JBAAR
Journal of Basic and Applied Research in Biomedicine
ISSN 2710-1479

Original Article

Ameliorative Potentials of *Garcinia kola* and Kolaviron on Bisphenol A Induced-renal Toxicity in Male Wistar Rats

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HISTORY
Received: 15-04-2026
Revised: 27-06-2026
Published: 31-10-2026

FUNDING
The authors declare that this research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST
The authors declare no conflict of interest in this study.

DATA AVAILABILITY
The data that support the findings of this study are available from the corresponding author upon reasonable request.

ABSTRACT

Background: Exposure to bisphenol A (BPA) has been linked to impaired renal function likely due to its ability to induce oxidative stress, DNA damage and apoptosis. Antioxidants, such as *Garcinia kola* and its biflavonoid extract, kolaviron, have been suggested as natural substances that may mitigate or ameliorate BPA induced toxicities.

Objective: This study was therefore designed to evaluate the ameliorative potentials of *G. kola* and kolaviron on BPA-induced renal toxicity.

Methods: Forty male Wistar rats were divided into five groups (n=8) and treated orally for 28 days as follows; Groups I (control) and II (vehicle control) received distilled water (1.5 mL/kg) and corn oil (1.5 mL/kg) while Groups III-V received BPA (50 mg/kg), BPA+*G. kola* (200 mg/kg), and BPA+kolaviron (200 mg/kg). Thereafter, urine samples were collected overnight in metabolic cages and analysed for urea, creatinine, total protein (TP), albumin, red blood cells (RBC) and glucose. Renal samples were excised after euthanasia by cervical dislocation and fixed in 10% buffered formalin for histological evaluation using Haematoxylin & Eosin and Periodic Acid Schiff stains, respectively.

Results: Group III had significantly elevated urea, creatinine, TP and albumin compared to control, whereas the increases in glucose and RBC count were not significant; TP and albumin were also significantly higher than in the vehicle group. In IV and V relative to III, TP, albumin, glucose and RBC count were lower, but not significantly. Renal structural and tubular aberrations consistent with tissue injury and inflammation were observed in III compared to I, IV and V, respectively.

Conclusion: This study suggests that bisphenol-A induced renal toxicity may be mitigated by *G. kola* and its biflavonoid extract, kolaviron.

Keywords: *Bisphenol A, Renal function, Garcinia kola, Kolaviron, Antioxidants*

Cite this article as: Taiwo, O.D., Omodon, A.C., Emediong, I.E., Adele, B.O., Ige A.O. (2026) Ameliorative Potentials of *Garcinia kola* and Kolaviron on Bisphenol A Induced-renal Toxicity in Male Wistar Rats. Journal of Basic and Applied Research in Biomedicine, 12(1): 51-57

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INTRODUCTION

Endocrine Disrupting Chemicals (EDC) are defined by the Endocrine Society as exogenous chemicals that alter any aspect of hormonal action (Gore *et al.,* 2015). They mimic, block and interfere with the body's endocrine system. Bisphenol A, is an EDC which mimics the hormone, estrogen, and has been shown to exert multi-organ toxic effects to the body (Yukta *et al.,* 2025). About 70% of bisphenol A produced is used in the production of polycarbonate plastics such as reusable water bottles, baby feeding bottles, food packaging materials, helmets, eyeglass lenses and safety goggles while about 25% is used in the production of epoxy resins that are used as adhesives and protective coatings such as those lining the inner surfaces of cans. The remaining 5% is used in the production of phenolic resins, unsaturated polyester resins, polyvinyl plastics, thermal paper, car tires and flame retardants (EFSA *et al.,* 2023). Bisphenol A has been observed to leach into food when BPA containing food packages are subjected to high temperatures, reused, or manipulated (Kursunoglu and Yurekli, 2022).

In humans, the main route of BPA exposure is via ingestion, but it can also be absorbed through inhalation from the air and dermal exposure (Li and Suh, 2019). However, exposure routes to BPA vary significantly across different population groups due to differences in lifestyle and occupation. Infants and young children are among the most susceptible groups, with exposure often occurring through food and drink containers, toys, and even breastfeeding if BPA has accumulated in the mother's body (Zheng *et al.,* 2024, Yesildemir *et al.,* 2024). Following exposure, BPA most commonly undergoes hepatic first-pass metabolism immediately after absorption, before it enters systemic circulation. Once in the bloodstream, BPA binds to plasma proteins, mainly albumin, facilitating its transport to various tissues, including the kidneys (Gayrard *et al.,* 2023).

