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Evaluation of Protective and Therapeutic Potentials of Aqueous Extract of Corn Silk on Gentamicin-Induced Nephrotoxicity in Albino Rats

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Authors' contributions

This work was carried out in collaboration among all authors. Author OEN designed the study and wrote the protocol. Author IE performed the statistical analysis. Authors IE and DO wrote the first draft of the manuscript. Authors ONB and NB managed the analyses of the study. All authors read and approved the final manuscript.

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ABSTRACT

Aim: To evaluate the protective and therapeutic potentials of corn silk extract on gentamicin (CN)-induced nephrotoxicity in albino rats.
Study Design: The rats were randomly selected and grouped as follows: Group 1 (NC): Were given only food and water. They served as negative control. Group 2 (PC): Were treated with 80 mg/kg/day of CN over a period of 7 days. They served as the positive control. Protective Treatment: Group 3a (CN+CSP 200 mg/kg): Concurrently treated with 200 mg/kg corn silk extract and 80 mg/kg/day of CN for 7 days. 200 mg/kg corn silk extract continued for 30 days. Group 3b (CN+CSP 400 mg/kg): Concurrently treated with 400 mg/kg corn silk extract and 80 mg/kg of CN for seven days. 400 mg/kg corn silk extract continued for 30 days. Therapeutic treatment: Group 4a (CN+CST 200 mg/kg): Induction of nephrotoxicity with 80 mg/kg/day of CN for seven days before the administration of 200 mg/kg of corn silk extract for 30 days. Group 4b (CN+CST 400

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mg/kg): Induction of nephrotoxicity with 80 mg/kg/day of CN for 7 days before the administration of 400 mg/kg of corn silk extract for 30 days.
Methodology: At the end of the treatment, the animals were allowed to fast for 18 hours and later anaesthetized using chloroform. Whole blood samples were collected via cardiac puncture and put into lithium heparin bottles. The samples were then spun at 3500 rpm for 5 minutes to obtain plasma. Kidney specimens harvested were fixed in 10% formol saline. Sections were prepared using histological techniques and stained using Haematoxylin and Eosin stain. Urea was analysed using Berthelot's enzymatic colorimetric method, creatinine using Jaffe's enzyme-kinetic method while the estimation of Na^+, K^+, and Cl^- were performed using Ion Selective Electrode (ISE) analyzer.
Results: Significantly lower ($p<0.05$) values of creatinine and urea were seen in protective and therapeutic treatment groups when compared against positive control. Potassium indicated significantly lower values especially in the therapeutic groups when compared against negative control while chloride indicated significantly higher values in 400 mg/kg rats compared with positive control at $p<0.05$. Histology of the protective treatment groups showed slightly distorted glomerular space, vacuolations, and dilated proximal and distal tubules. The positive control and the therapeutic treatment groups indicated severely damaged glomerulus, glomerular space, proximal and distal tubules as well as loss of parenchymal materials and presence of kupffer cell infiltration were seen but less severe in the therapeutic group compared to the positive control.
Conclusion: The results obtained suggest protective and therapeutic potentials of corn silk extract on gentamicin-induced nephrotoxicity in albino rats. However, the therapeutic efficacy was progressively gradual and not be fast-effective as documented in most traditional or herbal literatures.

Keywords: Nephrotoxicity; aqueous extract; corn silk; gentamicin; electrolytes; renal integrity.

ABBREVIATION

Cl^- : Chloride ion
CN : Gentamicin
Crt : Creatinine
CS : Corn Silk
CSP : Corn silk Protective group
CST : Corn silk Therapeutic group
K^+ : Potassium ion
Na^+ : Sodium ion
NC : Negative Control
PC : Positive Control
ROS : Reactive Oxygen Species

1. INTRODUCTION

Acute kidney injury (AKI) pathogenesis is complex, and promoting events may be completely different. Though ischaemia or toxins are major factors that precipitate in the injury, but similar pathways maybe involved in subsequent injury responses [1]. And as reported by Prohp & Onoagbe [2], one of the functions of a healthy kidney is to maintain constant blood electrolyte concentrations despite changes in physiological conditions.

