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Study of the Toxicological Effects of Acute and Chronic Exposure to Nano Polystyrene on Hematological and Oxidative Stress Indicators in Rats

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ABSTRACT

This study investigates the toxic effects of nano polystyrene plastic particles on laboratory rats using hematological and biochemical analyses. In both acute and chronic exposures, hematological alterations were evident, with a marked increase in white blood cell (WBC) counts, indicating an activated immune response and systemic stress. In contrast, red blood cell (RBC) counts and hemoglobin (HGB) levels showed a consistent decline, suggesting impaired erythropoiesis, reduced oxygen-carrying capacity, and possible hematological toxicity. These combined changes reflect a shift toward inflammatory and immune activation, alongside anemia-like effects, which may contribute to compromised physiological balance and overall health. In both acute and chronic exposures, oxidative stress biomarkers showed significant alterations, as catalase (CAT) activity and malondialdehyde (MDA) levels were markedly increased, reflecting enhanced lipid peroxidation and activation of antioxidant defense mechanisms. In contrast, superoxide dismutase (SOD) activity decreased, indicating a weakened primary antioxidant response and reduced capacity to neutralize superoxide radicals. These combined changes suggest an imbalance in the oxidative/antioxidant system, where elevated oxidative damage and insufficient enzymatic defense contribute to cellular stress and potential tissue injury due exposure to nano polystyrene. This study resulted in some behavioral and physiological alterations, including reduced appetite, weight loss, alopecia, lethargy, sleep disturbances, and heightened aggression, indicating that chronic nano polystyrene exposure disrupts neurological, metabolic, and systemic functions, indicating its potential classification as a cumulative toxicant with progressive adverse effects. In summary, both acute and chronic exposure to nano polystyrene in rats disrupts hematological function and induces oxidative stress.

INTRODUCTION

Microplastics are referred to as small particles ranging in size from 1 μm to 1000 μm (Ahmad, 2023). These synthetic particles are formed as a result of the gradual breakdown of larger plastic debris into smaller particles due to environmental factors, including physical, chemical, biological, and mechanical characteristics (Ghosh et al., 2023). They are generally spherical, irregular, cylindrical, and filamentous dark particles, the common sources of microplastics in the environment are usually through the disintegration and degeneration of plastic materials, coupled with the release of microplastics in the form of resistant, peel-off, and microporous fillers used in various household care products, such as cleansers, toothpaste, and facial scrubs (Carney Almroth et al. 2018).

The increasing production and disposal of plastics have led to growing concerns about the accumulation of microplastics in marine organisms, sediments, and other environments. These particles can disrupt hormones, reproduction, cardiovascular function, immune responses, and increase oxidative stress through ROS generation. To better understand their physiological impacts, it is essential to investigate microplastic accumulation in rats at different dosages and assess related blood parameters (Sulistyorini et al. 2024).

MPs strongly accumulated in the liver and showed stronger potential for harming rats compared with lower-level ones due to reactive oxygen species (ROS). Rats' whole-body physiological function in the blood antioxidant system was activated to maintain a balance under stress (Samawi, M.F. and Werorilangi, S., 2024). Brain, liver, and kidney ROS accumulation led to significant organ damage. In addition, MPs' accumulation in the liver affected cholesterol metabolism, inflammation, and immune-related functional lipid oxidation. The excretion of bile decreased, leading to oxidative damage and acid accumulation in rats. From the results of these three approaches, MPs had a strong potential to harm rats and could be transferred to a higher-level host through an ecological approach that considers the integrated oxidative effects on the body (Albazoni et al. 2024).

Nano polystyrene was selected for investigation because it represents one of the most common synthetic polymers extensively used in packaging, consumer products, and industrial applications (Abdelkareem et al. 2025). Its widespread production, use, and improper disposal contribute substantially to environmental contamination, where larger plastic debris progressively degrades into micro- and nano-sized particles (Vohl et al. 2024). At the nanoscale, polystyrene particles possess unique physicochemical properties, such as increased surface area, high reactivity, and the ability to cross biological barriers, which causes them to accumulate in tissues and interact with cellular systems compared to larger plastic fragments (Kelpsiene et al. 2022). Previous studies have suggested that nano polystyrene can induce oxidative stress, immune disturbances, and metabolic dysfunction in living organisms, highlighting the need for detailed toxicological assessment. Therefore, focusing on nano polystyrene allows for a clearer understanding of the potential health risks posed by nano-sized plastics and provides a model for evaluating the broader implications of nano plastic exposure. (Kelpsiene et al. 2022).

2. METHODOLOGY

The current study included a cohort of 40 albino female rats, each with a weight ranging from 180 to 200 grams, and at the age of 12 weeks. These subjects were procured from the Housing Animal facility located within the Faculty of Science at the University of Kufa. The experimental setup involved the use of six plastic cages, each fitted with metal covers, with dimensions of 43 cm in length, 27 cm in width, and 15 cm in height. For hydration, plastic bottles with corks featuring metal pipes were employed. The rats were accommodated five per cage (Techiplast, Kettering, UK) with sawdust serving as bedding in an environment with controlled temperature (22 ± 2 °C) and humidity (40 ± 5%). The light-dark cycle was maintained at 12:12 hours, with illumination set at 25 lux (Couto and Cates, 2019).

Fig. 1: The Animals and Cages Used in the Present Study.

1.1. Experiment Design: Acute and Chronic Toxicity Assessment of Nano Polystyrene

This study aimed to assess the acute and chronic toxicity of a nano polystyrene emulsion using female rats as an experimental model. The rats, aged 12 weeks and weighing between 180 and 200 grams, the ethical approval for animal handling obtained from the animal ethics committee of the University of Kufa. were divided into two main categories: an acute toxicity experiment and a chronic toxicity experiment. Each category included a control group (N = 10). The nano polystyrene, purchased from Sigma-Aldrich, with properties: particles size = 100 nm, concentration = 10% (solids), Purity = 100%, and density = 10.05 g/cm^3.

1.2. Acute Toxicity Experiment

In the acute toxicity experiment, rats in the treatment group received a daily dose of 6.783 mg/kg of the nano polystyrene emulsion for 7 days. In contrast, the control group was given distilled water to provide a baseline for comparison.

