EFFECTS OF AQUEOUS LEAF EXTRACT OF *ALCHORNEA CORDIFOLIA* ON THE KIDNEY OF ADULT WISTAR RATS.

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ABSTRACT
Background: *Alchornea cordifolia* is counted among the plants traditionally used in several African countries for the treatment of rheumatism, arthritis, inflammatory, malaria, etc.
Aim: This research aimed in evaluating the possible effects of *alchornea cordifolia* on the kidneys of adult wistar rats.
Methodology: Rats of both sexes (n=30), with an average weight of 197g were randomly assigned into 6 test (n=5) and control (n=5) groups. Rats in the test group were given the aqueous extract of *alchornea cordifolia* leaf at a single dose of 100mg/kg, 250mg/kg, 500mg/kg, 1000mg/kg and 1500mg/kg body weight daily for thirty days through the orogastric tube administration while the control group received equal volume of distilled water *ad libitum*. Rats were sacrificed by putting cotton wool into an enclosed container with about 45mls of chloroform as anesthesia, the rats were then placed in a supine position on a dissecting table. The Kidney was harvested and immediately fixed in 10% formal-saline for histological analysis. Blood samples were collected from abdominal aorta and heart through cardiac puncture.
Results: Findings indicated that the kidney in the test groups showed no changes of the cytoarchitecture of the renal cortical structure as compared to the control group. Findings also indicated that there was a significant ($P < 0.05$) decrease in weights (g) of the test kidney and significant increase on the urea level at dosages above 500mg/kg and no significant difference on the creatinine levels as compared to the control group.
Conclusion: It was concluded high dosage administration of *alchornea cordifolia* may have an adverse effect on the kidney of adult wistar rats.
Keywords: Morphology effects, *Alchornea cordifolia*, Kidney, Wistar rats.

INTRODUCTION
Alcornea cordifolia belongs to the family of *Euphorbiacea* and it is erect or straggling perennial shrub to a small tree (Enyiukwu *et al*., 2024). It is a common West African tropical flora (Mavar-Manga *et al*., 2007). The plant which has heart-shaped leaves with brown stem and green hanging fruits is widely distributed in West Africa, mostly Nigeria and Zaire republic. In Cross River State of Nigeria it is called 'Mbom' by the Efiks and 'Ashenshen' by the Bekwarra people, Epain (Ijaw), Ewe Pepe (Yoruba) Christmas bush (English), Bambami (Hausa), Ubebe (Igbo), Ebe-uhosa (Edo) (Alikwe *et al*., 2014).
The kidney is the major organ which excretes metabolic waste products in animals and humans, which complements the excretory function of the liver (Koomson *et al*., 2018).

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Thus, the kidney is prone to oxidative damage that is caused by oxidative stress, which may be induced by reactive oxygen species (ROS) (Ogbe *et al*., 2023).

The World Health Organization (WHO) estimates that nearly 70 % of the world population depend on traditional medicine, especially medicinal plants, for their primary health care needs (Ajibade and Olayemi 2018). Concerns have, however, been raised by researchers regarding the safety of such botanical products (Ansah *et al*., 2011).

Alchornea cordifolia is counted among the plants traditionally used in the pharmacopoeia of several African countries for the treatment of various diseases such as wound, rheumatism, arthritis, piles, inflammatory, malaria, worms, conjunctivitis, dermatomes, stomach ulcers, bronchitis, cough and toothache (Agyare *et al*., 2014). It is also used in the treatment of urinary tract infection, diarrhoea, dental caries, chest pain, yaws, rheumatic pain and anaemia (Lembè *et al*., 2014).

Several compounds possessing therapeutic virtues have been isolated and identified from this plant, including gallic acid, protocatechuic acid, quercetin, quercetin arabmose, Stigmasterol, Flavonoids, cardiac glycosides, anthraquinones, polyphenols, friedelin, methylgallate, L-chicoric acid, alkaloids, triterpenes, steroids, saponins and tannins; these provide *A. cordifolia* with its numerous pharmacological properties, including entomotoxicant, antiplasmodial, antidiabetic, antibacterial, antifungal activities (Mbembo *et al*., 2022).

