Review

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Micro- and Nanoplastic Entry Into the Human Body: Ingestion, Inhalation, Dermal Absorption, and Related Toxicity—A Scoping Review

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Since 1950, approximately 8.3 billion metric tons of virgin plastics have been produced, with 79% accumulating in the natural environment because of low recycling rates. These non-biodegradable materials fragment into micro- and nanoplastics (MNPs) that have become ubiquitous contaminants. Humans are continuously exposed, especially through the inhalation of urban dust and fibres and the ingestion of contaminated food and water. This scoping review aimed to summarise the current evidence regarding the deposition of MNPs in human tissues and their subsequent pathophysiological impacts, with a focus on pathological manifestations across organ systems. Following PRISMA-ScR guidelines for scoping reviews, a comprehensive search was conducted across the PubMed, Scopus, and Cochrane Library databases. Studies investigating human microplastic exposure, tissue deposition, and physiological/pathological consequences were included. Data extraction focused on exposure routes, deposition patterns, and associated tissue alterations or disease processes. Our analysis revealed that MNPs primarily enter the human body through respiratory and digestive pathways. Subsequent deposition was documented across multiple organ systems, with significant accumulation in respiratory tissues, neurological structures, and throughout the gastrointestinal tract. The evidence suggests that these deposited particles can disrupt normal tissue physiology through multiple mechanisms, notably an exacerbation of inflammatory conditions and potentially increasing the risk of malignancy in affected tissues. Dose-dependent relationships between microplastic burden and pathological severity were observed in several studies. This review highlights that microplastics not only penetrate and persist within human tissues but may significantly contribute to inflammatory disease processes and carcinogenesis. These findings underscore the urgent need for enhanced exposure monitoring and further research into the prevention and evaluation of long-term health implications.

Keywords: microplastics; nanoplastics; exposure; entry; toxicity; organs

Introduction

Plastics began to be produced worldwide around the 1950s, with an estimated 8.3 billion metric tons of virgin plastics produced to date [1]. Since then, they have become deeply embedded in our economies and daily lives through decades of mass production. However, due to low recycling rates, 79% of all plastic waste generated has accumulated in the natural environment [1]. Most environmental microplastics result from the deterioration and fragmentation of larger plastic products and waste [1]. Global annual plastic production reached approximately 350 million tons in 2018 and 400.3 million tons in 2023 [2,3]. Recent reports estimate that plastic use could triple by 2050 if current trends continue [1].

The cumulative impact of these diverse exposure routes has been quantified in large-scale analyses. Cox *et al.* [4] estimated that the average annual microplastics consumption is between 39,000 and 52,000 particles per person, depending on age and sex. When considering inhalation as an additional pathway, this increases significantly, reaching between 74,000 and 121,000 particles per person annually. Individuals who meet their recommended daily water intake through bottled water may ingest an additional 90,000 microplastic particles annually compared with those who consume only tap water [4].

Plastics, or synthetic organic polymers, are categorised by their versatile chemical compositions, predominantly consisting of polyethylene (PE), polypropylene (PP), polyvinyl chloride (PVC), polystyrene (PS), and polyethylene terephthalate (PET). Beyond the polymer itself, these materials often incorporate a variety of chemical additives,