BPA has been shown to affect multiple organs and systems including the kidneys mainly via initiating oxidative stress by creating an imbalance between antioxidants and reactive oxygen species (Ma *et al.,* 2019 & Chen *et al.,* 2022). Studies have therefore suggested that increased consumption of antioxidants, especially natural antioxidants, may prevent the development of multi-organ BPA induced toxicities including renal impairment **(**Abdelrazik *et al.,* 2022 & Mączka *et al.,* 2022**).**

Garcinia kola (G. kola) seeds, the mature seeds of *G. kola* Heckel also known as bitter kola, belongs to the genus *Garcinia* and are characterized by their bitter taste and smooth, elliptical morphology. It is primarily distributed in the tropical and humid regions of West and Central Africa, where they are widely consumed recreationally and serve as a customary offering symbolizing hospitality and reverence in traditional, ceremonial, and social settings (Emmanuel *et al.*, 2022). It is reported to be rich in antioxidants and has been shown to alleviate a series of toxicities via potentiation of antioxidant defense and anti-inflammation based mechanisms (Tauchen *et al.,* 2023). It has attracted considerable scientific interest due to its wide

ethnomedicinal applications and phytochemical profile. Phytochemical investigation of *G. kola* has identified several unique bioactive constituents, including kolaviron which takes credit for several of its therapeutic effects (Rotimi et al., 2022; Tauchen et al., 2023). Kolaviron, is a biflavonoid complex in *G. kola* that consist of Garcinia biflavonoid-1 (GB1), Garcinia biflavonoid-2 (GB2), and kolaflavanone (Rotimi *et al.,* 2022). *G. kola* and kolaviron have been linked to a broad spectrum of pharmacological activities, including antioxidant, anti-inflammatory, hepatoprotective, cardioprotective, renoprotective, antimicrobial, antidiabetic, neuroprotective and anticancer effects (Tauchen, *et al.,* 2023). However, whether *G. kola* or its active biflavonoid extract, kolaviron can prevent or alleviate BPA-induced renal impairment is largely under explored. This study was therefore designed to investigate the effects of *G. kola* and kolaviron on BPA-induced renotoxicity in male Wistar rats. Animals were exposed to BPA orally in order to mimic the main exposure route to the toxic substance as has been reported by Li and Suh (2019). The Null hypothesis for this study is that neither *G. kola* nor its biflavonoid extract, kolaviron exerts any significant preventive or alleviating effect on BPA induced renal impairment. As alternative hypothesis, animals treated with *G. kola* and to greater extent, kolaviron will show a significant preventive or alleviating effect against BPA-induced renal impairment.

MATERIALS AND METHODS

Preparation of plant material and extraction procedure

G. kola was purchased from a local market, its seeds were peeled, sliced, air dried, ground to a powder and stored in a sterile plastic container until needed. Powdered *G. kola* seed was suspended in distilled water daily and administered at a dose of 200mg/kg (Omodon *et al.,* 2024). Kolaviron was extracted from *G. kola* seeds as previously described (Omodon *et al.,* 2024). Briefly, powdered *G. kola* seeds (as described above) (500g) were defatted with n-hexane for 72 h, using the cold maceration method. The hexane extract was collected and the process repeated twice with fresh n-hexane each time. The defatted marc was then dried and then repeatedly extracted with acetone thrice in order to obtain crude kolaviron extract which was then concentrated using a rotary evaporator at 40 °C. This was diluted to twice its volume and then partitioned with ethyl acetate. The ethyl acetate fraction was concentrated to yield a golden-brown powder, kolaviron. The identity and purity of kolaviron was evaluated by subjecting it to thin-layer chromatography using silica gel GF 254-coated plates and solvent mixture of methanol and chloroform in the ratio 1:4 v/v (Adaramoye et al., 2005). The yield of the preparation was 6%.