The root and leaf decoctions are used as a mouthwash against mouth ulcers, toothache and decay, stopping post-partum bleeding, bleeding gums, hemorrhage, and treatment of vaginitis (Sinan and Gumes 2021). A poultice of leaves and stem bark is used to cure yaw, chancre and dried tissue powders are used to facilitate the healing of fractures (SHI, 2019).

A variety of bioactive compounds, including ellagic acid, hyperin, and eugenol have been isolated from the plant (Noundou *et al*., 2014). Also, strong anti-inflammatory compounds including 3, 5, 7, 3'-tetrahydoxyflavone-3-0-α-L-rhamnoside, lupenol (lup-20(29)-en-3c-ol, and methyl gallate has also been isolated from different parts of the plant (Enyiukwu *et al*., 2024).

Some workers reported the presence of bioactive fatty acids such as dodecanoic (lauric) acid, n-hexadecenoic (palmitic) acid, 9, 12-octadecadienoic acid (alpha-linolenic acid), pentadecanoic acid, nonacosane, 9-octadecenoic (oleic) acid, octadecanal, and terpinolene etc. in extracts of *Alchornea species* which contributed to the plants' bio-efficacy (Osadebe *et al*., 2012).

Antimicrobial, antiretroviral, antioxidant and antitoxin activities of *A. cordifolia* have been documented (Okwu *et al*., 2010). Organic extracts and isolates from the plant demonstrated antimicrobial activity against *Staphylococcus aureus, Escherichia coli* and *Plasmodium berghei* in vitro and mice, respectively (Amos-Tautaua *et al*., 2003). The root and bark extracts of *A. cordifolia* have shown strong antiviral activity against strains of HIV I, out-performing AZT in some trials (Mambé *et al*., 2016). The anti-HIV activity of this plant may be due to its content of hexadecenoic acid reported to bind directly to CD4 receptors and actively blocking HIV-1 entry and infection in humans (Ogbe *et al*., 2020). Methanol extracts of *A. cordifolia* similarly inhibited *Botrydiplodia theobromae* in vitro. This fungus has been implicated in invasive fungemenia in humans (Osadebe *et al*., 2012). The presence of dodecanoic acid in extracts of *Alchornea* known to exhibit antibacterial, antifungal and anti-inflammatory properties in both fungi and humans may account for these activities (Ahmadu *et al*., 2015).

Since the kidney is involved in the excretion of many toxic metabolic waste products, including the nitrogenous compounds, it would therefore be worthwhile to examine the effects of *alchornea cordifolia* on the kidney of adult wistar rats.

The purpose of this experiment is to evaluate the possible effects of *alchornea cordifolia* on the kidneys of adult wistar rats.

MATERIALS AND METHODS

Preparation of Extract

The fresh collected *Alchornea cordifolia* leaves were thoroughly washed and air dried in the shade at room temperature for two weeks to constant weight. The leaves were then pulverized to powder. The powder obtained was then boiled immediately in distilled water. The aqueous extracts were prepared by boiling the plant material in water. Filtration was then done to separate the filtrate from the residue. After filtration, the filtrate was then concentrated and the aqueous extract was obtained. The extracts obtained were weighed and stored in the refrigerator for preservation.

Animal Care and Management

Thirty adult Wistar rats weighing between 180g and 214g were used for the experiment. The rats were purchased from the animal house in the department of anatomy, University of Benin, Edo State. The rats were then acclimatized for two weeks (at the animal house in the department of anatomy, University of Benin, Edo State) before the commencement of the study. During this period, the animals were allowed free access to standard animal feed (Top feed growers mash) and clean water *ad libitum*.

Each animal procedure was carried out in accordance with approved protocols and in compliance with the recommendations for the proper management and utilization of laboratory animals used for research (Buzek and Chastel, 2010).

Method of Administration/Choice of Dosage

The dosage was given through an orogastric tube in order to ensure accuracy in treatment. Throughout the period of the experiment, the experimental animals had access to standard animal feed and clean water ad libitum and were weighed before commencement and during the period of the experiment.

Experimental Design

Thirty (30) experimental adult Wistar rats of either sex were randomly assigned into six (6) groups; Groups A – F comprising of five rats per group.

Group A: Served as control. They were fed with standard animal feed and clean water ad libitum.

Group B: Rats were treated daily with oral administration of 100mg/kg body weight of *Alchornea cordifolia* leaf extract for 30 consecutive days.

