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The Effect of Some Heavy Metals on Kidney Tissue and Function

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Abstract, *This research tested the effect of cadmium chloride and lead acetate on kidney function and their impact on kidney tissues. The study included (30) white rats that were randomly divided into (6) groups:- The control group takes plain water orally for 30 days, the group that was given $CdCl_2$ (5 mg/kg) of body weight, the group that was given $CdCl_2$ 10 mg/kg of body weight, the group that was given lead acetate 50 mg/kg of body weight, the group that was given lead acetate 100 mg/kg of body and the group that was given cadmium chloride 5mg/kg with lead acetate 50 mg/kg body weight with drinking water for a month .The results shown in Table (1) indicated a significant increase ($P < 0.05$) in the levels of urea, creatinine, and uric acid in the serum of groups treated with $CdCl_2$ at doses of 5 and 100 mg/kg, and the groups treated with lead acetate at doses of 50 and 100 mg/kg, as well as the group that received $CdCl_2$ at a dose of 5 mg/kg along with lead acetate at a dose of 50 mg/kg, comparison with the healthy group .As for histological sections, the results showed the following section of the renal of the group treated with cadmium chloride 5 mg/kg shows atrophic renal glomerulus, necrosis of cells lining Bowman's capsule , necrosis of cells lining the convoluted tubule and a large increase in the space between the glomerulus and the capsule. As for the group treated with high-dose cadmium chloride showing necrosis of cells lining the glomerulus and degeneration of cells lining the renal tubules Fragmentation of the glomerulus. As for the group treated with lead acetate at a dose of 50 mg/kg showing renal glomerulonephrosis, proximal and distal convoluted tubule necrosis, and periglomerular space in an almost normal manner. A section of the kidney of the group treated with with high-dose lead acetate, showing atrophy of some renal glomeruli and congestion of blood vessels and showing blood congestion within the kidney tissue, and decomposition of the cells lining the urinary tubules , Cross-section of the kidney of the group treated with cadmium chloride 5 mg/kg and lead acetate 50 mg/kg body weight Shows destruction of renal glomeruli and swelling of renal tubule cells and necrosis of the kidney tissue with the appearance of hemorrhage Comparison with the healthy group*
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Keywords: *(Cadmium chloride , lead acetate , Creatinine , Urea , Uric acid)*

1. INTRODUCTION

Heavy metals are among the most important pollutants that are widespread in all environmental sites (air, water, soil) produced by some natural and human activities. These heavy metals are directly linked to human and animal health through direct entry into the body and indirectly through their impact on the growth of plants that living organisms feed on (Zhang and Wang, 2020). Heavy metals are considered a widespread hazardous problem these days, and pollution with them causes many serious diseases due to their tendency to accumulate and accumulate within living environmental systems (Priya et al., 2023).

Cadmium is one of the poisonous elements that exists in the environment through various natural and human sources, and it is dangerous to most living organisms, including humans and animals. It is a non-biodegradable element by nature, and thus, once it enters the body, it remains in the bloodstream and accumulates in the nephrons, causing damage within the nephrons and the proximal convoluted tubule. (Saini and Dhania, 2020). Cadmium and lead have very wide poisonous effects that can lead to serious physiological damage to the liver, kidneys, bones, lungs,

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and testes. (Carmona et al., 2021). The poisonous effects of cadmium are characterized by liver and kidney damage, testicular necrosis, high blood pressure, diabetes, intestinal mucosal damage, pulmonary fibrosis, bone demineralization, and neurotoxicity, especially in the brain, as well as teratogen effects, cancerous tumors, genetic mutations in humans and animals, and oxidative stress (Yan et al., 2021)

Lead is one of the metals that are widely spread everywhere, and it is a toxic element that poses a great danger to the lives of living organisms, as it causes many functionalism, behaviorism , and biochemical risks in both humans and animals (Goto et al., 2020) , including the central nervio system, renal, liver, reproductive system, and cardiovascular system (Al-Rubaye, 2017). Lead causes many very serious health effects such as congenital deformities in fetuses, genetic diseases such as reproductive organ weakness (Ambiginous) and genetic syndrome, and an increase in deaths due to increased cancerous injuries and chromosomal abnormalities. Regarding genetic effects, prolonged exposure to lead leads to the occurrence of chromosomal deviations in human cells (AL-Imarah, 2000).