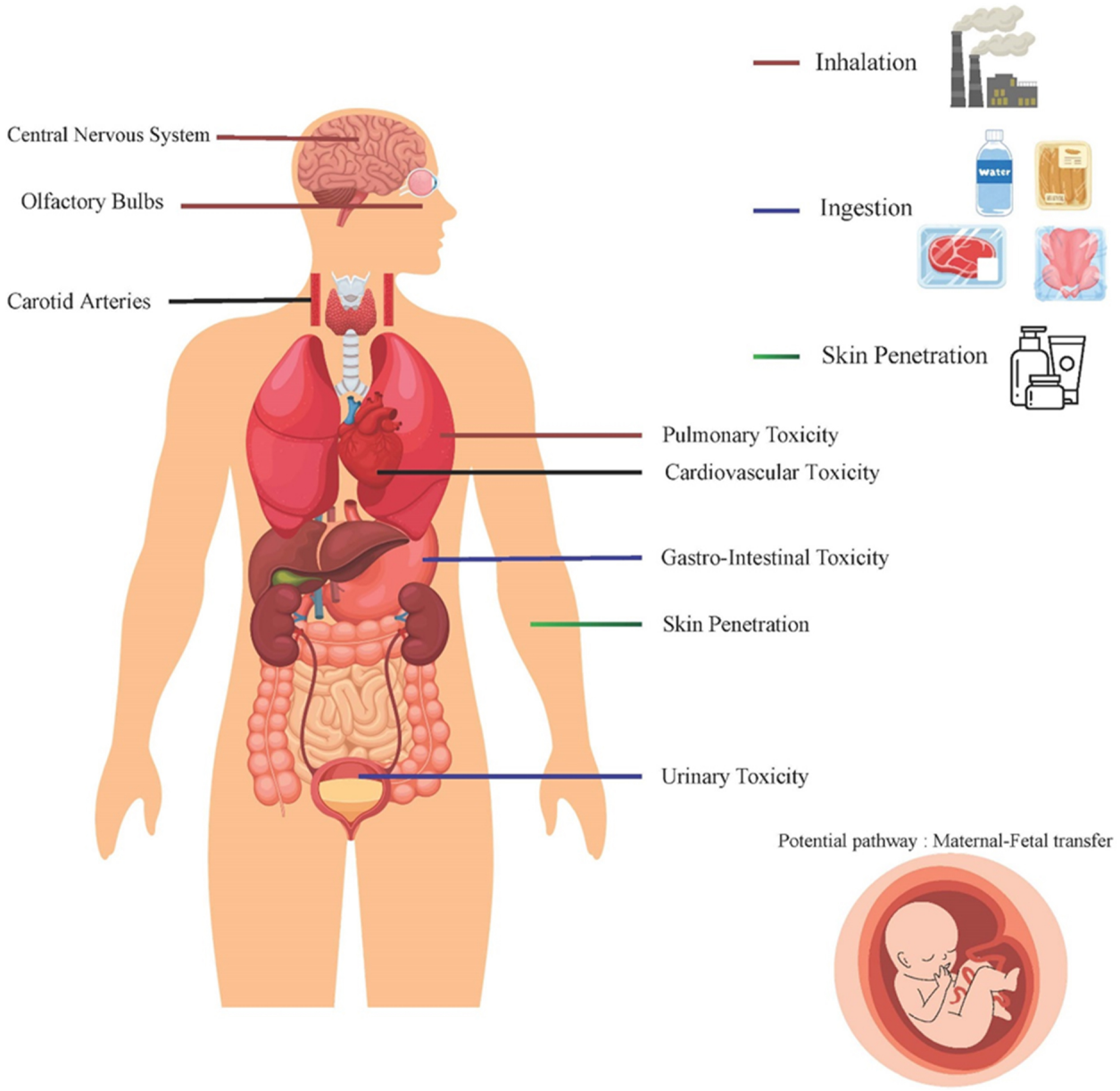

Fig. 1. Illustration of the three modes of entry of microplastics into the human body (inhalation, ingestion, and skin penetration) and the potential sites of toxicity. Drawn with Canva Pro (https://www.canva.com).

such as phthalates and bisphenols, that can leach into biological environments, potentially inducing endocrine disruption [5–8]. Phthalate esters (PAEs) are ubiquitous and used extensively as plasticisers to increase the fluidity of materials. Because of the absence of covalent bonds, PAEs are not chemically bound to the polymer matrix, meaning they are highly susceptible to leaching into the surrounding environment [8].

Under environmental triggers, such as ultraviolet (UV) radiation and mechanical abrasion, larger plastic debris undergoes continuous degradation and fragmentation. This process leads to the formation of microplastics (MPs; defined as particles ranging from 0.1 µm to 5 mm) and nanoplastics (NPs; $<$100 nm) [9].

Environmental and human exposure to these materials occurs through two distinct categories: primary and secondary plastics. Primary plastics are intentionally manufactured for specific applications, including industrial abrasives, exfoliating beads in personal care products, and specialised vectors for drug delivery. Conversely, secondary plastics arise from the progressive structural degradation and fragmentation of larger plastic debris under the influence of UV radiation, mechanical abrasion, and thermal oxidation [7,10].

Human exposure to these particles is now ubiquitous. Direct ingestion occurs through the global food chain, with MNPs detected in bottled water, soft drinks, table salt, and seafood [4,11,12]. Contamination can arise from en-

vironmental bioaccumulation and the degradation of food-contacting materials, such as plastic packaging. Furthermore, daily-use items, such as PP baby bottles or plastic tea bags, can release billions of particles directly into liquids during preparation [11].

Recent literature supports that plastic particles enter the human body through several pathways (Fig. 1), including the respiratory tract and digestive system [13–18]. An emerging body of literature has demonstrated the possibility of maternal–foetal transfer through the systemic circulation via the placenta, highlighting their potential to cross biological barriers [19,20].

MPs are therefore no longer considered merely as environmental pollutants, but rather as emerging biological factors impacting human diseases, as shown by Marfella *et al.* [21]. These authors found that patients with asymptomatic carotid stenosis (>70%) and evidence of MNPs had a greater incidence of stroke and myocardial infarction than those without evidence of MNPs in the atheroma, indicating that accumulation of MNPs in the arteries is a cardiovascular risk factor. In the study of Yan *et al.* [13], patients with inflammatory bowel disease (IBD) had higher levels of MNPs than healthy patients.

This scoping review aims to map the distribution of MNPs across human tissues and their multi-organ pathophysiological impacts, focusing on entry routes, tissue deposition sites, and the underlying biological mechanisms (inflammation, oxidative stress, genotoxicity, and carcinogenesis). Specifically, we analyse how tissue deposition triggers chronic inflammatory responses and oxidative stress, while also exploring evidence regarding cell death pathways.

