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Aqueous fruit pulp extract of *Adansonia digitata* (L) protects against lead-acetate-induced hepato-renal damage in rat model

Wusa Makena^{1*} , Eduitem Sunday Otong², Nathan Isaac Dibal¹, Barka Ishaku¹ and Sebastine Anthony Bazabang³

Abstract

Background: *Adansonia digitata* (L) fruit has a multi-purpose function one among many, is the antioxidant activities of the fruit by preventing oxidative stress. The effect of *Adansonia digitata* (L) fruit on lead-induced liver and kidney damage is not clear. Hence, the study was aimed to assess the protective role of *Adansonia digitata* (L) fruits against lead acetate induced changes in the liver and kidney function test parameters and the histology of both organ in experimental rats. The rats were divided into five groups with five rats each. All the rats were administered with respective assigned treatment once daily for 6 weeks. Rats in groups I were administered with just distilled water (2 ml/kg). Rats in groups II were administered with lead acetate (30 mg/kg) while rats in groups III–V were administered *Adansonia digitata* (L) fruit extract (250 mg/kg and 500 mg/kg) and Succimer (5 mg/kg) respectively, then additionally challenged with lead acetate (30 mg/kg) immediately after. At the end of the administration, the blood serum from the experimental rats were used for biochemical analysis. Then, the organs such as the liver and kidney collected for histological study.

Results: Rats administered with Lead acetate showed an increase in AST, ALP and ALT as well as increase in urea and creatinine level ($p < 0.001$), when compared with the control group (group I), where as *Adansonia digitata* (L) fruit prevented the effect (upsurge of serum, Urea, Creatinine, AST, ALP and ALT) of lead acetate. Rats administered with only Lead acetate revealed marked liver steatosis and the degeneration of the kidney glomerulus. The *Adansonia digitata* (L) fruit extract and Succimer prevented the histological liver steatosis, as well as the degeneration of the glomerulus of the kidney cytoarchitecture.

Conclusion: The findings in this study suggest that *Adansonia digitata* fruits extract has a protective potential against lead acetate induced liver and kidney toxicity by preventing the upsurge of liver function enzymes and kidney function parameters. Hence, *Adansonia digitata* fruits can serve as a natural plant agent that can prevent hepato-renal toxicity. Therefore, *Adansonia digitata* holds future prospects in preclinical framework to ameliorate organ toxicity for oral therapeutic applications.

Keywords: Lead acetate, *Adansonia digitata*, Succimer, Liver, Kidney, Creatinine

1 Background

Lead (Pb) is a non-biodegradable toxic heavy metal found in the water, soil and air, it has a widespread contamination that results in serious health problems [1, 2]. Report

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from Institute for health and metric evaluation indicated that Pb toxicity result in about 9.3 million disabilities and 494,550 deaths globally [3]. Pb occur naturally in the environment, it constitutes a major environmental hazard globally [4]. The hazard and burden of Pb poisoning is high in developing countries. In Nigeria, high cases of Pb poisoning have been reported in parts Niger and Zamfara states [5]. Pb has been reported to cause multiple organ failure leading to disability and death. The toxic effect of Pb depends on the amount and period of exposure [6, 7]. Pb gets into the body by inhaling Pb containing substances or by ingesting Pb-contaminated food and/or water that are eventually absorbed into the blood stream via the respiratory and gastrointestinal tracts respectively [8]. In the body, lead binds to the red blood cells, distributed to different tissues and eventually accumulates in bone [9]. Diet can affect Pb absorption. Food rich in copper, iron zinc and calcium can decrease Pb uptake while food rich in fat and/or protein can promote Pb absorption [10]. Children are more prone to Pb poisoning because their organs are still in the developmental stage [11].

