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AMELIORATIVE EEFECTS OF TIGER NUT (*Cyperus esculentus*) ON ALUMINUM CHLORIDE INDUCED RENAL HISTOPATHOLOGY ON ADULT WISTAR RATS

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ABSTRACT
Tiger nut (Cyperus esculentus) is known in Nigeria as aya in Hausa, "Ofio" in Yoruba and "Aki Hausa" in Igbo, is an edible perennial grass-like plant. Tiger nut tubers can be eaten snacked, roasted, fried or baked and liquid (Kunun aya). Tiger nut contain lipid, protein, and carbohydrate (fiber and starch included). Tiger nut can be used to 'mop up' and scavenge free-radicals generated by essential metabolic body reactions and environmental pollutants. The major route of aluminium elimination is by the kidneys.Due to its reactivity, aluminum in nature is found only in combination with other elements like chlorine as in aluminum chloride ($AlCl_3$). Al compound are used in a variety of foodstuffs, medications, domestic water supplies, kitchen equipments. herbs and cosmetics. If the kidney cannot excrete Al, it will accumulate in the body. The aim of this work was to evaluate the protective effects of tiger nut against aluminium chloride induced renal histopathology in the kidney of wistar rats. Twenty adult males and females wistar rats weighing 80 – 170g were grouped into 4. Group 1 - Control group, received normal saline for 14 days, Group 2 – received 1250mg of liquid tiger (ethanolic extract) nut extract daily by oral route for 14days. Group 3 – received aqueous aluminium chloride 500mg/kg followed by 2500mg/kg of liquid tiger nut extract daily by oral route for 14days and Group 4 – received aqueous aluminium chloride 500mg/kg followed by 3750mg/kg of liquid tiger nut extract daily by oral route for 14days. After sacrifice and tissue processing, groups 1 and 2 presented normal renal histology while groups 3 and 4 presented normal renal histology with lymphocytes between their distal convoluted tubules around the medulla. It was concluded that tiger nut has an ameliorative effect on $AlCl_3$ induced histomorphological changes in the histology of kidney and it has no any negative effect on the histology of kidney.
Keywords: Ameliorative, Tigernut, Aluminium Chloride, Kidney, Wistar Rats

INTRODUCTION

Tiger nut (*Cyperus esculentus)* is known in Nigeria as *aya* in Hausa, *ofio* in Yoruba and *akihausa* in Ibo. *Cyperus esculentus* grows mainly in the middle belt and northern regions of Nigeria where three varieties (black, brown and yellow) are cultivated Among these, only two varieties, yellow and brown are readily available in the market. The yellow variety is preferred to all other varieties because of its inherent properties like its bigger size, attractive colour and fleshier body (Raphael *et al.,* 2010). Tigernut also contributes to the reduction of cholesterol, it reduces the risk of coronary heart disease, arteriosclerosis and is recommended for those who have heavy digestion, flatulence and dysentery (Gambo & Da'u, 2014). Study has shown that there was no significant effect on serum cholesterol and protein and on total and differential white blood cell, red blood cell, haemoglobin, packed cell volume and erythrocyte sedimentation rate in the rat that were feed with tigernut (Raphael *et al.,* 2010). *Cyperus esculentus* is also used for the treating urinary tract and bacterial infection and assist in reducing the risk of colon cancer when eaten (Adejuyitan *et al*., 2009). Aluminum (Al) is the third most abundant element in the earth's crust (Abdel-Moneum & Gaafar, 2016; Klein, 2019; Sargazi *et al.,* 2001) after oxygen and silicon (Sargazi *et al.,* 2001), amounting to an estimated 8% of total earth mass (Priest, 1992) and it is widely distributed (Starkey,

1987).Due to its reactivity, aluminum in nature is found only in combination with other elements (Bernardo, 2021) like chlorine as in aluminum chloride ($AlCl_3$). Al is an ubiquitous element (Kutlubay *et al.,* 2007) which is naturally present or anthropogenically introduced in our environment (Cunat *et al.,* 1999), and its one of the most common substance that we frequently use them in our daily activities. Al compound are used in a variety of foodstuffs (e.g. tea), medications (e.g. vaccines, antacids), domestic water supplies (Shirley & Lote, 2005), kitchen equipments (Fitri *et al.,* 2020) herb and cosmetics (Okail *et al.,* 2020). Aluminium poisoning was first reported by Spofforth (1921).

