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Toxicity of lead bioaccumulation and its effects on liver, kidney and blood functions in laboratory rats

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سمية التراكم الحيوي للرصاص وتأثيراته على وظائف الكبد والكلى والدم لدى الفئران

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Abstract
This study aimed to determine the bioaccumulation of lead and its effects on blood, liver, and kidney function. The study included 40 male mice. The mice were divided into four groups. They were given intraperitoneal doses of lead daily for 4 weeks. as follows: Control group G1 received distilled water throughout the experiment, Group G2 was injected with a dose of lead of 10 mg/kg-1 .b. w, Group 3G was injected with 50 mg/kg-1.b. w, group G4 was injected with 100 mg/kg-1b. w, after 4 days from the end of the experiment, blood samples were collected and serum was obtained to measure hematological parameters and liver and kidney functions. The results of blood parameters showed a significant decrease ($P< 0.05$) in the rate of WBC, RBC, HB, HCT higher the lead dose compared to the control group. While MCV, PLT decreased at concentration 100 mg/kg-1. b. w, While the dose of 10 and 50 mg/kg-1 .b. w has the same effect. results showed a significant increase ($P< 0.05$) in the levels of AST, ALT, ALP, bilirubin, creatine, urea, and urea acid. The higher the lead dose. While Total protein recorded a significant decrease ($P< 0.05$) the higher the lead concentration. As for the electrolytes results, the results showed that the groups that took a concentration of 10 and 50 mg/kg-1. b.w, had the same effect on the potassium level, While the group that took dose 100 mg/kg-1 increased the potassium level compared to the control group. The results showed a significant decrease in calcium and magnesium levels with increasing lead concentration compared to the control group. While sodium recorded a significant increase at concentrations of 1.100 mg/kg-1. Lead levels were assessed in kidney, liver, and blood tissues, and the results showed that lead levels increase with increasing dose.

Keywords: Lead, bioaccumulation, hematological parameters, liver and kidney functions, rats.

الملخص
تهدف الدراسة تحديد التراكم الحيوي للرصاص وتأثيراته على وظائف الدم والكبد والكلى. شملت الدراسة 40 فأرًا ذكرًا. تم تقسيم الفئران إلى أربع مجموعات. تم إعطاؤهم جرعات يومية من الرصاص داخل الصفاق لمدة 4 أسابيع. على النحو التالي: تلقت المجموعة الضابطة G1 الماء المقطر طوال التجربة، حقنت المجموعة G2 بجرعة من الرصاص مقدارها 10 ملغم/كغم من وزن الجسم، المجموعة G3 بجرعة 50 ملغم/كغم من وزن الجسم، و حقنت المجموعة G4 بجرعة 100 ملغم/كغم من وزن الجسم، وبعد 4 أيام من نهاية التجربة، تم جمع عينات الدم والمصل لقياس المعايير الدموية ووظائف الكبد والكلى. أظهرت نتائج معايير الدم انخفاضًا كبيرًا ($P < 0.05$) في معدل خلايا الدم البيضاء و الحمراء والهيموغلوبين كلما زادت جرعة الرصاص مقارنة بالمجموعة الضابطة. بينما انخفضت MCV وPLT عند تركيز 100 ملغم/كغم. بينما كان للجرعة 10 و50 ملغم/كغم نفس التأثير. أظهرت النتائج زيادة معنوية ($P<0.05$) في مستويات AST، ALT،ALP ، البيليروبين، الكرياتين، اليوريا وحمض اليوريا. كلما زادت جرعة الرصاص، سجل البروتين الكلي انخفاضًا معنويًا ($P<0.05$) كلما زاد تركيز الرصاص. أما الإلكتروليتات فقد أظهرت النتائج أن المجموعات التي تناولت تركيز 10 و50

ملغم/كغم كان لها نفس التأثير على مستوى البوتاسيوم، بينما زاد مستوى البوتاسيوم في المجموعة التي تناولت الجرعة 100 ملغم/كغم مقارنةً بالمجموعة الضابطة. أظهرت النتائج انخفاضًا معنويًا في مستويات الكالسيوم والمغنيسيوم مع زيادة تركيز الرصاص مقارنةً بالمجموعة الضابطة. بينما سجل الصوديوم زيادة معنوية عند تركيز100 ملغم/كغم. وباستخدام جهاز (AAS) تم تقدير مستوي الرصاص في أنسجة الكلي والكبد والدم وأظهرت النتائج إن مستويات الرصاص تزداد مع زيادة الجرعة.

الكلمات المفتاحية: الرصاص، التراكم الحيوي، المعايير الدموية، وظائف الكبد والكلي، الفئران.

