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Ameliorative Effect of Onions (*Allium Cepa*) on the Kidney of Adult Albino Rats with Gentamicin Induced Toxicity

[1]Obasi Mark Chikadibia[1], [2]Okolie Nnaemeka JC, [3]Johnkennedy Nnodim
[1,2]Department of Medical Laboratory Science Imo State University, Owerri

ABSTRACT: Phytochemical constituents of plant had been the forerunners of curative and ameliorative substances in fight against human diseases and ailments. In this study, an investigation into the ameliorative effect of onion (Allium cepa) extract was carried out to determine its effectiveness against gentamicin induced nephrotoxicity. Maceration method of extraction was used to extract the onions using absolute ethanol. A total of 60 adult albino rats of both sexes were used and grouped into; nine 9 groups as follows Group I: normal control, which received food and water only ad libitum, Group ii the gentamicin group which received 15mg/kg bw intramuscularly with food and water only for 5days. Animals in group iii-ix also received gentamicin 15mg/kg bw for five days IM, food and water. Group iii and iv are the low dose group that received 37.5 mg/kg bw Allium cepa extracts via oral gavage for one week and two weeks respectively post gentamicin injection. Group v and vi are the medium dose group that received 75mg/kg bw Allium cepa extract via oral gavage for one week and two weeks respectively. Group vii and viii are the high dose groups and received 150mg/kg bw of extract for one week and two weeks respectively. Group ix is the vitamin E group and received 131.3mg Vitamin E for a total of 14days. Body weights of the animals were taken before inducement with gentamicin and then on day 7 post inducement, day 14, and day 21. Kidney organs were also harvested on these days for histological assessment and the weight taken. It was observed that gentamicin affected the body weight of the treated animals causing a decrease in weight. Further observation showed that the decrease in weight of the gentamicin group and the low dose group were further elongated though healing started at late stage of the study. The weight of the kidney were increased histological assessment showed necrosis and haemorhagic reaction in the liver, oedema and necrosis of the cells were observed in the kidney. Administration of Allium cepa extract ameliorated the body weight of the treated groups earlier than gentamicin group. It was also observed that the vitamin E group recovered in a more robust way by the massive gain in body weight and fast recovery of kidney morphology. This indicates that Allium cepa extract has an ameliorative effect on gentamicin toxicity at a high dose but the Vitamin E effect is pronounced more than that of Allium cepa extract.

KEY WORDS: onions , kidney, adult albino rats, gentamicin

INTRODUCTION

The use of plants and plants products is as old as human existence on the planet earth. Plants of various specie has been used by man either as food substances or as medicinal substances either by direct use of the plants or plan products [1].

One of such plants that is the subject of inve`stigation in this piece of work is onion botanically known as *Allium cepa* which has both nutritional and medicinal values. Onion is a vegetable bulb crop known to most cultures and consumed worldwide [2]. It is cultivated in many areas with different variants in storage life, skin colour and bioactive compounds [3]. Onion is consumed because of its nutritional and medicinal benefits [4]

Gentamicin is an aminoglycoside antibiotic employed in curing of many gram-negative infections [5]. Gentamycin posses bacteria – killing capabilities against aerobic gram-negative bacteria making it a nice choice in the treatment of several infectious diseases. Although it has good bactericidal values, Gentamicin toxicity is well known and is an issue of concern when it is being used in treatment.

Gentamicin is known for its nephrotoxic effect because of its concentration in the renal cortex and inner ear. This can lead to ear injury resulting in auditory and vestibular dysfunction therefore it becomes imperative to look for source of amelioration of toxic effects of gentamicin and this is objective of this project work.

The kidney is one of the important organs of the renal system with the main function being reabsorbtion and excretion of waste products including toxic substances. The kidney regulates plasma Osmolarily by modulating the amount of water, solutes and electrolytes in the blood, ensuring acid-base balance and produces erythropoietin which stimulates the production of red blood cells and rennin which regulates blood pressure [6]

Corresponding Author: Obasi Mark Chikadibia

The ingeston of some toxic substances can affect the function of the kidney which impedes its metabolic function. Adverse effects of certain drugs can affect kidney function and this work aims to investigate and evaluate ameliorative measures.

Albino rats are laboratory animals used in experimental research purposes for various laboratory conditions. The rat model also gives a useful biological system to stimulate human physiological condition suitable for testing therapeutics that can potentially benefit mankind [7]

In this research work, healthy adult albino rats will be used to investigate the ameliorative effect of onion in gentamicin induced toxicity in the kidney of these albino rats.

This study also aims to establish to a cheap, readily available and safe plant source (onion) to help patients and doctors manage toxic effects of Gentamicin.

Moreso, there has been no study investigating the effectiveness of *Allium cepa* extracts in the management of Gentamicin toxicity for which prompted this research work.

MATERIALS AND METHODS

Study Design

The study was carried out in the animal house, Imo State University Owerri, under the Anatomy Department, Imo State University is located at $5^0$30'28"N, $7^0$02'26"E South East Nigeria.

Plant Material Collection and Preparation: About 3000g of onion bulbs (*Allium cepa*) were purchased from vendors at World Bank Market Owerri, Imo State.

The Method of Maceration

The onion bulbs were cleaned by removing the outer dry layers. The bulbs were cut into pieces and grinded into fine paste using a blender. The paste were poured into a container and were mixed with 2.5L of absolute ethanol. This was stored for 72hrs with intermittent mixing for 12hrs interval homogenous mixing and proper maceration to ensure maximum extraction. The mixture was covered in the container with a tight lid to prevent evaporation.

At the end of 72hrs, the mixture was filtered using a sieve to separate sediment from the filterate. The filterate was evaporated in a hot water bath at a temperature of 30°c. At the end of evaporation of the alcohol, about 115grams of a dark coloured semisolid mass was extracted.

The extract was transferred to a clean dry container and stores in a fridge for a subsequent use.

Experimental Animals

Apparently healthy, purpose breed adult of mixed sexes were allowed to acclimatize before being used. Sixty animals were used. The rats were kept in deferent cages according to their group labels and maintained in 12hrs light and dark cycle at a temperature of about 28°c + 2°c in a well aerated animal house of Anatomy, department, Imo State University. Standard diet of growers feed by vital feeds ® Nigeria were being fed to the animals together with clean drinking water.

The environment was constantly cleaned to maintain good hygiene.

Table 2: Animal Groups

Groups of Rats	Treatment	Number of Rats	Duration
Group I	Normal control	6	3 wks
Group II	Gentamicin only	6	3 wks
Group III	Gentamicin + low dose extract	6	2 wks
Group IV	Gentamicin + low dose extract	6	3 wks
Group V	Gentamicin + medium dose extract	6	2 wks
Group VI	Gentamicin + medium dose extract	6	3 wks
Group VII	Gentamicin + high dose extract	6	2 wks
Group VIII	Gentamicin + high dose extract	6	3 wks
Group IX	Gentamicin + Vit E	6	3 wks

Table 2 shpows the different groups of rats and subsequent number of weeks they were treated and doses received.

Experimental Design

A total of 54 abino rats with body weigh 100-150gm were grouped into nine groups and their cages labelled. Pre-analytic test and history of the animals were taken:

- Animals physical activity eg agility rate, and respond to stimulus.
- Body weight of the animals were taken
- Provision of daily food and water examined for any deformity and signs of infirmity.

