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PROTECTIVE EFFECTS OF MANGANESE AND COBALT IN REDUCING CADMIUM TOXICITY WITH SPECIAL REFERENCE TO HEMATOLOGICAL PARAMETERS IN MALE ALBINO RATS

Short title: Manganese and cobalt role in reducing cadmium toxicity

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Abstract: This study focused on haematological parameters in male Albino rats treated with cadmium, manganese, and cobalt or cadmium + manganese and cobalt to examine the protective effects of manganese and cobalt on cadmium toxicity. Based on the observations and findings, it can be concluded that cadmium is toxic to rats even at modest doses, and exposure to it can cause changes in important hematological parameters. However, supplementation with manganese and cobalt can lower the toxicity of cadmium, leading to improved survival rates, body weight, and length in rats. The interaction between cobalt and manganese appears to be critical in reducing cadmium toxicity, and even lower levels of these supplements can have a significant impact. These findings suggest that the supplementation of manganese and cobalt could be a potential strategy to mitigate the negative effects of cadmium exposure in animals. However, further research is necessary to understand the mechanisms underlying this interaction and to determine the optimal doses for supplementation.

Index Terms **- Cadmium, Toxicity, Manganese and cobalt, Protective effects, Blood Biochemistry**

I. INTRODUCTION

All living things do not require the toxic metal cadmium. It presents numerous environmental risks that could ultimately lead to diseases to all the living organisms. As a result of its persistence, it might build up in many internal functions. Mining, smelting, and refining are a few examples of the anthropogenic and natural processes that release cadmium into the environment. Several more industrial uses for it include the production of polymers, pigments, enamels, ceramics, and steel plating. Cadmium toxicity is the outcome of cadmium exposure, which can occur through the soil, water, or air. [1-3]. Despite the fact that the exact mechanisms underlying cadmium toxicity are unknown, it is believed that the main way it affects cells is by generating reactive oxygen species (ROS) [4], which damage single-strand DNA and impair the synthesis of nucleic acids and proteins. As a result, it is crucial to keep an eye on the levels of heavy metals in ecosystems, and cadmium toxicity has consequently become a local as well as a global issue [5]. Cadmium is a transition metal that is a member of the d-block and the 12 group of the periodic table. It has an atomic mass of 112.411g and an atomic number of 48.

The *in vitro* studies indicate that cadmium exposure can cause cytotoxicity and DNA damage at doses ranging from 0.1 to 10 mM [6], while *in vivo* research in mice models showed that cadmium can affect male reproduction at a dose of 1 mg/kg body weight [7,8]. Furthermore, long-term exposure to cadmium has been linked to several health issues, including autoimmune diseases [9], cancer [10], cardiovascular disease [11], and hepatic dysfunction [12]. When cadmium is absorbed through the oral or respiratory route, it accumulates in the tissues and causes oxidative stress and metabolic disorders of essential elements, leading to tissue damage [13]. Cadmium can accumulate in various organs, such as the liver, kidney, and heart, and adversely affect organ function and overall health [14]. Manganese and cobalt are essential metals that are involved in protein structure, catalysis, and function regulation [15,16]. Few research, if any, have shown how manganese and cobalt can reduce the toxicity of cadmium, though. The mechanism of this relationship is also not well understood.

The current study sought to examine the impact of manganese and cobalt in lowering the toxicity of cadmium in rats since food supplements containing manganese and cobalt could be a potential strategy to minimise the adverse affects of cadmium exposure on health. Manganese and cobalt are essential micronutrients that play important roles in protein structure, catalysis, and regulation of function [15]. They are readily available as nutritional ingredients and have not been reported to have adverse side effects [17]. However, deficiency in these nutrients can increase cadmium absorption and toxicity. The study involved exposing rats to test solutions of cadmium, manganese, and cobalt, as well as a

combination of cadmium and manganese and cobalt for 90 days. Rats were chosen as the model of choice due to their easy maintenance, user-friendliness, and genetic similarity to humans. The researchers focused on evaluating the effects of manganese and cobalt on oxidative enzyme levels and blood biochemical analysis. Oxidative enzymes are involved in antioxidant defense mechanisms, and changes in their levels can indicate oxidative stress. Blood biochemical analysis can provide information on various physiological processes and can be used to monitor organ function and metabolic disturbances. Overall, the study aimed to provide insight into the protective effects of manganese and cobalt against cadmium toxicity and their potential role in reducing oxidative stress and promoting healthy organ function.

