Vitamin D in Modulating Liver And Kidney Functions Following Cadmium Exposure *In Vivo*

Walid Theib Mohammad [1*], Ahmad Maher AL Sayeh [1], Fernando Jesús Plaza del Pino [2]

Abstract

Background: Cadmium is known to affect liver and kidney function due to its toxicity detrimentally. Vitamin D reportedly mitigates cadmium-induced damage in various organs, yet its specific role in liver and kidney protection requires validation. Method: 24 male rats received cadmium chloride (CD) and nutritional vitamin D via intramuscular administration for 6 weeks. Liver and kidney function were assessed through ALT, AST, ALP, CRE, UA levels, and total protein concentration. Result: Groups A and B exhibited significant elevation (P<0.001) in ALT, AST, ALP, CRE, and UA levels compared to controls for 4 weeks, indicating cadmium-induced impairment. However, these markers significantly decreased after 6 weeks of vitamin D3 treatment, signifying improved liver and kidney function. Both groups showed increased TP levels compared to controls. Conclusion: Vitamin D mitigates liver and kidney damage induced by cadmium in adult male rats. The study highlights the protective effects of vitamin D against cadmium toxicity, potentially preserving organ function under toxin-induced stress.

Significance | The research determined how vitamin D plays a vital part in relieving kidney and liver damage from cadmium, thus having important implications for treatment.

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Introduction

For over two centuries, cadmium (Cd) has remained a significant threat to both the environment and human health globally (Van Horn, 2013). It infiltrates various environmental mediums such as food, water, and air, posing substantial risks (Bernard, 2016; Genchi, 2020; Schaefer, 2022; Yimthiang, 2022). The food chain serves as a primary pathway for cadmium exposure, with shellfish, liver, and kidney being significant sources of cadmium-rich foods. Soil, water, and the food supply are primarily contaminated through the use of phosphate fertilizers, resulting in widespread cadmium pollution (Nakata, 2021). Human activities such as mining, smelting, industrial production, and waste incineration significantly contribute to cadmium emissions, surpassing natural sources (Peana, 2022). Cadmium's mobility in soil is facilitated by its solubility and low affinity for soils and sediments (Schaefer, 2020). While natural processes like volcanic action, rock weathering, and forest fires also contribute to cadmium presence, industrial practices including mining, smelting, and tobacco smoking are major contributors to airborne cadmium emissions (Schaefer, 2020).

Cadmium inflicts detrimental effects on cells and organs, notably the liver and kidneys (Zoroddu et al., 2019; Schaefer, 2022; Zhang, 2019). It disrupts cellular metabolism enzymes and pathways, inducing toxicity at the organ level (Branca et al., 2020; Gasmi et al., 2021; Genchi, 2020). Cadmium's binding with high molecular weight proteins leads to its accumulation in the liver and kidneys,

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triggering metallothionein production, which detrimentally impacts hepatic and renal functions (Genchi, 2020). This is evidenced by reduced ALB levels and elevated B2M and U-ALB levels (Yu, 2019).

Exposure to cadmium (Cd) is acknowledged for inducing dysfunctions in vital organs such as the liver and kidneys. The liver experiences hepatotoxicity characterized by oxidative stress, elevated enzyme levels, and cellular damage due to Cd accumulation (Zongping, 2020; Yimthiang et al., 2022). Conversely, chronic Cd exposure leads to kidney injury in the tubules, resulting in proteinuria and altered filtration function, making the kidneys particularly susceptible to its toxicity (Peana et al., 2023). Prolonged exposure to cadmium causes its accumulation within the kidney tubules, leading to tubular injury and impairments in kidney function, notably decreased glomerular filtration rate (GFR) (Zhu, 2019). Therefore, chronic cadmium exposure is widely recognized to primarily adversely affect kidney function (Peana et al., 2023).

The liver and kidneys, vital for various physiological functions, depend on sufficient vitamin D support for optimal performance. Vitamin D metabolism is intricately linked with liver and kidney function, where disorders in these organs affect vitamin D metabolism and vice versa (Saponaro, 2016). Vitamin D deficiency is associated with kidney disease, while vitamin D supplementation has demonstrated improvements in renal function (Bragança et al., 2018; Santos, 2021).

