

Protective Role of Vitamin B1 in Mitigating Liver and Kidney Damage Induced by Lead Acetate in Rabbits

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ABSTRACT

Background: Lead is a well-studied toxic metal known for its harmful physiological effects, which depend on the duration and intensity of exposure. Its widespread presence in soil, water, and food makes it a significant public health concern. Given the limitations of conventional treatments, there is increasing interest in alternative therapies, including the use of Vitamin B1, to mitigate lead toxicity. This study aimed to evaluate the protective effects of Vitamin B1 against lead acetate-induced liver and kidney damage in rabbits. **Methods:** Twenty-eight local rabbits were randomly assigned to four groups and treated daily for eight weeks as follows: Group 1 (control) received distilled water; Group 2 (lead-only) received lead acetate (5 mg/kg BW); Group 3 received Vitamin B1 (75 mg/head) plus lead acetate (5 mg/kg BW); and Group 4 received Vitamin B1 (150 mg/head) plus lead acetate (5 mg/kg BW). Vitamin B1 was administered daily, while lead acetate was given every 48 hours. Blood samples were collected via cardiac puncture at weeks 1, 4, and 8 to measure liver enzyme levels (ALT and AST) and glutathione reductase. Histopathological changes in the liver and kidneys were also analyzed. **Results:** The AST and ALT enzyme levels showed no significant differences between groups at weeks 1 and 4. However, by week 8, Group 2 (lead-only) exhibited a significant increase in AST levels compared to Groups 1, 3, and 4 ($P < 0.05$). Within-group comparisons revealed significant elevations in AST levels in Group 2 between weeks 1, 4, and 8, whereas no significant changes were observed in the other groups. Histopathological examination indicated marked liver and kidney damage in Group 2, which was notably attenuated in the Vitamin B1-treated groups. **Conclusion:** Vitamin B1 demonstrated a protective effect against lead acetate-induced liver and kidney damage in rabbits, as evidenced by improved enzyme levels and reduced histopathological changes. These findings suggest that Vitamin B1 could be a potential therapeutic agent for mitigating the toxic effects of lead exposure.

Keywords: Histopathological Changes, Liver Damage, Lead Acetate, Oxidative Stress, Thiamin.

INTRODUCTION

B vitamins cannot be synthesized by mammals on their own. people have to put these into their diet in adequate amounts. despite the fact that the majority of them are made by plants, they can be consumed informally through foods made from animals, such as meat, dairy products, and eggs [1, 2]. In the control of fundamental metabolism, thiamine and its derivatives have both coenzyme- and non-coenzyme-related biological effects [1]. Therefore an eliminator of singlet oxygen and an inhibitor of lipid peroxidation, thiamine is also known to exert antioxidant properties [3]. Because thiamin can stop cells' SH group from oxidizing. In a rat model of acute ethanol intoxication, Mahdavi et al. [4] also demonstrated that vitamin B1 (thiamine) reduces hepatic levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), lipid peroxidation, and protein damage, and it could possess an indirect antioxidant function. In fact, thiamine (1-6 mM) attenuated the inhibition of the copper-induced radicals that inhibit pyruvate dehydrogenase and -ketoglutarate dehydrogenase. Thiamin may be able to prevent cell death brought on by oxidative stress in cell structures through minimizing the limitation of these enzymes [5]. Despite substantial health repercussions, lead (Pb) exposure has grown in the workplace and ecosystem across the world [6]. According to Assi et al. [7], lead is a toxicant that affects several essential organs, including the brain, heart, liver, kidney, and lung, producing various illnesses and malignancies. Due to two factors, Pb is primarily excreted from the body through the liver and kidneys, and these organs also include proteins with a high affinity for binding Pb, such as metallothionein,

acyl-CoA attaching protein, and thymosin 4 [8]. Different animal tissues may react differently to lead exposure depending on the dose and length of time exposed. It may result in instant and permanent harm. Additionally, lead exposure health hazards are seen as issues of health for the public [9, 10]. Liver is the foremost organ wide open to enter all absorbed nutrients and other xenobiotic. It is target organ affected by the toxicity of lead because it is stored and consists of highly active metabolic tissue acts as chief player in detoxification process of toxic substances, is of relevance in heavy metal poisoning [11]. After absorption, Pb primary accumulation in the liver [12]. That becomes a crucial organ for Pb poisoning, producing it. A limited amount of the absorbed Pb is eliminated in the kidney after being conjugated in the liver via the portal vein, while the majority accumulates in other bodily organs [13]. The buildup of Pb in the liver affects the endogenous antioxidant defense system, which includes superoxide dismutase, glutathione peroxidase, catalase, glutathione reductase, and glutathione S-transferase, as well as by depleting non-enzymatic antioxidants like reduced glutathione (GSH) [14]. The concentration of particular liver enzymes serves as a measure of liver function. In the processes of gluconeogenesis and amino metabolism, respectively, are the enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Pyridoxal phosphate is required for the activity of these enzymes. Additionally, according to Zareei et al. [15], they speed up the metabolism of proteins and carbohydrates. Lead and its byproducts, such as lead acetate, have been shown to harm the liver histologically and may interfere with regular biochemical processes,

