Research Article

Hematobiochemical changes induced by lead intoxication in male and female albino mice

Saeed A Alwaleedi

Department of Biology, Faculty of Science, Taif University (TU), Taif, Saudi Arabia.
Correspondence to: Saeed A Alwaleedi, E-mail: swaleedi@hotmail.com.

Received October 9, 2015. Accepted October 16, 2015

Abstract

Background: Lead is one of the main environmental contaminants that can threaten living organisms in many ways. Lead toxicity may affect multiple organs of human body and is associated with a number of physiological, biochemical, and morphological alterations. **Aims and Objective:** To investigate the risk that may result from exposure to different doses of lead acetate on the body weight and the weight of different organs, hematological indices, and the functions of liver and kidney. **Materials and Methods:** The experiment was performed on 80 mice. They were divided into four groups. The first group represented the healthy control animals, while groups II, III, and IV were given sublethal doses of lead acetate (0.4, 0.8, and 1.2 mg/kg body weight, respectively) in drinking water for 12 weeks. At the end of the experimental period, blood was collected and used for hematological and biochemical analysis. **Result:** The results indicated that mice treated with lead acetate showed significant reduction in total erythrocyte count, packed cell volume, hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration compared with the healthy control ones while there were significant elevations in total leukocyte count and the amount of platelets. The results also showed significant increase in the activities of alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transferase, alkaline phosphatase, and lactate dehydrogenase, indicating liver dysfunction. In addition, the serum levels of blood urea nitrogen and creatinine were also increased indicating renal deficiency. **Conclusion:** Treatment with lead acetate at low doses has harmful effects on experimental animals and induced hematological and biochemical alterations. Therefore, this study advises people to avoid any exposure to this toxic metal to prevent its hazardous effects on health.

KEY WORDS: Lead; Toxicity; Blood Indices; Biochemical; Liver; Kidney

Introduction

Lead is a widespread natural element in the environment. It is considered as one of the main persistent and common environmental pollutants.[1] Lead is used in the production of various manufactured products such as paints, printing, gasoline, batteries, water pipes, cosmetic products, pottery glazing, tank linings, brass faucets, and toys.[2] Owing to its toxic cumulative action in the environment, lead can affect all biological system via exposure from different sources including air, water, and food.

Access this article online	
Website: http://www.njppp.com	Quick Response Code:
DOI: 10.5455/njppp.2015.5.0910201578	

Lead can translocate through the food chain and cause harmful effects to human and other living organisms. It is one of the poisonous metals in the environment and has deleterious impact on most organs of the human body.[3] Lead enters into the body through three main routes, including digestive and respiratory tracts and skin. When it is absorbed into the blood, some of it is bound to erythrocytes, and the remaining stays in plasma to be distributed to other tissues.[4]

There are many evidences that report that lead is a poisonous factor, which targets numerous organs such as kidneys, liver,

nervous system, immune system, and hematopoietic system. Lead toxicity is associated with a number of physiological, morphological, and biochemical alterations such as liver dysfunction,[5,6] hematological disorders,[7] impairment of renal system functions,[8] glucose metabolism abnormality,[9,10] and nervous system disturbances.[11]

Accumulation of lead in the body could lead to destructive impacts on hematic, gastrointestinal, and renal systems.[12] Lead toxicity has been associated with multiple forms of cancer, cardiovascular disorders, nephrotoxicity, and distraction of nervous system. Lead poisoning is related to sex, age, exposure duration, exposure route, absorption rate, frequency of intake, solubility, and retention percentage.[11] Exposure to excessive amount of lead has been shown to elevate blood pressure and cardiovascular disorders in adults and to decrease the cognitive development and intellectual performance in children.[13]

