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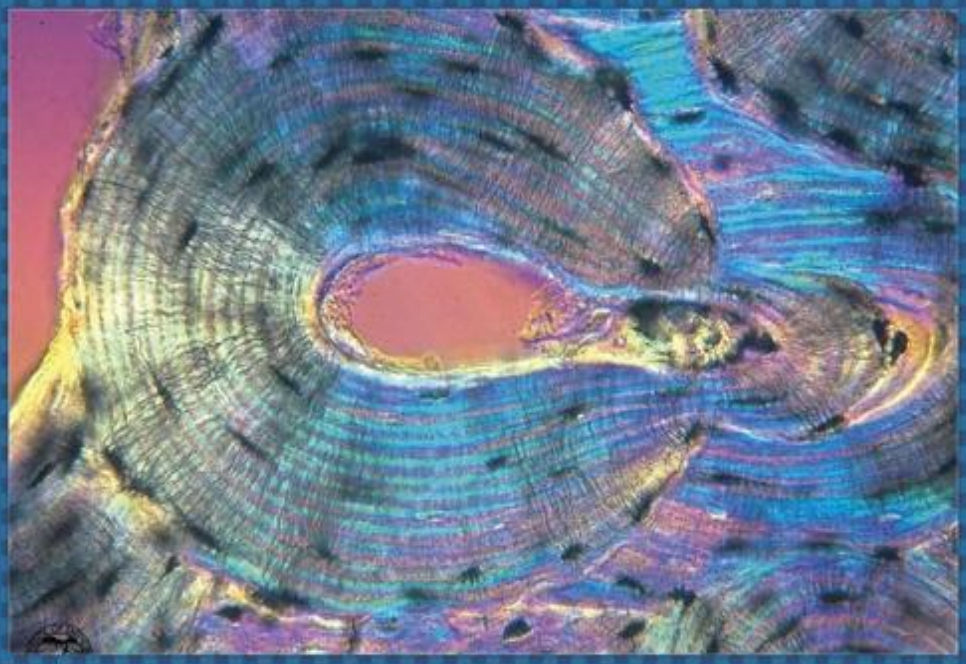

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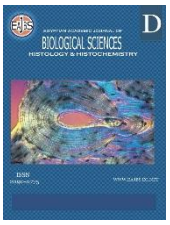

# Distribution and Tissue Damage After a Single Microplastic Exposure in Mice

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**ABSTRACT**

Microplastic (MP) is plastic particle smaller than five millimeters. As an emerging environmental pollutant, they can potentially harm human health, but direct evidence of MP particles entering the circulating blood, lungs, and brain is limited. This study aimed to provide an overview of MP distribution and tissue damage following a single MP exposure in mice. We performed short-term uptake studies, administering 200-nm fluorescent MPs to mice by gavage at a dose of 200 mg/kg body weight. The MP fluorescence intensity in the blood was measured using fluorescence imaging 1, 2, and 4 h after gavage, finding it to peak after 2 h. The distribution and tissue damage 2 h after MP gavage were investigated. Fluorescence imaging detected the highest MP fluorescence intensity in the digestive system, particularly the stomach and cecum, followed by the lungs and spleen. Histological examination showed mild congestion in the liver and lungs and a small number of shed epithelium cells in the stomach and cecum. Light microscopy detected MP particles in the stomach, cecum, lungs, kidneys, liver, spleen, and brain, providing direct evidence that MP particles enter the blood circulation and translocate to other tissues. These results are vital to understanding MP' acute toxicity and potential effects.

## INTRODUCTION

Plastic is one of the greatest inventions of the 20th century. It is mainly made of polyethylene, polypropylene, polyvinyl chloride, and polystyrene (Prüst *et al.,* 2020; Debnath *et al.*, 2024; Thompsom *et al.*, 2024; Liu *et al.*, 2025). The world produces 430 million metric tons of plastic annually, more than the total weight of all humans on Earth (Prüst *et al.,* 2020; Cole *et al.,* 2024; Liu *et al.,* 2025). It brings many benefits and conveniences to people, but it also brings potential harm because plastic is difficult to degrade and forms debris and pellets.