Kidneys perform several vital functions besides formation of urine. By excreting urine, kidneys play the principal role in homeostasis (Sembulingam & Sembulingam, 2012). Kidney being the main excretory organ for aluminium elimination, some microscopic changes may be induced by Al in the kidney (Savory *et al.,* 1985). If the kidney cannot excrete Al, it will accumulate in the body, resulting in manifestations of Al toxicity in chronic renal disease (Klein, 2019). There is no evidence that aluminium is essential to human life or health (Savory *et al.,* 1985). A study by Buraimoh and Ojo (2014) reported that there was strong correlation between $AlCl_3$ administration and weight loss in Al treated groups of wistar rats, hence, there was significant weight loss in the Al treated Wistar rats of both sexes (Buraimoh & Ojo, 2014; Fulton *et al.,* 1988).

The kidneys are two bean-shaped organs situated on the posterior abdominal wall, one on each side of the vertebral column, behind the peritoneum (Singh., 2014). The right kidney is generally smaller and lower than the left kidney, to make space for the liver (Singh., 2014). Each kidney weight (125 to 170g), in female (115 to 155g), in male (125 to 170g) (Emamian *et al* 1993). The weight of the left kidney is 10.2cm and that of the right kidney is 9.8cm (Gupta *et al*, 2010).

The kidney is made up of three layers; outer cortex, inner medulla and renal sinuses. The outer cortex is darker and granular in appearance, it contains the renal corpuscles and convoluted tubules (Bulchholz 2000). The inner medulla contains tubular and vascular structures arranged in parallel radial lines, medullary mass and is divided into 8 to 18 malphigian pyramid with broad base and apex which project into minor calyx (Saldarriaga 2008). Renal sinus consist of renal pelvis, major calyx, 8 minor calyces, branches of nerves and blood vessels, loose connective tissue and fat (Bergmen *et al* 1992).

The nephron is the functional unit of kidney, there are 0.8 to 1.2 million nephron in each kindney and greatly varies in its structure among different vertebrate; also the formation of nephrons shows a variable degree of differences among species. In birds, the kidney has two kind of nephrons. One is reptilian type of nephron and small sized, without loops of Henle, and other mammalian type large in size with long or intermediate length loops (Lentite 2017).

Aluminum is absorbed by several routes (oral, intranasal, transdermal and parenteral) (Saad *et al*., 2018). The bioavailability of aluminum from drinking water is approximately 0.1% (Walton, 2007; Walton, 2009). The absorption of aluminum from the diet is reported to be between 0.01% and 0.04% (Greger *et al.,* 1992). Transdermal absorption of aluminum has been reported after a single underarm application of Al hexahydrate, the absorption was found to be 0.012% of Al applied (Flarend *et al.,* 2001).

Aluminium that has accumulated in the body is thought to have a generalised cytotoxic effect (Nordal *et al.,* 1998). Aluminium accumulation is a potential hazard of end stage chronic renal failure (Opelz *et al.,* 1973). Aluminium toxicity is indicated by the accumulation of aluminium in bone and by symptoms and signs from several organs (Boyce *et al.,* 1982). It has also been reported that aluminum accumulates in all tissues of mammals such as the heart, liver, kidneys, blood, bones and brain (Al-Kahtani, 2014) and it was found that one of the main organs targeted by aluminium exposure is the kidneys which play a major role in preventing accumulation of aluminium by excreting it throughout urine (Stoehr, 2006).

Aluminum (Al) is an environmental and industrial pollutant that induces a broad spectrum of toxicity (Liu *et al.,*2016). Aluminium is presents in many manufactured foods and medicines and is also added to drinking water for purification purposes (Buraimoh & Ojo., 2013).