leading to elevated liver enzyme levels. It is generally recognized that liver enzymes (AST and ALT) are significant biomarkers for the identification of liver disorders (hepatotoxicity). Lead results in cytoskeletal changes that enhance cell membrane permeability and induce hepatocytes to lyse, which raises the serum levels of this biochemical [16]. Liver enzyme (AST and ALT) can be increase gradually in blood plasma with increasing lead levels in growing rabbits [17]. Also lead absorber, it deposits in kidneys which is one of the most important parts affected by lead toxicity with more blood and metabolic flows [18]. Nephrotoxicity from lead exposure is what doctors refer to when lead toxicity damages the kidneys. Lead is removed by the kidney in the renal tubules, which causes kidney damage. Proximal tubular cells take up lead and it attaches to certain lead protein molecules [18]. These lead binding proteins produce intercellular inclusions of proximal tubular cells [19]. In addition, in rabbit renal tissue, long-term exposure to lead acetate had histopathological effects such as dilatation, congestion, nuclei heterochromatic effects, an increase in renal tubule diameter, and urinary barrier thickness. The intensity of adverse effects is determined by quantitative the plasma concentration and duration of lead acetate exposure showed many histopathology side-effects, especially in the urinary barrier. Finally, the extent cellular damage is linked to noticeable changes in liver and kidney functions [9]. Multiple renal histopathological alterations were brought about by chronic lead exposure, including a decrease in microvillus density and degradation of the luminal epithelium of the proximal tubules [20]. The corpuscle, particularly podocytes and the capillary loop of the glomerulus, blood arteries, interstitial tissues, and renal tubules are all impacted by acute nephritis [21]. Additionally, after prolonged exposure to lead acetate, alterations in the ultrastructure of the renal tissues, including vacillation of the matrix, condensing of mitochondria, dilatation of the endoplasmic reticulum, and thickening of the basement membrane of the urinary filtration barrier, were noted [9]. The objective of the current investigation was to ascertain the protective benefits of vitamin B1 and track its potential to mitigate lead acetate-induced oxidative damage in rabbits. It was discovered that Pb is a

toxic element that harms the liver and renal tissues of rabbits. It has been established that vitamin B1 protects towards the adverse impacts of Pb.

MATERIAL AND METHODS

Twenty-eight healthy local rabbits at age of 5-6 months for period eight days. These animals divided into four equal groups as follows: Control group (G1) orally administered distill water, group G2 lead acetate (5mg/kg BW) group G3 reserved vitamin B1 (75mg/head) plus lead acetate (5mg/kg BW), group G4 reserved vitamin B1 (150 mg /head) plus lead acetate (5mg/kg BW). All rabbits had received their treatments vitamin B1 daily while lead acetate every 48 hours along eight weeks two months, the sample of blood were collected by cardiac puncture technique at 1st, 4th, 8th week of study for estimation some of liver enzymes (ALT and AST) and glutathione reductase (Cohesion biosciences / U.K); after that specimens of liver and kidneys was taken to be studying the histopathological changes.

Statistical Analysis

SAS (Statistical Analysis System - version 9.1) was used to analyze the data. P 0.05 is regarded as statistically significant when using the one-way, two-way, and least significant differences (LSD) post hoc tests to evaluate significant differences among means.

Results

Alanine Amino Transaminase (ALT)

Data in the table 1 that related with assessments (ALT) enzyme of means level of experimental groups which revealed no significant differences between groups at 1st week, but G2 group was recorded significant ($p < 0.05$), differences than other groups in 4th and 8th weeks of experiment period. At the same time the compression within group (from base line to end of experiment) it was noted that there was no significant differences in all experimental groups except G2 group recorded significant differences in 4th and 8th weeks, as compare with 1st week in level of ALT enzyme.

Table 1: Ameliorative the Effect of Vitamin B1 on Reducing Impact Lead Acetate on ALT Enzyme Level (U/L) of Local Female Rabbits Means $\pm$ SE

Groups/ALT	1 st Week	4 th Week	8 th Week
G1	A68.25 $\pm$ 6.52a	A67.81 $\pm$ 6.65b	A67.47 $\pm$ 7.21b
G2	B68.45 $\pm$ 7.22a	A99.49 $\pm$ 15.23a	A98.38 $\pm$ 3.47a
G3	A66.33 $\pm$ 6.43a	A59.86 $\pm$ 1.93b	A55.99 $\pm$ 1.37b
G4	A55.00 $\pm$ 6.09a	A49.59 $\pm$ 2.81b	A58.97 $\pm$ 4.86b
LSD	19.439		

The means in the same column that have a distinct tiny letter are statistically different (P 0.05). Means in the same row with different capital letters are significantly various (P 0.05).