Introduction

Lead is a harmful and toxic heavy metal that poses significant environmental and health risks in developing and industrialized countries [1]. It is considered a hazard to human health even at low concentrations [2]. The International Agency for Research on Cancer (IARC) has classified inorganic lead compounds as a group (B2) carcinogen [3], As in Figure 1. Exposure to lead occurs from natural sources such as volcanoes, rock erosion, and fires [4]. Industrial sources include its uses in water distribution pipes, lead-based paint, and gasoline additives [5]. Battery storage and use in welding production, alloy casting, radiation protection pipes, cable covers, pigments, ceramics, glass, and plastics [6]. Air polluted by dust, fuel combustion and fossil fuels [7, 8]. lead consumption was 8 million tons, with lead-acid battery production estimated at 71%, ammunition at 6%, dyes at 12%, and cable sheathing at 3%. Lead, which enters the body through inhalation or ingestion, is absorbed through the respiratory and gastrointestinal tracts [9]. About 30-40% of inhaled lead reaches the bloodstream once absorbed, and 99% of lead is retained in the blood for 30-35 days, accumulating in other tissues such as the liver, kidneys, bones, brain, spleen and lungs. In a report by the International Agency for Energy and Cancer Research in 1987, there is scientific evidence confirming that lead causes cancer through research conducted on laboratory animals [10]. [11] indicated the presence of brain tumors among professionals exposed to lead. One of the most important mechanisms of lead poisoning is the enhancement of oxidative stress through the generation of free radicals and the depletion of antioxidant enzyme systems such as (SOD) Super Oxide Dismutase Catalase (CAT), which reduces the level of glutathione and increases the production of reactive oxygen. Lead replaces cations in enzymes and proteins, leading to the loss of vital activities and functions, by inhibiting the glutathione reductase enzyme by binding to thiol groups. Lead also inhibits the aminolevulinic acid dehydrogenase enzyme (ALAD), as indicated by [11]. This leads to increased levels of aminolevulinic acid (ALA), which is known to stimulate ROS production, as reported by [12]. Lead can alter the biophysical properties of the membrane [13]. The process involves the oxidation of lipids in the cell membrane by binding to phosphatidylcholine, leading to the production of reactive oxygen species (ROS) [14]. The liver is the primary organ for storing lead, accounting for more than 33% of the lead content in the human body [15]. The kidneys are followed by the toxic effects of lead in the form of hepatitis and dysfunction, impairing their ability to detoxify and metabolize drugs [16]. Exposure to lead damages the kidneys, impairing their ability to filter waste products from the blood and reducing filtration, and lead toxicity has been shown to disrupt the normal functioning of blood and disrupt the function of normal blood cells [17]. Mainly through increased oxidative stress, which leads to impaired red and white blood cell production, decreased oxygen carrying capacity, impaired coagulation mechanisms, impaired immune function and hypertension, As in Figure 1. The mechanism responsible for the effects of lead on hematological parameters is not well understood. However, red blood cell baseline is a potential biomarker for detecting lead poisoning [18]. This study aimed to investigate the harmful effect of lead on hematological and biochemical parameters of liver and kidney in laboratory rats.

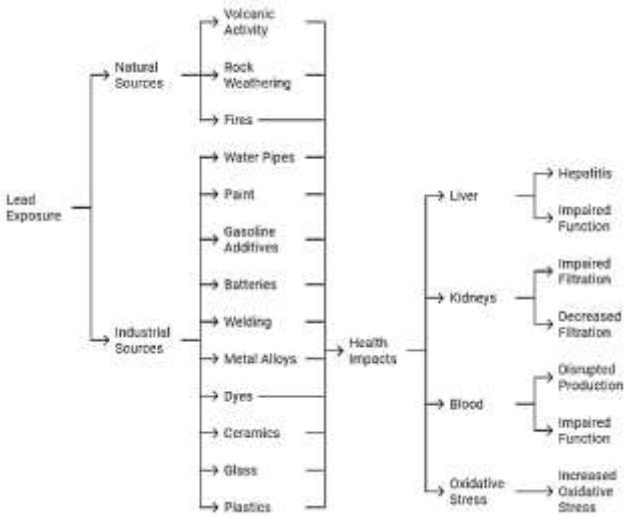

Figure 1. Sources of lead exposure and health risks.