MATERIALS AND METHODS

Chemicals: Aluminium chloride ($AlCl_3$) was used as solution for oral administration. It was collected from Department of Biochemistry, BUK. About 30g of $AlCl_3$ was used in this research.

Reagents: Hematoxylin and Eosin stains (H&E), 10% Neutral Buffered formalin (NBF), graded

alcohol (absolute ethanol, 90% ethanol, 80% ethanol, 70% ethanol and 50% ethanol), xylene, 1% acid alcohol, chloroform and paraffin wax were obtained from Department of Human Anatomy Bayero University Kano. Normal saline was purchased from pharmacy and distilled water was obtained from department of pharmacy, and tween eighty was obtained from Department of Microbiology.

Animals: Twenty adult males and females wistar rats weighing 80 – 170g were purchased from deparment of pathology in Aminu Kano Teaching Hospital (AKTH), Bayero University Kano (BUK).

Plant Collection and Extraction : Brown tiger nut was purchased from the Rimi market. Then it was taken to department of plant biology for identification (voucher no: BUKHAN367). The department of pharmacy for extraction. 4L of tiger nut was macerated using ethanol to give the ethanolic tiger nut that was use in this experiment. The weight of the tiger nut after the extraction was 205.31g.

METHODS

Study Design and Experimental Procedure

After the animals were acclimatized for one week, they were divided in to four groups on descending order of weight, each group has five rats. The groups are;

Group 1 - Control group, received normal saline.

Group 2 – Cyperus Esculentus (C.E) group, received liquid tiger nut extract 25% of LD50 daily by oral route .

Group 3 – Aluminium choloride ($AlCl_3$) and Cyperus Esculentus (C.E) 01 group, liquid tiger nut extract 50% of LD50 and aqueous aluminium chloride 500mg/kg daily by oral route.

Group 4 - Aluminium choloride ($AlCl_3$) and Cyperus Esculentus (C.E) 02 group, liquid tiger nut extract 75% of LD50 and aqueous aluminium chloride 500mg/kg daily by oral route.

Dose of the Substances that were Administered to each Rat.

Dose of normal saline for group 1

Normal saline has no any case of toxicity, therefore the selected dose for each rat is same as the stock.

$$\text{Dose} = \frac{\text{Selected dose} \times \text{weight of rat}}{\text{Stock}}$$

☐ the dose of normal saline for each rat in the control group is same as it is body weight in ml

Dose of aluminum chloride for groups 3 and 4

Aluminum chloride was reported to induce renal toxicity at 500mg (Ajibade *et al.*, 2019).

☐ 500mg is our selected dose for each rat in the groups that $AlCl_3$ will be administered.

LD50 = 3470mg/ml .

$$\text{Dose} = \frac{\text{Selected dose} \times \text{weight}}{\text{Stock}}$$

Slected dose = 500mg/ml

Stock = 500mg/ml

☐ the dose of $AlCl_3$ for rat is base on its weight in ml.

Dose of tiger nut extract for group 2

Since there is no any case of toxicity associated with tiger nut, the LD50 of tiger nut can be above 5000ml/kg. Therefore, 5000ml/kg is the LD50 of tiger nut used in this study.

$$\text{Dose} = \frac{\text{Selected dose} \times \text{weight}}{\text{Stock}}$$

Selected dose = 25%LD50= 1250mg/ml

Stock = 1000mg/ml

Dose of tiger nut extract for group 3

$$\text{Dose} = \frac{\text{Selected dose} \times \text{weight}}{\text{Stock}}$$

Selected dose = 50%LD50 = 2500ml/kg

Stock = 1000mg/ml

Dose of tigernut extract for group 4

$$\text{Dose} = \frac{\text{Selected dose} \times \text{weight}}{\text{Stock}}$$

Selected dose = 75%LD50 = 3750mg/ml

Stock = 1000mg/ml

Animal Sacrifice: Twelve rats three from each group were sacrificed. The rats were sacrificed at the last day of the experiment under chloroform anesthesia. A midline incision was done through the ventral abdominal wall and the kidney tissue was collected immediately and fixed in 10% formal saline (fixative) for the minimum of 24 hours. The tissue was processed using routine histological techniques and stained with hematoxylin and eosin stains for general tissue architecture.

