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Perspective

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Micro/nanorobots for the removal of microplastics and nanoplastics from the human body

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1. Introduction

In today's era, plastic products are ubiquitous in daily life and bring us great convenience. Meanwhile, the problem of microplastic pollution is spreading at an alarming rate, becoming an environmental and health hazard that cannot be ignored. Increasing concentrations of microplastics and nanoplastics (MNPs) in the global environment have raised concerns about human exposure and health consequences. Microplastics are not a single substance, but a complex mixture of plastic particles, fragments, and fibers smaller than 5 mm in diameter.[1] Further degradation leads to the formation of nanoplastics smaller than 1000 nanometers (1 μm). MNPs continuously enter the human body in many ways, such as ingestion, inhalation, and skin exposure, which trigger a range of toxicological effects and pose a potential threat to human health.[2]

The MNPs can easily pass through biological barriers and enter various tissues and organs of the human body.[3] Although the threat of MNPs to human health is becoming increasingly prominent, there is still no research on the removal of MNPs from the human body. Current research has mainly focused on the source and distribution of MNPs in the environment and their impact on the ecosystem, and detecting the presence of MNPs in human tissues, but less attention has been paid to how to remove MNPs that have entered the human body. The human body lacks a mechanism to degrade MNPs. Once these foreign substances enter the body, they may accumulate for a long time and continue to have adverse effects on cells, tissues, and organs. However, an effective solution has not yet been found to clear these MNPs lurking in the human body. Therefore, it is urgent to fill the gap in research on removing MNPs from the human body.

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2. Distribution of MNPs in the human body

In vitro and animal exposure studies indicate that MNPs may cause inflammation, oxidative stress, and cell apoptosis, but the relevance of concentrations to human exposure and body burden is unclear. "The dose makes the poison" (Paracelsus); therefore, it is of great significance to ascertain the tissue distribution and internal dose of MNPs in the human body.

In 2021, Ragusa and coworkers[4] demonstrated the presence of microplastics in human placenta. These microplastics, of spherical or irregular shape, ranged from 5 to 10 μm in dimension and were identified as polypropylene and pigments. This finding demonstrates that microplastics can cross the placental barrier, leading to exposure very early in life and potential cross-generational health effects. Microplastics were even detected in human breastmilk[5] proving that microplastics can be passed through breastmilk. Besides, microplastics were also present in human semen[6] and endometrium.[7] Taken together, MNPs have been prevalent in the reproductive system.

Inhalation is also a way that MNPs enter the human respiratory system. For example, researchers have validated the existence of microplastics in human lung tissue[8] and upper respiratory tract.[9] Due to the peculiarities of the human digestive system, ingestion is the main way for MNPs to enter the human body. As a consequence, MNPs have been detected in colon tissue,[10] cirrhotic liver tissue,[11] tumoral colon tissue,[12] and gallbladder.[13]

In 2022, Leslie and coworkers[14] conducted a pioneering study to determine the concentration (1.6 μg/mL) of MNPs in human whole blood from healthy volunteers. These MNPs were larger than 700 nm and composed of polyethylene terephthalate, polyethylene, polymers of styrene, and poly(methyl methacrylate). This first report showed that MNPs can enter the human bloodstream, which may be associated with cardiovascular and cerebrovascular diseases, causing health risks. Later, Wu and coworkers gave the first evidence on the presence of microplastics and pigment microparticles in human thrombi.[15] Recently, it was demonstrated that microplastics in blood even caused cerebral thrombosis and neurobehavioral abnormalities.[16] Microplastics were also discovered in human bone marrow.[17] In addition, MNPs were present in cirrhotic liver tissue,[11] saphenous vein tissue,[18] and heart.[19] Taken together, these results imply that MNPs can spread throughout the body and theoretically reach any organ or tissue via the bloodstream.

Although MNPs have emerged as a potential risk factor for cardiovascular disease, direct clinical evidence remains lacking. Recently, Marfella and coworkers[20] carried out a prospective, multicenter, observational study on patients undergoing carotid endarterectomy. A total of 304 patients participated in this

study, with detected polyethylene (58.4%) and polyvinyl chloride (12.1%) from atheromatous plaques. At 34 months of follow-up, patients with detected MNPs in atheroma had a higher composite risk of myocardial infarction, stroke, or death from any cause than those nondetected.