II. METHODOLOGY

***Animals and experimental protocol*:**
Rats were purchased from a local commercial dealer and acclimated in laboratory conditions for two weeks prior to the experiments. Rats were maintained at 26+10C under a photoperiod of 14:10 h light: dark cycle. Rats were fed daily with commercial food and Clean drinking water was provided *ad libitum*. Rules of the "Institutional Animal Ethics Committee of Sri Venkateshwara University" were strictly followed during the experiment and steps were taken to protect the welfare of experimental animals.

Experimental groups and sample preparation: Before recruitment to the study, the body weight, and food and water consumption of all the rats were recorded. Treated rats were randomly divided into four groups **(Figure 1)** as given below with 04 rats in each group and 4 rats bloods were used to assess haematological changes.

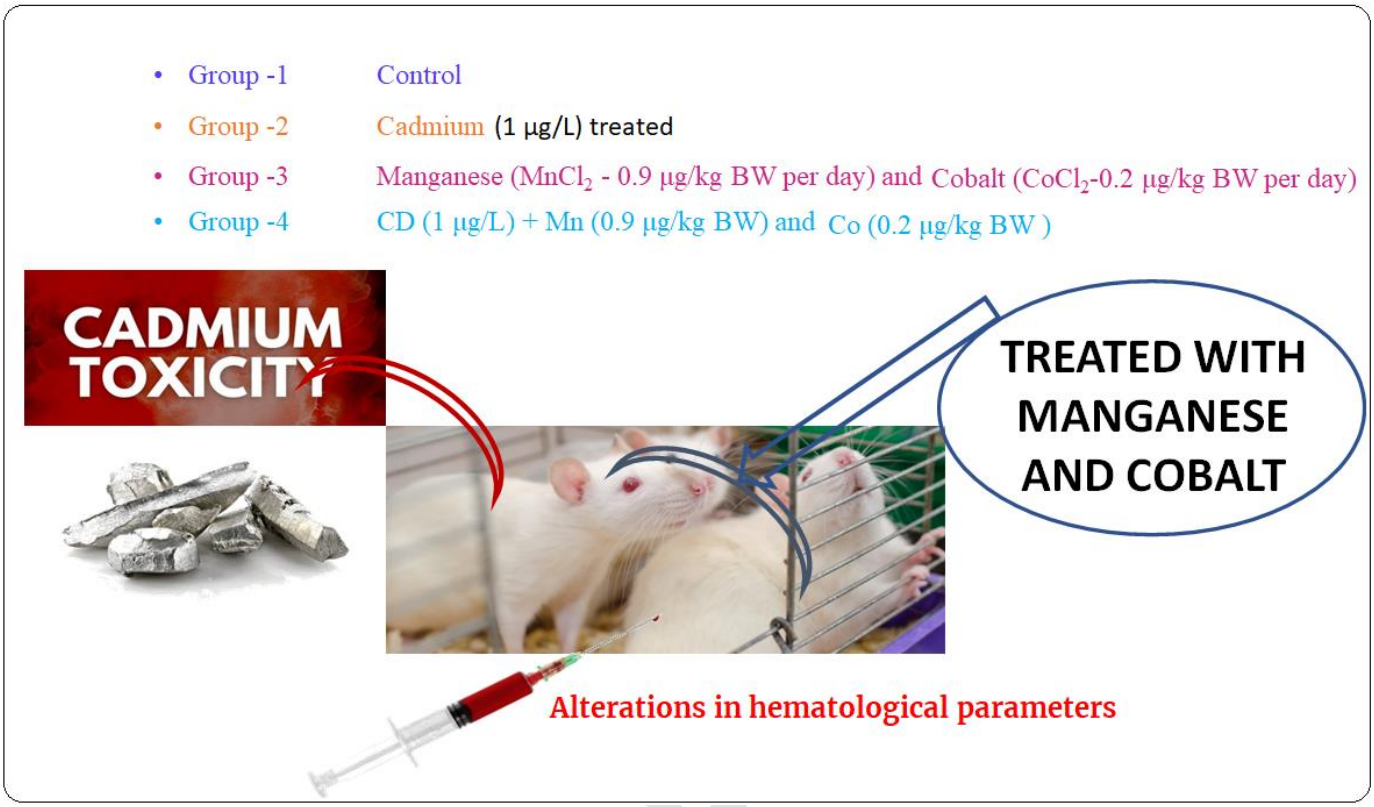

Figure 1 Experimental setup used in this study

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.

