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Histological Effects of Aqueous Extract of Carica papaya Seed on the Renal Tissue in Adult Wistar Rats**Ekundina, V.O.*¹, Ebeye, O.A.² and Odigie, B.O.³**Department of Medical Laboratory Science, Afe Babalola University Ado-Ekiti, Ekiti State, Nigeria¹,Department of Human Anatomy and Cell Biology, Delta State University Abraka, Delta State, Nigeria²,Department of Medical Laboratory Science, University of Benin, Benin City Edo State, Nigeria³

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Abstract

Attention has been given to some tropical fruit that are of medicinal importance among which is *Carica papaya*. Papaya is the fruit of the plant *Carica papaya* and the sole specie in the genus *Carica* of the *Caricaceae* family. The present study is designed to access the Histo-morphological changes on the kidney in adult Wistar rat exposed to oral administration of the aqueous extract. A total of twenty (20) male Wistar rat were divided into four (4) groups of five (5) animals. Group 1 (control) received water and feed liberally and three experimental groups (2-4) were administered with 100mg/kg, 200mg/kg and 300mg/kg aqueous extract once daily for 21 days. On completion of administration, the animals were sacrificed by cervical dislocation, dissected, kidney removed and fixed in 10% formol saline. The fixed tissues were processed for routine histological studies, sectioned at 5microns and stained with haematoxylin and eosin technique. Data obtained were expressed as mean \pm SEM. Result showed reduction in the total body weight in the treated group when initial weight is compared with the final body weight. Histopathology result showed no marked alteration in the Histo-morphological features of the renal tissue. Aqueous extract of *Carica papaya* seed showed weight reduction potentials without marked damage to the renal histomorphology. Subsequent studies should evaluate renal function parameters and ultra-structural evaluation to corroborate these findings.

Keywords: kidney, *Carica papaya*, Wistar rat, histopathology

Introduction

In the history of the world, plants have been used medically. A large and increasing number of patients use medicinal herbs or seek the advice of their physician regarding their use (O'Hara *et al.*, 1998). It has been estimated roughly that presently more than half of the total population of the world uses herbal drugs (Chang, 1987). Attention has been given to some tropical fruits that are of economic importance (Glombitza *et al.*, 1993) among which *Carica papaya* is one.

Papaya is the fruit of the plant *Carica papaya* and the sole specie in the Genus *Carica* of the plant family *Caricaceae*. *Carica papaya* is a large, tree-like plant with a single stem growing from 5 to 10m (16 to 33ft) tall, with spirally arranged leaves confined to the top of the trunk. The lower trunk is conspicuously scarred where the leaves and fruits were borne. The leaves are large, 50-70cm (20-28inches) in diameter, deeply palmate lobed with seven lobes and the tree is usually unbranched (Beckstrom-Sternberg *et al.*, 1994).

It is commonly grown in West Indies, Philippines, Sri Lanka, India, and Malaysia, other countries in tropical America and in Nigeria. In Nigeria, papaya is one of the most popular, cheapest economically important fruit trees grown and consumed for its nutritional content (Baiyewu and Amusa, 2005). There are a lot of commercial products prepared from different parts of *Carica papaya* plant such as fruit juice and seed oil. The different parts of the plant (the fruits, leaves, latex and seeds) can be eaten and also be used for medicinal purposes as claimed traditionally for the treatment of

different ailments (Wiert, 2002) and wound healing (Suhada *et al.*, 2008). The unripe fruit is used traditionally among the Yoruba tribe of Nigeria for the treatment of various human and veterinary diseases including malaria, hypertension, diabetes mellitus, hypercholesterolemia, jaundice, intestinal helminthiasis (Gill, 1992) and for the management of sickle cell anemia (Ogunyemi *et al.*, 2008).

Carica papaya can be used as food and the fruit contains several nutrients such as provitamin A carotenoids, vitamin C and folate. Papaya skin pulp and seeds contains a variety of phytochemicals including lycopene and polyphenols. The ripe fruit of *Carica papaya* is usually eaten raw without the skin and seeds, while the unripe green fruit can be cooked usually in curries, salad, and stews (Natty, 2013). *Carica papaya* is locally known as Ibepe, Gwanda, Okwere in Yoruba, Hausa, Igbo respectively. Various pharmacological actions and medicinal uses of different parts of papaya are well reported in the ancient literature (Kirtikur and Basu, 1998).