Adansonia digitata (Baobab) is a plant that is widely grown in the arid and semi-arid regions of Africa, America and Asia due to its ability to survive a long period of drought and high temperature [12, 13]. Baobab leaves and seed are used in making soup and as flavouring agent in many African dishes respectively while the fruit pulp is used for making beverages [14]. In Africa, baobab fruit is traditionally used in the treatment of dysentery and diarrhoea and to stimulate milk production in lactating women [15, 16]. *Adansonia digitata* fruit pulp is rich vitamin C, dietary fiber, calcium, potassium, procyanidins, kaempferol isomers, terpenoids, Flavonoids and thiamine [17, 18]. Baobab leaves and fruit are important sources of polyphenols, they are reported to have cardioprotective, antioxidant and hepatoprotective properties [19, 20]. The antioxidant property of baobab fruit is attributed to its vitamin C, polyphenols and flavonoids content [21]. With all the aforementioned beneficial effects of *Adansonia digitata* fruitpulp and leaves, the present study was aimed at evaluating the protective role

of *Adansonia digitata* fruits pulp against lead induced liver and kidney injury in Rats.

2 Methods

2.1 Chemical

Lead acetate (BDH Chemicals Ltd, England) was used as hepato-renal toxicant. Succimer (meso-2,3 Dimercaptosuccinic acid) (Sigma-Aldrich, MO, USA) was used as standard drug (Chelating agent). Ketamine hydrochloride (PVT Ltd, India) was used as an anesthetic agent. Also, creatinine, urea, uric acid, AST, ALT and ALP kits (Ran-dox test kits) were used.

2.2 Plant collection and authentication

Adansonia digitata (baobab) fruits were obtained from a local farm in Shika, Sabo Local Government, Kaduna state, Nigeria. The Fruit was authenticated at the Herbarium (specimen no. 2512) Department of Biological Sciences, Ahmadu Bello University (ABU), Zaria, Nigeria.

2.3 Extraction

The fruit pulp of *Adansonia digitata* was grounded and extracted with distilled water in a soxhlet apparatus for 10 h.

2.4 Experimental animals

A total of 25 albino Wistar rats (160–180 g) were purchased from the Department of Pharmacology, ABU Zaria. The rats were allowed to acclimatize to the animal house condition for two (2) weeks before the commencement of the study. The rats had free access to rat chow and water. The research was approved by Animal use and care committee (ABUCAUC/2018/064), Ahmadu Bello University Zaria, and conducted in accordance with the ARRIVE guidelines.

2.5 Experimental design

The rats were randomly distributed into five groups ($n=5$). The grouping and administration of Lead acetate, succimer and aqueous extract of *Adansonia digitata* fruits is summarized in Table 1.

Table 1 Summary of experimental design

Groups	Treatment	Period
1	Distilled water at 2 ml/kg	6 weeks
2	Lead acetate at 30 mg/kg	6 weeks
3	<i>Adansonia digitata</i> at 250 mg/kg + lead acetate at 30 mg/kg	6 weeks
4	<i>Adansonia digitata</i> at 500 mg/kg) + lead acetate at 30 mg/kg	6 weeks
5	Succimer at 5 mg/kg + lead acetate at 30 mg/kg	6 weeks

2.6 Biochemical studies

The rats were euthanized at the end of the six weeks, blood sample of each rat was collected in a plain tube. The blood samples were centrifuged at 3000 rpm for 5 min using a centrifuge machine. The serum obtained was used to estimate ALT, AST, ALP, creatinine, urea and uric acid.

2.7 Histological studies

The liver and kidneys were harvested and fixed in neutral buffered formalin, dehydrated in graded alcohol, embedded in paraffin wax, cleared in xylene, sectioned at 5 μm and stained with Hematoxylin and eosin (H & E).

2.8 Statistical analysis

Data were expressed as mean ± standard error (SE). One-way analysis of variance (ANOVA) test was followed by Tukey’s post-hoc test was conducted using Graphpad prism (Version 9.2). Statistical significance was considered at $p < 0.05$.