Material and methods

Preparing lead and calculating the dose: Lead was prepared from lead acetate and the dose was calculated based on dissolving the atomic weight of lead in 250 ml of distilled water, if every 3.75 g of lead acetate contains 1g of lead, dissolve it in 250 ml of distilled water. 119]

Lead acetate→ Lead, 3.79.33→ 106

X=Lead (1g)

$$X = \frac{379.33}{106} = 3.75g$$

Experimental Animal Preparation: All experimental procedures were conducted in accordance with established protocols [20]. Forty male rats, weighing between 180-210 grams and aged 7-8 weeks, were obtained from Sebha University's animal house. The rats were housed in plastic cages, cleaned daily to prevent contamination, and maintained under standard laboratory conditions, including a light-dark cycle, temperature range of 23-25°C, and relative humidity of 50-60% for acclimatization. The rats were provided with a commercial diet and pure drinking water prior to the experiment [21].

Experimental Design: The experiment lasted for 4 weeks, during which the rats were divided into four groups. Group G1 served as the control and received distilled water. Groups G2, G3, and G4 received lead injections at doses of 10 mg/kg^{-1}, 50 mg/kg^{-1}, and 100 $mg.kg^{-1}$ b. w, respectively. The rats were sacrificed after 4 days via chloroform anesthesia.

Blood Sample Collection: Blood samples were collected by puncturing the heart through the diaphragm, following the method described by [22]. As in Figure 2. The blood **samples were divided into two groups:** one for measuring blood indicators and the other for hematological analysis. The blood indicators measured included mean cell volume (MCV), hematocrit (HCT), mean cell hemoglobin (MCH), and mean cell hemoglobin concentration (MCHC). Hemoglobin (HGB) was measured using a Mindray device, Auto Hematology Analyzer, model BC-20s Germany.

Platelets (PLT): are measured using aluminum oxylate solution 5 ml mixed with 95% water and placed in a special bottle 20-micron blood + 0.05 ml of solution. Leave for 5 minutes and then counted using a platelet counting strip, where each square is divided. into 5 squares, then the numbers inside these squares are added and the result is shown in numbers according to what was stated in the method of [23].

White blood cell count (WBC): is measured using concentrated acetic acid and gel dye to distinguish the white cells in blue, and the reading is done with a reading bottle following the method [24].

Red blood cell count (RBC): I followed the method of [25]. The blood is diluted with a Formal Citrate solution consisting of 1% formalin and 38 g/L of sodium tricitrate. 20 microliters of blood are added to 0.4 cm3 of Formal Citrate solution, then the diluted blood is stirred. In the tube, the counting chamber is then filled with diluted blood using a pipette and then examined under an optical microscope with an eyepiece of 40X10 power.

RBC= RBC Calculated in 5 squares* 1000

Measurement of Biochemical Parameters in Blood Plasma:
Blood samples (3 ml) were collected and placed in tubes without anticoagulant, left at laboratory temperature for 15-30 minutes, and then centrifuged at 3000 rpm for 10 minutes to separate blood serum and plasma. The plasma and serum were then frozen at -80°C and 20°C, respectively, according to the method described by [26].
The following biochemical parameters were measured: blood urea (BUN), creatinine (CRE), uric acid (UA), total serum proteins (TP), albumin (ALB), direct bilirubin (DB), and total bilirubin (TB) using a Photometer 4040 V5+ device (ROBERT RIELE GmbH & Co KG, Germany). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were measured using a method that estimates the amount of baprovate and oxaloacetate released by their reaction with dinitrophenyl hydrazine. Alkaline phosphatase (ALP) was measured by estimating the amount of phenol released by its reaction with 4-aminoantipyrene.
Electrolytes such as inorganic calcium (Ca^{+2}), magnesium (Mg^{+2}), potassium (K^{+}), and sodium (Na^{+}) were measured using an Electrolytes MEDICA, model ORIGIN US, Germany.

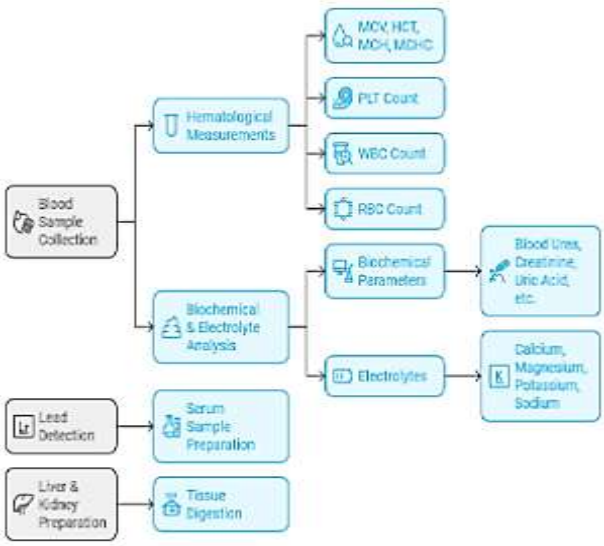

Figure 2. Tests required to measure biochemical parameters in blood, plasma, liver and kidney tissues.

