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Research Article

# Cassava effluent toxicity in the Urinary Bladder and its Implications on Renal Functions

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**Abstract**

This study investigated the effects of cassava effluent on the histo-structure of the urinary bladder of albino rats and the implication on renal function markers. A total of 20 adult male albino Wistar rats weighing between 113g to 205g were divided into 5 groups and designated as group 1, 2, 3, 4, 5. Group 1 served as control and was given feed and water, while group 2 to 5 served as experimental groups. Group 2 was administered 20ml/kg of Garri effluent, group 3 was administered 10 ml/kg of Garri effluent, group 4 was administered 20 ml/kg of Fufu effluent, group 5 was administered 10ml/kg of fufu effluent. All administration was carried out within 28 days and cassava effluent was administered orally using orogastric tubes. By the end of administration, the rats were sacrificed and their bladder harvested and fixed in 10% buffered formalin, processed and stained with Hematoxylin and Eosin and observed under the microscope. Blood sample was collected for renal function analysis. Results obtained from the study showed that cassava effluent caused damages in the bladder tissue, including hemorrhagic cystitis, disorganized epithelium, tissue edema, and detrusor muscle hypertrophy. Cassava effluent also altered the levels of renal function markers, such as serum creatinine, serum urea and blood urea nitrogen. The study suggests that consumption of poorly prepared cassava products may have deleterious effects on bladder function and renal function parameters.

**Keywords:** cassava effluent, urinary bladder, albino rat, cyanide, renal function marker

## Introduction

Cassava (*Manihot esculenta Crantz*), is a perennial shrub. It is currently the sixth world food crop for more than 500 million people in tropical and subtropical Africa, Asia, and Latin America [1]. It is cultivated mainly by resource-limited small farmers for its starchy roots, which are used as human food either fresh or in many processed forms or products, mostly starch, flour, and for animal feed. The crop is widely grown as a staple food and animal feed in countries of tropical and subtropical Africa, Asia, and Latin America with a total cultivated area of over 13 million hectares, more than 70% of it being in Africa and Asia [2, 3]. It is currently the most important food source for carbohydrates, after rice, sugarcane, and maize [3]. Its main value is in its storage roots with dry matter containing more than 80% starch. For consumption, cassava cultivars low in cyanogens are preferably used to avoid health hazards [2]. Cassava cultivars high in cyanogens contain high levels of hydrocyanic acid and can be removed from cassava roots and leaves by using a mix of complex traditional methods and modern technologies during food processing and preparation [4]. Cassava is grown in marginal, low fertility acidic soils under variable rain-fed conditions ranging from less than 600mm per year in semi-arid tropics [5] to more than 1000mm in the sub-humid and humid tropics [6]. Storage roots are generally harvested 7-24 months after planting, depending on the cultivar, the purpose of use, and growing conditions. Due to root perishability and rapid deterioration after harvest, roots have to be used immediately, either eaten raw, marketed for consumption, processed for starch extraction, dried for flour production, or roasted for food products [1]. Some of the processed food products are known as farinha da mandioca in Brazil, gablek in Indonesia, Garri and Fufu in West Africa. Garri is a roasted granular hygroscopic starchy food product, produced from cassava and consumed by millions of people in the West Africa subregion. Garri available in the market can be consumed directly without further processing in the dry form with peanut, coconut, smoked fish, soaked in water (sometimes with milk and beverage) or processed minimally using boiled water to form a stiff paste popularly called “eba” [7]. Fufu is a fermented wet paste made from cassava widely consumed in Nigeria and parts of West Africa [8]. It is ranked next to Garri as an indigenous food of most Nigerians. In Nigeria, it has commercial potential that has been reported to be increasing [9]. A safety concern among consumers of cassava processed products (Garri and Fufu) arises from the presence of cyanogenic glycoside which upon hydrolysis produces cyanohydrin that further breaks down to release hydrogen cyanide [10]. Other chemical constituents such as

nitrates and phosphates are found to be present in cassava-processed products. Chemical constituents such as cyanide, phosphate, nitrates at high levels have been seen to be highly toxic, thereby negatively impacting on organs of the body. These constituents are found to be present in cassava at high levels. Nigeria is populated with over 200 million people, and 7 in every 10 Nigerians consume, at least, a product of cassava once in a day [11]. These products include: cassava flakes (garri), cassava flour (pupuru and lafun) and cassava paste (fufu) which are derived from cassava roots [12]. Since cassava products are dietary staple food in Nigeria and other countries in Sub-Saharan Africa (SSA). It is pertinent to carefully study its impact on the bladder as well as its effects on renal function.