Aspartate Amino Transaminase (AST)

The results of table 2 demonstrate that AST enzyme level in experimental animals, showed non-significant differences between groups at 1st and 4th weeks of experiment, while a significant ($P < 0.05$)

increase in G2 group as compared with G1, G3 and G4 groups in the means value of AST enzyme (150.50 $\pm$ 17.09), (74.42 $\pm$ 5.82), (75.49 $\pm$ 8.30) and (71.72 $\pm$ 5.06) respectively. At the same time the compression from base line to end of experiment it was noted that there were no significant differences in all experimental groups except G2 group recorded significant differences in 8th weeks as compare with 1st and 4th week in level of AST enzyme.

Table 2: Ameliorative Effect of Vitamin B1 on Reducing Impact Lead Acetate on AST Enzyme Level (U/L) of Local Female Rabbits Mean $\pm$ SE

Groups/AST	1 st Week	4 th Week	8 th Week
G1	A69.35 $\pm$ 6.56a	A64.62 $\pm$ 7.61a	A74.42 $\pm$ 5.82b
G2	B66.39 $\pm$ 8.22a	B71.28 $\pm$ 6.70a	A150.50 $\pm$ 17.09a
G3	A62.80 $\pm$ 6.52a	A57.87 $\pm$ 6.38a	A75.49 $\pm$ 8.30b
G4	A73.72 $\pm$ 5.04a	A67.20 $\pm$ 3.67a	A71.72 $\pm$ 5.06b
Lsd	22.773		

The means in the same column that have a distinct tiny letter are statistically different (P 0.05). Means in the same row with different capital letters are significantly various (P 0.05).

Antioxidant levels (Glutathione Reducates)

Table 2 appears the impact of PbAc with and without vitamin B1 on glutathione reduces in female rabbits. From this result we can notice a significant ($P<0.05$) lower in mean values of glutathione reduces levels for G2 group as compared with control (G1) and other treated groups G3 and G4 that was at the end of study (8th week) 1.63 ± 0.02 , 2.18 ± 0.01 , 2.02 ± 0.03 and 2.05 ± 0.06 respectively. In addition to the control group recorded highest value significantly ($P<0.05$) as compared with all experimental groups.

Histopathological Examination

The result of histopathological examination showed liver of control negative group (G1) liver tissue section showed normal morphology and absent lesions (figure 1). Whereas, moderate

histological alteration was detected in liver tissue of control positive group (G2) characterized by extensive hepatic cell vacuolation and Central vein congestion (figure 2) other findings revealed sinusoids congestion with periportal MNCs infiltration accompanied with necrotic findings of hepatic cords while other sinusoids showed leukocytic infiltration with prominence of kupffer cell (figure 3).

Mild histological alteration was observed in major liver section of G3 that exhibit diffuse hepatic steatosis with obvious cytoplasmic fat droplets (figure 4). With minimal sinusoid dilation and congestion mainly at the periportal area with edematous substance and slight portal cellular infiltration (figure 5). Section of liver (G4) were getting closer in similar to those G1 figure and showed normal appearance of central vein and arrangement of hepatic cords (figure 6).

Table 3: Ameliorative Effect of Vitamin B1 on Reducing Impact Lead Acetate on Glutathione Reducates Levels ($\mu\text{mol/L}$) of Local Female Rabbits Mean $\pm$ SE

Groups	Glutathione Reducates (GR)
G1	$2.18\pm0.01a$
G2	$1.63\pm0.02c$
G3	$2.02\pm0.03b$
G4	$2.05\pm0.06b$
LSD	0.1234

Means with a different letter are significantly different ($P<0.05$)

