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ORIGINAL ARTICLE

Protective role of zinc against oxidative stress induced by cadmium in white rats

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ABSTRACT
The present study was conducted to determine the protective effects of zinc and vitamin C, individually or in combination with Cd, in order to monitor their ability to improve against cadmium-induced oxidative damage in albino rats. Through research, it was found that cadmium is a toxic element that harms liver tissue. Vitamin C and zinc have been shown to have an important protective role against the toxic effects of cadmium. The study was conducted on 40 male rats, and it was divided into two periods for each period of five groups, each group containing four rats. The duration of the first period was 3 weeks, and the second period was 6 weeks. This study was conducted on affected albino rats by administering a dose of cadmium with drinking water 10 mg/L individually for a period of (3 weeks, 6 weeks) and assessing the protective role. The biochemical results showed a significant increase, p<0.05, in the average level of AST, ALT, and LDH in the cadmium group compared with the control.As for LDH, ALT, there were significant differences, p<0.05, between the treated groups (cd+vt.c, cd+zinc, cd+vt.c+zinc) when compared with control, but AST did not show significant differences, p>0.05 between the groups (cd+vt.c ,cd+zinc, cd+vt.c+zinc) when compared with control. The results showed significant differences p < 0.05 in the cadmium group for all biochemical parameters. As for the antioxidants (SOD, CAT), the results showed a significant decrease p < 0.05 for the cadmium group when compared with the control and treated groups (cd+vt.c, cd+zinc, cd+ vt.c+zinc) for two (3,6) weeks, and significant differences (p<0.05) were observed between the two periods for the cadmium group. As for the (cd+vt.c+zinc) group, there were no significant differences (p>0.05 when compared with the control group). C is an essential nutrient for all animal species. In other words, these vitamins have been shown to have a protective effect against mineral-induced toxicity. In conclusion, this study showed that oral exposure to cadmium caused a decrease in biochemical and hematological activities in rats, and vitamin C had a reinforcing effect against metal-induced toxicity. It is a natural antioxidant.
Keywords: Zn, Antioxidant, Cd, ALT, LDH

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INTRODUCTION

Environmental pollutionthe primary cause of early death and disease in the globe (1). Since the first community and groups of people lived for a long time in one specific location from which the earth became polluted, the term "environmental pollution" has been used commonly and its effects have been greatly felt on the entirety of humanity and its surroundings whether knowingly or unknowingly (2,3) global issue that poses a serious threat to human existence (4,5,6).. 9 million deaths yearly, or 16% of all deaths worldwide, are attributed to pollution, which is three times more fatal than the combined effects of AIDS, malaria, and tuberculosis. One in every four death is brought on by environmental pollution (1). Moreover, (7) revealed that kids react to pollution in a precise way.Heavy metals are One of the biggest life-threatening problems in the globe is heavy metal pollution. Due to the continued growth of industrialization (8,9) around the world, the negative effects of heavy metals on living systems are continuously getting worse. One of the most dangerous elements, cadmium is present in air, water, and soil naturally. Because it is widely used in the plastics, battery, metal plating, pigment, fertilizer, and various alloy industries, there is a lot of Cd in the environment (10,11) The main ways that humans are exposed to Cd are through tainted food and water. Compared to individuals who are not exposed to a Cd-

infested workplace, those who work in the battery or paint production industries are more likely to get Cd-intoxicated. Smoking cigarettes and drinking tainted beverages are two additional common ways that Cd can develop in people (12,13) Human activity is mainly responsible for the accumulation of Cd in the environment. The delivery of Cd to humans has reportedly been linked to both acute and chronic tissue damage, as well as negative effects on vital organs including the liver (14,15). Cadmium is a heavy and dangerous metal. It is widely spread in the environment as well as in industries such as batteries, paint, and electroplating (16). Water and eating certain foods are among the main sources of exposure to cadmium (17).Cadmium affects different organs and tissues, but the first organ to be targeted is the liver. Cadmium causes significant damage and a deficiency of trace metal elements (18), and exposure to cadmium leads to a state of oxidative stress and damage to the narrow junction in the intestine, which causes disruption of the intestinal barrier and hypertrophy of cadmium absorption (19). Cadmium also interferes with the metabolism of basic metavalent minerals such as zinc and magnesium. The toxicity of cadmium was also explained by the structural disorder of the protein caused by the binding of cadmium to the sulfhydryl group (20). In addition, the response to cadmium toxicity involves macrophage inflammatory protein-2 (MIP-2) chemokine cytokine production and subsequent neutrophil infiltration (21). Cadmium induces oxidative damage to cell organelles through an increase in the production of reactive oxygen species (ROS). The interaction of ROS with cellular biomolecules initiates protein destruction, altered gene expression, apoptosis, and DNA damage (22) when the effects of ROS are not counteracted by the repair processes and affected cells undergo apoptosis or necrosis (23). Zinc is involved in many biological functions and cellular processes, including free radical defense, cell reproduction, and immune function. Zinc is rarely found in cells (24) and zinc has an effect on the metabolism of heavy and toxic metals and is one of the most important nutrients with this effect. There is ample evidence that zinc plays an important role as an antioxidant in protecting cellular components from oxidative stress (25).Once cadmium enters the body, it displaces zinc by interfering with covalent and ionic bonds. for sulfur, hydrogen, and oxygen (26). Thus, zinc will decrease and cause many essential zinc enzymes to malfunction (27). Therefore, increased zinc consumption helps prevent cadmium and toxicity from accumulating. On this basis, this study was conducted to investigate the histological and biochemical effects of cadmium on the intestinal wall and determine whether zinc had a protective role against these toxins.

