Journal of Pharmacognosy and Phytochemistry
Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
www.phytojournal.com
JPP 2025; 14(1): 09-12
Received: 13-10-2024
Accepted: 16-11-2024

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Effects of aqueous leaf extract of *Manihot esculentai* on the kidney of adult Wistar rats

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DOI: https://doi.org/10.22271/phyto.2025.v14.i1a.15213

Abstract
The kidneys play a crucial role in waste filtration and maintaining homeostasis but are susceptible to dietary compounds, including bioactive substances in *Manihot esculentai* leaves. These leaves, although traditionally utilized, contain cyanogenic glycosides that may impact renal health. This study assessed the safety of aqueous extracts of *M. esculenta* on the kidneys of adult Wistar rats. Twenty-five rats were divided into five groups: a control group and four treatment groups receiving varying doses (100, 500, 1000, and 1500 mg/kg) for 28 days via an orogastric tube. Post-treatment assessments included oxidative stress markers, kidney function tests, and histological evaluations. The results indicated no significant alterations in malondialdehyde, glutathione, superoxide dismutase, and catalase levels, suggesting that the extract did not cause oxidative stress. Furthermore, serum urea and creatinine levels remained unchanged, indicating no renal impairment. Histological analysis showed preserved kidney architecture across all doses, suggesting that *Manihot esculentai* extract is safe for kidney health at the administered doses.

Keywords: *Manihot esculentai*, kidney, nephrotoxicity, Wistar rats

Introduction
The kidneys are essential organs responsible for filtering waste products from the bloodstream, regulating electrolyte balance, and maintaining fluid homeostasis [1]. Given their complex and constant filtering functions, they are highly susceptible to damage from various internal and external factors, including toxins, metabolic by-products, and certain compounds found in plants and foods [2, 3]. Even substances consumed regularly in the diet can impact kidney health, with some exerting protective effects while others may contribute to renal stress or injury [4]. Consequently, evaluating the potential impacts of commonly consumed plants on kidney function is essential to understanding any possible health risks or benefits.
Manihot esculentai, commonly known as cassava, is widely cultivated and consumed in many parts of the world for its starchy tubers [5]. Although primarily valued as a food source, cassava leaves are also utilized in traditional practices and are known to contain various bioactive compounds, such as flavonoids, saponins, tannins, and cyanogenic glycosides [6, 7, 8]. These compounds, particularly when ingested in significant amounts, may exert physiological effects on organs, including the kidneys. While cassava is an essential food crop, its leaves contain cyanogenic glycosides that can release cyanide—a potentially toxic compound—when metabolized [9]. The presence of such compounds raises questions about their possible effects on organs involved in detoxification and filtration, such as the kidneys.
Given the kidneys' central role in filtering and metabolizing substances from the bloodstream, they are likely to interact directly with the bioactive and potentially toxic compounds present in cassava leaves. However, there is limited scientific research examining how the consumption of cassava leaf extract specifically affects kidney tissues and function. Determining whether these compounds cause cellular stress, inflammation, or other histological changes in kidney tissue is essential to understanding the possible renal impact of cassava leaf consumption. This study aimed to evaluate the safety margins of the aqueous leaf extract of *Manihot esculentai* at given concentrations on the kidney of adult Wistar rats.

Materials and Methods
Plant Extract: *Manihot esculentai* leaves were obtained from a nearby farm. It was identified, and authenticated at the Department of Plant Biology and Biotechnology, University of Benin, Nigeria. Were thoroughly washed to remove any dirt, it was air dried at room temperature for about two weeks.

After drying it was then pulverized into powder form using an electric blender. The pulverized extract was then soaked in distilled water for 24 hours with constant stirring and shaking every six (6) hours. After soaking for 24 hours the mixture was then filtered using filter paper. Thereafter the filtrates were turned into a container and concentrated over a hot water bath at 45 °C and then refrigerated afterwards.

Experimental Animals: Wistar rats were procured and bred in the Animal House, Department of Anatomy, University of Benin, Benin City, Edo State, Nigeria. The rats were acclimatized for 2 weeks before the commencement of the experiment and the animals were fed Top feeds grower mash and clean water. The animals were weighed at the commencement and weekly afterwards. Protocols for this experiment will be in accordance with the guide for the care and use of laboratory animals [10].