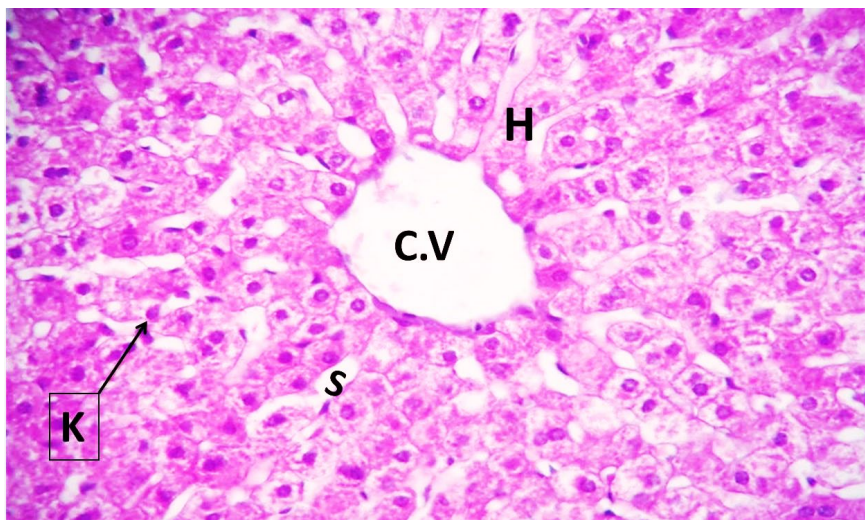


Figure 1: Liver section in Rabbit of Control Negative (G1) Showed Normal Cords of Hepatocytes (H) Radiating from (C.V) With Kupffer (k) Cell Appearance in Sinusoids (S). H&E stain X40

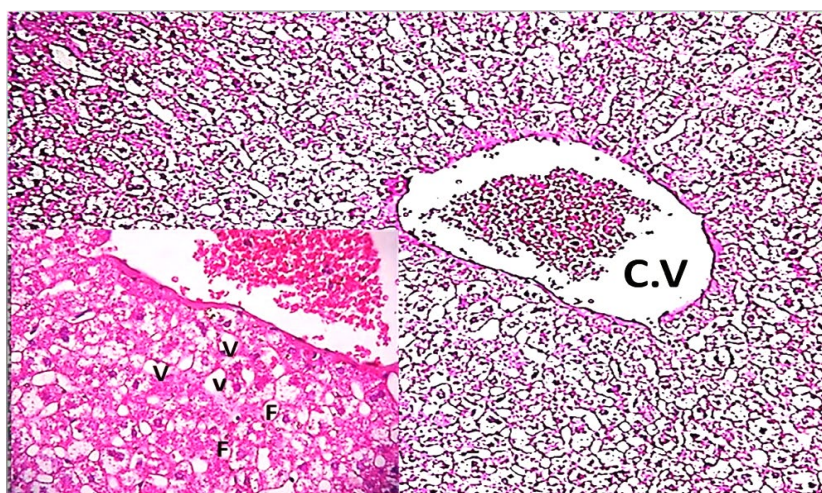


Figure 2: Showed liver Section in Control Positive (G2) Enlarged & Congestion C.V with Extensive Vacuolation (V), Diffuse Cytoplasmic Fat Droplets (f) & Extensive Hydropic Swelling of Adjacent Hepatocytes. H&E stain X10 and X40.

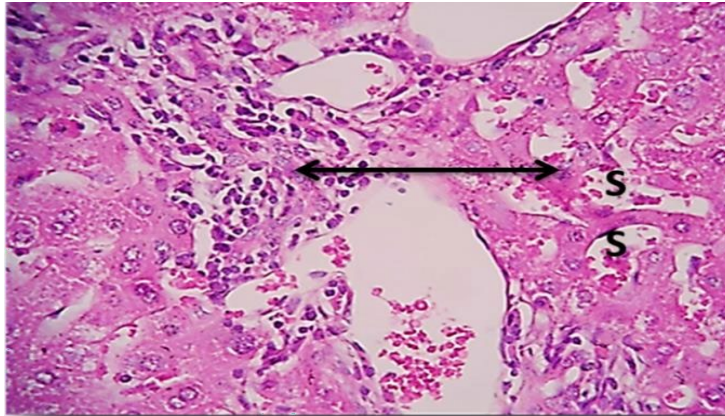


Figure 3: Showed Sinusoids Congestion (S) with Periportal MNCs Infiltration & Nuclear Pyknosis of Adjacent Hepatocytes $\leftrightarrow$, H&E Stain X40.

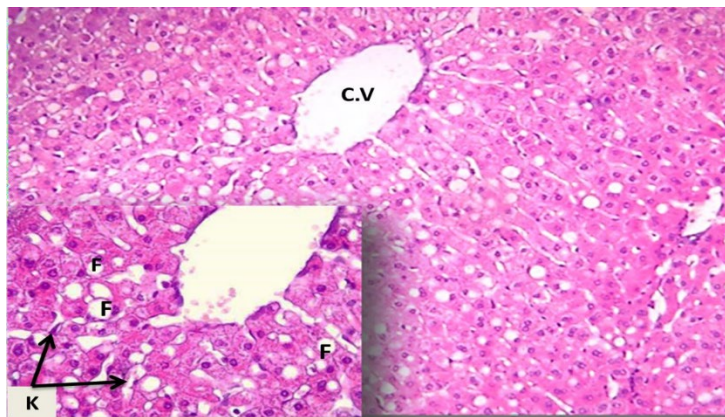


Figure 4: Liver Section of G3 Fatty Infiltration Showed Diffuse Cytoplasmic Fat Droplets with Minimal Presence of Kupffer Cells (k) H&E X10 & X40.