Methods

A PubMed, Cochrane Library, and Scopus database search was conducted for relevant peer-reviewed publications dedicated to the bioaccumulation and toxicity of MNPs in the human body according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) recommendations [22]. Initially, the systematic search yielded 331 studies. There were no language or date restrictions up to December 2025. The following MeSH and non-MeSH keywords were used ‘microplastics’, ‘nanoplastics’, ‘toxicity’, ‘inflammation’, ‘bioaccumulation’, ‘brain’, ‘tissue’, and ‘carcinogenesis’. The selection process was conducted in three stages to ensure rigorous screening of the literature by two investigators. First, a title screen was performed to remove 92 duplicates and irrelevant studies, leaving 239 unique articles. Second, an abstract screen was conducted to assess the eligibility of the remaining articles based on our predefined inclusion and exclusion criteria. Finally, a full-text screen was carried out on the selected papers to verify the relevance of the findings. Any disagreements during the screening process were resolved through discussion among the authors. This process resulted in a final selection of 42 articles, including studies on MNP detection in human tissues and *in vitro* models related to human cell lines, as well as secondary sources and foundational papers. Clinical prospective, retrospective, controlled, and uncontrolled studies, experimental research with application to the human body, meta-analyses, and systematic reviews were included. Case reports and studies without human translational relevance were excluded. Studies were considered if they had database abstracts, available full texts, or titles containing the search terms. For each article included, the following primary outcomes were extracted: study design, model or population, particle size, MP detection method (μ-FTIR, TEM, Raman spectroscopy, pyrolysis-GC-MS), organs studied, main results, and limitations. This scoping review covers human exposure pathways, with a focus on the central nervous system (CNS) because of the emerging evidence of MNP translocation across the blood–brain barrier and the potential for long-term neurotoxic effects. Ethics committee approval was not required for this review.

Results

MNP Entry

MNPs penetrate the human body via several pathways, but the primary routes of entry are ingestion and inhalation, as well as maternal–foetal transfer. The clinical evidence regarding these primary exposure pathways, including the specific polymer types detected and the biological samples analysed, is synthesised in Table 1 (Ref. [13–20]).

Ingestion

Ingestion is the most documented exposure pathway, occurring through contaminated food, bottled water, seafood, and others. Yan *et al.* [13] conducted a comparative observational study including 50 healthy individuals and 52 patients with IBD to quantify microplastic intake and clinical correlations. MPs were detected in the faecal samples of all participants (n = 102) with a PET scan and a polymer profile. Concentrations were higher in IBD patients (mean 41.8 items/g) than in healthy individuals (28.0 items/g). Schwabl *et al.* [14] detected MNPs in 100% of stool samples from eight healthy volunteers, identifying nine polymer types that were primarily attributed to food, drinking water, and plastic packaging. Hartmann *et al.* [15] performed an interventional study in which 15 volunteers alternated between low, normal, and high plastic-use dietary scenarios. MNPs were detected in all stool samples. PE, PP, PET, PA, and PS were frequently identified, and MNP levels significantly increased with the consumption of ultra-processed foods, use of plastic utensils, and plastic-based food packaging. Jahedi *et al.* [16] detected MNPs in human urine, predominantly fibres (20–100 μm, PE/PP/PS), implying gastrointestinal absorption followed by renal elimination.

Table 1. Clinical evidence of MNPs exposure in human subjects.

Author (references)	Study design	Model/population	Polymer type	Particle size	Exposure route	Method detection	Outcomes	Limitations/Bias
Yan *et al.* [13]	Observational study	Healthy controls (n = 50) and IBD patients (n = 52)	PET, PA, PP, PE, PC, PVC, POM, PTFE, EVA, PS, PMMA, PBT, AS, PES, TPU	Healthy: 4.4–333.2 µm; IBD patients: 1.7–393.8 µm	Ingestion	Raman microspectroscopy	Higher MP concentration in IBD patients; PET and PA dominant; MP load correlated with disease severuty.	Recall biais (self-reported 5 min questionnaire); single sample; geographic
Schwabl *et al.* [14]	Observational study	Healthy patients (n = 8)	PP, PET, PS, PE, POM, PC, PA, PVC, PU	50–500 µm	Ingestion	FTIR microspectroscopy	MPs detected in 100% of stool samples; median 20 particles/10 g; PP and PET dominant.	Small sample size (n = 8); origin and fate of MPs were not investigated
Hartmann *et al.* [15]	Interventional study	Healthy patients (n = 15)	PE, PP, PVC, PS, PET, PA, PU, PMMA, POM	5–5000 µm	Ingestion	FTIR microspectroscopy	MPs were detected in all stool samples; higher MP associated with plastic packaging, plastic ustensils and ultra-processed food intake.	Reliability of the participants; short duration; no analyze of the food and beveraves' MPs content
Jahedi *et al.* [16]	Observational study	Pulmonary conditioned patients (COPD or asthma) (n = 30)	PA, PE, PET, PP, PS, PU, PVC	20–500 µm	Inhalation (via sputum) and Ingestion (via urine sample	Raman microscpectroscopy	490 MPs were identified in the urine, sputum and BALF samples. Suggesting different pathways of MP filtration and fractionation.	Potential contamination during sampling and processing. Small sample size (n = 30)
Huang *et al.* [17]	Observational study (retrospective)	Lung disease patients (n = 22)	PU, PE, CPE, AV	20–500 µm; smaller than <500 µm	Inhalation	FTIR microspectroscopy	MPs were ubiquitous in all sputum; quantities of MPs are related to smoking.	Small sample size (n = 22); sputum was excreted through coughing; MPs in sputum may come from the food and drinks
Amato-Lourenço *et al.* [18]	Observational study	Olfactory bulbs of deceased individuals (n = 15)	PP, PA, PVA, PE	5.5–26.4 µm	Inhalation	FTIR microspectroscopy	Olfactory pathway may be an entry site for MPs. The anatomy of the cribriform plate of the ethmoid bone may serve as a gateway in the nasal passages.	Possibility of multiple entry routes as systemic circulation, crosing the BBB, respiratory pathway via the trigeminal nerve
Ragusa *et al.* [19]	Observational study	Human placentas (n = 6)	PP	5–10 µm	Maternal-fetal transfer	Raman microscpectroscopy	12 MPs were detected in four placentas of four women.	Small sample size (n = 6).
Sun *et al.* [20]	Observational study	Pregnant women (n = 12)	PA, PU, PET, CPE, PE, PMMA, ACR, PP, FKM, PS, PVC, BR	20–100 µm	Maternal-fetal transfer	Laser direct infrared	MPs in amniotic fluid was increased with the maternal age and BMI before pregnancy. No correlation was found between living habits and MPs abundance.	Small sample size (n = 12).