RESULTS

The photomicrograph of the kidney stained with hematoxylin and eosin (H&E) has shown that;

Group 1 – Control group that receive normal saline for 14days present normal kidney with normal glomerulus and normal tubules.

Group 2 – *Cyperus esculentus* group that received 1250mg/kg of tiger nut for 14days presnt normal kidney with normal glomerulus and normal tubules.

Group 3 – *Cyperus esculentus* and $AlCl_3$ group 01 that received 2500mg/kg of tiger nut followed by 500mg of $AlCl_3$ for 14days; they pesent a kidney with normal glomerulus, normal tubules and 3-4 foci of lymphocytes.

Group 4 – *Cyperus esculentus* and $AlCl_3$ group 02 that received 3750mg of tiger nut followed by 500mg of $AlCl_3$ for 14days they pesent a kidney with normal glomerulus, normal tubules and foci of lymphocytes.

The above result is shown in the photomicrographs below;

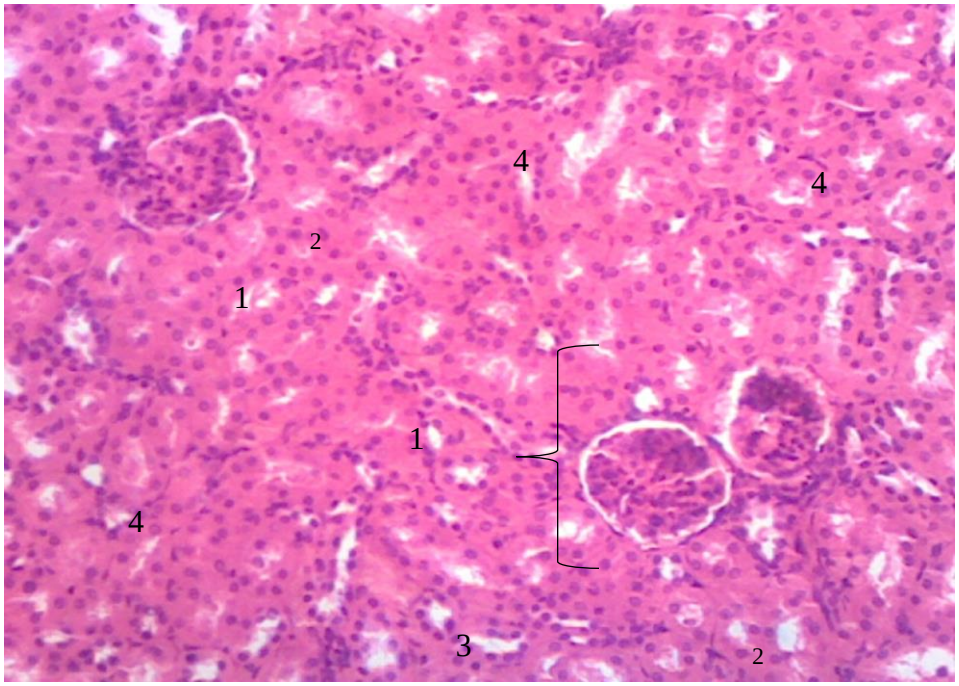

Plate I: Photomicrograph of group 1 kidney stained with H&E, ×100 magnification. Showing normal glomerulus, Bowman's capsule and renal tubules. They received normal saline.
1.Glomerulus 2. Bowmans capsule 3.Renal corpuscules 4.Renal tubules