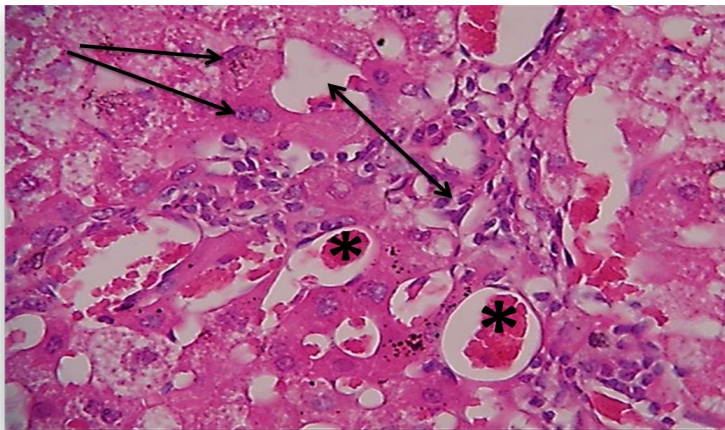


Figure 5: Liver section of G3 Showed Minimal Periportal Cellular Infiltration and Sinusoids Dilation ($\leftrightarrow$) with Edematous Substance * and Fewer Apoptotic Hepaticocytes ($\rightarrow$), H&E Stain X40.

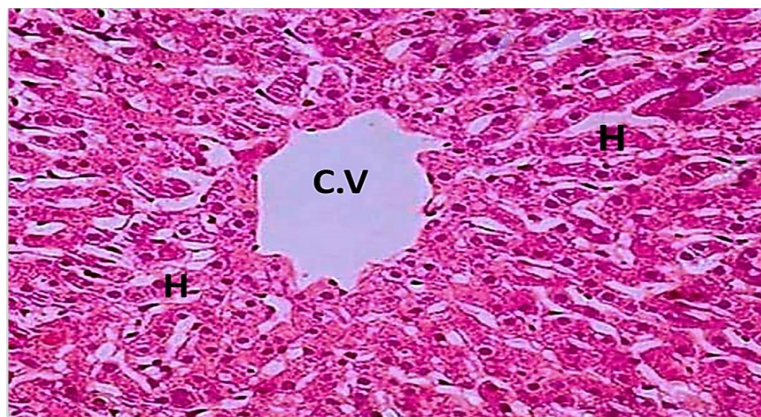


Figure 6: Liver in G4 Showed Normal Central Vein (c.v) and Arrangement of Hepatic Cords (H). H&E Stain x 10.

The result of histopathological changes in kidney section manifestation revealed normal structure of glomeruli and surrounding tubular in G1 (figure 7), while in G2 result in marked vascular congestion and renal interstitial blood vessels with extensive vacuolation of tubular epithelium (figure 8) with evidence of eosinophilic hyaline cast formation in other dilated tubules G2 (figure

9). The group G3 showed mild congestion of interstitial capillaries were detected mainly between renal tubules at medulla (figure 10) however some tubular epithelial vacuolation may persist and still seen in few sections (figure 11) while G4 with high level of thiamine showed various degree of tubular dilation however several tissue section with no obvious lesion (figure 12 and 13).

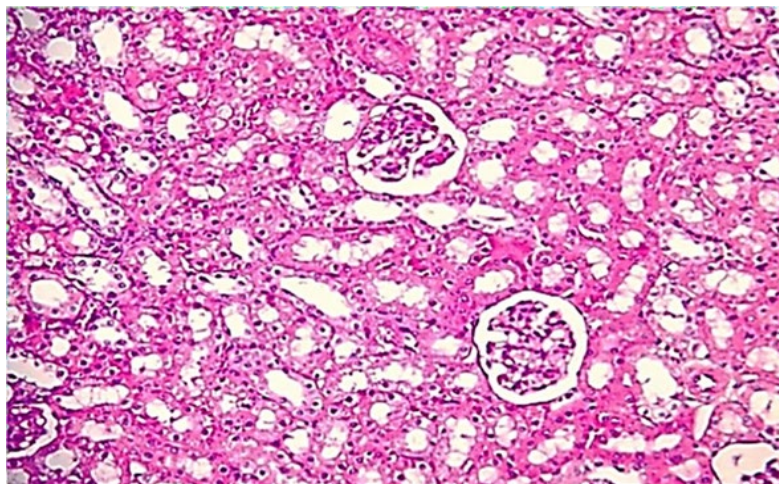


Figure 7: Kidney Section of Rabbit Control Negative (G1) Showed Normal Renal Structure. H&E Stain $\times 10$.