1.3. Chronic Toxicity Experiment

For the chronic toxicity experiment, rats in the treatment group were administered a lower daily dose of 2.8 mg/kg of the nano polystyrene emulsion over 30 days. As with the acute toxicity experiment, the control group received distilled water. This design aims to uncover any potential adverse effects of the emulsion in both the short and long term.

3. RESULTS AND DISCUSSION

3.1. Morphological and Behavioral Results

Nanoparticles of polystyrene can be taken up by the gastrointestinal system and subsequently enter the bloodstream, leading to accumulation in the cerebral regions of mice, which in turn results in neurobehavioral disturbances (Prust et al. 2020).

Table (1), Figures (2), and (3) below show the changes in the behavior of female rats exposed to varying doses of Nano polystyrene. Most behavioral changes appeared in the last days of the chronic exposure experiment. In addition to the change in stool color, laziness, and aggression appeared at the beginning of the acute exposure experiment. The most prominent changes included loss of appetite, weight loss, hair loss, and increased sleep hours.

Table 1: Behavioral Changes in Female Rats Exposed to Varying Doses of Nano polystyrene.

Observation	Control group	Acute group	Chronic group
Loss of appetite	-	-	+
Change the color of the feces	-	+	+
Loss of weight	-	-	+
Loss of hair	-	-	+
Refusal of drink	-	-	+
Wounds	-	-	-
Abscesses	-	-	-
Idleness	-	+	+
Aggressiveness	-	+	+
Sleep	-	-	+

The observed behavioral and physiological alterations indicate multiple toxicological implications of nano polystyrene exposure. Increased aggression, lethargy, and prolonged sleep duration suggest possible neurotoxic effects linked to central nervous system disruption and neurotransmitter imbalance (Howard et al.2024). Reduced appetite, weight loss, and changes in fecal coloration point toward metabolic and gastrointestinal dysfunction, while alopecia and overall lethargy reflect systemic stress and impaired homeostasis (Sweetser, 2022). Notably,

the more severe manifestations in the chronic exposure group highlight the cumulative and progressive nature of these adverse effects, emphasizing their dose- and time-dependent toxicity.

A variety of elements that may influence the neurotoxic effects of micro- and nanoplastics can be discerned. The extent of exposure to these particulates is crucial in assessing the possible neurotoxic ramifications of plastic particles (Wang et al. 2020). Nonetheless, the existing levels of exposure are significantly lower than those employed in laboratory conditions. Conversely, the duration of exposure in controlled experiments is often considerably shorter than what would be relevant for actual human exposure, despite findings suggesting that the neurotoxic outcomes of micro- and nanoplastics are contingent upon the exposure duration (Varo et al. 2019). In addition to the concentration and duration of exposure, the thermal conditions during exposure may also affect the neurotoxicity of micro- and nanoplastics, particularly in aquatic organisms, as increased toxicity has been observed at higher temperatures (Fonte et al. 2016).

In conjunction with the aforementioned exposure characteristics, the intrinsic properties of the particles themselves may markedly affect the neurotoxic potential of micro- and nanoplastics. It is posited that particle size is among the most significant attributes. Generally, nanoparticles are more readily assimilated and possess a heightened toxic potential relative to microparticles (Lin et al. 2024).

Fig. 2: Loss of Hair in Rat in Chronic Group.

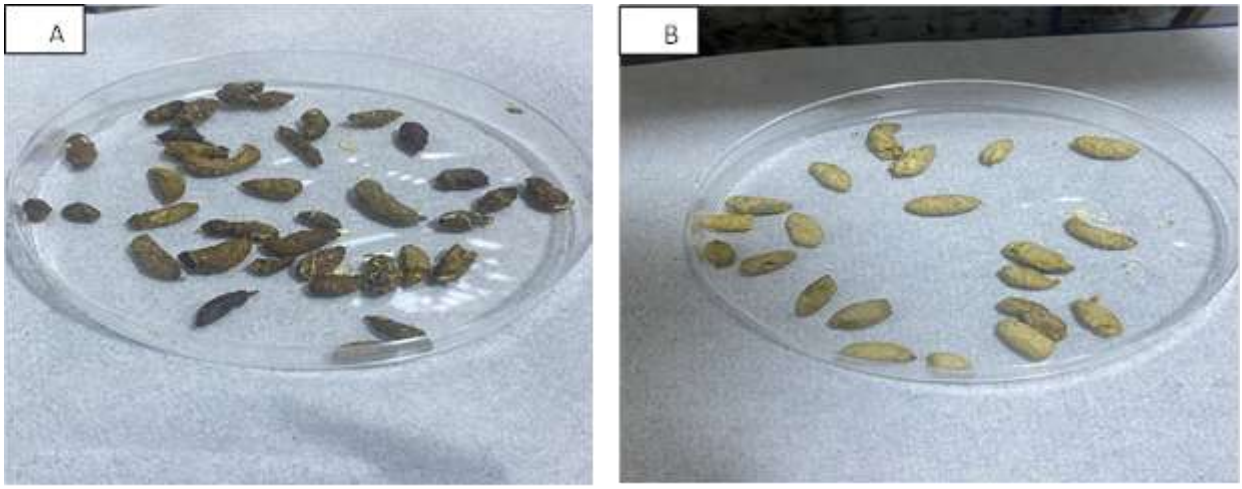

Fig. 3: Change of Feces Color in Chronic Group. (A) Control Feces, (B) Chronic Feces.

Some observational changes were observed in the rats' organs, including inflammation of the gastrointestinal tract and liver tissue damage in the acute group. While in the chronic exposure group, gastrointestinal inflammation, liver steatosis, and liver cysts, as shown in Figure (4).