Pattern of Treatment

The animals were fasted for 24hrs, weight taken before administration

Table 3

Groups of Rats	Treatment
Group I Normal group	Animals in this group were fed with food and water only: their body weights were taken before the experiment, then at one week interval for 3wks. At the end of the 3wks liver and kidney were harvested.
Group II Gentamicin	Rats in this groups received 0.4mls of gentamicin for 5days. They also had regular food and water. At the end of 7th days their body weights are recorded at interval for 7 days for 3weeks. Liver and kidney were harvested at the end of each week.
Group III Low dose extract 1 week	Animals in this group were given 0.4mls of gentamicin + 0.15ml extract, food and water. Gentamicin was given for 5days body weight recorded at one week intervals. The received *Allium cepa* extract for 1wk, liver and kidney harvested for analysis.
Group IV Low dose extract 2 weeks	The rats in this group received gentamicin 0.4mls, + *Allium cepa* 0.15mls food and water but received treatment with extract for extended one week making 2 weeks weight and organ were interval of one week at harvest.
Group V medium dose 1week	Rats in this group received 0.4mls gentamicin 0.3mls *Allium cepa* extract food and water. Treatment with extract commenced one week after inducement with gentamicin and lasted for 1week. Weight, organ harvest were taken at one week interval.
Group VI medium dose extract 2weeks	The rats were given gentamicin 0.4mls + *Allium cepa* 0.3mls + food and water. Treatment with extract commenced one week after inducement with gentamicin. The treatment in this group lasted for 2 weeks and organs and body weight takjen at 1wk interval.
Group VII High dose extract 1week	Received 0.4mls gentamicin + 0.6mls *Allium cepa* extract + food and water treatment with extract stated one week after inducement with gentamicin and lasted for 1week. Weight, taken at one week intervals and organs harvesting weekly.
Group VIII High dose extract 2weeks	These were given 0.4ml gentamicin + 0.6ml *Allium cepa* extract + food and water. Treatment with *Allium cepa* extract commenced one week after inducement with gentamicin and lasted for 2weeks. The weight and organ harvesting were taken at one week intervals.
Group IX Vitamin E Group	Group IX receive 0.4ml gentamicin + 1.3ml, Vitamin E + food and water. Treatment with Vitamin E started one week after inducement with gentamicin and lasted for 2weeks. Weight recording and harvesting of organs took place on interval of one week.

Table 3 shows the qwuantity of gentamicin and allium cepa extracts received by the animals and number of days administered.

Harvesting of Organs

The experimental animals were fasted for 24hrs prior to sacrificing and organ harvesting. The animals were individually placed in a jar of ether for suffocation. Weight of the rats were taken before suffocation and harvesting.

RESULT

Histological scoring of rat kidney after induction with gentamicin and treatment with *Allium cepa* extract

Histological Report

Table 4

Groups	No of Rats	Gentamicin (ml)	Day 7 after induction	Day 14 after treatment	Day 21 after treatment	No of death	Low dose	Medium dose extract (ml)	Highdose extract (ml)	Vitamin E (ml)
Normal group	6	-	Normal kidney structure	Normal kidney structure	Normal kidney	Nil				
Gentamicin	6	0.4	Severe oedema & necrosis	severe oedema and necrosis	Mild oedema and necrosis	Nil				
Low dose	12 (total)	0.4	Severe oedema & necrosis	Mild oedema & necrosis	Mild oedema & necrosis	Nil	0.15			
Medium dose	12 (total)	0.4	Severe oedema & necrosis	Mild oedema & necrosis	Mild oedema & necrosis	Nil		0.3		
High dose	12 (total)	0.4	Severe oedema & necrosis	Oedema & necrosis	Reparative cuages	Nil			0.6	
Vitamin E	6	0.4	Severe oedema & necrosis	Slight oedema and necrosis	Complete reparative changes	Nil				1.3

Table 4 shows the different results obtained from the diffent groups of the rats kidney

Table of average weight of rats in various groups at day 0, day 7, day 14 and day 21.
Table

	Initial weight	Day 7	Day 14	Day 21
Normal control	420	432	446	453
Gentamicin (G)	470	461	458	466
GLE	440	428	430	452
GME	458	449	456	474
GHE	484	475	483	497
GVE	500	491	507	516

Table repesents the average body weight of eact group pof rats

Bar chart representation of the body weight of rats different number of days pre-induction, post induction and treatment at weight days 0, 7, 14, and 21.
Figure 1

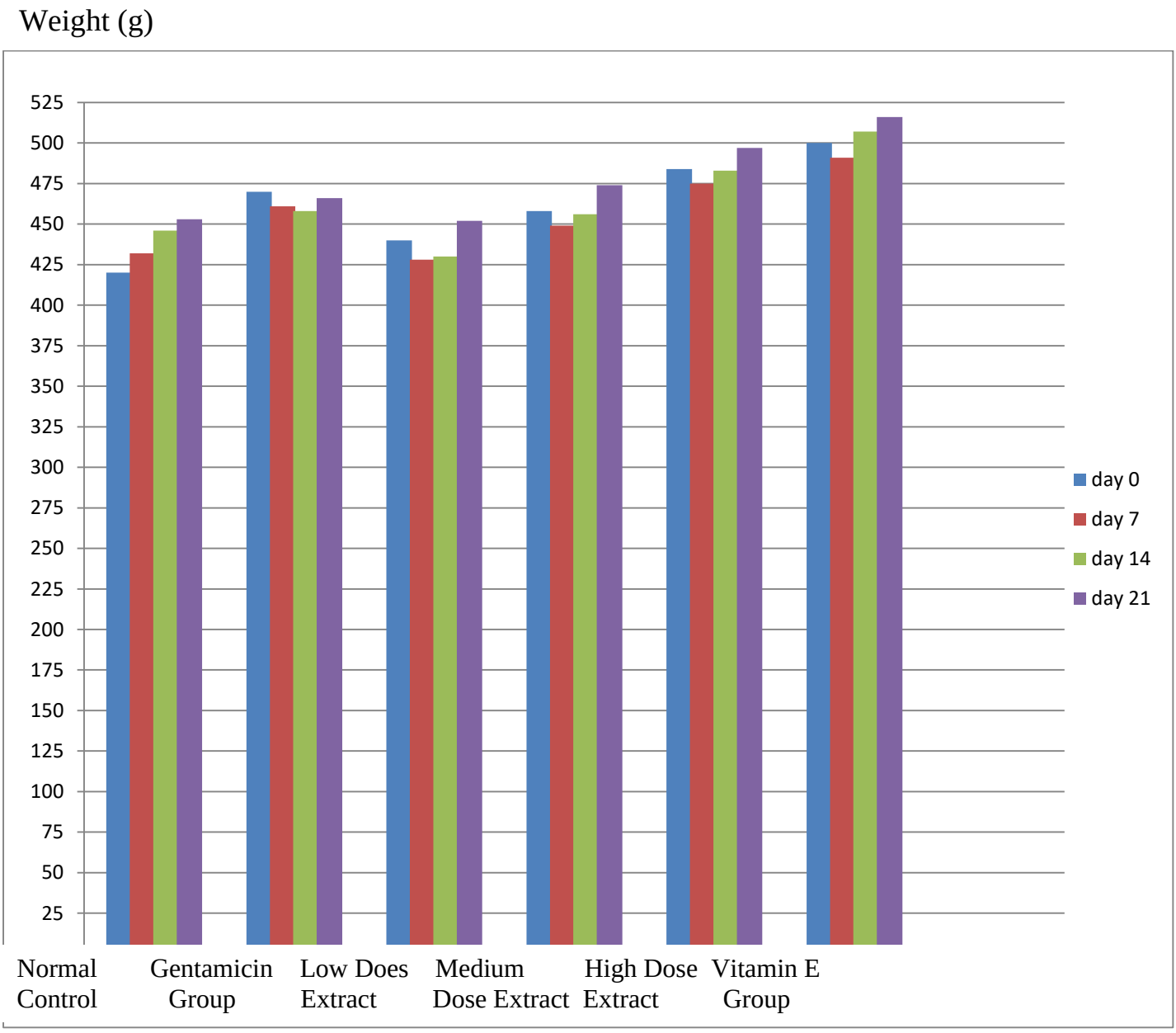


Figure 1. is the bar chart of average body weight of Rats for different group.