3 Results

3.1 Liver function enzymes

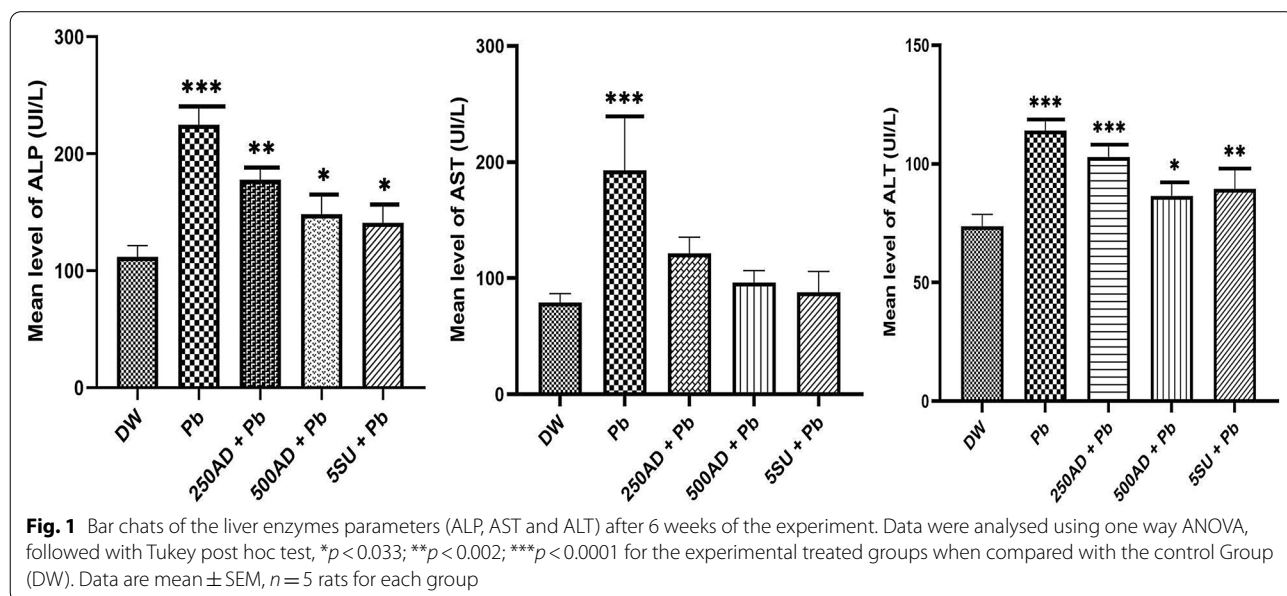
The levels of ALP, AST and ALT increased significantly ($p < 0.0001$) in the serum of lead acetate control rats when compared to control rats and rats treated with *Adansonia digitata* and Succimer (Fig. 1). Treatment with 500 mg/kg of *Adansonia digitata* were shown to be more effective. There was no significant difference ($p > 0.05$) in AST level between control rats and rats treated with *Adansonia digitata* and Succimer (Fig. 1).

3.2 Kidney function parameters

A significant increase ($p < 0.0001$) in creatinine and urea levels were observed in the kidney serum of rats treated with only lead acetate when compared with the control rats and rats that were treated with *Adansonia digitata* and Succimer (Fig. 2). There was no significant difference ($p > 0.05$) in creatinine level between control rats and rats treated with *Adansonia digitata* and Succimer (Fig. 2).

3.3 Histological study

Photomicrograph of the liver of normal control rats showed normal hepatocytes central vein and sinusoids (Fig. 3a). The liver of rats treated with only lead acetate showed marked steatosis, fat hepatocellular vacuoles and degenerating hepatocytes (Fig. 3b). The liver of rats treated concomitantly with lead acetate (30 mg/kg) and *Adansonia digitata* (250 mg/kg and 500 mg/kg) showed mild steatosis (arrow) and some macro vesicular fatty change (Fig. 3c, d). The liver of rats treated with Lead acetate (30 mg/kg) and Succimer (5 mg/kg) showed mild macro vesicular fatty change (Fig. 3e). For the histology of the kidney, the kidney of normal control rats showed histological structure of the kidney with normal glomerulus and renal tubules (Fig. 4a). The kidney of rats treated with only Lead acetate (30 mg/kg) showed marked degenerated glomerulus and spontaneous lipid vacuolation of the glomerulus (Fig. 4b). The Kidney of rats treated with Lead acetate (30 mg/kg) and *Adansonia digitata* (250 mg/kg and 500 mg/kg) simultaneously showed normal glomerulus and some mild tubular damage (Fig. 4c, d). The kidney of rats treated with Lead acetate (30 mg/kg)