Vitamin C Our general health and wellbeing depends on vitamin C. It need to be considered as a functional food element because it is a significant bioactive substance with antioxidant properties. A functional food is characterized as a natural or processed food that contains known or undiscovered bioactive components; These compounds, in required proportions, give a clinically proved and confirmed health benefit for treating, preventing, or managing chronic disease (28)

Experimental animals:

Male white rats weighing 130-240g were obtained from the animal house of the College of Science, University of Kufa, Iraq, and used for education. , inaIn the animal house at the University of Kufa, animals were housed typical setting (temperature 20-25°C) and the exact conditions of regular laboratory feeding with a regular diet (pellets), initially fed to the animals during the course of the experiments. The first period to3 weeks,, the second period 6weeks

MATERIAL AND METHODS

Chemicals

Cadmium as cadmium chloride ($CdCl_2$), , and vitamin C (ascorbic acid) zinc as zinc chloride ($ZnCl_2$)were obtained from India's Cd-Fine chemicals and Loba Chemicals. coming from Sigma Chemical Co. The maximum purity was used for all the substances used in this study.

Experimental Design

In this study, 40 male rats were used, and they were distributed into five groups, where each group included 8 males, 4 of which were used in each of the two experimental periods of 3 and 6 weeks for each group, and the five groups. groups were treated as follow:

1-The first group: control

2-The second group:The second group: 10 mg/L of $CdCl_2$ was dissolved in drinking water

3-The third group:The second group: 10 mg/L of $CdCl_2$ was dissolved in drinking water + vitamin C (500Mg/L of drinking water

4-fourth group: + zinc (50mg/L of drinking water

5-fifth group: The second group: 10 mg/L of $CdCl_2$ was dissolved in drinking water+ vitamin C (500mg/L of drinking water) + zinc (50mg/L of drinking water)

1-Liver function test
(ALT,AST,LDH)
2-Antioxidants determent
1-measurement of serum superoxide dismutase activity (SOD)
SOD activity estimated by colorimetric methods using Spectrophotometer, according to (29)
2-Measurement of serum Catalase activity (CAT)
Catalase was estimated according to (30)

RESULT
Liver function enzymes values
Table(1)) is about the differences in liver enzymes (ALT)between The treatment groups are 3 weeks (control, cd, cd+ vt.c, cd + zinc, cd+ vt.c+zinc) and the treatment groups being 6 weeks(control, cd, cd+ vt.c, cd + zinc, cd+ vt.c+zinc

Treated groups	ALT (U/L) Mean ± SD		Univariate Tests	Multivariate Tests
	3 W.	6 W.		
Control	25.33±1.53	21.33±1.52	0.0001*	LSD=4.747 p-value=0.233
Cd	39.67±2.52	35.00±6.24		
Cd + Vt.C	27.33±2.50	26.67±1.53		
Cd + Zinc	30.001±2.00	28.66±0.58		
Cd + Vt.C. + Zinc	26.32±2.08	28.67±1.15		
LSD	5.997	3.93		
p-value	0.0001*	0.007*		

Statistical analysis showed a significant increase, $p < 0.05$, in the mean concentration of ALT enzyme in the cadmium-treated group, compared to the control group for a period of (3,6) weeks. On the other hand, the statistical analysis showed that there were statistically significant differences for the treatment groups (cd + vt.c, cd + zinc, cd + vt.c + zinc when compared with the control group and with each other for both periods. (3, 6)The (cd + vt.c, cd + zinc, cd + vt.c + zinc) treated groups showed asignificant decrease $p < 0.05$ when compared to the cadmium group.
Table(2) is about the differences in liver enzymes (AST)between The treatment groups are 3 weeks (control, cd, cd+ vt.c, cd + zinc, cd+ vt.c+zinc) and the treatment groups being 6 weeks(control, cd, cd+ vt.c, cd + zinc, cd+ vt.c+zinc