Animal model

Forty (40) adult male Wistar rats (165 – 180g) were obtained from the Central Animal House, University of Ibadan, Nigeria and housed in well aerated laboratory cages and maintained at room temperature (25-27ºC) with alternate natural day and night time cycles. They were fed standard rat feed, had access to clean drinking water *ad libitum* and were maintained in humane conditions in accordance with the Guide for the Care and Use of Laboratory Animals (NRC, 2011). Only male rats were used in this study in order to avoid estrogenic cyclical confounding variables against a known oestrogen-mimic i.e., BPA. The animals were acclimatized for two weeks prior to commencement of experimental procedures and subsequently randomly divided into 5 groups (n=8) as follows; Groups I (Control) and II (vehicle control) received distilled water (1.5mL/kg) and corn oil (1.5mL/kg) respectively. Groups III-V received BPA (50mg/kg, Sigma Aldrich, USA) suspended in corn oil, BPA + *G. kola* (200 mg/kg) (Omodon *et al,* 2024) and BPA + kolaviron (200 mg/kg) (Kayinu *et al.,* 2024), respectively. All treatments were given for 28 days using an oral cannula.

Biochemical assays

At the end of experimentation, animals (n=5) were individually placed in metabolic cages and overnight urine samples were collected and analysed for urea (Orsonneau, *et al.,* 1992), creatinine (Thammitiyagodage, *et al.,* 2020), total protein (Lowry *et al.,* 1951), albumin (Chen *et al.,* 2004), red blood cells (Karamercan *et al*., 2011) and glucose (urine glucose assay kit; Crystal Chem, USA) using standard laboratory procedures and commercially available kit. Animals were then humanely euthanised using ketamine (75 mg/kg *i.p.*) followed by cervical dislocation.

Histological analyses

Animals (n=3) were also euthanised by cervical dislocation after ketamine (75mg/kg *i.p.*) anaesthesia, kidneys were harvested, washed in normal saline and then fixed in 10% buffered formalin solution. Tissues were processed, embedded in paraffin wax and stained with Haematoxylin and Eosin and Periodic Acid Schiff stains, respectively for evaluation of gross structural and renal tubular changes as described by Feldman and Wolfe (2014). Sections were examined by an investigator blinded to the treatment groups.

Statistical analysis

Statistical analyses were carried out using Prism by GraphPad (San Diego, USA) version 10. Data were presented as mean ± standard error of mean (SEM) and analyzed using one way ANOVA followed by Tukey multiple comparisons post hoc test. Each group was compared with the control (group I) and the vehicle control (group II), as indicated in Fig. 1. Normality and homogeneity of variance were not formally tested. Statistical significance between groups was taken at $p < 0.05$.

RESULTS

Effects of *G. kola* and kolaviron on urinary urea and creatinine levels following BPA exposure

Urinary urea levels (mmol/L) were significantly increased in group III (144.3±7.8) and IV (143.7±7.2) compared with I (108.0±5.8). In contrast, rats treated with BPA and kolaviron, i.e., group V, exhibited a 16.8% reduction in urea levels when compared to the BPA-only group (120.0±5.4 vs 144.3±7.8), which was not statistically significant. No significant difference was observed between groups I (108.0±5.8) and II (121.0±8.4). Values in group III were 19.3% higher than in II (vehicle), but this difference was not statistically significant (Fig. 1A). Urine creatinine levels (mg/dL) in groups II (80.2±3.0), III (93.3±5.9), IV (89.5±4.7) and V (86.4±4.7) increased by 20.2%, 39.9%, 34.2% and 29.5% compared with I (66.7±2.0), with values in III, IV and V being significantly increased compared to I. Values obtained in groups II (vehicle), IV and V were not significantly different from that in III (Fig. 1B).

Effects of *G. kola* and kolaviron on urinary total protein and albumin levels following BPA exposure

Urine total protein levels (mg/dL) in group III significantly increased by 52.1% and 32.3% when compared to control (I) and vehicle control (II), respectively. The values in groups IV (68.0±2.1) and V (58.7±4.6) were reduced compared with III (75.0±4.5). No significant difference was observed between values in groups I (49.3±3.5) and II (56.7±5.1) (Fig. 1C). Urinary albumin level (mg/L) in group III (39.3±2.9) significantly increased compared with I (20.3±1.5) and II (24.5±3.5), respectively. Values obtained in IV (30.7±3.8) and V (29.3±1.8) showed reduced urinary albumin levels compared with values in III (39.3±2.9). No significant difference was observed between group I (20.3±1.5) and II (24.5±3.5), respectively (Fig. 1D).