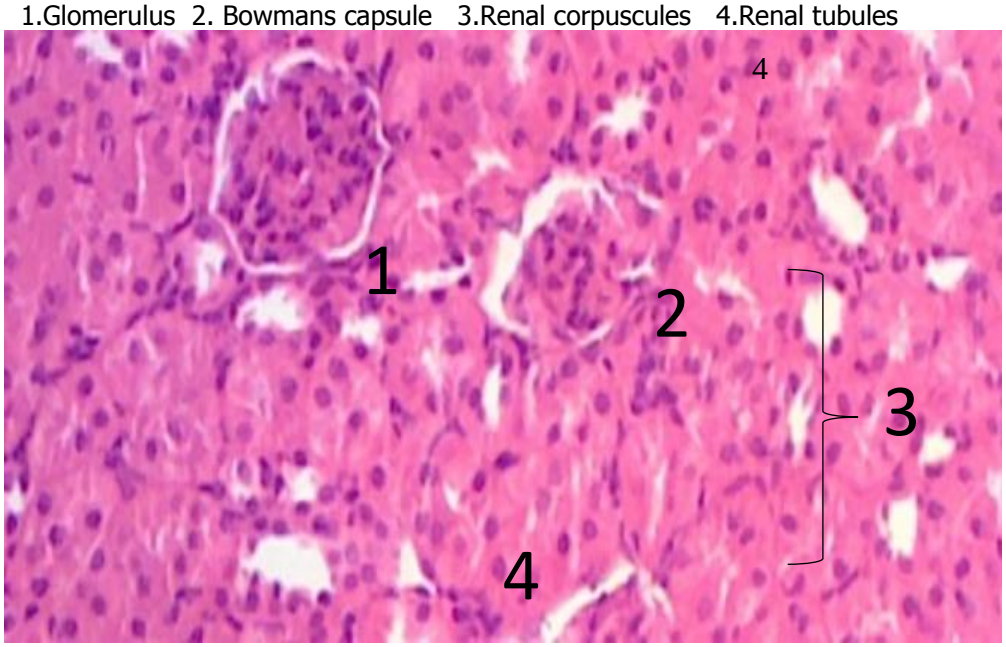

Plate II: Photomicrograph of group 2 kidney stained with H&E, × 100 magnifications. Showing normal glomerulus, Bowmans capsule and renal tubules. Received 1250mg/kg bwt of liquid tiger nut.
1. Glomerulus 2. Bowman's capsule 3. Renal corpuscle 4. Renal tubule

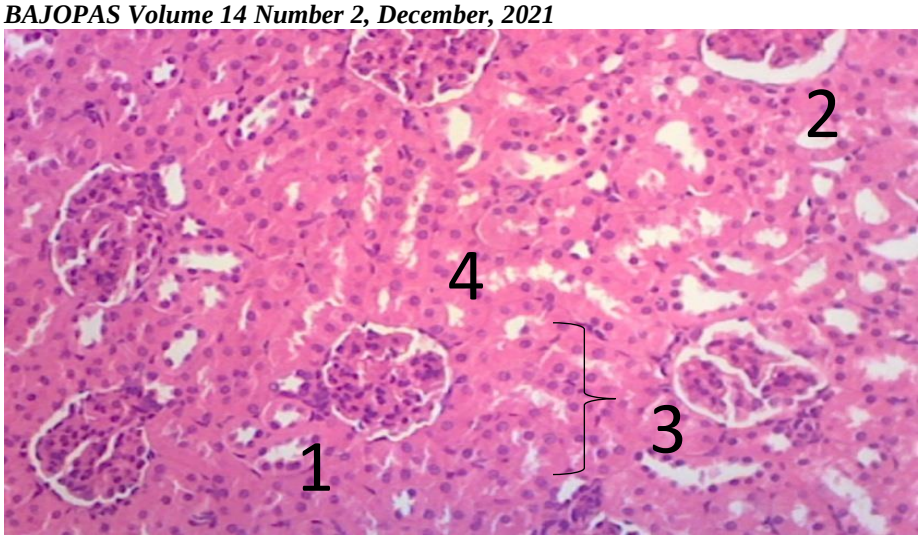

Plate III: Photomicrograph of group 3 kidney stained with H&E, ×100 magnification. Showing normal glomerulus, bowmans capsule and renal tubules. They received 2500mg/kg bwt of liquid tiger nut extract, followed by 500mg of $AlCl_3$.
1.Glomerulus 2.Bowman's capsule 3.Renal corpuscle 4.Renal tubule