ACR, Acrylates; AS, Acrylonitrile styrene; BALF, Bronchoalveolar lavage fluid; BR, Butadiene rubber; CPE, Chlorinated polyethylene; EVA, Ethylene-vinyl acetate; FKM, Fluororubber; FTIR, Fourier-transform infrared spectroscopy; MPs, Microplastics; PA, Polyamide; PBT, Poly(butylene terephthalate); PC, Polycarbonate; PE, Polyethylene; PES, Poly(ether sulfone); PET, Polyethylene terephthalate; PMMA, Polymethyl methacrylate; POM, Poly(oxymethylene); PP, Polypropylene; PS, Polystyrene; PTFE, Poly(tetrafluoroethylene); PU, Polyurethane; PVC, Polyvinyl chloride; TPU, Thermoplastic polyurethane.

Inhalation

Inhalation is the second primary route of human exposure to MNPs, which come from urban dust, textile fibres, tyre abrasion, industrial emissions, and indoor environments. Huang *et al.* [17] demonstrated direct evidence of inhaled MNPs in the human airway by analysing participants' sputum. Of 22 individuals, they detected MNPs (<500 µm) in 100% of samples and identified 21 polymer types, the most prevalent of which was polyurethane. Confirmation of lung deposition was provided by Jahedi *et al.* [16], who examined sputum and bronchoalveolar lavage fluid (BALF) in 30 patients with respiratory conditions. In sputum, they detected 359 MNPs and 123 in BALF, with the majority being fibres. Relative to the sputum, a greater proportion of MNPs (90%) were below 100 µm in size in BALF.

The study by Amato-Lourenço *et al*. [18] was the first in which MNPs in the human brain were detected, showing evidence of translocation of inhaled MNPs to extrapulmonary tissues via the human olfactory bulbs. MNPs were detected in eight olfactory bulbs out of 15 individuals. A total of 16 synthetic polymer particles were identified predominantly as fragments. The main polymer was polypropylene. The anatomical distribution suggests migration through the olfactory mucosa and neural pathways leading to the CNS. These studies show that inhalation is not only a continuous exposure pathway but also potentially involves neuro-translocation.

Maternal–Foetal Transfer

Emerging human studies provide evidence that MNPs can reach the maternal–foetal interface and may be present within foetal compartments. Using advanced spectroscopic techniques, such as Raman microspectroscopy, Ragusa *et al.* [19] found MNPs in human placental tissues collected from women after full-term delivery, with particles detected on both the maternal and foetal sides, as well as in the chorioamniotic membranes. Sun *et al.* [20] expanded these findings and reported MNPs are not only in the placenta but also in foetal appendages, such as the foetal membrane and umbilical cord, in addition to amniotic fluid and umbilical vein blood.

Detection and Identification Methods of MNPs in Human Tissues

The reliable identification of MNPs in complex biological matrices remains a significant analytical challenge because of the risk of background contamination and the physical limits of microscopy. Current research relies on a combination of spectroscopic and thermoanalytical techniques to confirm both the chemical nature and the concentration of these particles.

Spectroscopy Techniques

Micro-Fourier transform infrared (µ-FTIR) spectroscopy is the most commonly used method for identifying polymer types and works by measuring their specific infrared absorption patterns [23]. However, its spatial resolution is generally limited to particles higher than 10 µm. To detect smaller particles, Raman spectroscopy is used, as its higher resolution allows for the identification of particles down to 1 µm by analysing their inelastic scattering of light [24].