Experimental Design: Twenty-five (25) adult Wistar rats weighing between 137 g and 185 g were randomly assigned into five (5) groups of five (5) rats each. Group A – Control; Group B – 100 mg/kg *Manihot esculentai*; Group C - 500 mg/kg body weight of *Manihot esculentai*; Group D – 1000 mg/kg body weight of *Manihot esculentai*; Group E - 1500 mg/kg body weight *Manihot esculentai*. The administration lasted for 28 days and was done orally using an orogastric tube.

Sample collection: At the end of the treatment period (28 days), the rats were weighed and then sacrificed under chloroform anaethesia. Blood samples were collected into EDTA anticoagulant sample bottles for biochemical analysis and the kidney was harvested and immediately fixed on 10% formalin to avoid autolysis and used for histopathological evaluation.

Biochemical analysis: Creatinine and urea concentration assessment was carried out as previously described by Higgins [11]. Antioxidant activity evaluation was carried out as previously described; Malondialdehyde (MDA) [12]; Glutathione peroxidase (GSH) [13]; Superoxide dismutase (SOD) [14].

Histological Assessments: The harvested kidney tissues were processed and routinely stained using hematoxylin and eosin, according to the method previously reported by Drury and Wallington [15].

Results

Table 1: Showing the oxidative stress parameters across the experimental groups

	Control	100 mg/kg *Manihot esculentai*	500 mg/kg *Manihot esculentai*	1000 mg/kg *Manihot esculentai*	1500 mg/kg *Manihot esculentai*	P- value
MDA (mole/mg protein)	335.02±19.20	308.62±8.67*	281.01±6.19*	226.06±4.95*	234.82±2.48*	0.005
GSH (µM)	0.72±0.05	0.63±0.08	0.75±0.02	0.71±0.11	0.68±0.11	0.301
SOD (U/mg Protein)	3.49±0.42	3.68±0.18	3.60±0.07	3.51±0.17	3.43±0.20	0.239
CAT (U/mg Protein)	0.04±0.01	0.03±0.03	0.03±0.01	0.04±0.01	0.03±0.01	0.078

Values are given as mean ± SEM.

Table 2: Showing the urea, creatinine levels across the experimental groups

	Control	100 mg/kg *Manihot esculentai*	500 mg/kg *Manihot esculentai*	1000 mg/kg *Manihot esculentai*	1500 mg/kg *Manihot esculentai*	P- value
Urea (mg/dL)	30.00±3.00	32.50±0.50	32.00±0.61	32.00±0.70	31.50±0.75	0.216
Creatinine (mg/dL)	52.22±1.67	54.44±1.67	53.89±3.89	61.67±0.01	53.61±5.83	0.401

Values are given as mean ± SEM.

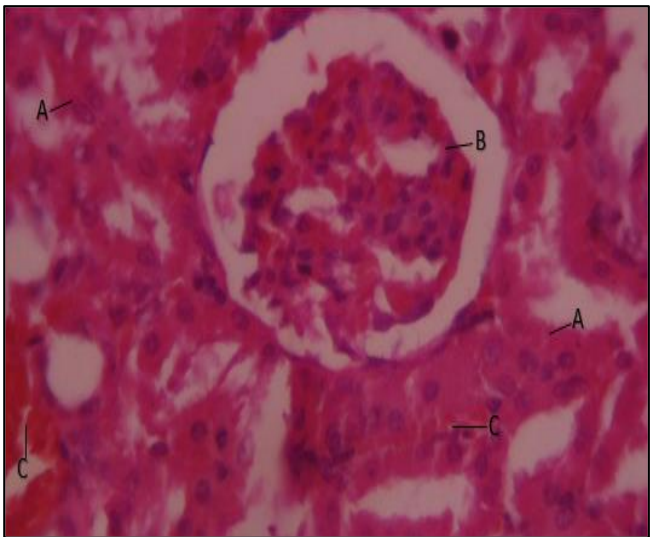

Plate 1: Rat kidney. Control. Composed of: A. tubules, B. glomeruli, all separated by C. interstitial space (H&E x 400).