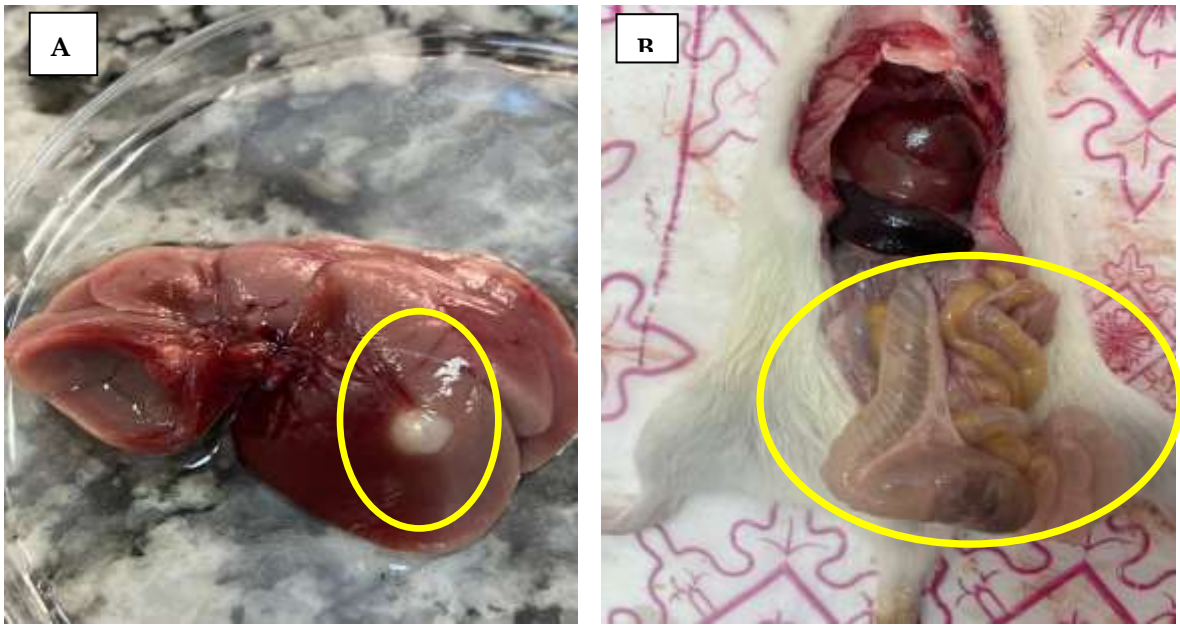

Fig. 4: (A) Liver cyst; (B) Gastrointestinal Inflammation.

3.2 Hematological Parameters

The provided figures (5,6,7) illustrate the impact of acute and chronic exposure on various hematological and biochemical parameters, comparing exposed groups to control groups. For White Blood Cells (WBC) count (10^3/ul), presented in Figure (5) increased in the exposed groups. Acutely, control WBCs were 7.045×10^3/ul, while exposed were 10.466×10^3/ul. In the chronic phase, control WBCs were 6.59×10^3/ul, but exposed WBCs were further elevated to 13.314×10^3/ul, indicating a more significant inflammatory or immune response over longer exposure.

Consequently, Red Blood Cells (RBC) count (10^6/ul), as shown in Figure (6), both acute and chronic exposure led to a decrease in RBC count in the exposed groups compared to controls. In the acute phase, control RBCs were 6.0483×10^6/ul while exposed RBCs were 5.281×10^6/ul. In the chronic phase, control RBCs were 6.166×10^6/µL, but exposed RBCs dropped significantly to 4.7975×10^6/µL, indicating a more pronounced reduction with prolonged exposure.

Hemoglobin (HGB) levels (g/dl), depicted in Figure (7) mirrored the trend of RBCs. In the acute exposure group, the control HGB was 12.544 g/dL, while the exposed group had an HGB of 11.282 g/dL. Chronically, control HGB was 11.329 g/dl, but exposed HGB showed a substantial decrease to 6.264 g/dl, suggesting a severe impact on oxygen-carrying capacity with chronic exposure.

Conversely, in comparison to the control group, those exposed to nano polystyrene exhibited significantly elevated white blood cell (WBC) counts. Conversely, the hemoglobin (HGB) and red blood cell (RBC) levels were greater in the control group than in the exposed individuals. There was a notable reduction in the average RBC and HGB levels in both acute and chronic cases among those not exposed.