Thermoanalytical Methods

To quantify the total mass of plastic in tissue samples, pyrolysis–gas chromatography–mass spectroscopy (Py-GC-MS) is the gold-standard approach [25]. Unlike spectroscopy, which counts individual particles, Py-GC-MS thermally decomposes the sample and analyses the resulting gases to determine the precise mass of specific polymers. This method is particularly effective for detecting MNPs in blood and highly vascularised organs such as the liver and placenta [26].

Translocation Across Biological Barriers

Fig. 2 shows the pathways of dissemination of MNPs and the mechanisms of toxicity for each organ.

Respiratory Interface

BALF studies demonstrate deep-lung deposition of MNPs [16,17]. Schraufnagel [27] proposed that particle size is the principal determinant of how deeply inhaled MNPs can penetrate the lungs: particles <1 µm remain airborne longer and reach the alveoli easily, while particles around 10 µm are deposited in the upper airways, and particles <100 nm (nanoplastics) can cross the alveolar epithelium transcellularly. Jenner *et al.* [28] analysed digested human lung tissue samples and found 39 MPs, and also showed that MPs were present at significantly higher levels in the lower lung (3.12 ± 1.30 MP/g) compared with the upper (0.80 ± 0.96 MP/g) and middle (0.41 ± 0.37 MP/g) regions.

Olfactory Bulbs

The presence of MNPs in human olfactory bulbs [18] is consistent with size-dependent deposition mechanisms, since particles smaller than 1 mm have been shown to migrate from the olfactory bulbs to the brain. The olfactory bulbs lie above the cribriform plate of the ethmoid bone, and since the plate has multiple foramina of less than 1 mm, it may lead directly to the brain.

Gastrointestinal Barrier

Increasing evidence suggests that MNPs can cross the intestinal barrier to gain access to the systemic circulation. As in the pulmonary system, this translocation appears to be strongly influenced by the particle size and surface charac-

