Journal of Complementary and Alternative Medical Research

Volume 24, Issue 1, Page 10-22, 2023; Article no.JOCAMR.104355
ISSN: 2456-6276

Mollification of Lead Induced Liver Injury by *Lycopersicon esculentum* (Tomato) Extract

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Authors' contributions

This work was carried out in collaboration between both authors. Author RSA conceptualized, designed and supervised the study. The experiments were carried out by author JCO. Both authors carried out literature search and analyses of the results. Draft manuscript was prepared by author RSA but read and approved by authors RSA and JCO.

Article Information

DOI: 10.9734/JOCAMR/2023/v24i1489

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/104355

Original Research Article

Received: 07/06/2023
Accepted: 12/08/2023
Published: 25/08/2023

ABSTRACT

Objective: Lead is a highly toxic, non-biodegradable heavy metal usually found in the environment largely as a pollutant of water, soil or air. Chronic lead exposure has adverse effects on human health. *Lycopersicon esculentum* has many phytochemicals that may ameliorate organ injury due to lead toxicity in humans. This study answered the question "Is aqueous extract of *Lycopersicon esculentum* (tomato) beneficent to lead toxicity induced liver injury?"
Methodology: The study had five groups with fifteen animals each. The control was group CN. The lead toxicity group (PbT) had 30 mg/kg/day of lead acetate crystals, the concomitant extract group (CE) had concurrent administration of lead acetate and aqueous extract of *L. esculentum* (at 400 mg/kg). The post lead toxicity low dose extract. (PLE) had sequential administration of lead acetate and aq. extract *L. esculentum* (at 400 mg/kg). The post lead toxicity high dose extract. (PHE) had sequential administration of lead acetate and aq. extract *L. esculentum* (at 800 mg/kg). Both the lead acetate and extract were administered orally for twenty one days. At specific periods, blood samples were collected for biochemical analyses and organs harvested for histopathological evaluation.

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Result: The total plasma protein levels of the extract groups (CE, PLE and PHE) were significantly higher than that of the PbT group. The PbT group had markedly elevated plasma liver enzymes. Oxidative stress was only evident in the PbT group but not in the extract groups as suggested by the significantly depressed anti-oxidant activities and elevated lipid peroxidation. A cystic lesion was observed in one of the liver specimens from the PbT group. Histopathological findings included fatty infiltration of the liver in the PbT group and presence of multinucleated hepatocytes in the extract groups. The latter feature suggested the ability of aqueous extract of *L. esculentum* to ameliorate the lead (Pb) toxicity induced liver damage.
Conclusion: Concurrent and post-exposure administration of aqueous extract of tomato fruit (*L. esculentum*) mollified the liver injury caused by lead toxicity.

Keywords: Hepatic lead toxicity; liver injury; Lycopersicon esculentum.

1. INTRODUTION

Lead is a highly toxic nonessential, non-biodegradable heavy metal found in the environment. It gets into the environment through human and industrial activities contaminating soil and surface water [1]. It serves as one of the raw materials in the manufacture of building paints, ductile pipes for conveyance of crude oil, refined petroleum products and industrial cum domestic gas. Lead is a component of crude oil [2] thus in geographic areas of crude oil exploration and exploitation activities, with high probability of surface water and soil contamination as a result of leakage which may be inadvertent or occasioned by pipe line vandalism, lead may thus be consumed either directly through water or indirectly through marine products such as fish, crabs and crustaceans [3,4]. Different organs in marine fish have been documented to have varying concentrations of heavy metals that are said to be within permissible levels [5]. It should be noted that consumption of these sea foods with permissible levels of heavy metals over a considerable time frame may be injurious to human health. Lead can also be consumed through plants such as cassava tubers and its staples, vegetables [6], palm kernel and its oils, banana and other arables cultivated in the polluted environment and contaminated soil. Thus human exposure to lead occurs either through inhalation of lead dust or consumption of lead contaminated food materials or lead containing substances. When lead gets into the human body it can affect all the systems. However, those whose functions are mostly affected are the gastrointestinal, reproductive, endocrine, hepatic and immune systems [7]. The blood level of lead equilibrates at about three months post absorption [8] and most of it is stored in the liver and to a lesser extent in the other organs [9]. Elimination of lead from the body is biphasic, the first being from the blood and soft tissues; this usually takes between 20 to 30 days and the second phase from the bones may take years. The biological half-life of lead in trabecular bone is about one year and in cortical bone it ranges from 10 to 20 years [10]. Lead exists in two forms which are inorganic and organic with the former being predominant. The inorganic lead is largely excreted in urine and the remainder in faeces after being metabolized by the hepatobiliary pathway [9]. Only 1% of blood lead is in the plasma and the remaining tagged to erythrocytes [8].

Lycopersicon esculentum (tomato) is a natural occurring fruity plant that has many phytochemicals with diverse biological and biochemical functions that are beneficial to human health. It may be of relevance either in the prevention or amelioration of organ injury sequel to lead toxicity.

It is obvious that lead is a ubiquitous heavy metal contaminant and readily gets into the human biologic systems. The toxicity and the resulting threat to human health of any contaminant depends on the concentration and duration of exposure. It is practically impossible to avoid lead contamination thus there is the need to explore nutritional supplement or additive that may serve as a decontaminant. This will reduce the incidences of pathologies involving vital body organs such liver, kidney, pancreas, bones etc that may result from lead toxicity. This formed the basis of the study being reported.