Effects of *G. kola* and kolaviron on erythrocyte count following BPA exposure

Erythrocyte count (RBC/high power field counts, HPFc) in urine was increased in group III (3.0±0.6) compared with I (1.7±0.7), although this increase was not statistically significant. Values in group IV (2.2±0.3) and V (2.1±0.1) were reduced compared with III. No significant difference was observed between groups I (1.7±0.7) and II (2.3±0.3). (Fig. 1E).

Effects of *G. kola* and kolaviron on urinary glucose level following BPA exposure

Urinary glucose levels (mg/dL) in group III (16.67±1.86) were 31.6% and 28.2% higher than in I (12.67±0.67) and II (vehicle) (13.00±1.00), respectively, but these differences were not statistically significant. Values in group IV (14.33±0.33) and V (13.67±0.33) were 14.0% and 18.0% lower than in III, respectively, although not significantly. No significant difference was observed between groups I (12.67±0.67) and II (13.00±1.00) (Fig. 1F).

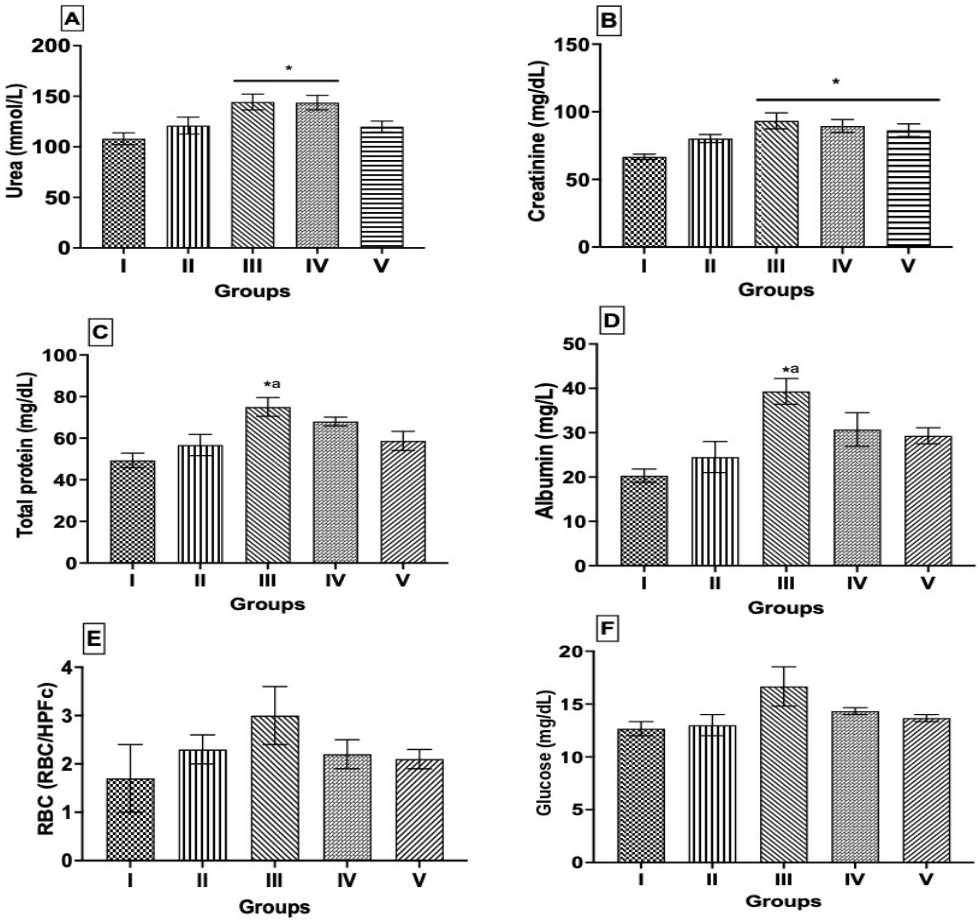


Figure 1: Urinary biochemicals in control and experimental groups assayed for urea (A), creatinine (B), total protein (C), albumin (D), red blood cell (E) and glucose (F). Values are expressed in Mean ± SEM, n = 5, * indicates values that are significantly different ($p < 0.05$) compared with group I (Control); ª indicates values that are significantly different ($p < 0.05$) compared with group II (vehicle).