TOTAL KIDNEY WEIGHT OF THE VARIOUS GROUPS OF RATS PRE-INDUCTION, POST INDUCTION WITH GENTAMICIN AND TREATMENT.

Table 5

Groups of Rats	Weight (g) Pre-Induction	Weight (g) Post-Induction	Weight (g) Difference
Group I (Normal)	2.68	2.71	0.03
Group II (Gentamicin)	2.67	2.79	0.12
Group III & IV (Low Dose Extract)	2.61	2.75	0.14
Group V & VI (Medium Dose Extract)	2.53	2.62	0.09
Group VII & VIII (High Dose Extract)	2.76	2.79	0.03
Group IX (Vitamin E)	2.73	2.74	0.01

Table 15 represents the weight of kidney of the rats preinduction and post treatment note the difference in weight

BAR CHART REPRESENTATION OF THE AVERAGE KIDNEY WEIGHT OF RATS PRE-INDUCTION AND POST TREATMENT

Figure 2

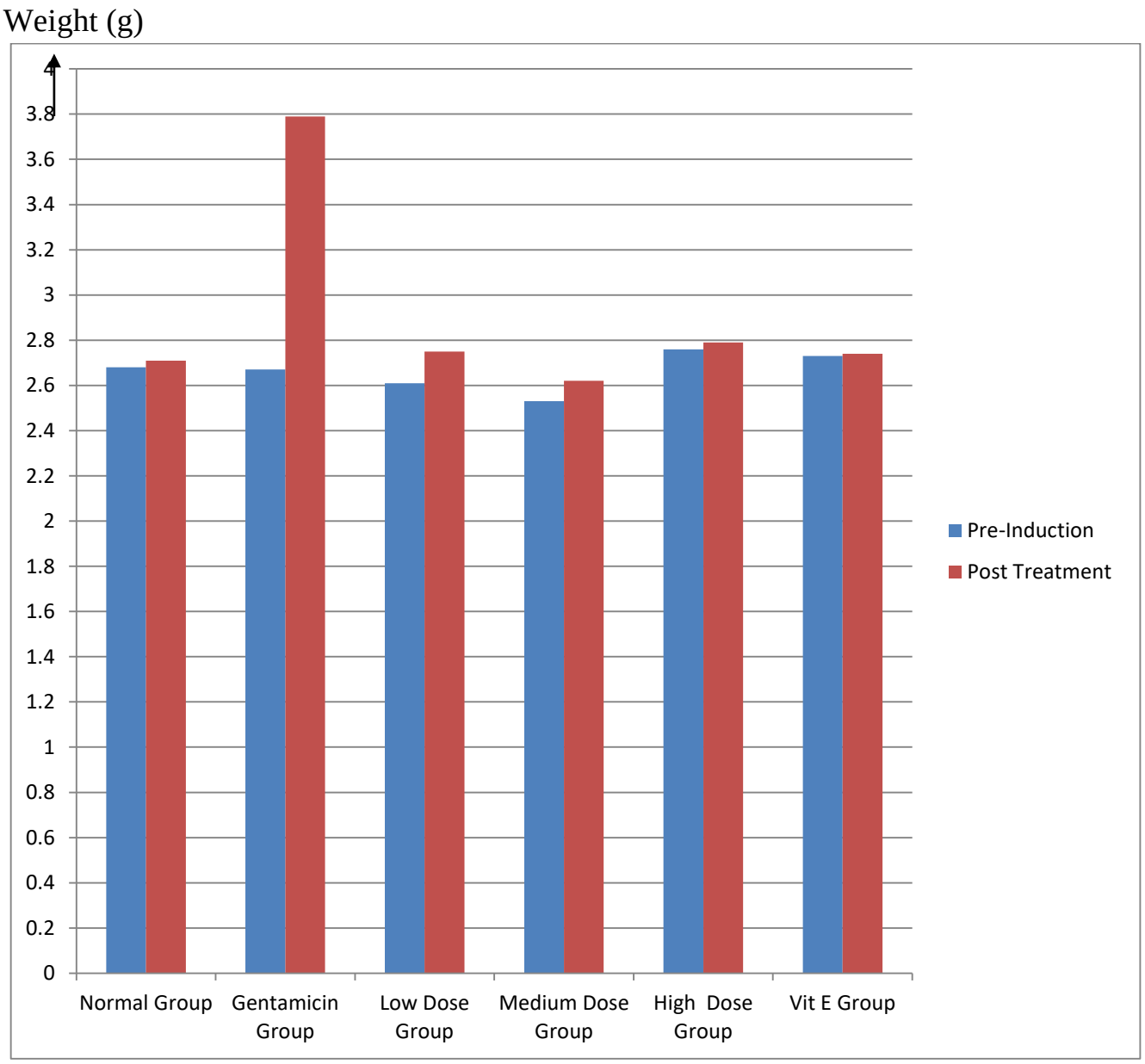


Figure 2. is the bar chart representing the weight of the kidney of rats pre-induction and ptost treatment on dy 21.

Different Rat Organs Pre-Induction, Induction and Post Treatment

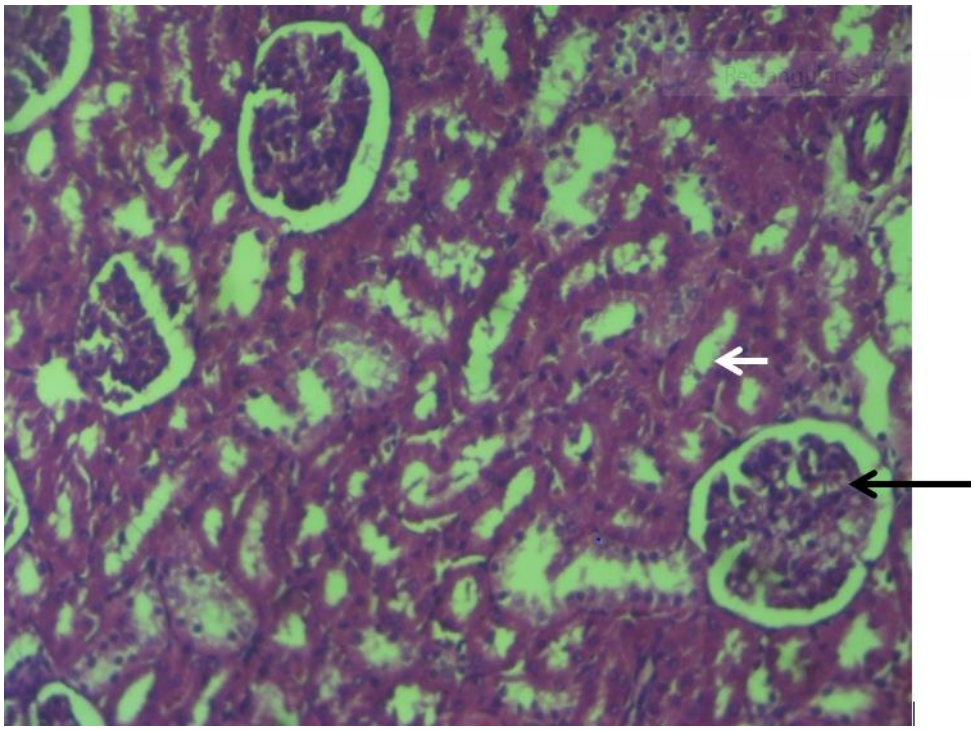


Plate 4a: Normal Kidney

Plate 4A: (Kidney Control Group)

Photomicrograph of the Kidney showing the glomeruli surrounded by narrow Bowmon's spaces. The tubules filled the bulk of the parenchyma between the corpuscles. The cortex consisting of mainly the proximal convulated tubules lined by more eosinoplilic epithelial cells.