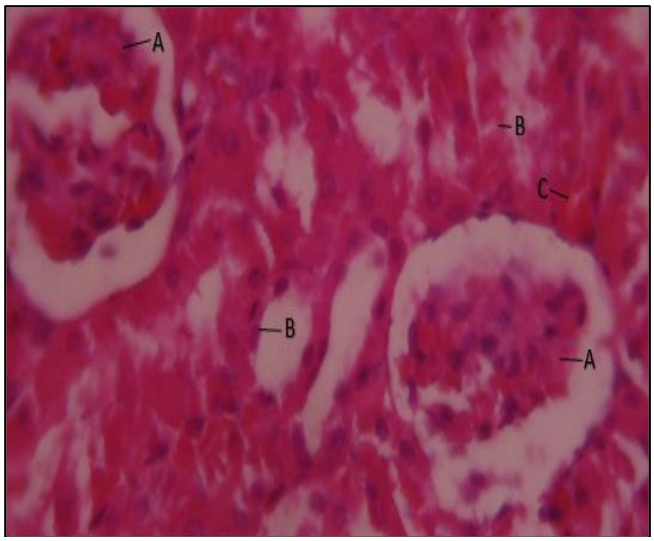

Plate 2: Kidney of Rat given low dose Extract showing: A normal nephron architecture composed of: A, glomeruli, B, tubules and C, active interstitial congestion (H&E x 400).

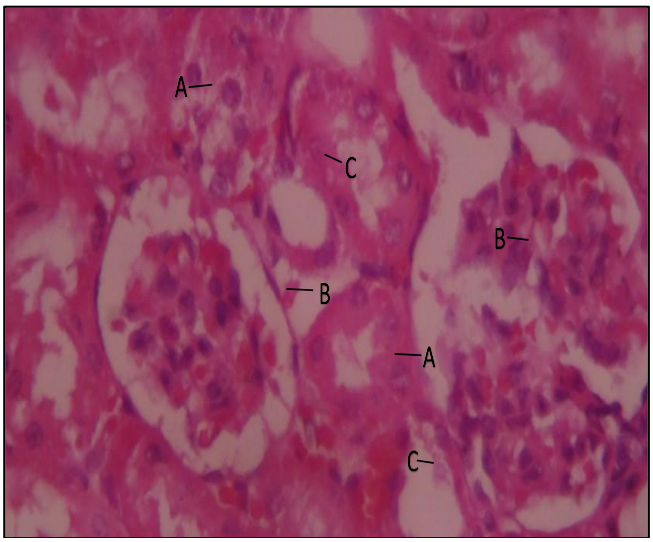

Plate 3: Kidney of Rat given medium dose extract showing: A, normal nephron architecture composed of: A, tubules, B, glomeruli and C, active interstitial congestion (H&E x 400).

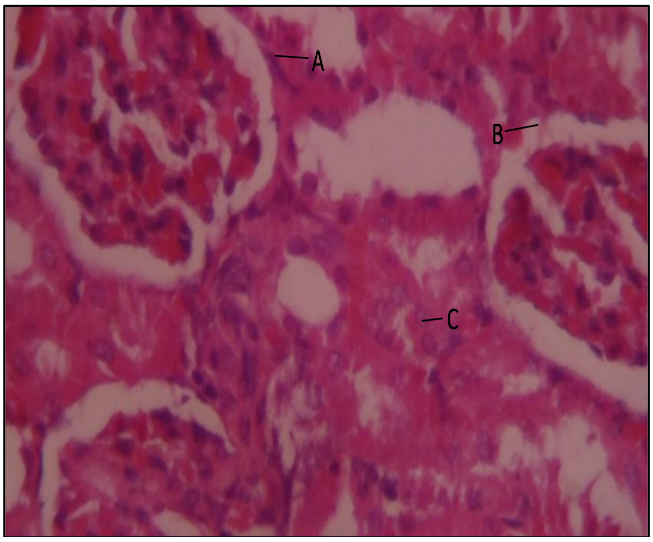

Plate 4: Kidney of Rats given high dose Extract showing normal nephron architecture composed of A. glomeruli, B, tubules and C, active interstitial congestion (H&E x 400).