2. MATERIALS AND METHODS

2.1 Plant Materials

2.1.1 Plant collection and authentication

Ripe and freshly harvested *Lycopersicon esculentum* (tomato) fruits were sourced from a metropolitan commodity and grocery market

situated in Ibadan, South West Nigeria. The Herbarium division of the Botany Department, University of Ibadan assisted in the botanical identification and specie confirmation of the *L. esculentum*.

2.1.2 Extract preparation

The *L. esculentum* fruits were initially washed under potable running water and thereafter blended till fine-textured. Aqueous extract was obtained by means of filtration resulting in a 12.5% yield that was refrigerated till use.

2.2 Animals

Seventy five adult Wistar rats weighing 140 to 220 g were sourced from the Central Animal house of the College of Medicine, University of Ibadan. They were acclimatized for three weeks in a well ventilated and illuminated environment with optimal ambient temperature (26±2°C, 12 hours light / dark cycle) that was conducive for the study. The animals were fed liberally with locally sourced but standard pelletized rat feed and had free access to water.

2.3 Design of the Experiment

The creation of the experimental groups was premised on lead toxicity and dosage of L. *esculentum* aqueous extract administered. Consequently, five groups were created and the animals were randomly allotted.

The details of the groups were;

(1) Control (CN)- lead toxicity not induced.
(2) Lead toxicity (PbT)- had lead acetate but extract was not administered.
(3) Concomitant extract (CE)- concurrent administration of aq. extract of L. *esculentum* and lead acetate
(4) Post lead toxicity low dose extract. (PLE). Sequential administration of lead acetate and low dose extract of *L. esculentum*.
(5) Post lead high dose extract. (PHE). Sequential administration of lead acetate and high dose extract of *L. esculentum*.

2.4 Induction of Lead Toxicity

Lead acetate crystals administered orally over a specific period has been documented to induce toxic injury of the liver [1,2]. Thus each rat in the PbT, CE, PLE and PHE groups had daily oral administration of lead acetate at 30mg/ kg for 21 days in order to induce toxic injury of the liver.

2.5 Conduct of the Experiments

The control group had only normal rat diet and water while the Lead toxicity group had 30 mg/kg/day of lead acetate crystals orally for 21 days. The Concomitant extract group (CE) had concurrent daily oral administration of lead acetate crystals at 30 mg/kg and aqueous extract of *L. esculentum* at 400 mg/kg for 21 days. While the Post lead toxicity low extract group (PLE) had initial daily single dose of lead acetate crystals at 30 mg/kg for 21 days and thereafter, daily oral dose of the *L. esculentum* at 400 mg/kg for 21 days. For the Post lead toxicity high extract group (PHE), the extract was administered at 800 mg/kg for 21 days. Both Pb and the extract were administered via a steel cannula.

Venous blood samples were collected through intraocular puncture from five animals in each group at day 28,35 and 42 for biochemical analyses. The biochemical parameters evaluated were the liver function test (Total protein plus globulin and albumen fractions; liver enzymes-alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase. The activities of catalase(CAT), glutathione peroxidase (GPx) and superoxide dismutase (SOD); and the degree of lipid peroxidation as measured by malondialdehyde (MDA) levels were used to assess the extent of oxidative stress occasioned by the lead toxicity.

Also, on day 28,35 and 42, each group had five animals (whose blood were collected) sacrificed by cervical dislocation with prior light sedation for the purpose of organ harvesting.

The harvested liver specimens were initially washed in buffered saline and thereafter stored in 10 % formaldehyde solution for subsequent light microscopy.

2.6 Data Analysis and Processing

The numerical aspects of the results were analyzed with Statistical Package for the Social Sciences (SPSS) version 24 and expressed as percentages, means plus standard deviation of means (SD). The student t- test was used for inter group comparison and level of significance was set at $p<0.05$.

3. RESULTS

All the experimental groups had significantly lesser percentage weight gain in comparison with the Control. The weight gain by the Post lead low

extract (PLE) and Post lead high extract (PHE) groups were markedly higher than that of the Lead toxicity group (PbT). The Concomitant extract (CE) and PLE groups had notably lesser weight gain than that of the PHE group.

As for the mean liver weight and the relative liver weight the values were similar across the groups. The total protein levels of group PbT were significantly lower than that of the Control group at Day 28,35 and 42. Also the total protein level of the PbT was observed to the markedly lower than those of CE, PLE and PHE at Day 42. The albumin fraction of the total protein level of the PbT group was significantly lower than those of the Control, CE, PLE and PHE groups at Day 28,35 and 42. It was only at Day 35 that the albumin fraction of the total protein levels of the CE, PLE and PHE were significantly lower than that of the Control. No remarkable difference was observed in the level of the globulin fraction of the total protein amongst the groups.

The alanine transaminase (ALT) levels of the PbT group at Day28,35 & 42 were markedly higher than those of the Control group. The ALT of the PbT was significantly higher than those of CE, PLE and PHE only at Day 42. The aspartate transaminase (AST) of PbT was significantly higher than those of the CN, CE and PHE at Day 42. The alkaline phosphatase (ALP) of PbT group at Day 42 was significantly higher than those of the other groups (CN, CE, PLE and PHE).

