

REVIEW ARTICLE

Health impacts and detection challenges of human exposure to microplastics

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Abstract

The widespread use of plastic has led to growing concerns about the release and impact of microplastics and nanoplastics (MPNPs) on both the environment and human health. The surge in plastic production during the COVID-19 pandemic increased the potential for human exposure through ingestion, inhalation, and dermal absorption. MPNPs pose significant health risks due to their mutagenic and carcinogenic properties, primarily through DNA damage and the adsorption of toxic contaminants. Their small size and large surface area-to-volume ratio increase their reactivity with biological tissues. Despite these potential hazards, limited technologies are currently available for detecting MPNPs in humans. This review provides a comprehensive overview of MPNPs, focusing on their origins, chemical compositions, and the mechanisms by which they contribute to carcinogenesis. In addition, it explores various types of cancers linked to microplastic exposure and outlines current methodologies for detecting microplastics in human tissues.

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1. Introduction

Plastics are ubiquitous worldwide, with only 9% of the 460 million tons produced annually in 2022 being recycled. Projections estimate that global plastic production could rise to 1.2 billion tons by 2060.¹ The discovery of microplastics (MPs) in most ecosystems has raised significant concerns regarding contamination and its potential impacts on human health. MPs have been linked to a range of health issues, including infections, inflammation, and disorders affecting the pulmonary, intestinal, and cardiovascular systems.² Over the past 70 years, global plastic production has surged to 359 million tons, with China leading production at 17.5% of the total output. Meanwhile, Turkey produces the highest amount of plastic waste in the Mediterranean region, generating 144 tons daily.³ Notably, 75% of marine debris consists of MPs, with 80 – 90% of this pollution originating from land-based sources.⁴ Even at low concentrations of 10 µg/mL, MPs can cause significant adverse effects in humans and animals, including cytotoxicity, immunological responses, oxidative stress, impaired barrier functions, and genotoxicity.⁵

Researchers have observed increased intestinal residence duration, inflammation, and depletion of energy reserves in the marine worm *Arenicola marina* following exposure

to MPs, which may be associated with reproductive issues. Similarly, juvenile fish (*Pomatoschistus microps*) exposed to pyrene-contaminated polyethylene (PE) MPs exhibited immunotoxicity in their muscle cells, with alterations in the antioxidant systems, lysosomal compartments, and peroxisomal reproduction. MPs can enter the body through ingestion, inhalation, and dermal absorption.⁶ Plastics are found in a wide range of consumer and industrial products, such as children's toys, household appliances, cosmetics, healthcare items, automotive components, textiles, packaging, and construction materials.⁷ The majority of plastic waste is neither recycled nor incinerated, leading to its accumulation in landfills and the environment. Plastic pollution is pervasive, contaminating ecosystems from terrestrial areas to rivers, streams, and oceans. Most plastics do not biodegrade; instead, they fragment over time due to environmental weathering, breaking down into microplastics and nanoplastics (MPNPs).⁸ Food items may also contain MPNPs due to environmental contamination during production. However, there is insufficient scientific evidence to support the notion that MPNPs from food packaging migrate into food and beverages. Humans may encounter these particles through food consumption, inhalation, and skin absorption from personal care products.⁹ MPNPs exhibit a wide range of sizes, shapes, and colors, varying in polymer types, degradation states, and chemical additives introduced during manufacturing.¹⁰ MPs, typically defined as plastic fragments measuring <5 mm in one dimension, can originate from resin pellets or degrade from larger plastic items in the environment. Nanoplastics (NPs) are even smaller, usually <1 µm in size, with a human hair's diameter measuring approximately 70 microns.¹¹ In marine environments, the most common plastic types include PE, polypropylene (PP), polystyrene (PS), and polyvinyl chloride (PVC). MPs enter marine ecosystems primarily through two mechanisms: The natural degradation of larger plastics and transport through rivers and waterways. MPs are typically classified into two categories: primary and secondary. Primary MPs include virgin plastic manufacturing pellets, widely used in both industrial and household items, such as shower gels, cosmetics, and hand and face cleaners. Secondary MPs result from the breakdown of larger plastic debris. It is estimated that, over the past 50 years, up to 0.3 million tons of MPs produced from personal care products have accumulated in aquatic environments worldwide. Due to their large surface area and hydrophobic properties, MPs readily adsorb microbes, heavy metals, and organic pollutants. These characteristics may complicate the evaluation of MP contamination and its associated toxicological risks.¹² The fishing industry is a major contributor to marine plastic pollution, with fishing

nets accounting for over 640,000 tons (10% of total marine waste). These nets fragment into MPs smaller than 5 mm due to processes such as hydrolysis, photodegradation, or biodegradation. Furthermore, MPs can adsorb toxic organic contaminants (OCs) from water, potentially posing cancer risks.¹³