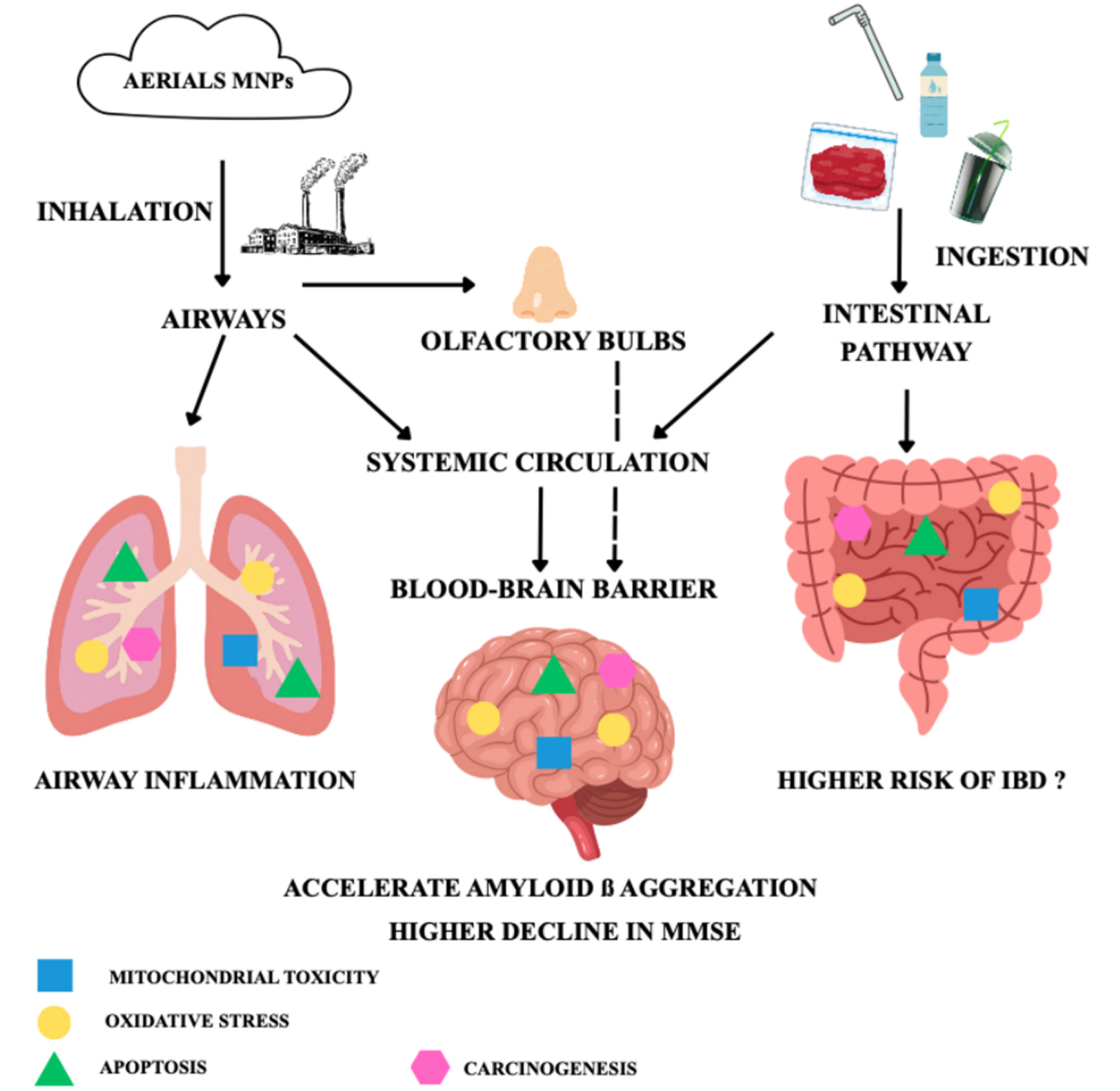

Fig. 2. Illustration of the pathways of dissemination of MNPs and the mechanisms of toxicity for each organ. Currently, the literature does not show that the mechanisms of toxicity differ between organs. Abbreviation: IBD, inflammatory bowel disease. Drawn with Canva Pro (https://www.canva.com).

teristics. The most discussed pathway involves endocytosis and transcytosis by intestinal epithelial cells [29]. Microfold cells are specialised intestinal epithelial cells found in the gut-associated lymphoid tissue, such as Peyer's patches, and represent a key portal of entry. Their main job is to take up luminal antigens and deliver them to the lymphoid follicles, facilitating immune surveillance [30]. This mechanism could be an entry route for MNPs. Another critical determinant of translocation is barrier integrity. Yan *et al.* [13] showed that more microplastics were found in faecal samples of patients with IBD (Crohn's disease and ulcerative colitis) than in healthy controls, and there were correlations between particle load and disease severity. Lifestyle was also a major component, as participants with a higher abundance of faecal MPs drank bottled water, consumed more plastic-packaged fast food, and were exposed to dust in their working and living conditions. Therefore, conditions associated with higher intestinal permeability, such as chronic inflammation, dysbiosis, or IBD, may enhance MP uptake.

While nanoplastics theoretically possess a higher capacity for transcellular passage, direct human evidence for their intestinal absorption remains limited.

Dermal Absorption

Dermal contact represents a complex and less understood exposure pathway. A recent review by McLean *et al.* [31] indicates that while the skin remains a highly effective barrier, a definitive size-based uptake threshold has not been established because of methodological heterogeneity in current studies. Most evidence shows that MNPs primarily localise in the stratum corneum (the outermost layer of the skin containing keratinised cells) and hair follicles. However, some studies have observed particles smaller than 2 µm penetrating deeper epidermal layers. This uptake is influenced by a complex interplay of physicochemical factors, including particle shape, surface charge, and hydrophobicity, rather than size alone. The clinical significance of this pathway remains uncertain, especially considering that impaired skin barrier function or repeated exposure through cosmetic formulations could facilitate deeper penetration.

Mechanistic Cascade of MNP-Induced Cytotoxicity

The cellular mechanisms of MNP toxicity, including oxidative stress and membrane disruption, are detailed in Table 2 (Ref. [32,34–36]). Oxidative stress is one of the earliest biological responses to MNP exposure. Across multiple studies and human tissues, MNPs induce an imbalance between reactive oxygen species (ROS) production and antioxidant defence systems, leading to cellular damage and tissue injury, disrupting homeostasis. However, Huang *et al.* [32] showed that ROS generation is not universally required to mediate cellular injury, finding that exposure to polystyrene nanoplastics induces dose-dependent cytotoxicity despite pharmacological suppression of oxidative stress via N-acetylcysteine (NAC).

Many neurodegenerative diseases have been reported to involve mitochondrial dysfunction, which leads to an increase in ROS levels. Human neuronal models support a causal role for mitochondrial-derived oxidative stress in the response to MNPs [33]. An increase in the MitoSOX level correlated with particle concentration-dependent neurotoxic effects, including neurite degeneration. Importantly, the suppression of ROS using NAC rescued MNP-induced neuronal degeneration. In addition, the intensity of ROS varied according to particle morphology and was least pronounced in neurons exposed to microfibers, but was similar between different concentrations (2 µm, 100 nm, and 20 nm).

Laganà *et al.* [34] showed that MNPs induce a rapid oxidative response in neuronal cells. In SH-SY5Y cells, ROS production was very fast for all particles. Peak ROS was observed as early as 1-hour post-exposure, followed by a slow decline over time that nonetheless remained significantly elevated compared with controls. This highlights the involvement of alternative mechanisms.

The initial oxidative stress directly triggers mitochondrial damage. Mitochondria play a role in cellular homeostasis, integrating energy production, intracellular calcium buffering, redox balance, and cell death signalling. The entry of Ca^{2+} into mitochondria is mainly driven by the mitochondrial membrane electrochemical gradient. Ca^{2+} is an essential secondary messenger in neuronal signalling and plays a pivotal role in maintaining physiological nerve conduction. Tang *et al.* [35] demonstrated that exposure to polystyrene nanoplastics (PS-NPs) significantly disrupts the regulation of this system. In differentiated SH-SY5Y cells, PS-NP treatment induced marked increase in Ca^{2+} levels, concomitant with a reduction in the mitochondrial membrane potential. These effects were observed at concentrations of 100, 200, and 500 mg/L. Therefore, this study shows strong evidence for direct mitochondrial damage [35].