***Blood Biochemical assays*:** Approximately 1 ml of blood was drawn from the tail vein of each rat after treatment. EDTA anti - coagulated blood was used in hematological investigations and serum was used in biochemical investigations. All the blood parameters were estimated by using diagnostic kits supplied by SD fine, Kanbaxy, span diagnostics Ltd., India, as per the procedures mentioned on the kit.

***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 study suggests that cadmium exposure has a significant negative impact on the growth rate and survival of rats (Tabe 1). The rats exposed to cadmium had decreased body weight and a higher mortality rate compared to control animals and those treated with Mn + Co. However, the administration of Mn + Co alongside cadmium treatment helped to restore the physiological properties of the rats, resulting in a higher survival rate. These findings suggest that protective agents like Mn + Co could potentially be used to mitigate the harmful effects of cadmium exposure. The study highlights the importance of protecting animals and humans from exposure to toxic substances, as well as the potential for interventions to minimize the negative effects of such exposure. Further research in this area could help to

identify additional protective agents and strategies for minimizing the impact of environmental toxins on human and animal health. The protective benefits of Mn + Co were also provided by blood biochemical properties (Table 2)

Table 1. Rat lengths (mouth to caudal peduncle), weight, and survival rate after and before treatment

PARAMETER	Group -1	Group -2	Group -3	Group -4
Body weight (g)	Before treatment			
	237 ± 18.43^{a}	225 ± 14.51^{a}	232 ± 27.53^{a}	$236^{a} \pm 15.43$
	After treatment			
	314 ± 14.34^{c}	248 ± 16.34^{a}	321 ± 12.52^{c}	274 ± 17.5^{b}
Survival (%) after treatment	100	70	100	90

Means ± S.E. in each row, followed by the same letter are not significantly different ($P \leq 0.05$) from each other according to DMR test.

Table 2. Effect of Mn + Co in reducing Cadmium toxicity with reference to blood biochemical analysis in rats

BLOOD PARAMETER	Group- 1	Group- 2	Group- 3	Group- 4	Range (%)
White blood cell differential counts					
Lymphocytes (%)	75.21 ± 3.21^{c}	54.34 ± 3.41^{a}	78.42 ± 43.21^{b}	73.62 ± 3.84^{b}	71-92
Monocytes (%)	11.31 ± 1.41^{d}	5.43 ± 0.32^{a}	11.21 ± 1.23^{c}	8.21 ± 0.32^{b}	5-15
Neutrophils (%)	12.12 ± 1.21^{d}	9.36 ± 2.34^{a}	12.71 ± 1.32^{c}	10.42 ± 0.25^{b}	2-18
Eosinophils	2.41 ± 0.02^{c}	1.51 ± 0.01^{a}	2.12 ± 0.04^{b}	1.74 ± 0.0^{b}	0-4
Basophils	1.05 ± 0.03^{c}	0.43 ± 0.02^{a}	1.39 ± 0.02^{b}	0.72 ± 0.12^{b}	0-2
Serum Biochemical analytes					
Albumin	3.4 ± 0.42^{c}	2.45 ± 0.25^{a}	3.1 ± 0.74^{b}	2.74 ± 0.21^{b}	4.3 g/dl
ALP	8.5 ± 0.31^{d}	4.31 ± 0.42^{a}	8.45 ± 1.16^{c}	6.31 ± 0.77^{b}	2.0 – 10.0 U/L[3]
ALT	364 ± 07.21^{d}	276 ± 13.5^{a}	375 ± 21.11^{c}	311 ± 4.31^{b}	343.0-410.0 U/L
BUN	3.8 ± 0.14^{d}	2.27 ± 0.05^{a}	3.21 ± 0.3^{b}	3.31 ± 0.54^{c}	3.0 – 4.0 mg/dl
	OTHER MAJOR COMPONENTS OF THE BLOOD				
Haemoglobin	15.4 ± 1.32^{c}	11.5 ± 2.14^{a}	15.6 ± 1.36^{c}	13.7 ± 2.43^{b}	11.0-18.0g/dL
RBC	8.18 ± 1.31^{c}	6.32 ± 1.2^{a}	8.65 ± 1.22^{c}	7.65 ± 0.92^{b}	7.0-9.2 cells/mcL
Platelets	$9,40,000^{b}$	$6,43,000^{a}$	$12,10,200^{c}$	$9,32,000^{b}$	700000 - 1400000
Total Protein	7.1 ± 0.14^{d}	6.15 ± 0.42^{a}	7.58 ± 1.14^{c}	6.42 ± 0.14^{b}	4.0 – 7.8 g/dl