2. Chemical components in micro/nanoplastics

2.1. Polystyrene MPs

MPs are frequently defined as plastic materials smaller than 5 mm. Due to their small size, MPs can interact rapidly with both organic and inorganic pollutants in the environment, including heavy metals, organic compounds, and microbes.¹⁴ These pollutants can be transferred to various environmental media by binding to MP particles. The accumulation of PS-MPs in various organs of organisms has been linked to numerous negative effects, such as decreased body weight, early mortality, respiratory disorders, neurological damage, transgenerational toxicity, oxidative stress, metabolic changes, environmental toxicity, immunotoxicity, and other functional impairments.^{15,16} Recent studies have shown that exposure to MPs of various sizes can alter the gut microbiome, affecting metabolism and leading to intestinal dysfunction and chronic inflammation. Because PS-MPs range in size from 0.5 to 500 µm, they can be readily ingested by a variety of organisms, potentially entering the human food chain.¹⁷ Neurotoxicity is one of the most notable toxic effects observed in a variety of aquatic animals exposed to MPs, with potential links to brain cancers. Moreover, transgenerational toxicity suggests that the effects of PS-MPs are not limited to a single generation, but may also affect subsequent generations.¹⁸

2.2. Bisphenol A (BPA)

First synthesized in the 1890s BPA, with the chemical formula $C_{15}H_{16}O_2$, is a synthetic carbon-based compound containing two 4-hydroxyphenyl groups, formed by condensing two equivalent amounts of phenol with acetone.¹⁹ BPA is widely used as a plasticizer in the production of polycarbonate plastics and food packaging materials. The estrogenic effects of BPA were first identified in the early 1930s, and more recently, the European Union's General.

Court has classified BPA as a "substance of serious concern" due to its endocrine-disrupting properties.²⁰ The European Chemicals Agency had also identified BPA as a harmful substance in plastic production. The compound is commonly found in food containers, water bottles, and receipts, and is associated with various health issues,

including cardiovascular disease, weight gain, reproductive disorders, and breast cancer.²¹

2.3. Phthalates

Phthalates are the most widely used class of synthetic chemicals in terms of plastic production,⁸ with approximately 6,000,000 tons produced globally each year. These compounds are primarily used as plasticizers, which are added to raw plastic materials to impart properties such as pliability, elasticity, and flexibility. Phthalates are colorless, odorless, low-volatility liquids with low solubility in water.²² However, certain phthalates have raised significant concerns due to their detrimental effects on ecosystems and human health. They are known to disrupt hormones in the body, and many are believed to interfere with animal and human reproduction or contribute to cancer development.²³

Dibutyl phthalate and diethyl phthalate can be found on three distinct types of MPs, with particle sizes smaller than 75 µm (PS, PE, and PVC). Other polymers, such as polyvinylidene chloride, polyvinyl acetate, polyurethanes, exterior coatings, non-slip coatings, finishing products, labels, prints, adhesives, sealants, inks, and paints, which are not silicone rubber or natural latex coatings, are also commonly used in plastic production.²⁴ These polymers are subjected to regulation, and restrictions on their use in certain products, including medical items, came into effect on July 7, 2020, under Annex I and Annex XVII of the European Union's regulation on the registration, evaluation, authorization, and restriction of chemicals (Table 1).²⁵

Outside of the water ecosystem, we discovered that the majority of plastic garbage enters the marine environment. Initially, plastics are typically large in size,²⁶ but over time, they degrade due to mechanical stress, ultraviolet

radiation, prolonged exposure to sunlight, oxidation, and hydrolysis, breaking down into smaller particles known as MPs.²⁷ These particles can come into direct contact with humans through inhalation, ingestion, or skin absorption. Marine organisms such as fish, crabs, shrimp, and lobsters may ingest MPs and become contaminated. When humans consume contaminated fish, MPs can enter the human body, potentially leading to cancer (Figure 1).²⁸

