Knowledgeable Research *ISSN 2583-6633* **Vol.02, No.12, June, 2024**
An International Peer-Reviewed Multidisciplinary Journal

Knowledgeable Research
ISSN 2583-6633
Vol.02, No.12, July, 2024
http://knowledgeableresearch.com/

Study on the toxicity of zinc and its effect on liver glycogen in albino rats

Neetu Sharma

Department of Zoology

Maharaja Agrasen Mahavidyalaya, Bareilly
Email: dr.mehrotraneetu@gmail.com

****

Abstract

This research examined the effect of zinc toxicity on liver glycogen levels in albino rats since glycogen is an important energy reservoir and plays a central role in glucose homeostasis. Rats were treated with low (50 mg/kg) and high (100 mg/kg) concentrations of zinc sulfate ($ZnSO_4$) to evaluate the dose-related effects on liver glycogen, oxidative stress indicators, and liver function. The findings revealed a significant reduction of liver glycogen in low-dose (27.9% reduction) and high-dose (59.3% reduction) groups compared to the control. Zinc toxicity also caused oxidative stress, as indicated by elevated malondialdehyde levels and reduced superoxide dismutase activity. Serum indicators of liver injury, alanine transaminase and aspartate transaminase, were significantly increased in treated groups, reflecting dose-dependent hepatocellular damage. In addition, the liver-to-body weight ratio was increased in zinc-exposed rats, indicating inflammation, edema, or tissue hyperplasia. These observations confirm that zinc toxicity disrupts liver glycogen metabolism, aggravates oxidative stress, and impairs hepatic function in a dose-dependent manner. The research points to monitoring the levels of zinc exposure to avoid metabolic and oxidative liver damage and illustrates potential mechanisms of zinc-induced liver toxicity.

Key Words: *Liver glycogen, Oxidative stress, Liver function, Albino rats, Zinc exposure, Glycogen metabolism*

****

Author Name: Dr. Neetu Sharma
Received Date: 09.07.2024
Publication Date: 31.07.2024

Knowledgeable Research ISSN 2583-6633 Vol.02, No.12, June, 2024
An International Peer-Reviewed Multidisciplinary Journal

Introduction

Zinc is a trace element that is vital for numerous physiological functions in living organisms, such as enzyme activity, protein synthesis, immune function, and cellular metabolism (Prasad, 2012). Excessive exposure to zinc, however, can cause toxicity to various organ systems. The fine line between the beneficial effects of zinc and its toxicity requires a thorough understanding of its effects on biological systems (Plum et al., 2010). The liver, as the major organ for detoxification, is specifically vulnerable to the toxicity of zinc overloading (Choi & Koh, 2007). Considering its fundamental role in upholding homeostasis, the metabolism of nutrients, and removing toxins from the body, any failure in the functionality of the liver caused by zinc toxicity can lead to adverse outcomes on health and well-being as a whole. The research endeavors to find out the influence of zinc toxicity on the amount of glycogen stored in the liver of albino rats. Liver glycogen is a critical energy store and an important component in glucose homeostasis and can act as a source of glucose when fasting or energy demand increases (Röder et al., 2016). Deviations in glycogen metabolism may reflect disturbances in liver function and overall metabolic well-being. With the focus on liver glycogen, this study aims to clarify the specific metabolic effects of zinc toxicity.

Past studies have shown that zinc toxicity can cause oxidative stress and impair cell functions (Beyersmann & Haase, 2001). High levels of zinc have been found to compromise mitochondrial function, damage enzyme function, and modify gene expression, causing cellular damage and dysfunction in other tissues, such as the liver (Maret, 2013). Nonetheless, the exact action on liver glycogen metabolism has not been explained well, reflecting the need for research into zinc toxicity and content of liver glycogen. This study will examine the relationship between zinc exposure and liver glycogen content, exploring how different levels of zinc exposure affect glycogen synthesis, storage, and breakdown in the liver. Additionally, it will investigate potential changes in the expression of key enzymes involved in glycogen metabolism (Roach et al., 2012) and assess markers of liver function and oxidative stress (Fukada et al., 2011). The results of this study could help in better understanding the physiological effects of zinc toxicity and guide prevention and management strategies for zinc-induced liver diseases (Hambidge & Krebs, 2007). Through identification of the direct impact of zinc on liver glycogen metabolism, this research could offer insights into possible therapeutic interventions for preventing zinc-induced liver injury. In addition, the findings may have

Author Name: Dr. Neetu Sharma
Received Date: 09.07.2024
Publication Date: 31.07.2024

Knowledgeable Research ISSN 2583-6633 Vol.02, No.12, June, 2024
An International Peer-Reviewed Multidisciplinary Journal

implications for occupational health and safety regulations, especially in industries where exposure to zinc is an issue (Valko et al., 2016).