Gentamicin (CN) belongs to the class of antibiotics called aminoglycosides and it has been in use for over a 50 years. It has been reported to be clinically effective against wide range of bacterial infections caused by *Staphylococcus* spp, *Enterococcus* spp and lots of gram-negative bacteria genus but it has also been seen to induce nephrotoxicity [3]. As reported by Gonzalez & Spencer [4], accumulation of CN in proximal renal tubules may cause brush border network damage as a result of nephrotoxicity effect. It was also reported that CN induces nephrotoxicity by initiating and propagating oxidative stress through the production of reactive oxygen species that react with cellular macromolecules, adversely resulting in the consumption of antioxidant defense mechanisms, glomerular and tubular damages leading to loss or reduced renal structural integrity and functions [3].

This study evaluates the protective and therapeutic potentials of aqueous extract of corn silk when CN is used to induce renal injuries or nephritis. Corn silk (CS) or stigmata is derived from (corn) maize (*Zea mays*) and commonly described as the "hair of maize". CS has been reported possess beneficial properties in humans as a medicinal herb in the treatment and management of some ailments [5,6,7,8]. Corn is a plant that is cultivated and consumed mostly as cereal in many parts of the world. Whole-grain corn is as healthy as any cereal grain, rich in

fibre and many vitamins, minerals, and antioxidants [9,10]. In herbal medicine, the part of the corn that is used is the long stigmas, called silks (commonly described as “corn hair”), which grow from the top end of the corn's 'ear'. They are silky, light, pale yellow strands that are seen when peeling the husks of corn on the cob [9, 10]. Once they are dried the CS look very different to their fresh form, becoming brown, curled, crinkly, and incredibly light-weight. CS in form of extract has been employed as herbal medicine in several parts of the globe like Asia, Africa, Europe and America [11,12]. The medicinal properties of corn silk are linked to the rich-reserves of minerals and anti-oxidants of mostly phenolic origins [12,13,14]. Anti-oxidants have been reported to neutralize or mitigate the adverse effect of reactive oxygen species (ROS) that may induce pathological conditions [13,14]. CS has been reported in several literatures as herbal medicine, it is used as a complement in the treatment of cystitis, edema, kidney stones, prostate related problems, and urinary infections as well as bedwetting and obesity [10,15]. Velazquez [16] documented that CS soothes and relaxes the lining of the bladder and urinary tubules, hence reducing irritation and increasing urine secretion.

Due to its documented potential benefits and considering the few scientific studies reported on the phytochemical, pharmacological and toxicological activities of CS. This current study seeks to provide more scientific evidence on the potential uses of corn silk in healthcare. The outcome of this study could provide further justification for the protective and therapeutic use of CS or limitation of its use. Therefore, the aim of this study was to evaluate the protective and therapeutic potentials of aqueous extract of CSon CN-induced nephrotoxicity in albino rats.

2. MATERIALS AND METHODS

2.1 Materials

Materials used include ampoule of 80 mg/2ml gentamicin (Emzor Pharmaceuticals, Nigeria), hypodermic syringes, 23 g needles, gavage tubes (Plymouth Meeting, USA), corn silk (fresh cut stigmata of *Zea mays* L. poaceae flowers), Haier thermocool refrigerator (China), Ohaus Scout-Pro Electronic weight balance (New Jersey, USA), MPW bucket centrifuge (Warsaw, Poland), digital Olympus microscope with camera (Japan), urea and creatinine reagents were purchased from Atlas Diagnostics (Cambridge, United Kingdom), Vis spectrophotometer (Axiom Medical Limited, United Kingdom), Ion selective electrolyte (ISE) 4000 analyzer (France), chloroform, and other chemicals of good quality and analytical grade (AR).

2.2 Experimental Animals

Thirty (30) adult male albino rats of 16 weeks old weighing 180.0±2.5 gms were used for this study. The animals were obtained from the animal farm of Pharmacology Department, University of Port Harcourt, and transported in a well-ventilated wired cage to the animal house at the Department of Medical Laboratory Science, Rivers State University, Port Harcourt. Prior to the study the rats were allowed to acclimatize for 14 days, with a 12 hr light/dark cycle, and were allowed access to solid poultry chow and water *ad libitum*.