ALP = Alkaline phosphatase; ALT – alanine transaminase; BUN – Blood Urea Nitrogen

Means ± S.E. in each row, followed by the same letter are not significantly different ($P \leq 0.05$) from each other according to DMR test

The study suggests that hematological parameters can be a useful tool for measuring the toxicity of heavy metals, such as cadmium, in mammals. The hematological parameters, including blood glucose, potassium, phosphorous, and various enzymes, can be affected by exposure to heavy metals and can serve as a predictor of physiological changes and health conditions (Table 2). The study found that cadmium exposure had a more significant negative impact on hematological parameters than the control and Mn + Co-treated groups. The cadmium-treated rats had significantly lower values for hemoglobin, RBC, and platelets compared to the control and Mn + Co-treated groups. Additionally, the cadmium-treated rats showed a significant drop in albumin, BUN, and other hematological parameters compared to the Mn + Co-treated rats. The findings suggest that supplementing the diet with protective agents like manganese and cobalt may help mitigate the negative effects of cadmium exposure on hematological parameters. Overall, the study highlights the importance of monitoring hematological parameters in animals and humans exposed to heavy metals and the potential

benefits of protective agents in reducing the toxicity of these metals. Further research in this area could help to identify additional protective agents and strategies for minimizing the impact of heavy metal exposure on health.

This study highlights the potential use of hematological parameters as a tool for measuring the toxicity of heavy metals in mammals and for assessing the effectiveness of interventions aimed at reducing their harmful effects. The mechanism by which cadmium is absorbed by cells is not yet fully understood, and further research is needed to determine the amount of cadmium in circulation and the pathway of its uptake in cells. However, studies have identified several cellular transporters and ion channels, including calcium channels, that are involved in transporting cadmium across the cell membrane [18.19]. Elevated blood cadmium levels have been linked to increased mortality from coronary heart disease. Therefore, it is important to understand the factors that can protect against cadmium-induced toxicity. The study cited found that supplementing with manganese and cobalt can protect organisms from cadmium-induced toxicity. The duration of supplement use was inversely associated with serum levels of manganese and cobalt, but there was no evidence of a relationship between supplement use and cadmium exposure. Manganese and cobalt are essential minerals for normal cellular function, but excessive levels can be harmful. To maintain homeostasis and prevent toxicity, cells have evolved mechanisms to regulate intracellular levels of these minerals, including transporters, ion channels, and metal-binding proteins. Overall, the study highlights the potential protective effects of manganese and cobalt against cadmium-induced toxicity and the importance of maintaining a balance of essential minerals in the body. Further research is needed to better understand the underlying mechanisms and potential therapeutic applications.

IV. SUMMARY AND CONCLUSION

It is evident that the body's manganese and cobalt status can play a critical role in the development of cadmium toxicity. Research suggests that increasing the supply of manganese and cobalt in the diet may help minimize cadmium absorption and accumulation, as well as mitigate its negative effects. Conversely, a deficiency in manganese and cobalt can increase cadmium accumulation and toxicity in animals. Supplementing with manganese and cobalt may be particularly important for animals, as these trace minerals are essential for proper growth, development, and immune function. In addition, manganese is involved in a variety of physiological processes, including bone formation, glucose metabolism, and antioxidant defense. Cobalt is a key component of vitamin B12, which is essential for nerve function and red blood cell production. Overall, it is important to ensure that animals have adequate levels of manganese and cobalt in their diets to help protect against the harmful effects of cadmium toxicity. However, it is also important to note that excessive supplementation with these trace minerals can have negative effects on animal health, so it is important to consult with a veterinarian or animal nutritionist to determine the appropriate levels of supplementation for specific species and circumstances.

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