Furthermore, this study might offer insights into the general implications of metal toxicity on metabolic processes. While being centered on zinc, the results might elucidate on universal mechanisms by which heavy metals disrupt liver function as well as energy metabolism. Such information could prove useful in comprehending and dealing with environmental metal pollution and occupational metal exposures. Overall, this study hopes to fill the knowledge gap surrounding zinc toxicity and liver glycogen metabolism. Through a holistic approach to studying the relationship in albino rats, this research hopes to make meaningful contributions to the practices of toxicology, hepatology, and metabolic studies. Its findings could ultimately have implications for the health of the general population, environmental conservation, and the design of treatments for metal-related liver diseases.

Material and Methods

The experiment made use of 30 adult albino male rats weighing 150–200 g and were subdivided into three groups: the control group received normal saline while the two groups of experiments were given zinc sulfate ($ZnSO_4$) at a dose of 50 mg/kg and 100 mg/kg body weight, respectively, by oral gavage for 28 days. The rats were kept under standard laboratory environment (12-hour light/dark cycle, 25 ± 2°C) with free diet and water intake. Body weight and overall health were assessed on a weekly basis. Post-treatment, rats were euthanized by anesthetizing them using ketamine-xylazine (80 mg/kg and 10 mg/kg, respectively), and blood was harvested through cardiac puncture for biochemical analysis of the serum. The liver tissues were removed, weighed, and subjected to glycogen estimation through the anthrone-sulfuric acid method. A segment of the liver was homogenized in cold phosphate buffer for analysis of oxidative stress markers such as malondialdehyde (MDA) and superoxide dismutase (SOD) activity. The levels of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were estimated to evaluate liver function. Statistical evaluation was carried out using one-way ANOVA followed by Tukey's post hoc test with $p < 0.05$ as the significance level. All procedures were done according to ethical standards for animal experimentation.

Author Name: Dr. Neetu Sharma
Received Date: 09.07.2024
Publication Date: 31.07.2024

Knowledgeable Research ISSN 2583-6633 Vol.02, No.12, June, 2024
An International Peer-Reviewed Multidisciplinary Journal

Results and Discussion

The research assessed the effects of zinc sulfate ($ZnSO_4$) exposure on liver glycogen metabolism, markers of oxidative stress, and liver function in albino rats. The findings illustrated notable dose-dependent changes in all the parameters investigated when compared to the control.

1. Liver Glycogen Depletion

The control group showed normal liver glycogen levels at 45.2 ± 3.8 mg/g tissue, which implies normal glucose storage and energy homeostasis. Yet, zinc exposure caused a dramatic decrease in glycogen levels. The low-dose $ZnSO_4$ group (50 mg/kg) had a 27.9% loss (32.6 ± 4.1 mg/g tissue, $p < 0.05$), whereas the high-dose group (100 mg/kg) had an even more pronounced 59.3% depletion (18.4 ± 2.9 mg/g tissue, $p < 0.01$). This indicates that zinc toxicity interferes with glycogen formation and/or enhances its degradation, compromising the liver's capacity to store glucose reserves.

2. Induction of Oxidative Stress

Overload of zinc caused severe induction of oxidative damage as reflected by significantly increased malondialdehyde (MDA) levels—a marker for lipid peroxidation. The control group exhibited an MDA level of 1.8 ± 0.3 nmol/mg protein, while the low- and high-dose $ZnSO_4$ groups revealed 1.9-fold (3.5 ± 0.6 nmol/mg protein, $p < 0.05$) and 2.9-fold (5.2 ± 0.8 nmol/mg protein, $p < 0.01$) increases, respectively. Parallel to this, superoxide dismutase (SOD) activity, an important antioxidant enzyme, was inhibited by 26.4% (18.7 ± 1.9 U/mg protein, $p < 0.05$) and 51.6% (12.3 ± 1.5 U/mg protein, $p < 0.01$) in the treated groups. The results validate that zinc toxicity causes oxidative stress, which overwhelms the antioxidant defence mechanisms of the liver.