The kidney is a bean shaped structure located at the posterior portion of the abdomen (Moore *et al.*, 2006). It is made up of nephrons which are its basic functional unit that play pivotal role in ultrafiltration of waste products from the blood stream. Hence, this present study is designed to assess the histo-morphological changes of the kidney in adult Wistar rats exposed to oral administration of *Carica papaya* seed extract.

Methodology

Carica papaya seed Extract Preparation

Carica papaya fruit was bought from a local market in Abraka. The fruits were peeled and the seeds were collected, air dried and later grounded. Then they were weighed, 36 g of the grounded seed were soaked with 180ml of distilled water for 48 hours and the residue was separated from the solvent. The solvent was concentrated to a paste-like solid with a heating mantle and the extract was kept in a clean container and refrigerated until use.

Animal Handling

Twenty (20) Wistar rats weighing between 160g and 270g obtained from the animal house of the Faculty of Basic Medical Science, Delta State University Abraka were used for this study. They were kept in rat cages that was well ventilated and exposed to 12 hours light and 12 hours darkness and they were fed with clean water and rat chow once daily. The rats were acclimatize for a period of two (2) weeks prior to the beginning of the experiment.

Experimental design

A total of twenty (20) male Wistar rats were divided into four (4) groups of 5 rats each, comprising of one control group (group 1) and three experimental groups (group 2-4).

- I. Group 1: Received rat chow and water daily without extract.
- ii. Group 2: Received rat chow and water daily with a dose of 100mg/kg body weight of aqueous extract of *Carica papaya* seed.
- iii. Group 3: Received rat chow and water daily with a dose of 200mg/kg body weight of aqueous extract of *Carica papaya* seed.
- iv. Group 4: Received rat chow and water daily with a dose of 300mg/kg body weight of aqueous extract of *Carica papaya* seed.

Extract Administration

The administration of the extract was done orally with the help of an orogastric cannula once daily between the hours of 12:00pm and 01:00pm for a period of 21 days (3 weeks).

Histological procedure

On the twenty-second (22nd) day of the experiment the animals were sacrificed by cervical dislocation. The dissected rats' kidneys were taken and fixed in 10% formal saline and sections were taken from them for processing. The tissues obtained was dehydrated with ascending grades of alcohol (ethanol), cleared with xylene, impregnated and embedded in paraffin wax. Tissue section of 5µm in thickness was prepared using a rotary microtome and stained with Haematoxylin and Eosin (H&E) and was observed using a light microscope.

Statistical analysis

All data are expressed as mean ± Standard error of mean (SEM). A p-value of < 0.05 was considered statistically significant in all statistical analysis.

Results

Body Weight

From table 1 above, the final body weight (220.97±35.32) of the control animals (Group 1) significantly increased (p<0.05), when compared with the initial body weight

(212.33±27.00). But mild reduction was observed with 200mg/kg of the extract treated animals (groups 3) when compared to their initial body weight (210.00±5.77) and final weight (205.27±15.75). A mild decrease was also observed in the final body weight (180.03±17.63) of the 300mg/kg (Group 4) of the extract treated animals when compared with their initial body weight (196.67±3.33). The body weights of the group 2 animals which received 100mg/kg body weight of the extract were also decreased.

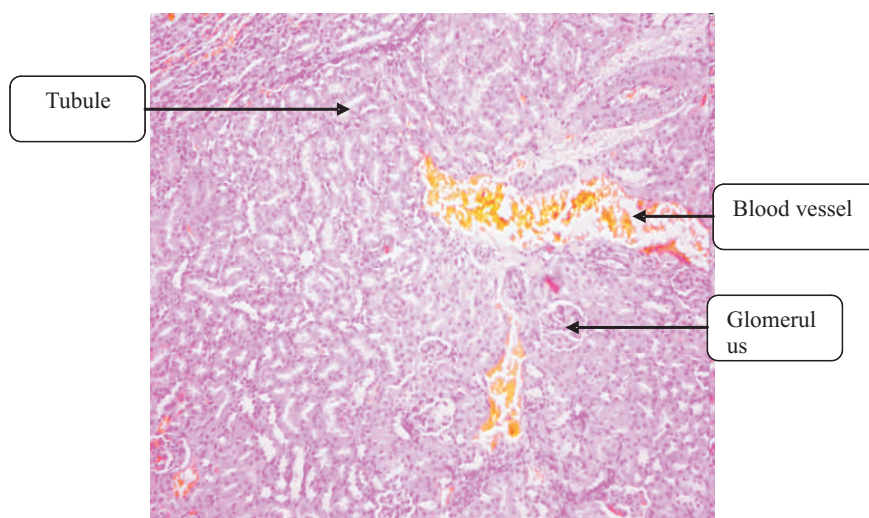
Table 1: Effects of Carica Papaya seed extract on body weight of Wistar rats