2. MATERIAL AND METHOD

This study used 30 male albino rats obtained from the animal shelter / College of Veterinary Medicine / University of Tikrit, aged between (14 to 16) weeks and weighing between (200 to 260) grams. They were randomly divided into (6 groups), each group included 5 animals, The animals were treated with cadmium chloride($CdCl_{2)}$ and lead acetate at different concentrations for a month as follows:

1- The control group takes plain water orally.

2- The group was treated with $CdCl_2$ 5 mg/kg.

3-The group was treated with $CdCl_2$ 10 mg/kg

4- The group was treated with lead acetate 50 mg/kg.

5-The group was treated with lead acetate 100 mg/kg.

6- The group that was given cadmium chloride 5 mg/kg with lead acetate 50 mg/kg.

After the end of the experiment, the rats were anesthetized with chloroform, then blood was drawn by cardiac stab and placed in test tubes free of anticoagulants. Then the serum was centrifuged at 3000 rpm for 15 minutes, and the serum was stored at a temperature of 20 degrees Celsius in new plastic tubes until creatinine and urea were analyzed. , and uric acid was performed.

The animals were then dissected, the kidneys were removed, and they were placed in formalin (10%) for the purpose of fixation for 72 hours, after which they were washed with water and preserved in 70% alcohol. (Al-Hajj , 1998).

3. THE RESULT

1- The results shown in Table (1) indicated that the group treated with $CdCl_2$ at a concentration of 5 and 100 mg/kg body weight, and groups dosed with lead acetate acetate at a concentration of 50 and 100 mg/kg, as well as the group that was given $CdCl_2$ at a concentration of 5 mg/kg with acetate. Lead, at a concentration of 50 mg/kg, showed a significant increase ($P< 0.05$) in the levels of urea, creatinine, and uric acid in blood serum compared to the healthy group.

Table (1) shows the concentration of blood serum urea , creatnine and uric acid

Transactions	Urea	Creatnine	uric acid
Control	24.7 ± 2.16 e	0.57 ± 0.17 f	5.2 ± 0.29 e
group that was given $CdCl_2$ 5 mg/kg	43.6 ± 3.70 d	1.5 ± 0.35 e	8.2 ± 0.35 d
group that was given $CdCl_2$ 10 mg/kg	5. 45 ± 4,17 d	2.2 ± 0.25 d	9.3 ± 0.46 d
group that was given lead acetate mg/kg50	54.7 ± 3.77 c	2.8 ± 0.095 c	10.6 ± 0.59 c
group that was given lead acetate 100 mg/kg	61.1 ± 1.01 b	3.3 ± 0.22 b	12.6 ± 1.0 b
group that was given $CdCl_2$ 5 mg/kg with lead acetate 50 mg/kg	70 ± 3.30 a	3.7 ± 0.095 a	13.4 ± 0.71 a

• Values represent the arithmetic mean ± standard error.
• Different letters vertically mean there is a significant difference at a significant level ($P \leq 0.05$).

2- However, regarding the kidney tissues, the results showed the following:-

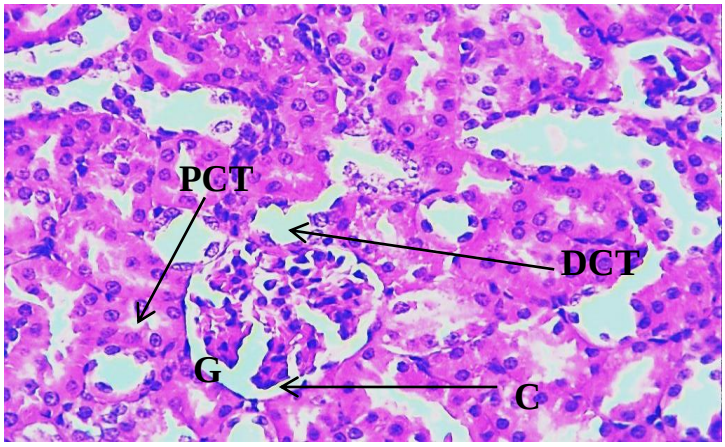


Image (1) Transvers section of a healthy group kidney showing the renal glomerulus (G), the proximal convoluted tubule (PCT), the distal convoluted tubule (DCT), and the periglomerular ,space(C) normally. H & E 400X