The British scholar Thompson RC first proposed the concept of 'microplastic' (MP) in 2004, referring to plastic fragments and particles smaller than five millimeters (Fournier *et al.*, 2020; Thompsom *et al.*, 2024; Liu *et al.*, 2025). Single-use plastic bags, bottles, and food packaging are easily broken into MPs or nano-scale particles (≤100 nm in diameter) under various chemical and physical conditions, including ultraviolet radiation, erosion, and sand abrasion (Sen *et al*., 2022; Alijagic *et al.,* 2024; Thompsom *et al.,* 2024).

Ordinary plastic, made from fossil fuels, takes centuries to degrade. Globally, most plastic products end up in landfills or are incinerated. Both processes produce MPs that are nearly impossible to remove from the air, ground, and water (Ziani *et al.*, 2023; Wei *et al.,* 2024; Liu *et al.*, 2025).

It can be imagined that MPs are so ubiquitous that they are absorbed by animals and plants everywhere all the time (Dovidat *et al.,* 2020; Liu *et al.*, 2025). Furthermore, plastics might contain toxic chemicals or act as vectors for contaminants, including heavy metals, pesticides, and even pathogens (Debnath *et al.,* 2024; Dar *et al.*, 2025; Liu *et al.,* 2025). These substances ultimately enter the human body through the food chain and accumulate in tissues, increasing the risk of cancer and damaging the human immune system (Turner *et al.,* 2020; Yang *et al.,* 2022; Dar *et al.,* 2025).

Researches in aquatic organisms have shown that MP can reduce oyster reproduction, affect energy storage in marine worms, cause toxicity to sea urchin embryos, induce oxidative stress and motility disorders in zebrafish, and cause lipid metabolism disorders, neurotoxicity, reproductive toxicity, and other effects in various aquatic organisms (Xie *et al.,* 2020; Jin *et al.*, 2021; Lee *et al.,* 2022; Debnath *et al.*, 2024; liu *et al.,* 2025 ). These findings increase the likelihood that exposure to MP might pose a threat to human health.

MPs are everywhere. In food production, processing, packaging, and storage, MPs easily mix into some foods, such as salt, sugar, bottled water, beer, and milk, and are ingested or inhaled into the body (Kutralam-Muniasamy *et al.*, 2020; Prüst *et al.,* 2020; Cole *et al.,* 2024; Martinchik *et al*., 2024). MPs have been detected in the human lungs, liver, blood, brain, placenta, breast milk, and feces (Antonio *et al.*, 2021; Sen *et al.,* 2022; Kopatz *et al.,* 2023; Cole *et al*., 2024; Wardani *et al.,* 2024). Some experiments have shown oxidative stress and cytotoxic effects caused by MPs to cultured human cerebral, epithelial, and astrocytoma cells (Jung *et al.,* 2020; Prüst *et al*., 2020); however, scientists are still unsure how these might affect the human body. Food safety agencies in some countries attempted to perform a risk assessment for MPs; however, detailed risk assessments are limited because exposure and effect data are insufficient (Yang *et al*., 2022; Kopatz *et al.,* 2023; Wardani *et al.,* 2024).

This study explored the time it takes for ingested MPs to enter the blood and reach peak levels and investigated the distribution and tissue damage after a single MP exposure in mice.

## MATERIALS AND METHODS

### Animals and Reagents:

Twelve female Kunming mice (5 weeks old, Specific Pathogen Free) were purchased from Beijing Vital River Laboratory Animal Technology Company. Red fluorescent-labeled polystyrene MPs with a diameter of 200 nm (λ excitation/emission 632/680 nm) suspensions (1.0% w/v, 10 mg/1 ml) were purchased from JUNYIJIA Scientific Corporation (Tianjing, China), stored at 4°C in the dark, and shaken gently before use.

All mice were given free access to sterile water and food and were kept in an isolated environment (12 h light/12 h dark; temperature 25 ± 2°C; humidity 55 ± 5 %). The mice were fasted for 12 h before exposure to MPs. All experimental procedures were approved by the Animal Ethics Committee of Anhui Agricultural University (Number, AHAUB2024006) and were conducted following the animal care and use regulations and guidelines of this committee.

### Study Design:

Experiment 1: Mice were randomly divided into two groups ($n$ = 3/group) that received 200-nm MPs (200 mg/kg body weight) or normal saline by gavage. Blood samples were collected from the orbital veins 1, 2, and 4 h after gavage and analyzed for the absorption of MPs into the blood using fluorescence imaging.