3. Carcinogenic impacts micro- and nanoplastics and their derivatives

It is well-established that heavy metals found in stabilizers, pigments, commercial goods, and biocides, contribute to the creation and persistence of plastics. Brominated flame retardants, BPA, phthalates, triclosan, bisphenone, and organotin are among the hazardous chemicals commonly added to plastics, many of which are linked to adverse health effects in humans.²⁹ These chemicals, along with waste products from the plastic industry, often contain neurotoxic, hormone-disrupting, and carcinogenic substances, which ultimately enter the environment through air, land, and water contamination.³⁰ Common chemicals found in polycarbonate plastics include vinyl chloride (in PVC), dioxins (in PVC), benzene (in PS), phthalates and other plasticizers (in PVC and other plastics), formaldehyde, and BPA. In addition, toxic gaseous pollutants, such as dioxins, hydrogen cyanide, and carbon monoxide, are released into the atmosphere by the plastic industry, posing serious risks to both human and animal health and contributing to environmental degradation.³¹

Plastic recycling, which emerged in the 21st century, has gained importance as a potential solution to global environmental concerns.³² A study on plastic reuse and recycling in Northern China revealed important findings

Table 1. Chemical compounds/heavy metals found in plastics and their toxicity/cancer risks

Name of chemical compound/hazardous element	Type of polycarbonate plastic	Toxicity/cancer risks
Polystyrene	-	DNA damage, cardiovascular damage, cancer
PCB	Polystyrene	Hepatocellular cancer
PA, PC, nylon	-	Cell damage, liver toxicity
Alkylphenols, PCB, BPA	BPA	Biliary tract cancer
Aluminium, Antimony	PVC, PBT	Breast cancer
DDT and PCBs	Phthalate	Pancreatic cancer
Cadmium, copper	PVC	DNA damage, cellular-related cancer
Arsenic	Polyester, PVC	Skin cancer, liver cancer, kidney damage, death
Lead	All PVC	Infertility, brain damage, hypertension, cell damage
Barium	PVC	Male estrogen effects, breast cancer

Abbreviations: BPA: Bisphenol A; DDT: Dichlorodiphenyltrichloroethane; DNA: Deoxyribonucleic acid; PA: Polyamide; PBT: Polybutylene terephthalate; PC: Polycarbonate; PCB: Polychlorinated biphenyls; PVC: Polyvinyl chloride.