Several studies have underscored the antioxidant protective role of vitamin D against cadmium-induced toxicity, consistent with the current study's findings. Moreover, research indicates that vitamin D supplementation enhances antioxidant defenses, ameliorates liver histology, mitigates serum oxidative stress indices, and restores liver integrity in cadmium-induced hepatic dysfunction (Al-Rahoo, 2020; El-Boshy et al., 2019). These insights prompted the current investigation into the potential ameliorative effects of vitamin D, particularly in conjunction with calcium, on cadmium-induced liver damage. The outcomes closely align with prior studies suggesting that vitamin D, especially when combined with calcium, effectively mitigates the deleterious effects of cadmium toxicity (Megahed et al., 2023; Al-Rahoo, 2020).

The present study aimed to elucidate the crucial role of vitamin D in liver and kidney functions and investigate its potential protective effects against cadmium toxicity. By assessing whether vitamin D mitigates cadmium-induced harm to the liver and kidneys, we aim to deepen our understanding of the complex interactions among vitamin D, cadmium, and organ health. This research endeavors to contribute modestly to existing literature, highlighting the significance of vitamin D—a widely consumed nutrient—in combating the environmental toxin cadmium. Ultimately, our findings advocate for the implementation of effective public health and environmental policies.

Materials and Methods

Chemicals:

Cadmium chloride (CdCl2) and Vitamin D3 were purchased from the Sana Pharma Medical AS factory.

Study Design:

The current study was approved by Al Hussein Bin Talal University of Scientific Research and Postgraduate Studies in cooperation with the College of Health Sciences, Nursing Department, and Medical Laboratories Department. Approval was given to use the university laboratory. 24 adult male Wistar rats, 8 weeks old and weighing 250–300g, were purchased from the Animal House, Biology Department, Al Hussein Bin Talal University. The rats were acclimatized to standard laboratory conditions for two weeks before the 10-week experiment. The rats were randomly and equally divided into Control, Group A and Group B, each containing eight rats. The study was completed in two phases. The first phase: Group A was exposed to CdCl2 by dissolving 40mg/L in drinking water, while Group B was given the same previous concentrations of CdCl2 plus nutritional vitamin D, mixed with a ground rat chow, orally for 6 weeks. The second phase: Group A and Group B were given an intramuscular injection of vitamin D3 600 IU/kg, 3 times/week for 4wks. All rats were given tap water and free access during the study. The average daily consumed water for rats is 100mL/kg. Cd exposure was induced by dissolving CdCl2 (40mg/L) in drinking water throughout experiment periods for groups A and B in phase one. Group B was given nutritional vitamin D (357 IU/kg/dose) orally only by gavage. The selection of the CdCl2 and vitamin D3 doses and the duration of exposure and treatment were based on the previous experimental studies for standardization. Such studies designed to react two different periods of high exposure resulting in toxicity which demonstrates sexual dysfunction or contaminant teratogenicity (Mohamed El-Boshy et al., 2019; Baraa Yaqoob Al-Rahoo et al., 2020; R. A. Almaimani et al., 2019).

Sample collection:

We collected 2ml blood samples from the rats via retro-orbital plexus technique in plain tube using auto Lancet, and the samples were kept at room temperature for 20 minutes. The blood sample was centrifuged at 1500xg for 10min to separate the serum, transferred to labeled Eppendorf vials, and stored at -20°C in the refrigerator for further biochemical analysis. Blood sampling was performed at three time points: at the beginning of the first stage (before treatment), at the end of the sixth week, and at the end of the 10th week of the experiment, respectively, in each rat of the different groups.