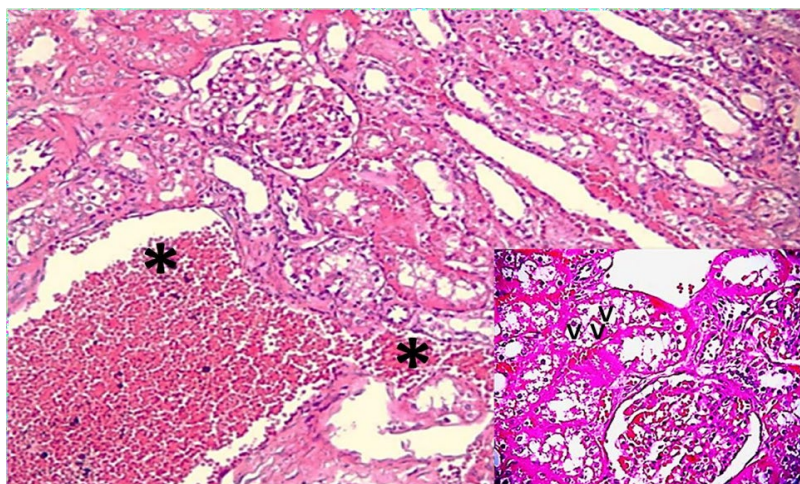


Figure 8: Kidney Section of G2 Showed Marked Vascular Congestion of Renal Vessels (*) with Extensive Vacuolation (v) of Tubular Epithelium H&E Stain $\times 10$ & $\times 40$.

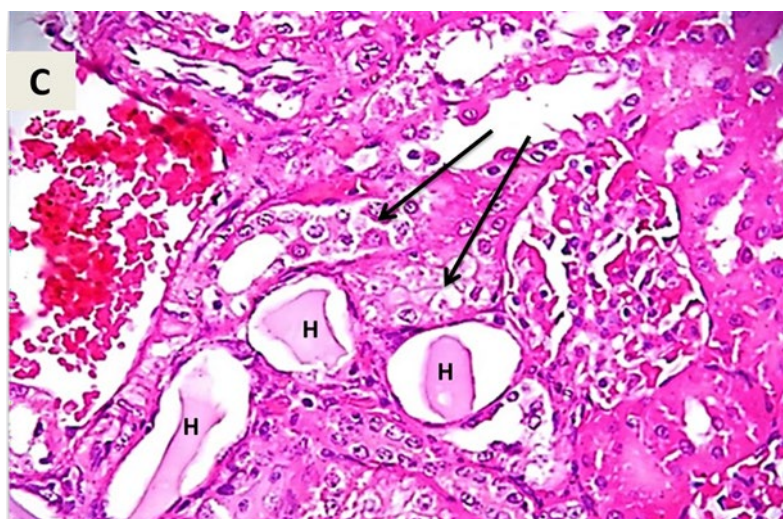


Figure 9: Kidney Section of rabbit of G2 Showed Appearance of Eosinophilic Hyaline Cast (H) in some Dilated Tubules Associated with Necrotic Findings of Adjacent Tubules → & Venous Congestion (C) H&E Stain $\times 40$.

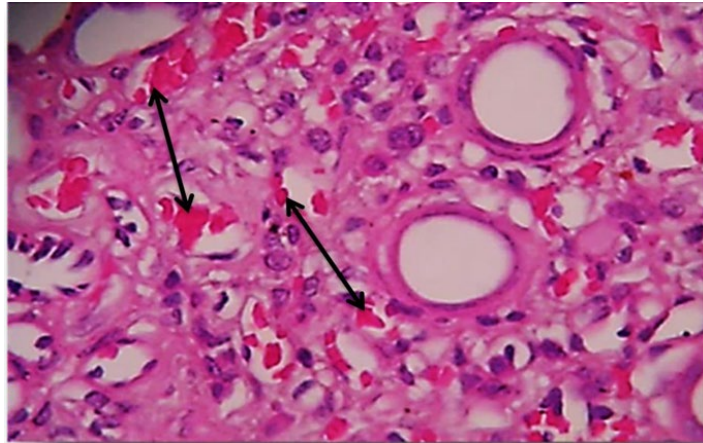


Figure 10: Kidney Section of G3 Showed Vascular Congestion of Intrestial Capillary in Medullary Portion (↔) H&E Stain X40.