In evaluating the severity of oxidative stress consequent on lead toxicity and its amelioration by *L. esculentum;* catalase(CAT) activities of the PbT were significantly reduced at Day 28,35 and 42 with reference to those of the Control, PLE and PHE. Amongst the extract groups, it was only at Day 28 that the CAT activity was markedly lower than that of the control and for the PLE it was at Day 35. Only the PLE had glutathione peroxidase (GPx) activities that were significantly higher than those of the Control and PbT groups and these were observed on Day 28. The superoxide dismutase (SOD) activities at Day 28,35 and 42 of the PbT were significantly lower than those of the Control and PLE. Lipid peroxidation was very pronounced in the PbT but mild in the extract groups. This conclusion was drawn from the levels of malondialdehyde (MDA) of the PbT that were markedly elevated than those of the Control and extract groups at the three periods of quantification (Table 1).

One of the harvested liver specimens from the PbT group had a cyst that contained lead particles (Fig 1).

Photomicrographs obtained from the liver specimens at day 28 revealed hepatocytes with vacuolation in the PbT group, presence of multinucleated hepatocytes in groups CE, PLE and PHE. Macrophages were observed in considerable number in the PbT group all through the duration of the study. On day 28,35 and 42, fewer hepatocytes were observed in the lead toxicity group relative to the control and extract groups. The architecture of the liver was preserved in all the groups and at the three periods of evaluation (Plates 1-3).

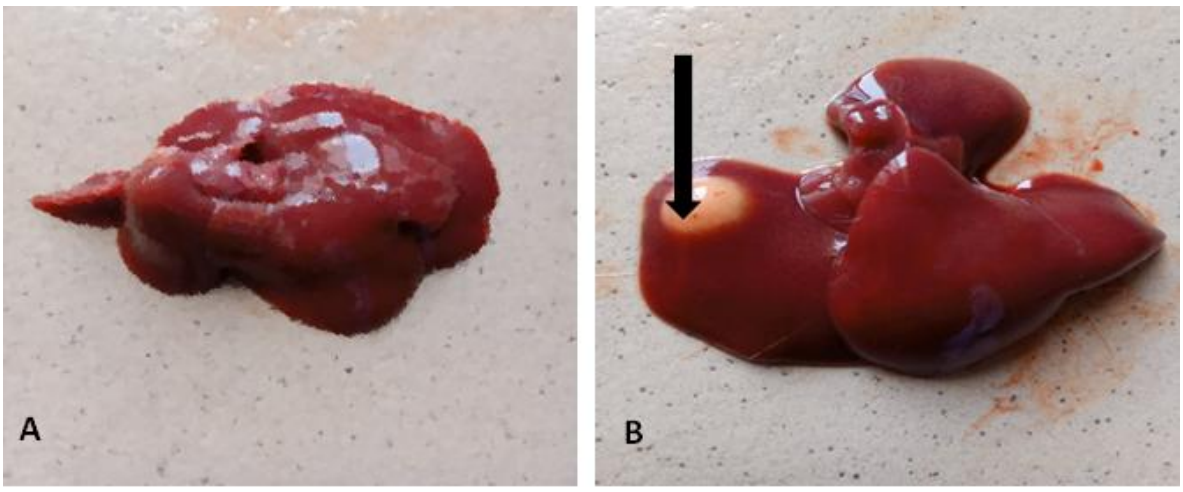

Fig. 1. Normal liver specimen (A); Liver specimen with a cyst (B)

Table 1. Morphological, biochemical and antioxidants parameters (mean values)