Detection of lead in blood: Serum samples were wet digested following the method of [27]. 1ml of blood serum was treated with 5 ml of nitric acid and then centrifuged for minutes. Atomic spectrometer was used to measure the lead concentration [28].

Preparation of Liver and Kidney Organs: After dissecting the animals, the liver and kidney organs were washed with cold saline, wiped with filter paper, and stored at -20°C for lead analysis [29]. Tissue samples (500 mg) were weighed and placed in a sterile container, dried in an oven at 85°C for 15 hours [21].

Digestion of Tissue Samples for Lead Determination: Tissue samples were digested by adding 2 ml of highly purified concentrated nitric acid at 120°C for two hours. Peroxide 30% was then added to finish the process. The volume was replenished with high-purity water, and the samples were stored in glass tubes until analysis [30]. The chemicals used are of analytical nature from CARLO ERBA Reagents (S.r.l), Italy. Standard solutions of 0.1, 0.5, 1.0, 2.0 and 5.0 mg.ml were prepared in one-litre measuring flasks according to the standard method of the instrument for lead at a wavelength of 283.3 nm. using an atomic absorption spectrophotometer(AAS) type Nov AA400 located in the Scientific Laboratory for Research and Consulting at Sebha University.

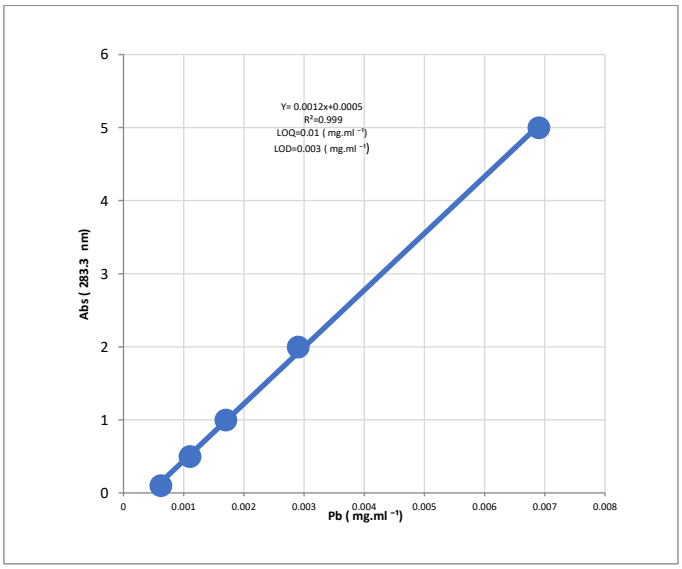

Figure 3. Calibration curve for standard Lead solution.

statistical analysis: The statistical program SPSS was used to analyze the data. The arithmetic mean and standard error values were extracted, and a one-way analysis of variance (ANOVA) was performed to determine the significant differences between the rates of the studied standards (blood and biochemical standards). A p-value of less than 0.05 was considered statistically significant.

Results and discussion

Blood parameters: The results presented in Table 1 show the levels of blood parameters measured in the four tested groups of experimental rats. The data reveal significant changes in blood parameters in response to lead exposure.

WBC: The results showed that the **WBC** rate decreased when the Rats were exposed to lead compared to the control group. The dose of 50 mg and 10 mg had the same effect on the WBC with an average of 3.780± .1135, while the rats that took a concentration of 100 mg of lead had an average WBC of 2.810±.567, and the control group had an average of 4.23±.2626. This indicates that lead works to reduce the rate of WBC. These results are consistent with the study [31]. **RBC:** results showed that as the lead increased, the RBC rates decreased, as the average was 4.87±.530, 3.53±.204, 2.99±.368 compared to the control group 6.66±.558, and these results are consistent with [32]. **HB:** The rate of HB decreased with increasing lead dose, as the averages of hemoglobin in the tested groups were respectively 8.529±.246, 7.248±.268, 5.33±.176 compared to the control group, 12.63±.682. These results are consistent with [32]. **HCT:** The HCT rate decreased as the lead dose increased, as the average was 28.98±.575, 22.82±.476, 18.43±.258 compared to the control group, 39.89±.552. These results are consistent with [29]. **MCV:** The MCV rate decreased at the 100 mg dose with an average of 52.972±1.204, while the groups that took 50 mg and 10 mg had the same effect on the MCV with an average of 65.43±.2672, and the control group 72.868±8.378. These results are consistent with [33]. **PLT:** The results of PLT indicate that there is no difference in the average of the groups that took the dose of 10 and 50 mg, 507.75±65.67, while the results of the group that took the dose of 10 and 50 mg showed a decrease in PLT values for the group that took 100 mg had an average of 424.19±53.09 compared to the control group with an average of 536.728±3.968.
The decrease in RBC, HGB, and HCT levels may be attributed to intravascular hemolysis, which occurs when lead binds to red blood cells, leading to anemia and activation of free radicals and lipid peroxidation. This oxidative stress disrupts cell components and increases membrane fragility, ultimately contributing to the decrease in RBC, HGB, and HCT levels [34].
Furthermore, the decline in HB levels may be due to lead's ability to inhibit erythropoiesis or its association with RBC, resulting in decreased HB content and a shortened lifespan of RBC, respectively [31] Additionally, lead may displace iron from HB or inhibit aminolevulinic acid dehydratase (ALAD) activity, all of which contribute to reducing the level of Hb and the lifespan of red blood cells [35].

