

Impact of Micro and Nanoplastics on Inflammatory and Antioxidant Gene Expression in the Gastrointestinal System

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Micro and Nanoplastics (MNPs) are emerging contaminants characterized by particle sizes smaller than 5 mm and less than 1 μ m, respectively ¹. Microplastics (MPs) are categorized into primary and secondary sources of origin ². Primary MPs are intentionally produced as tiny particles, such as microbeads, in personal care products. Secondary MPs are generated when larger plastic materials degrade owing to factors such as sunlight exposure, biological interactions, mechanical forces, and various environmental conditions ^{3, 4}. MNPs are present in a wide range of ecosystems and affect both marine and terrestrial organisms. They can disrupt the feeding patterns, development, and reproductive processes of various organisms ^{5, 6}. Moreover, MPs can carry harmful pollutants, such as toxic chemicals ⁷ and antibiotic-resistant bacteria ⁸, thereby amplifying their negative effects on the environment ⁹. Recent studies have highlighted concerns regarding the presence of MPs in human tissues and bodily fluids ¹⁰. Studies have revealed that MPs are present in various human organ

systems, including the cardiovascular, digestive, respiratory, and reproductive systems ¹¹. Additionally, they have been identified in biological samples such as breast milk, urine, stool, and blood ^{12, 13}. Moreover, MNPs have been detected in a diverse range of food products, including fruits, vegetables, seafood, livestock (such as chicken), and drinking water. MPs contamination has been found in various food products, including beer, honey, sugar, cow's milk, and sea salt. Additionally, more than 220 marine species, such as mussels, oysters, clams, and shrimp, have been reported to contain these particles in their gastrointestinal tracts, making their way into numerous seafood products ^{14, 15}. Therefore, upon ingestion, MNPs interact directly with the intestinal epithelium and are exposed to the local immune system, gut microbiota, and inflammatory bowel disease (IBD)¹⁶. IBD, which includes Crohn's disease and ulcerative colitis, affects over 6.8 million people globally, with cases in China projected to exceed 1.5 million by 2025 ¹⁷. Patients with IBD, with their compromised

intestinal microenvironment, are particularly vulnerable to environmental particulate matter, such as MNPs, which can exacerbate intestinal damage¹⁸. An in vivo study on mice exposed to MNPs (10–150 µm) at concentrations of 2, 20, and 200 µg/g over five weeks revealed an increase in gut microbial species, bacterial abundance, and flora diversity, along with enhanced secretion of proinflammatory cytokines¹⁹. These interactions can have significant biological consequences, particularly through the modulation of gene expression²⁰. Evidence indicates that exposure to MNPs disrupts the regulation of genes related to inflammation, oxidative stress, and gut barrier integrity, raising concerns about their potential effects on human health^{21, 22}. An initial study found that oral exposure to MNPs disturbs redox balance and activates the TLR4/NF-κB inflammatory signaling pathway in the intestines of mice. Consequently, this results in oxidative stress, inflammation, and intestinal epithelial cell apoptosis through the mitochondrial pathway, leading to intestinal barrier impairment, mucosal damage, and intestinal toxicity²³.

Inflammatory Gene Expression

Studies have demonstrated that MNPs can cause inflammatory damage in various murine organs through the TLRs/MyD88/NF-κB signaling pathway in in vivo models²⁴. Prior studies have suggested that MNPs may play a significant role in initiating inflammatory gene expression following activation of endogenous molecules released from damaged cells by contributing to intestinal dysbiosis and inflammation triggered by the activation of the Toll-like receptor 4 (TLR4) signaling pathway¹⁹. TLR4, a crucial component of the innate immune system^{25, 26}. Once activated, TLR4 triggers two primary signaling pathways: MyD88-dependent and TRIF-dependent pathways, with the MyD88-dependent pathway mainly activating NF-κB. This activation promotes the production of pro-inflammatory cytokines, such as IL-6, TNF-α, and IL-1β, as well as chemokines that help recruit immune cells to sites of infection or injury^{27, 28}. Inflammatory processes contribute

to tissue damage and disease progression in the body.

In addition to their inflammatory effects, MNPs, such as polystyrene MNPs (PS-MNPs), exhibit significant cytotoxicity, even at the lowest tested concentrations. PS-MNPs increase apoptotic cell counts and reduce cell viability²⁹. They also disrupt molecular markers, as indicated by elevated levels of LDH, ALT, and AST activity in the supernatants, along with reduced GST activity and SOD and GSH levels in liver organoids^{30, 31}. Elevated MDA levels further confirmed oxidative stress induced by PS-MNPs. Additionally, PS-MNPs caused lipid buildup, reduced ATP production, elevated ROS levels, and the release of proinflammatory markers, such as IL-6 and COL1A1. These effects are further intensified by increased hepatic CYP2E1 and HNF4A expression, which heightens the risk of fibrosis and steatosis. These findings highlight the potential of MNPs to disrupt cellular and molecular homeostasis and trigger inflammation and oxidative stress, which may exacerbate underlying health conditions²⁹.