Parameter	CN (n=15)	PbT (n=15)	CE (n=15)	PLE (n=15)	PHE (n=15)
Body weight gain (%)	63.14±13.06	17.27±11.92$^{\alpha}$	16.63±12.14$^{\alpha\mu}$	28.13±17.12$^{\alpha\delta}$	43.57±15.28$^{\alpha\beta}$
Liver weight (g)	7.51±1.19	6.69±0.60	7.23±0.44	6.71±0.66	7.08±0.94
Relative liver weight (g/100g body weight)	3.30±0.01	2.94±0.05	3.43±0.03	2.99±0.03	3.05±0.04
Total protein (g/dl)					
Day 28	14.34±0.14	8.84±2.01$^{\alpha}$	12.54±1.86	11.17±0.5$^{\alpha}$	12.33±1.85
Day 35	12.99±0.78	9.37±017$^{\alpha}$	12.89±2.5	12.23±1.42	12.23±1.58
Day 42	13.29±1.07	8.85±0.93$^{\alpha}$	13.04±0.29$^{\beta}$	13.14±1.00$^{\beta}$	13.09±1.22$^{\beta}$
Albumin (g/dl)					
Day 28	5.69±1.13	1.93±0.08$^{\alpha}$	3.06±0.11$^{\beta}$	3.47±0.12$^{\beta}$	3.59±0.04$^{\beta}$
Day 35	6.40±0.03	1.99±0.07$^{\alpha}$	3.31±0.10$^{\alpha\beta}$	3.33±0.1$^{\alpha\beta}$	3.44±0.07$^{\alpha\beta}$
Day 42	5.87±1.20	1.89±0.23$^{\alpha}$	3.07±0.05$^{\beta}$	3.47±0.11$^{\beta}$	3.30±0.10$^{\beta}$
Globulin (g/dl)					
Day 28	8.67±0.98	6.91±2.09	9.48±1.85	7.70±0.38	8.74±1.81
Day 35	6.59±0.82	7.39±0.25	9.58±2.40	8.90±1.24	8.78±1.50
Day 42	7.42±2.27	6.96±1.16	9.97±0.23	9.67±0.88	9.79±1.12
Alanine transaminase (u/l)					
Day 28	27.49±2.29	45.29±4.57$^{\alpha}$	35.58±4.57	29.11±4.57	30.73±2.29
Day 35	24.26±2.29	50.14+11.54$^{\alpha}$	27.50±2.28	27.50±2.29	24.26±2.29
Day42	25.88±9.15	69.55±2.29$^{\alpha\beta}$	32.35±4.57$^{\beta}$	21.03±2.28$^{\beta}$	21.03±2.29$^{\beta}$
Aspartate transaminase (u/l)					
Day 28	67.94±4.57	121.31±25.16	69.55±2.29	55.00±4.57	58.23±9.15
Day 35	69.55±11.44	103.52±4.54	72.79±6.86	101.90±20.59	80.88±9.15
Day42	64.70±13.72	148.81±22.87$^{\alpha}$	74.41±13.72$^{\beta}$	77.64±9.14	72.79±6.86$^{\beta}$
Alkaline phosphatase (u/l)					
Day 28	22.61±0.39	27.29±4.67	17.51±9.94	19.57±0.38	23.29±1.94
Day 35	20.68±1.95	28.81±6.82	23.16±1.95	26.74±0.39$^{\alpha}$	22.33±0.77
Day 42	17.51±2.53	31.71±0.78$^{\alpha}$	16.13±7.60$^{\beta}$	21.23±1.56$^{\beta}$	15.03±1.75$^{\beta}$
Catalase (µM/mg)					
Day 28	41.90±3.40	15.65±1.47$^{\alpha}$	21.82±3.28$^{\alpha}$	30.20±1.52$^{\beta}$	35.12±4.90$^{\beta}$
Day 35	43.22±1.94	19.80±1.28$^{\alpha}$	29.92±10.7$^{\beta}$	29.43±0.33$^{\alpha\beta}$	36.92±6.55$^{\beta}$
Day42	39.84±2.33	16.75±1.98$^{\alpha}$	26.49±13.97	39.96±0.81$^{\beta}$	41.95±0.32$^{\beta}$

Parameter	CN (n=15)	PbT (n=15)	CE (n=15)	PLE (n=15)	PHE (n=15)
Glutathione peroxidase(µmol/mg)					
Day 28	9.11±0.10	8.94±0.51	10.43±1.48	11.47±0.36$^{\alpha\beta}$	10.56±1.56
Day 35	10.02±0.51	8.42±1.59	10.26±1.90	10.63±1.04	10.58±1.40
Day 42	9.86±0.80	7.78±0.51	9.94±0.15$^{\beta}$	9.84±0.73	9.90±0.83
Superoxide dismutase(µmol/mg)					
Day 28	13.28±0.06	9.46±0.78$^{\alpha}$	14.40±2.14	14.27±0.55$^{\beta}$	13.39±1.77
Day 35	13.38±0.58	8.38±0.59$^{\alpha}$	14.01±2.17	14.52±0.71$^{\beta}$	13.59±1.67
Day 42	13.35±0.52	8.90±1.23$^{\alpha}$	13.28±2.15	14.70±0.81$^{\beta}$	14.89±1.07$^{\beta}$
Malondialdehyde (mmol/l)					
Day 28	17.93±2.71	70.08±0.69$^{\alpha}$	22.46±4.60$^{\beta}$	44.72±6.65$^{\alpha\beta}$	34.21±0.25$^{\alpha\beta}$
Day 35	21.99±1.18	68.62±9.00$^{\alpha}$	25.67±5.91$^{\beta}$	32.71±0.81$^{\alpha\beta}$	34.68±1.33$^{\alpha\beta}$
Day42	22.12±1.63	82.46±6.56$^{\alpha}$	23.12±3.48$^{\beta}$	22.72±0.88$^{\beta}$	24.51±4.77$^{\beta}$

α-indicates significant difference from that of the Control group.

β-indicates significant difference from that of the Lead toxicity (PbT) group

δ-indicates significant difference from that of the Post lead toxicity high extract group (PHE) group

µ-indicates significant difference from that of the Post lead toxicity high extract group (PHE) group

CN-Control group, CE- Concomitant extract group, PbT- Lead toxicity group, PLE-Post lead toxicity low dose extract group and PHE- Post lead toxicity high dose extract group