2.3 Collection, Preparation, and Phytochemical Analysis of Corn Silk Extract

Corn silks (fresh cut stigmata of *Zea mays* L. poaceae flowers) were purchased in Port Harcourt from farmers and was identified and confirmed by a botanist in the Department of Applied and Environmental Biology, Rivers State University, Nigeria. In the preparation of the extract, the corn silks were sun-dried, ground into powdered form, 36 grams was weighed using Scout-Pro electronic weigh balance and dissolved in 1 liter of boiling water at 120±5°C for 40 minutes, and then sieved to obtain the filtrate (extract). This implies that 1.0ml of aqueous extract contains 0.036 g of corn silk extract when given to 180.0±2.5 gms of rats which is equivalent to 0.2 g/kg or 200 mg/kg bodyweight of CS. In this study water (aqueous extraction method) was chosen because of consideration of safety and time factor. In addition, the quantitative analysis of phytochemicals constituents of the extract was carried out in the Department of Chemistry, Rivers State University, Port Harcourt using Gas Chromato-graphy-Mass Spectrometry (GC-MS)

2.4 Experimental Design and Treatment

In the experimental design, the animals were randomly selected and grouped (each group consisting of 5 rats) as shown below. The administration of CN was done intraperitoneally (i.p) while that of the CS extract was done orally using an orogastric gavage tube. Nephrotoxicity was confirmed by observing elevated creatinine

and urea levels. The experimental protocol and method of induction of nephrotoxicity were according to Gharaei et al. [17].

I. Group 1 (NC): Animals in this group were given only food and water. They served as negative control.
II. Group 2 (PC): Animals in this group were treated with 80 mg/kg/day of CN over a period of 7 days. This group was NOT given CS extract and therefore served as the positive control.

2.4.1 Protective treatment

I. Group 3a (CN+CSP 200 mg/kg): Animals in this group were concurrently treated with 200mg/kg CS extract and 80 mg/kg/day of CN for 7 days. 200 mg/kg CS extract continued for 30 days.
II. Group 3b (CN+CSP 400 mg/kg): Animals in this group were concurrently treated with 400 mg/kg CS extract and 80 mg/kg of CN for 7 days. 400 mg/kg CS extract continued for 30 days.

2.4.2 Therapeutic treatment

I. Group 4a (CN+CST 200 mg/kg): Induction of nephrotoxicity with 80 mg/kg/day of CN for 7 days before the administration of 200 mg/kg of CS extract for 30 days.
II. Group 4b (CN+CST 400 mg/kg): Induction of nephrotoxicity with 80 mg/kg/day of CN for 7 days before the administration of 400 mg/kg of CS extract for 30 days.

2.5 Specimens Collection, Preparation and Laboratory Analysis

At the end treatment, the animals were anaesthetized using chloroform after which a cardiac puncture was performed. 5ml of fasting blood samples was collected into lithium heparin bottles. The whole blood was spun at 3500 rpm for 5 minutes to obtain plasma. The collected plasma was used for analyses of electrolytes, urea and creatinine. Urea was analysed using Berthelot's enzymatic colorimetric method as described by Patton & Crounch [18], Creatinine using Jaffe's enzyme-kinetic method as documented by Vaishya et al. [19] while the estimation of Na^+, K^+, and Cl^- were performed using Ion Selective Electrode (ISE) analyser as described by Buck & Linder [20]. Renal specimens harvested were washed in physiological saline and fixed in 10% formol saline. The sections were prepared using histological techniques, stained using Haematoxylin and Eosin stain, viewed and photomicrographs collected using digital Olympus microscope with camera.

2.6 Statistical Analysis

Data obtained from evaluation of parameters were presented as Mean±SD. Statistical analysis was done using GraphPad prism (version 5.03). Inferential statistics was done using one way ANOVA while post-hoc was carried out using Tukey's multiple comparison tests. Statistical significance was set at $p< 0.05$.

3. RESULTS

3.1 Phytochemical Analysis and Composition of Corn Silk

The estimation of phytochemical of the CS used in this study indicated phenol had the highest content in the sample with 75.18%, followed by flavonoid with 17.87%, saponin with 6.96% while and phytosterol had the least concentration with 0.72% of the prepared sample (Table 1).