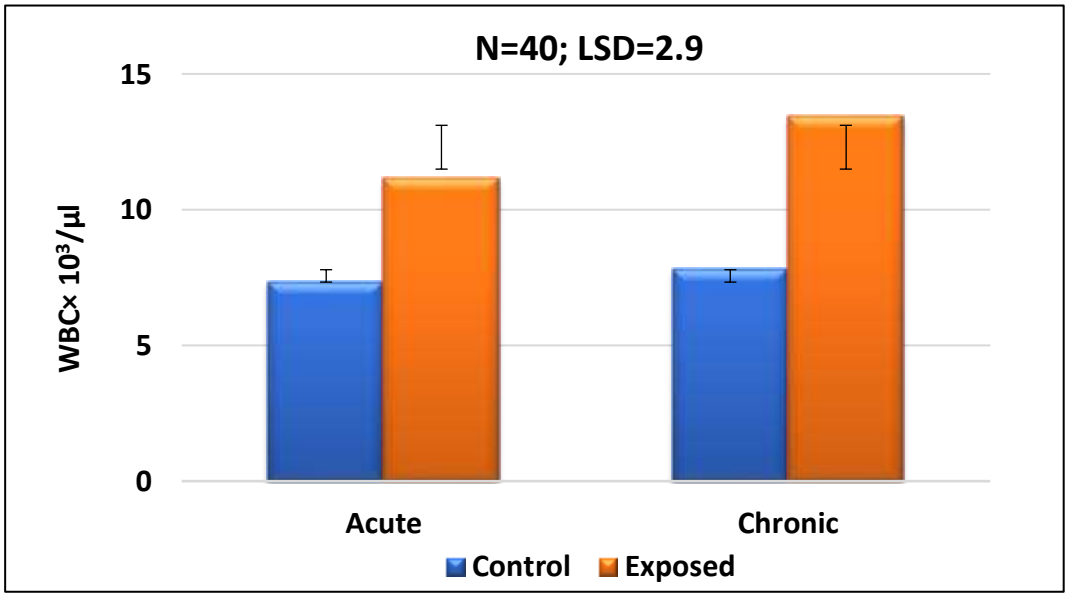

Fig. 5: Comparison of WBCs in Control vs. Exposed Groups**.**

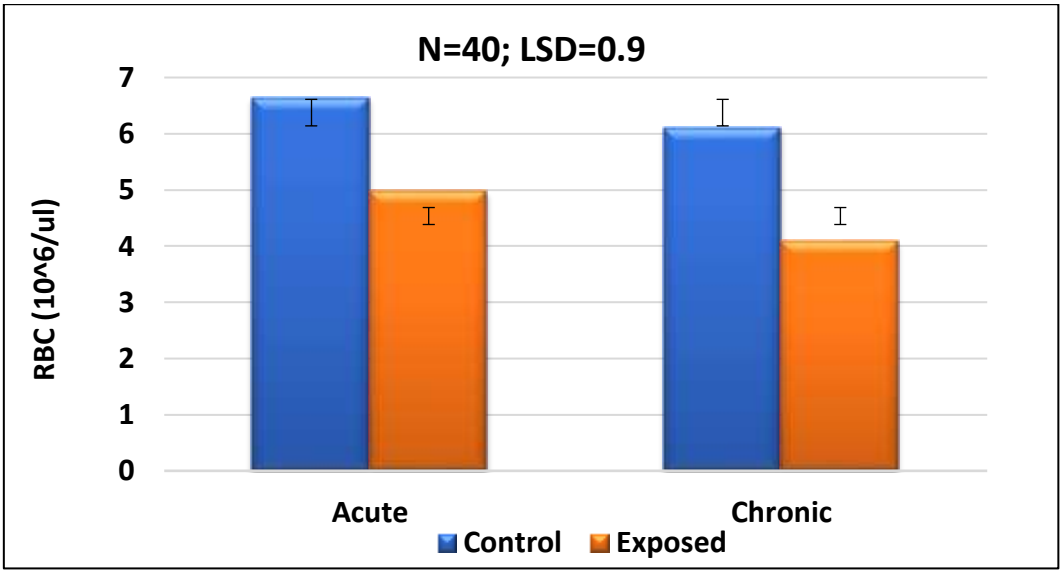

Fig. 6: Comparison of RBC in Control vs. Exposed Groups.

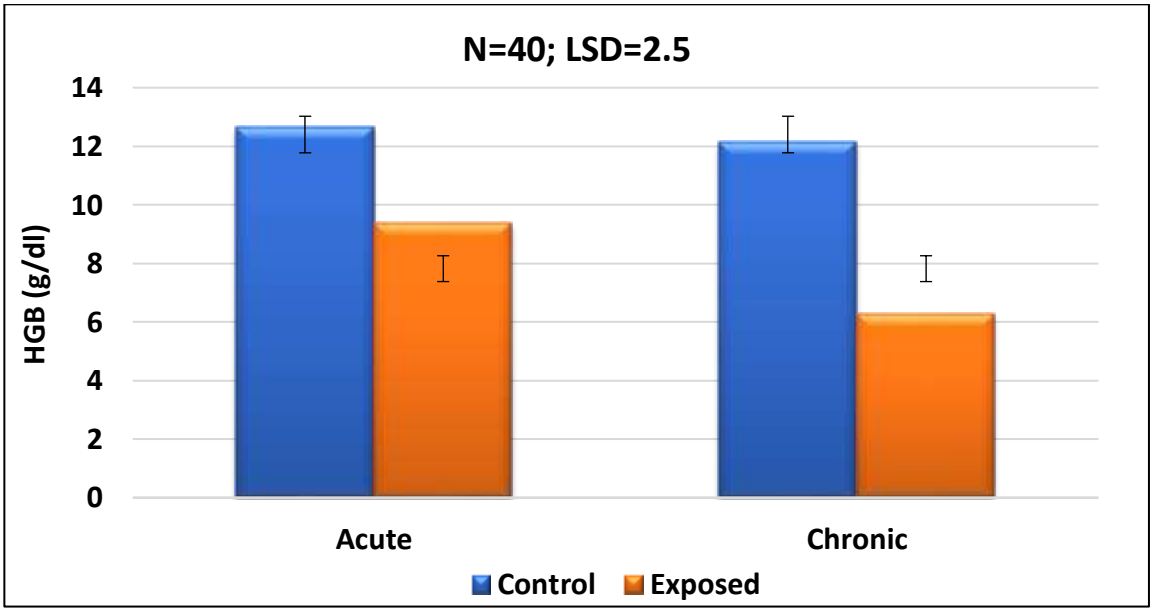

Fig. 7: Comparison of HGB in Control vs. Exposed Groups**.**

The observed increase in white blood cell counts suggests an immunological response likely triggered by oxidative and inflammatory stress induced by nano polystyrene exposure (Dey Chowdhury et al. 2025). Conversely, the significant reductions in RBC and hemoglobin levels point toward the development of anemia, potentially resulting from oxidative damage to erythrocytes or impaired erythropoiesis. The simultaneous elevation in WBCs and suppression of RBC and Hb levels reflect a dual hematological stress response, characterized by immune activation and reduced oxygen-carrying capacity (Spinelli et al., 2025). This hematological profile, marked by leukocytosis alongside anemia, highlights the compound effects of immune and oxidative stress on the body's homeostasis, particularly under chronic exposure conditions. These findings underscore the importance of monitoring both immune and red cell parameters in early toxicological assessments, as they serve as integrative markers of systemic physiological stress.

A study by Abdel-Zaher et al. (2023) investigated the hemotoxic properties of polyethylene microplastics (MPs) in murine models. They found that MP concentrations of 60 µg/ml and 600 µg/ml significantly affected red blood cells (RBCs), and hemoglobin (Hbs), with statistical significance ($p < 0.05$). Even during recovery periods, these hematological parameters, including RBCs, HCT, and Hbs, remained sensitive to MP exposure at both concentrations. Compared to control and 6 µg/ml MP groups, mice exposed to MPs exhibited notable differences in their hematological profiles. While significant changes in red blood cells and HCT were observed post-recovery, other hematological parameters did not show substantial alterations. These findings suggest that individual variations among the subjects might influence the observed effects, and importantly, the study indicated that MP concentration is a critical factor in determining adverse effects, with a 15-day recovery period positively impacting hematological parameter improvement.

In a separate preliminary study, Sun et al. (2021) assessed the impact of micro polystyrene on hematological parameters and gene expression in mice. This study revealed that polystyrene microparticles (MPs) adversely affect white blood cell populations, encompassing monocytes, lymphocytes, neutrophils, eosinophils, and basophils. This could potentially weaken the immune system and lead to broader health issues. The observed harmful effects included DNA damage, altered cytokine expression, heightened oxidative stress, changes in immune responses, modifications in antigen processing pathways, and degranulation, all contributing to inflammatory and stress responses. A significant reduction in leukocyte counts was specifically noted in C57BL/6 mice exposed to 0.5 mg of 5 µm PSMP, reinforcing the established detrimental effects.