Exposure to lead has been shown to increase the production of reactive oxygen species (ROS) and, consequently, induce lipid peroxidation and alteration of antioxidant defense systems in mice[14] resulting in oxidative stress.[15] ROS are the by-products of numerous degenerative reactions in various tissues, which affect the regular metabolism by damaging the cellular components.[16] Decreasing the possibility of lead interacting with critical biomolecules and stimulating oxidative damage or bolstering the cell's antioxidant defense might be attributed to the beneficial role of antioxidant nutrients through exogenous supplementation of antioxidant molecules.[17] Binding of lead to phosphatidylcholine in the cell membrane of red blood cells (RBCs) resulted in reduction of phospholipid levels. Lipid peroxidation has also been determined in tissue from different parts of the brain of lead-intoxicated rats. Lead exposure may cause hypochromic and normochromic anemias, which result from ROS production and subsequent erythrocyte hemolysis.[18] Therefore, this study was designed to investigate the risk that may result from exposure to different doses of lead acetate on body weight, hematological indices, and the function of liver and kidney.

Materials and Methods

Experimental Animals

The study was conducted on 40 male and 40 female white wool albino mice, *Mus musculus*, aged 3 months. The animals were kept in standard compartmented, rectangular, and well-ventilated cages. They were maintained on standard healthy laboratory conditions at a temperature of 18°C–24°C and 12-h light and darkness. Animals were adapted to the new environment for 14 days prior to the beginning of the study. All animals received humane care in accordance with the guidelines of the National Institutes of Health, USA, for ethical treatment of laboratory animals. All mice had free access to drinking water and food, ad libitum, during the experimental period. They were fed with standard pellet diet (LabDiet, MO) consisting of 60% starch, 20% casein, 10% cotton seed oil, 4% salt mixture, 5% cellulose, and 1% vitamin mixture.

Lead Dosage

The animals were divided into four equal groups. Each group comprised 10 male and 10 female separately and was marked as groups I, II, III, and IV. The first group represented the healthy control animals, while the second, third, and fourth groups were given 0.4, 0.8, and 1.2 mg/kg body weight of sublethal doses of lead acetate (Sigma-Aldrich, Ltd., UK), respectively, in their daily supply of drinking water for 12 weeks. Each mouse was weighed every week, and its daily water intake was determined.

Blood Collection and Analysis

For hematological and biochemical investigations, blood was collected from each mouse individually. The animals were fasted for 12 hours prior to blood collection. All animals were anesthetized by chloroform and blood samples collected immediately from their hearts using heart puncture technique with the aid of disposable sterile syringe and needle (Sigma). Blood sample of each mouse was then transferred to a sterile capped tube containing anticoagulant EDTA (Greiner Bio-One, Frickenhausen, Germany) for hematological estimation. Some of the blood was transferred to another sterile anticoagulant-free tube and centrifuged at 3000 rpm for about 10 min using centrifuge 5418 R (Eppendorf, Ontario, Canada) to obtain the serum for biochemical examination.

Blood cell counter URIT-2900 automated hematology analyzer (Dhanwantari Medical Systems, DMS, India) was used to determine hematological indices including total erythrocyte count (TEC), total leukocyte count (TLC), packed cell volume (PCV), hemoglobin (Hb) concentration, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and the amount of platelets.

Serum biochemical parameters were analyzed using auto serum analyzer, Selectra ProS (Merck, Ltd., Germany) and Ecoline kits (Merck, Ltd.) in accordance to manufacturer's instructions. These parameters included aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin concentration, gamma-glutamyl transferase (GGT), lactate dehydrogenase (LDH), alkaline phosphatase (AKP), the concentration of blood urea nitrogen (BUN), and serum creatinine concentration.

Statistical Analysis

The data provided in this study were analyzed using statistical-based methods, analysis of variance and Student's *t*-test to compare the difference between parameters. Results were expressed as mean values ± standard error. All statements of significance were based on probability of less than 0.05 ($P < 0.05$).