Mitochondria are also the primary site of adenosine triphosphate (ATP) synthesis, which is essential for neuronal function, synaptic transmission, and axonal transport. ATP is produced in the inner membrane folds of mitochondria. Mitochondrial damage induced by NPs has been associated with impaired mitochondrial membrane voltage-dependent anion channels and reduced ATP availability. In SH-SY5Y cells, the ATP levels were reduced by 13.2% and 17.3% at concentrations of 200 and 500 mg/L, respectively.

Ultimately, these mitochondrial alterations and oxidative stress activate cell death pathways. Tang *et al.* [35] showed that in SH-SY5Y cells, exposure to MNPs induced dose-dependent apoptotic cell death. In addition, a significant correlation between the apoptosis ratio and MNP concentration has been observed at concentrations $>$100 mg/L. Cytochrome c is released into the cytoplasm because of mitochondrial damage, resulting in the formation of a complex that activates caspase-3 and results in apoptosis [35].

A critical limitation of current *in vitro* research is the use of MNP concentrations (up to 500 mg/L) that far exceed those detected in the human body. Consequently, these findings should be interpreted with caution, as they may overstate the immediate toxicological risk compared with human exposure.

Microglial cells play a central role in maintaining CNS homeostasis by clearing debris and regulating neuroinflammatory processes. Exposure to MPs has been shown to significantly alter microglial behaviour. Kwon *et al.* [36] showed that in human microglial HMC-3 cells, exposure to MNPs induced marked cellular activation and increased apoptotic cell death. Transcriptomic analyses revealed alterations in genes involved in immune responses. These findings suggest that MNPs not only activate microglia but also induce immune dysfunction.

Multi-Organ Effects

MNPs have a biological effect across multiple organ systems. These effects arise from a combination of oxidative stress, activation of apoptosis, mitochondrial dysfunction, and immune dysfunction.

Table 2. Summary of cellular responses and molecular pathways for *in vitro* studies.

Author (references)	Cell line	Type	Size	Exposure concentration	Exposure duration	Evaluated endpoints	Outcomes	Limitations/Bias
Huang *et al.* [32]	SH-SY5Y (Human Neuroblastoma cells)	PS	50 nm	0.5 to 500 µg/mL	24 hours	Cell viability, ROS production, mechanism of protection	Excessive mitophagy via AMPK/ULK1 pathway; mitochondrial dyfunction, ATP depletion, and ROS production.	Limited to PS, smooth spherical beads, higher concentration than the real exposure
Laganà *et al.* [34]	SH-SY5Y (Human Neuroblastoma cells)	PS	Nano (40–70 nm) and Micro (1–2 µm)	1 to 50 µg/mL	24 hours	Cell viability, oxidative stress and metabolomic profilling	Microplastics was more pro -oxidant than nanoplastics. Alterations in energy metabolism and neurotransmission.	Higher concentrations than the real exposure; static cell culture doesn't mimic blooc brain barrier filtration
Tang *et al.* [35]	SH-SY5Y (Human Neuroblastoma cells)	PS	50 nm	12.5 to 100 µg/mL	24 hours	Cell viability, ROS, mitochondrial membrane potential	Induced mitochondrial dysfunction and oxidative stress.	Lack of long-term exposure data
Kwon *et al.* [36]	HMC-3 (Human Microglial cells)	PS	0.5 µm	10 to 100 µg/mL	24 to 48 hours	Phagocytosis, Cytokine release (IL-6, TNF-α, apoptosis markers)	MPs are phagocytosed by microglia inducing pro-inflammatory responses and apoptosis	Lack of long-term exposure data

PS, polystyrene.

Cardiovascular System

Recent clinical studies have established a significant association between MNP accumulation and cardiovascular pathologies. Marfella *et al.* [21] conducted one of the best-known studies concerning the effects of MNPs in human tissues. In this study, they enrolled 312 patients who were undergoing carotid endarterectomy and found that PE was present in the carotid artery plaque of 150 patients, and PVC was present in 31 patients. Even though these results do not prove causality and the study has some limitations, patients with MNPs in plaques had a higher risk of non-fatal stroke than patients with no MNPs. These findings were supported by Yu *et al.* [37], who reported significantly higher levels of PVC and polyamide 66 (PA66) in the blood of patients with extracranial carotid artery stenosis (ECAS) compared with healthy controls.

It has been proposed that MNP accumulation promotes plaque instability through a dual mechanistic pathway involving endothelial inflammation and localised oxidative stress. Once embedded within the vascular wall or atheromatous plaque, MNPs may act as a persistent irritant that triggers a chronic inflammatory response in the endothelium. This inflammation, coupled with the MNP-induced production of ROS, weakens the fibrous cap of the plaque, thereby increasing the risk of rupture and subsequent thromboembolic events [21,37].

