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MITIGATING CADMIUM TOXICITY THROUGH MANGANESE AND COBALT: EMPHASIS ON OXIDATIVE STRESS IN MALE ALBINO RATS

Short title: Alleviating Cadmium Toxicity with Manganese and Cobalt

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Abstract: The study investigated the impact of cadmium exposure and the combined influence of manganese (Mn) and cobalt (Co) on the levels of oxidant enzymes in male albino rats. The results revealed a significant increase in oxidant enzyme levels in the cadmium-exposed group compared to the control group (*p<0.05 Vs Control). However, the group exposed to both cadmium and Mn + Co exhibited a noteworthy reduction in these oxidant enzyme levels when compared to the cadmium-exposed group. Intriguingly, no significant difference in oxidant enzyme levels was observed between the control and Mn + Co groups (#p<0.05 Vs Cadmium). These findings suggest that cadmium exposure leads to an elevation of oxidant enzymes, indicative of oxidative stress, and that the combined treatment with Mn + Co effectively mitigates this effect. The protective influence of manganese and cobalt against oxidative stress caused by cadmium holds potential implications for counteracting cadmium-induced toxicity. This research contributes to the understanding of mechanisms underlying cadmium toxicity and highlights the promise of using manganese and cobalt to alleviate its adverse effects in the context of oxidative stress in male albino rats.

Index Terms **- Cadmium, Toxicity, Manganese and cobalt, Protective effects, Oxidative enzymes**

I. INTRODUCTION

Heavy metals, due to their persistence and toxic nature, pose a significant threat to both environmental ecosystems and human health. Among these heavy metals, cadmium (Cd) has attracted substantial attention for its adverse effects on various biological systems [1]. Cadmium is ubiquitous in the environment, primarily stemming from industrial processes, agricultural activities, and waste disposal, leading to its accumulation in soil, water, and the food chain [2,3]. As a result, organisms, including humans, are exposed to cadmium through various routes, with dietary intake being a prominent avenue of exposure [4,5]. The deleterious effects of cadmium on organisms are well-documented, particularly in the context of oxidative stress. Oxidative stress occurs when there is an imbalance between the production of reactive oxygen species (ROS) and the cellular antioxidant defense mechanisms [6]. The excessive accumulation of ROS can lead to oxidative damage to lipids, proteins, and DNA, thereby disrupting cellular functions and contributing to a range of pathological conditions [7]. Cadmium-induced oxidative stress has been implicated in various physiological and pathological processes, including cellular dysfunction, inflammation, and organ damage. The liver and kidneys are especially vulnerable due to their roles in detoxification and excretion, rendering them primary targets of cadmium toxicity [8,9]. Given the severity of these consequences, there is a growing interest in identifying strategies to mitigate the toxic effects of cadmium and alleviate oxidative stress.

Manganese (Mn) and cobalt (Co) are essential trace elements that have gained attention for their potential protective effects against heavy metal toxicity, including cadmium [10,11]. Manganese is a cofactor for several antioxidant enzymes, such as superoxide dismutase (SOD), which plays a crucial role in neutralizing ROS [12]. Cobalt, similarly, is involved in the synthesis of vitamin B12, which is essential for maintaining proper cellular functions and protecting against oxidative stress. The combined effects of manganese and cobalt in countering oxidative stress caused by cadmium have been explored in various biological systems, including animal models [11]. However, their potential to mitigate cadmium-induced oxidative stress in specific organs such as the liver and kidneys remains an area of active investigation. This study aims to contribute to this understanding by investigating the effects of cadmium exposure and the concurrent administration of manganese and cobalt on oxidant enzyme levels in male albino rats, with a focus on the liver and kidney tissues. The rationale behind this research stems from the potential of manganese and cobalt to modulate antioxidant defenses and attenuate oxidative stress. If successful, this study could shed light on the mechanisms through which manganese and cobalt exert their protective effects, particularly within the context of cadmium-induced oxidative stress. Understanding the interplay between these elements and their impact on oxidant