Treated groups	AST (U/L) Mean ± SD		Univariate Tests	Multivariate Tests
	3 W.	6 W.		
Control	52.31±2.52	58.03±3.00	0.007*	LSD=6.734 p-value=0.022*
Cd	63.00±2.64	78.67±3.06		
Cd + Vt.C	47.33±7.51	52.00±3.00		
Cd + Zinc	54.30±5.03	56.66±3.05		
Cd + Vt.C. + Zinc	48.33±4.49	47.33±2.08		
LSD	8.737	5.21		
p-value	0.017*	0.001*		

The study's findings showed a statistically significant increase ($p< 0.05$) in the average concentration of the AST enzyme treated with cadmium when compared to the control group and groups treated for two (3,6) weeks with cd+vt.c, cd+ zinc, and cd+vt.c+zinc The average concentration of this enzyme is lower in the treatment groups (cd+vt.c, cd+ zinc, and cd+vt.c+zinc) compared to the cadmium group both during time periods (3,6)
.

Table(3) is about the differences in liver enzymes (LDH)between. The treatment groups are 3 weeks (control, cd, cd+ vt.c, cd + zinc, cd+ vt.c+zinc) and the treatment groups being 6 weeks(control, cd, cd+ vt.c, cd + zinc, cd+ vt.c+zinc

LDH (U/L)	3 W.	6 W.	Univariate Tests	Multivariate Tests
Control	15.67±1.50	16.67±1.52	0.001	LSD=2.488 p-value=0.0001*
Cd	31.7±1.53	34.33±1.53		
Cd + Vt.C	24.33±1.52	26.00±1.73		
Cd + Zinc	25.32±1.52	27.31±1.50		
Cd + Vt.C. + Zinc	21.10±1.00	19.00±1.00		
LSD	2.615	2.698		
p-value	0.001*	0.0001*		

In the cadmium group compared to the control for two (3,6) weeks, the results demonstrated a significant increase (p <0.05When compared to control and to one another for both periods, the treatment groups (cd+vt.c, cd+zinc, and cd+vt.c+zinc) did not differ significantly (p>0.05), according to the statistical analysis. On the other hand, treatment groups (cd+vt.c, cd+zinc) experienced, cd+vt.c+zinc) significantly decreased (p>0.05) in compared to the cadmium group) .

Oxidative Stress indications

Table(4) is about the differences in Oxidative Stress parameters Values SOD between The treatment groups are 3 weeks (control, cd, cd+ vt.c, cd + zinc, cd+ vt.c+zinc) and the treatment groups being 6 weeks(control, cd, cd+ vt.c, cd + zinc, cd+ vt.c+zinc

SOD (U/ml)	3 W.	6 W.	Univariate Tests	Multivariate Tests
Control	0.186±0.007	0.198±0.032	0.0001*	LSD=0.044 p-value=0.0001*
Cd	0.06±0.016	0.11±0.026		
Cd + Vt.C	0.126±0.034	0.133±0.045		
Cd + Zinc	0.153±0.021	0.194±0.047		
Cd + Vt.C. + Zinc	0.174±0.011	0.164±0.043		
LSD	0.036	0.055		
p-value	0.0001*	0.002*		

A significant increase (p 0.05) was seen in the results. As compared to the control and treatment groups (cd+vt.c, cd+zinc, cd+vt.c+zinc), the results for the cadmium group showed a significant decrease in SOD concentration (p0.05). For the treatment groups cd+vt.c, cd+zinc, and cd+vt.c+zinc, there was a significant difference (p0.05) when compared to the control, but there was no significant difference (p>0.05) for the group (cd+vt.c+zinc) when compared to the control .Between the two periods (3,6 weeks), the cadmium group showed significantly difference (p<0.05).

Table (5) is about the differences in Oxidative Stress parameters Values CAT)between The treatment groups are 3 weeks (control, cd, cd+ vt.c, cd + zinc, cd+ vt.c+zinc) and the treatment groups being 6 weeks(control, cd, cd+ vt.c, cd + zinc, cd+ vt.c+zinc

Treated groups	CAT (Umol/min) Mean ± SD		Univariate Tests	Multivariate Tests
	3 W.	6 W.		
Control	82.77±4.03	78.56±2.87	0.0001*	LSD=11.314 p-value=0.0001*
Cd	70.54±5.95	41.02±2.38		
Cd + Vt.C	53.78±12.30	21.68±6.06		
Cd + Zinc	44.00±5.60	70.96±8.95		
Cd + Vt.C. + Zinc	38.85±5.92	71.41±6.41		
LSD	13.355	10.665		
p-value	0.0001*	0.0001*		

The results showed a significant increase (p <0.05). When compared to the control and treated groups (cd+vt.c, cd+zinc, cd+vt.c+zinc) over two (3,6) weeks, the results showed a significant decrease in the CAT

concentration of the cadmium group (p <0.05 For the cadmium group, there was a significant difference (3,6 weeks) between the two periods (p< 0.05).