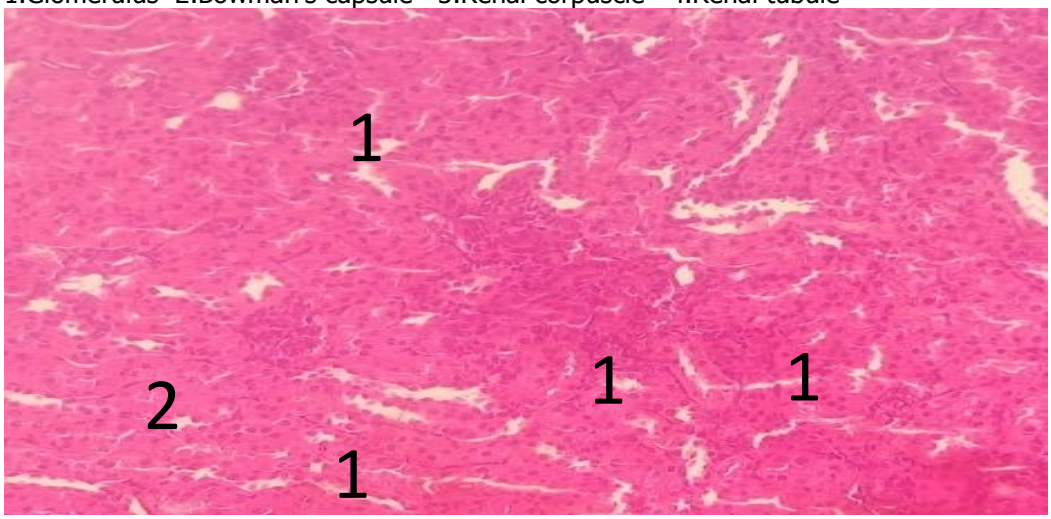

Plate IV: Photomicrograph of group 3 kidney ×100 magnification. Showing lymphocytic aggregates (1) due interstitial nephritis and distal convoluted tubules. They received 2500mg/kgbwt of liquid tiger nut extract, followed by 500mg of $AlCl_3$.
1.Lymphocytic aggregates 2.Distal convoluted tubules

