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Effects of Crude Saponins Extract of *Parkia biglobosa* Fruit-Husk on Some Liver and Kidney Indices on Gentamicin-Induced Nephrotoxicity in Male Wistar Rats

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ABSTRACT

The present study was undertaken to determine the effects of crude saponins extract of *Parkia biglobosa* fruit husk on gentamicin-induced nephrotoxicity in male Wistar rats. The study was aimed to determine the effects of crude saponins extract of *Parkia biglobosa* fruit-husk on some liver and kidney indices on gentamicin-induced nephrotoxicity in male Wistar rats. Nephrotoxicity was induced in male Wistar rats (80±20g) by intraperitoneal administration of 80 mg/kg b.w of gentamicin for 9 days. Forty-two male rats were divided into six groups of 7 each, as follows: group 1: normal control, group 2: negative control, group 3: standard control, groups 4 and 5 were gentamicin-induced nephrotoxic but treated with 400 mg/kg and 800 mg/kg b.w of crude saponins extract respectively. Group 6: received normal saline with 1200 mg/kg b.w of crude saponins extract. Administration of extract occurred daily for 12 days. A serum sample was used for the determination of kidney function parameters and liver function parameters. Kidney tissues were used for histological evaluations. At dose up to 500 mg/kg b.w does not cause any mortality or sign of toxicity. Thus the extract is considered safe. Gentamicin administration induced marked nephrotoxicity as evidenced by a significant increase ($p< 0.05$) in serum levels of creatinine, urea, uric acid and bun. A significant increase ($p< 0.05$) in ALT, ALP, AST, TP, GGT and ALB. Treatment of rats with crude saponins of *Parkia biglobosa* fruit-husk extract was found to improve kidney and liver indices, as well as histological changes in the kidney. Administration of crude saponins of *Parkia biglobosa* fruit husk extract was found to improve kidney and liver indices, as well as antioxidant activities and histological changes in the kidney.

INTRODUCTION

Saponins are glycosides that are surface-active and have a distinct foaming feature that develops spontaneously on the surface of surfaces. Although plants account for the vast majority of their creation, bacteria and other lesser marine creatures also contribute to its development. Nephrotoxicity is a situation in which the kidneys have been poisoned by an external agent [1]. There is evidence that several medicines, including prescription medications as well as hazardous substances, might negatively influence kidney function. In addition, many medications can have a variety of negative effects on the kidneys, and some medications can have several effects on renal function. On the second Thursday of March each year, World Kidney Day is marked to recognise the importance of the kidney and associated diseases in the human body and to raise awareness of these issues. Continuing at this rate, the situation in Sub-Saharan African countries such as Nigeria would deteriorate significantly more.

A total of 36.8 million Nigerians are believed to be suffering from various stages of renal disease, accounting for around 23% of the total population (23 percent of the population). Approximately seven out of every ten Nigerians is at risk of getting a disease at any time. In the current economic climate, it is nearly hard to offer replacement treatment to all of

the patients that require it. In light of the fact that these therapies are necessary to preserve renal function, the next step for doctors is to identify viable alternatives that would either slow the course of the illness or allow patients to avoid dialysis [2-4].

Plants used for medicinal purposes are extremely important in the field of human health care. In accordance with Ameesh and Murugan [5] traditional medicine, which is mostly comprised of plants, is utilised by around 80% of the world's population, according to the authors. It's a dicotyledonous flowering plant that belongs to the Fabaceae-Mimosoideae family, and it blooms in the spring. In the world of vascular plants, spermatophytes constitute a prominent classification. Medical and pharmacological investigations on Parkia biglobosa seeds have revealed that the seeds contain hepatoprotective, hypolipidemic, antimicrobial, and anti-inflammatory properties, among other things. The major goal of this study is to determine how a crude saponin extract of Parkia biglobosa fruit husk affects certain liver and kidney parameters in male Wistar rats after they have been given gentamicin to cause nephrotoxicity, which is the primary goal of this study.

MATERIALS AND METHODS

Collection of Plant Material

The fruit husk of *Parkia biglobosa* was collected from Gombe town of Gombe state and authenticated by a botanist with the department of biological sciences, Gombe State University. a voucher specimen no. 37 as *Parkia biglobosa* was deposited at the department herbarium.

Chemicals, Reagents and Equipment

All of the chemicals and reagents used in the study were of the analytical grade, according to the researchers. In addition, the laboratory equipment that was used was of standard class.