3.2 Results of Renal Parameters

3.2.1 Administration of gentamicin (CN) and concomitant treatment with corn silk (Protective treatments)

Results obtained when rats were treated with CN and concomitantly with corn silk at low (200 mg/kg) and high dose (400 mg/kg) showed significant lower values of creatinine, urea and higher values of potassium compared against rats treated with CN alone (positive control). However, non-significant increases were observed when CS at low (200 mg/kg) and high dose (400 mg/kg) were compared against negative control. Chloride and sodium indicated non-significant higher and lower values in CS at low (200 mg/kg) and high dose (400 mg/kg) as well as negative control when compared against positive control (Table 2).

3.2.2 Treatment with corn silk after gentamicin (CN) induced-nephrotoxicity (Therapeutic treatments)

In this case, renal results obtained indicated significant differences in the values of Crt, urea, K^+ and Cl^- in negative control rats against rats treated with CN only (PC) and rats treated with CS after the induction of nephrotoxicity. Creatinine and urea indicated significantly higher values compared against negative control. In addition, significantly lower values were also

observed in rats treated with low (200 mg/kg) and high dose (400 mg/kg) compared with positive control. However, no significant difference was observed between low (200 mg/kg) and high dose (400 mg/kg). When potassium was considered, non-significant differences were seen in low (200 mg/kg) and high dose (400 mg/kg) compared to Positive controls but significant lower values were seen when compared against negative control. However, no significant difference was observed between low (200 mg/kg) and high dose (400 mg/kg). When chloride was considered, significantly higher values were seen in high dose (400 mg/kg) compared against positive control. In Sodium (Na), non-significant lower values were observed in low (200 mg/kg) and high dose (400 mg/kg) CS treatments at $p<0.05$ (Table 3).

3.3 Histological Examination of Renal Tissues

The histological investigations indicated normal structural architecture in the negative control. In the positive control, severely distorted glomerular and glomerular spaces, loss of parenchymal materials as well as that of the proximal and distal tubules were observed. In the protective treatment, CN+CSP (200 mg/kg) group indicated intact glomerulus with slightly distorted glomerular space and vacuolations. In the CN+CSP (400 mg/kg) group, mildly distorted glomerulus and glomerular space as well as dilated proximal and distal tubules were observed unlike the positive control (Fig. 1). In the therapeutic treatments, CN+CST (200 mg/kg) group indicated severely damaged glomerular and glomerular space, proximal and distal

Table 1. The quantitative phytochemical analysis of corn silk

Parameters	Phytosterols	Saponins	Flavonoids	Phenols	
Yield (mg/ml)	0.34±0.04	3.27±0.08	8.40±0.48	35.34±0.21	
Relative %	0.72%	6.96%	17.87%	75.18%	100%