Table 1. mean ± SD for some blood parameters in tested and control Rats after exposure to different dose of lead.

Parameter	100 mg.Kg^{-1}.Pb	50 mg.Kg^{-1}.bP	10 mg. Kg^{-1}. Pb	Control
WBC($\times 10^9$/L)1	^{c}2.810±.567	^{b} 3.780±.113	^{b}3.770 ±.323	^{a}4.23 ±.262
RBC ($\times 10^{12}$/L)1	^{d}2.992±.368	^{c} 3.539±.204	^{b}4.877±.530	^{a}6.66 ±.5585
HB(g/dl)	^{d}5.337±.176	^{c}7.248 ±.268	^{b} 8.529±.246	^{a} 12.639±.682
HCT(%)	^{d}18.43±.258	^{c}22.82 ±.476	^{b}28.98 ±.575	^{a}39.89±.552
MCV(fL)	^{c}52.972±1.204	^{b}65.43±.267	^{b}66. 344±.681	^{a}72.868±8.378
PLT($\times 10^9$/L)1	^{b}424.19±53.09	^{a}507.75±65.67	^{a}507.75±65.67	^{a}536.728±3.96

Data are expressed as mean ± S.D of (40) animals per group.
Means for groups in homogeneous subsets are displayed.
a. Uses Harmonic Mean Size = 10.000.
Subset for alpha= 0.05.

Through the results shown in Table 2, which shows the levels of liver and kidney biochemical parameters measured in the four tested groups of experimental Rats, which are considered important factors in detecting liver and kidney dysfunction, the following is revealed:

AST: AST results indicate that as the dose of lead increased, the rate of AST increased, as the average AST for the 10 mg dose was 136.15±2.38, the 50 mg dose had an average of 144.69±2.908, and the average 100 mg dose was 163.74±1.727, while the control group had an average of 51.21±1.516.5. **ALT:** The tested groups showed higher activity of the ALT enzyme compared to the control group, which increases as the lead dose increases, 48.081±1.222, 51.723±1.220, 56.51±.561, respectively. While the mean of the control group was 43.316±1.139, these results are consistent with the study of [36]. An increase in the ALT enzyme, along with an increase in its concentration in the body, is an indication that lead causes hepatotoxicity. **ALP:** The effect of the three doses of lead varied. As the dose increased, the rate of ALP increased, as the averages were 51.797±.7758, 59.33±.617, and 62.790±.4493, respectively. While the mean of the control group was 45.321±.633, these results are consistent

