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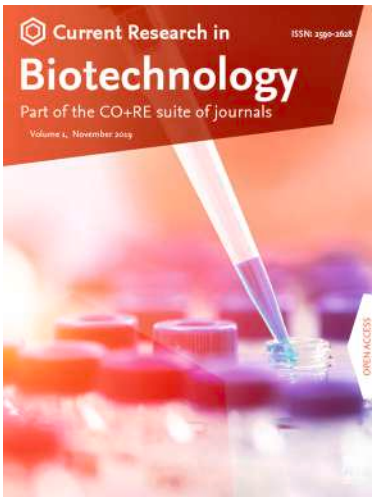

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Review

Microplastics Contamination in Food Products: Occurrence, Analytical Techniques and Potential Impacts on Human Health

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Abstract: Chemically, microplastics (MPs) are synthetic materials composed of plastic monomers and additives and vary in size from 0.1 to 5,000 μm. Due to their chemical stability and the widespread use of plastics for various purposes, MP contamination of the environment has increased dramatically, leading to the contamination of daily consumer products as well. Although previous studies have reported the environmental impacts of MPs, only a few studies have highlighted the occurrence of MPs in food products and their possible effects on human health. Recent investigations have identified MP particles in drinking water and other beverages, seafood, plant products, salt, sugar, and honey, raising an alarm over the safety and quality of these food items. Ingestion, inhalation, and dermal contact of such food and other consumer goods are the common routes through which MPs may enter the human body and can have several deleterious health impacts including oxidative stress, inflammation, immunotoxicity, increased risk of neoplasia, cellular metabolism impairment, neurotoxicity, gut microbiome dysbiosis, disruption of reproductive system among others. A collective approach employing source control, recycling, biodegradable plastics, strengthening legislation, and bioremediation could be a promising and sustainable solution to control the MP pollution. The key challenge appears to standarize detection methods along with reducing the MP contamination from the food products as well as from the environment. Therefore, this review focuses on the occurrence of MPs in several food products, current methods of analysis, potential health impacts, and strategies to mitigate the widespread MP pollution. It also adds novel findings, knowledge gaps, and recommendations that can guide future research in this field.

Keywords: Microplastics, Food Contamination, Analytical Methods, Human Health

1. Introduction

Plastics are materials made from long chains of polymer molecules created by combining smaller monomers and incorporating specific additives (Hahladakis et al., 2018; Udovicki et al., 2022). There are two major types of plastics: thermoplastics and thermosetting plastics. The fundamental difference between these two is that thermosetting plastics cannot be remolded, while thermoplastics can be. Some of the major thermosetting plastics include polyurethane (PU), epoxy resins, vinyl esters, and silicones, while polyvinyl chloride (PVC), polyethylene (PE), polypropylene (PP), polystyrene (PS), polyethylene terephthalate (PET), polyamide (PA), and polycarbonate (PC) are examples of thermoplastics. Among these, PE, PP, PVC, PS, and PET

are the major plastics commonly encountered in microplastics (MPs) (Udovicki et al., 2022). Additionally, these five types also account for more than 70% of the global demand for plastic (Plastics Europe 2022). Studies have indicated that in 2021, the production of plastic reached an astonishing 390.7 million tons (Plastics Europe 2022), which is predicted to reach 33 billion tons by 2050 (Cincinelli et al., 2019).

MPs are a diverse assortment of materials with varying shapes, including fragments, fibers, spheroids, granules, pellets, flakes, and beads, with dimensions ranging from 0.1 to 5,000 μm. Based on their origin, MPs can be classified as primary MPs and secondary MPs. Primary MPs are synthetic materials manufactured for specific dimensions and are commonly used in textiles, pharmaceuticals, sandblasting, and personal care items like facial and body exfoliants (Browne, 2015; Cole et al., 2011). Secondary MPs primarily come from the breakdown of larger plastic materials (macro and MPs) and are more prevalent in the environment (Andrady, 2017). Further differentiation can be made to nanoplastics (NPs) based on particle size. NPs are described as substances with either an external dimension in the nanoscale range (0.001-0.1 μm) or an internal or surface structure within that same size range. NPs are usually formed from the breakdown of MP debris through various biotic and abiotic processes (CONTAM, 2016). Due to their smaller size, NPs can easily permeate through biological membranes and are considered more damaging than MPs (Yee et al., 2021).

Generally, two types of chemicals are found in MPs: additives and polymeric raw materials like monomers or oligomers that come from the plastics themselves, as well as chemicals absorbed from the environment. Additives are substances deliberately added during plastic production to impart properties like color and transparency. They enhance the plastic's resistance to factors such as temperature, humidity, light, microbes, ozone, etc., and improve its mechanical, thermal, and electrical strength. These additives consist of fillers, plasticizers, UV stabilizers, antioxidants, coloring agents, lubricants, and flame retardants (Hahladakis et al., 2018). While the primary purpose for use of these additives is to enhance the characteristics of the plastics, most of them are known toxins and pose a significant risk of contaminating the soil, air, and water. In addition to these additives, plastics also absorb chemicals from their surroundings, which leach plastic particles out of the plastic polymer into the environment (Campanale et al., 2020). Studies have shown that toxic substances such as polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), as well as heavy metals, have been absorbed by MPs, leading to various toxic effects when consumed by organisms. Other hazardous chemical additives such as bisphenol A (BPA), phthalates, triclosan, bisphenols, organotin, and brominated flame retardants (BFR) are also present in plastics that can seriously impact human health (Galloway, 2015). On the other hand, recent investigations have demonstrated that MPs themselves can have serious negative health impacts including inflammation, oxidative stress, immunity suppression, promotion of carcinogenesis, and alteration of reproductive and cognitive functions (Prata et al., 2020; Yee et al., 2021; Q. Zhang et al., 2022). A recent study predicted the plastic-attributable disease burden in the USA, which was estimated

to be $249 billion, accounting for about 1.22% of the total gross domestic product (Trasande et al., 2024). The majority of the economic burden was caused by PBDE exposure. This raises a serious concern about the impact that MPs and other chemicals associated with MPs can have on human health.