Study Groups	Changes in Body Weight (g)				
	Initial	Week 1	Week 2	Week 3	Final
Control	212.33±27.00	213.33±27.28	221.00±32.32*	225.00±29.30*	220.97±35.32
100mg/kg extract	220.00±26.46	226.67±29.63	208.33±21.86	197.00±32.65	193.70±32.94^
200mg/kg extract	210.00±5.77	210.00±11.55	210.00±10.00	202.33±8.09	205.27±15.75
300mg/kg extract	196.67±3.33	193.33±8.82	188.33±11.67	184.00±13.32	180.03±17.63

Values are expressed as mean ± Standard error of mean (S.E.M), n=4 *p<0.05: Significant increase and ^p<0.05: Significant decrease when body weights were compared initial weight and final B.W at end of the experiment.

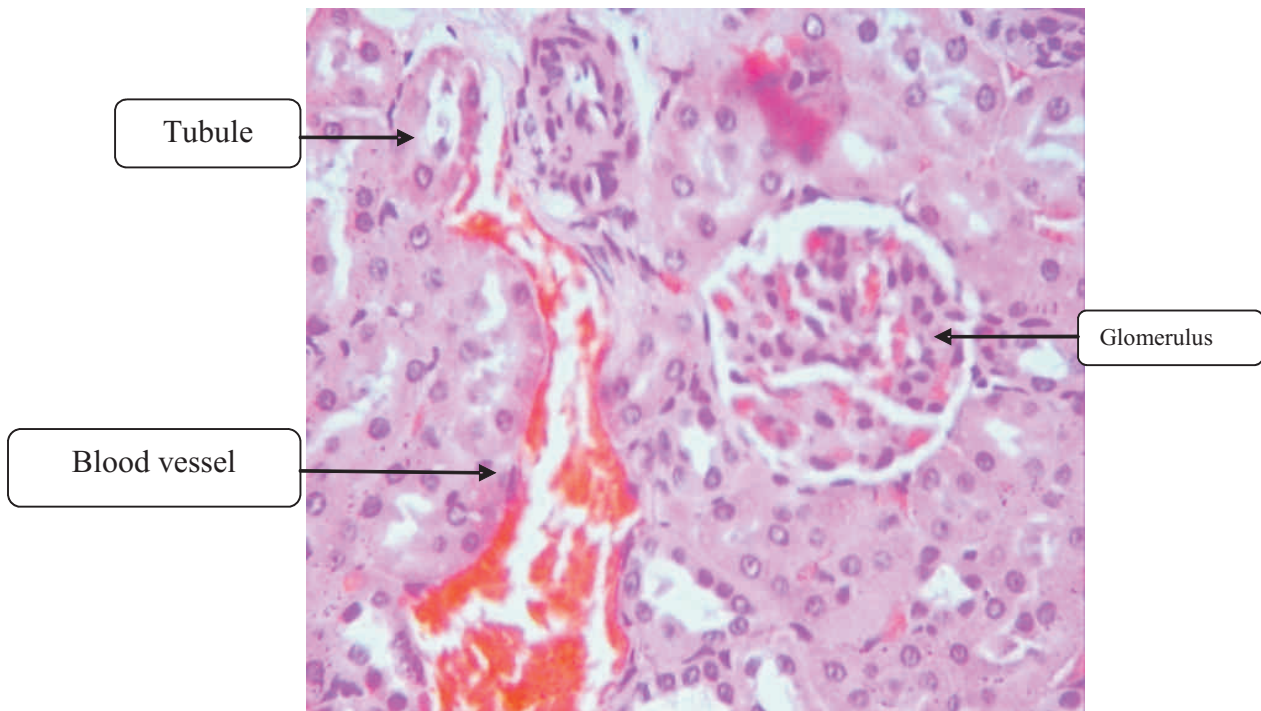
Photomicrographs of the Kidney

The photomicrographs of kidney sections from control and experimental rats (administered with different doses of aqueous extract of carica papaya seed for 21 days) stained with haematoxylin and eosin (H&E) are shown below.