Result

The results of this investigation revealed that the mean body weight of the experimental animals decreased significantly

Table 1: Lead toxicity on the body and organs weight of the experimental animals after 12 weeks of treatment

Lead acetate dose	Sex	Body weight	Liver weight	Kidney weight	Heart weight
Group I (control), 0.0 mg/kg b. wt.	♀	60.17 ± 2.23	3.54 ± 0.06	1.01 ± 0.06	0.75 ± 0.05
	♂	61.18 ± 1.56	3.78 ± 0.25	1.00 ± 0.10	0.73 ± 0.09
Group II, 0.4 mg/kg b. wt.	♀	48.79 ± 2.92*	4.12 ± 0.99*	1.10 ± 0.09*	0.82 ± 0.08*
	♂	48.82 ± 2.68*	4.16 ± 0.42*	1.08 ± 0.12*	0.79 ± 0.11*
Group III, 0.8 mg/kg b. wt.	♀	46.97 ± 2.36*	4.23 ± 0.03*	1.19 ± 0.11*	0.94 ± 0.10*
	♂	47.56 ± 3.01*	4.27 ± 0.55*	1.17 ± 0.04*	0.91 ± 0.06*
Group IV, 1.2 mg/kg b. wt.	♀	42.45 ± 1.74*	4.31 ± 0.22*	1.18 ± 0.03	0.96 ± 0.02*
	♂	43.61 ± 2.08*	4.33 ± 0.37*	1.19 ± 0.07	0.98 ± 0.12*

Data are represented as mean ± SE, $n = 10$.
*$P < 0.05$.

($P < 0.05$) in all treated groups in both genders after 12 weeks of treatment with lead acetate (Table 1). They were reduced to 80%, 77%, and 71% in male mice, while 82%, 78%, and 70% in female mice of groups II, III, and IV, respectively, when compared with the healthy normal control mice. The harmful effect of lead acetate on the body weight increased significantly with the increase in its dose. The current study also observed an obvious increase in the weight of liver, kidney, and heart of intoxicated mice relative to the control mice.

The results in Table 2 indicated significant ($P < 0.05$) reduction in the TEC following exposure of lead acetate in groups II, III, and IV in comparison with the control group in both sexes. A marked decrease was observed in the levels of Hb and PCV. MCV, MCH, and MCHC also reduced significantly ($P < 0.05$) in treated mice in relative to the healthy mice. In addition, TLC and platelets elevated significantly ($P < 0.05$) in all groups that were administered lead acetate relative to the control in both genders (Table 2).

The findings of this study also indicated a significant increase ($P < 0.05$) in the enzymatic activities of ALT and AST in male and female of the intoxicated animals relative to the healthy control mice (Table 3). The elevated activities of these enzymes paralleled with the increase in lead acetate doses. The results in Table 3 also showed that the marked elevation of LDH gradually increased with the increasing lead acetate dose in both male and female of all treated animals. The activity of AKP markedly ($P < 0.05$) increased in groups II, III, and IV compared with the control group of both sexes. In addition, the results of GGT showed that the stimulation of serum GGT under the effect of lead acetate also increased with the increasing lead acetate dose in both male and female mice (Table 3).

Regarding kidney function, the serum levels of BUN and creatinine were used to check kidney function in the intoxicated animals relative to the healthy control. The data in Table 3 showed significant elevation ($P < 0.05$) in blood concentration of BUN and creatinine in lead-treated animals.

Table 2: Alteration in hematological values of the experimental animals after 12 weeks of treatment with lead