Antioxidant Gene Expression

MNPs can produce reactive oxygen species, causing cellular damage and disturbing cellular balance upon ingestion^{30, 31}. In the gut, oxidative stress plays a crucial role in the activation of antioxidant defense mechanisms, particularly through the Nrf2 (Nuclear factor erythroid 2-related factor 2) pathway³². Under oxidative conditions, Nrf2 is activated and moves to the nucleus, where it attaches to antioxidant response elements³³ in the promoters of antioxidant genes. These genes include those encoding enzymes such as glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase, which work together to neutralize ROS and protect cells from oxidative damage³⁴. However, the capacity of the gut to mount an adequate antioxidant response to MNP-induced oxidative stress may be insufficient, especially after prolonged or high-level exposure to these particles³⁵.

In addition to their direct effects on cellular

antioxidant systems, MNPs can alter gut microbiota, further influencing oxidative stress and inflammation. MNP-induced dysbiosis can lead to an imbalance in gut bacteria, which may exacerbate oxidative stress and disrupt the regulation of antioxidant gene expression²². Changes in the microbiome may also affect the production of proinflammatory cytokines, thereby modulating the activation of antioxidant pathways³⁶. The cumulative effect of these disruptions can impair the gut defense mechanisms, potentially contributing to the development of gastrointestinal disorders, such as IBD, colorectal cancer, and other diseases associated with chronic inflammation and oxidative stress³⁷.

MNPs pose a significant threat to gastrointestinal health by interfering with the expression of important genes related to inflammation and oxidative stress. Comprehending these molecular interactions is essential for developing approaches to reduce harmful effects and protect human health.

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References

- Bai C-L, Wang D, Luan Y-L, et al. A review on micro- and nanoplastics in humans: implication for their translocation of barriers and potential health effects. *Chemosphere*. 2024;361:142424.
- Catarino AI, Macchia V, Sanderson WG, et al. Low levels of MicroPlastics (MP) in wild mussels indicate that MP ingestion by humans is minimal compared to exposure via household fibres fallout during a meal. *Environmental pollution*. 2018;237:675-84.
- Ziani K, Ioniță-Mândrican CB, Mititelu M, et al. Microplastics: a real global threat for environment and food safety: a state of the art review. *Nutrients*. 2023;15(3):617.
- Ranjdoost F, Abbasi S, Asadi-Ghahhari M, et al. On the nature and sources of MicroPlastics (MPs) and MicroRubbers (MRs) in urban snow. *J Environ Manage*. 2024;370:122851.
- de Souza Machado AA, Kloas W, Zarfl C, et al. Microplastics as an emerging threat to terrestrial ecosystems. *Glob Chang Biol*. 2018;24(4):1405-16.
- Rezaei Rahimi N, Fouladi-Fard R, Rezvani Ghalhari M, et al. The links between microclimatic and particulate matter concentration in a multi-storey car parking: a case study Iran. *J Environ Health Sci Eng*. 2022;20(2):775-83.
- Vithanage M, Ramanayaka S, Hasinthara S, et al. Compost as a carrier for microplastics and plastic-bound toxic metals into agroecosystems. *Curr Opin Environ Sci Health*. 2021;24:100297.
- Liu Y, Liu W, Yang X, et al. Microplastics are a hotspot for antibiotic resistance genes: progress and perspective. *Science of the Total Environment*. 2021;773:145643.
- Amobonye A, Bhagwat P, Raveendran S, et al. Environmental impacts of microplastics and nanoplastics: a current overview. *Front Microbiol*. 2021;12:768297.
- Barceló D, Picó Y, Alfarhan AH. Microplastics: detection in human samples, cell line studies, and health impacts. *Environ Toxicol Pharmacol*. 2023: 104204.
- Jenner LC, Rotchell JM, Bennett RT, et al. Detection of microplastics in human lung tissue using μ FTIR spectroscopy. *Science of the Total Environment*. 2022;831:154907.
- Rotchell JM, Jenner LC, Chapman E, et al. Detection of microplastics in human saphenous vein tissue using μ FTIR: a pilot study. *PLoS One*. 2023; 18(2): e0280594.
- Schwabl P, Köppel S, Königshofer P, et al. Detection of various microplastics in human stool: a prospective case series. *Ann Intern Med*. 2019;171(7):453-7.
- Zhang Y, Wang S, Olga V, et al. The potential effects of microplastic pollution on human digestive tract cells. *Chemosphere*. 2022;291:132714.
- Covello C, Di Vincenzo F, Cammarota G, et al. Micro(nano)plastics and their potential impact on human gut health: a narrative review. *Curr Issues Mol Biol*. 2024;46(3):2658-77.
- Li W, Chen X, Li M, et al. Microplastics as an aquatic pollutant affect gut microbiota within aquatic animals. *J Hazard Mater*. 2022;423: 127094.
- Hu L, Zhao Y, Xu H. Trojan horse in the intestine: a review on the biotoxicity of microplastics combined environmental contaminants. *J Hazard Mater*. 2022;439:129652.
- Zhao Y, Liu S, Xu H. Effects of microplastic and