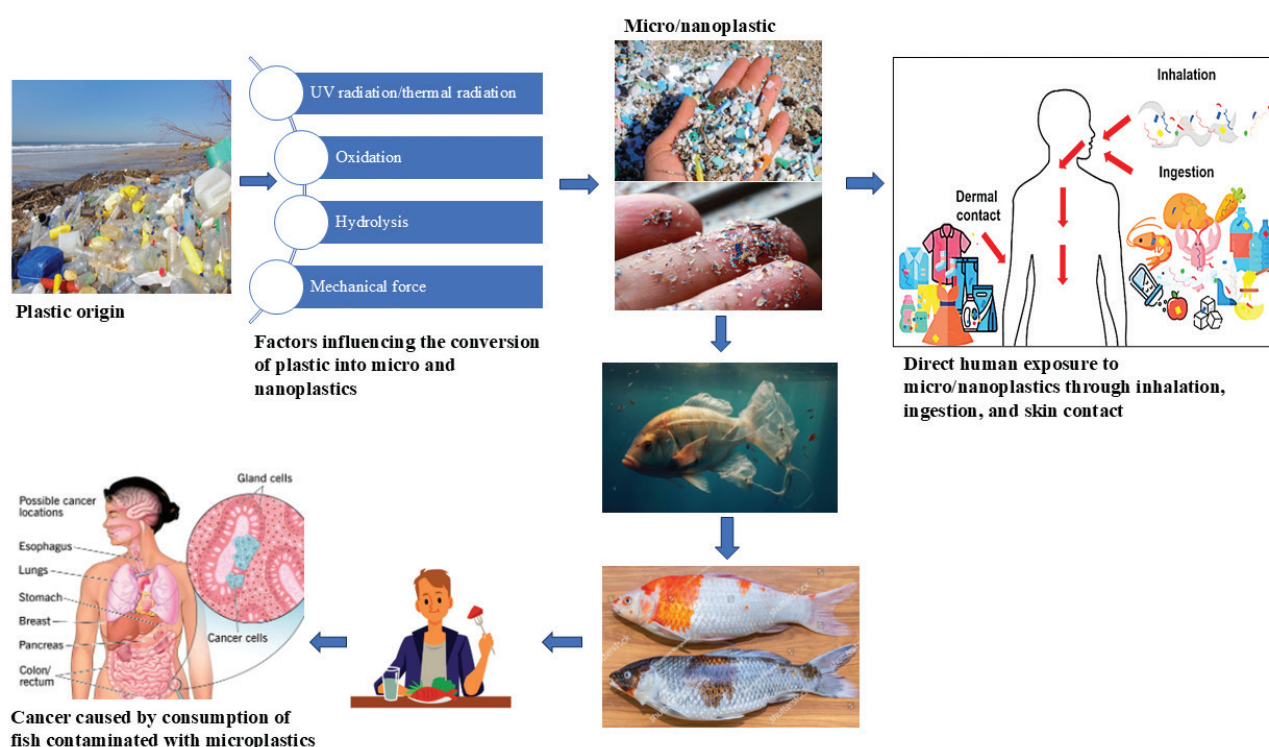


Figure 1. Toxicity process and carcinogenic effects of micro/nanoplastic on humans
Abbreviation: UV: Ultraviolet.

related to the removal of toxic heavy metals from soil samples.³³ Many plastics contain small, potentially toxic elements, such as cadmium and mercury, which can settle in nearby lakes, rivers, and soils. Both carcinogenic and non-carcinogenic effects from exposure to these substances can affect human health, and it is crucial for medical professionals to be aware of potential risks associated with local recycling plants.³⁴ Exposure to these substances can occur through ingestion, dermal contact, and inhalation, with workers in recycling industries being at heightened risk of exposure, potentially disrupting their metabolic processes.³⁵

3.1. Endocrine-related cancers

Endocrine disruptors – substances that interfere with the endocrine system – can lead to cancerous tumors, birth defects, and other diseases that affect development.³⁶ These chemicals alter the synthesis, secretion, transport, binding, or elimination of natural hormones, which are crucial for regulating development, behavior, fertility, homeostasis, and disease onset. Endocrine disruptors are present in numerous consumer and industrial products and can interfere with the body's hormonal function, leading to developmental and non-malignant diseases, as well as various cancers. Bruno *et al.* emphasized the

role of hormone-receptor interactions, such as estrogen/testosterone binding, in cancer types, such as colon, pleural, and bladder cancer.³⁷ Notably, testicular cancer has been found to be more prevalent among workers in the plastics and construction industries.³⁸ MPs and their toxic additives can disrupt several hormone axes, including the hypothalamic-pituitary-thyroid, hypothalamic-pituitary-adrenal, and hypothalamic-pituitary-gonadal (HPG) axes. These substances can cross biological membranes, including the blood-brain barrier, and interfere with hormone receptors. Research using animal models (rats and mice) has shown that exposure to MPs results in metabolic diseases, gut dysbiosis, and intestinal barrier dysfunction.³⁹ Similarly, neurobehavioral changes, altered thyroid function, and metabolic stress have been observed in rats exposed to MPs. Chemicals of concern include alkylphenols, polybrominated diphenyl ethers, phthalates, organotins, perfluorinated compounds, dioxins, BPA, and heavy metals, such as chromium, lead, and cadmium. Approximately 1,000 chemicals are categorized as endocrine-disrupting compounds (EDCs), which alter hormone receptor expression and disrupt hormone synthesis, secretion, transport, and action, leading to endocrine and developmental disorders.⁴⁰