with [20]. [30] pointed out that increased ALP activity poses a danger to cells that depend on phosphate esters for cellular processes, and also pointed out that increased ALT, ALP and AST enzymes are an indication that lead increases the phagocytic activity of hepatic sinusoidal cells. The significant increase in ALT, ALP and AST levels may be due to leakage from tissues as a result of damage caused by lead. It can linked to membrane damage resulting from oxidative stress caused by lead. This led to increased permeability of enzymes from liver cells to the circulation, and this was indicated by [37]. **Total protein (TP):** As the dose of lead increased, the rate of total proteins decreased. The average was 6.407±.1459 at a dose of 10 mg. While the dose of 50 mg had an average of 4.709±.2771, and the dose of 100 mg had an average of 4.089±.0589, while the control group had an average of 7.257±.2303 mg, [30]. **Bilirubin:** Bilirubin level increased with increasing lead dose, as the averages were 0.472±.0175, 0.526±.0150, and 0.724±.0189 respectively, while the control group averaged 0.377±.0211 mg, The cause is attributed to nephrotoxicity and kidney dysfunction. These results are consistent with [38]. **Albumin:** The higher the lead dose, the lower the albumin rate, as the averages were 3.402±.291, 2.59±.2213, and 1.694±.2752 mg respectively. While the control group had a score of 3.78±.0879. These results are based on the study [30]. [39]. indicated that exposure to lead causes a significant decrease in serum albumin. Albumin depletion can enhance lead toxicity. One way that lead causes albumin to reduce is by forming a complex with the protein, causing it to lose its biological function. **Urea:** The results showed that the rate of urea increased with an increase in the dose of lead, as the average was 38.07±.8732, 43.106±1.114, and 56.43±3.296 mg respectively, while the control group was 30.737±.694. These results are consistent with [30] and may be attributed to the increase in Urea indicates the presence of acute and chronic kidney inflammation, suprarenal gland prolapse, and a high level of urea and creatine is a vital indicator of weak excretory function in the kidney. **Creatinine:** The rate of creatine increased as the lead increased, as the averages were 0.424±.0227, 0.552±.0239, 0.655±.031, while the control group was 0.382±.0078. These results are consistent with [40]. Creatine increases due to kidney inflammation, kidney dysfunction, high urea rate, and urinary tract obstruction [41]. **Urea acid:** The results showed that as the dose of lead increased, the levels of urea acid increased, as the averages were 32.26±.5518, 42.26±1.002, 49.59±.670, 54.57±.375. [42]. indicated that the increase in uric acid levels resulting from lead toxicity is due to the decomposition of purines as a result of the action of the enzyme xanthine oxidase and hypoxanthine, which is believed to be caused by damage to the renal tubules.

Table 2. mean ± SD liver and kidney functions and the level of kidney proteins in the plasma in the plasma of tested and control Rats after exposure to different dose of lead.

Parameter	100 mg.Kg^{-1}.Pb	50 mg.Kg^{-1}.bP	10 mg. Kg^{-1}. Pb	Control
AST(UlL)	^{a}163.74±1.727	^{b}144.69±2.908	^{c}136.15±2.38	^{d}51.216±1.489
ALT(UlL)	^{a}56.51±.561	^{b}51.723±1.22	^{c}48.081±1.22	^{d}43.316±1.139
ALP(UlL)	^{a}62.790±.449	^{b}59.33±.617	^{c}51.797±.775	^{d}45.321±..633
Total protein (mgldl)	^{d}4.089±.058	^{c}4.709±.277	^{b}6.407±.145	^{a}7.257±.230
Bilirubin BiT mg/dl	^{a}0.724±.018	^{b}0.526±.015	^{c}0.472±.017	^{d}0.377±.021
Albumin g/dl	^{d}1.694±.275	^{c}2.59±.2213	^{b}3.402±.291	^{a}3.78±.087
Urea mg/dl	^{a} 56.435 ±3.296	^{b} 43.106 ±1.114	^{c} 38.077 ±.873	^{d} 30.737 ±.694
Creatinine mg/dl	^{a}0.655±.031	^{b}0.552±.0239	^{c}0.424±.0227	^{d} 0.382±.007
Urea acid mg/d	^{a}54.57 ±.375	^{b}49.592 ±.670	^{c}42.27 ±1.002	^{d}32.261±.551

See footnote Table 1.

the results shown in Table 3. which shows the levels of electrolytes measured in the four tested groups of experimental Rats, it is clear that:

Potassium: The results of Table 3. showed that the potassium level of the groups that took a dose of 10 and 50 mg had the same effect on the level of potassium, as the average was 3.89±.094, while the group that took a dose of 100 mg was 5.15±.426, compared to the control group, 3.50±. 223 [43]. **Calcium:** the results showed a decrease in the calcium level as the lead dose increased, 3.67±.151, 3.08±.330, 1.83±.363, while the control group was 4.18±.441, and these results are consistent with [44]. **Sodium:** results showed that the group that took the dose of 10 mg did not affect the sodium level compared to the control group, where the average was 94.927±7.43, while the sodium level increased at the doseof 50 and 100 mg with an average of 115.28±.986, 135.13±2.72, and these results are consistent with [43]. **Magnesium** decreased as the lead dose increased, 1.13±.046, 0.848±.059, 0.613±.588, compared to the control group 1.36±.045, and these results are consistent with a study [45]. The levels of potassium and sodium increased significantly, and the levels of calcium and magnesium decreased with an

increase in the dose of lead compared to the control group due to functional disorders in the adrenal gland, which causes altered metabolism. We agree with the study [46, 47], which confirmed that exposure to organic pollutants causes an imbalance in calcium due to oxidative damage to the membranes of red blood cells. It also confirmed that exposure to organic pollutants leads to an increase in sodium and potassium and is accompanied by a decrease. In the levels of calcium and magnesium, this is an indication of increased lipid peroxidation and disturbance.