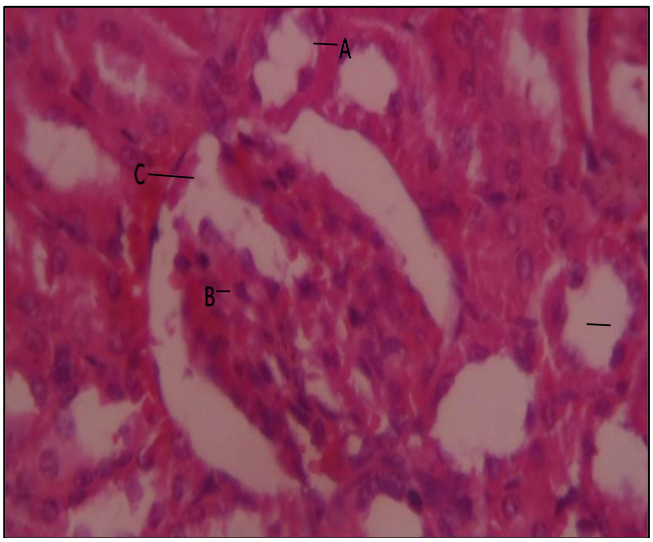

Plate 5: Kidney of Rats given high dose Extract showing normal nephron architecture composed of A. glomeruli, B, tubules and C, active interstitial congestion (H&E x 400).

Discussion

The oxidative stress markers—malondialdehyde (MDA), glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT)—are key indicators of oxidative balance within kidney tissue [16, 17]. The MDA levels, indicative of lipid peroxidation, showed no significant changes across control and treatment groups. This consistency suggests that *Manihot esculentai* extract, even at the highest dose (1500 mg/kg), did not induce lipid peroxidation. Studies on other plant extracts, such as *Moringa oleifera* and *Azadirachta indica*, have demonstrated reductions in MDA levels at therapeutic doses, suggesting antioxidant potential [18-20]. However, the presence of significant reductions in MDA here implies that *Manihot esculentai* possesses notable antioxidant effects in renal tissues or that its antioxidant activity is dose-independent.

Similarly, GSH, an endogenous antioxidant that counters oxidative damage, showed no significant alterations among groups. This aligns with studies by Ofoego *et al*. [21] on *Cucumis sativus* extract, where high doses did not significantly increase GSH levels in the kidneys, suggesting that not all plant extracts induce marked antioxidant responses. Additionally, SOD and CAT activities, both crucial enzymatic defenses against superoxide radicals and hydrogen peroxide, respectively, remained stable across control and treated groups. In comparison, studies on *Camellia sinensis* extracts demonstrated increased SOD and CAT activities [22], which indicates a more pronounced antioxidative impact than observed with *Manihot esculentai* in this study.

Kidney function was assessed by measuring serum urea and creatinine levels, reliable indicators of glomerular filtration efficiency and kidney health. Urea levels showed no significant differences between control and treated groups, and creatinine levels also remained comparable. The lack of significant elevation in these markers suggests that the *Manihot esculentai* extract did not impair renal function or induce nephrotoxicity. These results are consistent with studies by Obeten *et al*. [23] on *Curcuma longa* extracts, which similarly showed no alterations in urea and creatinine at various doses. The stability of these markers indicates that *Manihot esculentai* may be safe for the kidneys at the tested concentrations.

Histological examination of the kidneys provided further insights into the effects of *Manihot esculentai* extract. The kidneys in the control group displayed normal tubular and glomerular structures, with minimal congestion. In the treated groups, the histological architecture remained preserved across all doses, showing well-defined tubules, intact glomeruli, and only mild interstitial congestion. These findings are in agreement with other studies on *Ocimum gratissimum*, where even high doses did not induce structural alterations in renal tissues. The observed mild interstitial congestion in *Manihot esculentai*-treated kidneys could be a transient response to the plant's phytochemicals.

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