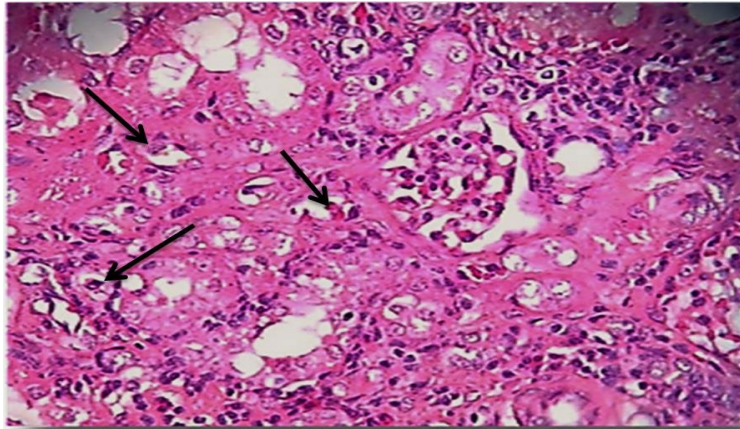


Figure 11: Kidney Section of G3 Showed Mild Vacuolated Epithelial Lining of Some Cortical Tubules (→) H&E Stain X40.

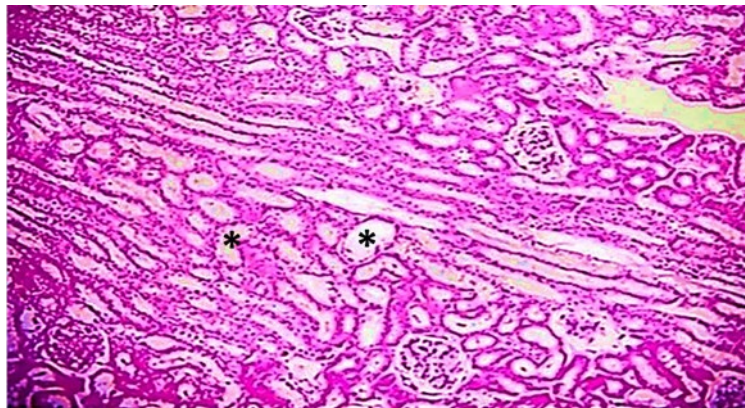


Figure 12: Kidney Section of G4 Showed Moderate Cyst Dilation of Cortical Tubules (*). H&E Stain X10

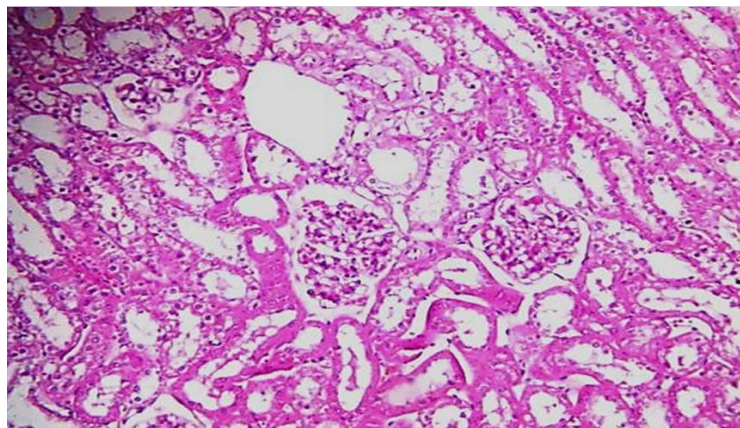


Figure 13: (Magnificent) Kidney Section of G4 Showed no Obvious Histological Alteration, H&E Stain X10.

Discussion

Among the key metabolic organs, the liver is crucial for a number of intricate metabolic activities, such as the metabolism of macronutrients, vitamin activation and storage, and the excretion of waste materials [22, 23]. The current study observed treatment of rabbits with only PbAC caused increased in values of ALT and AST levels from result in table 1 and 2 respectively, that concerned to second group G2 compared with control and others treated groups in this study. The major cause of the rising levels of liver enzymes (AST and ALT) in infected animals' blood plasma was the leaking of these enzymes from the liver cytosol into the blood stream. Whereas enzyme release through damaged hepatic cells into the blood causes the AST level to increase considerably in the plasma. Once the liver organ experiences cellular deterioration or destruction, ALT also rises in plasma levels. According to a laboratory animal study, large levels of transaminases, which are typically found in the hepatocyte cytosol and indicate either a cell's normal state or damage that results in liver malfunction, can be inferred [24, 25]. Increased concentration of ALT and AST in serum of rabbits with increasing lead levels, that agreement with previous studies [17, 25].