Lead acetate dose	Group I (control), 0.0 mg/kg b. wt.		Group II, 0.4 mg/kg b. wt.		Group III, 0.8 mg/kg b. wt.		Group IV, 1.2 mg/kg b. wt.	
Gender	♀	♂	♀	♂	♀	♂	♀	♂
TEC ($\times 10^3/\mu L$)	6.52 ± 0.71	6.31 ± 0.63	6.12 ± 0.44*	5.99 ± 0.09*	5.71 ± 0.48*	5.68 ± 0.78*	5.2 ± 0.05*	5.31 ± 0.93*
TLC ($\times 10^3/\mu L$)	7.12 ± 0.32	7.00 ± 0.09	7.80 ± 0.85	7.74 ± 0.39	8.00 ± 0.73*	8.22 ± 0.26*	8.50 ± 0.81*	8.90 ± 0.02*
PLT ($\times 10^3/\mu L$)	253 ± 4.63	255 ± 3.98	340* ± 5.26	349* ± 4.35	370 ± 3.88*	368 ± 5.61*	382 ± 3.72*	379 ± 4.11*
Hb (g/dL)	13.91 ± 1.55	14.2 ± 1.08	11.75 ± 1.92*	12.03 ± 1.02*	10.82 ± 1.42*	11.6 ± 1.59*	10.1 ± 1.30*	9.34 ± 1.05*
MCV (fl)	62.3 ± 1.95	61.8 ± 2.33	60.24 ± 2.70	60.61 ± 1.06	58.80 ± 1.25*	58.01 ± 2.91*	58.1 ± 2.22*	57.95 ± 1.08*
MCH (pg)	19.74 ± 1.82	19.51 ± 1.04	15.62 ± 1.22*	16.33 ± 1.73*	13.81 ± 1.90*	14.03 ± 1.41*	12.4 ± 1.00*	12.71 ± 1.37*
MCHC (%)	31.81 ± 2.02	32.00 ± 1.46	25.80 ± 1.88	25.68 ± 2.50	23.53 ± 1.09*	22.84 ± 2.39*	21.4 ± 1.58*	21.12 ± 2.04*
PCV (%)	46.52 ± 2.77	46.03 ± 2.00	45.33 ± 1.71*	46.00 ± 1.49*	34.98 ± 1.80*	32.63 ± 1.13*	31.09 ± 2.08*	30.87 ± 1.12*

Hb, hemoglobin; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; PCV, packed cell volume; TEC, total erythrocyte count; TLC, total leukocyte count.
Data are represented as mean ± SE, $n = 10$.
*$P < 0.05$.

Table 3: Lead toxicity on the functions of liver and kidney of the experimental animals after 12 weeks of treatment

Lead acetate dose	Group I (control), 0.0 mg/kg b. wt.		Group II, 0.4 mg/kg b. wt.		Group III, 0.8 mg/kg b. wt.		Group IV, 1.2 mg/kg b. wt.	
Gender	♀	♂	♀	♂	♀	♂	♀	♂
AST (U/L)	22.8 ± 1.2	26.7 ± 0.62	36.5 ± 1.86*	35.4 ± 2.98*	41.9 ± 2.04*	64.6 ± 2.86*	63.8 ± 2.52*	68.2 ± 1.48*
ALT (U/L)	18.9 ± 1.8	21.0 ± 1.90	33.5 ± 1.72*	44.3 ± 2.04*	44.9 ± 2.12*	64.2 ± 1.96*	61.1 ± 2.04*	77.3 ± 1.80*
AKP (U/L)	74.3 ± 3.28	69.9 ± 1.56	85.8 ± 1.82*	72.9 ± 2.5*	91.4 ± 1.34*	79.3 ± 1.78*	115.3 ± 3.74*	112.6 ± 4.10*
LDH (U/L)	101.2 ± 5.34	95.2 ± 2.54	111.5 ± 5.10*	99.5 ± 3.24*	121.2 ± 3.4*	135.7 ± 2.20*	138.4 ± 3.88*	145.2 ± 4.74*
GGT (U/L)	33.4 ± 1.14	38.3 ± 2.14	43.2 ± 3.04*	42.4 ± 1.56*	46.4 ± 2.28*	65.5 ± 3.20*	61.4 ± 4.14*	80.3 ± 2.70*
Bilirubin (mg/dL)	0.72 ± 0.13	0.83 ± 0.30	3.02 ± 0.23*	2.97 ± 0.42*	2.25 ± 0.16*	3.10 ± 0.82*	3.18 ± 0.19*	3.51 ± 0.75*
Creatinine (mg/dL)	0.93 ± 0.03	0.89 ± 0.09	1.06 ± 0.27*	1.27 ± 0.29*	1.62 ± 0.42*	2.71 ± 0.05*	2.74 ± 0.08*	3.03 ± 0.61*
BUN (mg/dL)	16.87 ± 1.06	16.69 ± 1.11	17.54 ± 1.32*	19.11 ± 1.68*	22.72 ± 1.01*	21.02 ± 1.54*	26.45 ± 1.48*	28.03 ± 1.07*

AKP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; GGT, gamma-glutamyl transferase; LDH, lactate dehydrogenase.
Data are represented as mean ± SE, $n = 10$.
*$P < 0.05$.