Various studies have been published regarding the environmental impact of MPs in recent years. Since there is an increasing level of MPs in terrestrial and aquatic environments, they can easily contaminate food products used for human consumption reaching human body. Which is supported by recent studies reporting MPs in human placenta (Zhu et al., 2023), breast milk (Ragusa et al., 2022), and stool samples (Yan et al., 2021) and blood (Leslie et al., 2022). Recent research on commonly consumed protein products (seafood, terrestrial meats, and plant-based proteins) conducted by Milne and colleague showed contamination of MPs. Based on which, they estimated that in USA, adult annually consumes 11,000 ± 29,000 MP particles, with a maximum yearly exposure of 3.8 million MPs (Milne et al., 2023), raising a serious concerns over MP contamination of food products and the potential health impacts of MPs on humans. Although there are still less studies on common food to find MPs contamination, some research had shown presence of MPs in common food products, including beverages, plant-based items, marine products, as well as common additives like salt and sugar, which are summarized in Figure 1. These food products serve as potential sources through which MPs can enter our bodies. Therefore, this review aims to provide an overview about the occurrence of MPs in several food products, current methods of analysis, potential impacts on human health, and applicable strategies to mitigate and prevent the MP pollution.

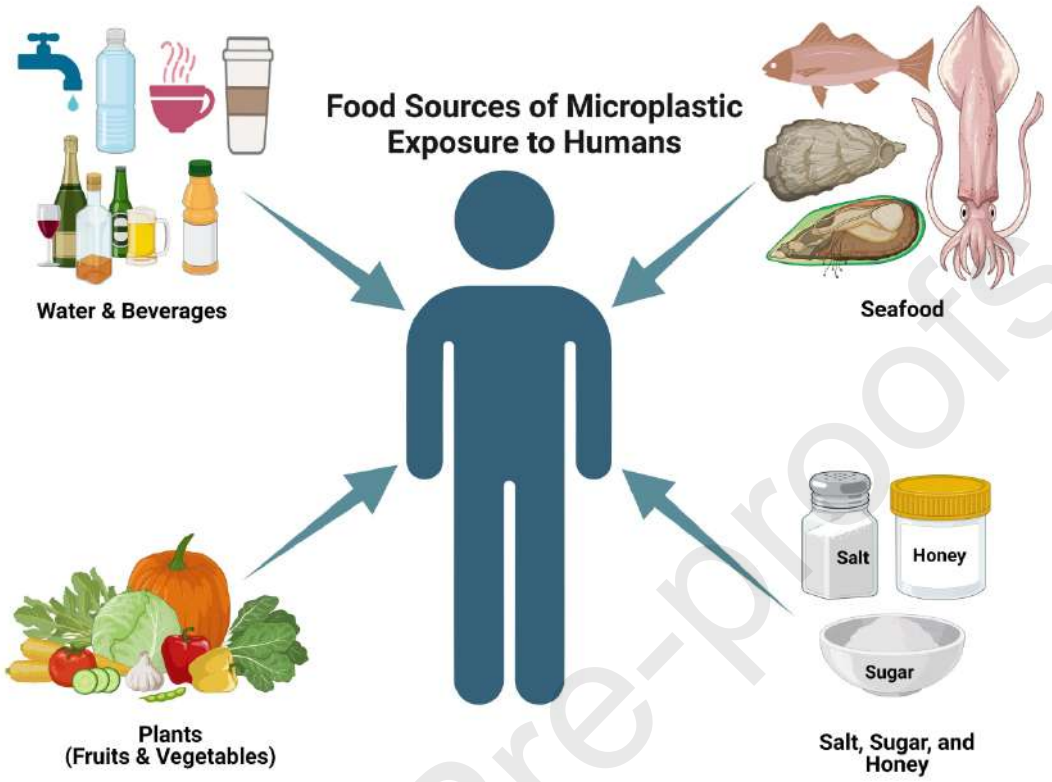

Figure 1. Various food products that can be contaminated by microplastics.

2. Methodology

PubMed and Google Scholar were used to search for related information on sources, analytical methods, routes of exposure and health impacts of microplastics. The keywords “microplastic”, “beverage”, “drinking water”, “carbonated water”, “mineral water”, “sea food”, “analytical methods” and “health impacts” were used individually or jointly to search for papers published in between 2000 and 2024 which were further collected, analyzed and appropriate information were used for the preparation of the manuscript.

3. Global Occurrence of Microplastics in Food Products

3.1 Water and beverages

Water is considered the major source of MPs in our diet, as it is consumed on a daily basis, potentially leading to chronic exposure. Moreover, water is substantially utilized for various purposes, including the production of food, cleaning and sanitizing food processing facilities, and serving as a component in food ingredients and various processing steps (Udovicki et al., 2022).

MPs can enter drinking water sources through various means, such as surface runoff after rain, treated and untreated wastewater effluent, combined sewer overflows, discharge from industries, degraded plastic waste, and atmospheric deposition (WHO, 2019). Several research studies have investigated the presence of MPs in water. Additionally, other studies have found MPs in various beverages and alcoholic drinks, as shown in the **Table 1** below.