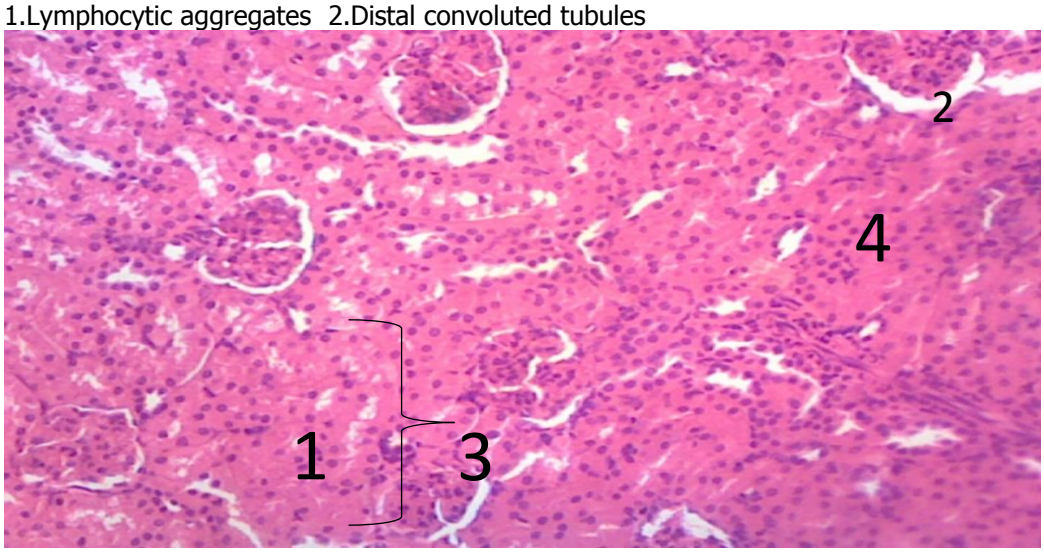

Plate V: Photomicrograph of Group 4 kidney ×100 magnification. Showing normal glomerulus, bowmans capsule and renal tubules. They received 3750mg/kgbwt of liquid tiger nut extract, followed by 500mg of $AlCl_3$.
1.Glomerulus 2.Bowman's capsule 3.Renal corpuscle 4.Renal tubule

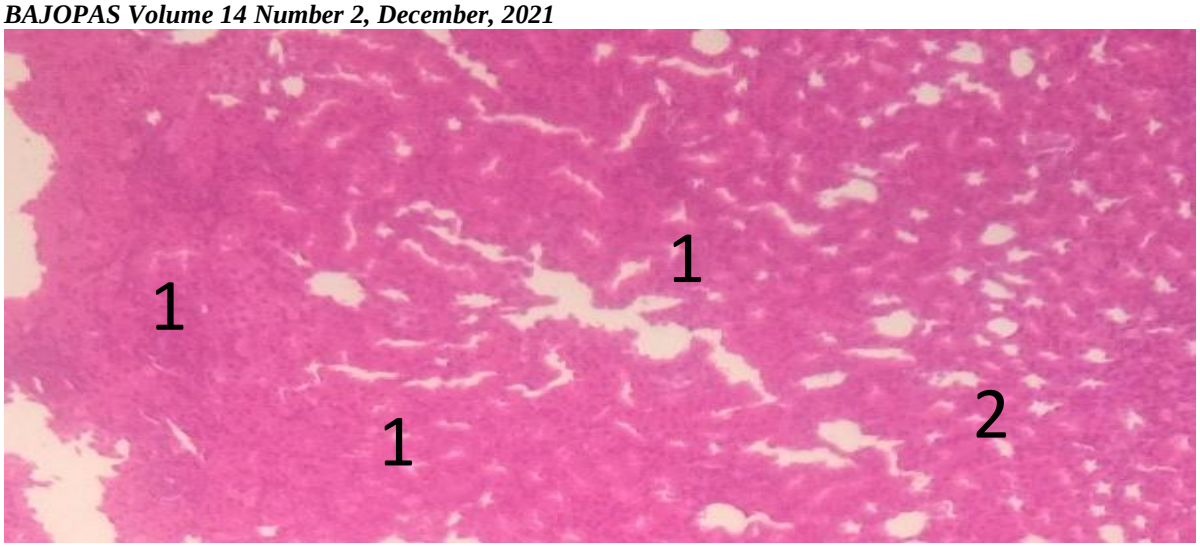

Plate VI: Photomicrograph of group 4 kidney ×100 magnification. Showing lymphocytic aggregates (1) due interstitial nephritis and distal convoluted tubules. They received 3750mg/kg bwt of liquid tiger nut extract, followed by 500mg of $AlCl_3$.
1. Lymphocytic aggregates 2. Distal convoluted tubules