- engineered nanomaterials on inflammatory bowel disease: a review. *Chemosphere*. 2023;326:138486.
19. Ali N, Katsouli J, Marczylo EL, et al. The potential impacts of micro-and-nano plastics on various organ systems in humans. *EBioMedicine*. 2024;99:104901.
 20. Cheng J, Meistertzheim A-L, Leistschneider D, et al. Impacts of microplastics and the associated plastisphere on physiological, biochemical, genetic expression and gut microbiota of the filter-feeder amphioxus. *Environ Int*. 2023;172: 107750.
 21. Wang X, Jian S, Zhang S, et al. Enrichment of polystyrene microplastics induces histological damage, oxidative stress, Keap1-Nrf2 signaling pathway-related gene expression in loach juveniles (*Paramisgurnus dabryanus*). *Ecotoxicol Environ Saf*. 2022;237:113540.
 22. Hu Y, Lin S, Tang J, et al. Effects of microplastics and lead exposure on gut oxidative stress and intestinal inflammation in common carp (*Cyprinus carpio* L.). *Environmental Pollution*. 2023;327: 121528.
 23. Jia R, Han J, Liu X, et al. Exposure to polypropylene microplastics via oral ingestion induces colonic apoptosis and intestinal barrier damage through oxidative stress and inflammation in mice. *Toxics*. 2023;11(2):127.
 24. Xia Q, Wei Y, Hu L-j, et al. Inhalation of microplastics induces inflammatory injuries in multiple murine organs via the toll-like receptor pathway. *Environ Sci Technol*. 2024;58(42):18603-18.
 25. Haynes LM, Moore DD, Kurt-Jones EA, et al. Involvement of toll-like receptor 4 in innate immunity to respiratory syncytial virus. *J Virol*. 2001;75(22): 10730-7.
 26. Peri F, Piazza M. Therapeutic targeting of innate immunity with Toll-like receptor 4 (TLR4) antagonists. *Biotechnol Adv*. 2012;30(1): 251-60.
 27. Duan T, Du Y, Xing C, et al. Toll-like receptor signaling and its role in cell-mediated immunity. *Front Immunol*. 2022;13:812774.
 28. Xia Q, Wei Y, Hu L-j, et al. Inhalation of microplastics induces inflammatory injuries in multiple murine organs via the toll-like receptor pathway. *Environ Sci Technol*. 2024;58(42):18603-18.
 29. Cheng W, Li X, Zhou Y, et al. Polystyrene microplastics induce hepatotoxicity and disrupt lipid metabolism in the liver organoids. *Science of The Total Environment*. 2022;806:150328.
 30. Barboza LGA, Vieira LR, Branco V, et al. Microplastics increase mercury bioconcentration in gills and bioaccumulation in the liver, and cause oxidative stress and damage in *Dicentrarchus labrax* juveniles. *Sci Rep*. 2018;8(1):15655.
 31. Cheng W, Li X, Zhou Y, et al. Polystyrene microplastics induce hepatotoxicity and disrupt lipid metabolism in the liver organoids. *Sci Total Environ*. 2022;806(Pt 1):150328.
 32. Kadac-Czapska K, Oško J, Knez E, et al. Microplastics and oxidative stress-current problems and prospects. *Antioxidants (Basel)*. 2024;13(5):579.
 33. Tamargo A, Molinero N, Reinosa JJ, et al. PET microplastics affect human gut microbiota communities during simulated gastrointestinal digestion, first evidence of plausible polymer biodegradation during human digestion. *Sci Rep*. 2022;12(1):528.
 34. Ngo V, Duennwald ML. Nrf2 and oxidative stress: a general overview of mechanisms and implications in human disease. *Antioxidants (Basel)*. 2022;11(12): 2345.
 35. Wu H, Xu T, Chen T, et al. Oxidative stress mediated by the TLR4/NOX2 signalling axis is involved in polystyrene microplastic-induced uterine fibrosis in mice. *Science of the Total Environment*. 2022;838:155825.
 36. Liang B, Deng Y, Huang Y, et al. Fragile guts make fragile brains: intestinal epithelial Nrf2 deficiency exacerbates neurotoxicity induced by polystyrene nanoplastics. *ACS Nano*. 2024;18(35): 24044-59.
 37. He Y, Li Z, Xu T, et al. Polystyrene nanoplastics deteriorate LPS-modulated duodenal permeability and inflammation in mice via ROS driven-NF-κB/NLRP3 pathway. *Chemosphere*. 2022;307:135662.