Table 1: Occurence of MPs in drinking water and beverages

Type of product	**Sample origin**	**Composition of MPs**	**MPs size (*μ*m)**	**Analytical method**	**Total count of MPs (MP/L)**	**Reference**
Packaged ice cubes	Mexico	PP, PE, PVA, PA,	20-500	SEM-EDX+ATR-FTIR spectroscopy	19 ± 4 - 178 ± 78	(Shruti et al., 2022)
Processed drinking water,	Germany	PE, PET, PP, PA	5-1000	Raman microspectroscopy	0.001 - 0.197	(Pittroff et al., 2021)
Single-use plastic bottled water		PET, PES, PE, PP, PA	5-100	Micro-Raman spectroscopy	14 ± 14	(Schymanski et al., 2018)
Returnable plastic bottled water		PET, PES, PP, PE, PA	5-100		118 ± 88	
Glass bottled water		PET, PES, PE, PP, PA	5-100		50 ± 52	
Water from beverage cartons		PET, PES, PP, PE, PA	5-1500		11 ± 8	

Plastic bottled water Glass bottled water Tap water	Saudi Arabia	PE, PS, PET	25–500	Micro-FTIR	1.9 - 4.7	(Almaiman et al.)
Tap water	China	PE, PP, PPS, PS, PET	3-4453	Micro-Raman spectroscopy	440 ± 275	(Tong et al., 2020)
Bubble tea	China	PE, PET, PE/PEA, PE/PP	20- > 1000	Micro-Raman spectroscopy	70.7 ± 149	(Bai et al., 2022)
Coffee		PE, PET, PS, PE/PEA			21.3 ± 29.8	
Single use plastic bottled mineral water	Germany	PET, PET+olefin, PP	1.5-10	Micro-Raman spectroscopy	2649 ± 2857	(Oßmann et al., 2018)
Reusable plastic bottled mineral water		PET, PP, PET+olefin, PP	≤1.5 - ≥10		4889 ± 5432	
Glass bottled mineral water		PE, PP and styrene-butadiene-copolymer, PET	≤1.5 - ≥10		6292 ± 10521	
Single use plastic bottled water			6.5 - ≥ 50	Optical & Fluorescence	140 ± 19	

Glass bottled mineral water	Thailand	PET, PE, PP, PA	6.5 - ≥ 50	microscope, ATR-FTIR, Confocal Raman spectroscopy	52 ± 4	(Kankanige & Babel, 2020)
Plastic bottled water	United Kingdom	PET, ethyl p-ethoxybenzoate	0.6 – 5	Optical microscopy, FTIR, TD-GC/MS		(Y. Huang et al., 2022)
Cold tea	Mexico	PA, PEA	100-2000	SEM-EDX, Micro-Raman spectroscopy	11 ± 5.26	(Shruti et al., 2020)
Soft drinks		PA, PEA, ABS	100-3000		40 ± 24.53	
Energy drinks		PA, PEA	100-3000		14 ± 5.79	
Beers		PA, PET, PEA	100-3000		152 ± 50.97	

3.2 Seafoods

Seafood accounts for more than 17% of global protein consumption (Lusher et al., 2017). It serves as a major source of nutrition for humans due to its richness in high-quality proteins and healthy fats such as polyunsaturated fatty acids (PUFAs), along with various micronutrients that have been shown to offer numerous health benefits (Jin et al., 2021).

Plastics can enter the aquatic ecosystem through both land-based and marine or freshwater sources. However, plastics originating from land-based sources, such as garbage, industrial discharges, wastewater effluents, plastic transported by winds or tides, account for more than 80% of plastic debris in the marine environment (Jambeck et al., 2015). These plastic particles may be ingested by marine organisms due to their resemblance to natural food sources or may adhere to the external appendages of these organisms. This poses a risk of trophic transfer of MPs in the

marine ecosystem, as organisms in higher trophic levels may indirectly accumulate MPs through the consumption of tainted prey. Ultimately, there is a risk of human exposure to MPs when consuming contaminated seafood, such as fish. This risk is more relevant in the case of small fish species that are consumed whole, like sardines, anchovies, and other small-sized fish. The risk is relatively lower for larger fish species since they are gutted before consumption (Lusher et al., 2017). Various studies have found the presence of MPs in fish, shellfish, bivalves, and crustaceans obtained from both wild and aquaculture farms or markets, in packaged seafood and some of these findings are highlighted in the **Table 2** below.

Table 2: Occurrence of MPs in seafood

Type of seafood	**Sample origin**	**Composition of MPs**	**MPs size (*μ*m)**	**Analytical method**	**Concentration**	**Reference**
Fish (46 species)	Brazil	PA, Rayon, PE	380-4160	ATR-FTIR	1.2 ± 5.0 particles/individual	(Schmid et al., 2018)
Fish (27 species)	China	CP, PET, PES, PE-PP	40-5000	Micro-FTIR	0.2 - 17.2 particles/g	(Jabeen et al., 2017)
Fish (14 species)	China	PET, PE, Rayon, PS, PA	20-5000	Micro-FTIR	0.33-5.3 particles/individual	(Su et al., 2019)
Fish (10 species)	UK	PA, Rayon, PES, PS, PE	130-5000	FTIR	1.9 ± 0.10 particles/individual	(Lusher et al., 2013)
Fish (26 species)	Portugal	PP, PE, Alkyd resin, Rayon, PES	217-4810	Micro-FTIR	0.27 ± 0.63 particles /individual	(Neves et al., 2015)