Ethical Clearance

Ethical clearance for the animal experimental procedure was granted by the department of veterinary services ethics committee of the Ministry of agriculture, Gombe state with reference number GS/DVS/ECR/VII/53.

Preparation of crude saponins

For the mining of saponins as described by Obadoni and ochuko, the dried fruit husk of *Parkia greatlobosa* [8] was utilised. A conical flask was added to the ground fruit husk (50 g) and 20 per cent aquatic ethanol were added to a 100 cm^3 flask. For 4 h, the sample was heated with a constant agitation at 55 ^oC. The mixture was filtered and 200 mL 20 percent ethanol was added to the residual. In addition, a water bath at 90 ^oC reduced the mixture to 40 mL. The concentrates have been transferred and shaken vigorously into 250 mL funnel and 20 mL diethyl ether. The aqueous layer has been recovered while the ether layer has been removed. Repeat and add 60 mL of n-butanol to the cleaning process. Tweaked with 10 mL aqueous sodium chloride, the combined n-butanol extract washed. In a water bath at 60 ^oC the rest of the solution was heated. The material was dried at 20 ^oC to constant weight in an oven following evaporation.

Experimental Animals

Animals were obtained from the animal facility centre of the department of physiology, Gombe State University, Gombe. They were housed in polypropylene cages and were given a standard grower diet (vital feeds) and water *ad libitum* for 7 days before the commencement of the experiment. throughout the experiment, it was maintained under laboratory conditions of 29±2^o c and 12 h light and dark cycle. The guide for the care and use of laboratory animals was strictly followed.

Experimental Design

Nephrotoxicity was induced by the method described by Paoulomi *et al.* [9] with slight modifications in male Wistar rats (80±20g) by intraperitoneal administration of 80 mg/kg b.w of gentamicin for 9 days. Forty-two male rats were divided into six groups of 7 each, as follows: group 1: normal control, group 2: negative control, group 3: standard control, groups 4 and 5 were gentamicin-induced nephrotoxic but treated with 400 mg/kg and 800 mg/kg b.w of crude saponins extract respectively. group 6: received normal saline with 1200 mg/kg b.w of crude saponins extract only. Administration of extract occurred daily for 12 days.

Biochemical Analysis Serum Collection

After the last dose, 8 h were taken in the rats, chloroform vapour and blood samples were anaesthetized and collected in labelled centrifuge tubes from the animals via heart puncture. The samples were permitted to be cloaked and spun for 5 minutes in a tabletop centrifuge at 3000 rpm. The serum was tested for an estimation of several biochemical parameters in labelled specimen test tubes.

Histology Examination

A random selection of kidneys of each experimental group in the research work was identified, isolated and transferred into 10 % formalin to preserve the tissue until when required for the histological studies. tissue processing was carried out by an automatic tissue processing machine and the prepared 5-micron thickness sections were mounted on a slide and stained with hematoxylin and eosin [10].

Statistical Analysis

All values are expressed as Mean± S.E.M of seven (7) replicates. Mean values with a different superscript in a column were significantly different at $p<0.05$ using one-way analysis of variance (ANOVA) followed by Bonferroni Multiple Comparison Test. Graph Pad Instant Statistical Package Version 5.0 was used for the statistical analysis.

RESULTS AND DISCUSSION

Table 1. Effects of crude saponins extract of *Parkia biglobosa* fruit husk on the body and relative kidney weights in gentamicin-induced nephrotoxicity in male Wistar rats.

Groups /days	Day 1	Day 7	Day 14	Day 21	Relative Kidney weight
Group 1	84.6±2.33	75.8±2.02^a	87.1±3.02^a	103.2±3.94^a	0.91±0.15^a
Group 2	80.9±3.45	72.3±4.91^a	64.4±5.22^b	76.3±7.13^b	0.81±0.07^b
Group 3	81.8±4.69	66.0±1.37^b	67.6±2.29^b	83.6±2.78^c	0.97±0.05^a
Group 4	84.3±4.05	71.8±5.63^a	76.3±6.52^c	94.9±6.75^{ab}	0.96±0.05^a
Group 5	85.4±4.94	68.5±2.82^b	67.8±3.02^b	84.4±2.78^c	0.83±0.02^b
Group 6	87.5±3.50	70.5±3.93^a	81.6±4.76^a	91.1±4.12^d	0.83±0.04^b

Note:Values are expressed as Mean ± SEM of seven (7) replicates. Mean values with different superscripts in a column are significantly different at ($p< 0.05$).