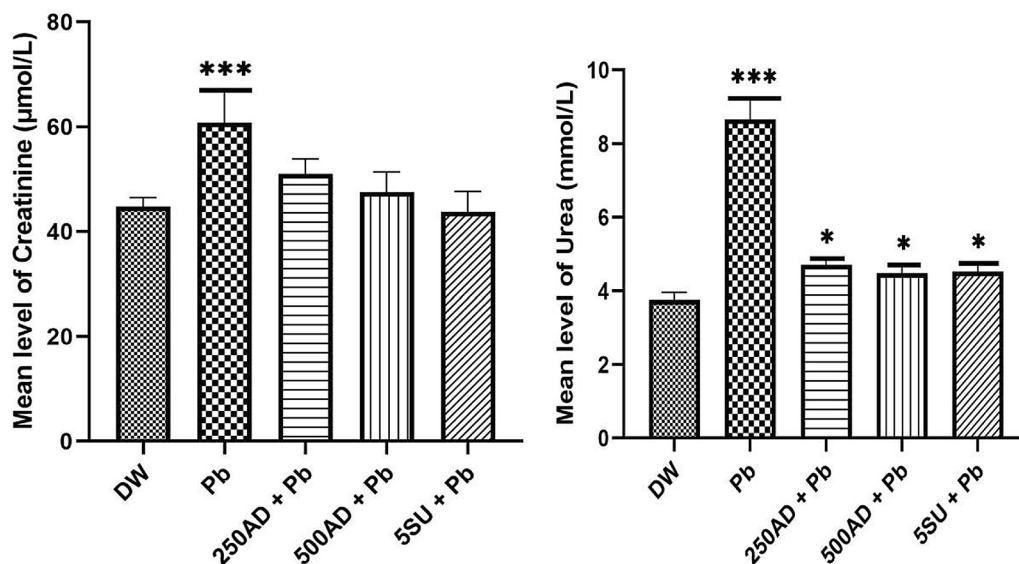


Fig. 2 Bar charts of the creatinine and Urea serum level after 6 weeks of the experiment. Data were analysed using one way ANOVA, followed with Tukey post hoc test, * $p < 0.033$; ** $p < 0.002$; *** $p < 0.0001$ for the experimental treated groups when compared with the control Group (DW). Data are mean \pm SEM, $n = 5$ rats for each group