Fish (22 species)	Germany		22-4986		0.2 - 0.5 particles/individual	(Roch et al., 2019)
Fish (3 species) ~~Commercially important~~	Turkey	PE, PES, PA	300-2500	FTIR	0.8 - 1.2 particles/individual	(Kılıç, 2022)
Fish (4 species) Commercially important	Persian Gulf		< 300	SEM	18.50 ± 4.55 - 5.66 ± 1.69 particles/10 g fish muscle	(Akhbarizadeh et al., 2018)
Fish (6 species)	South Korea	PTFE, PE, rayon	100-5000	Micro-FTIR	5 - 56 particles/individual	(Park et al., 2020)
Bivalve (3 species)	Iran	PE, PET, PA	10-5000	FTIR, SEM	0.2 - 2.2 particles/g	(Naji et al., 2018)
Bivalve (8 species)	China	PE, PET, PA	5-5000	Micro-FTIR	2.1 - 10.5 particles/g	(J. Li et al., 2015)
Bivalve (*Meretrix meretrix*)	India	PU, PVCA, PVC, PET,	21.06-1500	Fluorescence microscope, Raman spectroscopy	0.18 ± 0.04 particles/g	(Dowarah et al., 2020)
Bivalve (*Mytilus edulis*)	UK	PES, PP, PE	5-5000	Micro-FTIR	0.7 - 2.9 particles/g	(J. Li et al., 2018)
Bivalve (*Mytilus galloprovincialis*)	Greece	PE, PP, PTFE	<100 to 1000	FTIR	1.9 ± 0.2 particles/individual	(Digka et al., 2018)

Bivalve (*Mytilus edulis*)	France, Belgium, Netherlands	PE, PS	15-500	Micro-Raman spectroscopy	0.2 ± 0.3 particles/g	(Van Cauwenberghe et al., 2015)
Bivalve (*Zygochlamys patagonica*)	Argentina	PET, PE, PP, PEP, PEPD	5-5000	Micro-FTIR	0.32 ± 0.11 particles/g	(Akoueson et al., 2020)
Bivalve (*Manila clams*)	Canada	PP, PS, nylon		Optical microscopy	0.07 ± 5.47 particles/g	(Davidson & Dudas, 2016)
Fish (52 species)	USA	PP, PET, PMMA, PS, PA	330-475	FTIR		(Phillips & Bonner, 2015)
Packaged powdered spirulina	Turkey	PP, PS, PE, PES	70-5691	Stereomicroscopy, Micro-Raman spectroscopy	17.34 ± 4.22 MPs/100g dw	(Tutaroğlu et al., 2023)
Capsule/tablet spirulina					10.43 ± 2.45 MPs/100g dw	
Breaded shrimp	USA	PET/PES, PE, PP, PS, PU	40-27300	Raman Spectroscopy	1.3 ± 1.9 MP/g	(Milne et al., 2023)

3.3 Plants

Only a handful of studies have investigated MPs in fresh foods such as vegetables and fruits. A recent study analyzed the occurrence of MPs in commonly consumed fruits and vegetables in Turkey and found that tomatoes were mostly contaminated with MPs, namely PE, PP, and PET, with an estimated annual intake of 398,520 particles per individual per year (Aydın et al., 2023). Likewise, another study on common edible fruits and vegetables in Italy showed that apples, carrots, and lettuce were mostly contaminated with MPs. Moreover, the researchers indicated that fruits were more contaminated with MPs than edible vegetable parts, probably due to their greater size, complexity, high vascularization of the fruit pulp, and age of the tree (Conti et al.,

2020). Similarly, Tympa and colleagues observed that acrylonitrile butadiene styrene MPs accumulated in the roots of radish plants (*Raphanus sativus*) after two weeks of treatment with the powder of the same MPs (Tympa et al., 2021). Another study demonstrated the uptake of PS-MPs by carrot roots. The authors observed that PS-MPs of size 1 *μ*m can enter and accumulate in the intercellular layers of the carrot roots, while 0.2 *μ*m-sized PS-MPs can transfer to the leaves. Furthermore, the study concluded that the presence of arsenic in groundwater (used in hydroponics) aids in the increased entry of PS-MPs into the carrot roots (Y. Dong et al., 2021). A recent study on lettuces grown in urban vegetable gardens with high traffic density in Portugal showed higher levels of MPs (Canha et al., 2023). Additionally, retention of MPs in plants, such as radish, Italian lettuce, wheat, and corn plants, was reported through their roots, even at a very early growth stage (Gong et al., 2021). Therefore, humans have direct exposure to MPs through fresh fruits and vegetables.

3.4 Salt, sugar, and honey

Salt, sugar, and honey also represent sources through which MPs can enter the human body. We regularly use table salt and sugar in our daily lives as taste enhancers and food additives. They are also exploited as additives, stabilizers, and thickeners in both the pharmaceutical and cosmetic industries. The contamination of honey has been attributed to environmental sources. It is believed that contaminant particles may be carried into the hives by the bees or introduced during honey processing, or both (Liebezeit & Liebezeit, 2013). Based on their origin, salts can be categorized into sea salt, lake salt, rock salt, river, or well salt. Evaporation is used to produce sea and lake salt, while mining is employed for rock salt. River and well salt are obtained from wells located in non-coastal areas (Iñiguez et al., 2017). Various studies that reported MPs on salts, honey, and sugar from different countries around the globe are summarized in **Table 3** below.