The skeletal system is the system of bones, joints, and ligaments in the human body that provides structure and support, protects internal organs, and assists muscle movement. Caused by multiple factors such as bloodstream and surgery, microplastics were also present in human bone and skeletal muscle tissues, as evidenced by Lu et al.,[21] which poses a threat to individual athletic ability. It is known that the complex anatomical structure of the brain and the presence of blood–brain barrier pose severe challenges to drug delivery[22]; similarly, MNPs can hardly cross these natural barriers and enter the human brain. However, in a recent study, Nihart et al confirmed the existence of MNPs in the decedent human brains, largely in the form of nanoscale shard-like fragments.[23] Such findings manifest the urgency to figure out the potential routes of exposure and uptake of MNPs in the human nervous system and their health outcomes. Moreover, in the same study, MNPs were also detected in the human urinary system (kidney).[23] Table 1 summarizes the distribution of MNPs in the human body reported in representative literature.

3. Removal strategies for MNPs from the human body

Based on the existing preclinical and clinical studies, it is anticipated that the ubiquitous presence of MNPs makes human exposure inevitable. MNPs have been found in the bodies of both healthy people and patients; particularly, more MNPs are present in the organs or tissues of patients. Researchers have demonstrated the abnormal accumulation of MNPs in diseased tissues such as tumors,[12] atheromas,[20] and the brain with dementia.[23] Therefore, the relationship between MNPs and diseases needs to be clarified. In the field of environmental remediation, various strategies have been exploited to eliminate MNPs, including catalytic degradation and catalytic recycling.[24] However, to date, there are no studies on the removal of MNPs from the human body, which calls for urgent action to address this serious health challenge and meet medical needs.

Micro/nanorobots are a type of miniature artificial machine with a maximum size of microns. Their greatest feature is the ability to move autonomously or under field control.[25–27] Micro/nanorobots have shown great promise for a variety of biomedical applications, such as single-cell microsurgery,[28,29] smart drug delivery,[30,31] and cell manipulation and delivery.[32,33] Zhou et al.[34] developed magnetic microrobots carrying polydopamine and lipase to capture and degrade microplastics from an aqueous environment. Considering that micro/nanorobots can reach narrow and hard-to-reach locations in the human body, such as blood vessels, digestive tract, and bile duct, they can be functionalized with catalysts or enzymes that degrade MNPs. There are microbial strains that can efficiently degrade MNPs in nature, which can be engineered into biohybrid microbe microrobots to degrade MNPs. Moreover, hydrogels can be exploited to fabricate micro/nanorobots for removing MNPs due to their excellent biocompatibility, favorable biodegradability, and high cargo loading capacity.[35,36] Taken together, these strategies can be exploited in the future to eliminate MNPs in the human body. Nevertheless, the design of these micro/nanorobots should take into account their degradability or retrievability after completing their tasks. More details are discussed in the next section.

4. Conclusion and outlook

When researchers identified MNPs deep within the human placenta, in a newborn's first mouthful of breastmilk, and in the plaques of arteries that sustain life, it was a deafening wakeup call about living with the ubiquity of MNPs rather than just a scientific discovery. Increasing human exposure to MNPs will greatly raise human health risks and be associated with a variety of diseases. The potential toxicity effects and mechanisms of MNPs on the human body, such as the nervous system, cardiovascular system, reproductive system, digestive system, and respiratory system, should be elucidated from the clinical perspective in the future. For example, large-scale, long-term prospective population cohort studies can be conducted to establish a definitive causal relationship between the burden of human exposure to MNPs and the risk of specific diseases (such as neurodegenerative diseases, cardiovascular diseases, metabolic diseases, and reproductive disorders). It is also suggested to focus on the special risks of vulnerable groups such as fetuses, infants, and occupationally exposed populations.

There is currently no research in the area of the removal of MNPs from the human body. In this context, we call on more researchers to pay attention to this field. First, in vitro studies and animal experiments on MNPs removal should be carried out in the laboratory, despite being extremely far from clinical application. Completely different from environmental remediation, when developing novel strategies to remove MNPs from the human body, several core challenges should be carefully tackled, encompassing excellent biosafety to be compatible with tissue cells, high efficiency and specificity to precisely target MNPs of different types, sizes, and distributions, and adaptability to the complex physiological environment of the human body.