enzyme levels in vital organs could hold implications for developing strategies to mitigate heavy metal-induced toxicity and its associated health risks. In conclusion, cadmium toxicity is a pressing concern due to its widespread environmental presence and its detrimental effects on organisms, particularly through the induction of oxidative stress. The potential protective effects of manganese and cobalt in alleviating cadmium-induced oxidative stress present a promising avenue for further exploration. This study seeks to uncover the intricate interactions between cadmium, manganese, and cobalt, focusing on oxidant enzyme levels in liver and kidney tissues of male albino rats. The insights garnered from this investigation could contribute to a deeper understanding of the mechanisms underlying cadmium toxicity and offer potential strategies for ameliorating its adverse effects, ultimately safeguarding both environmental ecosystems and human health.

II. METHODOLOGY

Animal Procurement and Experimental Procedure:

Healthy rats (12 weeks old) were procured from a local reputable commercial supplier and allowed a two-week acclimatization period in controlled laboratory conditions before initiating the experiments. The rats were housed at a stable temperature of 26±1°C, following a light-dark cycle of 14 hours of light and 10 hours of darkness. Their sustenance included a daily provision of commercial rat feed, while access to clean drinking water was unrestricted. Adherence to the guidelines stipulated by the "Institutional Animal Ethics Committee of Sri Venkateshwara University" was scrupulously upheld throughout the study, ensuring the ethical treatment and wellbeing of the experimental animals.

Group Classification and Sample Preparation:

The treated rats were subsequently randomized into four distinct experimental groups (Figure 1), with each group consisting of four rats. For the assessment of oxidative enzyme levels, the liver (n4) and kidneys (n4) of four rats from each group were utilized. This comprehensive approach aimed to ensure robust and reliable data collection and analysis in the subsequent phases of the research.