Table 3: Occurrence of MPs in salt, sugar and honey

Type of food	**Sample origin**	**Composition of MPs**	**MPs size (*μ*m)**	**Analytical method**	**Concentration (particles/kg)**	**Reference**
Sea salt	India	PE, PS, PET, PA, PES	<500-5000	Digital microscope + FTIR	56 ± 49 - 103 ± 39	(Seth & Shriwastav, 2018)

Sea salt	China	PET, PE, CP, PES, PB, PP	45-4300		550 – 681	(Yang et al., 2015)
Sea salt	Japan	PP, PE, PET, PI-PS, PAN, PA-6	160-980	Stereomicroscope + Raman spectroscopy	1	(Karami et al., 2017)
Sea salt	Malaysia				0 – 2	
Lake salt	Iran				1	
Sea salt	South Africa				4	
Sea salt	France				0 – 2	
Sea salt	Portugal				0 – 10	
Sea salt	Australia				0 – 9	
Unidentified	New Zealand				1	
Sea salt, Rock salt, Lake salt	Turkey	PE, PET, PU, PP, PMMA, PA-6, PVC	20-5000	Raman spectroscopy	16 - 84 (sea) 9 - 16 (rock) 8 - 102 (lake)	(Gündoğdu, 2018)
Commercial salt, Rock salt	Sri Lanka	PE, PP, PU, PET, PVC	65-25000	Stereo-microscope +FTIR	11 - 193 (commercial) 64 (rock)	(Kapukotuwa et al., 2022)
Sea salts	Croatia, Italy	PET, PVC, PE, PS, PA, PP	10-150	Microscopy + Micro FTIR	70 - 200 (Croatia)	(Renzi et al., 2019)

					170 - 320 (Italy)	
Sea salt, well salts	Spain	PET, PE, PP	30-35000	Stereo- microscope +FTIR	50 - 280 (sea salt) 115 - 185 (well salt)	(Iñiguez et al., 2017)
Sugar	Germany	Colored fibers and fragments	10-9000	Stereomicroscope	217±123 (fibers) 32±7 (fragments) 1100 (total fibers and fragments)	(Liebezeit & Liebezeit, 2013)
Sugar	Bangladesh	ABS, PVC, PET, EVA, CA, PTFE	<300	Stereo- Microscope +FTIR	343.7 ± 32.08	(Afrin et al., 2022)
Honey	Germany	Synthetic fibers and fragments	40-3100	Stereo-microscope	10-336 (fibers) 2-82 (fragments)	(Liebezeit & Liebezeit, 2015)
Honey	Ecuador	PP, PE, Polyacrylamide	5.15-5174.01	Inverted microscope + FTIR	22 – 114	(Diaz-Basantes et al., 2020)
Honey	Germany, France, Italy, Spain, Mexico	Colored fibers and fragments	10-9000	Stereomicroscope	166 ± 147 (fibers)	(Liebezeit &

					9 ± 9 (fragments)	Liebezeit, 2013)

4. Routes of Exposure of Microplastics

There are three major routes through which MPs can enter the human body: ingestion, inhalation, and dermal contact. As discussed above, ingestion of MPs can occur from foods and drinks contaminated by MPs. Inhalation of MPs can happen through airborne particles originating from synthetic textiles, urban dust, and rubber tires (Prata, 2018). Dermal exposure may occur through wounds, sweat glands, or hair follicles, which can be present in cosmetics products, textiles, or dust (Revel et al., 2018; Schneider et al., 2009). These routes will be further explained in the following sections.

4.1 Ingestion

The major route through which humans consume MPs is ingestion (Lehner et al., 2019). Studies have found the presence of MPs in human stool samples, primarily PET, PA, and PP, suggesting consumption of MPs by them possibly through contaminated food and drinks (Schwabl et al., 2019; Yan et al., 2021). Additionally, other studies have identified MPs in human placenta (Zhu et al., 2023), breastmilk (Ragusa et al., 2022), blood (Leslie et al., 2022), infant formulas (Kadac-Czapska et al., 2023) and in oral healthcare products as well (Protyusha et al., 2023). However, studies have not yet explored the fate of MPs in humans once they enter the gastrointestinal (GI) tract. Investigating the route of MP particles through the GI tract would be significant.

Particles may enter the GI tract through contaminated food products or drinks and through mucociliary clearance after inhalation (Salim et al., 2014). As discussed earlier, MPs have been found in various foodstuffs and drinks, such as seafood, salt, sugar, honey, bottled water, beer, etc., making their ingestion likely. Cox and colleagues reported an annual intake of 39,000 to 52,000 MP particles per individual based on the American diet (Cox et al., 2019). Similarly, it is estimated that Europeans consume 11,000 MPs per individual per year through the intake of bivalves (Van Cauwenberghe & Janssen, 2014)., whereas from the consumption of table salt 37 MPs per individual per year in Europe (Karami et al., 2017) and 100 MPs per individual per year in China (Yang et al., 2015) were reported.

After ingestion, permeation of MPs at a paracellular level is not likely, as the relevant pores at the tight junction channels have a maximum functional size of approximately 1.5 nm (Yee et al., 2021). It is more probable that MPs enter the body through the lymphatic tissue and could potentially do so through endocytosis and permeate microfold (M) cells in the Peyer's patches (Bergmann et

al., 2015). After intraperitoneal injections in mice, it was observed that peritoneal macrophages engulfed 1, 5, and 12 μm PMA and PS particles through phagocytosis (Carr et al., 2012). The intestinal mucus can be penetrated by insoluble particles due to an increase in solubility resulting from the adsorption of particles in the "corona" (a collection of proteins) of intestinal contents (Powell et al., 2007).