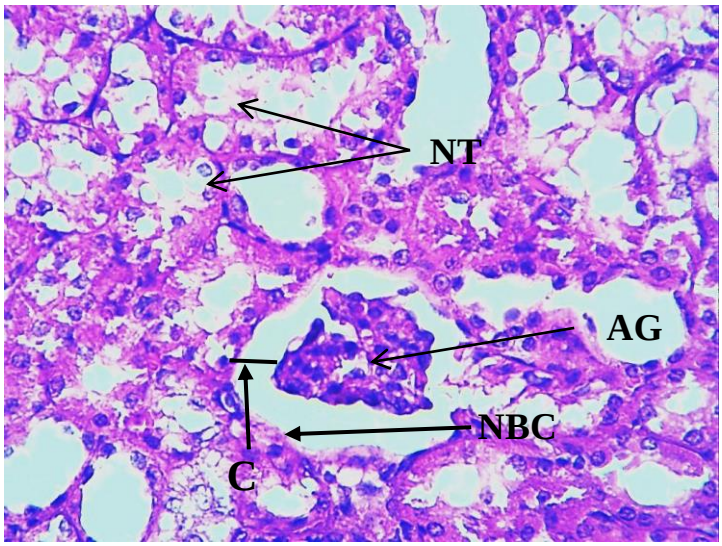
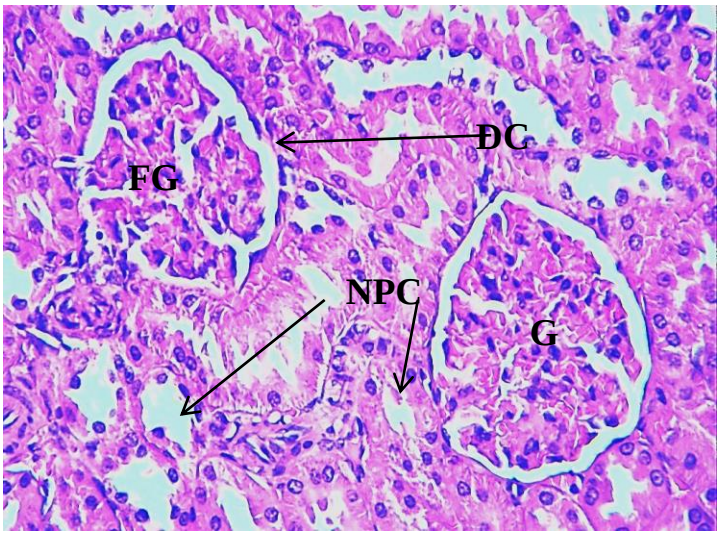


Image (2) Histological section of the kidneys of group dosed with $CdCl_2$ 5 mg/kg of weight shows atrophic renal glomerulus (AG), necrosis of cells lining Bowman's capsule (NBC), necrosis of cells lining the convoluted tubule (NT) and a large increase in the space between the glomerulus and the capsule (C). .H&E 400X:



Image(3) Histological section of the kidneys of group dosed with $CdCl_2$ 10 mg/kg showing necrosis of cells lining the glomerulus (DG) and degeneration of cells lining the renal tubules (DC). Fragmentation of the glomerulus (FG): H & E 400X.