3.3 Oxidative Stress Test

The provided figures (8,9,10) illustrate the impact of acute and chronic exposure on key biochemical markers: Catalase (CAT) activity, Superoxide Dismutase (SOD) activity, and Malondialdehyde (MDA) levels, comparing exposed groups to control groups. In the acute phase, CAT activity in the exposed group (78.286 µmol min^{-1} mg^{-1} protein) was elevated compared to the control (63.7317µmol min^{-1} mg^{-1} protein), suggesting an initial compensatory response to oxidative stress. However, under chronic exposure, CAT activity in the exposed group (55.367 µmol min^{-1} mg^{-1} protein) significantly declined below the control (68.362µmol min^{-1} mg^{-1} protein), indicating a potential depletion or impairment of this antioxidant enzyme over time. SOD activity consistently showed a decrease in the exposed groups for both acute (0.166 Unit/ml vs. control 0.2181 Unit/ml) and chronic (0.0944 Unit/ml vs. control 0.201 Unit/ml) exposures, with the chronic reduction being more pronounced, suggesting a sustained suppression of this critical antioxidant defense. Conversely, MDA levels, an indicator of lipid peroxidation and oxidative damage, were markedly increased in the exposed groups under both acute (35.0054 µmol/l vs. control 17.034 µmol/l) and chronic (24.759 µmol/l vs. control 15.29µmol/l) conditions. This consistent elevation of MDA strongly implies that the exposure leads to significant oxidative stress and cellular damage, with the initial antioxidant responses (like the acute CAT increase) seemingly insufficient to counteract the damage, especially during prolonged exposure when key antioxidant enzymes like SOD and CAT are compromised.

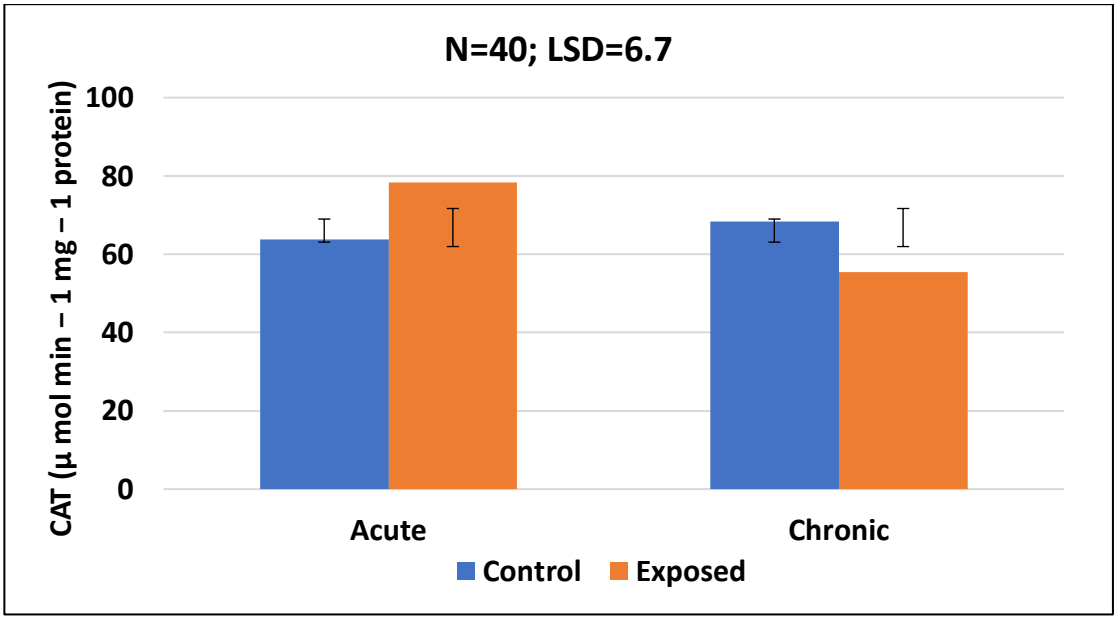

Fig. 8: CAT Activity in Exposed vs. Control Groups

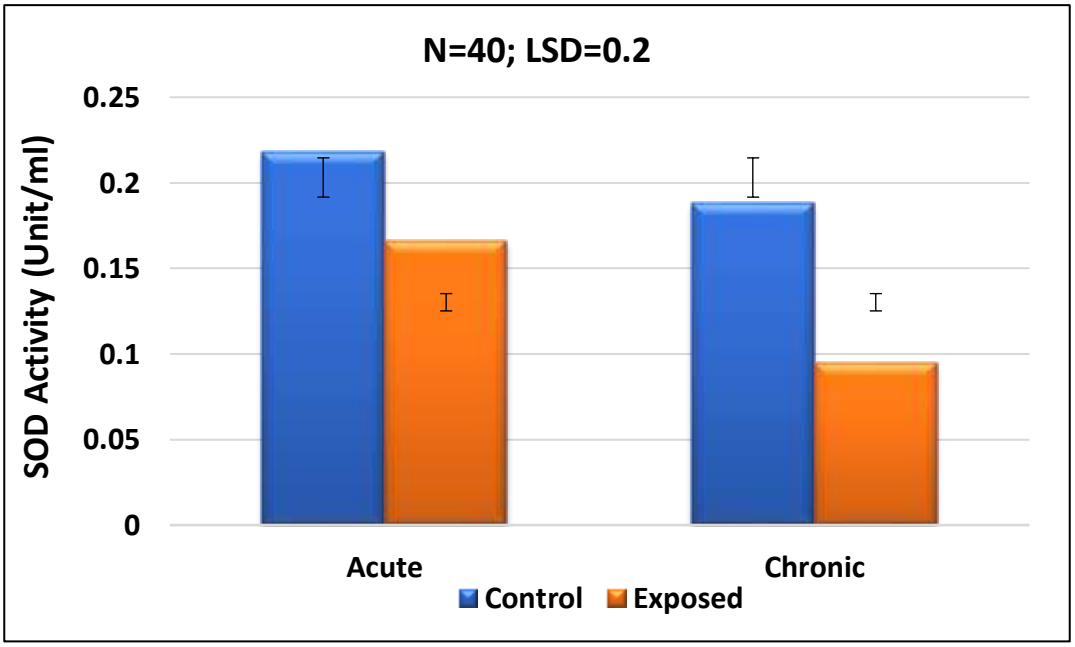

Fig. 9: SOD Activity in Exposed vs. Control Groups.