Micro/nanorobots can actively move around and search for targets in a space of interest, which holds great promise for the removal of MNPs from the human body, as illustrated in Figure 1. This direction is the most revolutionary, but also the most difficult, facing huge scientific obstacles such as immunogenicity, off-target effects, and delivery efficiency. When designing micro/nanorobots for this purpose, many factors need to be considered. (1) Micro/nanorobots can be integrated with novel catalysts, enzymes, or bacteria that can safely and controllably degrade MNPs in specific locations of the human body (such as blood and brain), thereby achieving targeted degradation. (2) To enable micro/nanorobots to eliminate MNPs from the human body, synthetic biology may bring breakthroughs in designing highly specific, safe, and controllable MNPs-degrading enzymes or engineering bacteria. (3) Regarding the materials design of orally administered micro/nanorobots, nonabsorbable hydrogels and clay minerals can be combined to efficiently adsorb MNPs in the intestine, prevent them from penetrating the intestinal barrier into the circulatory system, and promote their excretion with feces. (4) Micro/nanorobots possess better locomotion performance in body fluids, where MNPs are present in large quantities. Through body fluids, MNPs can spread to various tissues and organs throughout the body. Therefore, it is of great importance to develop safe micro/nanorobots that can specifically bind to MNPs in blood or tissue fluids and enhance their excretion through the hepatobiliary system (bile) or kidney system (urine) after capture and degradation. We

Table 1

Distribution of MNPs in the human body.

Location		Materials	Morphology	Dimension	Concentration (abundance)	Year	References
Reproductive system	Placenta	Polypropylene, pigments	Spherical or irregular shape	5 –10 μm	12 microplastics in 6 human placentas	2021	[4]
	Breastmilk	Polyethylene, polyvinyl chloride, polypropylene	Irregular fragment, sphere	2 –12 μm	0.13~2.72 particles/g	2022	[5]
	Semen	Polypropylene, polyethylene, polyethylene terephthalate, polystyrene, polyvinyl chloride, polycarbonate, polyoxymethylene, acrylic	Spherical or irregular shapes	2 –6 μm	16 particles in 6 semen samples	2023	[6]
	Endometrium	Ethylene-acrylic acid, fluororubber, chlorinated polyethylene, polyethylene, acrylate	Irregularly shaped	20 –100 μm	Median 21 particles/100 mg tissue	2024	[7]
Respiratory system	Lung tissue	Polypropylene, polyethylene, polyvinyl chloride, etc.	Particulate, fibrillar	Fragments: 3.92 μm, fibers: 11.23 μm	33 fragments and 4 fibers in 13 decedent lung tissues	2021	[8]
	Upper respiratory tract	Polycarbonate, polyvinyl chloride, polyamide, polyethylene	Fibrous, particle, etc.	NA	Sputum: 102.9 –134.3 particles per gram, nasal lavage fluid: 0.8 –2.6 particles per gram	2022	[9]
Digestive system	Colon tissue	Polycarbonate, polyamide, polypropylene	Filaments or fibers	1.1 mm	28.1 particles per gram tissue	2021	[10]
	Cirrhotic liver tissue	Polystyrene, polyvinyl chloride, polyethylene terephthalate, polymethyl methacrylate, polyoxymethylene, polypropylene	Fragments	4 –30 μm	3.2 particles per gram tissue	2022	[11]
	Tumoral colon tissue	Polyethylene, poly(methyl methacrylate), polyamide	Irregular shape	1 –613 μm	702.68 particles per gram tissue	2023	[12]
	Gallbladder	Polystyrene, polyethylene, polypropylene, polyethylene terephthalate, ethylene–vinyl acetate copolymer	Irregular shape	NA	0.56~5.25 particles gram gallstone	2024	[13]
	Liver	Polyethylene, polypropylene, polyvinyl chloride, styrene-butadiene rubber, nylon-6, nylon 66, etc.	Rod-shaped, shard-like	1 –5 μm (rod-shaped), <0.4 μm (shard-like)	141.9 (2016), 465.3 (2024)*	2025	[23]
Cardiovascular system	Blood	Polyethylene terephthalate, polyethylene, polymers of styrene, poly(methyl methacrylate)	NA	≥700 nm	1.6 μg mL^{-1}	2022	[14]
	Thrombi	Phthalocyanine, polyethylene, pigments	Irregularly block-shaped	2.1 –26.0 μm	Phthalocyanine: 21 particles in 16 thrombi, polyethylene: 1 particle in 16 thrombi, pigments: 63 particles in 16 thrombi	2022	[15]
	Saphenous vein tissue	Alkyd resin, poly(vinyl propionate/acetate), nylon-ethylene-vinyl acetate, tie layer, etc.	Irregular-shaped fragment/film	119.59 μm length, 41.27 μm width	14.99 particles per gram tissue	2023	[18]
	Heart	polyethylene terephthalate, polyurethane, poly(methyl methacrylate), polyethylene	Threads, rods	20 –469 μm	3 –74,116 particles per gram tissue	2023	[19]
	Atheromatous plaque	Polyethylene, polyvinyl chloride	Jagged-edged	<1 μm	Polyethylene: 21.7 μg mg^{-1} plaque, polyvinyl chloride: 5.2 μg mg^{-1} plaque	2024	[20]
Skeletal system	Bone marrow	Polyethylene, polystyrene, polyvinyl chloride, polyadiohexylenediamine, polypropylene	Irregularly shaped	20 –100 μm	Polyethylene: 30.02 μg g^{-1}, polystyrene: 5.27 μg g^{-1}, polyvinyl chloride: 17.01 μg g^{-1}, polyadiohexylenediamine 66: 6.81 μg g^{-1}	2024	[17]
	Bone, skeletal muscle	Bone: polypropylene, polyphenylene oxide, polybutyleneadipate-co-terephthalate, polycarbonate, polyethylene, etc.; muscle, polyphenylene oxide, polyethylene, polyurethane	Bone: fragments	Bone: >100 μm, <10 μm; muscle, >500 μm	Bone: 30.1 –62.2 particles per gram, muscle: 15.22 –56.82 particles per gram	2024	[21]
Nervous system	Brain	Polyethylene, polypropylene, polyvinyl chloride, styrene-butadiene rubber, nylon-6, nylon 66, etc.	Shard-like	<1 μm	3420 (2016), 4763 (2024)*	2025	[23]
Urinary system	Kidney	Polyethylene, polypropylene, polyvinyl chloride, styrene-butadiene rubber, nylon-6, nylon 66, etc.	Irregularly shaped, shard-like	1 –5 μm (irregularly shaped), <0.4 μm (shard-like)	538.1 (2016), 666.3 (2024)*	2025	[23]