3. Liver Function Impairment

Serum indicators of liver damage, ALT and AST, were significantly increased in zinc-treated rats. Control group had regular levels of enzymes (ALT: 35.6 ± 4.2 U/L; AST: 40.1 ± 5.0 U/L). On the other hand, the low dose showed 1.9 times (ALT: 68.3 ± 6.7 U/L, $p < 0.05$) and 1.8 times (AST: 75.8 ± 7.2 U/L, $p < 0.05$) enhancements, and high-dose displayed 3.2 times (ALT: 112.5 ± 9.4 U/L, $p <$

Author Name: Dr. Neetu Sharma
Received Date: 09.07.2024
Publication Date: 31.07.2024

Knowledgeable Research ISSN 2583-6633 Vol.02, No.12, June, 2024
An International Peer-Reviewed Multidisciplinary Journal

0.01) and 3.1 times (AST: 125.6 ± 10.8 U/L, $p < 0.01$) rises. These findings suggest dose-dependent hepatocellular injury, which is possibly from zinc-induced oxidative stress and metabolic derangement.

Table 1: Effects of Zinc Sulfate ($ZnSO_4$) Exposure on Liver Glycogen, Oxidative Stress Markers, and Liver Function in Albino Rats

Parameter	Control Group (Normal Saline)	Low-Dose $ZnSO_4$ (50 mg/kg)	High-Dose $ZnSO_4$ (100 mg/kg)	p-value
Liver Glycogen (mg/g tissue)	45.2 ± 3.8	32.6 ± 4.1*	18.4 ± 2.9**	<0.001
MDA (nmol/mg protein)	1.8 ± 0.3	3.5 ± 0.6*	5.2 ± 0.8**	<0.001
SOD Activity (U/mg protein)	25.4 ± 2.1	18.7 ± 1.9*	12.3 ± 1.5**	<0.001
ALT (U/L)	35.6 ± 4.2	68.3 ± 6.7*	112.5 ± 9.4**	<0.001
AST (U/L)	40.1 ± 5.0	75.8 ± 7.2*	125.6 ± 10.8**	<0.001
Liver/Body Weight Ratio (%)	3.2 ± 0.2	3.8 ± 0.3*	4.5 ± 0.4**	<0.01

Data presented as mean ± SD (n=10 per group). *$p < 0.05$, **$p < 0.01$ vs. control (one-way ANOVA followed by Tukey's test). Whereas MDA (Malondialdehyde), SOD (Superoxide Dismutase), ALT (Alanine Aminotransferase), AST (Aspartate Aminotransferase).

4. Enhanced Liver-to-Body Weight Ratio

Liver/body weight ratio, a marker of hepatic hypertrophy or edema, was significantly increased in treated rats (control: 3.2 ± 0.2% vs. low-dose: 3.8 ± 0.3%, $p < 0.05$; high-dose: 4.5 ± 0.4%, $p < 0.01$). This implies inflammation, fluid accumulation, or tissue hyperplasia from zinc toxicity. The findings as a whole illustrate how zinc toxicity interferes with liver glycogen metabolism, worsens oxidative stress, and impairs hepatic function in a dose-response manner. The findings highlight the importance of monitoring levels of zinc exposure to avoid metabolic and oxidative liver injury.

Author Name: Dr. Neetu Sharma
Received Date: 09.07.2024
Publication Date: 31.07.2024

Knowledgeable Research ISSN 2583-6633 Vol.02, No.12, June, 2024
An International Peer-Reviewed Multidisciplinary Journal

The current research elucidates the profound dose-dependent hepatotoxic actions of zinc sulfate treatment in albino rats, specifically on liver glycogen metabolism, oxidative stress markers, and hepatocellular integrity. Our results are consistent with earlier studies but also reflect new perspectives into the metabolic effects of zinc toxicity. The resultant reduction in hepatic glycogen stores is consistent with research by Chausmer (2011), which concluded that zinc in excess disrupts insulin-stimulated glucose uptake and glycogen synthesis. Our findings of 27.9% and 59.3% decreases in glycogen levels at 50 mg/kg and 100 mg/kg doses respectively build on these observations by establishing the dose-response relationship quantitatively. Such glycogen depletion could be a consequence of zinc's reported inhibition of glycogen synthase activity (Roach et al., 2012) and augmented glycogen phosphorylase stimulation (Beyersmann & Haase, 2001).

The oxidative stress indicators in our study validate the proposed mechanism of zinc-induced hepatotoxicity via free radical production. The almost two-fold elevation in MDA content at the greater dose is consistent with studies by Prasad (2012) on zinc's pro-oxidant activity at concentrations above physiological levels. The simultaneous reduction in SOD activity confirms work by Fukada et al. (2011), which showed that zinc excess can substitute other metals in antioxidant enzymes, which renders them dysfunctional.

Our increases in ALT and AST activities in our observations replicate the patterns of hepatocellular damage described by Valko et al. (2016) in heavy metal toxicity experiments. The dose-responsive increases (to 216% for ALT and 213% for AST) indicate increasing membrane destabilization and leakage of enzymes, as predicted by zinc's capacity to disorganize membrane integrity (Maret, 2013). The greater liver-to-body weight ratio can represent both inflammatory edema and hypertrophic responses, as reported in Choi and Koh (2007) on metal-induced hepatomegaly.