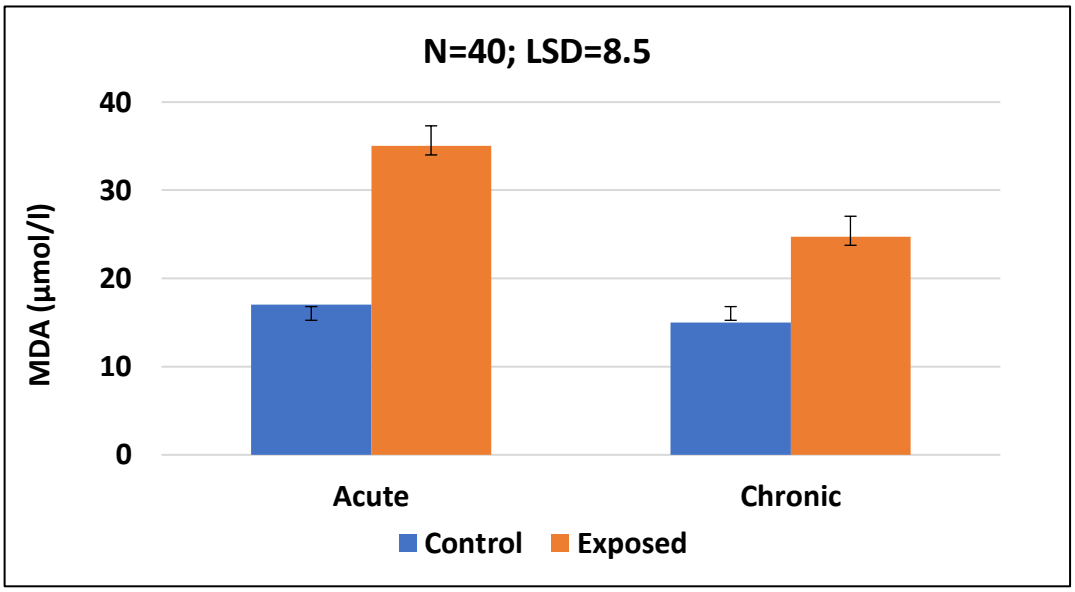

Fig. 10: MDA Activity in Exposed vs. Control Groups.

In both acute and chronic exposures to nano-polystyrene, oxidative stress markers demonstrated pronounced dysregulation. Catalase (CAT) activity and malondialdehyde (MDA) levels were significantly elevated, reflecting an adaptive response to excessive hydrogen peroxide generation and increased lipid peroxidation within cell membranes. The rise in MDA further indicates that nano polystyrene particles induce oxidative damage by promoting the breakdown of polyunsaturated fatty acids, leading to structural alterations in cellular and subcellular membranes (Bovolin et al. 2023). Conversely, superoxide dismutase (SOD) activity was reduced, suggesting that prolonged or excessive production of superoxide anions overwhelmed this primary line of antioxidant defense. The decline in SOD may result from direct interaction of nano polystyrene with the enzyme, depletion of essential cofactors, or oxidative modification that impairs its activity (Babaei et al. 2022). Together, these changes highlight that nano polystyrene exposure disrupts the delicate balance between pro-oxidants and antioxidants, driving cells toward a state of oxidative stress. This imbalance not only compromises redox homeostasis but may also trigger downstream consequences such as mitochondrial dysfunction, protein oxidation, and DNA damage, ultimately contributing to systemic toxicity in both acute and chronic conditions (Patel et al. 2024).

Overall, these results indicate that the exposure, whether acute or chronic, induces significant oxidative stress, leading to cellular damage. While there might be an initial compensatory antioxidant response (increased CAT acutely), prolonged exposure appears to overwhelm and eventually deplete the antioxidant defense mechanisms (decreased SOD and chronically decreased CAT), leading to persistent and detrimental lipid peroxidation.

This investigation is consistent with the observations made by Hou et al. (2021), who analyzed the impact of micro polystyrene on the initiation of pyroptosis and apoptosis in ovarian granulosa cells of rodent models,

specifically through the NLRP3/Caspase-1 signaling pathway. Their longitudinal study, spanning 90 days, involved 32 healthy female Wistar rats subjected to diverse concentrations of 0.5 μm PS microplastics dispersed in deionized water. These results substantiated that the presence of nanoparticles heightened MDA concentrations while undermining the organism's antioxidant defenses. As a result, the research concluded that PS microplastics instigated oxidative stress in the rats, resulting in reduced antioxidant capacity and subsequent oxidative injury (Li et al. 2020; Wang et al. 2020).

These antioxidant enzymes function as pivotal biomarkers for evaluating initial oxidative damage incurred due to exogenous agents. It has been recorded that SOD levels, while CAT activity fell in mice that were exposed to microplastics (Deng et al. 2017). In addition, numerous studies have highlighted the changes in the antioxidant capabilities of aquatic species due to exposure to microplastics. (Xie et al. 2020). The infusion of microplastics into the biological design of an organism may result in the emergence of Reactive Oxygen Species (ROS), initiating an immune response that later releases these compounds (Das, 2023). The relationship between oxidative stress and inflammation is deeply rooted, and microplastics may incite tissue inflammation in areas of their buildup. The inflammatory mechanisms in question may cause the emergence of reactive oxygen species (ROS) and the activation of pathways linked to oxidative stress (Hu and Palic, 2020). The unique pathways that are activated and the level of oxidative stress provoked by microplastics may fluctuate based on different variables like plastic type, particle size, exposure time, and the physiological responses of the organism impacted (Solomando et al. 2020).