The morphological features are in keeping with of normal kidney (H&E x 100).

Key:

Small arrow → Convoluted tubules

Long arrow → Glomeruli

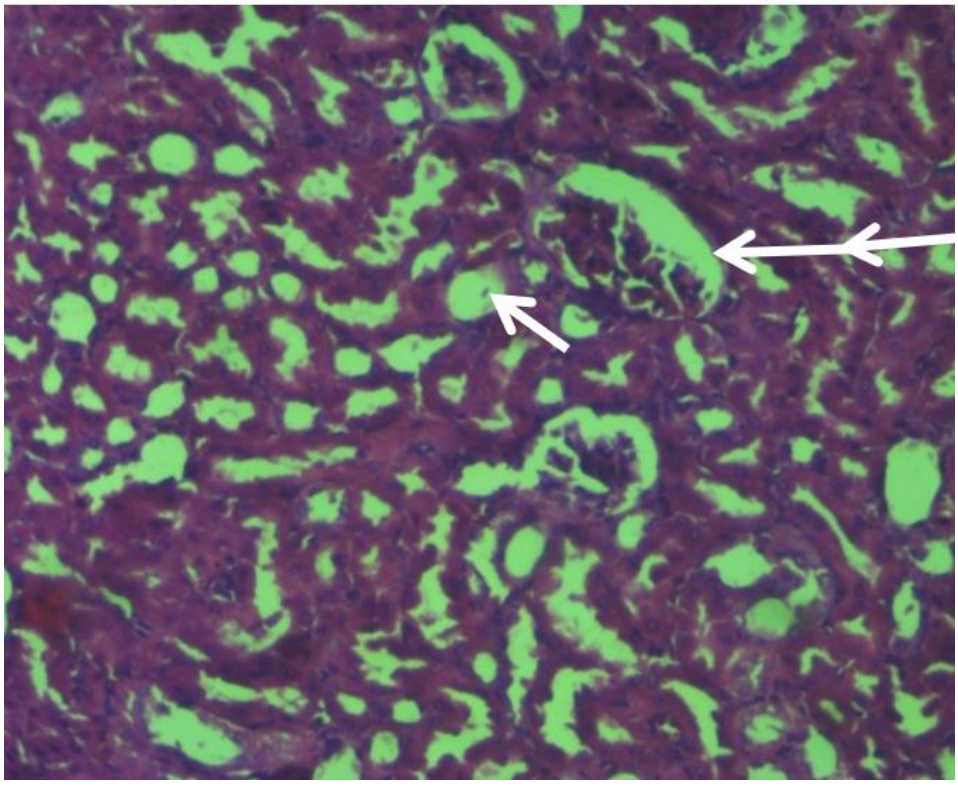


Plate 4ci: Day 7 Kidney

The photomicrograph of rat kidney at day 7 (plate 4ci and day 14 plate 4cii) showing varying degree of increased tubular epithelium with features of oedema.

Key:
Double arrow → loose glomemlar membrane
Single arrow → oedema\

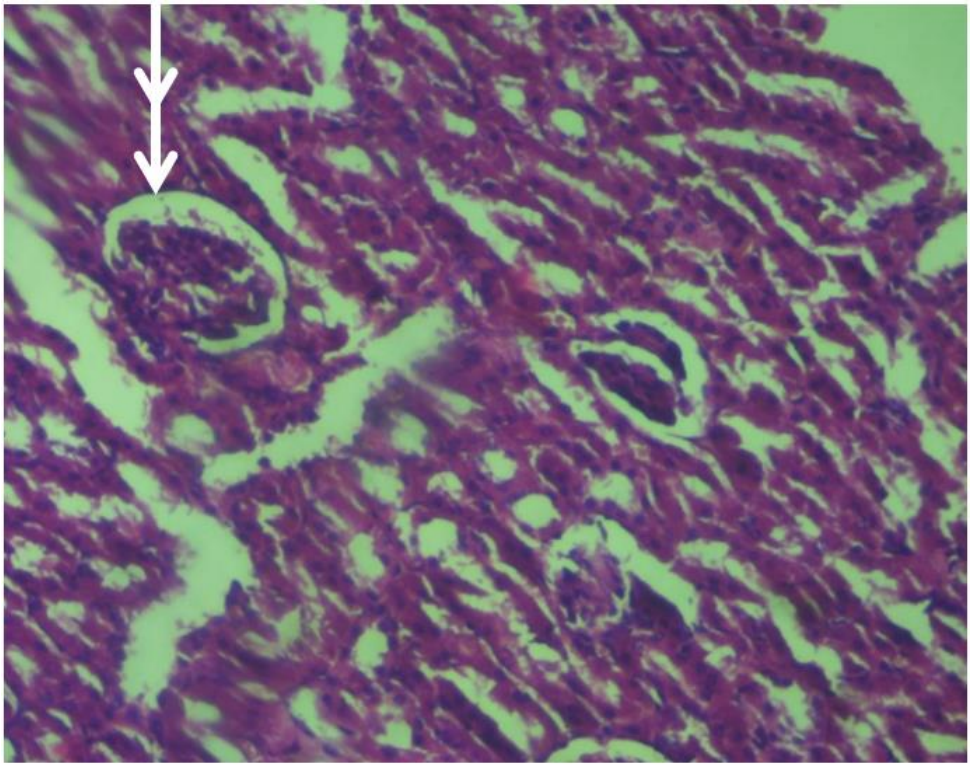
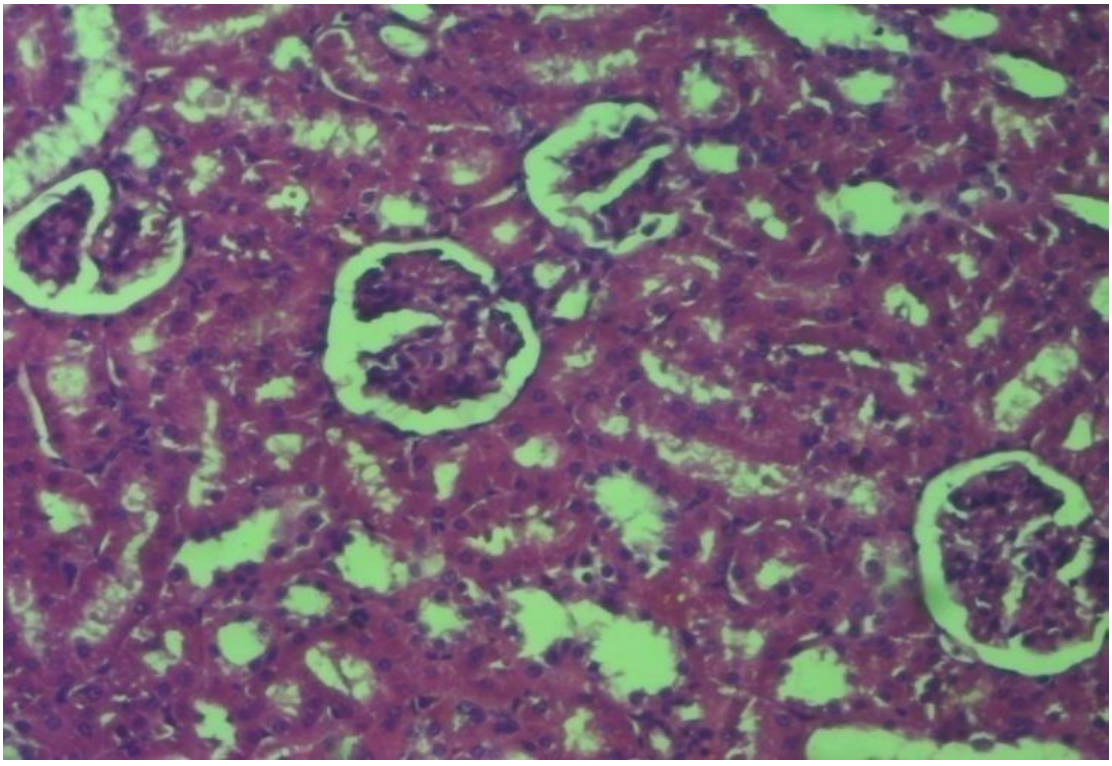