Group C: Rats were treated with oral administration of 250mg/kg body weight of *Alchornea cordifolia* leaf for 30 consecutive days.

Group D: Rats were treated with oral administration of 500mg/kg body weight of *Alchornea cordifolia* leaf extract for 30 consecutive days.

Group E: Rats were treated daily with oral administration of 1000mg/kg body weight of *Alchornea cordifolia* leaf extract for 30 consecutive days.

Group F: Rats were treated daily with oral administration of 1500mg/kg body weight of *Alchornea cordifolia* leaf extract for the 30 consecutive days.

Method of Sacrifice and Sample Collection

At the end of the thirty (30) days treatment, the rats were weighed using a weighing scale. Cotton wool was put into an enclosed container with about 45mls of chloroform as anaesthesia. After anaesthetizing the rats for about two minutes, the rats were then placed in a supine position on a dissecting table. An abdominal incision was made to expose the abdominal viscera. The Kidney was harvested and immediately fixed in 10% formal-saline for histological analysis. Blood samples were collected using 5mls syringes from abdominal aorta and heart through arterial and cardiac puncture. The samples were put into heparin bottles for renal function analysis.

Renal Function Test

To asses kidney function, the following parameters were assayed

i. Urea: using Chaney and Marbach (1962) procedure.

ii. Creatinine: using Bartels and Bohmer (1972) procedure.

RESULTS

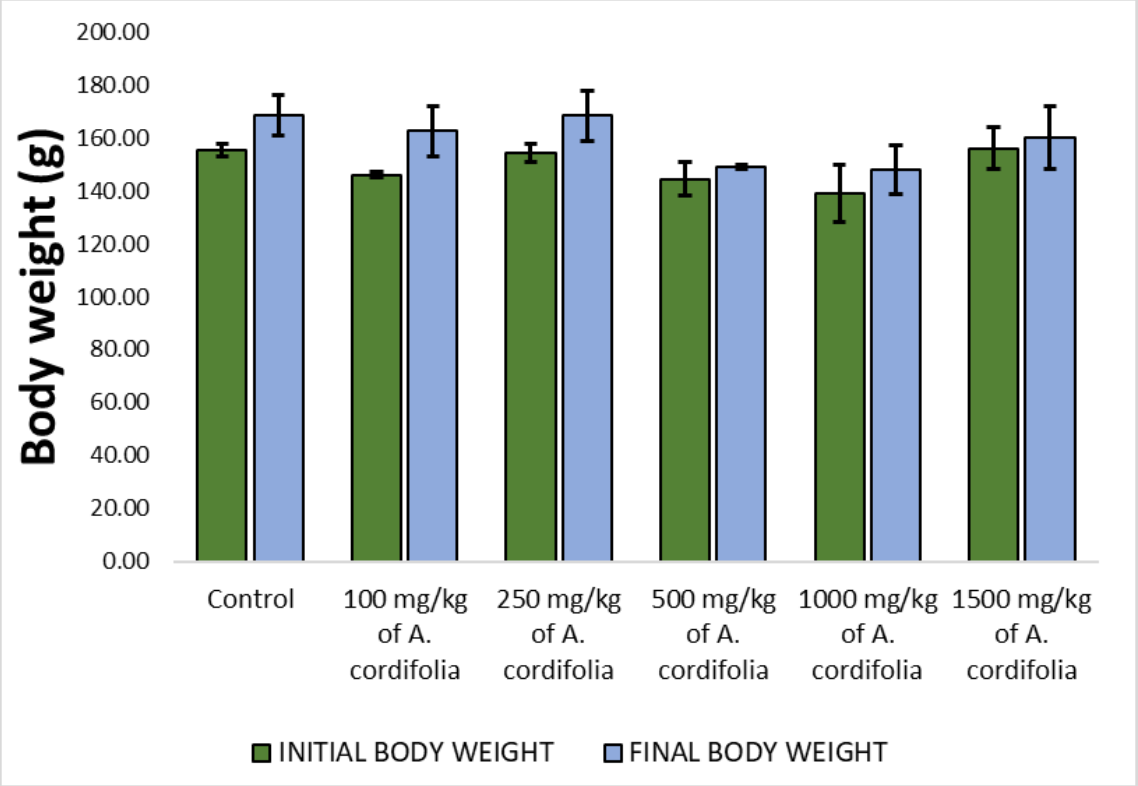

Figure 1: Chart showing body weights; both initial and final, across all groups

There were no significant differences (P<0.05) of body weights when the initial body weights were compared with the final body weights across the groups. But group D, E, F shows significant difference in final body weight compared to control.