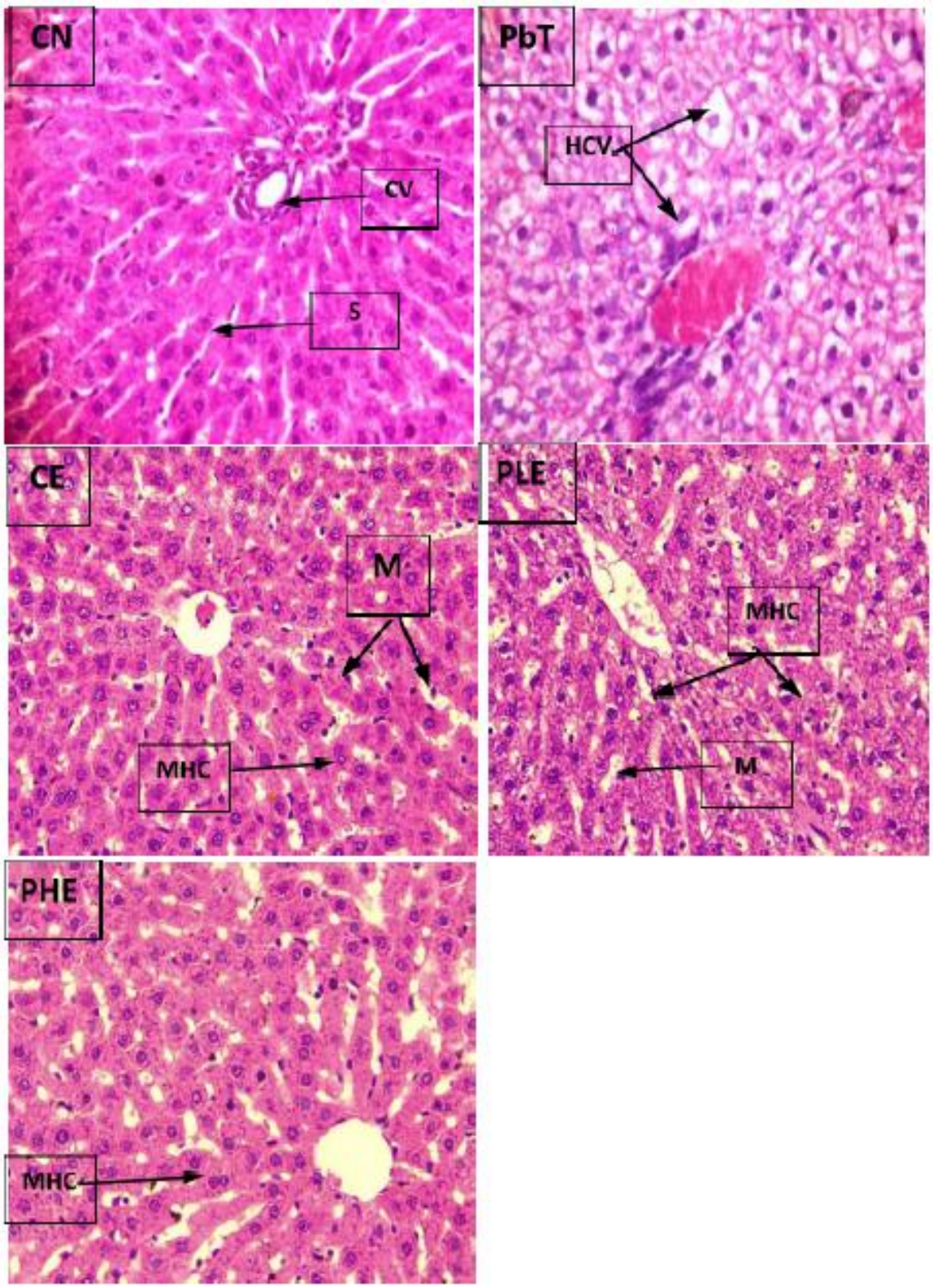

Plate 1. Photomicrographs of the liver specimens of the groups at Day 28 (H & E x400)

Legend: CV- Central vein, HCV- Hepatocytes with steatosis, M-Microphage, MHC- Multinucleated hepatocytes, S-Sinusoid, CN-Control group, CE- Concomitant extract group, PbT- Lead toxicity group, PLE-Post lead toxicity low dose extract group and PHE- Post lead toxicity high dose extract group