H and E x 100

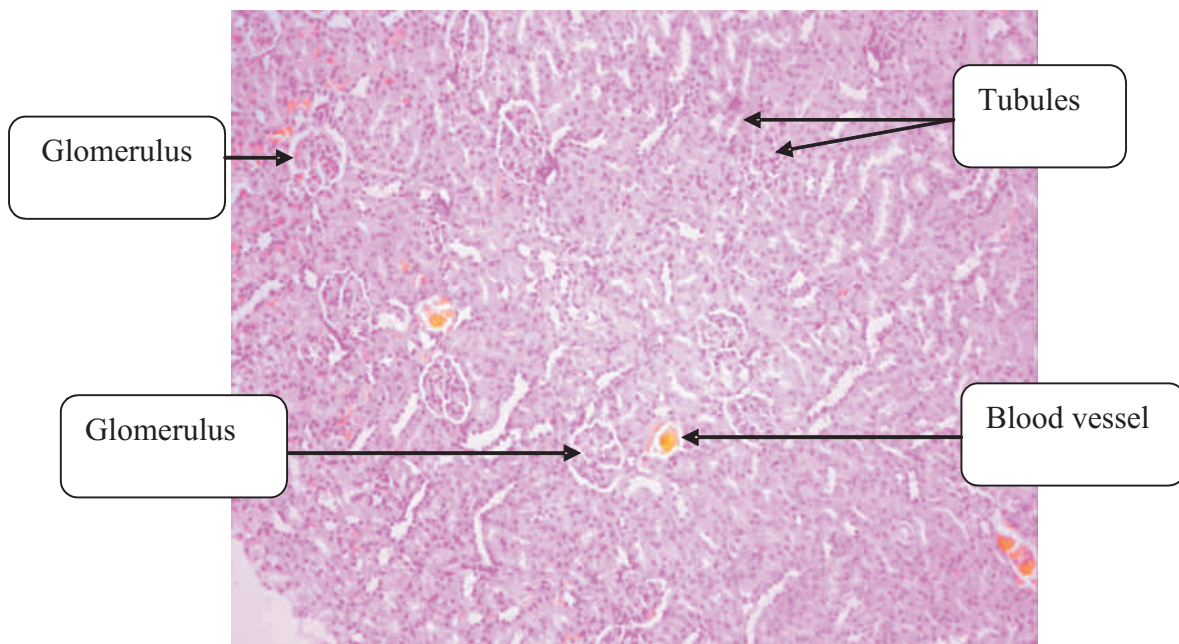
Plate 1a (group 1): Control group of photomicrograph of the kidney showing a kidney section stained with H&E. A section showing glomeruli of variable sizes disposed within tubules, which are lined by simple cuboidal epithelium. The tubular cells have centrally placed vesicular nuclei. Also seen are blood vessels.



H and E x 400

Plate 1b (Group 1): Control group of photomicrograph of the kidney showing a kidney section stained with H&E.

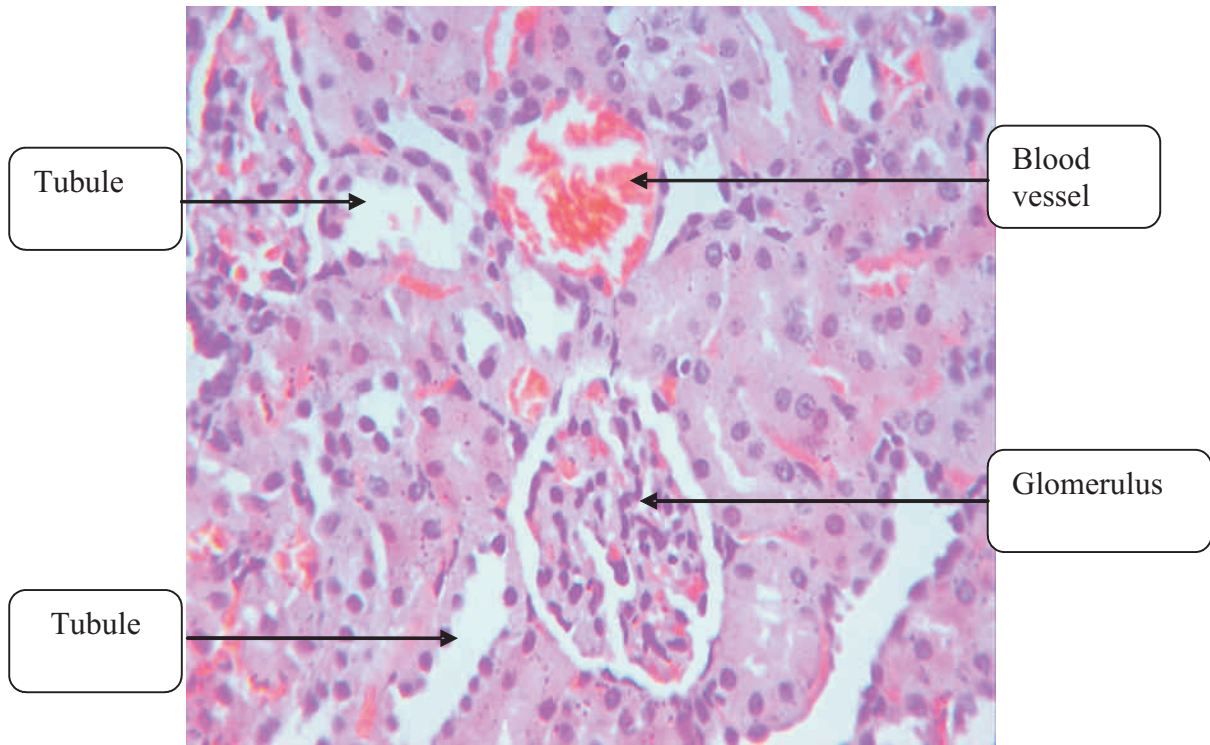
Section of the kidney show glomeruli of variable sizes disposed within tubules, which are lined by simple cuboidal epithelium. The tubular cells have centrally placed vesicular nuclei. Also seen are few blood vessels.