Discussion

Effects on Body and Organs Weight

The effect of lead on the weight of body and the weight of different organs markedly elevated during the experimental period of all treated groups of both sexes. Although the amount of food intake by the experimental animals was unchanged, the final body weight of intoxicated animals was significantly lower than that of the control group. The harmful effect of oral administration of lead acetate on the body weight markedly increased with the increase in its dose. These observations are in accordance with the result of previous studies that reported that lead caused reduction in growth rate in experimental animals fed with lead.[19,20] A reduction of body weight in lead-induced toxicity in rats has been observed.[21,22] The body weight gain decreased after treatment with lead in a dose of 400 mg/kg of the fodder.[23] The body weight loss might be resulting from the interruption of lead acetate in the absorption and metabolism of feed nutrients essential for health.[17]

The current investigation also observed an obvious increase in the weight of liver, kidney, and heart of intoxicated mice. The detected increase in the weight of different organs under the effect of lead might be because of necrosis and apoptosis, which were accompanied by the accumulation of lipids in the tested organs. Accumulation of lipids in kidney cells of intoxicated rats after treatment with lead has previously been reported.[24] This could be an indicator for the increase in the weight of different organs. An increase in the dry weight of the kidney and liver relative to the body weight has been observed, whichmight be because of nutritional disturbances caused by pair feedings.[25]

Effects on Blood Indices

The reduction in levels of TEC, Hb, PCV, MCV, MCH, and MCHC are other concordant hematological alterations observed in the groups where lead acetate was administered,[25,26] resulting in microcytic hypochromic anemia.[7,8] Similarly, progressive decrease in TEC count, PCV, Hb, and MCV was found following exposure of rats to lead acetate.[21,27] These hematological changes might be attributed to the toxic effect of lead on cell metabolism, interaction with some reactions where calcium is their secondary mediator, and inhibition of some enzymatic activities such as aminolevulinic acid dehydratase, which plays a key role in heme biosynthesis,[28] and other erythrocyte enzymes, for example, GA3PD and G6PD.[29]

Continuous exposure to lead might adversely affect the heme biosynthesis in the body owing to the inhibition of cytoplasmic and mitochondrial enzymes.[5] The depressing effects of lead acetate on the activity of major enzymes in the heme biosynthesis might be referred to imperfection of iron metabolism.[25,30] The inhibitory effect of lead acetate on conversion of coproporphyrinogen III to protoporphyrin IX results in shortening of erythrocyte life span and a decrease in the production of Hb.[28] The reduction of hematological values might be attributed to binding of lead to RBCs, which increase membrane fragility and destruction of RBCs.[31]

Analysis of TLC indicated leukocytosis and lymphocytosis in higher-dose groups of both sexes. This increase might be attributed to the toxic action of lead on leukopoiesis in lymphoid organs. This suggests that the increase in TLC is directly related with their increased production from the germinal center of lymphoid organs under the influence of lead toxicity. It has been reported that treatment with lead induced inflammation, which lead to increase in white blood cells count,[25] which concur this study. Platelets count revealed a considerable increase in the intoxicated animals compared with the control mice. This may be because of thrombocytopenia after lead intoxication,[32] followed by thrombocytosis.[25,32]

Effects on Biochemical Parameters

To assess the effect of lead on liver function, the activities of serum AST and ALT were investigated. AST is widely used to evaluate the liver function. ALT is a cytoplasmic enzyme, while AST is found in both mitochondria and cytoplasm. Treatment with lead acetate in this study was found to induce ALT and AST activities in male and female mice. The effect on the enzymatic activity gradually paralleled with the increase in lead dose. This suggests that the stimulation might be dose dependent. The elevation in the enzymatic activity of ALT and AST might be owing to the increase in cell membrane permeability or cell membrane damage of hepatocytes under the influence of lead.