Comment: Data are Mean±SD of triplicate determination

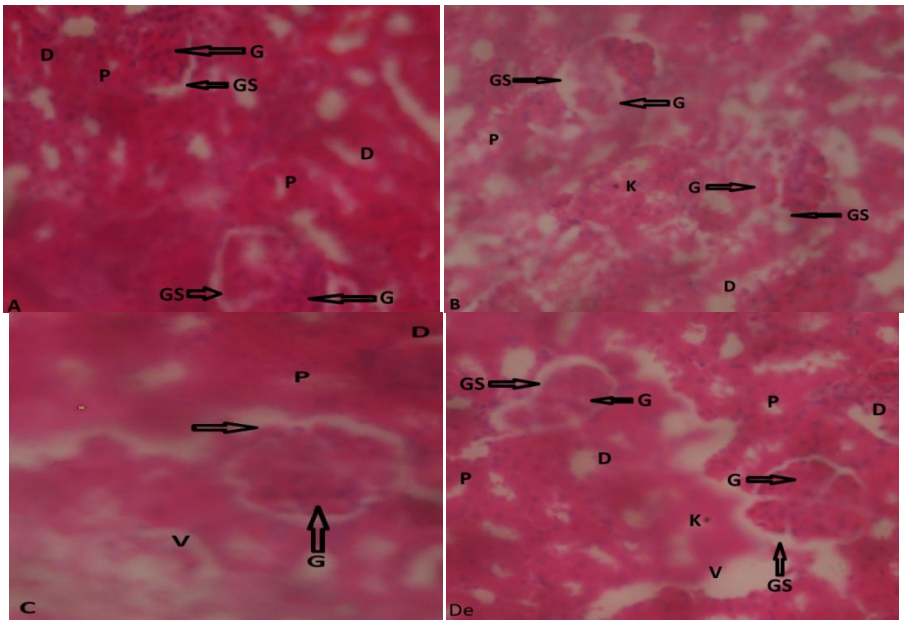

Fig. 1. A. Negative control (NC). Histology indicates normal glomerulus (G) and glomerular space (GS). Proximal (P) and distal tubules (D) appear intact. B. Positive control (PC): G and GS appear severely distorted. Distortion of the P and D were also observed. Loss of parenchymal materials and Kupffer cell was also observed. Protective Treatment: C. CN+CSP (200 mg/kg). G appears intact with the glomerular space (arrow) slightly distorted. Vacuolations were also seen. De. CN+CSP (400 mg/kg). G and G appear mildly damaged unlike plate B. P and D appear slightly dilated. Mag. 400X, H& E

Table 2. Renal parameters in rats concomitantly treated with gentamicin (CN) and corn silk (200mg/kg and 400mg/kg over a period of 30 days

Parameters	NC (n=5)	PC (n=5)	CN+CSP-200 mg/kg (n=5)	CN+CSP-400 mg/kg (n=5)	p value
CRT (µmol/L)	81.50 ± 18.89^{a}	163.9 ± 33.24^{bc}	109.26 ± 41.71^{ade}	103.34 ± 13.87^{ade}	0.0366^{*}
Urea (mmol/L)	5.69 ± 1.28^{a}	15.54 ± 8.92^{bc}	7.74 ± 3.76^{ade}	7.40 ± 2.48^{ade}	0.0182^{*}
K^{+} (mmol/L)	4.45 ± 0.37^{a}	2.88 ± 0.74^{bc}	4.88 ± 0.89^{ade}	5.10 ± 1.82^{ade}	0.0291^{*}
Cl^{-} (mmol/L)	88.75 ± 2.06^{a}	79.20 ± 3.70^{ab}	83.60 ± 1.95^{abc}	85.80 ± 5.22^{abc}	0.1098
Na^{+}(mmol/L)	123.0 ± 7.67^{a}	145.4 ± 8.44^{ab}	134.2 ± 15.13^{abc}	137.5 ± 10.60^{abc}	0.9048

*CRT, Urea, & K^{+}: Values in the same row with different superscripts (a, b) differ significantly when NC was compared against PC, CN+CSP, and CN+CSP. Also, values in the same row with different superscripts (c, d) differ significantly when PC was compared against CN+CSP and CN+CSP. More so, values in the same row with same superscripts (e) do not differ significantly when CN+CSP (200 mg/kg) was compared against CN+CSP (400 mg/kg). Cl^{-} & Na^{+}: However, values in the same row with same superscripts (a) do not differ significantly when NC was compared to PC, CN+CSP, and CN+CSP, same superscripts (b) do not differ significantly when PC was compared to CN+CSP (200 mg/kg) & CN+CSP (400 mg.kg) as well as same superscripts (c) do not differ significantly when CN+CSP (200 mg/kg) was compared CN+CSP (400 mg.kg) at p<0.05. Results are expressed as mean ±SD. Key: n=no of rats per group.NC=Negative Control, PC=Positive Control, CN = Gentamicin, CSP = Corn silk protected, *= Significant at P<.05*

Table 3. Results of renal parameters in rats treated with corn silk (200 and 400mg/kg) after CN-induced Nephrotoxicity over a period of 30 days

Parameters	NC (n=5)	PC (n=5)	CN+CST-200mg/kg (n=5)	CN+CST-400mg/kg (n=5)	pvalue
CRT (µmol/L)	81.50 ± 18.89^{a}	163.9 ± 33.24^{bc}	128.18 ± 9.22^{bde}	124.90 ± 14.23^{bde}	0.014^{*}
Urea (mmol/L)	5.69 ± 1.28^{a}	15.54 ± 8.92^{bc}	9.42 ± 1.69^{bde}	9.77 ± 1.26^{bde}	0.025^{*}
K^{+} (mmol/L)	4.45 ± 0.37^{a}	2.88 ± 0.74^{bc}	2.84 ± 0.39^{bcd}	3.42 ± 0.96^{acd}	0.041^{*}
Cl^{-} (mmol/L)	88.75 ± 2.06^{a}	79.20 ± 3.70^{ab}	85.20 ± 2.17^{abd}	101.80 ± 4.97^{acd}	0.012^{*}
Na^{+}(mmol/L)	123.0 ± 7.67^{a}	145.4 ± 8.44^{ab}	122.8 ± 27^{abc}	139.2 ± 8.88^{abc}	0.3252