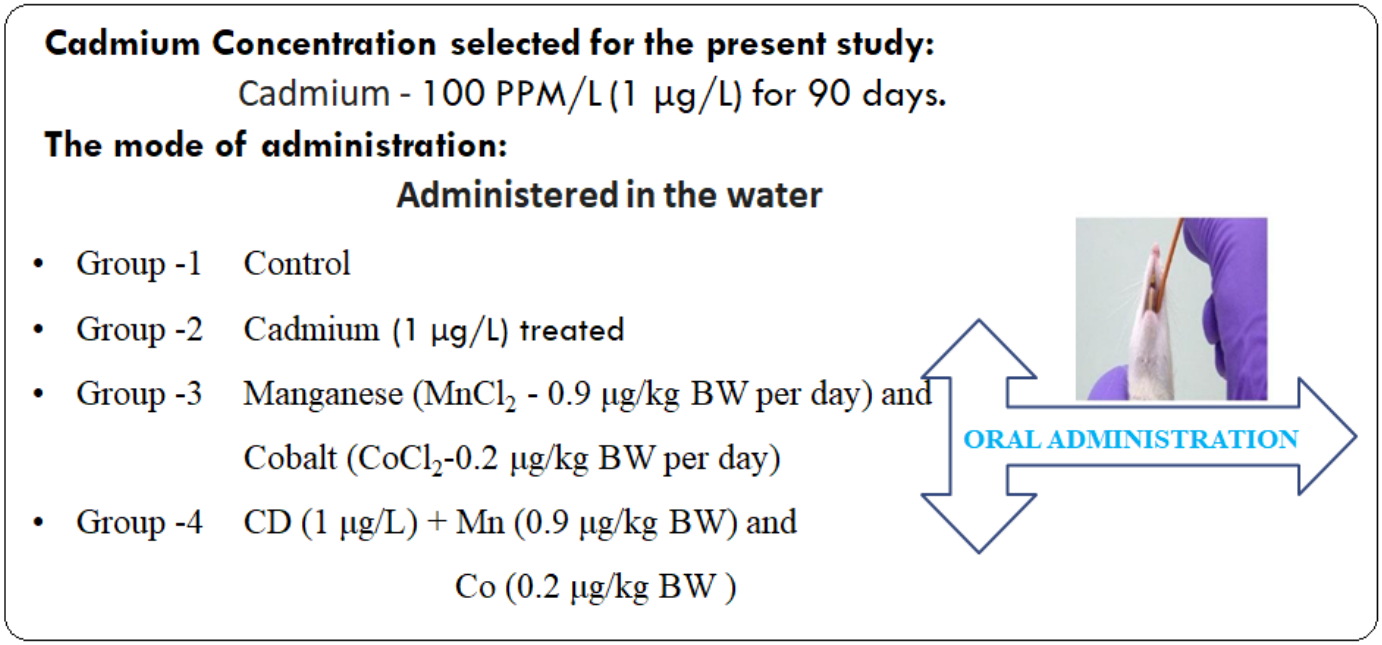

Figure 1 Experimental setup used in this study

As stated in Figure 1, Control Group were not exposed to Cadmium and Manganese and cobalt. Figure 1 also represents the experimental setup of the present study.

Oxidative enzyme activity:

In an icy cold 0.25 M sucrose solution, 10% (W/V) homogenates of the liver and kidney tissues were prepared, and they were centrifuged at 12,000g for 15 minutes at 4°C. LDH, SDH, and G-6-PDH enzyme tests were conducted using the supernatant fraction.

Lactate dehydrogenase (LDH): With only minor changes to Prameelamma and Swami's [13] methodology, the formazone was measured at 495 nm in a spectrophotometer to estimate the activity of LDH. The results were expressed in moles of formazone formed/mg protein/min.

Succinate dehydrogenase (SDH): Margulius and Seligman [14] developed a method to check the specific activity of SDH by the measuring the absorbance at 495 nm in a spectrophotometer as enzymes utilize Flavin Adenine Dinucleotide (FAD) and 2-(p-iodophenyl)-3-(p-nitrophenyl)-5-phenyltetrazolium chloride (INT) to form formazone and this was expressed in µ moles of formazone formed / mg protein / min.

Glucose-6-Phosphate dehydrogenase (G-6-PDH): G-6-PDH activity was calculated by measuring the intensity of colour formed when enzyme reacts with INT and NADPH and it was read at 495 nm against the toluene blank in

spectrophotometer and expressed in µ moles of formazone formed / mg protein / min. This method was developed Dror and group in 1970 [14]

***Statistical analysis*:** All the experimental data given in the results were means of quadruplicates and followed Duncan's new Multiple ranges (DMR) tests to find the significant difference (P<0.05) between values of each sampling.

III. RESULTS AND DISCUSSION.

The impact of cadmium exposure and the co-administration of Mn and Co on the levels of oxidant enzymes was rigorously examined. In the cadmium-exposed group, a pronounced elevation of oxidant enzyme levels was observed compared to the control group (*p<0.05 Vs Control). This alarming increase in oxidative stress markers indicated a perturbed redox balance induced by cadmium toxicity. Conversely, the group subjected to both cadmium and Mn + Co exhibited a noteworthy and statistically significant reduction in the levels of the aforementioned oxidant enzymes when contrasted with the cadmium-only group. This outcome suggests that the presence of manganese and cobalt may play a pivotal role in ameliorating the oxidative stress associated with cadmium exposure. Furthermore, intriguingly, no significant difference in oxidant enzyme levels was observed between the control group and the Mn + Co-treated group (#p<0.05 Vs Cadmium). This suggests that the administration of manganese and cobalt alone did not significantly influence oxidant enzyme levels, signifying the potential specificity of their protective effects against cadmium-induced oxidative stress. The presented values are expressed as mean±SEM (n=3), ensuring robustness and reliability in the reported findings.