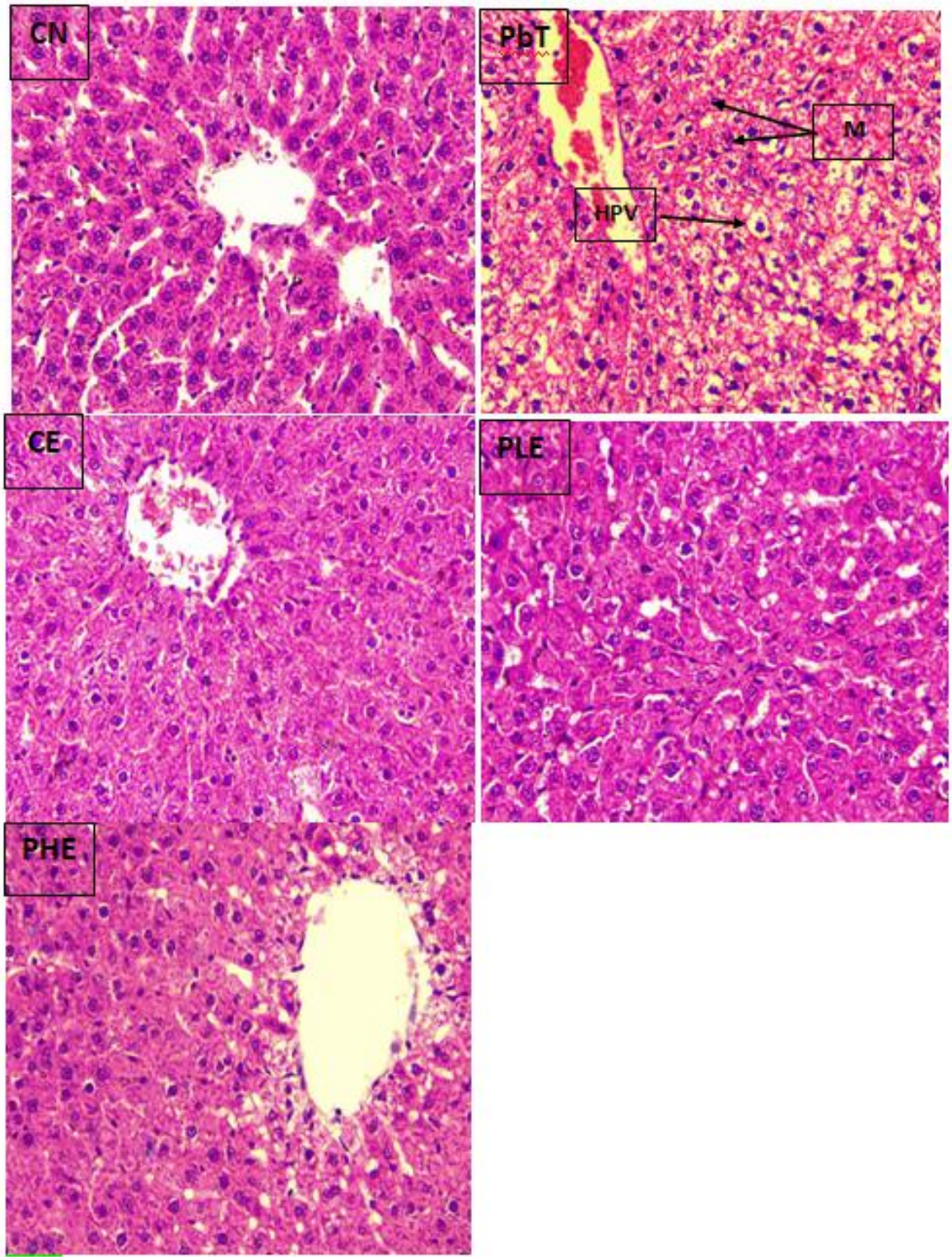

Plate 2. Photomicrographs of the liver specimens of the groups at Day 35 (H & E x400)

Legend: HPV-Hepatocyte with steatosis, M- Macrophage, CN-Control group, CE- Concomitant extract group, PbT- Lead toxicity group, PLE-Post lead toxicity low dose extract group and PHE- Post lead toxicity high dose extract group