These results concur with previous studies that reported an elevation in AST and ALT levels after treatment with lead caused by acute hepatitis, jaundice, and liver cirrhosis.[33,34] Lead has hepatotoxic effect resulting in liver cell damage, which causes increase in serum levels of AST and ALT.[35] It has been observed that lead has toxic effects on rat liver, leading to liberation of AST and ALT.[36] The high activities of plasma AST and ALT are attached by high liver microsomal membrane fluidity, production of free radicals, and alteration in the liver cells when animals were treated with lead acetate.[37] Increase in ALT and AST enzymatic activities might be resulting from lead acetate toxicity, which causes increased cellular basal metabolic rate, irritability, and destructive alteration of liver.[6,38] The elevated level of serum bilirubin following exposure to lead may be because of induction of heme oxygenase that plays an important role in heme catabolism and can convert heme to bilirubin.[19,39]

The stimulation of LDH in intoxicated animals was increased with the increasing lead acetate dose when compared with the control mice. Similar findings were achieved in studies where rats were dosed with lead acetate[19,37] and found a gradual stimulation in the activity of LDH in intoxicated rats. This study also investigated the changes in serum level of AKP. The AKP activity of lead-treated mice was stimulated compared with the healthy control mice. An increase in serum AKP activity resulting from liver, kidney, and bone damage leading to releasing of AKP has been found.[40] These results are according to findings of other studies[36] in which stimulation of AKP had been noted in rats under the effect of lead. The analysis of GGT showed that the stimulation of serum GGT under the effect of lead acetate also increased with the increasing lead acetate dose in both sexes. This elevation of serum GGT is an indication of hepatotoxicity
and oxidative damage in liver cells.[41]

In the case of kidney function, the concentrations of BUN and creatinine were examined to check how well kidney works in intoxicated mice compared with the healthy mice. Significant increase in blood concentration of both BUN and creatinine was detected in male and female mice. The elevation of BUN and creatinine values following oral administration of lead acetate might be because of kidney dysfunction and considered as a functional evidence of lead-induced nephrotoxicity.[42,43] Similar results were found in other studies after oral administrationof lead in rats,[6,7] goat,[44,45] and sheep.[46]

Conclusion

Lead is one of the main persistent and common environmental pollutants. Lead toxicity may affect multiple organs of human body and is associated with a number of physiological, biochemical, and morphological changes. Treatment with lead acetate at low doses has harmful effects on experimental animals and induced hematological and biochemical alterations. Therefore, this study advises people to avoid any exposure to this toxic metal to prevent its hazardous effects on health.

References

1. Joworaski Z. Stable and Radioactive Lead in Environment and Human Body. Warsaw: Nuclear Energy Information Center, Review Report, 1968, 29. pp. 17–30.
2. Harbison RD. Lead In:(Ed.) *Hamilton & Hardy's Industrial Toxicology*, 5th edn. Philadelphia, PA: Mosby, 1998. pp. 70–6.
3. Duruibe JO, Ogwuegbu MC, Egwurugwu JN. Heavy metal pollution and human biotoxic effects. Int J Phys Sci. 2007;2:112–8.
4. Stowe DM, Goyer RA, Krigman M, Wilson M, Cates M. Experimental oral lead toxicity in young dogs. Arch Pathol. 1973;95:106–16.
5. ATSDR . Agency for Toxic Substances and Disease Registry *Toxicological Profile for Lead, Update*. Prepared by Clement International Corporation under contact no. 205-88-060 for ATSDR. Atlanta, GA: US Public Health Services, 1993.
6. Elayat W, Bakheelf MS. Effects of chronic lead toxicity on liver and kidney functions. J Med Lab Sci. 2010;1:29–36.
7. Mugahi MN, Heidari Z, Sagheb HM, Barbarestani M. Effects of chronic lead acetate intoxication on blood indices of male adult rat. DARU. 2003;11:147–51.
8. Suradkar SG, Ghodasara DJ, Vihol P, Patel J, Jaiswal V, Prajapati KS. Haemato-biochemical alterations induced by lead acetate toxicity in wistar rats. Vet World. 2009;2:429–31.
9. Ahrens FA. Effects of lead on glucose metabolism, ion flux, and collagen synthesis in cerebral capillaries of calves. Am J Vet Res. 1993;54:808–12.
10. Yokoyama K, Araki S, Akabayashi A, Kato T, Sakai T, Sato H. Alteration of glucose metabolism in the spinal cord of experimental lead poisoning rats: microdetermination of glucose utilization rate and distribution volume. Ind Health. 2000;38:221–3.
11. Pitot CH, Dragan PY Please confirm the changes made in Reference 11.Chemical carcinogenesis In:(Ed.) *Casarett and Doull's Toxicology: The Basic Science of Poisons*, 5th edn. , New York: McGraw-Hill, 1996. pp. 201–60.
12. Correia PM, Oliveira E, Oliveira PV. Simultaneous determination of Cd and Pb in foodstuffs by electro-thermal atomic absorption spectrometry. Anal Chim Acta. 2000;405:205–11.
13. Commission of the European Communities. Commission regulation (EC) No. 221/2002 of 6 February 2002 amending regulation (EC) NO. 466/2002 Setting Maximum Levels for Certain Contaminants in Foodstuffs. Brussels: Official Journal of the European Communities, 2002.