3.1.1. Biliary tract cancer

Baj *et al.* conducted a comprehensive multicenter study across six European countries, and their findings suggest a potential relationship between workplace exposure to EDCs and an increased risk of extrahepatic biliary tract cancer in men, specifically in the extrahepatic bile duct and the ampulla of Vater.⁴¹ Polychlorinated biphenyls (PCBs) may be a significant risk factor. The data gathered suggests that the complexity of endocrine disruption has increased due to the presence of multiple MP derivatives. The researchers acknowledged the limitations in data collection and the restricted specificity for both liver cancer and gallbladder carcinoma.⁴² Although the results are informative, further clarification and precision are needed. The researchers further emphasized that exposure to EDCs with known estrogenic activity (e.g., PCBs, BPA, and alkylphenols) increased the incidence of extrahepatic biliary tract cancer, with PCB exposure showing a statistically significant association.⁴³ Estrogen receptors may be an important factor to consider in future research, given the similarity in carcinogenic properties related to pathophysiology and this compelling finding. Biliary cancer, sometimes referred to as cholangiocarcinoma, is a type of cancer that develops in the bile ducts. These ducts are part of the digestive system and transport bile from the liver and gallbladder to the small intestine. Intrahepatic cholangiocarcinoma develops in the bile ducts of the liver, perihilar cholangiocarcinoma occurs near the hilum where the bile ducts exit the liver, and distal cholangiocarcinoma develops in the bile ducts outside the liver, near the small intestine.⁴⁴

3.1.2. Hepatocellular cancer

Hepatocellular carcinoma (HCC) is often characterized as an insidious malignancy that can take years to develop. However, its progression may be expedited by exposure to various toxic agents, including both cytotoxic and non-cytotoxic compounds that can cause DNA damage.⁴⁵ Numerous studies have demonstrated that combinations of PCBs can induce hepatic lesions, alongside abnormalities in other organ systems. Axley *et al.* analyzed patients with HCC who exhibited elevated serum PCB levels before diagnosis. The findings of this study corroborate earlier observations linking liver involvement to hepatitis B virus, hepatitis C virus, and excessive alcohol consumption (over 60 g/day for 10 years).⁴⁶ This evidence suggests a potential link between PCB exposure and the development of HCC, particularly in heavily industrialized regions. PCBs, a class of synthetic organic chemicals, are implicated in carcinogenic processes affecting multiple organ systems.⁴⁷ Studies also indicate that MPs may interfere with the neuroendocrine system and affect the production of sex hormones by acting on the HPG axis.⁴⁸ MPs disrupt the blood-testis barrier

in the reproductive system, affecting spermatogenesis in males and causing placental dysfunction, ovarian atrophy, endometrial hyperplasia, and fibrosis in females. Furthermore, the reproductive and lipid metabolism of progeny may be impacted by MPs. However, research in this area is hampered by the complex compositions of MPs and limitations in detection techniques. It is essential to implement mitigation strategies to address reproductive consequences and adopt sustainable practices to minimize MP pollution.⁴⁹

3.1.3. Pancreatic cancer

A multicenter investigation evaluated the relationship between occupational history and serum concentrations of OCs in patients with exocrine pancreatic cancer (EPC). The study proposed an approach that could enhance understanding of the links between OCs and serum concentrations.⁵⁰ Interestingly, the data revealed lower OC serum levels in agricultural workers but higher PCB interactions with elevated serum concentrations in metal sector workers. Sana *et al.* emphasized the need for further serum analysis and research on OCs to identify key occupational sources of OC contamination in EPC and to understand how OCs may contribute to the association between specific industries and EPC risk.⁵¹ A limited number of studies have also suggested that diet influences blood OC concentrations and Kirsten rat sarcoma viral oncogene homolog (*K-Ras*) mutations in EPC. One study specifically highlighted a positive correlation between higher levels of PCB 138, PCB 153, and p,p'-dichlorodiphenyltrichloroethane (DDT) with increased consumption of milk and dairy products (excluding butter). In addition, there is strong evidence linking elevated blood OC levels with milk and dairy consumption.⁵² No significant correlation was found between meat, fish, or meat sausages and p,p'-DDT levels. However, both OCs and pancreatic cancer may play critical roles in the development of cancerous changes. A small number of studies have mentioned the influence of diet on serum OC concentrations and *K-Ras* mutations in EPC. One investigation pointed to dairy products (excluding butter), demonstrating that increased consumption of milk and other dairy products is significantly associated with higher levels of p,p'-DDT, PCB, and PCB 153.⁵³ Increased intake of milk and other dairy products was also found to be significantly associated with blood levels of OCs. Other food groups, such as meat and fish, showed negligible links, and no significant negative relationship was found between meat or sausage consumption and p,p'-DDT levels. The correlation between *K-Ras* mutations in EPC and the widespread intake of dairy products has piqued the curiosity of researchers.⁵⁴