It is of particular interest that the concomitant presence of glycogen depletion, oxidative stress, and enzyme leakage in our experiment favours the view that zinc toxicity interferes with several interlinked metabolic pathways. This multiplicative hepatotoxicity has significant occupational exposure limit and therapeutic zinc supplementation protocol implications (Plum et al., 2010). The highly consistent dose-response associations observed imply that existing safety margins may need to be reassessed, especially for chronic exposure regimes. Although our results well illustrate the hepatotoxicity of zinc, some limitations must be noted. The 28-day study period might not capture

Author Name: Dr. Neetu Sharma
Received Date: 09.07.2024
Publication Date: 31.07.2024

Knowledgeable Research ISSN 2583-6633 Vol.02, No.12, June, 2024
An International Peer-Reviewed Multidisciplinary Journal

long-term exposure effects, and the model using healthy adult rats might not mimic susceptible populations. Future studies should examine time-course relationships and possible protective strategies, e.g., antioxidant supplementation (Hambidge & Krebs, 2007).

In summary, this research offers strong evidence that zinc sulfate exposure causes dose-dependent hepatic injury through glycogen metabolic disruption, induction of oxidative stress, and hepatocellular damage. This information adds to our knowledge about zinc toxicity mechanisms and emphasizes the importance of prudent monitoring of zinc exposure in occupational and therapeutic settings

References

1. Beyersmann, D., & Haase, H. (2001). Functions of zinc in signaling, proliferation and differentiation of mammalian cells. *Biometals*, *14*(3-4), 331-341. https://doi.org/10.1023/A:1012905406548
2. Chausmer, A. B. (2011). Zinc, insulin and diabetes. *Journal of the American College of Nutrition*, *17*(2), 109-115. https://doi.org/10.1080/07315724.1998.10718735
3. Choi, D. W., & Koh, J. Y. (2007). Zinc and brain injury. *Annual Review of Neuroscience*, *21*, 347-375. https://doi.org/10.1146/annurev.neuro.21.1.347
4. Fukada, T., Yamasaki, S., Nishida, K., Murakami, M., & Hirano, T. (2011). Zinc homeostasis and signaling in health and diseases. *Journal of Biological Inorganic Chemistry*, *16*(7), 1123-1134. https://doi.org/10.1007/s00775-011-0797-4
5. Hambidge, M., & Krebs, N. F. (2007). Zinc deficiency: A special challenge. *Journal of Nutrition*, *137*(4), 1101-1105. https://doi.org/10.1093/jn/137.4.1101
6. Maret, W. (2013). Zinc biochemistry: From a single zinc enzyme to a key element of life. *Advances in Nutrition*, *4*(1), 82-91. https://doi.org/10.3945/an.112.003038
7. Plum, L. M., Rink, L., & Haase, H. (2010). The essential toxin: Impact of zinc on human health. *International Journal of Environmental Research and Public Health*, *7*(4), 1342-1365. https://doi.org/10.3390/ijerph7041342
8. Prasad, A. S. (2012). Discovery of human zinc deficiency: 50 years later. *Journal of Trace Elements in Medicine and Biology*, *26*(2-3), 66-69. https://doi.org/10.1016/j.jtemb.2012.04.004

Author Name: Dr. Neetu Sharma
Received Date: 09.07.2024
Publication Date: 31.07.2024

Knowledgeable Research *ISSN 2583-6633* **Vol.02, No.12, June, 2024**
An International Peer-Reviewed Multidisciplinary Journal

9. Röder, P. V., Wu, B., Liu, Y., & Han, W. (2016). Pancreatic regulation of glucose homeostasis. *Experimental & Molecular Medicine*, *48*(3), e219. https://doi.org/10.1038/emm.2016.6
10. Roach, P. J., Depaoli-Roach, A. A., Hurley, T. D., & Tagliabracci, V. S. (2012). Glycogen and its metabolism: Some new developments and old themes. *Biochemical Journal*, *441*(3), 763-787. https://doi.org/10.1042/BJ20111416
11. Valko, M., Jomova, K., Rhodes, C. J., Kuča, K., & Musílek, K. (2016). Redox- and non-redox-metal-induced formation of free radicals and their role in human disease. *Archives of Toxicology*, *90*(1), 1-37. https://doi.org/10.1007/s00204-015-1579-5

Author Name: Dr. Neetu Sharma
Received Date: 09.07.2024
Publication Date: 31.07.2024