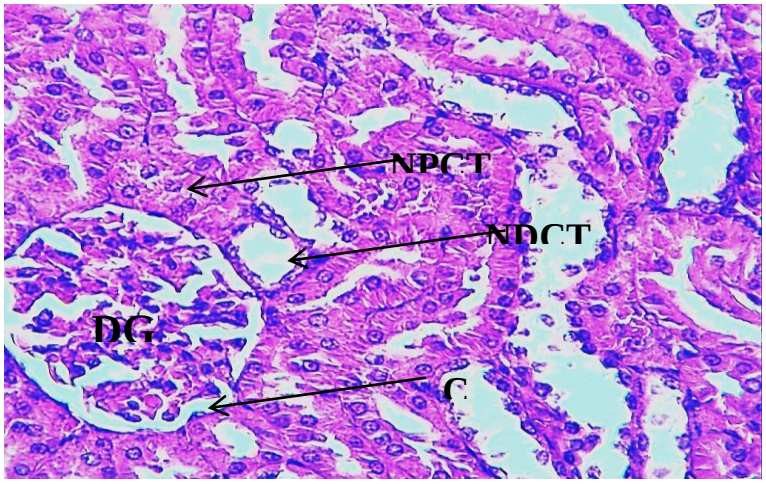
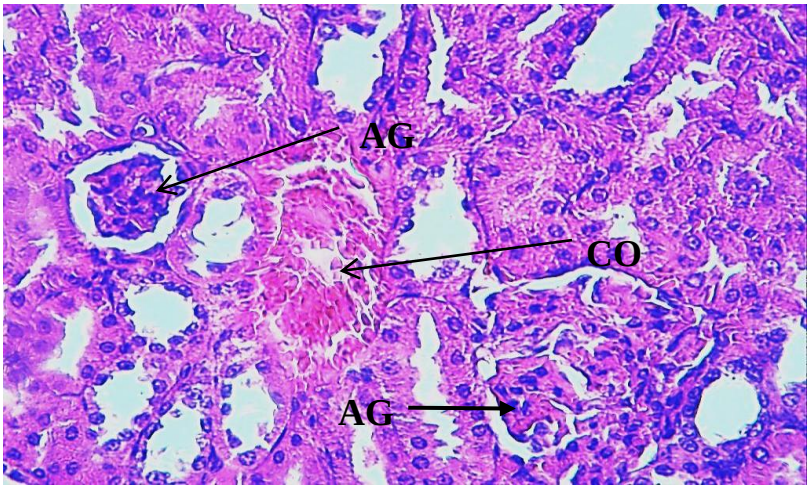
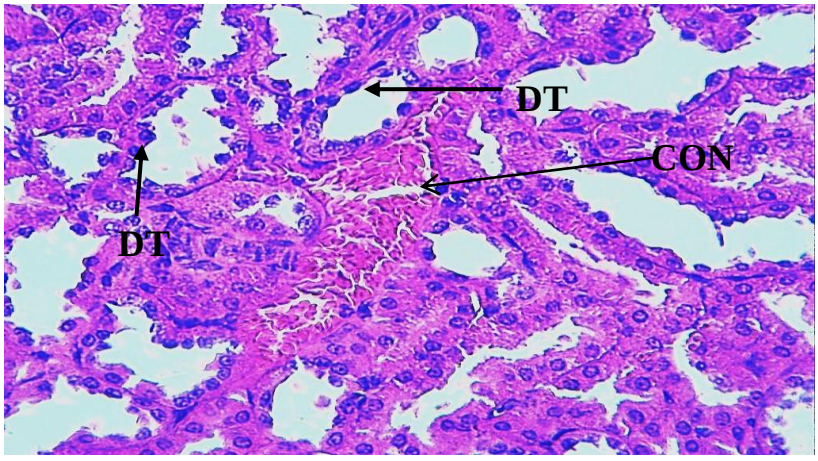


Image (4) Transvers section of the kidney of the group dosed with lead acetate at a concentration of 50 mg/kg showing renal glomerulonephrosis (DG), proximal and distal convoluted tubule necrosis (NPCT), and periglomerular space (C) in an almost normal manner. H & E 400X



Image(5A):Histological section of kidney of the group dosed with lead acetate, at a concentration of 100 mg/kg, showing atrophy of some renal glomeruli (AG) and congestion of blood vessels (CON). H & E 400X



Image(5B) A Histological section of kidney of the group dosed with lead acetate , at a concentration 100 mg/kg showing blood congestion (CON) within the kidney tissue, and decomposition of the cells lining the urinary tubules (DT). H & E 400X.