3.1.4. Blood cancer/leukemia

Micro- and nanoplastic particles may pose a risk for the development of hematological cancers, in addition to solid tumors. A recent study by Prata *et al.* suggests that plastic particles can accumulate in the human bloodstream.⁵⁵ These particles are primarily composed of PE terephthalate, PE, and polymers such as styrene and poly(methyl methacrylate). However, it remains unclear whether plastic particles can be detected in plasma or which specific cell types are responsible for their transport. Chen *et al.* found that exposure to PS-MPs in mice led to hematotoxicity and disruptions in metabolic pathways, including Janus kinase/signal transduction and transcription activation signaling and T cell homeostasis.⁵⁶ Researchers have also shown that PS-MPs inhibit the ability of bone marrow cells to form colonies and reduce the number of white blood cells in peripheral blood. These findings suggest that hematotoxicity may also be caused by plastic particles in human blood.⁵⁷ Barrier cells, including bronchial epithelial and endothelial cells, can facilitate the movement of particles through the circulatory system. PSNPs, with a size of 5 nm, have been found to travel through the bloodstream to various organs, including the stomach, intestines, liver, and bones in mice.⁵⁸ Plastic particles smaller than 100 nm can enter tissues and the circulatory system through the pulmonary and gastrointestinal pathways in mammalian animal models. MNPs can interact with the blood and vascular endothelium, leading to cell injury, and acute and chronic inflammation. This interaction may cause a range of related pathophysiological events, including oxidative stress, genotoxicity, and cytotoxicity.⁵⁹

3.1.5. Inflammatory bowel disease (IBD)/colorectal cancer (CRC)

The incidence of IBD is often higher in rapidly developing nations, likely due to severe environmental contamination. The intestinal environment in IBD patients differs significantly from that of healthy individuals, and MPs may exacerbate intestinal damage and accelerate disease progression.⁶⁰ However, knowledge about the impact of MNPLs on IBD patients and the underlying mechanisms remains limited. Notably, MNPL levels in CRC biopsies are significantly higher than in non-tumoral colon tissues, suggesting a potential link between MNPL exposure and CRC development. This is further supported by the increasing frequency of CRC in individuals under 50 years old.⁸ Ingested MNPLs can cause intestinal injury and inflammation, potentially entering the bloodstream and spreading to other tissues. Once in systemic circulation, MNPLs may pose risks to the cardiovascular system. Although research on the cardiovascular effects of MNPL exposure is still in its early stages, recent findings indicate

their presence in various cardiovascular tissues and blood.⁶¹ MNPLs may damage vascular endothelial cells, leading to adverse cardiovascular outcomes through interactions with blood and immune cells. MPs in the diet can disrupt the balance of microbiota and mucus in the colon.⁶² As such, they may modify colonocyte exposure to potentially hazardous gut microbiota components, influencing the development of CRC. Furthermore, given MPs' tendency to adsorb hydrophobic compounds from their surroundings, direct contact between colonocytes and MP-associated carcinogens may heighten the risk.⁶³ The presence of substantial amounts of MPs in stool samples shows that most MPs pass directly from the small bowel to the colon. Evidence from human blood and tissue samples indicates that not all ingested MPs travel through the gastrointestinal system.⁶⁴ Instead, particle size is expected to influence the distribution, deposition, and/or accumulation of MPs, as the distribution of particles throughout the respiratory tract depends strongly on particle size.⁶⁵

3.1.6. Effect on the reproductive system

Recent years have seen a significant rise in environmental contamination from MPNPs, accompanied by growing concerns about their potential toxicity to human health, particularly regarding the reproductive system. Infertility affects over 15% of couples globally, with environmental factors being among the most significant contributors.⁶⁶ However, the effects of MPs and NPs on reproductive organs, including the ovaries and testes, remain poorly understood. These particles can enter the body through ingestion, inhalation, and dermal contact, targeting the reproductive system in a size-dependent manner and disrupting the development of germ cells and other somatic cells.⁶⁷ Research indicates that MPs and NPs, when combined, can cause a range of reproductive effects, such as reduced female fertility and abnormal offspring development in various species. Under certain conditions, these particles may significantly affect female reproduction, with potential consequences extending beyond reproductive health.⁶⁸