H and E x 100

Plate 2a (Group 2): Experimental group of photomicrograph of the kidney showing a kidney section stained with H&E.

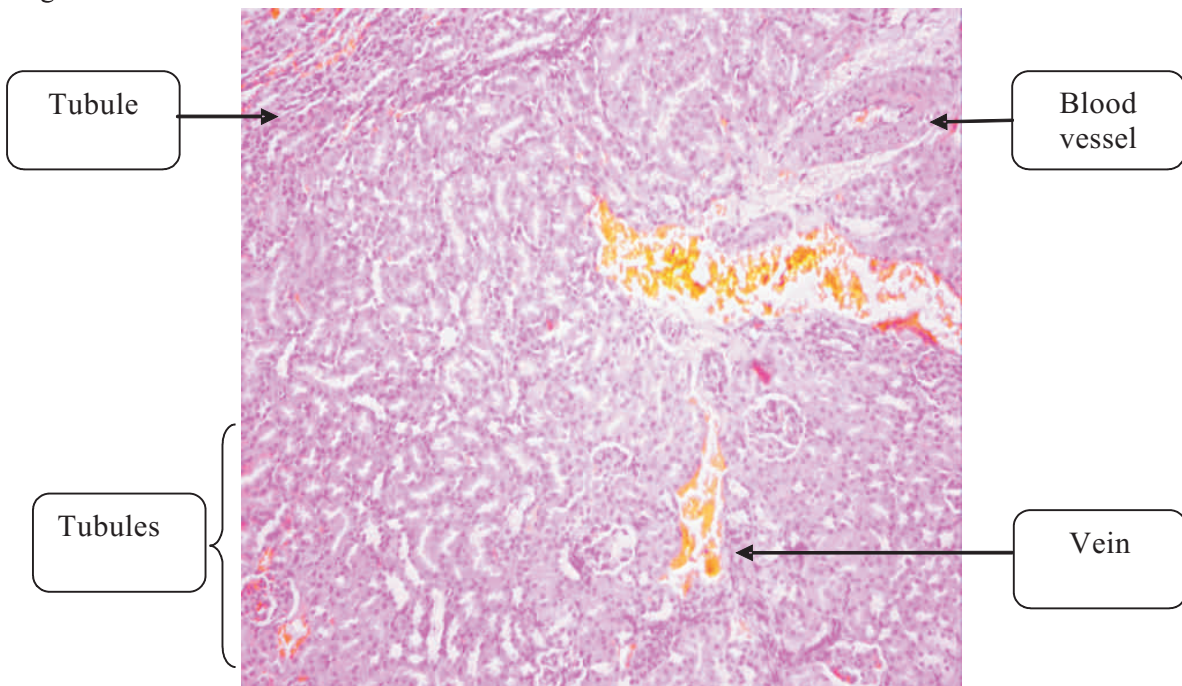
A section showing glomeruli of variable sizes disposed within tubules, which are lined by simple cuboidal epithelium. The tubular cells have centrally placed vesicular nuclei. Also seen are few congested blood vessels.



H and E x 400

Plate 2b (Group 2): Experimental group of photomicrograph of the kidney showing a kidney section stained with H&E.