## Materials and Methods

### Animal Handling and Care

Twenty (20) male Wistar rats, ranging in weight from 113 to 205g were acquired from the Animal House of the Faculty of Basic Medical Sciences, University of Uyo, Nigeria. Water was provided freely to the animals along with pelletized feed. The cages were kept in good condition by routinely replacing the sawdust bedding daily.

### Administration of Cassava Effluent

Adminstration of cassava effluent to the animals was done according to a method described by Edem et al. [2]. The animals were divided into five groups (4 rats each). The groups were organized as follows: Group 1 rats (control group) were fed a normal diet and tap water; Group 2 rats were given 20ml/kg of Garri effluent; Group 3 rats were given 10ml/kg of Garri effluent; Group 4 rats were given 20ml/kg of Fufu effluent and Group 5 rats were given 10ml/kg of Fufu effluent. Administration of cassava effluent took place for 28 days.

### Renal Function Test

Plasma aspirates were analyzed for creatinine, serum urea, and blood urea nitrogen using COBAS C111 Automated Analyzer, according to standard biochemical methods.

### Animal sacrifice, Tissue Processing and microscopy

The bladders of both the experimental and control groups were removed after sacrifice and placed in 10% neutral buffered formalin. The tissues passed through different stages of tissue processing which include; fixation dehydration, clearing, infiltration, embedding, sectioning (microtomy), staining and mounting. After these procedures, the tissue was then viewed with a microscope. Staining of bladder tissue was done using H&E.

### Statistical Analysis

Data obtained from this study were subjected to One-way Analysis of Variance (ANOVA) using Graphpad Prism (version 8.0.2) to compare the experimental and control groups and presented as mean ± standard error of mean.

## Results

### Effect of Cassava Effluent on Serum Creatinine (SC), Serum Urea (SU) and Blood Urea Nitrogen (BUN) Levels of Male Albino Wistar Rats

Results showed that there was significant increase in serum creatinine levels in all experimental groups after administration of cassava effluent.

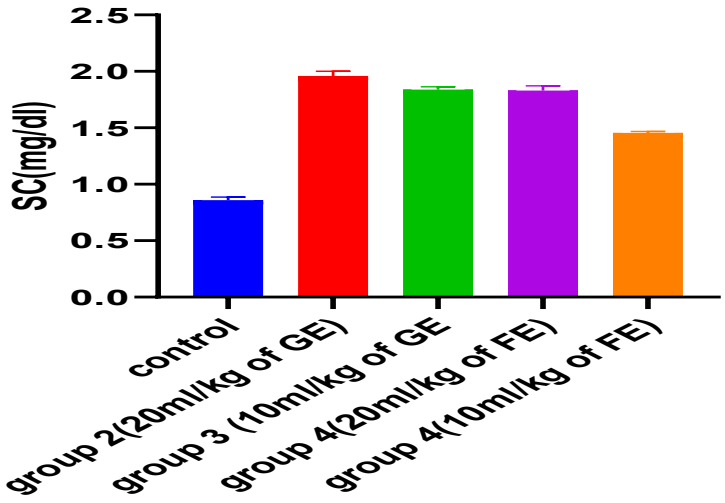


**Figure 1: Serum Creatinine Level after the Administration of Cassava Effluents**

Similarly, our results also showed a significant increase in serum urea levels in all the experimental groups after administration of cassava effluent. The most significant increase was observed in group 2 that was administered 20ml/kg of Garri effluent.