Experiment 2: Mice were randomly divided into two groups ($n$ = 3/group) that received 200-nm MPs (200 mg/kg body weight) or normal saline by

gavage. Two hours after gavage, the mice were anesthetized by a small animal anesthesia machine (R500IE, RWD, China) with 2.0% isoflurane (RWD, China), underwent fluorescence imaging analysis, and then sacrificed and bled. The liver, spleen, lungs, kidneys, stomach, cecum, and brain were collected and divided for fluorescence imaging analysis and paraffin embedding for histological examination.

All surgical instruments, glass slides, tubes, filter papers, and black papers used in the experiments were assessed to prevent fluorescence contamination.

**Experimental Procedure:**

Tissue fluorescence intensity that indicated MP content was measured by a small-animal imaging system (IVIS Lumina LT Series III, Perkinelmer, USA) with a 632 nm excitation filter and a 680 nm emission filter. The MP-exposed and control mice or their tissues were imaged on a black paper. The exposure time, gain, and other parameters were adjusted automatically using Living Image software (Perkinelmer, USA) to obtain the best image quality. The images were saved for later fluorescence signal analysis. Blood samples (100 μL) were placed in microwell plates and measured using the same method as solid tissues. The total radiant efficiency units from selected regions were used to calculate the fluorescence intensity of the various tissues. Radiant efficiency was corrected for tissue weight (g) and volume (μL) in all calculations.

To avoid interference from the autofluorescence of tissues, we followed the method of Yang *et al*. (2022) to calculate the fluorescence intensity using the fold change value between the exposed and control groups (fold change = total radiant efficiency [p/s] / [$\mu W/cm^2$] of the tissues in the exposed group/total radiant efficiency [p/s] / [$\mu W/cm^2$] of the tissues in the control group).

Tissues were immersed in 4% paraformaldehyde for at least 24 hours. Subsequently, they were placed in a 75–100% ethyl alcohol gradient, xylene, and paraffin for dehydration, transparency, and paraffin embedding, respectively, for appropriate durations. The embedded paraffin blocks were trimmed, sectioned, stained with hematoxylin and eosin (H&E), observed, and scanned by a digital slide scanner (Pannoramic Scan II, 3DHISTECH Ltd., Hungary).

**Statistical Analysis:**

The fluorescence intensity (i.e., radiant efficiency) of the various tissues was analyzed using GraphPad Prism 9.5 software (GraphPad, La Jolla, CA). The results are presented as means ± standard deviations (SDs). Differences between groups were analyzed using one-way analysis of variance, followed by Tukey's correction for multiple comparisons. Statistical significance was set at $p < 0.05$, while $p < 0.01$ indicated a highly significant difference.

## RESULTS

**Fluorescence Intensity of MPs in the Blood at Various Time Points:**

The fluorescence intensity (fold change value) of MPs in the blood increased 1 and 2 h after gavage, peaking at 2 h after gavage, and then returning to the 1-h level at 4 h after gavage. However, the levels at the three time points were statistically similar, as shown in Figure 1.

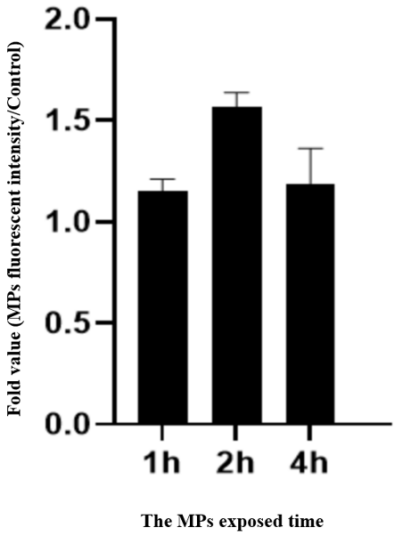


**Fig. 1.** Fluorescence intensity fold change values in the mice's blood at 1, 2, and 4 h after gavage.
Data are shown as means ± SDs ($n$ = 3).