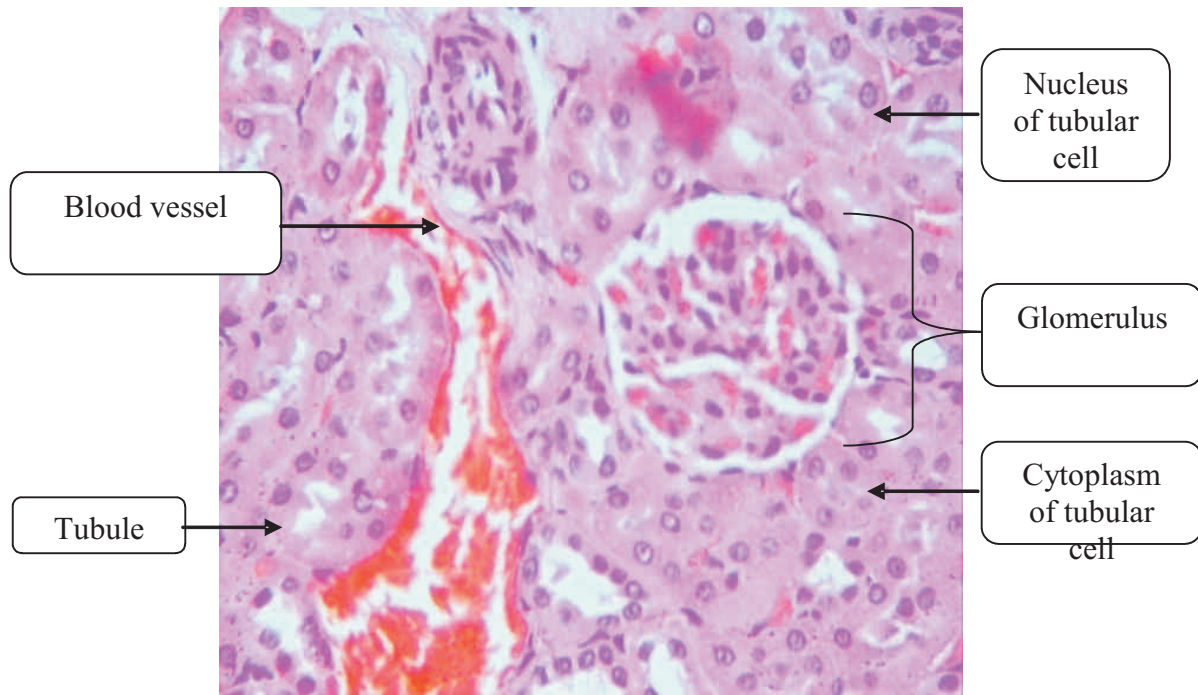
Section of the kidney show glomeruli of variable sizes disposed within tubules, which are lined by simple cuboidal epithelium. The tubular cells have centrally placed vesicular nuclei the interstitium and blood vessels are congested.



H and E x 100

Plate 3a (Group 3): Experimental group of photomicrograph of the kidney showing a kidney section stained with H&E.