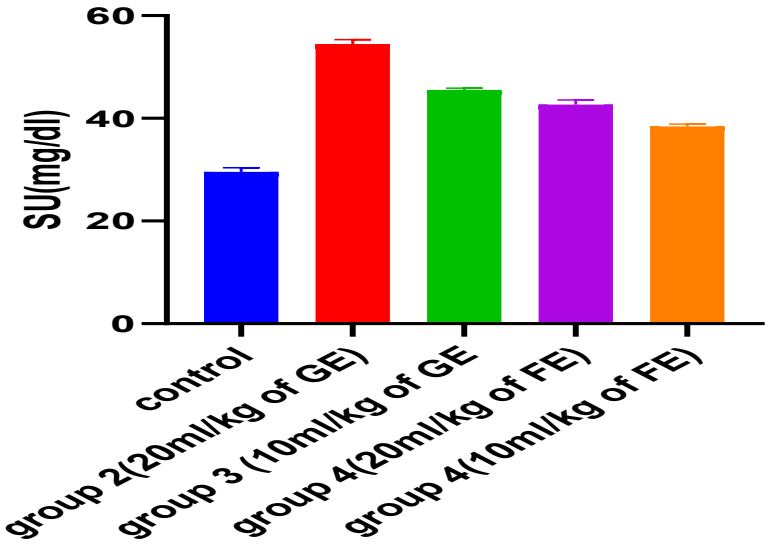


**Figure 2: Serum Urea Level after the Administration of Cassava Effluents**

Moreso, significant increase in blood urea nitrogen levels were evident in all the experimental groups after administration of cassava effluent.

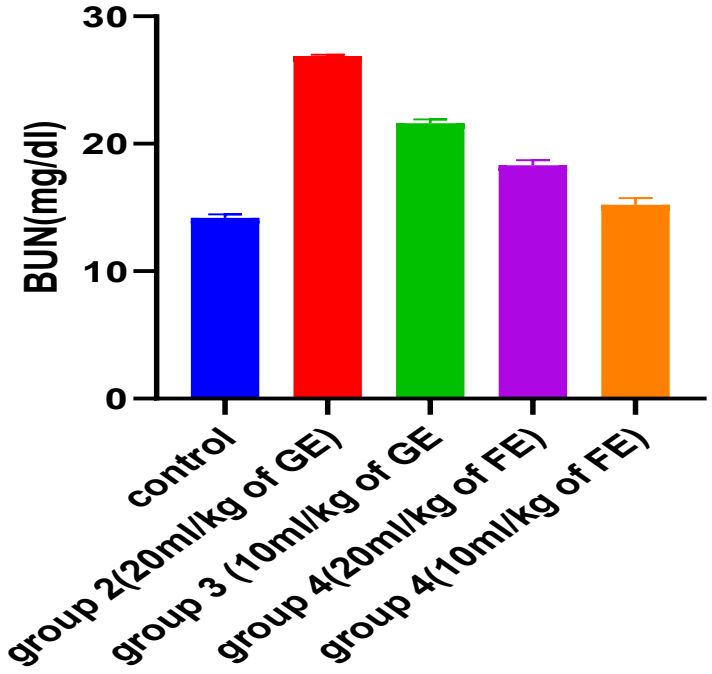


**Figure 3: Blood Urea Nitrogen Level after the Administration of Cassava Effluent**

**Histo-structural Appearance of Urinary Bladder after Administration of Cassava Effluent**

Histological findings of group 1 showed a section of the urinary bladder with normal histological structure including a well-defined urothelium with transitional epithelium, intact lamina propria and usual detrusor muscle layer (Figure 4). Histological findings on the urinary bladder of albino rats in group 2 given 20ml/kg of Garri effluent showed a disorganized/eroded epithelium, tissue edema, and detrusor muscle hypertrophy (Figure 5).

Histological findings on the urinary bladder of albino rats in group 3, given 10ml/kg of Garri effluent showed disorganized/eroded epithelium, hemorrhagic cystitis, tissue edema and detrusor muscle hypertrophy (Figure 6). Furthermore, histological findings on the urinary bladder of albino rats in group 4, given 20ml/kg of Fufu effluent showed disorganized/eroded epithelium, hemorrhagic cystitis within disorganized lamina propria, tissue edema and hypertrophied detrusor muscle (Figure 7) and finally, histological findings on the urinary bladder of albino rats in group 5, given 10ml/kg of Fufu effluent revealed thickened epithelium, hemorrhagic cystitis, mild tissue edema and detrusor muscle hypertrophy (Figure 8).