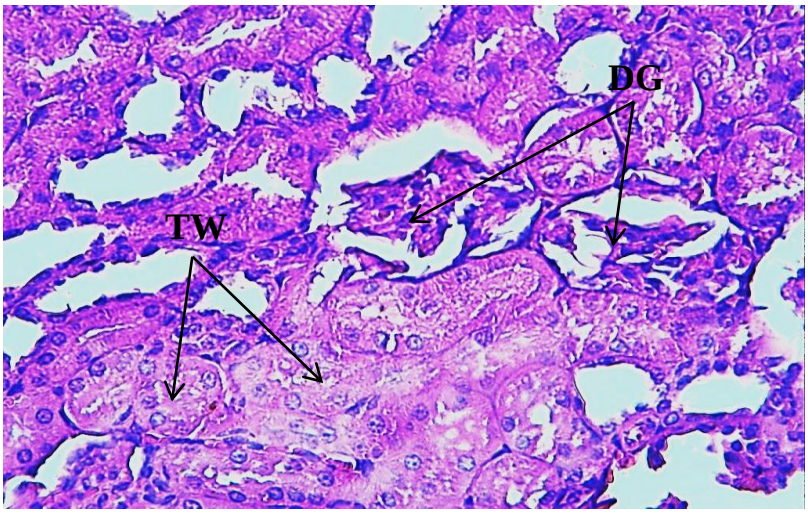
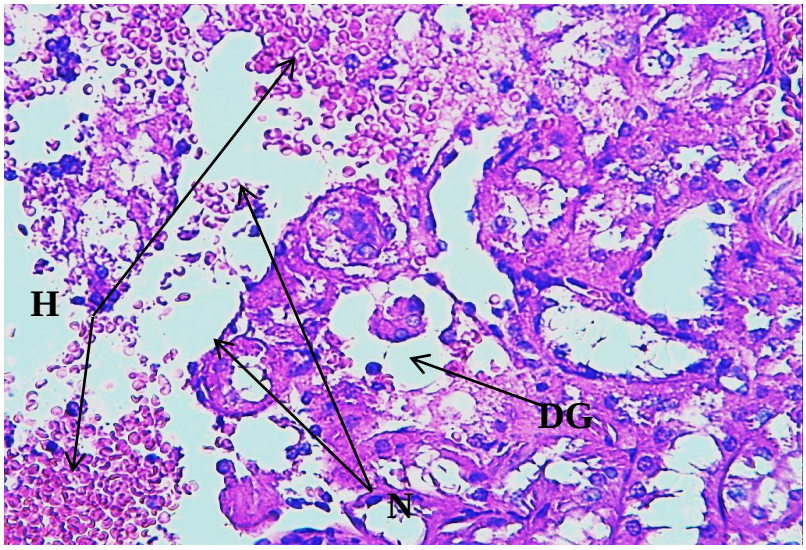


Image (6A) Transvers section of the kidney of the group dosed with $CdCl_2$ 5 mg/kg and lead acetate 50 mg/kg Shows destruction of renal glomeruli (DG) and tumefaction of renal tubule cells (TW). H & E 400X



Image(6B) Crosssection of the renal of the group dosed with $CdCl_2$ 5 mg/kg and lead acetate 50 mg/kg showing the destruction of the renal glomeruli (DG) and necrosis of the renal tissue (N) with the appearance of hemorrhage (H). H & E 400X.

4. DISCUSSION

This experiment was conducted to evaluate the function and structure of the kidneys after exposing rats to different concentrations of CdCl2 (5, 10 mg/kg) and lead acetate (50, 100 mg/kg) with drinking water for one month. They were assessed based on pathological histological

analyses, and we evaluated kidney functions by measuring the levels of creatinine, urea, and uric acid in the serum.

The results showed a significant increase (P>0.05) in the levels of urea, creatinine, and uric acid in the serum of rats exposed to different concentrations of cadmium chloride compared to the control group, as shown in Table (1).

The kidneys perform important functions by filtering excess fluids, chemicals, and waste, separating these substances from the blood, and then excreting them from the body through urine, including urea, uric acid, and creatinine. (Sharma and Tiwari, 2021).

Through glomerular filtration and reabsorption processes, it maintains acid-base balance in the blood and regulates fluid balance and the concentration of sodium, potassium, and other ions. (Rennki and Dinker, 2020). They also secrete hormones that are involved in controlling and regulating hemodynamics, producing red blood cells, and maturing vitamin D. Additionally, The kidneys are also susceptible to damage caused by other factors such as ischemia, drug toxicity, and environmental exposure to heavy metals.(Othman et al., 2021). Cadmium has the ability to bind to thiol groups (R-SH) and can be selectively selected bind to clusters containing proteins and peptides with available cysteine residues to bind cadmium after consuming water contaminated with cadmium. Cadmium can be absorbed into the bloodstream through the digestive system, respiratory system, or epidermis (Wang et al., 2020).

When it reaches the blood, it binds to albumin and other proteins and peptides that contain the amino acid cysteine, such as glutathione, and is transported through various pathways to the liver where it is released and stimulates the expression of metallothionein (MT), which subsequently binds tightly to cadmium Where cadmium-metallothionein (Ca-MT) complex is formed. (Ware et al., 2021). This binding serves a detoxification purpose, as the (Ca-MT) complex is generally considered non-toxic, and (Ca-MT) can be released into the blood and then filtered in the glomerulus and reabsorbed by the proximal convoluted tubule (Sotomayor et al., 2021). This is followed by the release of cadmium from the degradation of the (Ca-MT) complex. Its free form in the tubular area near the nephron can then bind to pre-existing renal metallothionein. When metallothionein is depleted (Trewin et al., 2019), free cadmium accumulates in the kidneys and causes nephrotoxicity, primarily in the proximal tubular area, by generating reactive oxygen species. Up to 50% of cadmium accumulation in the body can be deposited in the kidneys (Brand, 2020). The toxicity resulting from the accumulation of cadmium chloride in the kidneys leads to

kidney failure, accumulation of toxins, wastes, and blood, and high levels of urea, creatinine, and uric acid.(Pinheiro et al., 2020)