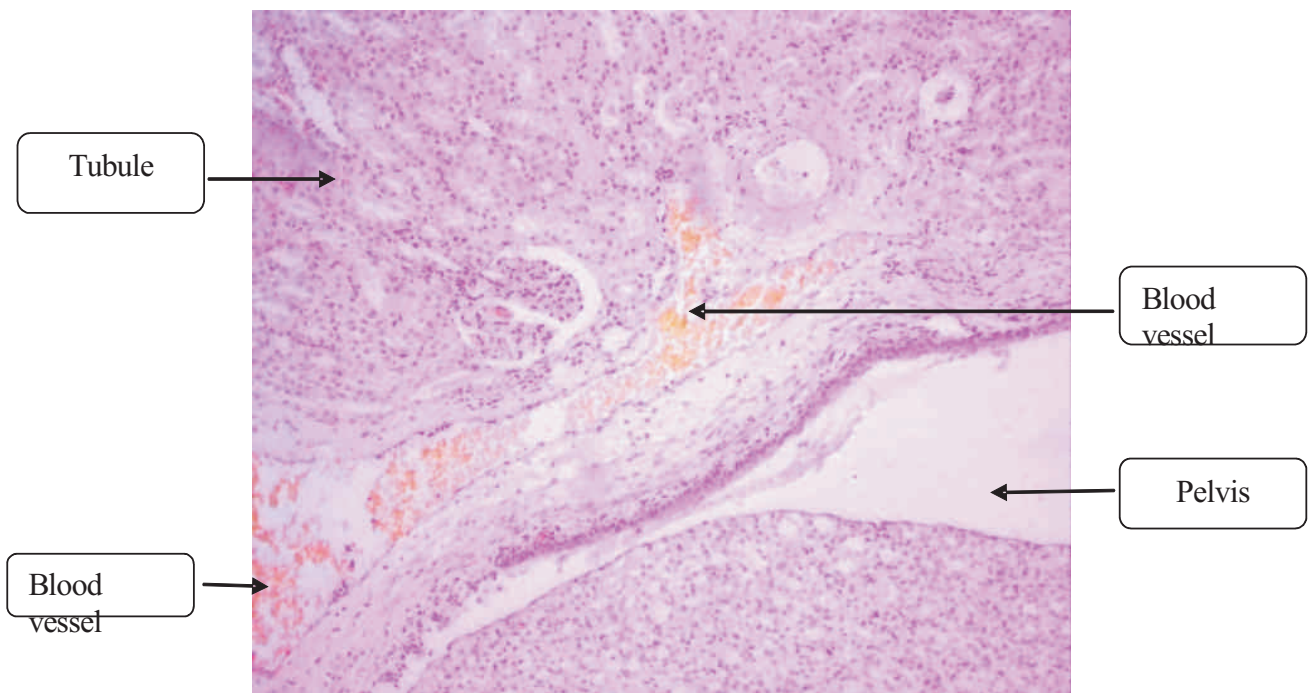
A section of the kidney showing glomeruli of variable sizes disposed within tubules, which are lined by simple cuboidal epithelium. The tubular cells have centrally placed vesicular nuclei. Also seen are congested blood vessels.



H and E x 400

Plate 3b (Group 3): Experimental group of photomicrograph of the kidney showing a kidney section stained with H&E.

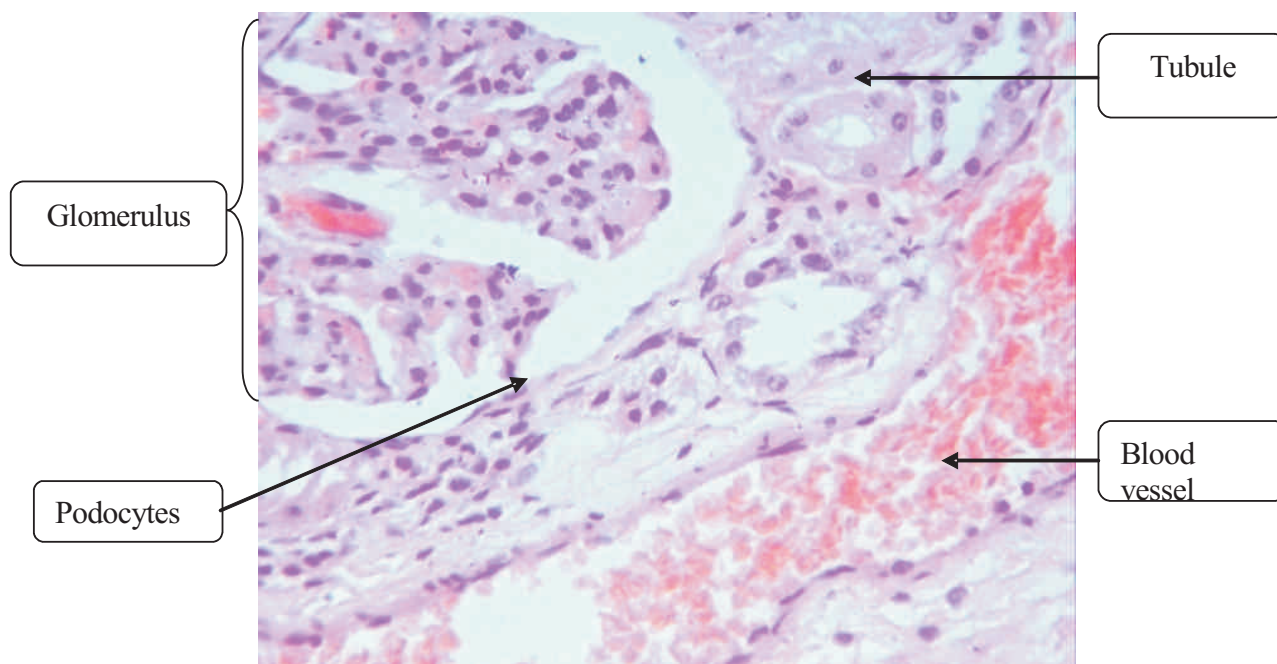
Section of the kidney show glomeruli of variable sizes disposed within tubules, which are lined by simple cuboidal epithelium. The tubular cells have centrally placed vesicular nuclei. Also seen are congested blood vessels.