**Tissue Distribution of the Fluorescent MPs 2 h After Gavage:**

Fluorescence imaging showed that the fluorescence intensity levels differed among tissues. The digestive system had the highest fluorescence intensity (**Fig.** 2). The highest level was noted in the cecum, followed by the stomach, lungs, and spleen (**Fig. 3**). The fluorescence intensity in the stomach and cecum of the exposed group was significantly higher than in the control group ($p < 0.01$), while those in the lungs, spleen, liver, kidneys, and brain were statistically similar to the control group (Fig. 4-1). These results were consistent with the fluorescence intensity using fold change values between the MPs-exposed and control groups (Fig. 4-2).

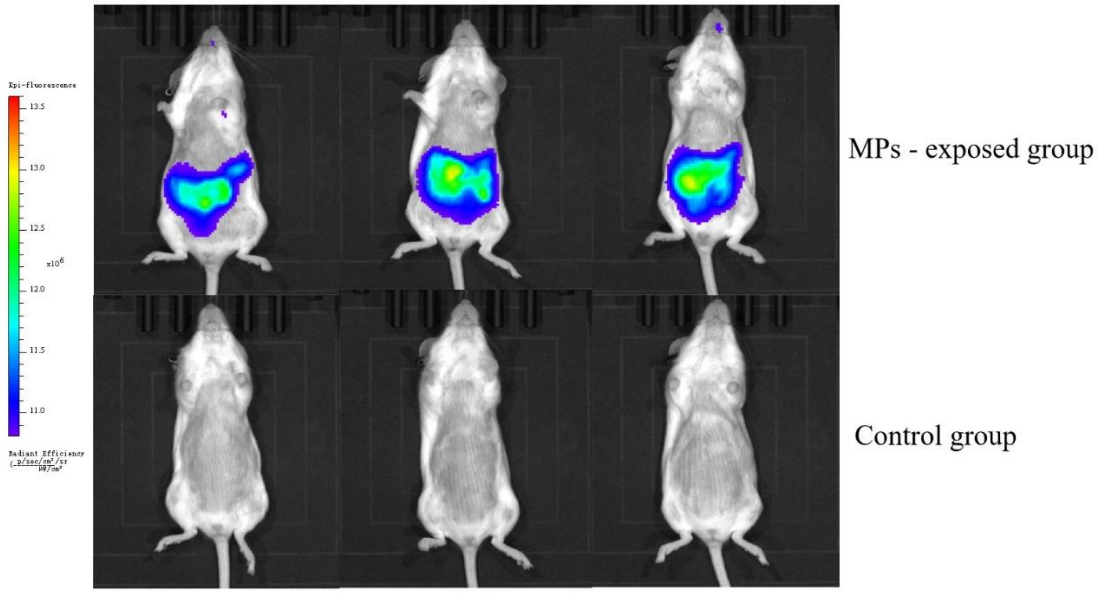


**Fig. 2.** Fluorescence intensity in mice 2 h after gavage.
Fluorescence imaging of mice treated with 200-nm fluorescent MPs by gavage at a dose of 200 mg/kg body weight ($n$ = 3) vs. Control. The images were taken two hours after gavage.

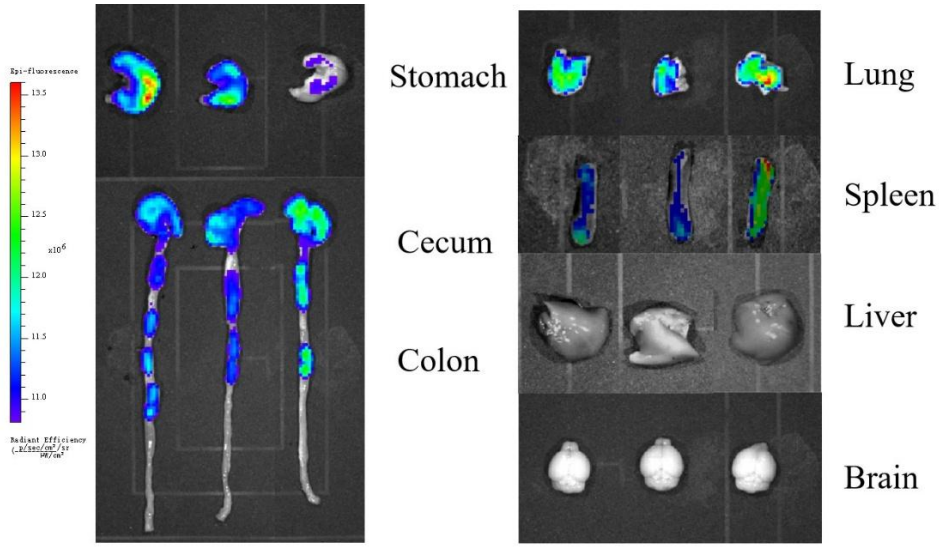


**Fig. 3**. Fluorescence intensity in various tissues 2 h after gavage.
Fluorescence imaging of various tissues of mice treated with 200-nm fluorescent MPs by gavage at a dose of 200 mg/kg body weight ($n$ = 3). The images were taken two hours after gavage.