Plate 4cii: Day 14 Kidney
Photomicropraph of rat kidney of the Gentamicin group indicating tubular necrosis by the long arrow.
Plate 4ciii: Day 21 Kidney
Rat kidney induced with gentamicin toxicity at 21st.



Kidney structure shows some degree of oedema in kidney structure.

Key:

Long arrow → loose glomerulus

Short arrow → oedema

Plate 4e: (low dose group)

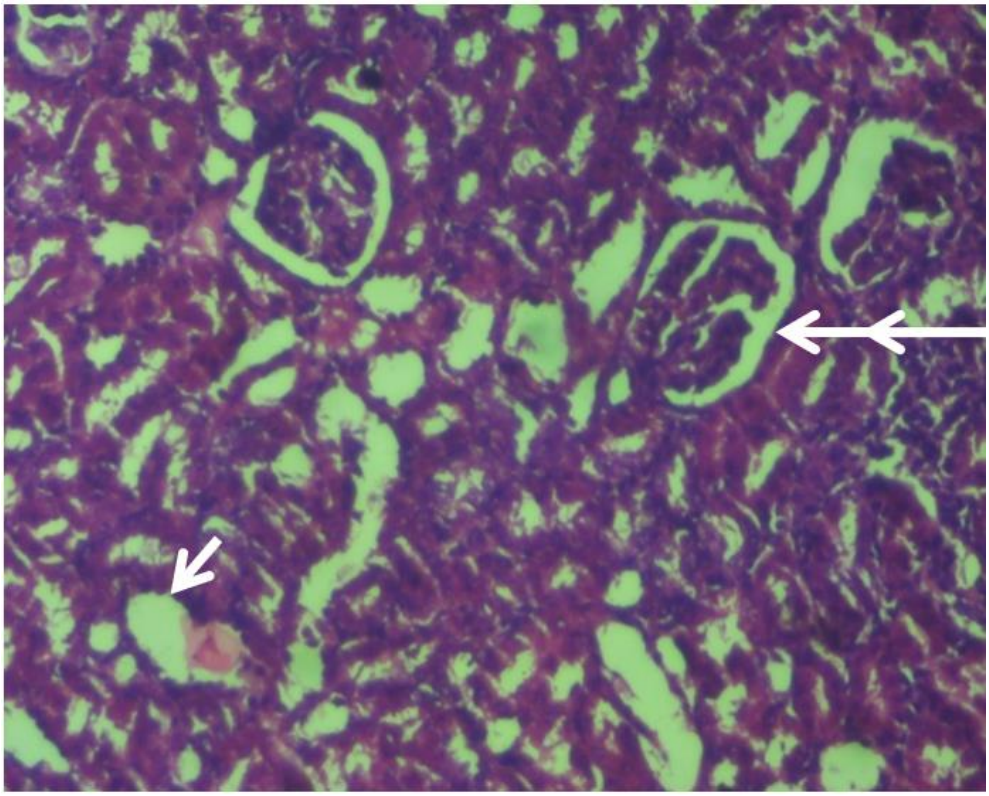


Plate 4ei: Kidney day 14

(H&E x 100)

Photomicrograph of rats in the low dose *Allium cepa* extrtract group at day 14. The double arrow indicate loose gromeruli and short arrow indicate oedema

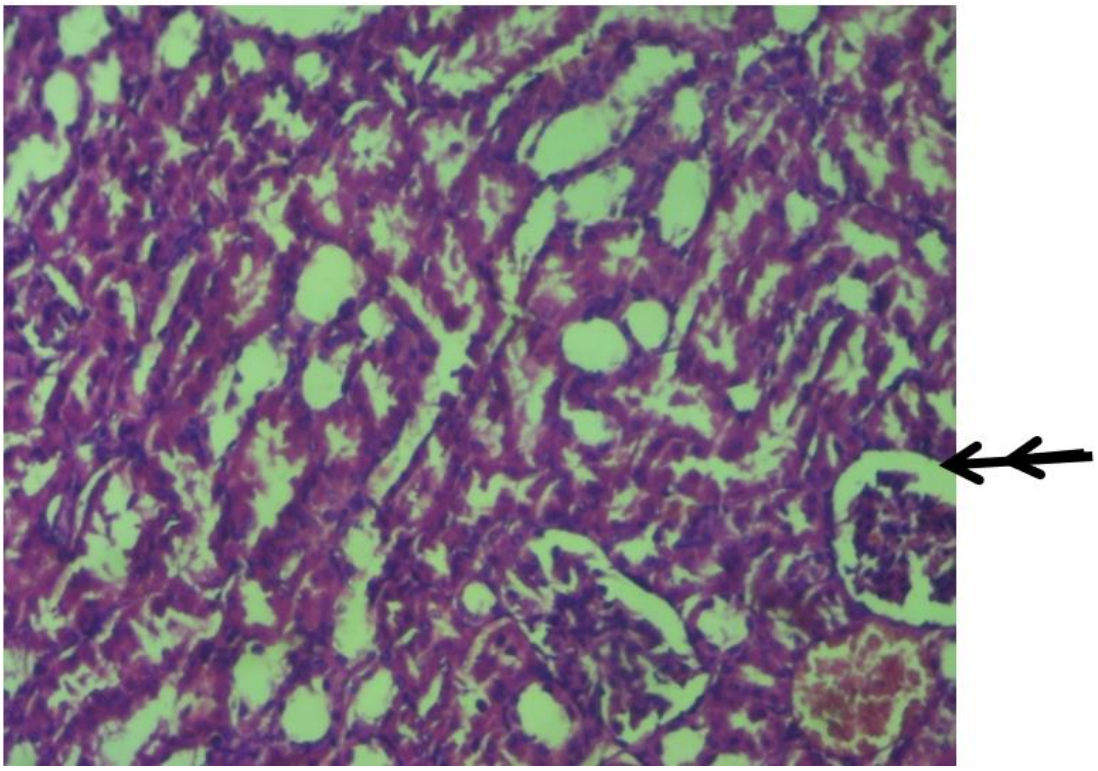


Plate 4eii: Kidney day 21
(H&E x 100)
Photomicrograph of rat kidney of the low dose group at day 21. Traces of oedema and loose glomeruli can be seen in the diagram