Blood Biochemistry:

The liver function parameters such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase

Table 1. The Mean levels activity of the AST, ALT and ALP in serum for all groups. Values expressed as mean ±SD (n=8). P < 0.05 indicate comparisons with respect to the control group

Group N (8)	ALT	%	AST	%	ALP	%
CONTROL	**29.1375 ± 0.1767**	**100%**	**76.22 ± 0.2251**	**100%**	**92.237 ± 0.2133**	**100%**
	PHASE 1					
A (CdCL2)	40.1237 ± 0.3615	**137%**	99.4675 ± 0.0260	**130%**	295.1813 ± 3.9131	**321%**
B (CdCL2 + VD)	36.3125 ± 0.3775	**124%**	94.2162 ± 0.2294	**123%**	185.2625 ± 0.7347	**200%**
	PHASE 2					
A (VD)	30.45 ± 0.2777	**104%**	83.125 ± 0.7265	**109%**	109.525 ± 3.8137	**118%**
B (VD)	30.3125 ± 0.1885	**104%**	81.0375 ± 0.7008	**106%**	95.1 ± 0.3817	**103%**

Table 2. The Mean levels activity of the CRE, UA and P in serum for all groups. Values expressed as mean ±SD (n=8). P < 0.05 indicate comparisons with respect to the control group.

Group N (8)	CRE	%	UA	%	Total Protein(P)	%
CONTROL	**0.3125 ± 0.1726**	**100%**	**2.8 ± 0.4**	**100%**	**6.975 ± 0.2659**	**100%**
	PHASE 1					
A (CdCL2)	1.2125 ± 0.1642	388%	4.175 ± 0.3991	149%	5.55 ± 0.3338	79%
B (CdCL2 + VD)	0.5875 ± 0.1457	188%	3.3875 ± 0.2799	120%	6.5875 ± 0.3313	94%
	PHASE 2					
A (V D)	0.5125 ± 0.0640	164%	3 ± 0.5756	107%	6.925 ± 0.2251	99%
B (V D)	0.4 ± 0.0755	128%	2.325 ± 0.1908	83%	6.925 ± 0.2251	99%

(ALP) in serum were measured by using commercial kits according to the methods of NV (1972) with modifications. The activity of ALT was determined by using the UV-kinetic method as previously reported 14 with suitable commercially available diagnostic kits (Biolis 24 i/Solis 100 video, United Kingdom). The serum's determination of AST was estimated using a commercially available kit (Randox Laboratories Ltd.). The activity of ALP in the serum was determined using the commercially available kit (Randox Laboratories Ltd), according to Bowers and McComb (1966). Kidney function parameters such as creatinine (CRE) and uric acid (UA) in serum were determined using Jaffe´s and RP-HPLC methods as previously reported 15. Total protein was determined at 660 nm by day-binding and refractometry 16. Serum biochemistry analysis was performed using an auto biochemical analyzer XN-1000 (Sysmex, Japan) according to the manufacturer protocols. A trained professional blind performed the analyses to the experimental details.

Statistical Analysis:

The mean ± standard deviation (SD) for each parameter was determined from the data we received. We used a one-way ANOVA by statistical software SPSS 21.0 to compare the means of all parameters between three groups. The significance cutoff was a p-value of <0.05.

Results

The liver function test results of female albino mice treated with CdCl2 and Vitamin D3 for 6 weeks are summarized in Table 1. Both group A and group B exhibited a significant elevation in alanine aminotransferase (ALT) compared to the control group treated with distilled water. Specifically, the ALT level increased by 130% in group A and by 123% in group B compared to the control. This finding is consistent with Mathiazhagen (2017), who suggested that the reduction of ALT in group B may offer protection against CdCl2 exposure. Interestingly, treatment with vitamin D for six weeks led to a significant reduction in ALT levels. In group A, ALT levels decreased from 137% to 104%, while in group B, they decreased from 130% to 124%. Notably, there was no significant difference in ALT levels between groups A and B after six weeks of vitamin D treatment.

Aspartate aminotransferase (AST) levels also showed a significant increase in groups A and B compared to the control group, with levels reaching 137% and 124%, respectively. However, group B appeared to be less affected by CdCl2 exposure. Following treatment with doses of 1 and 0.5 µg/kg of vitamin D for 6 weeks, a significant decrease in AST levels was observed, with levels dropping to 109% of those in the CdCl2-treated groups. After treatment, no significant difference in AST levels was noted between groups A and B.

In the second test measuring alkaline phosphatase (ALP) levels, both Group A and Group B exhibited significant increases compared to the control group, with P-values of 0.0001 and 0.009, respectively. ALP levels rose by 321% for Group A and 200% for Group B compared to the control group. These findings align with previous observations (Zongping, 2020) indicating the reduced susceptibility of Group B to CdCl2 exposure. However, after 6 weeks of vitamin D treatment, ALP levels significantly decreased compared to CdCl2 exposure, showing a reduction to 118% compared to CdCl2-exposed mice, with a P-value of 0.001. No significant difference was observed between Group A and Group B after treatment.