The results of the effects of crude saponins of *Parkia biglobosa* fruit husk extract on the body and relative kidney weights in gentamicin-induced nephrotoxicity in male Wistar rats are presented in **Table 2**. The result showed that there was no significant difference ($p<0.05$) in the weight of disease control rats when compared with that of normal control rats on day 7. There was a significant decrease ($p<0.05$) in the weight of standard control rats when compared with disease control on day 7. There was no significant difference ($p<0.05$) in the weight of crude saponins of *Parkia biglobosa* fruit-husk 400mg

and 1200 mg/kg body weight treated groups when compared with the disease control rats on day 7.

There was a significant decrease ($p<0.05$) in the weight of 800mg/kg of the crude saponins of the *Parkia biglobosa* fruit-husk treated group when compared with the disease control. There was a significant decrease ($p<0.05$) in the weight of disease control rats as compared with normal control rats on day 14. There was no significant difference ($p<0.05$) in the weight of standard control rats and 800mg/kg of the crude saponins of *Parkia biglobosa* fruit-husk treated group when compared with disease control rats on day 14. There was a significant increase ($p<0.05$) in weight of 400 mg/kg and 1200 mg/kg of the crude saponins of *Parkia biglobosa* fruit-husk treated group when compared with disease control rats on day 14.

There was a significant decrease ($p<0.05$) in the weight of disease control rats when compared with the normal control rats on day 21. There was a significant increase ($p<0.05$) in weight in the standard control-treated rats and 400 mg/kg, 800 mg/kg, 1200 mg/kg body weight of crude saponins of *Parkia biglobosa* fruit husk extract when compared with the disease control rats in day 21. There was a significant decrease ($p<0.05$) in the relative kidney of disease control rats when compared with the normal control rats.

There was a significant increase ($p<0.05$) in weight in the standard control-treated rats and 400mg/kg body weight of crude saponins of *Parkia biglobosa* fruit-husk extract when compared with the disease control rats. There was no significant difference ($p<0.05$) in the relative kidney of 800 mg/kg and 1200 mg/kg body weight of crude saponins of *Parkia biglobosa* fruit-husk extract as compared with the disease control rats. This result is in agreement with that by
Manimala *et al.* [16].

Table 2. Effects of crude saponins extract administration on liver function indices in gentamicin-induced nephrotoxicity in male Wistar rats.

Groups	AST (U/l)	ALP(U/l)	ALT(U/l)	GGT(U/l)	Alb(g/dl)	Tp (g/dl)
Group 1	52.3 ± 1.49^{a}	65.1 ± 1.15^{a}	43.7 ± 1.80^{a}	20.3 ± 0.20^{a}	4.9±1.08a	6.6 ± 0.37^{a}
Group 2	76.1 ± 0.74^{b}	84.9 ± 0.97^{b}	91.7 ± 2.07^{b}	35.7 ± 1.94^{b}	7.4 ± 0.23^{b}	8.8 ± 0.69^{b}
Group 3	53.4 ± 0.62^{a}	71.6 ± 0.59^{ab}	79.7 ± 2.52^{ab}	33.3 ± 1.26^{b}	5.5 ± 1.18^{c}	8.3 ± 0.26^{b}
Group 4	52.6 ± 0.57^{a}	78.1 ± 2.21^{ab}	84.4 ± 3.94^{c}	28.6 ± 1.82^{ab}	4.5 ± 1.09^{a}	10.1 ± 0.44^{ab}
Group 5	50.6 ± 1.56^{a}	77.3 ± 2.52^{ab}	86.7 ± 2.83^{c}	33.3 ± 1.17^{b}	2.6 ± 0.65^{ab}	7.3 ± 0.85^{c}
Group 6	53.2 ± 0.57^{a}	68.9 ± 1.92^{a}	83.1 ± 1.18^{c}	23.1 ± 2.35^{a}	2.4 ± 0.20^{ab}	6.3 ± 0.90^{a}

Note: Values are expressed as Mean ± SEM of seven (7) replicates. Mean values with different superscripts in a column are significantly different at ($p< 0.05$).

The results of the effects of crude saponins extract administration on liver function markers in gentamicin-induced nephrotoxicity in male Wistar rats is presented in **Table 3**. The result shows that there was a significant increase ($p<0.05$) in ast, alt, alp, ggt, alb and tp in the disease control rats when compared with the normal control rats. Administration with crude saponins of *Parkia biglobosa* fruit husk extract and standard drug decreases significantly ($p<0.05$) the levels of Ast, Alt, Alp, Ggt, Alb and Tp when compared with the disease control rats.