4. CONCLUSION

The findings of this study reveal that nano-polystyrene (NPS) has a significant potential to induce alterations in hematological parameters. Acute exposure led to an increase in white blood cell (WBC) count, suggesting an immune or inflammatory response. Conversely, red blood cell (RBC) and hemoglobin (Hb) levels were found to decrease in the subjects under investigation, indicating a potential risk for the development of anemia. Chronic exposure resulted in even more pronounced elevations in WBC counts, along with further reductions in RBC and Hb concentrations. Together, the hematological alterations observed in this study not only signal immune and inflammatory stress but also raise concern for anemia-related complications. These parameters thus serve as critical biomarkers for evaluating the systemic impact of nano-polystyrene exposure. Evidence of oxidative stress was apparent, the early and consistent alterations in oxidative stress biomarkers, particularly elevated malondialdehyde levels and suppressed antioxidant enzyme activities, positioning them as valuable early warning indicators. Their responsiveness to both acute and chronic exposure makes them crucial tools for preemptive toxicological screening and risk assessment in environments where nano-polystyrene and similar agents are present. This decrease in antioxidant enzyme levels suggests an acceleration of the apoptotic process, which may ultimately lead to necrosis. Behavioral and physiological changes were observed in the exposed rats, including reduced appetite, weight loss, alopecia, prolonged sleep duration, changes in fecal coloration, lethargy, and increased aggression effects, which were especially prominent in the chronic exposure group. Future

studies should focus on longer-term and environmentally relevant exposures, including chronic low-dose regimens and recovery groups, to better assess cumulative and delayed effects. Comparative assessments of different nanoplastic types, sizes, and shapes were recommended, with rigorous physicochemical characterization. The inclusion of both sexes will help identify sex-specific responses, while expanding endpoints to histopathology, oxidative stress, inflammation, genotoxicity, and molecular pathways will provide broader toxicological insight.

5. PATENTS

There are no patents resulting from the work reported in this manuscript.

Author Contributions: Hamza Jasim Albazoni: Writing – review and editing, Writing–original draft, Methodology, Conceptualization. Mohammed Jawad Salih Al-Haidarey and Afyaa Sabah Nasir: Writing–review and editing, Supervision.

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REFERENCES

1. Abdelkareem, S.T., Elemam, Y.A., Subaih, R.A., Elhefnawy, H.I., Saada, M.A. and Hassabo, A.G., 2025. Safety polymers for food packaging. *Journal of Textiles, Coloration and Polymer Science*, *22*(1), pp.355-370.10.21608/jtcps.2024.259207.1291
2. Abdel-Zaher, S., Mohamed, M. S., Sayed, A. E. D. H., 2023. Hemotoxic effects of polyethylene microplastics on mice. *Frontiers in Physiology*., 14, pp.1072797. https://doi.org/10.3389/fphys.2023.1072797.
3. Albazoni, H. J., Al-Haidarey, M. J. S., Nasir, A. S. 2024. A Review of Microplastic Pollution: Harmful Effect on Environment and Animals, Remediation Strategies. Journal of Ecological Engineering, 25(2), 140-157. https://doi.org/10.12911/22998993/176802.
4. Babaei, A. A., Rafiee, M., Khodagholi, F., Ahmadpour, E., and Amereh, F. 2022. Nanoplastics-induced oxidative stress, antioxidant defense, and physiological response in exposed Wistar albino rats. *Environmental Science and Pollution Research*, *29*(8), 11332-11344. https://doi.org/10.1007/s11356-021-15920-0.
5. Bovolin, P., Saraceni, A., Cottone, E., Mognetti, B., Gallo, M. P., Merlo, G., and Dal Bello, F. 2023. Microplastics and associated contaminants: Potential impact on cells and developing organisms. *EUROPEAN JOURNAL OF HISTOCHEMISTRY*, *67*(s2), 5-5.*https://dx.doi.org/10.4081/ejh.2023.3804*
6. Carney Almroth, B. M., Åström, L., Roslund, S., Petersson, H., Johansson, M., Persson, N. K., 2018. Quantifying shedding of synthetic fibers from textiles; a source of microplastics released into the environment. Environmental Science and Pollution Research., 25, pp.1191–1199. https://doi.org/10.1007/s11356-017-0528-710.1007/s11356-017-0528-7
7. Couto, M., Cates, C., 2019. Laboratory guidelines for animal care. In: Vertebrate Embryogenesis: Embryological, Cellular, and Genetic Methods, pp.407–430.10.1007/978-1-4939-9009-2_25
8. Das, A., 2023. The emerging role of microplastics in systemic toxicity: involvement of reactive oxygen species (ROS). *Science of The Total Environment* ., 879, pp.165076. https://doi.org/ 10.1016/j.scitotenv.2023.165076

9. Deng, Y., Zhang, Y., Lemos, B., Ren, H., 2017. Tissue accumulation of microplastics in mice and biomarker responses suggest widespread health risks of exposure. *Scientific Reports*., 7(1), pp.46687. https://doi.org/10.1038/srep46687
10. Dey Chowdhury, S., Mishra, S. K., Bhunia, P., Surampalli, R. Y., and Zhang, T. C. 2025. Human Exposures to Microplastics: Impact of Different Routes. *Microplastics in the Environment: Fate, Impacts, Removal, and Management*, 347-381. https://doi.org/10.1002/9781394251100.ch13.
11. Ghosh, S., Sinha, J. K., Ghosh, S., Vashisth, K., Han, S., Bhaskar, R., 2023. Microplastics as an emerging threat to the global environment and human health. *Sustainability*, 15(14), pp.10821. https://doi.org/10.3390/su151410821
12. Hou, J., Lei, Z., Cui, L., Hou, Y., Yang, L., An, R., Zhang, L., 2021. Polystyrene microplastics lead to pyroptosis and apoptosis of ovarian granulosa cells via NLRP3/Caspase-1 signaling pathway in rats. *Ecotoxicology and Environmental Safety*., 212, pp.112012. https://doi.org/10.1016/j.ecoenv.2021.112012
13. Howard, R., Al-Mayhani, T., Carr, A., Leff, A., Morrow, J., and Rossor, A. 2024. Toxic, metabolic and physical insults to the nervous system. *Neurology: a Queen Square textbook*, 903-943. https://doi.org/10.1002/9781119715672.ch26.
14. Hu, M., Palić, D., 2020. Micro-and nano-plastics activation of oxidative and inflammatory adverse outcome pathways. *Redox Biology* ., 37, pp.101620. https://doi.org/10.1016/j.redox.2020.101620
15. Jassim, A. K., 2023. Effect of microplastic on the human health. IntechOpen. https://doi.org/10.5772/intechopen.107149
16. Kelpsiene, E., Ekvall, M. T., Lundqvist, M., Torstensson, O., Hua, J., and Cedervall, T. 2022. Review of ecotoxicological studies of widely used polystyrene nanoparticles. *Environmental Science: Processes & Impacts*, *24*(1), 8-1. https://doi.org/10.1039/D1EM00375E
17. Li, B., Ding, Y., Cheng, X., Sheng, D., Xu, Z., Rong, Q., Zhang, Y., 2020. Polyethylene microplastics affect the distribution of gut microbiota and inflammation development in mice. *Chemosphere*, 244, pp.125492. https://doi.org/10.1016/j.chemosphere.2019.125492
18. Liu, P., Zhan, X., Wu, X., Li, J., Wang, H., Gao, S., 2020. Effect of weathering on environmental behavior of microplastics: properties, sorption and potential risks. *Chemosphere*, 242, pp.125193. https://doi.org/10.1016/j.chemosphere.2019.1251931
19. Nader, E., Skinner, S., Romana, M., Fort, R., Lemonne, N., Guillot, N., Connes, P., 2019. Blood rheology: key parameters, impact on blood flow, role in sickle cell disease and effects of exercise. *Frontiers in Physiology*., 10, pp.1329. https://doi.org/10.3389/fphys.2019.01329
20. Patel, K. D., Keskin-Erdogan, Z., Sawadkar, P., Sharifulden, N. S. A. N., Shannon, M. R., Patel, M., and Kim, H. W. 2024. Oxidative stress modulating nanomaterials and their biochemical roles in nanomedicine. *Nanoscale horizons*, *9*(10), 1630-1682.https://doi.org/10.1039/D4NH00171K**.**
21. Prokic, M. D., Petrovic, T. G., Gavric, J. P., Despotovic, S. G., Gavrilovic, B. R., Radovanovic, T. B., Saičic, Z. S., 2018. Comparative assessment of the antioxidative defense system in subadult and adult anurans: a lesson from the Bufotes viridis toad. *Zoology*, 130, pp.30–37. https://doi.org/10.1016/j.zool.2018.09.004
22. Prust, M., Meijer, J., Westerink, R. H., 2020. The plastic brain: neurotoxicity of micro-and nanoplastics. Particle and Fibre Toxicology., 17(1), pp.1–16. https://doi.org/10.1186/s12989-020-00358-y