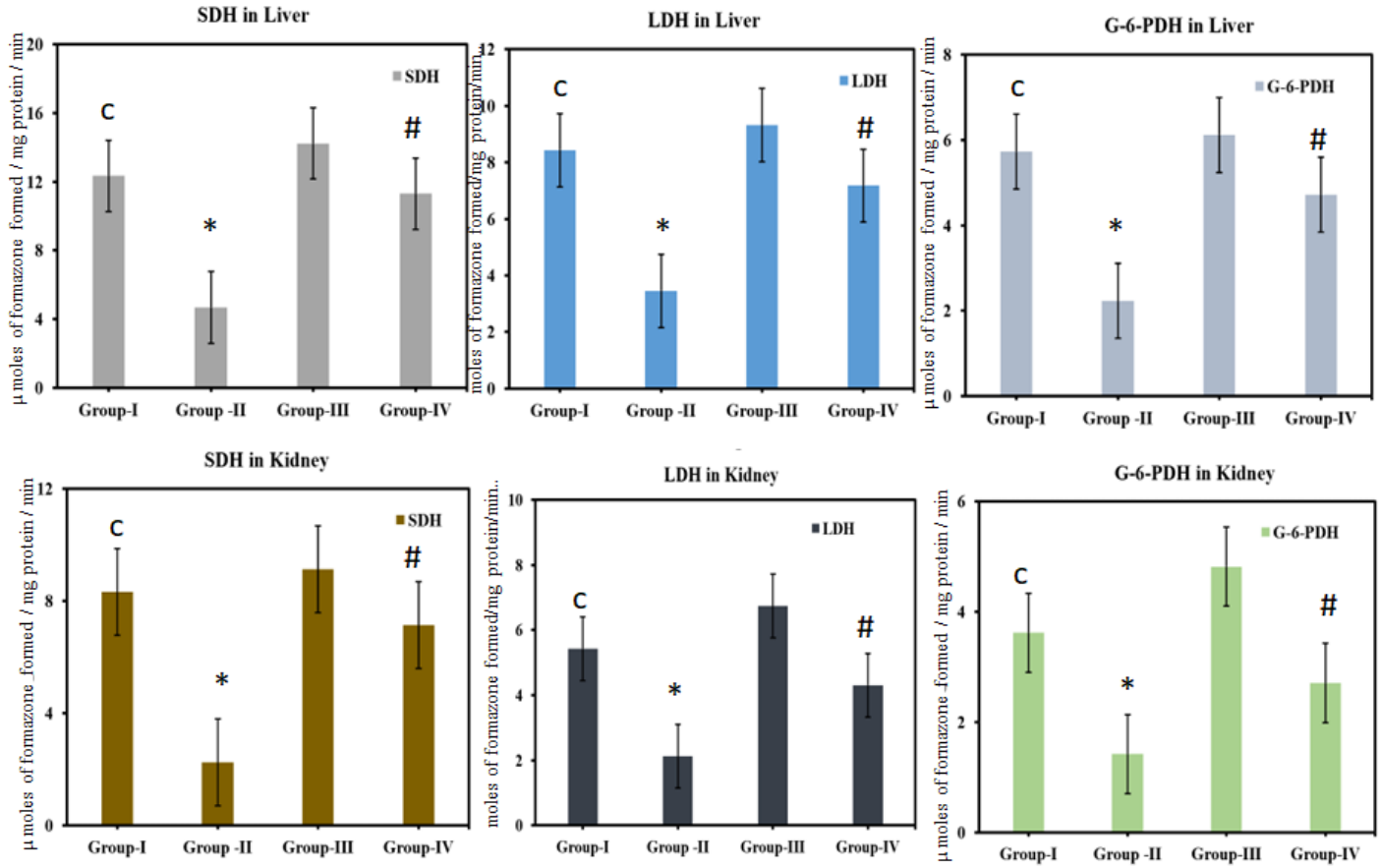

Figure 2. Level of Oxidative enzymes after treatment in liver and kidney tissue

The findings of this study underscore the critical role of oxidative stress in the context of cadmium toxicity and its potential modulation by manganese and cobalt. The substantial increase in oxidant enzyme levels observed in the cadmium-exposed group aligns with previous research, highlighting the well-documented ability of cadmium to induce oxidative stress by disrupting the equilibrium between ROS production and antioxidant defense mechanisms. This imbalance, in turn, can trigger cellular damage and contribute to various pathological conditions. The significant reduction in oxidant enzyme levels upon concurrent administration of cadmium and Mn + Co suggests a possible protective role for manganese and cobalt against cadmium-induced oxidative stress. This aligns with previous studies that have suggested the antioxidant properties of manganese and cobalt, particularly their involvement in the activation of antioxidant enzymes. The coordinated action of these enzymes is pivotal in quenching excess ROS and maintaining redox homeostasis. The lack of a significant difference in oxidant enzyme levels between the control group and the Mn + Co-treated group highlights the potential specificity of manganese and cobalt's protective effects against cadmium-induced oxidative stress. This suggests that the administration of manganese and cobalt alone might not significantly alter basal oxidant enzyme levels, emphasizing their potential selective targeting of cadmium-mediated oxidative stress pathways. The results presented here pave the way for further investigations into the intricate molecular mechanisms

underlying the interplay between cadmium, manganese, and cobalt. Future studies could delve into the modulation of antioxidant enzymes and other biochemical pathways, shedding light on the molecular pathways through which manganese and cobalt exert their protective effects. The present study offers valuable insights into the impact of cadmium toxicity on oxidant enzyme levels and the potential mitigation of these effects by manganese and cobalt. The observed reduction in oxidant enzyme levels upon concurrent administration of cadmium and Mn + Co holds promise for developing strategies to counteract the oxidative stress associated with cadmium exposure. These findings contribute to our understanding of the potential therapeutic applications of manganese and cobalt in mitigating heavy metal-induced oxidative stress and provide a foundation for future research endeavors in this domain.