Table 3. Effects of crude saponins extract administration on kidney function parameters in gentamicin-induced nephrotoxicity in male Wistar rats.

Group	Creat (mg/dl)	Ua (mg/dl)	Bun (mg/dl)	Urea (mg/dl)
Group1	2.3 ± 0.18^{a}	2.1 ± 0.21^{a}	25.1 ± 0.71^{a}	39.8 ± 0.91^{a}
Group 2	3.5 ± 0.06^{b}	4.3 ± 0.19^{b}	33.4 ± 1.00^{b}	81.6 ± 1.31^{b}
Group 3	1.3 ± 0.01^{c}	3.3 ± 0.07^{ab}	26.0 ± 0.72^{a}	53.1 ± 1.08^{ab}
Group 4	2.3 ± 0.21^{a}	2.8 ± 0.16^{c}	22.4 ± 0.31^{ab}	45.0 ± 1.33^{c}
Group 5	1.6 ± 0.23^{c}	2.5 ± 0.08^{c}	24.1 ± 0.26^{a}	47.4 ± 1.78^{c}
Group 6	1.3 ± 0.07^{c}	2.2 ± 0.04^{a}	21.2 ± 0.82^{ab}	37.4 ± 1.23^{a}

Note: Values are expressed as Mean ± SEM of seven (7) replicates. Mean values with different superscripts in a column are significantly different at ($p< 0.05$).

Creatinine and urea are considered biomarkers of renal function efficiency [11]. The results of the effects of crude saponins extract administration on kidney function parameters in gentamicin-induced nephrotoxicity in male Wistar rats is presented in **Table 4**. The result showed that there was a significant increase ($p<0.05$) in creatinine, uric acid, blood urine nitrogen and urea in the disease control rats (group 2) an indication of renal damage [12] when compared with normal control rats. Administration of crude saponins of *Parkia biglobosa* fruit husk extract and standard drug decreases ($p< 0.05$) the level of creatinine, uric acid, blood urea nitrogen and urea when compared with the disease control rats, an indication of metastable dialyzing power of the extract [13].

Histology examination

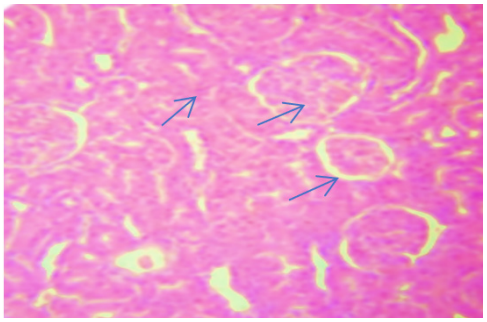

Plate 1a: light photomicrograph showing normal kidney architecture containing the glomerulus and renal tubules with erythrocytes and essential space (x400).

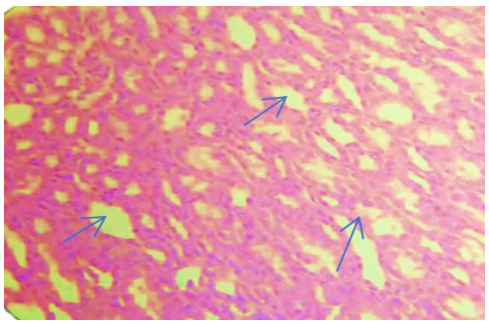

Plate 1b: light photomicrograph showing scanty lymphocytic infiltrates in the interstation, multiple dilated tubules, distortion of normal kidney architecture (x400)

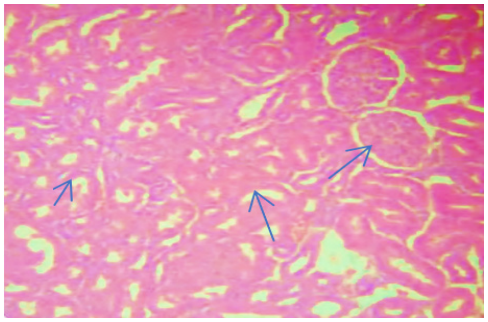

Plate 1c: section of the kidney showed marked reduced tubular damage with distal and proximal tubule similar to normal glomeruli. (x400).

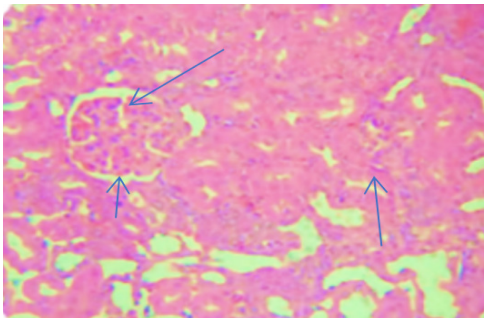

Plate 1d: Section of the kidney showed minimal disrupted architecture of kidney with the glomerular area, messengial space membrane in a regenerative fashion (x400).