23. Samawi, M.F. and Werorilangi, S., 2024. Characteristics, Abundance and Polymer Type of Microplastics in Anadara granosa (Blood Clam) from Coastal Area of Palopo City. *Nature Environment and Pollution Technology,* 23(3), pp.1589-1596. https://doi.org/10.46488/NEPT.2024.v23i03.028
24. Solomando, A., Capó, X., Alomar, C., Álvarez, E., Compa, M., Valencia, J. M., Sureda, A., 2020. Long-term exposure to microplastics induces oxidative stress and pro-inflammatory response in the gut of Sparus aurata Linnaeus, 1758. *Environmental Pollution*., 266, pp.115295. https://doi.org/10.1016/j.envpol.2020.115295
25. Spinelli, S., Marino, A., Remigante, A., and Morabito, R. 2025. Redox Homeostasis in Red Blood Cells: From Molecular Mechanisms to Antioxidant Strategies. *Current Issues in Molecular Biology*, *47*(8), 655.https://doi.org/10.3390/cimb47080655.
26. Sulistyorini, L., Arfiani, N.D., Rizaldi, M.A., Lutpiatina, L. and Samad, N.I.A., 2024. Assessment of Microplastic Pollution in Fresh Fish and Pindang Fish and its Potential Health Hazards in Coastal Communities of Banyuwangi Regency, Indonesia. *Nature Environment & Pollution Technology*, 23(3). https://doi.org/10.46488/NEPT.2024.v23i03.038
27. Sun, R., Xu, K., Yu, L., Pu, Y., Xiong, F., He, Y., Pu, Y., 2021. Preliminary study on impacts of polystyrene microplastics on the hematological system and gene expression in bone marrow cells of mice. *Ecotoxicology and Environmental Safety.,* 218, pp.112296. https://doi.org/10.1016/j.ecoenv.2021.112296
28. Sweetser, S. 2022. Gastrointestinal manifestations of systemic diseases. *Yamada's Textbook of Gastroenterology*, 2231-2273. https://doi.org/10.1002/9781119600206.ch111.
29. Varo, I., Perini, A., Torreblanca, A., Garcia, Y., Bergami, E., Vannuccini, M. L., Corsi, I., 2019. Time-dependent effects of polystyrene nanoparticles in brine shrimp Artemia franciscana at physiological, biochemical and molecular levels. *Science of The Total Environment*., 675, pp.570–580. https://doi.org/10.1016/j.scitotenv.2019.04.215
30. Vohl, S., Kristl, M., and Stergar, J. 2024. Harnessing Magnetic Nanoparticles for the Effective Removal of Micro- and Nanoplastics: A Critical Review. *Nanomaterials*, *14*(14), 1179. https://doi.org/10.3390/nano14141179
31. Wang, S. Y., Ni, X., Hu, K. Q., Meng, F. L., Li, M., Ma, X. L., Su, G. H., 2020. Cilostazol alleviate nicotine induced cardiomyocytes hypertrophy through modulation of autophagy by CTSB/ROS/p38MAPK/JNK feedback loop. *International Journal of Biological Sciences*., 16(11), pp.2001–2016. https://doi.org/10.7150/ijbs.42305
32. Wang, Y. L., Lee, Y. H., Chiu, I. J., Lin, Y. F., Chiu, H. W., 2020. Potent impact of plastic nanomaterials and micromaterials on the food chain and human health. *International Journal of Molecular Sciences*. 21(5), pp.172. https://doi.org/ 10.3390/ijms21050172
33. Wu, D., Wang, T., Wang J., Jiang L., Yin Y., Guo H., 2021. Size-dependent toxic effects of polystyrene microplastic exposure on Microcystis aeruginosa growth and microcystin production. *Science of The Total Environment*., 761, pp.143265. https://doi.org/10.1016/j.scitotenv.2020.143265
34. Xie, X., Deng, T., Duan, J., Xie, J., Yuan, J., Chen, M., 2020. Exposure to polystyrene microplastics causes reproductive toxicity through oxidative stress and activation of the p38 MAPK signaling pathway. *Ecotoxicology and Environmental Safety.,* 190, pp.110133. https://doi.org/10.1016/j.ecoenv.2019.110133