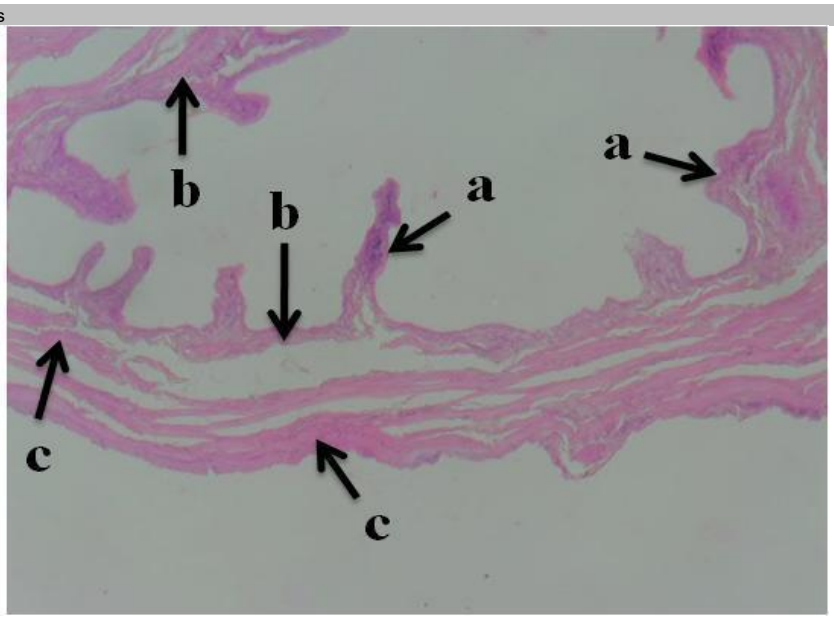


**Figure 4: Photomicrograph of urinary bladder of control animals given water and feed alone showing, a-well-defined urothelium with transitional epithelium, b-intact lamina propria and c- usual detrusor muscle layer. (H&E). 10x magnification. Inference: normal histo-structure.**

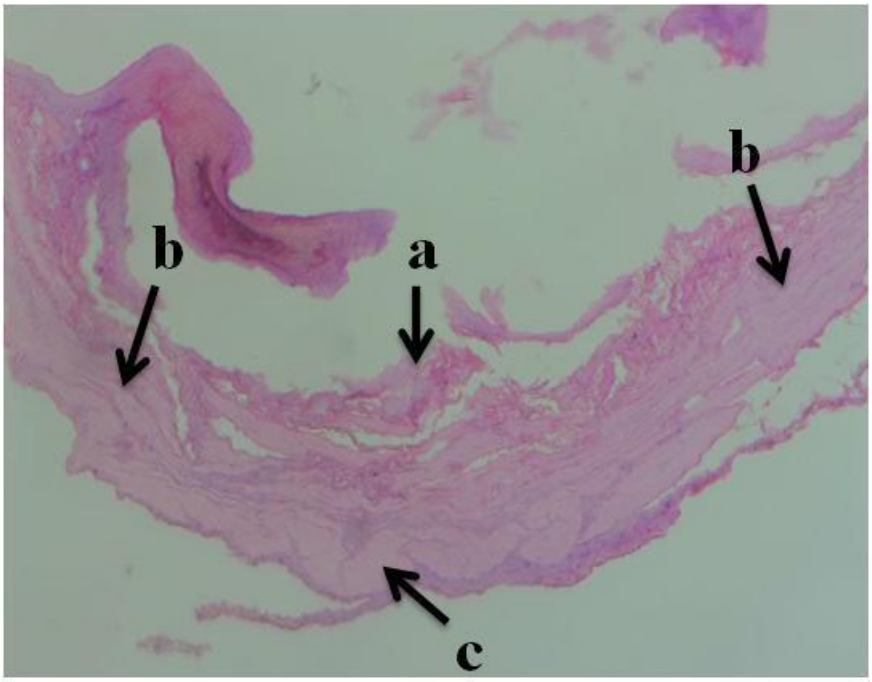


**Figure 5: Photomicrograph of urinary bladder of group 2 animals given 20ml/kg of garri effluent showing, a-disorganized/eroded epithelium, b- tissue edema, and c-detrusor muscle hypertrophy. (H&E). 10x magnification. Inference: severely affected due to inflammation.**