Histological Investigation

Structural evaluation of renal tissues in control and experimental groups

The structural histological assessment of the renal tissues (Figure 2) at lower (x100, A1-E1) and higher magnification (x400, A2-E2) showed normal renal histoarchitecture with intact glomeruli, normal mesangial cells and Bowman's capsular spaces (white arrow), preserved renal tubules (blue arrows), and normal interstitial spaces (slender arrow) in groups I and II (Fig. 2A1-A2 and 2B1-B2). The BPA only-treated group (III) exhibited marked histopathological alterations characterized by disrupted renal architecture (white arrow), few tubules exhibit eosinophilic fluid within their lumen (green arrow), interstitial spaces appear widened with infiltration by inflammatory cells (slender arrows), and evidence of tubular degeneration (blue arrow) (Fig. 2C1-C2). In group IV, renal samples exhibited markedly ameliorated renal damage, with restoration of near-normal glomerular (white arrow) and tubular architecture (blue arrow) and reduced interstitial inflammation (slender arrow) (Fig. 2D1-D2). Similarly, group V showed improved renal architecture with preserved glomeruli and tubules (white arrow), although few tubules exhibit eosinophilic fluid within their lumen (green arrow) and mild inflammatory cell infiltration within the interstitium (slender arrow) still persisted (Fig. 2E1-E2).

Evaluation of renal tubules in control and experimental groups

Samples (Figure 3) at lower (x100, A1-E1) and higher magnification (x400, A2-E2) from the control groups (I) and vehicle (II) showed normal basement membranes of the glomeruli and renal tubules (white arrow). The mesangial cells and the brush border of the Proximal Convoluted Tubule (PCT) were PAS positive (Fig.3A1-3A2 and 3B1-3B2). Group III showed poor architecture, the glomeruli showed degrees of sclerosis and the mesangial cells appeared fused (white arrow), the basement of the glomeruli (slender arrow) and the tubules (blue arrow) appeared thickened and there was considerable loss of brush borders (red arrow) within the PCTs (Fig.3C1-3C2). Groups IV and V showed normal, non-thickened basement membranes of the glomeruli (white arrow) and renal tubules (blue arrow). The mesangial cells and brush border of PCT in these groups were also PAS positive (slender arrow) (Fig.3D1-D2 and 3E1-E2)