DISCUSSION

It is crucial to assess liver function after calculating the activity of the liver enzymes since doing so not only aids in diagnosing the functional disorder of the liver but also identifies the type of disease because it shows where the disorder is located in the injured tissue (31). A number of experts concurred that either chronic or acute exposure to cadmium, whether through drinking water (33). If this activityWith increasing dose and exposure time, the activity of the liver enzymes ALT and AST increases. The results of the current study confirmed the findings of the aforementioned researchers, with many researchers attributing this elevation to liver tissue damage caused by cadmium, which is represented by its direct toxic action on liver cells and the degeneration of those cells, which results in the exudation of significant amounts of these two enzymes into blood serum (34). 35 36 The direct toxicity of the cadmium ion and the creation of free radicals, which damage the cellular membranes of the liver cells and cause their exudation and high concentration in serum, may be the cause of the high concentration of these two enzymes. Despite the fact that the liver enzymes AST and ALT are more effective when compared to each other, the results of the current investigation revealed a substantial positive link between their activities, which is consistent with what was previously discovered (38). The presence of AST in the cytoplasm of hepatocytes, as is the case with ALT, in addition to its presence in the mitochondria of these cells, as well as its presence in the heart muscle, where it is another source of excretion into the blood, was used to explain this increase in the effectiveness of AST (39). We can infer from the results that cadmium toxicity is to blame for the liver tissue damage observed in pathological examinations. The detoxification process, Dependence of storage and secretion of bacteria on the liver and kidneysThe liver's physiological and biochemical processes suggest that it is particularly prone to injury. In this study, an effort was made to assess the effects of cadmium poisoning in rats before attempting to alleviate them by co-administering Vitamin C and zinc together or both limit blood enzymes including LDH, ALT and AST were primarily used as biomarkers to evaluate liver damage in the presence of cadmium toxicity Activity levels of several blood enzymes, including LDH, ALT, and AST, were significantly increased by exposure to cadmium. Thus, the elevated activity of ALT and AST in plasma may be the result of these enzymes escaping from the liver cytosol and entering the bloodstream. He noted that there was a significant increase in the activity level recorded for AST and ALT; Alterations in ALT activities may also lead to the significant damage that occurs during cadmium toxicity. As previous reports indicated, lysosomal instability caused by cadmium toxicity resulted in leakage of liver enzymes, including ALT and AST, into the bloodstream (40). Conducted to examine the potential ameliorative effects of zinc vitamin C, , and cadmium supplementation, both separately and together, on the toxics effects of cadmium in male rats. Cadmium is one of the most hazardous elements found in industrial and environmental contaminants, and it is thought to damage cells through oxidation. According to earlier reports from a number of authors, cadmium is well renowned for its capacity to cause oxidative damage in rats [41,42]. Depending on the exposure route, dose, and duration, cadmium can be administered into the biological system [43]. The cytoplasm showed the highest rate of cadmium accumulation at 70%, followed by the nucleus at 15%, and the endoplasmic reticulum and mitochondria at very low levels [44]. According to a prior study, administering cadmium combined with particular compounds, minerals, or vitamin supplements made it easier to 'reduce It was found that antioxidant redox cycle enzyme activity had diminished, and that SOD, CAT, and T activity had all fallen off significantly. In addition, the rat liver tissues showed an increase in lipid peroxidation. This result has been associated with oxidative stress. Zinc, vitamin C, and Cd treatment to rats resulted in increased SOD and CAT activity than Cd treated alone. The reason for the decreased SOD and CAT activity could be related to the associated rise in the production of free radicals in rat tissues as a result of cadmium treatment. The interaction between cadmium and essential trace elements may be one explanation for the decrease in antioxidant enzymes in rat organs, since cadmium can occupy the zinc site of Cu/Zn-SOD and produce inactive forms of the enzyme (Cu/Cd-SOD).cadmium-induced toxicity as much as feasible [42]. In this study including the liver [44].However, rats given more zinc, vitamin C, and had higher Cu/Zn-SOD activity. This could be the result of supplementation's protection against Cd cytotoxicity, which allows for the maintenance of normal cellular redox balance by halting the production of free radicals.

Due to the inactivation of peroxyl lipid radicals and their breakdown products, the liver's SOD activity was dramatically reduced

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