Table 1: Table showing Mean levels of Urea across all groups

Control (mmol/L)	Group B (mmol/L)	Group C (mmol/L)	Group D (mmol/L)	Group E (mmol/L)	Group F (mmol/L)
20.2±0.645	18.0±0.197	22.1±0.481	19.6±0.446	27.0±0.308	35.1±0.615*

*significant (P < 0.05) Values represent mean ± SEM

There was no statistically significant difference in urea level of groups B, C and D when compared to control, but there were significant increase in the levels of urea in Group F, when compared to the control group.

Table 2: Table showing Mean levels of creatinine across all groups

Control (mmol/L)	Group B (mmol/L)	Group C (mmol/L)	Group D (mmol/L)	Group E (mmol/L)	Group F (mmol/L)
0.6±0.571	0.7±0.107	0.6±0.489	0.8±0.235	0.9±0.542	0.8±0.338

There was no statistically significant difference (P<0.05) in creatinine when compared to the control group.

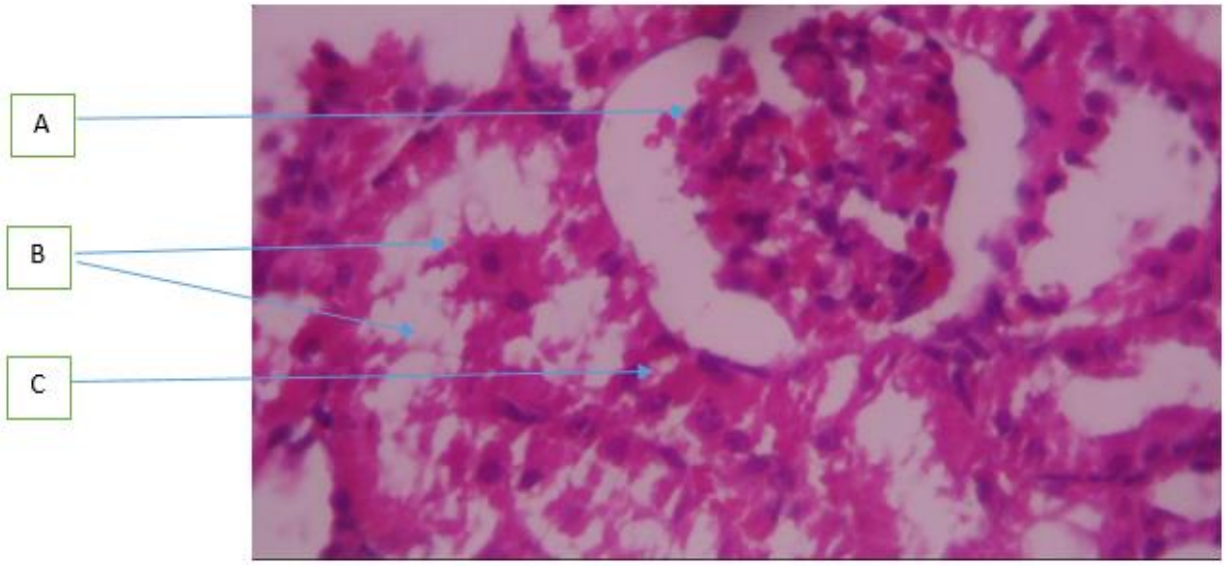

Plate 1. Kidney. Control. Composed of A; glomeruli, B, tubules and C, interstitial space (H&E x 400).