Additionally, in line with prior investigations, the serum of quails that had been exposed to lead showed an increase in ALT and AST activity [26, 27]. While the result in G3 and G4 showed that administration vitamin B1 with PbAC lead to decline enzymes concentration in levels nearly to G1 (control group), this result may be activity of vitamin B1 in reduce oxidation damage in liver cells by ROS, assisted that to keep cells contains. Antioxidant's therapy has protective role against lead induced hepatotoxicity, lining those fits with [28-30]. Furthermore, some researchers pointed that uses of thiamin at a dose 100 mg/animal has a positive effect on liver cells in reducing damage to cells poisoning by lead acetate in rabbits [31]. However, even at large dosages, oral forms of thiamine have not been linked to unfavorable effects, ALT increases, or liver damage. Thus, neither blood enzyme increases nor cases of clinically obvious liver impairment have been associated with oral or parenteral high dosage thiamine treatment [32]. Can be concluded from that the dosages used from vitamin B1 (75 and 150 mg /animals) in current study had a positive effect to maintaining cells and enzymes of liver in rabbits' contamination with lead acetate. Respecting anti-oxidant in Current study the results in table 3 indicate that a change in oxidative status of the animals' tissues in treated groups, the result in group G2 getting reducing in the glutathione due to treated with PbAC cause the oxidative stress, oxidative stress-induced by lead causing body tissues injury and formation of ROS including different pathways including hydroperoxides, singlet oxygen and hydrogen peroxides and resulting to a cellular dysfunction. These results are in agreement with [33, 34].

The role of sulfhydryl groups in molecules of thiamin which serves as configurations of thiamin and lead complexes. Despite of the reported in the effect of it as an antagonizing to lead toxicity need some clearly. The any defect in body cells (antioxidant enzymes) lead to increased ROS and-induced bio membrane disruption that might be alteration in function of cells membrane integrity in the body [35]. In the current study, it's have been the lead acetate significantly depressed the cell glutathione reductase and that agreement with our observation by, Ning et al.[28] reported considerable reduction in the

internal anti- oxidant like glutathione reductase following lead toxicity. Largely, this investigation is rare to study thiamine's ability to shield female rabbits from the effects of lead acetate through improvement of antioxidant status that was founded in groups G3 and G4, lining with Wathji and Almusawi [31] in lead acetate intoxicated rabbits, and in protection against oxidative stress caused by exhaustive exercise [36]. Farther more the previous investigators documented that lead might inactivate cellular glutathione by binding to the sulfhydryl groups [37]. The result showed that high level of thiamine prevented liver from toxic damage of lead while low doses of thiamine lowed the toxic effect of lead. Thiamine exhibits antioxidant effects as a result of chemical interactions, and its water-soluble nature may be related to the complexes that form between it and lead and then lead's elimination [38]. In addition to acting as a cofactor of the enzymes involved in the pentose phosphate cycle, it also raises the concentrations of NADPH and antioxidants [39]. It could be explained by the excretion of lead after complexes between thiamine and lead form.

Thiamine has also been shown to shield rat liver against lead-induced lipid peroxidation [40]. The first organ to be exposed to ingested nutrients is the liver, medications, and environmental toxins that enter the hepatic portal vein from the digestive system, and liver function can be negatively impacted by damage brought on by acute or long-term exposure to toxicants. Additionally, the current study demonstrated histopathological changes in the liver of G2 subjects who received lead treatment. Lead causes oxidative stress in hepatic tissues due to an increase in lipid peroxidation and a disruption in the antioxidant defense system in hepatocytes, which results in liver damage and hepatocyte apoptosis [41]. This result agree with many scientific researchers showed that intoxication with Pb, Hg, Cd and Cu caused several hepatic damages in experimental animals [42, 43]. The results in figure (7, 8 and 9) showed the toxic effect of lead exposure on renal tissue resulted in alterations, the outcomes are consistent with those of earlier research [44]. These alterations could be a sign that renal cells are unable to process residues that have accumulated as a result of lead-induced metabolic and problems with structure [45].

The group treated with low level of thiamine G3 (figure 10 and 11), while G4 with high level of thiamine showed various degree of tubular dilation however several tissue section with no obvious lesion (figure 12 and 13) this finding reflex the role of thiamine in protecting kidney tissue from toxic effect of lead, the pyrimidine ring of thiamine facilitates its communication to Pb, resulting in the inhibition of its buildup and/or enhanced clearance from organs, which may explain why the lead acetate levels in the kidney are reduced [46]. Our study chose the liver and kidney to describe the histological changes after lead exposure because lead is one of the most common toxic metals, and the most common way to get exposed to it is by consuming lead-contaminated food or water. Lead is first absorbed from the gastrointestinal tract, where it binds to erythrocytes and is then widely distributed to soft tissues like the liver, kidney, brain, and spleen.

Conclusion

Thiamine interacts with lead, which leads to preventing its accumulation and increasing its clearance from tissues, which leads to improved liver and kidney functions.

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