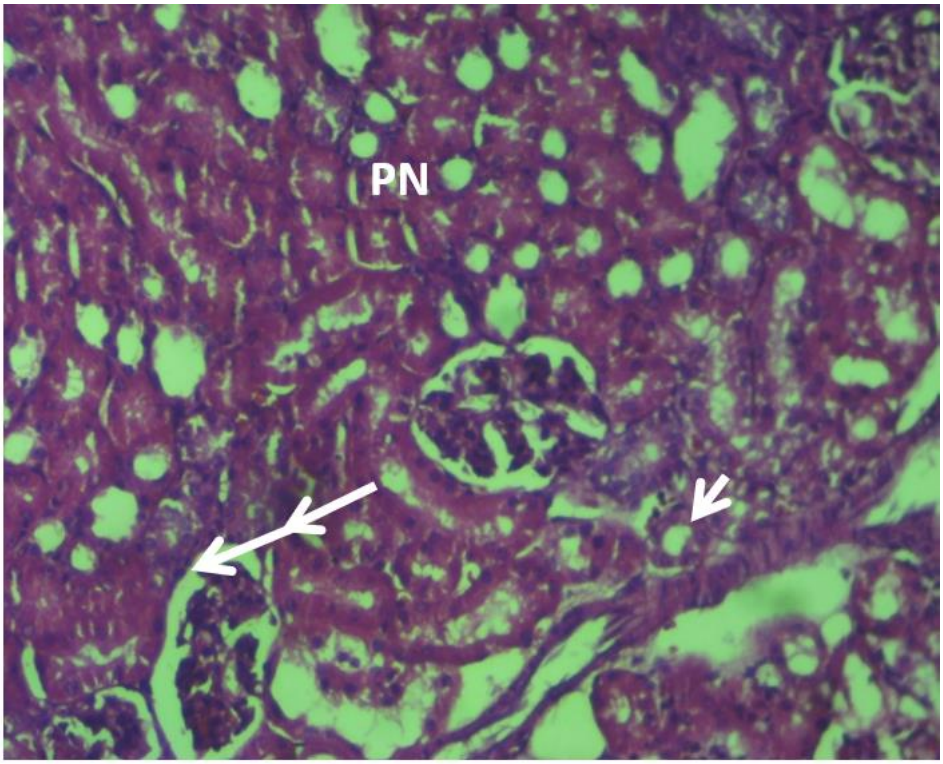


Plate 4fi: Kidney at day 14
(H&E x 100)

Photomicrograph of rats in the medium dose group showing kidney with mild necrosis and mild cellular proliferation within the glomeruli as shown by the long arrow.
The short arrow shows tubular necrosis.

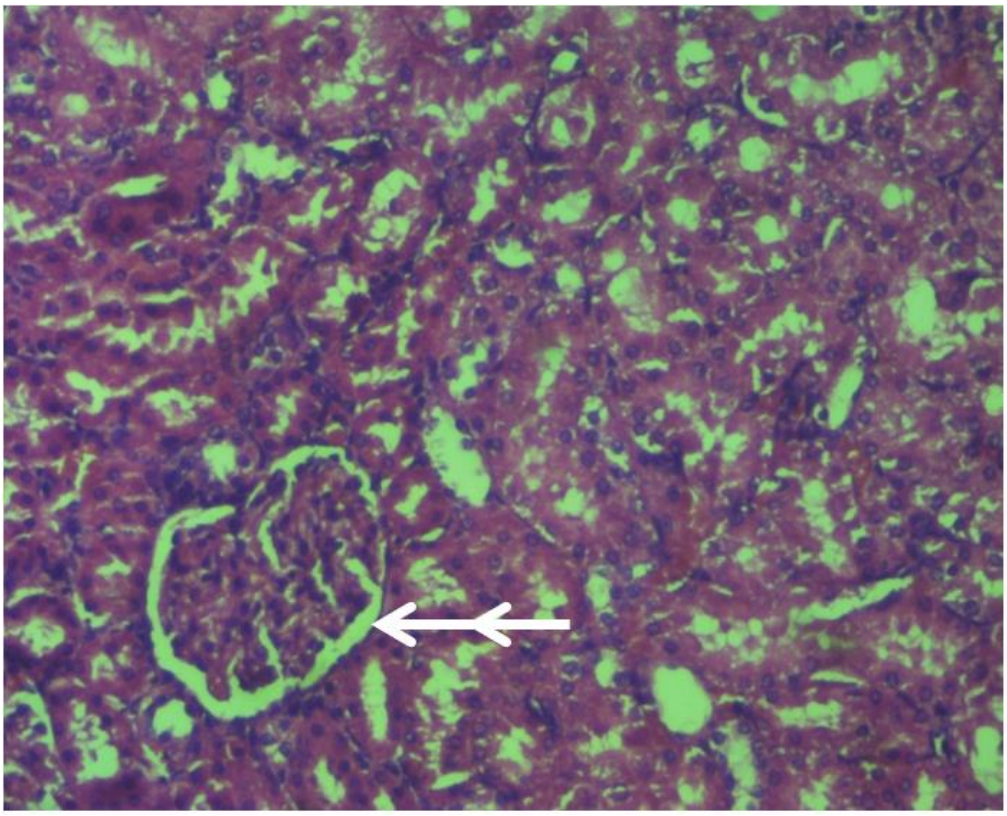


Plate 4fii: Kidney at day 21
(H&E x 100)
Photomicrograph of the kidney of rats in the medium dose group at day 21. The arrow indicates mild tubular necrosis