Moving on to the kidney function tests detailed in Table 2, notably different levels of creatinine (CRE) were observed in both Group A and Group B compared to the control group. Group A exhibited a 388% increase, while CdCl2 exposure led to a 188% increase compared to the control. The impact of CdCl2 appeared to be less pronounced in Group B. Previous research has noted variations in the impact of CdCl2 on the kidneys among different species (GGkce atikeler, 2016). Following six weeks of vitamin D treatment, there was a significant decrease in CRE levels in both groups compared to CdCl2 exposure. Group B showed a marked improvement (128%) compared to Group A (164%).

There were significant increases in uric acid (UA) levels in both groups A and B compared to the control. Group A showed a 149% increase, while group B exhibited a 120% increase compared to the control group. Consistent with previous findings, group B demonstrated less susceptibility to CdCl2 intoxication, possibly due to prior adaptation to the same dose and duration of CdCl2 exposure. After 6 weeks of vitamin D treatment, both groups A and B showed a significant decrease in UA levels compared to CdCl2 exposure. The improvement in group B (83%) was also noteworthy compared to group A (107%).

Furthermore, there was a significant reduction in total protein levels in both groups A and B compared to the normal control. Group B exhibited a more pronounced reduction (94%) compared to group A (79%). This finding aligns with previous studies indicating the lower susceptibility of group B to CdCl2 exposure. Following 6 weeks of treatment with vitamin D, there was a significant improvement in total protein levels in both groups A and B compared to CdCl2 exposure. No significant difference was observed between group A and B following treatment.

Discussion

Liver and kidney functions in individuals exposed to cadmium have been extensively studied, primarily highlighting the early impact of liver function toxicity and the gradual decline in kidney function during later stages of cadmium toxicity (Schaefer & Stolz, 2022). This applied experimental study aimed to replicate previous

findings to identify practical implications. Initial results align with previous studies by El-Boshy et al. (2019), Al-Rahoo et al. (2020), Almaimani et al. (2019), Abnosi et al. (2017), and Zou et al. (2017), providing further support for their conclusions.

Initially, we investigated the impact of vitamin D (VD) supplementation alongside CdCl2 on liver function enzymes. At the end of the 6th week, two groups of 14 rats each were examined: Group A received CdCl2 (4mg/kg body weight), while Group B received CdCl2 (4mg/kg body weight) along with VD (100 units/kg body weight). Both groups exposed to CdCl2 exhibited significant increases in liver function enzyme markers ALT, AST, and ALP compared to the control group. However, Group B, exposed to cadmium along with VD, showed lower levels of these hepatic dysfunction markers compared to Group A. This supports previous findings indicating the protective effect of vitamin D against cadmium-induced liver damage (Zou et al., 2019).

In the second stage of the study, after adding vitamin D to both groups, we observed significant decreases in the levels of ALT, AST, and ALP compared to the post-exposure levels observed in the first stage. These results approached levels similar to those of the control group that did not receive cadmium. This further underscores the ability of vitamin D to enhance liver function and counteract the damage caused by cadmium exposure (Al-Rahoo et al., 2020; El-Boshy et al., 2019; Megahed et al., 2023).

The results of the renal function tests revealed significant increases in both creatinine (CRE) and uric acid (UA) levels, accompanied by a decrease in total protein level following cadmium exposure in the first phase. Moreover, group B exhibited a lesser renal functional defect compared to group A. The rise in CRE and UA levels indicates renal functional impairment due to cadmium toxicity, which likely contributed to the decrease in total protein level. These findings align with previous studies (de Bragança et al., 2016; Atikeler et al., 2016).

In both groups, there was a significant decrease in the mean values of creatinine (CRE) and uric acid (UA) levels, as well as total protein, during the phase treated with vitamin D following exposure in phase 1. However, these values remained higher than those observed pre-exposure in phase 1, indicating partial improvement. This underscores the role of vitamin D in enhancing renal function post-toxin exposure and confirms its potential in ameliorating cadmium-induced renal dysfunction.