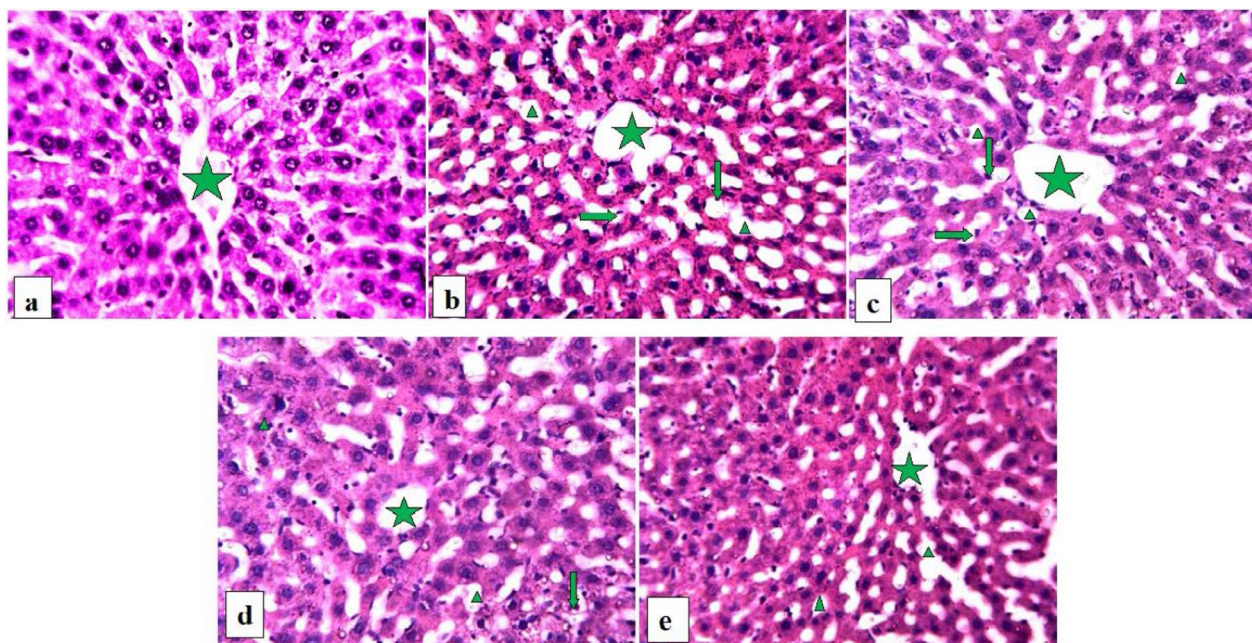


Fig. 3 Photomicrographs of sections of liver of a control (a) showing normal histological structure of the liver with the central vein (star), Lead acetate treated micrograph (b) showing marked steatosis (arrow) and some macro vesicular fatty change (arrow head), Extract 250/500 mg/kg + lead acetate 30 mg/kg (c, d) respectively showing mild steatosis (arrow) and some macro vesicular fatty change (arrow head), Succimer 5 mg/kg + lead acetate 30 mg/kg micrograph (e) showing mild macro vesicular fatty change (arrow head). H&E stained X 250, $n = 5$

kg) and Succimer (5 mg/kg) showed mild degenerated glomerulus (star) marked tubular damage (Fig. 4e).

4 Discussion

In this present study, the hepatic and renal toxicity due to lead acetate was seen by a significant increase in the