Table 3. Mean ± SD level of electrolytes in the serum of tested Rats and the control group after exposure to different dose of lead

Parameter	100 mg.Kg^{-1}.Pb	50 mg.Kg^{-1}.bP	10 mg. Kg^{-1}. Pb	Control
K^{+}(mmol/L)	[a]5.15±.426	[b]3.89±.094	[b] 3.89± .095	[c] 3.50±.223
Ca^{+2}(mmol/L)^{2}	[d] 1.83±.363	[c]3.08 ±.330	[b]3.67 ±.151	[a]4.18 ±.441
Na^{+}(mmol/L)	[c]135.13± 2.72	[b]115.28± .986	[a] 94.92±7.43	[a] 94.92 ±7.43
Mg^{2+} (mmol/L) ^{2}	[d] 0.613±.588	[c] 0.848±.059	[b] 1.13±.046	[a] 1.36 ±.045

See footnote Table 1

The results presented in Table 4, which displays the levels of accumulated lead in the liver, kidney, and blood of the four groups of experimental Rats, the level of lead in the kidneys, liver and blood increases with increasing doses, with the highest concentrations recorded at a dose of 100 mg. Kg^{-1} of 3.37± .297, 4.06± .084, and 2.47±.314 mg. Kg^{-1} respectively. The high levels of lead in the liver can be attributed to the increased synthesis of metallothionein (MT) in the liver, which in turn affects the total protein values in the blood. As the liver is the primary organ responsible for producing plasma proteins, particularly albumin, the elevated lead levels in the liver likely disrupt this process, as suggested by [48].

Table 4. Mean ± SD level of lead accumulation in the kidneys, liver, and blood of the tested Rats and the control group after exposure to different dose of lead.

Parameter	100 mg.Kg^{-1}.Pb	50 mg.Kg^{-1}.bP	10 mg.Kg^{-1} .Pb	Control	Permissible limit
Pb $_{Liver}$	[a]3.37±.297	[b] 2.36±.256	[c]1.31±.132	[d]0.14 ±.027	[e] 0.5-5.0
Pb $_{Kidney}$	[a]4.06±.084	[b]2.81±.112	[c]1.48 ±.043	[d]0.17 ±.009	[f] 1.0-10.0
Pb Blood$_{(ug.dl)}$	[a]2.47±.314	[b]1.167±.120	[c]0.645±.071	[d] 0.13±.009	[g] 0.1- 5.0

See footnote Table 1.

(f)= [19], (e)= [49], (g)= [50].

A one-way analysis of variance (ANOVA) was employed to assess the differences in the effects of various lead doses on hematological and biochemical parameters of the liver and kidney in laboratory rats. The results presented in Table 5 indicate significant differences in blood and biochemical parameters at a significance level of $P < 0.05$. This may be attributed to the fact that the dose of lead in the body is directly proportional to the level of lead poisoning. These findings are consistent with previous studies [51], which highlight the dose-dependent effects of lead exposure on hematological and biochemical parameters.

Table 5. One-way analysis of variance (ANOVA) showing the variation of different doses of lead on hematological and biochemical parameters in the liver and kidneys of laboratory rats.

Parameter		Sum of Squares	Df	Mean Square	F	Sig.
WBC	Between Groups	10.733	3	3.578	71.274	.000
	Within Groups	1.807	36	.050		
	Total	12.540	39			
RBC	Between Groups	80.256	3	26.752	138.841	.000
	Within Groups	6.937	36	.193		
	Total	87.193	39			
Hb	Between Groups	286.890	3	95.630	607.501	.000
	Within Groups	5.667	36	.157		
	Total	292.557	39			
HCT	Between Groups	2601.151	3	867.050	372.995	.000
	Within Groups	8.377	36	.233		
	Total	2609.528	39			