14. Demirezen D, Kadiriye U. Comparative study of trace elements in certain fish, meat and meat production. Meat Sci. 2006;74:255–60.
15. Xienia U, Foote GC, Van S, Devreotes PN, Alexander S, Alexander H. Differential developmental expression and cell type specificity of Dictyostelium catalases and their response to oxidative stress and UV light. Biochim Biophys Acta. 2000;1492:295–310.
16. Foyer CH, Noctor G. Oxygen processing in photosynthesis: regulation and signaling. New Phytol. 2000;146:359–88.
17. Marija V, Piasek M, Blanusa M, Saric M, Juresa D, Kostial K. Succimer treatment and calcium supplementation reduce tissue lead in suckling rats. J Appl Toxicol. 2004;24:123–8.
18. Patrick L. Lead toxicity part II: the role of free radical damage and the use of antioxidants in the pathology and treatment of lead toxicity. Altern Med Rev. 2006;11:114–27.
19. Seddik L, Bah TM, Aoues A, Benderdour M, Slimani M. Dried leaf extract protects against lead-induced neurotoxicity in Wistar rats. Eur J Sci Res. 2010;42:139–51.
20. Ali MA, Awal MA, Mostofa M, Islam MA, Ghosh A. Effects of selenium and vitamin B6 with their combination in lead acetate induced toxicities in long Evans rats. Bangl J Vet Med. 2010;8:63–73.
21. Teijon C, Olmo R, Blanco D, Romero A, Teijon JM. Low doses of lead: effects on reproduction and development in rats. Biol Trace Elem Res. 2006;111:151–65.
22. Aseth J, Jacobsen D, Andersen O, Wickstrom E. Treatment of mercury and lead poisoning with dimercaptosuccinic acid (DMSA) and sodium dimercapto-propanesulfonate (DMPS). A review. Analyst. 1995;120:853.
23. Szymezak J, Zechalko A, Biernat J. Effect of fodder fat type on blood plasma lipids in rats intoxicated with lead. Bromatol Chem Toksykol. 1983;16:94–8.
24. Hwang DF, Wang LC. Effect of taurine on toxicity of cadmium in rats. Toxicology. 2001;167:173–80.
25. Yagminas AP, Franklin CA, Villeneuve DC, Gilman AP, Little PB, Valli VE. Subchronic oral toxicity of triethyl lead in the male weanling rat. Clinical, biochemical, hematological, and histopathological effects. Fundam Appl Toxicol. 1990;15:580–96.
26. Falke HE, Zwennis WM. Toxicity of lead acetate to female rabbits after chronic subcutaneous administration. 1. Biochemical and clinical effects. Arch Toxicol. 1990;64:522–9.
27. Helmy MA, El-Naga NI, Helal SM. Effect of administration of milk and Kareish cheese on hematological values and histopathological changes of liver and brain in rat treated with lead. Alexandria J Agril Res. 2000;45:103–18.
28. Klaassen CD. *Casarett and Doull's Toxicology: The Basic Science of Poisons*, 6th edn. , New York: McGraw-Hill Medical Publishing Division, 2001. pp. 812–41.
29. Calderon-Salinas V, Hernandez-Luna C, Maldonado M, Saenz D. Mechanisms of the toxic effects of lead. I. Free lead in erythrocytes. J Expo Anal Environ Epidemiol. 1993;1:153–64.
30. Chmielnicka J, Zareba G, Nasiadek M. Combined effect of tin and lead on heme biosynthesis in rats. Ecotoxicol Environ Saf. 1994;29:165–73.