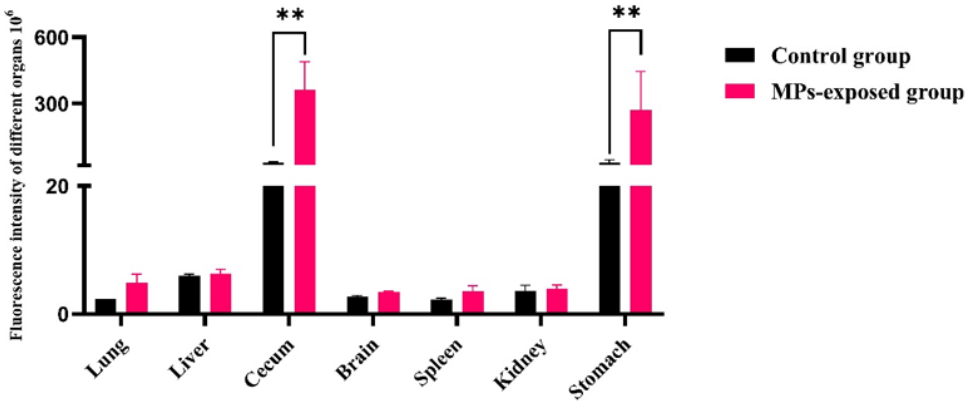


**Fig. 4-1**. Fluorescence intensity in the various tissues 2 h after gavage.
Data are shown as means ± SDs ($n$ = 3). $^{**}p < 0.01$ vs. Control.

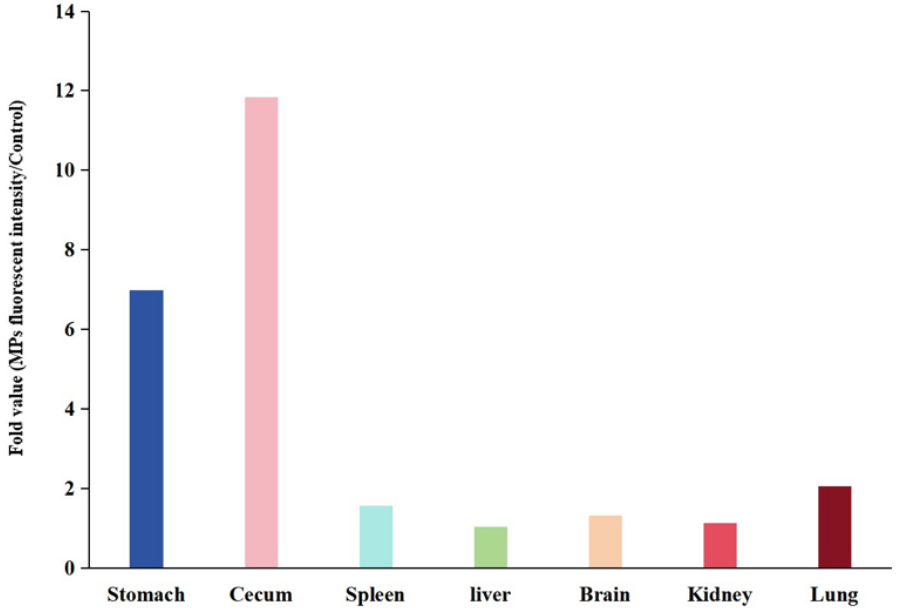


**Fig. 4-2**. Fluorescence intensity (fold change values) in various tissues 2 h after gavage.
Fold change = total radiant efficiency [p/s] / [μW/cm$^2$] of the tissues in the exposed group/control group.