JBAAR
Journal of Basic and Applied Research in Biomedicine
ISSN 2710-1479

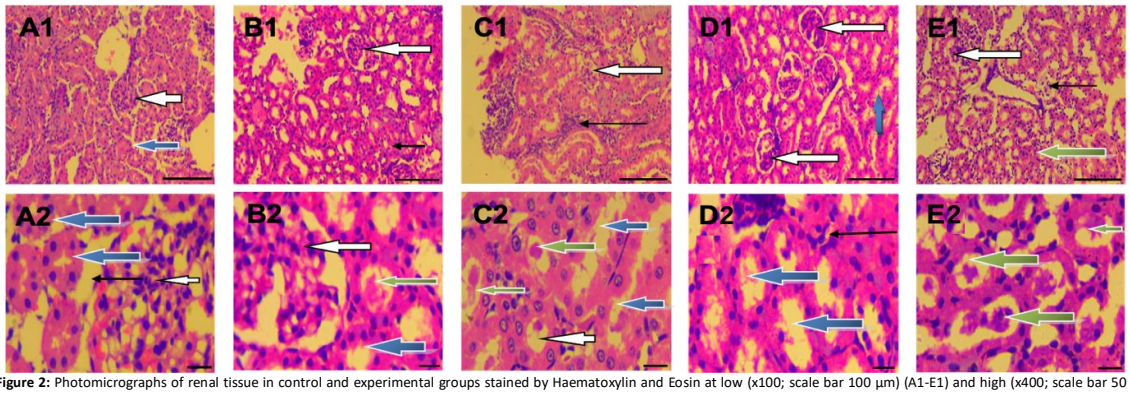


Figure 2: Photomicrographs of renal tissue in control and experimental groups stained by Haematoxylin and Eosin at low (x100; scale bar 100 µm) (A1-E1) and high (x400; scale bar 50 µm) (A2-E2) magnification. A = Control; B = Vehicle; C = BPA; D = BPA + *G. kola*; E = BPA + kolaviron. In A1-A2 and B1-B2, renal histoarchitecture preserved with intact glomeruli, normal mesangial cells and Bowman's capsular spaces (white arrow), preserved renal tubules (blue arrows), and normal interstitial spaces (slender arrow). In C1-C2, disrupted renal architecture (white arrow), few tubules exhibit eosinophilic fluid in lumen (green arrow), widened and inflammatory cell infiltrated interstitial spaces (slender arrows) and tubular degeneration (blue arrow) are seen. In D1-D2, renal samples had near-normal glomerular (white arrow) and tubular architecture (blue arrow) and reduced interstitial inflammation (slender arrow). The E1-E2, shows preserved glomeruli and tubules (white arrow). Few tubules exhibit eosinophilic fluid within their lumen (green arrow) and mild inflammatory cell infiltration within the interstitium (slender arrow).

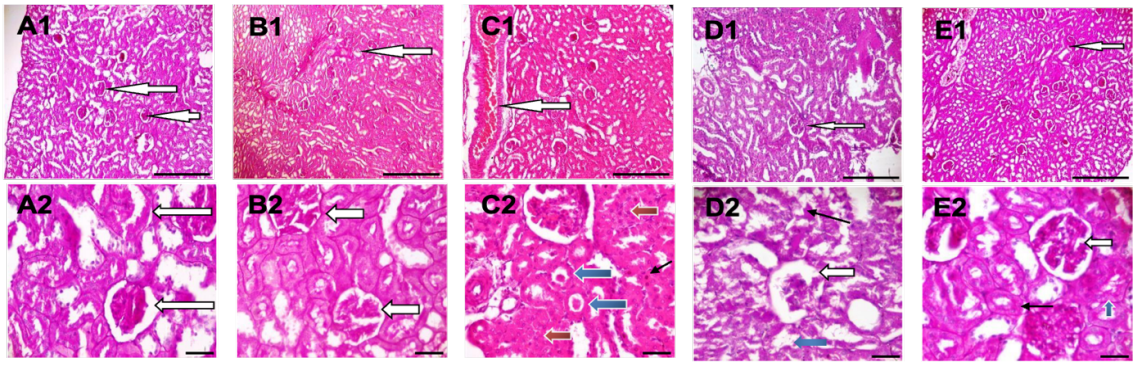


Figure 3: Photomicrographs of renal tissue stained by Periodic Acid Schiff technique at low (x100) (A1-E1) and high (x400) (A2-E2) magnification (scale bars: 100 µm in A1-E1 and 50 µm in A2-E2) in control and experimental groups. A = Control; B = Vehicle; C = BPA; D = BPA + *G. kola*; E = BPA + kolaviron. A1-A2 and B1-B2 show normal basement membranes of the glomeruli and renal tubules (white arrow). The mesangial cells and the brush border of the PCT were PAS positive. C1-C2 shows glomeruli with degrees of sclerosis and fused mesangial cells (white arrow). Glomeruli basement membrane (slender arrow) and tubules (blue arrow) appeared thickened and with loss of brush borders (red arrow) within the PCTs. D1-D2 and E1-E2 show normal, non-thickened basement membranes of the glomeruli (white arrow) and renal tubules (blue arrow). The mesangial cells and brush border of PCT are PAS positive (slender arrow).

DISCUSSION

The present study demonstrates that oral exposure to BPA induces significant renal dysfunction in male Wistar rats, as evidenced by alterations in urinary biomarkers and histopathological architecture of the kidney. Exposure to BPA resulted in increased urinary protein, albumin, creatinine and urea excretion, along with non-significant rises in urinary glucose and erythrocytes, indicating a compromised glomerular filtration barrier and possibly impaired tubular reabsorption. These biochemical distortions are consistent with previous reports that BPA impairs renal excretory function through oxidative stress-mediated mechanisms and inflammatory responses (Kobroob *et al.,* 2018, Hameed *et al.,* 2023, Kini *et al.,* 2024). Oxidative stress is central to the development of BPA-induced nephrotoxicity. BPA has been widely shown to increase the generation of reactive oxygen species (ROS) and lipid peroxidation products such as malondialdehyde (MDA), while simultaneously reducing the activity of endogenous antioxidant enzymes (e.g., superoxide dismutase, catalase, glutathione peroxidase) in rat liver (Tang et al., 2024) and mouse kidney (Tang et al., 2023) tissue. These shifts in redox balance contribute to oxidative injury of glomerular and tubular cells, leading to increased membrane permeability, protein leakage, and metabolic dysfunction of nephrons.