Central Nervous System

Beyond neurotoxicity, Gou *et al.* [38] suggested that MNPs may directly interfere with protein aggregation processes leading to neurodegenerative diseases. Amyloid-ß (Aß) aggregation follows a nucleation-dependent pathway, and in this study, PS nanoparticles were shown to accelerate the nucleation phase of both Aß40 and Aß42 aggregation. This observation is relevant from a clinical perspective, as the aggregation of Aß is known to play a role in neurodegenerative diseases, such as Alzheimer's disease. He *et al.* [39] provide preliminary clinical evidence linking MP exposure to neurodegenerative pathologies. Analysis of cerebrospinal fluid revealed significantly higher levels of PE and PVC MPs in amyloid-positive patients compared with amyloid-negative controls. They even showed that higher baseline cerebrospinal fluid PE levels correlated with a greater decline in the Mini-Mental State Examination (MMSE) score over one year, indicating possibly accelerated Alzheimer's disease cognitive deterioration. Bashirova *et al.* [40] confirmed these findings, as they found that PET nanoplastics accelerate the aggregation process, as shown by a reduction in both the lag time and the fibrillation time.

Nihart *et al.* [41] studied postmortem brain samples from the frontal cortex that were from 2016 and 2024. Brain samples showed higher levels of MNPs than the liver or kidney. However, of note, the liver and brain samples from 2024 had higher concentrations of MNPs than the 2016 samples. To explore the relevance in neurodegenerative conditions, Py-GC was used to analyse 12 individuals with Alzheimer's disease, vascular dementia, or other subtypes of dementia. MNPs were higher in neurodegenerative pathologies than in the normal frontal cortex. The authors suggested that brain atrophy, blood–brain barrier dysfunction, and impaired clearance mechanisms may facilitate MNP accumulation. However, these findings indicate an association rather than a causal relationship.

Respiratory System

MNPs induce the production of ROS, which triggers aberrant autophagy, activating ferroptosis and exacerbating epithelial damage. Wei *et al.* [42] showed a correlation between MNPs and the severity of chronic obstructive pulmonary disease (COPD). Significant epithelial cell death was observed after 24 hours of exposure at >200 µg/mL, indicating that high exposure may compromise airway epithelial integrity. They also showed that the concentrations of MNPs in the lung tissue of patients with COPD were significantly higher than in the control group. Thus, airway MNPs may trigger inflammation in COPD.

Conclusion

This scoping review synthesises the evidence that MNPs are not only environmental contaminants but also biologically active particles that can enter the body, where they accumulate and interact with human tissues. The current literature indicates that the primary routes of entry are ingestion and inhalation, which are followed by systemic distribution and deposition across organ systems, including the gastrointestinal tract, respiratory epithelium, cardiovascular tissues, and the CNS. MNP exposure is associated with a range of pathological processes, including oxidative stress, mitochondrial dysfunction, inflammation, and immune dysregulation, as well as the activation of cell death pathways, such as apoptosis, autophagy, and ferroptosis. In humans, accumulating evidence suggests clinically relevant effects. In the respiratory system, MNPs induce epithelial injury and oxidative cell death pathways that contribute to chronic airway inflammation. Cardiovascular studies report associations between circulating MPs and atherosclerotic disease severity, supporting a potential role in vascular injury. In the CNS, studies suggest that MNPs may contribute to neuroinflammation, mitochondrial dysfunction, and protein aggregation processes, including amyloid-ß-related diseases, with cognitive decline and neurodegenerative disorders.

Despite the increasing number of studies identifying MNPs in human tissues, several limitations remain. First, there is significant methodological heterogeneity in the detection and quantification of particles. As noted in Jin *et al.* [11], the lack of standardised protocols for sample preparation and the varying detection limits of spectroscopic tech-

niques (e.g., µ-FTIR vs Raman) make it difficult to compare concentrations across studies. Second, most current research focuses on larger MPs, while the toxicological impact of the nanometric fraction remains underrepresented. A critical gap in current knowledge is the lack of direct clinical studies in humans. Most available toxicological data are derived from *in vitro* models or animal studies, which may not accurately reflect the complex physiological responses, long-term bioaccumulation, and chronic health outcomes. Finally, there is a lack of long-term longitudinal studies establishing a direct causal link between MNP accumulation and specific chronic diseases in humans. Future research should focus on the development of standardised analytical methods for MP detection in human tissues and biological samples, longitudinal human studies assessing exposure/disease relationships, and particle characteristics. From a public health perspective, strategies aimed at reducing environmental and dietary exposure to MNPs, particularly ultrafine particles, may represent a prudent and preventive approach.

Availability of Data and Materials

Not applicable.

Author Contributions

Study conception and design: YF, MM, JRL; literature search and review: YF, JRL; manuscript drafting and critical revision: YF, MM, JRL. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest. Mario Manto is serving as one of the Editorial Board members of this journal. We declare that Mario Manto had no involvement in the peer review of this article and has no access to information regarding its peer review.

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