4.2 Inhalation

Next to ingestion, another major route of human exposure to MPs is through inhalation. MPs are released into the atmosphere through various sources, such as synthetic textiles and the abrasion of materials like car tires and buildings (Prata et al., 2020). The lungs possess a large alveolar surface area, around 150 m^2, with a very delicate tissue barrier that is less than 1 μm thick. This thin tissue barrier of the lungs allows NPs to permeate and reach the capillary bloodstream, enabling NPs to travel throughout the human body and have toxic effects (Lehner et al., 2019).

Prata (2018) estimated that 26-130 airborne MPs are inhaled per day, while Vianello and colleagues reported daily inhalation of 272 MPs if a male person engages in light activity (Prata, 2018; Vianello et al., 2019). These estimations depend on sampling techniques and factors related to space usage, such as cleaning schedules, activities, types of furniture materials, and seasons. The deposition of particles in the respiratory system is influenced by their characteristics, like size and density, and smaller, less dense particles can reach deeper areas of the lungs. Such deposited particles are subsequently cleared by macrophages or are translocated to the systemic circulation or lymphatic system. However, the extensive surface area of small particles can trigger an intense release of chemotactic factors in the respiratory system, hindering macrophage migration and increasing permeability, leading to chronic inflammation referred to as dust overload (Prata et al., 2020). *In vitro* studies on normal human lung epithelial cells BEAS-2B exposed to PS-MPs (1.67–2.17 μm) resulted in cytotoxic and inflammatory effects through the induction of ROS formation (Dong et al., 2020). The authors reported that PS-MPs reduced the levels of α1-antitrypsin in cells, suggesting an increased risk of chronic obstructive pulmonary disease (COPD). Moreover, a previous study on exposure of PS nanospheres (size 64 nm) to rats has also shown to cause infiltration of neutrophils and inflammatory conditions in the lungs together with the expression of proinflammatory genes in the epithelial cells (Brown et al., 2001). The study suggested that the smaller the particles, the greater the inflammatory response, as smaller particles have a greater surface area.

4.3 Dermal exposure

Exposure to MPs through skin contact is considered a less important route than ingestion and inhalation. However, NPs (<100 nm) are believed to be able to permeate through the skin barrier (Revel et al., 2018). The use of cosmetic products, such as facial and body scrubs, which are topically applied to the skin, represents a significant source of MP exposure through dermal

contact (Browne, 2015; Cole et al., 2011). Additionally, nanocarriers used for drug delivery via topical application represent another source of dermal exposure (Schneider et al., 2009).

The stratum corneum is the topmost layer of the skin that acts as a shield against external harm, chemicals, and microbes. It is composed of corneocytes encased in sheets of hydrophilic lipids, such as ceramides, long-chain fatty acids, and cholesterol (Bouwstra et al., 2001). Since MPs are hydrophobic in nature, it is speculated that their entry into the body through the stratum corneum is unlikely via contaminated water, but they might enter through sweat glands, hair follicles, or skin wounds (Schneider et al., 2009). Several external factors may cause NPs to permeate through the stratum corneum. Skin damage caused due to UV rays exposure makes the skin barrier more fragile, which may facilitate the penetration of NPs through the stratum corneum (Biniek et al., 2012). The potential for NPs to penetrate the skin barrier has been shown to be increased by some common ingredients found in body lotions, including urea, glycerol, and *α*-hydroxyl acids (Jatana et al., 2016).

Alvarez-Roman et al. studied the route and distribution of PS particles (20-200 nm) through the skin. They found a greater deposition of NPs of 20 nm compared to 200 nm in the hair follicles (Alvarez-Román et al., 2004). Similarly, another study conducted by Campbell et al. also found that PS particles (20-200 nm) can permeate only the upper layer of the skin, to a depth of 2 to 3 *μ*m (Campbell et al., 2012). Subcutaneous administration of PE disks of size less than 10 mm for 98 days resulted in the encapsulation of PE particles with minimal signs of inflammation. However, PVC stabilized with organo-tin or plasticizers induced encapsulation with moderate degeneration, necrosis, and neutrophilic infiltration (Van Tienhoven et al., 2006).

5. Analysis of Microplastics

5.1 Sampling

Sampling of MPs can be performed using one of the following methods: selective, bulk, or volume-reduced (Hidalgo-Ruz et al., 2012). Selective sampling involves directly extracting the MPs from environmental samples that are visually recognizable. This method is useful for surface sediment samples, typically for plastics with particle sizes ranging from 1-6 mm (Karlsson et al., 2017). Bulk sampling is a technique in which the entire volume of the sample is collected without reducing it. This method is suitable for MPs that are visually difficult to identify. On the other hand, volume-reduced sampling refers to a process in which the bulk sample is reduced, and only the portion of the bulk sample that is relevant for further processing is retained during sampling. Both bulk and volume-reduced samples require additional laboratory processing (Hidalgo-Ruz et al., 2012).

5.2 Sample pretreatment

After sampling, it is usually not possible to directly analyze the MP samples, as the samples collected from the environment typically contain impurities. Therefore, it is essential to separate and extract the collected samples. Various pretreatment methods can be used, including sieving, filtration, flotation (density separation), visual sorting, and chemical digestion (Hidalgo-Ruz et al., 2012; M. Jin et al., 2021).

MP extraction by the screening method involves passing the samples through several sieves of different mesh sizes. Particles that are retained in the sieve are collected, while those that pass through the sieve, including the impurities, are removed. The sieves are usually made of stainless steel or copper (Hidalgo-Ruz et al., 2012).