In summary, our findings support the protective effect of vitamin D against cadmium-induced liver and kidney damage. Future research should utilize advanced techniques to explore the molecular mechanisms underlying vitamin D's action and establish consistent approaches for targeting the prevention and management of cadmium-induced toxicity.

Conclusion

Supplementation with vitamin D showed promise in ameliorating hepatic and renal functions in individuals previously exposed to cadmium (CD). Our results demonstrated greater beneficial effects of vitamin D on hepatic functions compared to renal functions. Importantly, supplementation with vitamin D concurrent with CD exposure (group B) proved more effective than post-exposure administration (group A). However, while liver function significantly improved with vitamin D3 + Cd treatment, renal function saw minimal improvement. Future studies should explore longer durations or higher doses of vitamin D to enhance its effectiveness against CD-induced renal dysfunction and consider its potential in medical interventions for liver and kidney protection.

Author contribution

W.T.M.A. designed and conducted the experiment, analyzed data, prepared the initial draft, supervised the project, and corresponded with the journal. A.M.A.S. contributed to the design, assisted in analysis, and reviewed the manuscript. F. J.P.D.P. guided data analysis, revised, and finalized the manuscript.

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Competing financial interests

The authors have no conflict of interest.

References

Abnosi MH, G. S. (2017). Cadmium chloride treatment of rats significantly impairs membrane integrity of mesenchymal stem cells via electrolyte imbalance and lipid peroxidation, a possible explanation of Cd related osteoporosis. Iran J . Basic Med Sci; 20:28.

Ana Carolina de Bragança, D. C. (2016). Vitamin D Deficiency Aggravates the Renal Features of Moderate Chronic Kidney Disease in 5/6 Nephrectomized Rats.

Ana Carolina de Bragança, D. C. (2018). Vitamin D Deficiency Aggravates the Renal Features of Moderate ChronicKidney Disease in 5/6 Nephrectomized Rats. frontires of medicin.

ANSES. (2017.). Exposure to cadmium: proposals of toxicological values of reference by ingestion, health values reference in biological environments.

Baraa yaqoob Al-Rahoo, B. R. (2020). The Role of Vitamin D3 as an Antioxidant and Hepatic Treatment against the Toxic Effect of Cadmium Chloride in The Rats. Indian Journal of Forensic Medicine & Toxicology, , Vol. 15, No 2 .

Bernard, A. (2016). Confusion about cadmium risks: the unrecognized limitations of an extrapolated paradigm. Environ. Health Perspect. 124.

Branca, J., Pacini, A., Gulisano, M., Taddei, N., Fiorillo, C., & Becatti, M. (2020). Cadmium-Induced Cytotoxicity: Effects on Mitochondrial Electron Transport Chain. .

Dongmei Yu, L. Z. (2019). Association of liver and kidney functions with Klotho gene methylation in a populatio. International Journal of Environmental Health Research,, https://DOI:10.1080/09603123.2019.1572106.

Federica Saponaro, A. S. (2016). An Update on Vitamin D Metabolism . Department of Surgical, Medical and Molecular Pathology and Critical Area, University of Pisa.

Gasmi, A., Peana, M., Arshad, M., Butnariu, M., Menzel, A., & Bjørklund, G. (2021). inhibitors and their roles in the modulation of carcinogenesis. . Krebs cycle: Activators.

GGkce Atikeler, M. Z. (2016). Effect of vitamin D on free radical metabolism in renal tissues of septic rats. Turkish Journal of Biochemistry.

Giuseppe Genchi, M. S. (2020). Review: The Effects of Cadmium Toxicity. . Public Health, 17, 3782;, https://doi:10.3390/ijerph17113782.

Gkçe Atikeler, M. Z. (2016). Effect of vitamin D on free radical metabolism in renal tissues of septic rats. Turkish Journal of Biochemistry – Türk Biyokimya Dergisi ; 41 (5): 316–321.

Heather R. Schaefer, B. M.-D. (2022). A systematic review of adverse health effects associated with oral cadmium exposure. US Food and Drug Administration, Center for Food.

Heather R. Schaefer, B. M.-D. (2022). A systematic review of adverse health effects associated with oral cadmium exposure . Elsevier , Regulatory Toxicology and Pharma.

