conversion of arginine to urea, by the extract thereby reducing urea production. This needs to be further investigated.

Transaminases, are extensively recognized as the most specific indicators of hepatocellular necrosis (liver cell death). They are the most commonly used and specific indicators of hepatocellular necrosis.[26] Significantly raised plasma activity of alanine and aspartate transaminases, are a strong indication of liver injury especially one involving liver inflammation. Studies from Ezeuko et al showed that Curcuma longa significantly attenuated the activities of aspartate aminotransaminases and alanine aminotransaminases in the serum and liver tissue upon CCl_4-induced liver injury in rats.[27,28] Lee et al further indicated that hepatic enzymes, including AST and ALT were noticeably lowered in rats that were treated with *Curcuma longa*.[28] This observation supports our study's findings which demonstrated that the plasma transaminases of rats that received the medium and large of doses of CAE was lower but not significantly different from the control (GM), however, rats given 100 mg/kg of CAE had plasma activity of transaminases that was significantly reduced compared to the control (GM). The hepatoprotective ability of CAE from CAE is indicative of the membrane-stabilizing properties of its phytochemical constituents.

The liver is responsible for synthesizing almost all plasma proteins in the body, including albumin, binding globulins, protein C, protein S, and all intrinsic and extrinsic clotting factors.[29] Destruction of liver cells results in lower serum levels of total protein, albumin and globulin caused by disruption and dissociation of polyribosomes on rough endoplasmic reticulum. The total protein and albumin concentration in the plasma of the rats exposed to GM only was not notably different from the rats given the extract. However, the liver tissue protein and albumin of the rats treated with the GM only was notably higher than in the extract-treated rats. This possibly arose from rapid mitosis of the hepatocytes in order to compensate for the loss hepatic cells. This is supported by the photomicrographs of this group's liver cells, which exhibited centrilobular necrosis.

Limitations

This study did not identify the specific bioactive compound responsible for CAE 's rhizome protective effects. Additionally, the molecular mechanisms behind the rhizome's therapeutic action were not investigated.

CONCLUSION

CAE was found to effectively protect against GM-induced kidney and liver damage in rats. Interestingly, the lowest dose of 100 mg/kg was the most effective, suggesting the plant's protective effects aren't dependent on a higher dose. This therapeutic action is likely due to the plant's phytochemicals, making CAE a promising candidate for new drug development to treat kidney and liver injuries.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee National Institutes of Bowen University, Iwo, Nigeria with approval number (BUTH/REC/2357).

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Cite this article as: Olukiran OS, Adeniran IA, Adeniran EE, Orekoya EA, Akomolafe RO. Effects of *Curcuma Aeruginosa* Roxb. on selected biomarkers of renal and liver function following gentamicin-induced nephrotoxicity and hepatic damage in male Wistar rats. Int J Res Med Sci 2025;13:3940-9.