Studies indicate that MPs may interfere with the neuroendocrine system and affect the production of sex hormones by acting on the HPG axis. MPs can also disrupt the blood-testis barrier in the reproductive system, which affects spermatogenesis in males and causes placental dysfunction, ovarian atrophy, endometrial hyperplasia, and fibrosis in females.⁶⁹ Furthermore, the reproductive and lipid metabolism of progeny may be impacted by MPs. However, research is hampered by the complex compositions of MP and limitations in detection techniques. It is essential to implement mitigation strategies for reproductive consequences while adopting sustainable practices to minimize microplastic pollution. Exposure to

PS during the first trimester poses unknown hazards to the maternal-fetal immune balance, which is crucial for a healthy pregnancy. Understanding the biological effects and processes of MP exposure during pregnancy is an important area for future research.⁷⁰

3.2. Techniques for detecting microplastics in the human body

The majority of human samples, including placenta, stool, colon, lung, sputum, liver, breast milk, and blood, have been found to contain MPs. Although some links have been observed – such as MPs being found only in liver tissues from patients with cirrhosis and their higher MP concentrations in the feces of IBD patients compared to healthy individuals – these findings have not yet been conclusively proven due to several limitations. Given the limited information available on the toxicity of MPs in humans, this topic requires thorough investigation in future studies.⁷¹ Future research should include more representative sample sizes, as studies identifying the presence of MPs in the human body are sparse and often involve a small number of samples. To address concerns about the impact of MPs on human and animal health, it is essential to implement validated methods for their detection and characterization.⁷¹ Current approaches for analyzing MPs in human samples can be grouped into several categories. Commonly used techniques include microscopy, spectroscopy,⁷² and chromatography; however,

a significant portion of MPNPs remains undetectable using these methods (Table 2). The detection of MPs in humans is still in its early stages, and additional research is needed to fully comprehend the situation. While the existence of MPs in human populations is concerning, it remains unclear how severe their effects will be.⁷³

3.2.1. Detection of MPs and nanoplastics in the human body

Several recent studies provide substantial evidence that MPs can enter the human body, as MPs have been detected in various human samples. These investigations utilized previously established analytical methodologies. Here, we present a concise summary of research exploring the presence of MPs in human matrices, highlighting significant findings and conclusions. MPs and NPs can be absorbed by humans, as particles smaller than 150 µm are capable of passing through the mammalian gastrointestinal epithelium, although only about 0.3% of these particles are likely absorbed. Like other foreign substances, MPs may enter tissues through various passive and active transport mechanisms that are not yet fully understood. Generally, particles under 10 µm in size can penetrate various parts of the human body, crossing barriers and cellular membranes.⁷⁴ MPs may accumulate and cause localized toxicity by triggering or exacerbating immune responses, impairing the body's defense against infections, and disrupting energy reserves.

Table 2. Analytical methods employed in the detection of microplastics⁷⁴⁻⁸⁴

Name of compound	Method of detection	Reference
LDPE, PE, PET	FTIR spectroscopy	77
Polyethylene, polypropylene, polystyrene, and polyethylene terephthalate, were	FTIR and TED GC-MS	78
PVC	Raman spectroscopy	79
polyethylene, polypropylene, polystyrene, and polyethylene terephthalate, were	Hyperspectral imaging technology	80
Polyesters, Polyphenols, PE, PP	Thermo-analytical analysis	81
Polystyrene, PET, LDPE, HDPE	Electron microscopy, GC-MS	82
Polyethylene, polypropylene, polyethylene terephthalate, polyvinyl chloride, polyamide - PA	Infrared spectroscopy/microscopy	83
Polypropylene and polyethylene	Tandem mass spectrometry with pyrolysis-gas chromatography	84
BPA	GC-MS, LC-MS	85
Phthalates, BPA	LC-MS, GC-MS, Py-GC-MS	86
Polyvinylidene difluoride, heavy metals	SEM, ATR-FTIR, (ICP-OES)	87

Abbreviations: ATR-FTIR: Attenuated total reflectance- Fourier transform infrared spectroscopy; BPA: Bisphenol A; FTIR: Fourier transform infrared spectroscopy; GC-MS: Gas chromatography-mass spectrometry; HDPE: High-density polyethylene; ICP-OES: Inductively-coupled plasma optical emission spectroscopy; LC-MS: Liquid chromatography mass spectrometry; LDPE: Low-density polyethylene; PE: Polyethylene; PET: Polyethylene terephthalate; PVC: Polyvinyl chloride; SEM: Scanning electron microscope; TED GC-MS: Thermal extraction-desorption gas chromatography mass spectrometry.