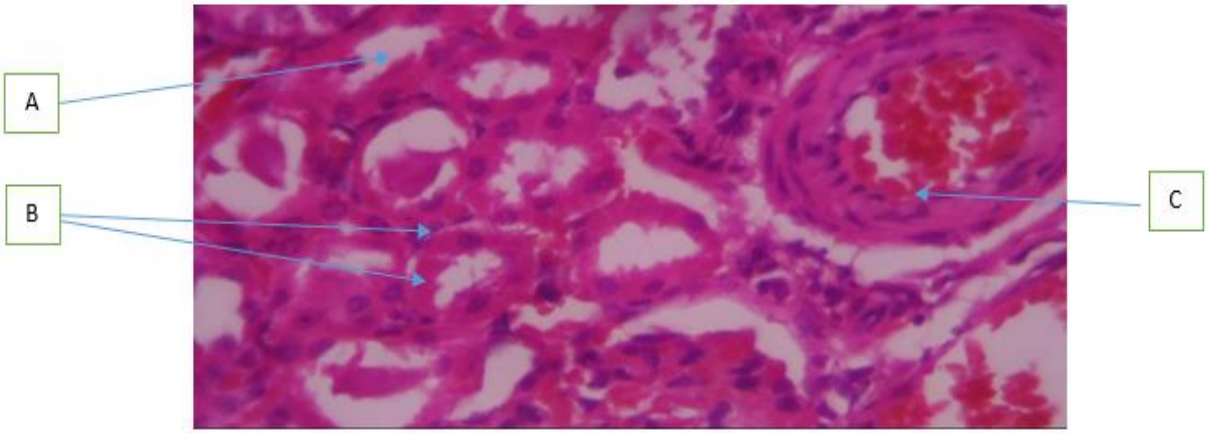

Plate 2. Rat given 100mg extract showing: A, normal interstitial space, B, normal tubular architecture and C, normal vascular microstructure (H&E x 400)

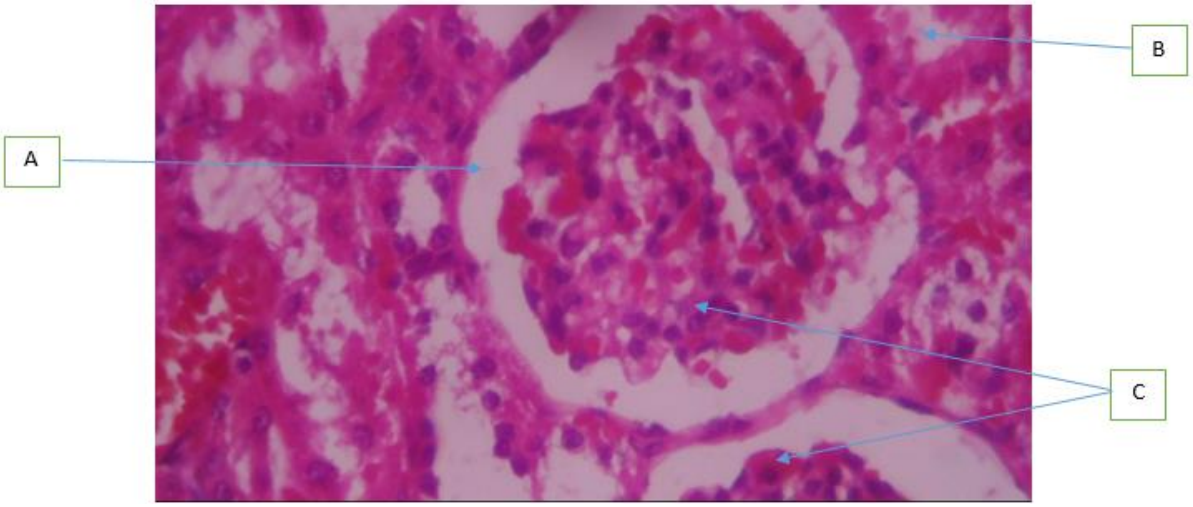

Plate 3. Rat given 250mg extract showing: A, normal interstitial space, B, normal tubular architecture and C, normal vascular microstructure (H&E x 400)