IV. SUMMARY AND CONCLUSION

In this study, the impact of cadmium toxicity and the potential protective effects of Mn and Co on oxidant enzyme levels were thoroughly investigated. The results revealed a significant increase in oxidant enzyme levels in rats exposed to cadmium, indicative of heightened oxidative stress. This finding aligns with the established knowledge of cadmium's ability to disturb the delicate balance between ROS production and antioxidant defenses, resulting in oxidative damage. Remarkably, the group of rats exposed to both cadmium and Mn + Co exhibited a noteworthy decline in oxidant enzyme levels compared to the cadmium-exposed group. This observation suggests that the simultaneous administration of manganese and cobalt may confer a protective effect against cadmium-induced oxidative stress. This protective mechanism could involve the activation of antioxidant enzymes, which are known to counteract the harmful effects of ROS and promote cellular redox balance. Moreover, the lack of a significant difference in oxidant enzyme levels between the control group and the Mn + Co-treated group highlights the potential specificity of manganese and cobalt's protective effects against cadmium-induced oxidative stress. This further underscores the selective nature of manganese and cobalt in targeting pathways perturbed by cadmium exposure, while leaving basal oxidative stress levels relatively unaffected. In conclusion, this study elucidates the intricate relationship between cadmium toxicity, oxidative stress, and the potential protective role of manganese and cobalt. The results underscore the critical importance of oxidative stress in the context of cadmium-induced toxicity and highlight the potential of manganese and cobalt to mitigate these effects. The findings open doors for future research exploring the underlying molecular mechanisms through which manganese and cobalt exert their protective effects. Overall, this study contributes to our understanding of novel strategies to mitigate heavy metal-induced oxidative stress, potentially paving the way for therapeutic interventions aimed at safeguarding biological systems from the detrimental consequences of cadmium exposure.

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