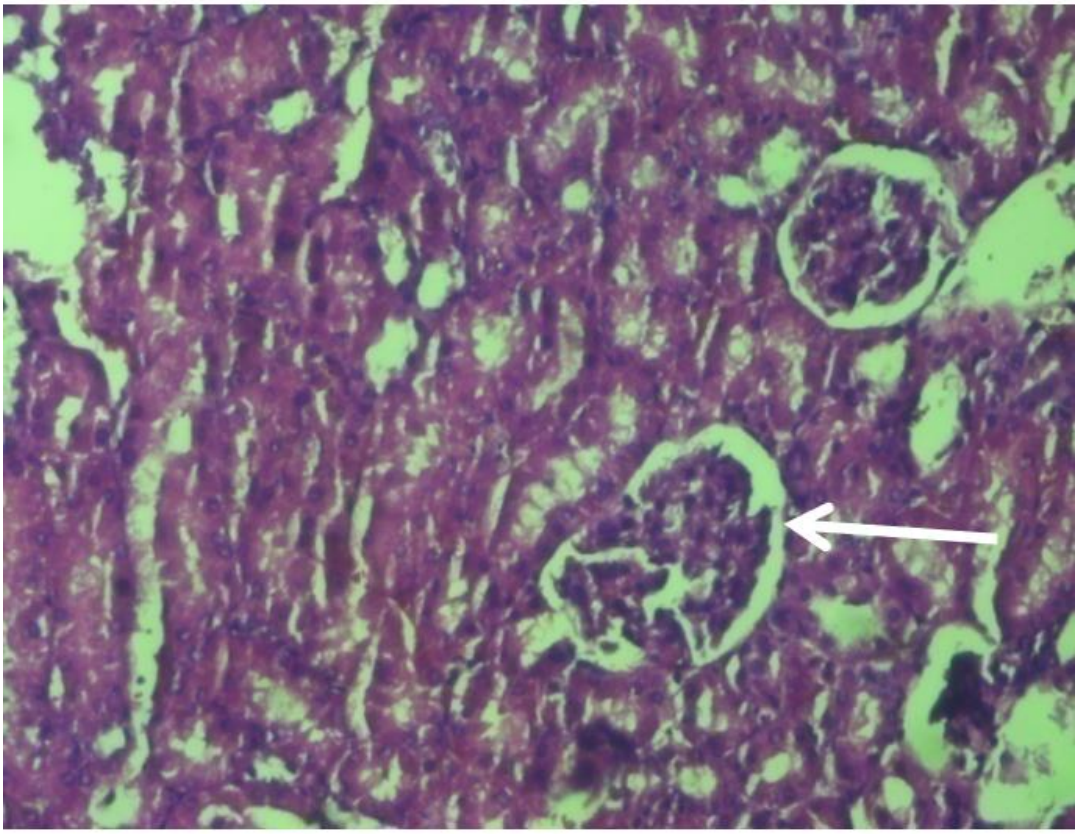


Plate 4gi: Kidney at day 14
(H&E x 100)

Photomicrograph of rats kidney treated with high dose extract of *Allium cepa* at day 14. The arrow shows reduction in tubular necrosis.

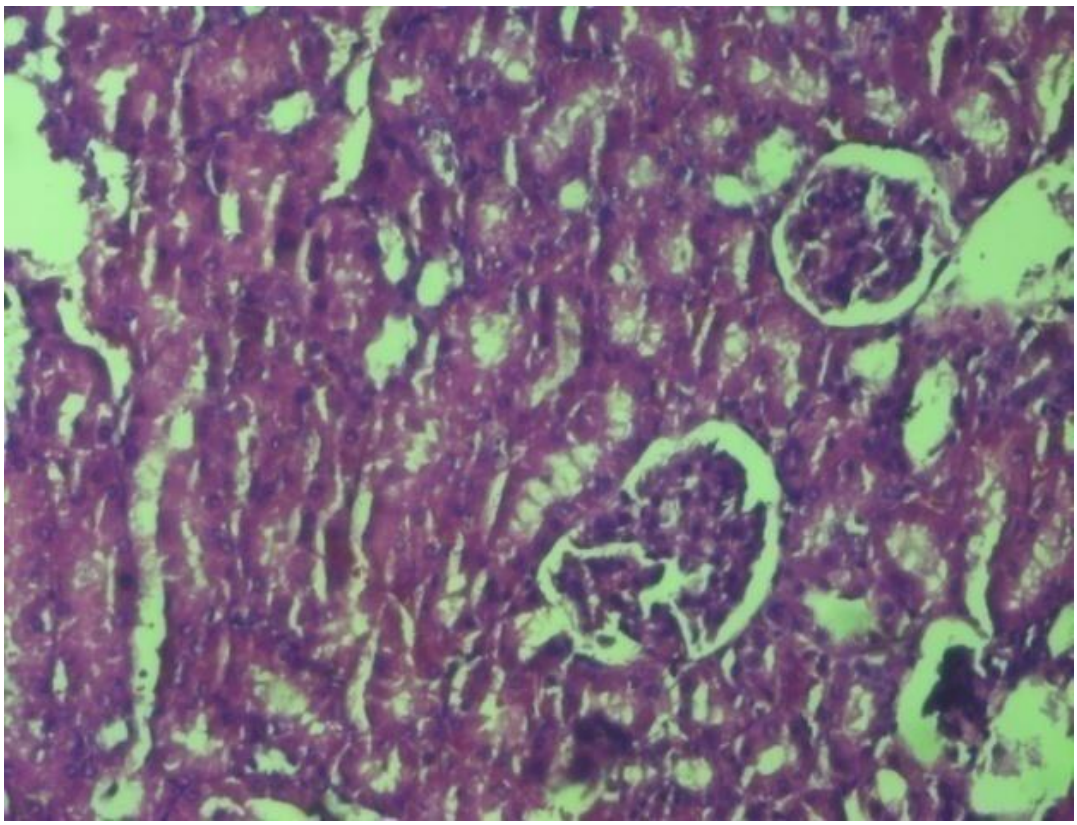


Plate 4gii: Kidney at day 2`1
(H&E x 100)

The photomicrograph at rats kidney treated with high dose extract of *Allium cepa* at day 21. The arrow show some reparative changes in tubular structure.

Plate 4h (Vitamin E Group)

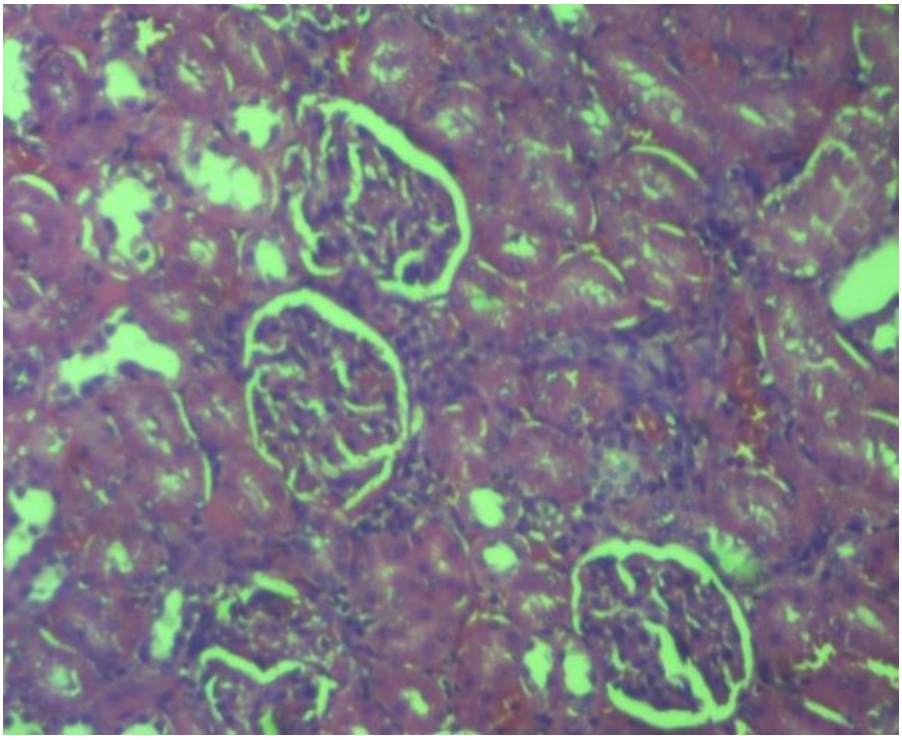


Plate 4hi: Kidney at day 14
(H&E x 100)

The photomicrograph of animals in the Vitamin E group at day 14. This shows the kidney with mild necrosis as indicated by the arrow. This is evidence of reparative restoration.