The results of the experiment appeared a significant increase (0.05>P) in the levels of urea, creatinine, and uric acid in the serum of groups administered different concentrations of lead acetate compared to the healthy group. The results of the study were consistent with (Yokoyama et al., 2000), who pointed out that a decrease in urea in urine and an increase in urea in serum indicate kidney impairment, which in turn reduces the kidney's efficiency in blood purification. The findings were also in agreement with (Cameron et al., 1998) and (Swarup and Dwivedi ,1992), where both studies indicated a significant increase in both urea and creatinine in serum, confirming renal dysfunction after oral administration of lead to goats. The results of the study were consistent with (Haneef et al., 1998) and (Tieraztl et al., 1992), who observed a moral increase in serum urea in animals orally administered lead. Urea is the final outcome of protein metabolism, and amino acids are used for glycogen synthesis (gluconeogenesis) after the removal of the amino group (deamination). This, in turn, leads to an increased level of urea in the serum. On the other hand, the rise in urea levels leads to the destruction of red blood cells. Lead poisoning is accompanied by an increase in uric acid levels, as indicated by (Ankrah et al., 1996). Experiment results also agreed with (Yasir et al., 2008), which indicated that the increase in uric acid is due to the increased breakdown of purine bases or an increase in its production and the inability to excrete it from the body.

The results of the tissue sections for the groups treated with cadmium chloride and lead acetate showed different concentrations as illustrated in figures (1,2,3,4,5,6) including atrophy of the renal glomeruli, necrosis of the cells lining Bowman's capsule, necrosis of the cells lining the convoluted tubule, and an increased large space between the glomeruli and the capsule. There was also degeneration of the renal tubular epithelial cells, fragmentation of the renal glomeruli, dissolution of the renal glomeruli, and necrosis of both the proximal and distal convoluted tubules, along with the space around the glomeruli. Additionally, there was atrophy of some renal glomeruli, congestion of blood vessels, blood congestion within the kidney tissue, dissolution of the cells lining the urinary tubules, destruction of the renal glomeruli, and swelling of the renal tubular cells. The destruction of the renal glomeruli and necrosis of the kidney tissue were noted, with the appearance of hemorrhage compared to the healthy group.

The concentration of cadmium in the kidney cortex reaching 200 micrograms/g of kidney weight is a dangerous indicator because it leads to damage to the renal tubules (Lee et al.,2024).

Cadmium chloride has a density five times greater than that of water, which makes it a cause of damage to the kidneys and may cause acute renal failure and thus death, in addition to its effect on the liver, which constitutes an important site in the body that plays a role in the processes of biotransformation, excretory of xenobiotic waste, and ridding the body. Of toxic waste, it is a center for its treatment within the living body ((Merce, 2024, Kim, 2018)

Cadmium causes dysfunction in kidney tissue by causing damage to the functioning of the renal tubules, failure in the process of normal absorption of substances, and reduces the absorption of phosphate by the renal tubules (Satarug, 2024). The rate of transport of cadmium, which is in the form of a cadmium-metallothionein (MT) complex, depends on Cd from the liver to the kidney depends on the time required to synthesize metallothionein (Nasiadek, e al., 2022), When the complex reaches the renal tubules, the complex is analyzed by lysosomes, which contain digestive enzymes that work to liberate cadmium, and this in turn leads to the synthesis of renal metallothionein, which accumulates it in the kidneys at levels higher than in the liver (Bautista et al., 2024). As the period of its remaining free in the kidney is a long period that may reach 3 months compared to the average half-life of the MT-Cd complex, which reaches (only 3-4 days) (Yuzbaşıoglu et al., 2024).

The effects of lead on the histological structure of the kidney may be through the direct effect of lead on the functioning of the renal tubules and the excretion of urine containing amino acids, which leads to high blood pressure with an increase in the level of urea and creatine in the blood, which ultimately leads to the appearance of pathological histological changes in the kidneys and then The occurrence of kidney failure (Weeden et al., 1986) and then death as a result of kidney poisoning, as indicated by(Cooper et.al 1985) in a study on workers in battery and metal smelting factories.

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