DISCUSSION

This study was designed to assess the ameliorative effect of tiger nut extract on $AlCl_3$ induced histomorphological changes in the kidney. Some of the damaging effect of $AlCl_3$ was established on the kidney like the interstitial nephritis around the distal convoluted tubules in group 3 and 4 leading to lymphocytic aggregates. In this study, there were no any alterations in the histomorphology of the kidney of the control and Cyperus esculentus groups (1&2). But there was a little sign of inflammation (lymphocytes aggregates) in group 3 and 4 due to interstitial nepritis. Interstitial nephritis with severe inflammatory cells infiltration as sign of aluminum induced histological change is the only change that was observed in the experimental groups (3&4) and this corresponds to the findings of Saad *et al. (*2018) when 2.5mg/kgbwt was administered to some group of rabbits five times per week for 3 months even though the duration of their study was 6 times (90 days) the duration of this study (14 days), and their duration is approximately 61 days of administration. But the concentration of the $AlCl_3$ in this study (500mg/kg) is 200 times the concentration of $AlCl_3$ in their study (2.5mg/kg), and this is indicating that the histological changes that were observed in their study which include; widening of the Bowman's space, increased urinary spaces and necrosis of glomerular capillary tufts, vacuolar degeneration, tubular epithelium attenuation to necrosis, enlargement of epithelial cells toward the tubular lumen, congested blood vessel, interstitial nephritis with severe inflammatory cells infiltration, mesangiolysis of mesangium, ischemic glomerular necrosis are supposed to be observed in the experimental groups that reecieved both tiger nut and $AlCl_3$, but due to the protective effect of tiger nut against aluminium chloride, only interstitial nephritis with severe inflammatory cells infiltration was observed.

Mohammed *et al.* (2017) has administered 37 mg\kg bwt of $AlCl_3$, for 60 days in his study and his result showed that the kidney of the treated group showed inflammatory cell infiltration particularly neutrophils, macrophages and lymphocytes between renal tubules, with the congested blood vessels and vacuolar degeneration of epithelial cells and severe congested blood vessels between renal tubules, and also the kidney showed inflammatory cells infiltration in the wall of collecting tubules with hyperplasia of epithelial cells of collecting ducts and these cells aggregated as hyperchromatic pleomorphic cells arranged as mass or sheath or glandular structure and atrophy of glomerular tufts with dilated Bowman's space ,congested blood vessels and acute cellular degeneration. But in this study, only the inflammatory cell infiltration was observed in the experimental groups. Even though their duration was 4 times (60 days) higher than this study's duration, but this study dose (500mg/kg) was 13 times their dose (37mg/kg), and the remaining pathologic changes were not observed in the experimental groups of this study. This is showing the powerful protective effect of tiger nut against $AlCl_3$.

Ajibade *et al.*(2019) has administered same dose of $AlCl_3$, as in this study (500mg/kg) to some groups of rats for 31days.

And their result has shown that there was mild disarrangement of kidney architecture with decreased capsular space and mild degeneration of glomerulus, but none of these pathologies was observed in our experimental groups. This is also proving the protective effect of tiger nut against $AlCl_3$ induced histological changes.

Berlyne *et al* (1972) has subjected some group of rats to 2/3 nephrectomy that was done on the other side under chloroform anaesthesia. The animals were allowed to recover for 1-2 weeks from the operation and were then divided into control and test groups. The test groups received 180mg of $AlCl_3$ and the control received distilled water. The rats of the test groups died within 8 days and that of the control group recovered from their injury. The concentration of the $AlCl_3$ dose in this study is 2.5 times their dose (180mg) which means the effect supposes to be high in this study's experimental groups, but our rats were healthy so there was no death. But due to the protective effect of tiger nut, there was no dangerous effect talk less of death, which means tiger nut was the ameliorating agent.

A small amount of Al is excreted in bile, but the major route of Al elimination is by the kidneys and typical value for total body Al in a healthy subject is 30 mg (Shirley & Lote, 2005), But in this study, 16 times of the dose of healthy subject was administered to rat, which means the dose (500mg) was enough to cause renal histopathology, but due to the protective effect of tiger nut, only sign of inflammation (lymphocytic aggregate) was observed. Aluminium is protein bound and therefore unfilterable, and that the filtration of elevated plasma Al concentrations is very much dependent on the nature of the anion species with which the excess Al forms complex, therefore, patients with renal insufficiency are more susceptible to Al toxicity (Shirley & Lote, 2005).

CONCLUSION

Based on this study, it was concluded that tiger nut has an ameliorative effect on $AlCl_3$ induced histomorphological changes in the histology of kidney and it has no any negative effect on the histology of kidney.

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