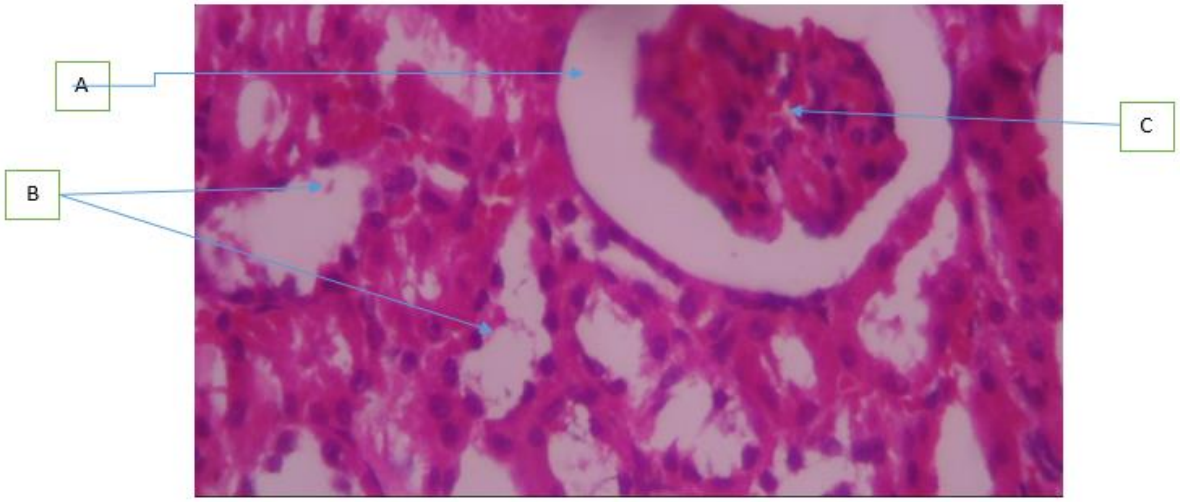

Plate 4. Rat given 500mg extract showing: A, normal interstitial space, B, normal tubules and C, normal glomeruli (H&E x 400)

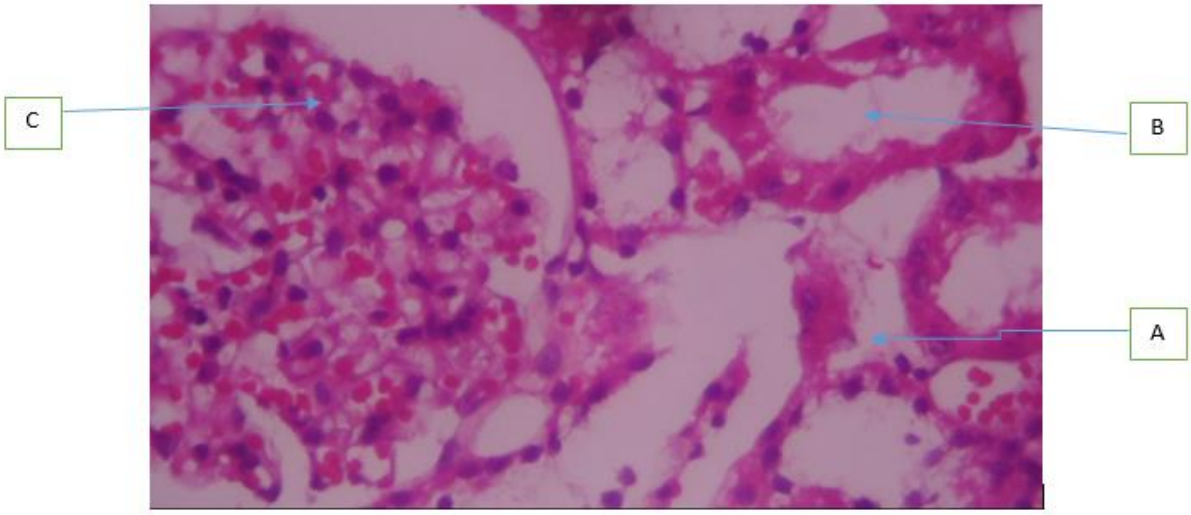

Plate 5. Rat given 1000mg extract showing: A, normal interstitial space, B, normal tubules and C, normal glomeruli (H&E x 400)