Similar to the sieving method, the filtration method uses a filter medium such as glass fiber, polycarbonate, and nitrocellulose filter, with a specific pore size to separate the plastic particles, commonly from liquid samples. Vacuum can be applied to increase the efficiency of filtration. The pore size of the filter can range from 0.45-20 μm (Crawford & Quinn, 2017a).

Sample pretreatment by the density separation method uses the principle of density differences between the target MP particles and impurities. In this method, the sample is mixed with a saturated solution (e.g., NaCl, NaI, $ZnCl_2$), followed by shaking for a certain time to promote thorough mixing. The high-density particles settle to the bottom, while the lighter particles with MPs float on the surface of the solution. Finally, the supernatant with the plastic particles is collected and separated for subsequent processing. The density of the MP particles ranges from 0.8 to 1.4 g cm^{-3} (e.g., PP, PE, PS, etc.) (Hidalgo-Ruz et al., 2012). A saturated solution of NaCl (1.2 g cm^{-3}), which is cheap, easily available, and non-toxic, is mostly used to separate low-density MPs such as PP, PS, PE, etc. from water or salt samples, while NaI solution (1.8 g cm^{-3}) and $ZnCl_2$ (1.6 g cm^{-3}) are used for sorting high-density MPs like PVC, PET from water, salt, or seafood samples (M. Jin et al., 2021).

Visual sorting and separation is an easy and convenient method for MP analyses. It is crucial for separating MP particles from other items like animal parts, seaweed, shell fragments, glass, and metal particles, etc. This is commonly performed by direct observation of the sample or simply by using a microscope. Furthermore, other materials like soil, sand, etc., which are attached to the plastic fragments, can be removed by washing. Plastic materials separated this way can then be dried and stored in the dark with temperature-controlled settings (Hidalgo-Ruz et al., 2012).

Preprocessing by digestion or chemical methods is commonly used for samples of biological origin (such as aquatic organisms, vegetables, and fruits) to remove organic impurities. The digestion process includes acidic, alkaline, or enzymatic digestion by acidic, alkaline, or enzyme solutions, respectively. For acidic digestion, 30% hydrogen peroxide (H_2O_2), 65% nitric oxide (HNO_3), hydrochloric acid (HCl), perchloric acid ($HClO_4$), or their mixture is used to digest the

biological samples. A combination of both enzymatic followed by acidic or alkaline digestion is also used (Karlsson et al., 2017).

5.3 Detection methods

In general, the detection of MPs involves two phases: first, the physical characterization of the particles, followed by the chemical characterization, which confirms the chemical profile of the particles. For physical characterization, various microscopy methods are employed, such as stereo- and fluorescence microscopy, transmission electron microscopy (TEM), scanning electron microscopy (SEM), and atomic force microscopy (AFM) (Sridhar et al., 2022). Among these methods, fluorescence, TEM, and SEM help characterize and evaluate the physical and chemical properties of polymers. Whereas, for chemical characterization, Fourier-transform infrared spectroscopy (FTIR), Raman spectroscopy, and thermal techniques like differential scanning calorimetry, thermogravimetry, pyrolysis-gas chromatography-mass spectrometry (py-GC-MS), and combinations of these methods can be used. The sole purpose of these identification techniques is to differentiate MPs from false MPs and quantify MPs (Tirkey & Upadhyay, 2021).

Some of the common methods employed in the detection, identification, and quantification of MPs are discussed in detail below:

5.3.1 Visual identification

Direct observation of MPs with the naked eye is the simplest, easiest, and most cost-effective method for identifying MPs. A microscope can also be used for better visualization. However, this technique can only detect large particles, and there can be variations in results from person to person. The potential for confusion in visualization due to the similar appearance of contaminants like algae, charcoal, seeds, and leaves with MP fibers cannot be ignored. The use of dyes to visualize MPs has also been explored to aid in the visual identification of MPs (Lv et al., 2021). An empirical study by Hidalgo et al. found that 70% of particles assumed to be MPs were actually non-plastic materials when examined using FTIR spectroscopy. Despite its simplicity, this method has many limitations, making it a highly unreliable method for identifying MPs (Hidalgo-Ruz et al., 2012).

5.3.2 Scanning electron microscopy (SEM)

SEM is one of the most widely used analytical techniques for physical characterization, primarily focusing on surface characteristics and identifying additives present in MPs samples (Tirkey & Upadhyay, 2021). SEM functions by directing a high-intensity electron beam into the samples, which interacts with the samples and emits secondary electrons. The analysis of these secondary electrons provides information about the topography and morphology of MPs in the samples. Additionally, the interaction of the samples with the incident electron beam produces X-ray photons, characteristics to the elements present in the samples. The installation of an EDS

(energy dispersive spectroscopy) detector with SEM allows for the differentiation of these characteristic X-ray spectra to identify elements present in MPs samples (Schwaferts et al., 2019). An example of this is seen in a study by Pan et al., where they found a strong nitrogen peak on polystyrene, polypropylene, and polyethylene samples, representing bioaccumulation resulting from the interaction between MPs and biota (Pan et al., 2019).

SEM offers several advantages. Firstly, it provides images with high resolution, facilitating the examination of MPs' topography. Secondly, SEM, when coupled with an EDS detector, can rapidly distinguish non-plastic particles from small plastic particles that are difficult to categorize visually. Plastic microparticles exhibit a strong carbon signal, along with other elemental signals from additives, while non-plastic MP samples lack a sharp carbon peak (Blair et al., 2018; Cooper & Corcoran, 2010). A noteworthy use of this method is the detection of MPs in marine samples where MPs are embedded in thin biofilm, fish scales, mineral crust, radiolarians, and crustaceans, often resembling marine organisms. These MPs can be easily identified by the presence of a strong C-peak, while natural mineral particles mentioned later exhibit brighter scattered electrons due to their high calcium and silica content. Another advantage of this method is that the samples used for SEM are artifact-free and do not degrade during the sample processing, allowing for further analysis using FTIR and Raman spectroscopy (Wagner et al., 2017).