G. kola has been reported to contain biflavonoids (especially kolaviron) and other polyphenolic compounds which have the ability to act as potent antioxidants by donating hydrogen atoms to neutralize ROS, upregulate endogenous antioxidant enzymes and modulate nuclear factor erythroid 2–related factor 2 (Nrf2) signalling thereby resulting in an enhancement of cellular resilience against oxidative damage (Farombi et al., 2002, Ayepola et al., 2014). *G. kola* and kolaviron have also been reported to exert reno-protective effects by inhibiting pro-inflammatory cytokines via a downregulation of NF-κB signalling, resulting in reduced inflammation-driven tubular injury and fibrosis (Farombi & Owoeye, 2011). They have also been observed to improve mitochondrial dysfunction and modulate caspase-mediated apoptosis, resulting in mitigation of renal injury in diabetic rats (Sun et al., 2024) and cisplatin-induced renal oxidative damage in rats (Okoko & Ndoni, 2018).

In this study, co-exposure to BPA and either *G. kola* or its bioflavonoid, kolaviron, lowered several urinary biomarkers of renal injury (although not significantly relative to the BPA-only group), aligning with their previously reported potent antioxidant and anti-inflammatory properties. These agents i.e., *G. kola* and kolaviron, may have exerted renal protection by scavenging free radicals, enhancing endogenous antioxidant defenses, stabilizing cellular membranes of glomerular and tubular structures and mitigating apoptosis. The lower urinary protein and albumin levels in co-treated groups, although not significantly different from the BPA-only group, are compatible with preservation of glomerular barrier integrity, while the lower glucosuria and erythrocyte excretion are compatible with improved tubular re-absorptive and structural status compared with BPA alone; these biochemical trends need confirmation in larger samples. These findings correspond with observations in

other nephrotoxicity studies where *G. kola* and kolaviron mitigated oxidative damage markers and histological injury (Alabi *et al.,* 2018, Okoko & Ndoni, 2018, Sun et al., 2024).

The reno-protective mechanisms of *G. kola* and kolaviron may also involve modulation of inflammatory signaling pathways, as oxidative stress and inflammation are tightly linked in chemical-induced tissue injury. Previous studies demonstrate that BPA elevates pro-inflammatory cytokines in rat tissues, exacerbating structural deterioration, while antioxidant co-treatments reduce inflammatory marker expression alongside improvements in oxidative balance (Oviosun *et al.,* 2025). The present study demonstrates that exposure to bisphenol A (BPA) induced marked renal histoarchitectural alterations, as observed in both H&E and PAS-stained sections. BPA-treated rats showed disrupted glomerular structure, widened interstitial spaces with inflammatory cell infiltration, tubular degeneration, thickened basement membranes, and loss of proximal tubular brush borders. These findings are consistent with previous reports describing BPA-induced nephrotoxicity, which is largely mediated through oxidative stress and inflammatory pathways (Priego *et al.,* 2021).