*CRT & Urea: Values in the same row with different superscripts (a, b) differ significantly when NC was compared against PC, CN+CST, and CN+CST. Also, values in the same row with different superscripts (c, d) differ significantly when PC was compared against CN+CST and CN+CST. More so, values in the same row with same superscripts (e) do not differ significantly when CN+CST (200 mg/kg) was compared against CN+CST (400 mg/kg). K^{+}: Values in the same row with different superscripts (a, b) differ significantly when NC was compared against PC, CN+CST, and CN+CST. Also, values in the same row with different superscripts (c) do not differ significantly when PC was compared against CN+CST and CN+CST. More so, values in the same row with same superscripts (d) do not differ significantly when CN+CST (200 mg/kg) was compared against CN+CST (400 mg/kg). Cl^{-}: Values in the same row with same superscripts (a) do not differ significantly when NC was compared to PC, CN+CST, and CN+CST and the different superscripts (b, c) differ significantly when PC was compared to CN+CST (200 mg/kg) & CN+CST (400 mg.kg). However, the values with same superscripts (d) do not differ significantly when CN+CST (200 mg/kg) was compared CN+CST (400 mg.kg). Na^{+}: Values in the same row with same superscripts (a) do not differ significantly when NC was compared to PC, CN+CST, and CN+CST, same superscripts (b) do not differ significantly when PC was compared to CN+CST (200 mg/kg) & CN+CST (400 mg.kg) as well as same superscripts (c) do not differ significantly when CN+CST (200 mg/kg) was compared CN+CST (400 mg.kg) at p<0.05. Results are expressed as mean ±SD. Key: n=no of rats per group. NC=Negative Control, PC=Positive Control, CN = Gentamicin, CST = Corn silk therapeutic, NS= Not Significant, *= Significant at P<.05*

tubules as well as loss of parenchymal materials due to vacuolations, and presence of kupffer cell infiltration. In the CN+CST (400 mg/kg) group, glomerular and glomerular spaces were less severely distorted while the proximal and distal tubules appeared mildly dilated (Fig. 2).

3.3.1 Histology of protective treatment

The histologic examinations of renal tissues when CN was administered concomitantly with CS extract are shown below in Fig. 1 alongside the histology of the negative and positive controls.

3.3.2 Therapeutic treatment

The histologic examinations of renal tissues after the induction of nephritic damages using CN followed by administration of CS given are shown below in Fig. 2 alongside the histology of the negative and positive controls.

4. DISCUSSION

In the present study, in the protective and therapeutic treatments in was observed that the administration of aqueous extract of CS ameliorated the adverse effect of CN on the kidneys due to the observed significantly lowered levels of creatinine and urea in the corn silk treated rats compared against the positive control. Our findings are in line with the reports of Sukander et al. [21]. They reported that CS alone and in combination with binahong leaves alcoholic extracts repaired and improved renal damages resulting in improved renal markers such as creatinine and urea as well as antioxidant capacities. A study by Sepheriet al. [22] reported that the consumption of CS methanol extract (80%) at concentrations of 200 and 300 mg/kg showed a significant decrease of serum creatinine levels in CN- induced nephrotoxicity. In addition, Sabiu et al. [23] also reported ameliorative effect of