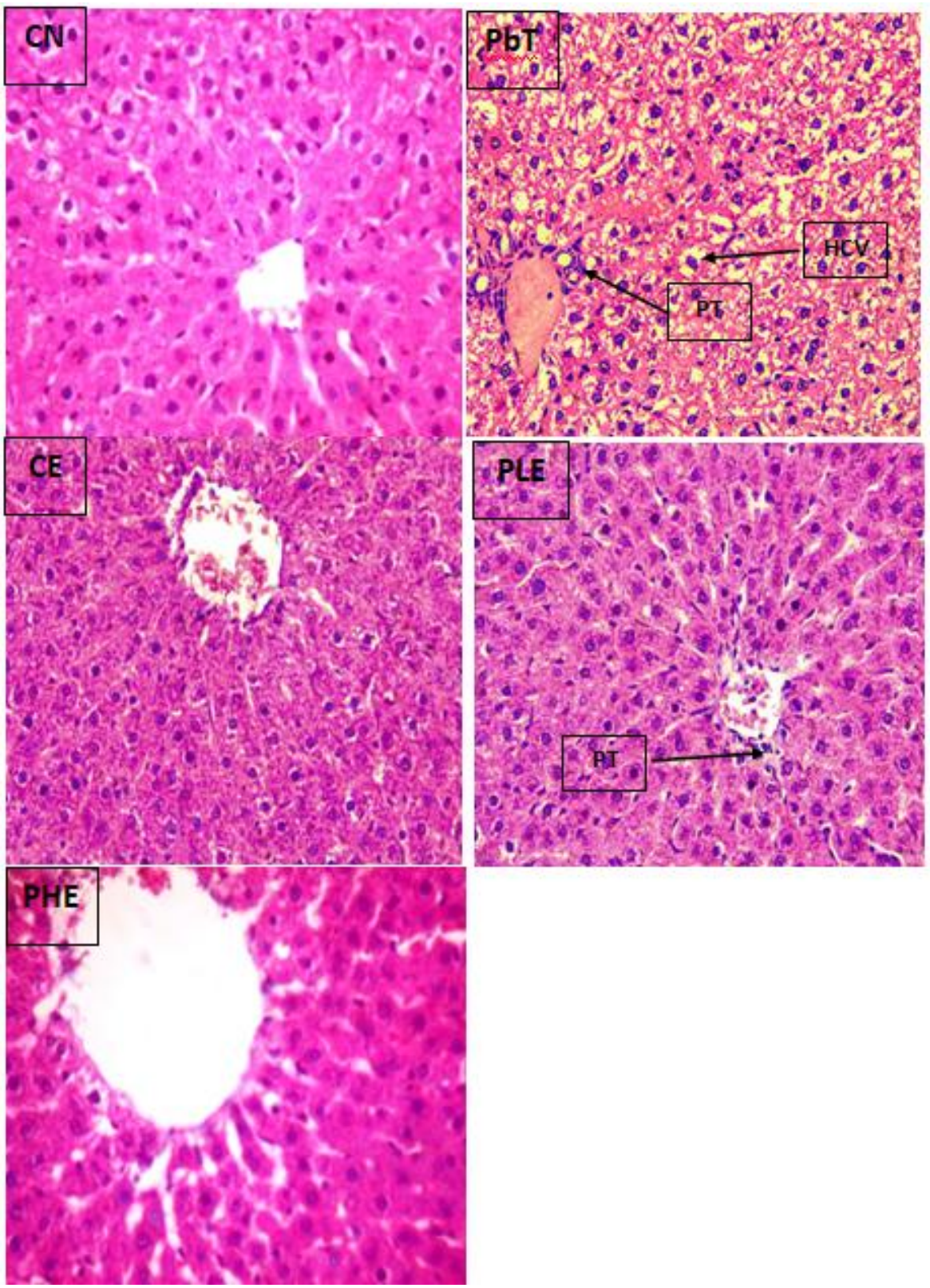

Plate 3. Photomicrographs of the liver specimens of the groups at Day 42 (H&E x400)

Legend: PT-Portal triad, CN-Control group, CE- Concomitant extract group, PbT- Lead toxicity group, PLE-Post lead toxicity low dose extract group and PHE- Post lead toxicity high dose extract group

4. DISCUSSION

High blood level of lead (Pb) in humans has been documented to cause anorexia, nausea, vomiting, diarrhea and constipation [11]. All these clinical symptoms will invariably lead to increased catabolism and reduced anabolism with resultant weight loss. This might explain the significantly least mean weight gain by the Lead toxicity (PbT) and Concomitant extract (CE) groups. Both low and high extract groups (PLE & PHE) had remarkable weight gain that was more pronounced in the latter. This showed that aqueous extract of *L. esculentum* administered following lead exposure is ameliorative in a dose-dependent fashion while administration during the period of Pb exposure may not be ameliorative in terms of body weight dynamics.

The mean liver weight was similar across the groups this could be due to large reserve of the liver and also the duration of the exposure. In humans, exposure to Pb for years will result in morphological alterations in liver such as fatty changes and fibrosis.

The synthetic function of the liver was remarkably depressed by Pb toxicity as evidenced by the low blood protein levels of the Lead toxicity (PbT) group after short (28 days), medium (35 days) and long (42 days) durations of Pb ingestion. The blood total protein levels of the experimental groups (CE, PLE & PHE) were similar to those of the control. Thus oral administration of the aqueous extract of *L. esculentum* was able to restore hepatic synthetic function following lead toxicity. This pattern was also observed for the blood levels of the albumin fraction of the total protein. However, the levels of the globulin fraction were similar across the groups. Thus it can be reasonably concluded that *L. esculentum* has the ability to restore hepatic synthetic function following toxic injury. This pattern of alterations in the blood levels of protein and its fractions was observed in a previous hepatic toxicity study. In that study by us, hepatic toxic injury was induced by administration of carbon tetrachloride and the interventional agent was extract of *Vitex angus castus* [12]. Also in another study in which the injurious agent was alcohol and the ameliorating agent was *Phyllanthus amarus* extract, the blood protein profile was similar [13]. Also, aqueous fruit pulp extract of *Adansonia digitate* has been documented to protect against Pb induced hepatorenal injury [14]. In summary, plant extracts play prominent role in the restoration of hepatic synthetic function following toxic injury.

Liver enzymes such as alanine transaminase (ALT) and aspartate transaminase (AST) reside within the cytosol of the hepatocytes. Thus necrosis of hepatocytes will result in elevation in the blood levels of these enzymes. In this study, Pb toxicity caused elevated transaminases as the levels for the PbT group were significantly higher than those of the Control while the values for the three extract groups were similar to those of the Control at all the reference periods of 28,35 and 42 days. The inference that could be drawn from this observation is that extract of *L. esculentum* either protected against hepatocyte necrosis or increased hepatocyte regeneration. Whichever of these postulations is correct supports the assertion that tomato (*L. esculentum)* is protective against lead toxicity.

In the human body, lead causes rapid depletion of antioxidants and also increases the production of free oxygen radicals leading to oxidative stress [15,16]. Oxidative stress is the main mechanism responsible for its toxicity. It alters the composition of fatty acids in membranes thus affecting processes like exocytosis, endocytosis and signal transduction [9]. In this study, administration of lead caused oxidative stress as evidenced by the markedly depressed activities of antioxidants such as catalase and superoxide dismutase in the Lead toxicity (PbT) group. The activities of these antioxidants in the two extract groups that had the tomato extract following established lead toxicity were not remarkably different from those of the Control. Antioxidant parameters of this study also showed that lead toxicity caused significant lipid peroxidation as the malondialdehyde levels of the PbT group were significantly higher than those of the Control and the three extract groups at the three reference periods. That the activities of antioxidants of the tomato extract groups were similar to those of the control serves as an objective evidence of *L. esculentum* possessing antioxidant property thereby attenuating the negative effects of exposure to Pb. This will be of immense health benefit to people habiting areas where lead contamination of the soil, domestic water sources, aquatic life and plants are unavoidable due to industrial and economic activities.

A cystic lesion is a fluid containing space lined by epithelial cells and it may be congenital or acquired. It may occur in any structure or organ. Hepatic cysts are usually parasitic in aetiology. A liver specimen harvested from the PbT group had a solitary cystic in one of its lobes

that contained lead particles. The formation of this cyst might have been due to the inflammatory process initiated in the liver by the prolonged administration of Pb. Inflammatory response is usually a way to limit extent of injury.