*Total MNP concentrations in decedent specimens, μg/g.

NA, data not available.

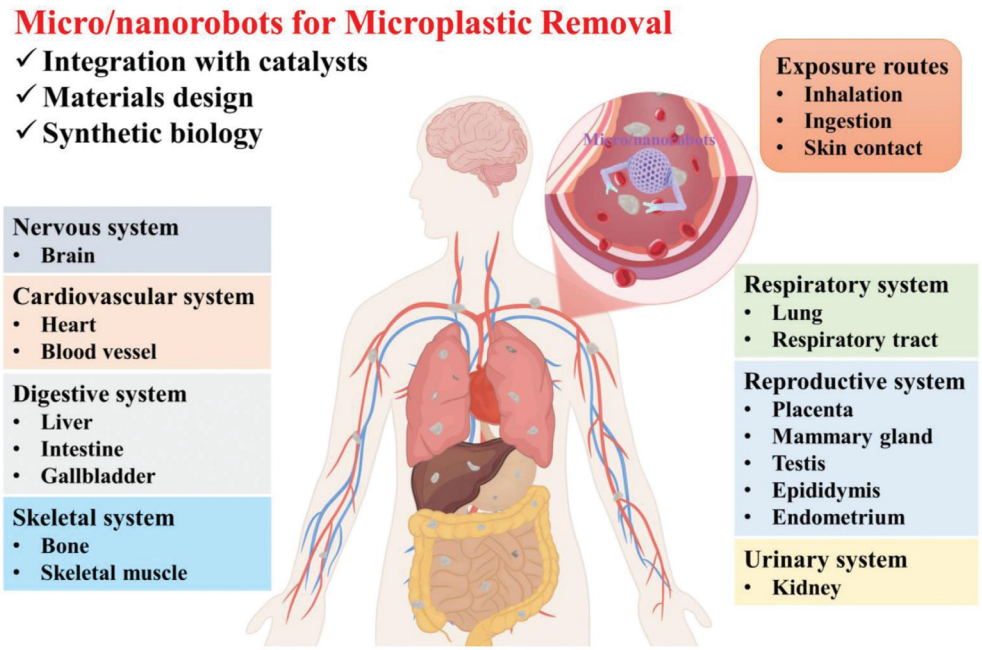

Figure 1. Schematic illustration of exploiting micro/nanorobots for the removal of MNPs from the human body.

expect this perspective will shed light on the impact of MNPs exposure on human health and pave the way for developing micro/nanorobotic strategies to eliminate MNPs from the human body.

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Conflicts of interests

The authors declare that they have no conflicts of interest.

Author contributions

H.Z.: funding acquisition, writing—review and editing, and writing—original draft; Y.Y. and P.L.: investigation; J.L.: conceptualization, supervision, funding acquisition, writing—review and editing, and writing—original draft.

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