Historical workplace studies have shown respiratory symptoms and diseases among workers in industries producing flocculent materials, vinyl chloride, and synthetic textiles, supporting inhalation as a route of MP exposure.⁷⁵ Humans can inhale MPs present in the air, potentially allowing them to enter and persist in the lungs. In addition, the gastrointestinal tract serves as a primary pathway for the ingestion and absorption of MPs in humans. Studies using two human intestinal cell lines (Caco-2 and NCM 460) assessed the effects of both pristine and *in vitro* digested PS-MPs (simulating passage through the gastrointestinal tract). Results showed considerable accumulation of 0.1 and 1 μm PS-MPs in both cell lines after 24 h of treatment.⁷⁶

3.3. Microplastic/nanoplastic-triggered molecular pathways

The toxic effects of MPs and NPs on the human body have raised significant concerns. MPs have been reported to increase oxidative stress, leading to tissue damage, developmental abnormalities, metabolic disorders, epigenetic changes, reproductive issues, and reduced gamete quality.⁸⁸ Recent studies have identified dysregulated proteins in cancer-related signaling pathways, including the mitogen-activated protein kinase pathway (receptor tyrosine kinase, RAS, extracellular signal-regulated kinase, c-Jun N-terminal kinase, P38, nuclear factor erythroid 2-related factor 2 [NRF2], tumor necrosis factor α , and tumor necrosis factor α receptor) and the phosphatidylinositol 3-kinase- protein kinase B pathway. Boran *et al.* reported that PS-MPs affect oxidative processes in ovarian tissues, reducing anti-Müllerian hormone levels and inducing apoptosis and oxidative stress through the Kelch-like ECH-associated protein 1 (KEAP1)/NRF2/heme oxygenase 1 signaling pathway in both rats and granulosa cells.⁸⁹ Furthermore, C57BL/6J mice exposed to PSNPs exhibited systemic oxidative stress, indicated by increased malondialdehyde levels. In addition, as PSNP doses increased, the fluorescence intensity of KEAP1 and P53 in femur sections rose, along with the expression of the cell oxeiptosis pathway (KEAP1, mitochondrial serine/threonine protein phosphatase, apoptosis inducing factor mitochondria associated 1) and the cell senescence pathway (P53/P21).⁹⁰ Overall, these findings suggest that PSNP exposure induces oxidative stress, potentially leading to cell oxeiptosis, senescence, and hematotoxicity.

MPNPs also activate inflammatory pathways, with response kinetics varying by cell type, as seen in the upregulation of P50 and P38 expression and elevated Toll-like receptor 4 expression.⁹¹ Another study demonstrated that polystyrene nanoplastic (Pst-NP) disrupts

mitochondrial function by affecting complex I, leading to excessive mitophagy through the AMP-activated protein kinase/serine/threonine-protein kinase pathway, which results in dopaminergic neuron death. Notably, melatonin can counteract PS-NP-induced mitochondrial dysfunction and motor impairments by regulating mitochondrial autophagy, offering insights into the neurodegenerative mechanisms of MPNP-induced Parkinson's disease-like symptoms and highlighting melatonin's protective potential in mitigating environmental MPNP risks.⁹² Collectively, these studies strongly suggest that MPNP toxicity may involve multiple inflammatory pathways.

4. Conclusion

Humans are inevitably exposed to MPs due to their widespread presence in the environment, leading to their accumulation in various tissues. This situation highlights the urgent need to investigate the potential health impacts of MPs, particularly their role in carcinogenesis. Extensive research involving laboratory rodents and human-derived cells has identified toxicity targets and underlying mechanisms, aiming to clarify the link between MP exposure and cancer. Given that cancer remains one of the leading causes of death globally, this review is of critical importance. However, the lack of standardized methods, validated reference materials, and consistent analytical procedures hinders the accurate quantification of human NP exposure. While PS is often used in studies due to its ease of synthesis, plastics such as polyolefins (e.g., PE, PP), polyesters, and polyurethanes are more prevalent in commercial use. Given the diversity in particle sizes, shapes, and chemical compositions of plastics, the health effects of different types of MPNPs remain unclear. Therefore, future research should focus on the risks of long-term exposure to various MPNPs, considering realistic doses and exposure conditions.

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Conflict of interest

The authors declare that they have no competing interests.

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