**Histological Examination for MPs in Various Tissues 2 h After Gavage:**

Histological examination showed that MP particles were scattered or clustered around the stomach and cecal epithelium, alveolar cavity, renal tubular lumen, and cerebral capillary extracellular space (Fig. 5). Figure 5B shows MP particles adhered to the cecal epithelium, where they seem to have passed through the epithelium and lamina propria to reach the muscle layer. Mild congestion was noted in the liver and lungs (Figs. 6B, D), and a small number of epithelial cells were shed in the stomach (Figures 6F) and cecum. Other tissues had no apparent pathological lesions.

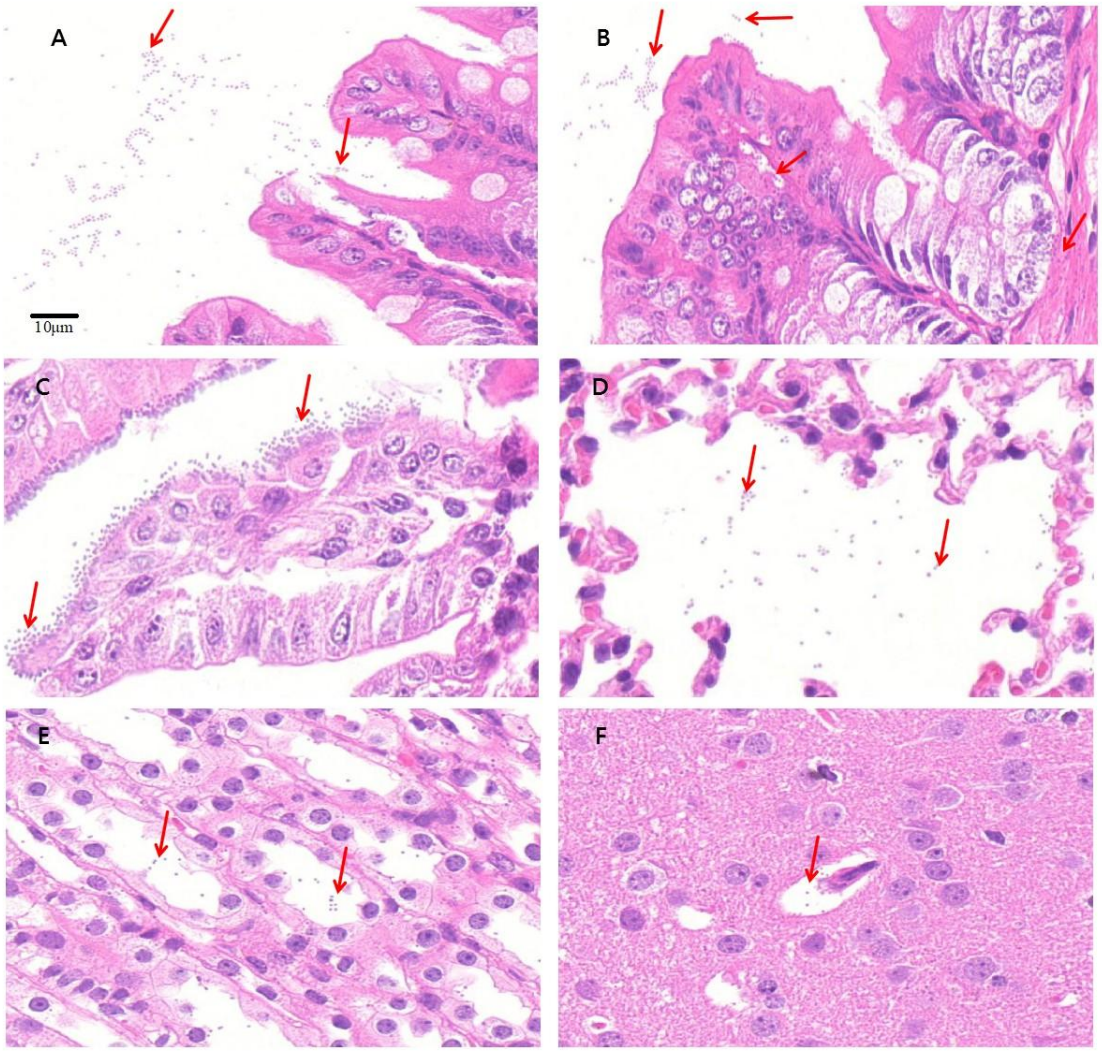


**Fig. 5:** MP particles in the cecum, stomach, lungs, kidneys, and brain.
A and B, cecum. C, Stomach. D, Lung. E, Kidney. F, Brain. The arrows point at MP particles (H&E, ×1,000).