31. Rous P, Jelinek P. [The effect of heavy metals boundary contaminated soil on haematological and selected biochemical parameters in blood plasma of rabbits]. Acta Univ Agric Silvic Mendel Brun. 2000;48:93–9.
32. Sudakova AI, Shevchenko ZT, Nosova LI. [Peripheral blood and bone marrow cell status of white rats with long-term lead exposure]. Tsitol Genet. 1983;17:3–7.
33. Patil AJ, Bhagwat VR, Patil JA, Dongre NN, Ambekar JG, Das KK. Occupational lead exposure in battery manufacturing workers, silver jewelry workers, and spray painters in western Maharashtra (India): effect on liver and kidney function. J Basic Clin Physiol Pharmacol. 2007;18:87–100.
34. Mehta A, Kannan GM, Dube SN, Pant BP, Pant SC, Flora SJ. Hematological, hepatic and renal alterations after repeated oral or intraperitoneal administration of monoisoamyl DMSA. I. Changes in male mice. J Appl Toxicol. 2002;22:359–69.
35. Abdou ZA, Attia MH, Raafat MA. Protective effect of citric acid and thiol compounds against cadmium and lead toxicity in experimental animals. J Biol Chem Environ Sci. 2007;2:481–97.
36. Shalan MG, Mostafa MS, Hassouna MM, El-Nabi SE, El-Refaie A. Amelioration of lead toxicity on rat liver with vitamin C and silymarin supplements. Toxicology. 2005;206:1–15.
37. Ibrahim NM, Eweis EA, El-Beltagi HS, Abdel-Mobdy YE. Effect of lead acetate toxicity on experimental male albino rat. Asian Pac J Trop Biomed. 2012;2:41–6.
38. Ghorbe F, Boujelbene M, Makni AF, Guermazi F, Kammoun A, Murat J, et al. Effect of chronic lead exposure on kidney function in male and female rats: determination of lead exposure biomarkers. Arch Physiol Biochem. 2001;109:457–63.
39. Murrey RK, Granner DK, Rodwell VW. *Harper's Illustrated Biochemistry*, 27th edn.New York: McGraw-Hill. 2006.
40. Kaplan MM, Righetti A. Induction of rat liver alkaline phosphatase: the mechanism of serum elevation in bile duct obstruction. J Clin Invest. 1970;49:508–16.
41. Tatjana J, Gordana K, Dusica P, Ivana S, Tatjana C, Ducan S, et al. Effects of captopril on membrane associated enzymes in lead induced hepatotoxicity in rats. Acta Fac Med Naiss. 2003;20:183–8.
42. Patterson C. Contaminated and natural lead in environments of man. Arch Environ Health. 1965;11:344–60.
43. Zook BC, Carpenter JL, Roberts RM. Lead poisoning in dogs: occurrence, source, clinical pathology, and electroencephalography. Am J Vet Res. 1972;33:891–902.
44. Swarup D, Dwivedi SK. Changes in blood and cerebrospinal fluid indices in experimental lead toxicity in goats. Ind J Animal Sci. 1992;62:928–31.
45. Haneef SS, Swarup D, Dwivedi SK, Dash PK. Effects of concurrent exposure to lead and cadmium on renal function in goats. Small Rum Res. 1998;28:257–61.
46. Ahmed YF, Shalaby SA. Clinicopathological and histopathological studies on chronic lead intoxication in male Barki sheep. Afr J Agric Sci. 1991;18:19–37.

How to cite this article: Alwaleedi SA. Hematobiochemical changes induced by lead intoxication in male and female albino mice. Natl J Physiol Pharm Pharmacol 2016;6:46-51.

Source of Support: Nil, **Conflict of Interest:** None declared.