H and E x 100

Plate 4a (Group 4): Experimental group of photomicrograph of the kidney showing a kidney section stained with H&E.

A section of the kidney showing glomeruli of variable sizes disposed within tubules, which are lined by simple cuboidal epithelium. The tubular cells have centrally placed vesicular nuclei. Also seen are congested blood vessels.



H and E x 400

Plate 4b (Group 4): Experimental group of photomicrograph of the kidney showing a kidney section stained with H&E.

Section of the kidney show glomeruli of variable sizes disposed within tubules, which are lined by simple cuboidal epithelium. The tubular cells have centrally placed vesicular nuclei. Also seen are congested blood vessels.

Discussion

It has been reported that the safety assessment in the experimental animals of both medicinal and non-medicinal biological active chemicals has been very successful in predicting toxicity in humans, (Gu *et al.*, 1995). Therefore, this present study was carried out in order to assess the effect of aqueous extract of *Carica papaya* seed on the histo-morphology of the kidney.

From table 1, the final body weight (220.97 ± 35.32) of the control animals (group 1) was significantly increased ($p < 0.05$) when compared with the initial body weight (212.33 ± 27.00). But there was reduction in the body weight of the experimental animals (Group 2, 3 and 4) that received 100mg/kg, 200mg/kg and 300mg/kg body weight of aqueous extract of *Carica papaya* seed. This finding is consistent with a previous report (Das, 1980) which indicated that the seed of *carica papaya* is black and contains an active enzyme carpesemine which is a plant growth inhibitor and can cause reduction in body weight in male albino rats. Our finding is however at variance with a previous report (Nale *et al.*, 2012) which demonstrated

significant ($p < 0.05$) increase in the body weight of the animals that were administered with *Carica papaya* seed extract.

The photomicrographs of plate 1a and 1b Control (Group 1) stained with H&E is a section of the kidney of rats that received clean water and rat chow only and these sections revealed normal histological features such as the glomeruli in variable sizes disposed within tubules which are lined with simple cuboidal epithelium, the tubular cells having centrally placed vesicular nuclei. The photomicrographs of plate 2a and 2b (Group 2) of rats that received rat chow and clean water and was administered with 100mg/kg body weight of aqueous extract of *carica papaya* seed and it showed no histological distortion of the kidney. The photomicrographs of plate 3a and 3b (Group 3) of rats that received rat chow and clean water and was administered orally with 200mg/kg body weight of aqueous extract of *carica papaya* seed revealed no histological damage of the kidney sections. The photomicrographs of plate 4a and 4b (Group 4) of rat that received rat chow and clean water and was administered orally with 300mg/kg body

weight of aqueous extract of carica papaya seed highlighted no histological damages. These results obtained revealed that aqueous extract of Carica Papaya seed had no effect on the histology of the kidney when compared with the control group, reason might be because of the short duration of this study which lasted for three weeks but this is in consonance with Oduola *et al.*, (2010) who revealed in their study that no lesions was noted in all tissue sections such as the liver, kidney, heart and small intestines of Wistar rats administered with aqueous extract of unripe pawpaw. Our finding is consistent with a previous report (Nale *et al.*, 2012) which indicated that administration of aqueous extract of Carica papaya seed prevent disruption of kidney structures, hence stating that this extract is nephroprotective which might be due to the presence of phytochemicals like Flavanoids and tannins which act as antioxidants individually or synergistically. Our finding is however at variance with a previous report (Dikibo *et al.*, 2012) which indicated mild to severe glomerular degenerations, tubular wall distortions and vacuolation glomerular shrinkage following the administration of Carica papaya seed extract. The reason for this difference could be because of the longer duration of the extract (carica papaya seed) administered to the rats. However, our finding is in agreement regarding their study on this extract on the kidney which demonstrated loss in body weight.

The evaluation of the possible effects of aqueous extract of Carica Papaya seed on the kidney did not record any histological damage using H&E stains and light microscopy but there was decrease in the body weight of the treated animals. The decrease of body weight caused by this extract is significant to humans especially the obese persons because it will help to reduce their body weight since the response of human is similar to that of experimental animals.

Recommendations

It is recommended that more research on this area should be carried out using electron microscopy where cellular organelles can be studied in detail also evaluating other functional parameters to corroborate the findings from these studies.

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