Hokuto Nakata a, 1. S. (2021). Clinical biochemical parameters associated with the exposure to multiple environmental metals in residents from Kabwe, Zambia. elsevier.

Hokuto Nakata, S. M. (2021). CClinical biochemical parameters associated with the exposure to multiple environmental metals in residents from Kabwe, Zambia.. Chemosphere.262(127788)., https://doi.org/10.1016/j.chemosphere.2020.127788.

Hui Zou, J. S. (2017). Effects of Cadmium and/or Lead on Autophagy and Liver Injury in Rats . J .Biological Trace Element Research, https://doi.org/10.1007/s12011-020-02045-7.

Hui Zou1, 2. &. (2019). Effects of Cadmium and/or Lead on Autophagy and Liver Injury in Rats.

Iwona Markiewicz-Górka 1, *. ,. (2019). Alleviating EFFEect of _-Lipoic Acid and Magnesium on Cadmium-Induced Inflammatory Processes, Oxidative Stress and Bone Metabolism Disorders in Wistar Rats . journal of environmental research and public health.

Massimiliano Peana, A. P. (2022.). Biological Effects of Human Exposure to Environmental Cadmium . . Biomolecules, https://DOI:10.33.

Megahed, A., Gadalla, H., Abdelhamid, F., Almehmadi, S., Khan, A., Albukhari, T., & Risha, E. .. (2023). Vitamin D Ameliorates the Hepatic Oxidative Damage and Fibrotic Effect Caused by Thioacetamide in Rats. Biomedicines.

Megahed, A., Gadalla, H., Abdelhamid, F., Almehmadi, S., Khan, A., Albukhari, T., & Risha, E. (2023). Vitamin D Ameliorates the Hepatic Oxidative Damage and Fibrotic Effect Caused by Thioacetamide in Rats. . Biomedicines , 424, https://doi.org/10.3390/biome.

Michele Santiago dos Santos, D. C. (2021). The Restoration of Vitamin D Levels Slows the Progression of Renal Ischemic Injury in Rats Previously Deficient in Vitamin D. frontiers of medicin.

Mingkun Zhu, W. Z. (2019). Dietary Cadmium Chloride Supplementation Impairs Renal Function and Bone Metabolism of Laying Hens. J Animals, 998. , https://doi:10.3390/ani9110998.

Mohamed El-Boshy1, 2. |. (2019). Vitamin D3 and calcium cosupplementation alleviates cadmium hepatotoxicity in rat. wileyo.

Peana, M., Pelucelli, A., Chasapis, C., Perlepes, S., Bekiari, V., Medici, S., & Zoroddu, M. .. (2023). Biological Effects of Human Exposure to Environmental Cadmium. Biomolecules .

Schaefer, H. D. (2020). Cadmium: mitigation strategies to reduce dietary exposure. J.Food Sci. 85.

Tianfeng Zhanga, X. G. (2019). The effects of long-term exposure to low doses of cadmium on the health of the next generation of mice . Chemico-Biological Interactions 312 .

Van Horn, J. K. (2013). Reveow:Cadmium Physical and Chemical Properties. J. Encyclopedia of Metalloproteins.

Yimthiang, S., Pouyfung, P., Khamphaya, T., Kuraeiad, S., Wongrith, P., Vesey, D., . . . Satarug, S. (2022). Effects of Environmental exposur to CD and lead on risk of the diabetes and kidney dysfunction. envirion res public health.

Yimthiang, S., Pouyfung, P., Khamphaya, T., Kuraeiad, S., Wongrith, P., Vesey, D., . . . Satarug, S. (2022). Effects of Environmental Exposure to Cadmium and Lead on the Risks of Diabetes and Kidney Dysfunction. . Int. J. Environ. Res. Public Health.

Zongping, L. H. (2020). Effects of Cadmium and/or Lead on Autophagy and Liver Injury in Rats. Biological Trace Element Research ., https://doi.org/10.1007/s12011-020-02045-7.

Zoroddu, M., Aaseth, J., Crisponi, G., Medici, S., Peana, M., & Nurchi, V. .. (2019). The essential metals for humans: A brief overview.