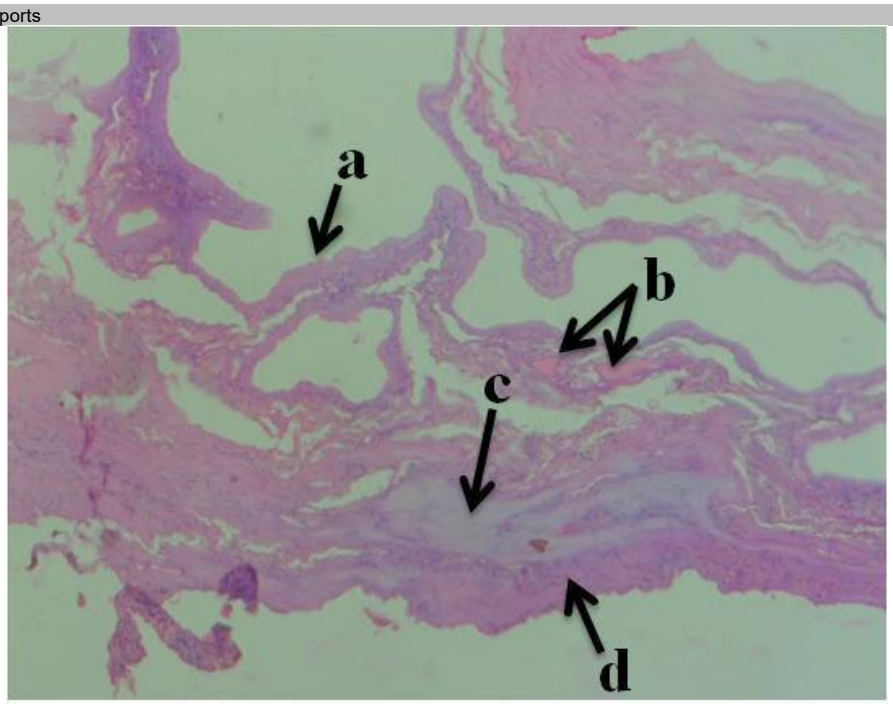


**Figure 6: Photomicrograph of urinary bladder of group 3 animals given 10ml/kg of garri effluent showing, a-disorganized/eroded epithelium, b-hemorrhagic cystitis, c-tissue edema and d-detrusor muscle hypertrophy. (H&E). 10x magnification. Inference: severely affected due to inflammation.**