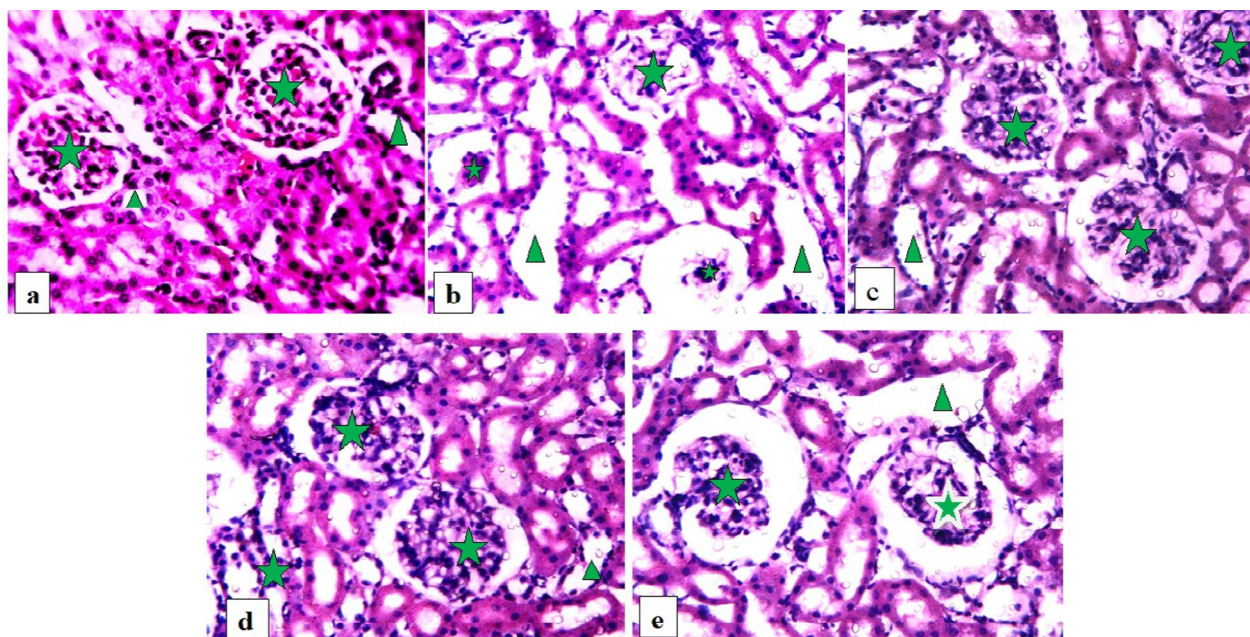


Fig. 4 Photomicrographs of sections of kidney of a control (a) showing histological structure of the kidney with normal glomerulus (star) and renal tubules (arrow head), Lead acetate treated micrograph (b) showing marked degenerated glomerulus and spontaneous lipid vacuolation of the glomerulus (star), Extract 250/500 mg/kg + lead acetate 30 mg/kg (c, d) respectively showing normal glomerulus (star) and some mild tubular damage (arrow head), Succimer 5 mg/kg + lead acetate 30 mg/kg micrograph (e) showing mild degenerated glomerulus (star) marked tubular damage (arrow head). H&E stained X 250, $n = 5$

levels of parameters like ALT, AST and ALP as other studies also observed same outcome [22, 23]. This could be explained by the fact that Pb disrupt the liver cell membrane [24], hence the increased concentration of the liver enzymes parameters. The marked increase in serum creatinine and urea level in lead acetate administered rats (Fig. 2), this could due to the toxic effect of lead acetate on the cells of renal tubules, hence the impairment of the permeability of creatinine and urea [25, 26]. the outcome in this experiment is consistent with that of previous studies [5].

Adansonia digitata fruit administered rats markedly protected the disruptions induced by lead acetate by reducing the level of the liver enzymes parameters (AST, ALP and ALT) likewise the serum level of urea and creatinine. This might be due to the antioxidant potential of *Adansonia digitata* fruit [21], which plays a significant role to protecting the liver and kidney against the lead acetate induced renal toxicity as reported in previous studies [27, 28]. The distortion induced by lead acetate on both tissue (liver and kidney) confirmed the biochemical parameters result and might be due the formation of free radicals generated by the lead acetate [25]. The histopathological findings of Rats administered with *Adansonia digitata* fruit reveal the restoration of cyto-architectural of the liver and kidney. The protective

activities of *Adansonia digitata* fruit might be due to the fruit bioactive components, as it was reported that the fruits is rich in vitamin C, urosolic acids, and sitosterol [29], This components have been report to mediate against free radical, lipidemic and inflammatory activities [30, 31], hence, the hepatic and renal architectural protection by the *Adansonia digitata* fruit. The result is in agreement with previous studies [32].

5 Conclusions

This study suggested the protective role of *Adansonia digitata* fruit extract against lead acetate induced liver and kidney toxicity. *Adansonia digitata* fruit extract exerts this protective role by mitigating the upsurge of both liver function enzymes and kidney function parameters (creatinine and Urea) level. Likewise the study revealed the protective efficacy of the fruit extract against lead acetate induced hepatic and kidney cyto-architectural degeneration in rats.

Abbreviations

AD: *Adansonia digitata*; ALP: Alkaline Phosphatase; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; DW: Distil Water (Normal Control group); Pb: Lead; SU: Succimer (Standard drug group).

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None.

Authors' contributions

Conception and design: All authors. Provision of study materials: WM, ESO and NID. Data collection: WM, ESO and SAB. Data analysis and interpretation: All authors; Initial draft of manuscript: WM, BI, SAB and NID. Critical review of the manuscript: WM and NID. All authors read and approved the final manuscript.

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Availability of data and Material

Not applicable.

Declarations**Ethics approval and consent to participate**

The research was approved by ABU Directorate of Academic Planning and Monitoring (Approval No: ABUCAUC/2018/064) and was conducted according to the ARRIVE Guidelines.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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