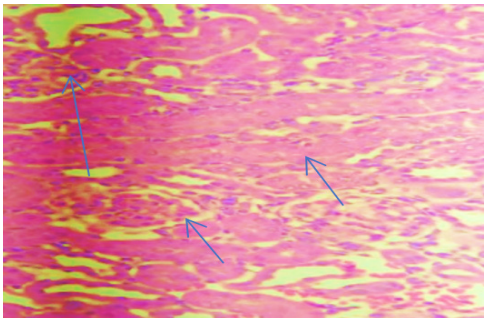

Plate 1e: sections of the kidney show normal glomeruli with minute dilations in tubules, messengial space and erythrocytes(x400).

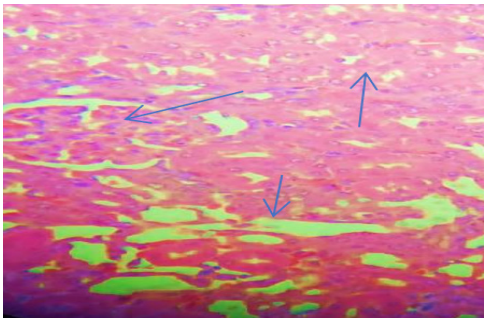

Plate 1f: sections of the kidney showed normal glomeruli architecture with the marked glomerular area, podocyte, renal and distal tubules(x400).

Note: **Plate** 1a: light pictomicrograph of a section of normal rat kidney for group 1. **Plate** 1b: light pictomicrograph of a section of disease control rats for group 2. **Plate** 1c: light pictomicrograph of standard control group 3. **Plate** 1d: light pictomicrograph of 400 mg/kg treated rats group 4. **Plate** 1e: light pictomicrograph of 800 mg/kg b.w treated rats group 5. **Plate** 1f: light pictomicrohraph of 1200 mg/kg b.w administered for group 6.

The kidney of control rats showed normal histological features of glomerular, tubular and Interstitial components of the cortex and messengial space (**Plate 1a**). Significant tubular and interstitial changes in the kidneys of rats in the gentamicin-induced groups may be attributable to a decrease in antioxidant defence system enzymes in group 2 [14]. Tubular changes caused by gentamicin therapy manifested early in the form of necrosis, degeneration, and vacuolization. Swelling and loss of the proximal tubular brush boundary were seen in the degenerative tubules. These modifications were seen in the majority of the proximal convoluted tubules and, to a lesser extent, the distal tubules (**Plate 1b**). In contrast, groups treated with the standard drug showed a rapid response in regeneration and repair of the degenerated tissues, inhibiting necrosis and tubular alterations, reduced lymphocytic infiltrations (**Plate 1c**).

The concurrent treatment with crude saponins extracts of *Parkia biglobosa* fruit husk (400 and 800 mg/kg, p.o) reduced such changes in kidney histology (**Plate 1d** and **1e**). Furthermore, in group 6, the changes extended to the distal convoluted tubules and collecting ducts which showed a lot of lysosomal structures and large glomerulus (**Plate 1f**). The renal structure of rats in this group 6 (1200 mg/kg) showed no significant degeneration from the extract of the crude saponins that may result in alterations. The observed renal histological changes and the accompanying levels of liver and kidney indices indicate dialyzing power potential as postulated by Sodipo *et al.* [15].

CONCLUSION

Crude saponins of *Parkia biglobosa* fruit-husk extract produce nephrocurative potentials in the rats as the oral administration in gentamicin-induced nephrotoxic rats resulted in a significant reduction in some live and kidney indices, as well as histological changes in the kidney caused by gentamicin. Therefore, *Parkia biglobosa* fruit-husk crude saponins can be better used for the development of new therapeutics to manage kidney disease.

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COMPETING INTERESTS

The authors have declared that no competing interests exist concerning the publication of this manuscript.

AUTHORS' CONTRIBUTIONS

Abubakar I. Was responsible for the study concept, Mukhtar A. And Abubakar I. Contributed to all necessary laboratory analyses. Aishatu B. And Daniel D. assisted with all data analysis and also provided critical revision of the manuscript for intellectual support. Sani AM was responsible for all necessary histological examinations. All authors critically reviewed the content and approved the manuscript for publication.

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