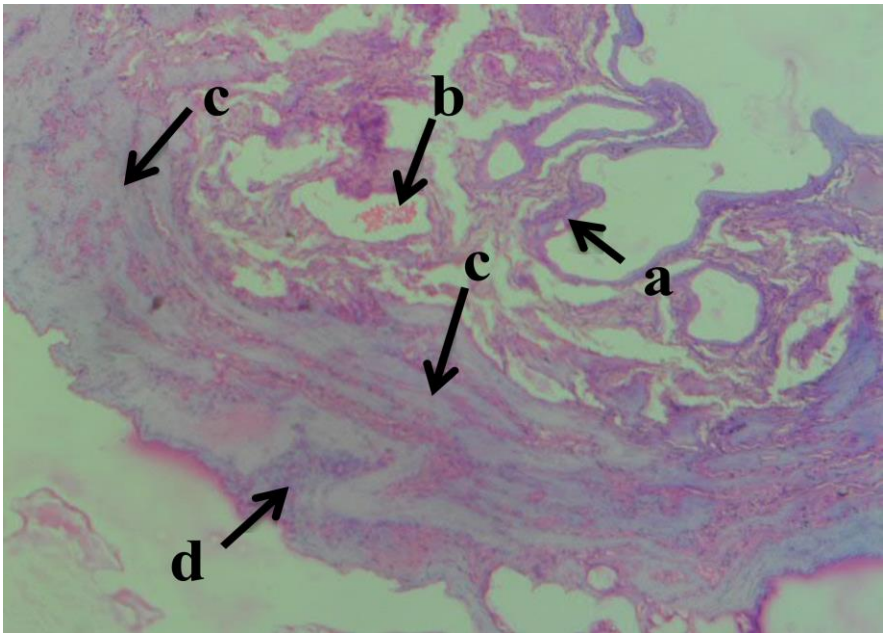


**Figure 7: Photomicrograph of urinary bladder of group 4 animals given 20ml/kg of fufu effluent showing, a-disorganized/eroded epithelium, b-hemorrhagic cystitis within disorganized lamina propria, c-tissue edema and d-hypertrophied detrusor muscle. (H&E). 10x magnification. Inference: severely affected due to inflammation.**

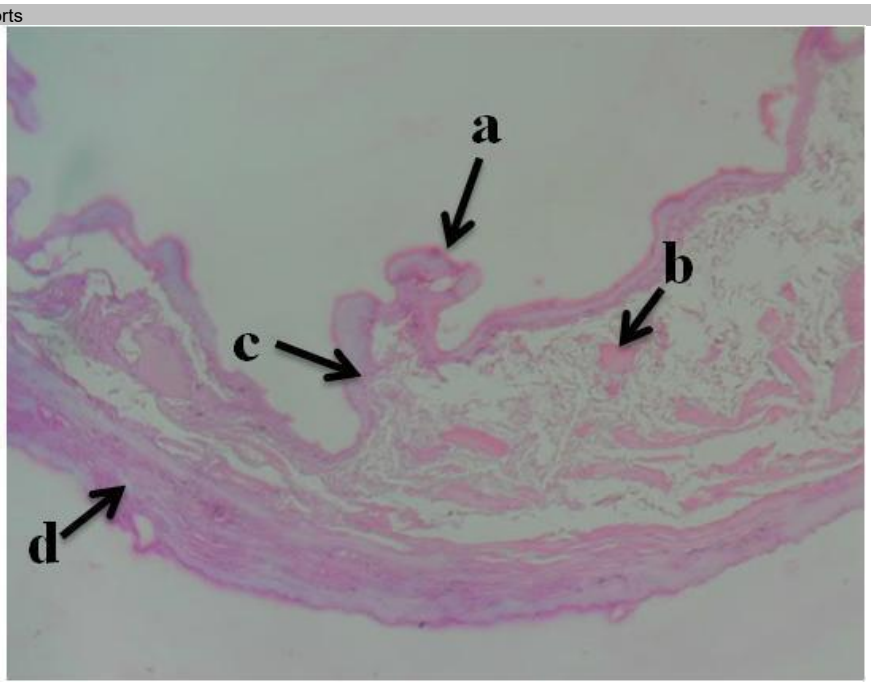


**Figure 8: Photomicrograph of urinary bladder of group 5 animals given 10ml/kg of fufu effluent showing, a-thickened epithelium, b-hemorrhagic cystitis, c-mild tissue edema and d-detrusor muscle hypertrophy. (H&E). 10x magnification. Inference: mildly affected due to inflammation.**