The PAS staining revealed pronounced thickening of glomerular and tubular basement membranes, mesangial cell fusion, and reduced PAS positivity of proximal tubular brush borders following BPA exposure. These alterations suggest impairment of carbohydrate-rich basement membrane components and proximal tubular re-absorptive capacity. Similar PAS-positive basement membrane thickening and glomerulosclerosis have been reported in experimental models of BPA toxicity, indicating compromised filtration barrier integrity and early fibrotic changes (Abbas *et al.,* 2021). The observed histological damage may be attributed to BPA-induced reactive oxygen species generation, depletion of endogenous antioxidant defenses, and activation of inflammatory responses, which collectively promote cellular injury, tubular epithelial degeneration, and interstitial inflammation (Tang *et al.,* 2023). Loss of proximal tubular brush borders further reflects tubular epithelial damage and impaired renal functional capacity. Co-treatment with *G. kola* markedly ameliorated BPA-induced renal damage, as evidenced by near-normal glomerular and tubular architecture, reduced interstitial inflammation, and preservation of PAS-positive basement membranes and brush borders. These protective effects are consistent with the known antioxidant and anti-inflammatory properties of *G. kola*, which have been shown to mitigate xenobiotic-induced renal injury (Nnamdi *et al.,* 2025). Kolaviron also improved renal architecture, with preserved glomeruli, intact basement membranes, and restored PAS positivity of mesangial cells and proximal tubular brush borders, although mild interstitial inflammation and a few tubules with eosinophilic luminal fluid persisted. The protective effect of kolaviron may be attributed to its potent biflavonoid composition, which exerts strong antioxidant and anti-inflammatory actions. This is supported by previous reports demonstrating that kolaviron reduces renal oxidative stress and modulates inflammatory responses in chemically induced nephrotoxicity models (Ayepola *et al.,* 2014).

This study however has a few limitations. Clinical assessment of renal function is reported to rely on a combination of serum tests, to evaluate the rate of waste filtration or accumulation, and urine analysis in order to detect renal filtration capacity, structural damage, infection or tubular defects (Mouton and Holder, 2006). This study only investigated one aspect of renal function assessment and therefore represents a limitation of study. Evaluating serum biochemistry (creatinine and blood urea) in addition to urinalysis would have presented with a full assessment of renal function. Another limitation, is the use of qualitative histological descriptions (which is well suited for the study design) rather than blinded, semi-quantitative histopathological scoring systems which would have contributed significantly to transforming descriptive, qualitative tissue observations into numerical data in order to be able to evaluate disease severity and therapy efficacy. This will however be factored into subsequent studies. Finally, this study utilized a 28-day duration of exposure, which reflects sub-chronic studies and may not capture chronic human environmental exposure profiles. This and an evaluation of the influence of sex differences on BPA induced-renal toxicity and its amelioration by either *G. kola* or otherwise, will form the crux of subsequent investigations. In addition, markers of oxidative stress and inflammation were not measured, so the proposed antioxidant and anti-inflammatory mechanisms remain inferential, and urinary values were not normalised to urine volume or creatinine. Finally, because BPA was administered in corn oil, the vehicle group (II) is the most appropriate comparator for the BPA effect, and some vehicle-related differences were observed (e.g., urinary creatinine).

CONCLUSION

Bisphenol A exposure induces significant renal toxicity in male Wistar rats, as evidenced by proteinuria, albuminuria, and structural renal damage. Co-treatment with *G. kola* and kolaviron lowered several urinary markers of renal injury (without reaching statistical significance versus the BPA-only group) and preserved renal histoarchitecture, suggesting partial nephroprotection. These effects may be mediated through antioxidant and anti-inflammatory mechanisms, which warrant confirmation in future studies. Collectively, the findings support the potential of *G. kola* and kolaviron as protective agents against BPA-induced renal dysfunction.

ETHICAL APPROVAL

All animal procedures were approved by the Department of Physiology, College of Medicine, University of Ibadan, Ibadan, Nigeria (Ref. No. PHY/EDT/IV; protocol presented and approved at a departmental seminar in March 2023). Procedures followed the National Research Council (2011) Guide for the Care and Use of Laboratory Animals.

DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

The authors acknowledge that AI-assisted technologies were partially used in the preparation of this manuscript. Generative AI (ChatGPT) was used to support language refinement and grammar correction. No AI tools were used to generate data, interpret results, or replace the authors' intellectual contribution. All content was critically reviewed, edited, and approved by the authors.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST

The authors declare no conflict of interest in this study.

FUNDING

The authors declare that this research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

AUTHOR'S CONTRIBUTION

I.A.O. conceived and designed the study and supervised the experiments. T.O.D., O.A.C., and E.I.E. performed the laboratory experiments, analyzed the data, and drafted the manuscript. T.O.D., A.B.O. and I.A.O. conducted the statistical analysis and generated the figures. All authors contributed to manuscript revision, read, and approved the submitted version.

ACKNOWLEDGMENTS

The authors thank Prof. K. O. Soetan of the Department of Veterinary Physiology and Biochemistry, Faculty of Veterinary Medicine, University of Ibadan, Nigeria, for technical assistance.

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