Vacuolation of hepatocytes is indicative of accumulation of fat in the cytoplasm. This is known as fatty change. Hepatic fatty change may be due to malnutrition, alcohol abuse, chemical and bacterial toxins [17]. This fatty change was seen only in the Lead toxicity (PbT) group and not in the extract groups. Thus aqueous extract of *L. esculentum* administered concurrently or sequentially ameliorated lead toxicity. Steatosis (hepatic fatty change) is said to be reversible once the precipitating factor no longer exists [18]. This may also explain why fatty change was not observed in the liver specimens from the PLE and PHE groups.

Presence of multinucleated hepatocytes is an evidence of recovery following extensive liver cell necrosis [19]. In this study the induced lead toxicity resulted in necrosis of the hepatocytes as evidenced by both the quantitative and qualitative results of the PbT group. Observation of multinucleated hepatocytes in the extract groups provides a conclusive evidence that the aqueous extract of *L. esculentum* reversed the hepatic cellular injury occasioned by lead toxicity.

Lead is known to increase bone turnover, reduce mineralization and bone mineral deposit thus leading to osteoporosis [19]. This will increase the incidence of pathological fracture in people that are chronically exposed to Pb.

Consumption of game animals hunted with gunshot is a source of chronic low level exposure to Pb. In these animals, the muscle Pb concentrations comprise of biologically incorporated lead and shot-in lead. In some European countries, some measures have been put in place to reduce the use of lead gunshot for animal gaming as a way of reducing exposure to lead [20]. In Nigeria both the use of lead gunshot for hunting animals and the consumption of meats from such animals are not regulated and in fact it will be difficult to regulate. This makes the beneficial effect of aqueous extract of *L. esculentum* on lead toxicity as documented by the results of this study to be of relevance in our communities. Plants like cabbage and ginger have been documented to ameliorate the severity of lead induced liver injury in ways similar to those of *L. esculentum* (tomato) as documented by this study [21,22]

Children can absorb 40% to 50% of an oral dose of water-soluble lead compared with 3% to 10% for adults. Lead is a known abortifacient and has been implicated in increased fetal deaths and reduced birth weights. Lead is a potent neurotoxin, and childhood lead poisoning has an impact on many developmental and biological processes such as intelligence, behavior and overall life achievement [23]. Thus chronic lead exposure is a serious health hazard to children and finding a nutritional remedy against lead toxicity will enhance the health of children.

Lead is the second most toxic metal after arsenic and constitutes 0.002% of the Earth's crust. However, its natural level remains below 50 mg/kg. Recent research findings suggest that traces of Pb (~29 ng/g diet) is important for enzyme activities and cellular systems, especially during cell development, hematopoiesis, and reproduction [24]. Some studies conducted in northern Nigeria have reported the presence of Pb at values greater than the World Health Organization permissible levels in some green vegetables such as lettuce and cabbage thus making the consumption of such leafy vegetables in such areas hazardous to human health [25,26]. It is obvious that these plants got the Pb from the contaminated soil which would have been from human and industrial Pb related activities [27,28].

The importance of environmental lead exposure cannot be overemphasized. The United States Center for Disease Control and Prevention had to issue a press release in October 2020 to warn that some 3.6 million U.S. families risk permanent harm to their children because their homes were contaminated with lead-based paint [29]. Similar statistic for Nigeria and other African countries may be lacking thus the finding of *L. esculentum* aqueous extract as remedy to lead toxicity will be of immense benefit if translatable to humans. Countries like Canada have established permissible blood lead level (0.30 – < 0.50 µmol/L) and management protocol for elevated values [30]. In most African countries such values are not available thus the main finding of this study which is *L. esculentum* being able to counter the deleterious effect of Pb poisoning will improve the quality of life of inhabitants of Pb polluted environment. Arising from the fact that children absorb 40% of the exposed Pb and retain 30% (respective values for adults being 10 and 1%) [31]. They are at a

greater risk of lead toxicity thus the aqueous extract of *L. esculentum* will serve as prophylaxis in children living in areas of high Pb contamination. The most reliable estimation of recent lead exposure in adults is the blood level while for life time cumulative exposure is the Pb content of the tibia.

5. CONCLUSION

Lead toxicity negatively affects mitochondrial function and interferes with calcium homeostasis and may thus trigger multi organ/system dysfunctions. The exact permissible safe levels in both children and adults may be difficult to ascertain as clinical entities attributable to lead have been reported in patient with values below these permissible levels. Through advocacy and legislation, environmental lead pollution can be abated but not eliminated. Thus recommending aqueous extract of *L. esculentum* as nutritional supplement will reduce the health challenges occasioned by lead toxicity in residents of areas that have persistent environmental lead exposure or pollution.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The animals used in this study were handled in accordance to the guidelines as prescribed by the ethical conduct of animal research of the University of Ibadan. Also, the principles of laboratory animal care as contained in the 8th edition (2011) of the Guide for the Care and Use of Laboratory Animals by the National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals were observed [32].

ACKNOWLEDGEMENT

We are grateful to the Department of Anatomy, University of Ibadan for the partial funding of this research through the Year 2021 Department Research Grant.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/104355