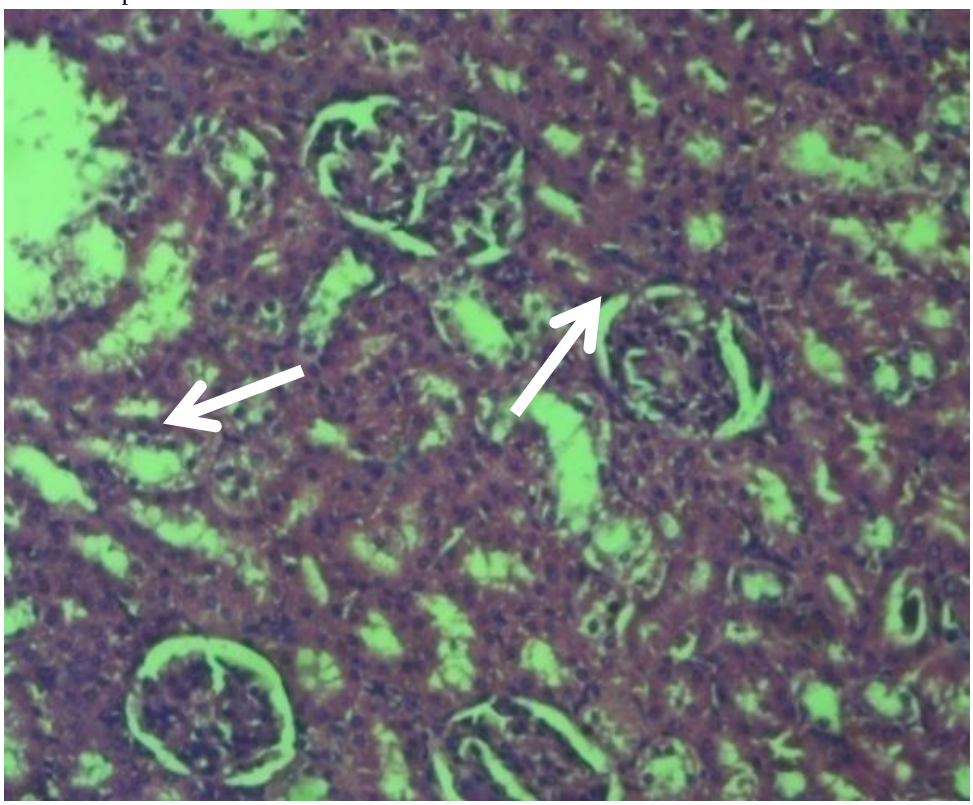


Plate 4hii: Kidney at day 21
(H&E x 100)

Photomicrograph of kidney structure of rats treated with vitamin e at day 21. There is restorative and repartative showing compared with gentamicin group. The glomeruli is more of normal structure as indicated by the arrow.

DISCUSSION

This study was carried out to determine the toxicity effect of gentamicin on the kidney and liver of rats and see if the extract of *Allium cepa* can ameliorate this toxic effect. From the results obtained, it clearly evident that gentamicin induced toxic effects on the kidney of the rats. This agrees with the works of [8] which stated that gentamicin acts on the mitochondria directly and indirectly to induce nephrotoxicity. It was reported that the nephrotoxic effect of gentamicin concerning the toxic effect of gentamicin, this piece of work agrees with the findings of [9] which states that gentamicin exerts its hepatoxicity effect on the liver through the creation of free radicals which causes liver damage.

Before the inducement of the animals with gentamicin, body weights of the animals were taken and the weights of the kidney were taken also. After the inducement the animals were observed for any changes in behaviour.

Animals had raised furs from about the 4th day of gentamicin administration. Body and organ weight of the animals were also retaken after 7th day, 14th day and 21st day post inducement. It was observed that the animals in all the induced groups had a general decline in body weight. This loss in body weight of the animals after inducement agrees with the works of Abdelrahman (2018) which recorded that animals induced with gentamicin recorded loss of body weight.

Animals in group, II (gentamicin) and group III (low dose group) started recovering latter than the animals in high dose group and vitamin E group. Animals treated with *Allium cepa* extract especially the high dose group recorded appreciable reparation both on the kidney and liver structure. At day 21, there were reduced necroses, oedema in the kidney structure as well as reduced liver haemorrhagic necrosis in the liver of the animals. Animals in the group treated with vitamin E after inducement with gentamicin only had a faster recovery on body weight and reparation in both liver and kidney structure. The ameliorative effect of the medum and high dose group of *Allium cepa* extract is comparable to that of Vitamin E group which is a standard recognized antioxidant.

The reparative and ameliorative effect of *Allium cepa* extract observed in this study agrees with the work carried out by [10] which also recorded improvement in the body weight of the animals and corresponding reparative changes in the kidney of animals treated with *Allium cepa* extract and Vitamin E. The vitamin E group had the most significant improvement in weight gain and improved structure of organs compared to other groups induced with gentamicin and this also agrees with the findings of [11]

The physiological disposition of the kidney which involves filteration and excretion of waste and toxic products from the circulatory system exposes it to toxic effect of harmful substances.

According to [12] gentamicin increases the generation of Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) in the renal cortex which subsequently leads to kidney damage.

The oxidative stress induced by gentamicin can be seen in the following ways:

- Interference with antioxidant enzymes such as catalases and superoxide dismutase due to accumulation of gentamicin. By disrupting these enzymes, gentamicin causes proteinuria, inflammation etc.
- Gentamicin affects lactate dehydrogenase (LDH) enzyme which is located in proximal tubules. This results in L-γ-Glutamyl – Lysteinyle-glycine (GSH) decreased levels and an elevated lipid peroxidation.
- Reactive oxygen species generated by gentamicin reacts with cellular components such as proteins, lipids, DNA and causes their damage. The ROS produced by gentamicin causes poly unsaturaled falty acid peroxidation (PUFAs) and the production of malondialdehyde (MDA) which is the basis of lipid peroxidation of lipids in the cellular damage and necrosis [13]

It is well known that antioxidants play a crucial role in neutralizing destructive effect of reactive oxygen species (ROS) and free radicals in the body. *Allium cepa* is known to possess a reasonable amount of antioxidants that are capable of ameliorating the toxic effect of free radicals and reactive oxygen species generated by gentamicin in the body of the experimental rats. The phytochemical constituents of *Allium cepa* such as polyphenols, organosulphur compounds, and flavinolds are among the natural antioxidant compounds found in *Allium cepa* [14. 15].An experiment carried out to evaluate the effect of phenol-rich *Allium cepa* on the development digestion and antioxidant activity and immune response on a broiler chickens, it was revealed that phenol-rich *Allium cepa* extract increased antioxidant enzymes such as catalases (CAT), superoxide dismutase (SOD) and glutathione peroxidase and these are taken to be as a result of the presence of high amount of Phenol and flavonoid content of *Allium cepa* extract [16. 17]

Based on the above evidence it can be seen that *Allium cepa* extract actually has the ameliorative property required to neutralize the free radicals generated by gentamicin. Thus so far the healing effect of *Allium cepa* extract is rooted in its ability to balance and neutralize free radicals and reactive oxygen species in the body system thus establishing an equilibrium of oxidants and antioxidant.

CONCLUSION

Based on the results obtained, it is evident that gentamicin has a toxic effect on kidney and therefore calls for caution during administration.

It is also evident that *Allium cepa* extract has the ability to ameliorative the toxic effect of gentamicin in the kidney at least at moderate dose due to its antioxidant characteristics.

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