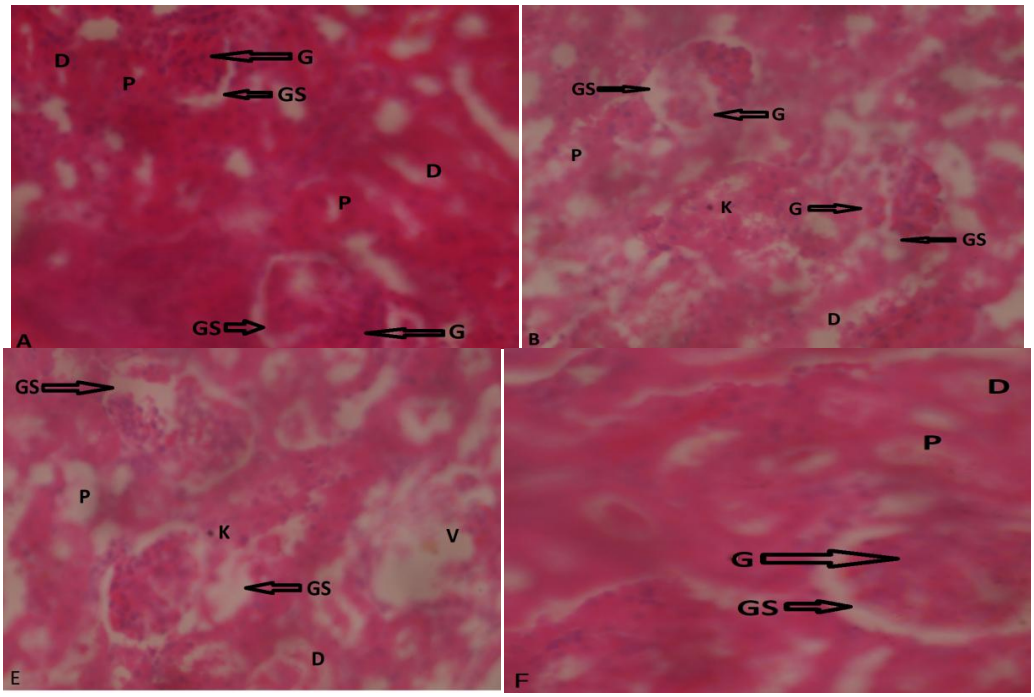

Fig. 2. A. Negative control (NC). Histology indicates normal glomerulus (G) and glomerular space (GS). Proximal (P) and distal (D) tubules appear intact. B. (postivite control) PC: G and G appear severely distorted. Distortion of the P and D were also observed. Loss of parenchymal materials and Kupffer cell was also observed. Therapeutic Treatment:E. CN+CST (200mg/kg). G and GS appear severely distorted. Distortion of the P and D tubules were also observed. Loss of parenchymal materials due to vacuolations and Kupffer cell were also observed. F. CN+CST (400mg/kg). G and GS appears less severely distorted unlike positive control. P and D appeared mildly dilated. Mag. 400X, H& E

CS extract on acetaminophen -induced kidneys damages in wistar rats by stabilizing membranes and detoxifying the toxic effect of the acetaminophen. Creatinine and urea are used as bio-markers in the indicating the state of the kidneys. These bio-markers are increased in the plasma when the glomerular filtration or renal integrity has been compromised. The deranged levels of creatinine and urea seen in the rats treated with corn silk especially in the therapeutic treatment groups concur with our histological findings. The histology indicated severely distorted glomerulus, glomerular space, proximal and distal tubules, and loss of parenchymal materials which are indicative of glomerulus nephritis and renal tubular dysfunction. The presence of kupffer cell further indicates the inflammation reactions and damages of the kidneys. However, these changes were less severe compared against the positive control rats that were given only CN without corn silk extract. This difference in the severity of damages seen in the treatment groups (whether protective or therapeutic) against the positive control group is an indication that corn silk extract possesses potentials of ameliorating CN-induced nephrotoxicity in albino rats.