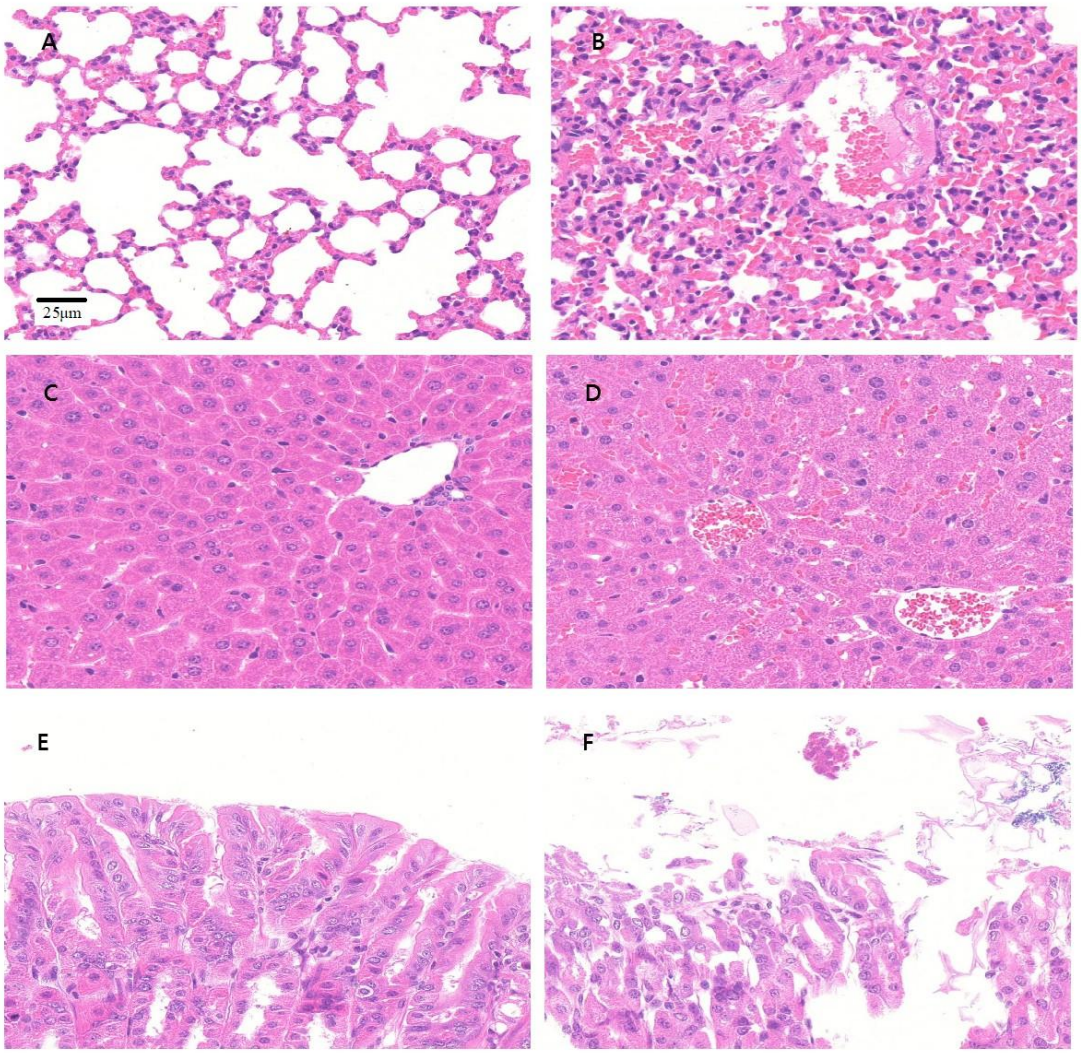


**Fig. 6:** Lesions caused by the MPs in various tissues.
A, C, E, Control group; B, D, F, MP-exposed group. Congestion in the lung (B) and liver (D); Epithelial cells shed in the stomach (F). (H&E, ×400).