Parameter		Sum of Squares	Df	Mean Square	F	Sig.
	Between Groups	2071.421	3	690.474	38.262	.000
MCV	Within Groups	649.653	36	18.046		
	Total	2721.074	39			
	Between Groups	70767.971	3	23589.324	8.236	.000
PLT	Within Groups	103105.787	36	2864.050		
	Total	173873.758	39			
	Between Groups	74522.418	3	24840.806	5132.161	.000
AST	Within Groups	174.248	36	4.840		
	Total	74696.666	39			
ALT	Between Groups	936.598	3	312.199	271.495	.000
	Within Groups	41.397	36	1.150		
	Total	977.996	39			
	Between Groups	1832.120	3	610.707	1540.691	.000
ALP	Within Groups	14.270	36	.396		
	Total	1846.390	39			
Total	Between Groups	64.729	3	21.576	556.732	.000
	Within Groups	1.395	36	.039		
	Total	66.125	39			
Billrubin	Between Groups	643.	3	.214	640.479	.000
	Within Groups	.012	36	.000		
	Total	655.	39			
Albumin	Between Groups	25.803	3	8.601	158.375	.000
	Within Groups	1.955	36	.054		
	Total	27.758	39			
Urea	Between Groups	3518.061	3	1172.687	351.215	.000
	Within Groups	120.202	36	3.339		
	Total	3638.263	39			
Creatinine	Between Groups	.464	3	.155	292.815	.000
	Within Groups	.019	36	.001		
	Total	.483	39			
Urea acid	Between Groups	2819.290	3	939.763	1978.897	.000
	Within Groups	17.096	36	.475		
	Total	2836.386	39			
K^+	Between Groups	15.446	3	5.149	82.435	.000
	Within Groups	2.248	36	.062		
	Total	17.694	39			
Ca^{2+}	Between Groups	30.692	3	10.231	88.988	.000
	Within Groups	4.139	36	.115		
	Total	34.831	39			
Na^+	Between Groups	11139.795	3	3713.265	43.346	.000
	Within Groups	3083.976	36	85.666		
	Total	14223.771	39			.
Mg^{2+}	Between Groups	3.225	3	1.075	371.346	.000
	Within Groups	.104	36	.003		
	Total	3.329	39			
Lead Liver	Between Groups	57.947	3	19.316	364.434	.000
	Within Groups	1.908	36	0.53		
	Total	59.855	39			
Lead Kidney	Between Groups	84.668	3	28.223	5191.698	.000
	Within Groups	.196	36	.005		
	Total	84.864	39			
Lead Blood	Between Groups	32.805	3	10.935	368.236	.000
	Within Groups	1.069	36	.030		
	Total	33.874	39			

Groups I to IV are as defined in the text. Normally distributed data are expressed in mean ± SE and are compared using (ANOVA) ;
The groups have the same superscript letter have no significant difference between them while groups have significant difference have different superscript letter. *: Statistically significant at $P < 0.05$.

Cconclusions:

This study investigated the effects of lead exposure on hematological, biochemical, and electrolyte parameters in laboratory rats. The results showed significant dose-dependent changes in various parameters.

1- Hematological Parameters:

White blood cell (WBC) count decreased with increasing lead dose. Red blood cell count (RBC) decreased compared to the control group with increasing lead dose. Hemoglobin levels decreased compared to the control group with increasing lead dose. Hematocrit (HCT) rate decreased compared to the control group with increasing lead dose. Mean corpuscular volume (MCV) rate decreased at a dose of 100 mg, while groups receiving 10 mg and 50 mg showed no significant differences. Platelet (PLT) rate decreased for the group receiving 100 mg, while groups receiving 10 mg and 50 mg showed no significant differences.

2- Biochemical Parameters:

Aspartate aminotransferase (AST) levels increased with increasing lead dose. Alanine aminotransferase (ALT) levels increased with increasing lead dose. Alkaline phosphatase (ALP) levels increased with increasing lead dose. Total protein levels decreased with increasing lead dose. Bilirubin levels increased with increasing lead dose. Urea levels increased with increasing lead dose. Creatinine levels increased with increasing lead dose. Uric acid levels increased with increasing lead dose.

3- Electrolytes:

Potassium levels increased in the group receiving 100 mg, while groups receiving 10 mg and 50 mg showed no significant differences. Calcium levels decreased with increasing lead dose compared to the control group. Sodium levels increased gradually with increasing lead dose, except for the group receiving 10 mg. Magnesium levels decreased with increasing lead dose compared to the control group.

4- Lead Bioaccumulation:

The study revealed that lead bioaccumulation in the blood, liver, and kidneys is a significant issue, with lead concentration in the liver being higher than in the blood or kidneys.

Recommendations:

1- Conduct more studies to know the harmful effects of lead on different tissues and organs of the body.
2- Conduct more anatomical and histological studies to understand the carcinogenic effect of lead on the kidneys, liver and other organs of the body.
3- Studying the long-term effects of lead to assess health risks.
4- Studying the effects of antioxidants in reducing the toxic effects of lead.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

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