When the electrolytes were considered, though the K^+ levels in the protective treatment were not grossly affected as seen in our results, but that of the therapeutic treatments were significantly affected with resultant lowered values of K^+ in the 200 mg/kg and 400 mg/kg corn silk treated rats compared against the negative control rats. However, there were improvements in the K^+ levels seen especially in the 400 mg/kg corn silk treated groups of both the protective and therapeutic groups. The higher level of K^+ observed in corn silk treated rats may be due to K^+-sparing activities, which is one of the mechanisms through which some diuretic drugs exerts their effects. This finding correlated with work of Okunade et al. [24] on the effect of aqueous CS (*Stigma maydis*) extracts on serum electrolytes in male wistar rats. Our finding also concurs with the reports of Ha et al. [25]. They documented that CS extract even at 500 mg/kg were observed not to be toxic. It was further reported that at 400 mg/kg, corn silk extract did not induce biochemical or haematological toxicity rather improved results of these analytes were seen. More so, Sabiu et al. [23] also reported that CS extract improved the glomerular and tubular functions of rats treated with corn silk at 100 mg/kg and 200 mg/kg after the induction of renal damages using acetaminophen. The lower values of potassium in this present study could be attributed to the loss of renal tubular function of re-absorption of useful electrolytes from the urinary mainly from the distal tubules. In acidic conditions (as predicted by hypokalamia) as seen in oxidative induced derangements, as K^+ migrates from intracellular to extracellular compartments, they are excreted and their re-absorption is poor especially at the distal tubules due to failure to build up H^+ concentration gradient between the distal lamina and the laminal cells. The histological findings of distorted and dilated tubules further support our biochemical results concerning the state of the electrolytes especially K^+. Though, the other electrolytes did not show significant difference except chloride that indicated higher values in 400 mg/kg treated rats in the therapeutic treatments groups. However, it was also observed that there was a corresponding lower and higher level of the other electrolytes corresponding to that of lower and higher levels of K^+ respectively. These observations further suggest that the loss of electrolytes due to these tubular dysfunctions (proximal and distal) was not specific to K^+ alone but it was severely affected. The improved statue of the electrolyte state of the 400 mg/kg of CSgroup also indicates that the CS treatment ameliorated the toxic effect of the CN as a result of their anti-oxidant properties and their supply in electrolytes. This observation is also in line with the reports of Eteng et al. [26]. They reported that antioxidants such as vitamin E and selenium are vital in ameliorating the depletion of electrolytes under acidic or oxidative conditions.

Furthermore, the significant higher values of creatinine and urea as well as the significant reduction of K^+ in the therapeutic treatment (group) of low and high dose of CS compared against the negative control also indicates that the therapeutic efficacies of CS may be gradual and recovery may occur over a period of time which is contrary to the reports seen in literatures that corn silk is used to treat or completely reverse renal diseases or nephrotoxicity within a short time frame. In addition, it was also observed that the protective of potentials of corn silk given concomitantly with CN were more effective compared with the therapeutic treatments. The observation is further supported by the biochemical and histologic findings where deranged values of creatinine, urea and K^+ as well as severe distortion of the glomeruli, glomerular spaces, tubules, and loss of parenchymal materials were seen in the low and

high doses of CS aqueous extract in the therapeutic treatment unlike the protective treatments were mild distortions were seen in the glomerular space and tubules. In other words, the protective efficacies of CS extracts were more pronounced than that of the therapeutic potentials of CS extract which may take longer time frame.

The ameliorative effect observed whether in the protective or therapeutic groups could be attributed to the phytochemical constituents of the extracts as observed in our phytochemical analysis. Phytosterols, saponins, flavonoids, and phenols were the constituents observed in our CS extract and they are known biochemical with anti-oxidant properties that reduce or mitigate the disastrous activities of reactive oxygen species viz-a-viz oxidative stress and damages in cells or biological entities. As reported by Foster et al. [27], CN is a mitochondrial toxin can exert various morphological damages to the kidney due amplified intracellular and intra-mitochondrial reactive oxygen species content pathological conditions as seen in nephrotoxicity. Therefore, these anti-oxidants probably facilitated the detoxifying of reactive oxygen species that mediated the CN-induced nephrotoxicity through the induction enzymes responsible for the detoxification of ROS thereby halting or mitigating the effect oxidation on macromolecules of the renal organ-system.

5. CONCLUSION

The results obtained suggest protective and therapeutic potentials of CS extract on gentamicin-induced nephrotoxicity in albino rats. However, the therapeutic efficacy was progressively gradual and not be fast-effective as documented in most traditional or herbal literatures.

6. RECOMMENDATIONS

There is few or no study on the therapeutic and protective effects of CS extract on CN treatment, so more studies are recommended. Also, future studies with larger sample size and using the best extraction method for CS extract is warranted in order to confirm beneficiary effects of corn silk extract.

7. LIMITATION OF THE STUDY

The study/treatment duration did not cover a longer period in order to ascertain the protective and therapeutic potentials of the aqueous extract of corn silk in CN-induced nephrotoxicity. Also, the results observed in this study of this cannot be translated directly in human. Therefore, the need for human studies.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

We hereby declare that the Principles of Laboratory Animal Care (Nih Publication No. 85-23, Revised 1985) were followed. All the animal experiments were conducted according to the ethical norms approved by the Institutional Ethical Committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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