## DISCUSSION

Direct evidence of MPs entering the blood circulation and translocating to other tissues remains limited (Vagner *et al.*, 2022; Wardani *et al.*, 2024). Most studies used fluorescence-labeled MPs (Sen *et al.*, 2022; Yang *et al.*, 2022; Kopatz *et al.*, 2023); however, due to spontaneous fluorescence interference of some tissues, fluorescence microscopy imaging is not absolutely reliable. Transmission electron microscopy has high experimental operational requirements (Sen *et al.*, 2022; Vagner *et al.*, 2022), and missing MP detection due to the low dose is easy. Small-animal imaging systems are more convenient for detecting tissues with high MP concentrations (Shan *et al.*, 2022; Yang *et al.*, 2022); however, the detection by these systems is limited when very low tissue MP levels are concerned. Consequently, we used histological examination in this study. By combining optical microscopy and digital slide scanning, we observed MP particles in the stomach, cecum, lungs, kidneys, spleen, liver, and brain. The method can digitally magnify the images up to 1,000 times on a computer, making it easy to determine which tissues the MPs have translocated to. This method helped confirm that MPs were transferred to various tissues through the bloodstream (Sen *et al.*, 2022; Vagner *et al.*, 2022).

Reports on MP toxicity are inconsistent, and available mammal data are scarce (Prüst *et al.*, 2020; Kopatz *et al.*, 2023). Prolonged *in vivo* observations were impossible in this

study due to the easy quenching of the fluorescence-labeled MPs. Therefore, we selected a shorter exposure duration. We observed no abnormalities in the mice within 4 h of gavage; however, the histological examination revealed mild congestion in the liver and lungs. MP particles were found scattered in or clustered around the stomach and cecal epithelium, causing the shedding of epithelial cells. This indicates that short-term exposure to high MP doses results in very slight tissue damage, perhaps representing a kind of stress response.

How MPs reach the bloodstream from the gastrointestinal tract remains unknown. Rubio *et al*. (2020) speculated that internalization through M cells and paracellular absorption in the intestine are the most likely mechanisms underlying MP uptake. Kopatz *et al*. (2023) suggested that MPs can enter cells by endocytosis, in which the cell membrane engulfs the particles and brings them into the cell without forming phagosomes. As a foreign substance, continuous MP internalization by epithelial cells might elicit a cascade of signaling events, resulting in oxidative stress, cytokine/chemokine release, and inflammation (Vethaak and Legler, 2021; Alijagic *et al*., 2024). It is crucial to understand the interaction MPs have with the immune system to understand their potential health effects.

Many critical factors can influence the absorption, bioaccumulation, biodistribution, and toxic effects of MP exposure (Alijagic *et al*., 2024). Consistent answers are lacking due to limitations in experimental methods and observation techniques. Most studies used short exposure durations and high exposure levels (Prüst *et al*., 2020; Kopatz *et al*., 2023), while humans are chronically exposed to low levels. Evidently, the experimental exposures used so far are unrealistic simulations of human exposure. Future experiments should consider various MP exposure concentrations and durations (a single acute dose or chronic exposure), particle characteristics (type, size, shape, and charge) (Prüst *et al*., 2020; Zingaro *et al*., 2023; Wardani *et al.*, 2024), and routes of exposure (ingestion, inhalation, and intravenous injection) (Prüst *et al.*, 2020; Sen *et al.*, 2022). It will be particularly important to study the long-term effects of MP exposure and their potential to accumulate and cause damage to tissues.

## CONCLUSION

After a single 200-nm MP exposure in mice, MP particles were observed in the stomach, cecum, lungs, spleen, liver, kidneys, and brain by fluorescence imaging and light microscopy. Histological examination showed mild congestion in the liver and lungs and a small number of shed epithelium cells in the stomach and cecum. This study reports direct evidence that MPs are absorbed from the gastrointestinal tract into the bloodstream and transferred to other tissues. This knowledge is vital to the understanding of MP' acute toxicity and the potential effect of long-term exposure.

**Declarations:**

**Ethics Approval:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

**Conflict of Interest:** The authors declare no conflict of interest.

**Author contribution:** Qian Zhou and Yongyi Shen contributed to data interpretation and preparation of the manuscript. Xinyuan Chen, Chenxiao Wang, Yongyi Shen and Qian Zhou contributed to study design, execution, data interpretation and revision of the manuscript. All authors have read and agreed to the published version of the manuscript.

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