## Discussion

This study evaluated the effect of cassava effluent on the urinary bladder and kidney function parameters of Wistar rats. Cassava effluent is a liquid waste generated during cassava processing into either Garri or Fufu. The effluent is known to contain cyanide and acidic pH in addition to other chemical characteristics such as heavy metals, chemical oxygen demand, biological oxygen demand among others [13]. Increase in serum urea and serum creatinine as seen in this study due to cassava effluent toxicity may be linked to disturbances in protein catabolism, a consequence of elevated synthesis of the arginase enzyme involved in urea production [14, 15]. In assessing kidney function, creatinine, a by-product of creatine phosphate in muscles, assumes a crucial role. Produced consistently by the body, creatinine is predominantly cleared from the bloodstream by the kidneys [14]. As the foremost endogenous marker, creatinine holds significant importance in evaluating glomerular function [14]. Estimating the glomerular filtration rate (GFR) is the clinically preferred method for assessing renal function, representing the rate (mm/min) at which substances are filtered or cleared from the blood through the kidney glomerulus [14]. Serum urea is the final metabolite of protein nitrogen balance. These measurements permit the assessment of the overall metabolism of proteins and amino acids through the exclusive hepatic urea cycle. Once in the bloodstream, urea is predominantly excreted by the kidneys. After undergoing glomerular filtration, a substantial percentage, varying between 40% and 60%, is reabsorbed at the tubular level, establishing it as a marker for renal function. Serum urea concentration increases with reduced glomerular filtration rate (GFR), and vice versa [14]. This means that serum urea increases in conditions where renal clearance decreases due to renal impairment. Blood Urea Nitrogen (BUN) denotes the nitrogen content, primarily in the form of urea circulating in the bloodstream and was reported to be significantly increased in rats induced with cadmium, indicating renal disturbances [14]. In the case of healthy animals, the renal glomerulus filters urea from plasma, although some urea returns to the blood through renal tubules, the major route of elimination is through urine. If the kidney is not operating effectively, it results in insufficient removal of urea from plasma, causing elevated BUN levels that vary in response to various physiological conditions like increased protein intake, intestinal bleeding, infection, fever, dehydration, medications, burns, and poisoning [16]. In this study, it was observed that rats given cassava effluent showed heightened serum urea levels compared to the control group, suggesting potential kidney damage. The pathogenesis of chemical-induced bladder damage hinges on oxidative damage, where free radicals play a central role in the mechanisms leading to urinary bladder toxicity [14]. Our study suggests that cassava effluent inflicted considerable bladder impairments on experimental rats. This claim was supported by examining photomicrographs from the histopathological analysis of bladder sections taken from control and experimental animals. Histological examinations revealed impaired bladder tissues, aligning with depreciated kidney function markers. This strongly supports the potential toxicity of cassava effluent on bladder tissues. The histopathological findings in this study align with the observations of Romaniuk et al [17] who demonstrated significant morphological changes in the tissue wall structures of the urinary bladder caused by heavy metal salts. Our study may point to a buildup of cyanide, nitrate and phosphate in urinary bladder tissue, providing an explanation for the observed histological alterations. According to studies by Feki-Tounsi and Hamza-Chaffai [18] and Golabek et al [19], bladder cancer tissues exhibited elevated cyanide concentrations compared to those in control animals. Due to the kidneys' function of expelling toxic substances, such as cyanide, nitrate and phosphate, through urine, these toxic substances can be held in the bladder, leading to their accumulation in its walls and potentially causing impairment of its function. Histological modifications were observed in the urinary bladder of rats administered cassava effluent. These include disorganized epithelium, hemorrhagic cystitis, tissue edema, and detrusor muscle hypertrophy. Lining the walls of the urinary bladder is a specialized stratified epithelium called the urothelium. The urothelium appeared rough and scattered due to cassava effluent toxicity. There was damage to the inner lining of the bladder and the blood vessels that supply blood to the bladder. The bladder was shown to be inflamed, and blood was seen in the lining of the bladder. The tissue of the bladder appeared swollen due to fluid accumulation caused by leakage of blood vessels in the bladder. The fibers of the detrusor muscle of the bladder were hypertrophic to compensate for increased workload of the bladder emptying. This is very common in conditions that obstruct the urine outflow, such as benign prostatic hyperplasia. An acidic environment in the bladder can lead to irritation and inflammation of the urothelium. Prolonged exposure to an acidic environment can cause chronic inflammation (cystitis) [20]. Furthermore, the urothelial barrier could be compromised by acidic pH, weakening the barrier in the process. The bladder tissues become more susceptible to damage and infection from harmful substances in urine, increasing the risk of pathological conditions [20]. Another study by Keay et al [21] reported that acidic environments can also lead to cellular damage

within the bladder's epithelial cells, increasing the permeability of the bladder wall and allowing toxins and irritants to penetrate deeper layers, potentially causing ulceration. Chronic exposure to an acidic pH can cause long-term damage to the urothelium.

## Conclusion

Cassava effluent poses significant risk of damage to bladder urothelium and development of bladder diseases. In our study, cassava effluent had a significant effect on the histomorphology of the bladder and kidney function. We conclude that cassava effluent has detrimental effects on the bladder and serious care should be adopted during cassava processing.

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