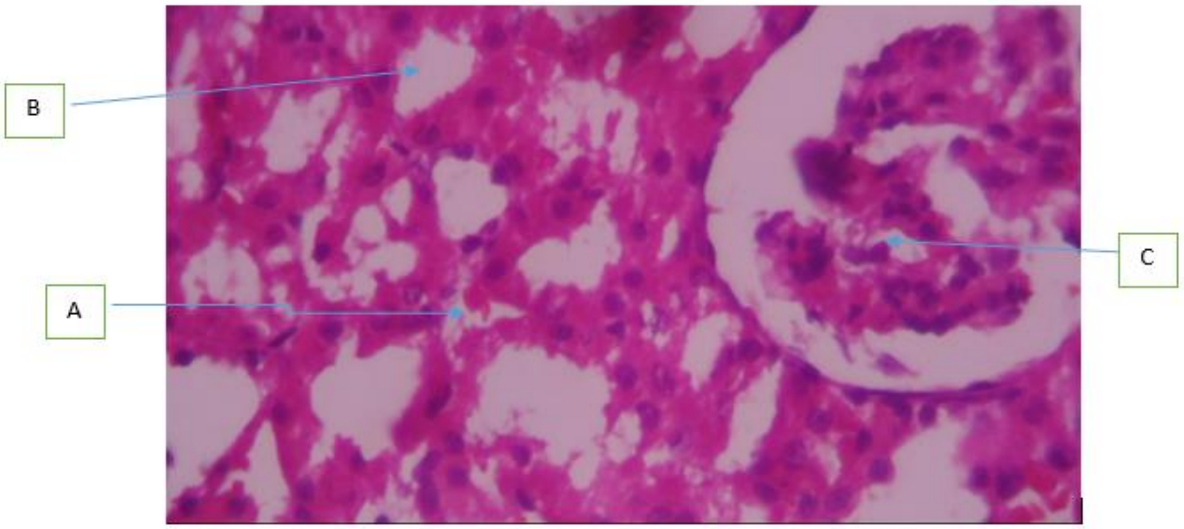

Plate 6. Rat given 1500mg extract showing: A, normal interstitial space, B, normal tubules and C, normal glomeruli (H&E x 400)

DISCUSSION

The slight increase in body weight in Figure 1 after administering the extract can be ascribed to normal growth of the animals over the period. Food and water intake were normal within groups and no deaths occurred. Groups B and C are similar to the work done by Alikwe *et al*. (2014), who administered 200mg/kg of the extract. However groups D, E and F are similar to that of Alikwe *et al*. (2014) who administered high dosage of the extract. Group F is different from that of Ezeokeke *et al*. (2017) who registered an increase in the weight of the animals at a high dosage. Our findings is in disagreement with that of Ejeh *et al*. (2023) where no significant change in body weight occurred.

Groups B, C, D and E are in accordance with the work done by Ezeokeke *et al*. (2017) and Arsene *et al*. (2022). The significant difference observed in groups F maybe due to the high dosage of the extract administered when compared to that of Ezeokeke *et al*. (2017) whose maximum dosage was 750mg/kg, but in contrast with the work of Arsene *et al*. (2022) who recorded a significant decrease at high dose. The findings of our study is in disagreement with that of Ogbe *et al*. (2020) who recorded a significant in the levels of urea at 342mg/kg, the increase maybe due to the fact that the rats were exposed to diclofenac sodium.

The findings of this work is in accordance with the work done by Ezeokeke *et al*. (2017) and Arsene *et al*. (2022), but different at higher dosage where a significant decrease was recorded when compared to Arsene *et al*. (2022). The findings of our study is in disagreement with that of Ogbe *et al*. (2020) who recorded a significant in the levels of creatinine at 342mg/kg, the increase may be due to the fact that the rats were exposed to diclofenac sodium.

As tissue shrinks as seen in this study, the activity of the cellular transporters is approximately modified by the up or down regulations as has been reported in the case of hyponatramia or hypernatremia. There are many different causes of cell swelling or shrinkage, including drug poisoning, water intoxication, hypoxia and acute hyponatremia (Johanson, 1995). Under such conditions, there is a net shift of water from the extracellular space to the interior of the cells (Johanson, 1995).

The significant decrease associated with the weight of the kidney in this experiment usually involves intracellular swellings or shrinkage of the endothelia (Johanson, 1995). The photomicrograph section of the tested kidney showed no changes in the interstitial space, glomeruli and tubules of the test groups when compared to the control section. The findings of this study is in accordance with that of Ansah *et al*. (2011) where no changes were observed.

CONCLUSION

Administration of dosages above 500mg/kg of aqueous extract of *alchornea cordifolia* leaf resulted in a significant decrease in weight, significant increase on the urea level and no significant difference on the creatinine levels and no changes of the cytoarchitecture of the renal cortical structures of the test kidney as compared to the control. There is a need to exercise caution when using the plant at higher treatment doses and for prolonged periods of exposure.

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