5.3.3 Thermal methods

This is one of the easiest, cheapest, and most reliable methods for characterizing MPs by analyzing their degradation products. Degradation products are examined using techniques such as gas chromatography, mass spectrometry, thermogravimetry, differential scanning calorimetry, and more to identify MPs. This method is destructive and is particularly suitable for environmental samples from aquatic animals, water, and sediments, which may face challenges in dissolution, extraction, and hydrolysis. There is an increasing trend in the use of thermal methods for the analysis of MPs, as evidenced by the growing number of publications citing their use, from one article in 2019 to seven articles ((Peñalver et al., 2020).

Some of the techniques used for analyzing MPs through thermal methods include pyrolysis gas chromatography coupled with mass spectrometry (py-GC-MS), thermogravimetry (TGA), TGA-MS, TGA-differential scanning calorimetry (TGA-DSC), DSC, TGA-thermal desorption-GCMS (TGA-TD-GC-MS), and others (Peñalver et al., 2020).

5.3.4 Raman spectroscopy

Raman spectroscopy provides information about the chemical structure of molecules present in MPs through their spectral fingerprint. Inelastic scattering of light by molecules generates vibrational spectra that are specific to different molecules (Araujo et al., 2018). This technique allows the detection of very small-sized MPs, down to 1 μm, which would be challenging to detect using other methods (Crawford & Quinn, 2017a). Raman spectroscopy offers several advantages,

including better resolution for samples containing small-sized MP particles, high sensitivity in detecting non-polar functional groups, narrowed spectral bands, and reduced interference from water (Tirkey & Upadhyay, 2021).

Schymanski et al. conducted point mapping and identified MPs released into bottled water from packaging materials using Raman spectroscopy (Schymanski et al., 2018). Ghosal et al. made efforts to optimize Raman spectroscopy for MP analysis by developing an algorithm to remove background fluorescence and obtain clear Raman spectra of polymers. Thus obtained spectra, when compared with a library, provide information about the size, morphology, and chemical composition of MP particles (S. Ghosal et al., 2018). Sobhani et al. utilized a confocal Raman microscope to visualize MP particles from natural soil/sand samples, identifying five different types of MPs (PVC, PET, PS, PE, and PP). The use of a microscope allowed the selection and analysis of samples from each pixel, facilitating comparisons and analyses based on a reference library of spectra (Sobhani et al., 2019). Recently, Qian and co-workers developed a new data-science-driven hyperspectral stimulated Raman scattering (SRS) imaging technique that enables single-particle analysis of micro-nano plastics. Unlike traditional Raman spectroscopy which has relatively poor resolution and sensitivity, SRS microscopy has an imaging contrast mechanism that allows rapid identification of MPs as well as NPs with high sensitivity, specificity, and throughput (Qian et al., 2024).

5.3.5 FTIR

The FTIR technique has been widely employed for the detection of MPs due to its reliability, simplicity, and non-destructive nature. Different types of plastics can be identified by observing specific IR spectra band patterns (Tirkey & Upadhyay, 2021). When a sample is exposed to IR radiation, MPs absorb this radiation by altering the dipole moment of their bonds, making it possible to detect polar functional groups in MPs. By identifying the functional group, we can determine the polymer type and assess the physicochemical weathering of MPs by analyzing oxidation intensity using the FTIR technique (Büchtemann, 1993; Cooper & Corcoran, 2010; Käppler et al., 2016). Importantly, this technique provides accurate chemical properties of MPs without causing damage to the samples. MPs with particle sizes of up to 20 μm can be analyzed using this method (Tirkey & Upadhyay, 2021).

Furthermore, this technique has been further optimized to enhance reliability and expand the detection range of MPs, leading to the development of Micro-FTIR, attenuated total reflection FTIR, and focal plane array FTIR methods.

5.3.5.1 Micro FTIR

FTIR alone is unable to detect MPs below 20 μm. To address this limitation, an optimized Micro-FTIR method was developed, allowing the detection of samples below 10 μm. Reflectance and transmittance FTIR are two widely used modes for analyzing small-sized MPs. Observations have

indicated that this technique can detect MPs in marine sediments, natural fibers, and semisynthetic fibers by comparing the obtained spectra of samples with standard spectra in a library (Cai et al., 2019; Harrison et al., 2012; Löder & Gerdts, 2015).

5.3.5.2 Attenuated total reflection FTIR (AT-FTIR)

This technique is a rapid and reliable method for detecting polymer samples from water and other biological origins (Büchtemann, 1993; Cooper & Corcoran, 2010; Käppler et al., 2016). It identifies particles through surface contact analysis, where the plastic sample needs to be in contact with a crystal (Shim et al., 2017). Song et al. employed this technique to identify MPs smaller than 50 *μ*m in sea surface and beach sand samples, and they observed increased detection efficiency with decreasing particle size. The increased efficiency was due to a higher concentration of MPs as the particle size decreased. Additionally, this technique can identify polymer type, polymer origin, and polymer behavior (Song et al., 2015). Furthermore, this method can detect MPs with uneven surfaces, providing stable spectra regardless of the surface morphology. However, there are limitations to this technique, including the high pressure produced by the probe, which can damage fragile and weathered MPs, and the electrostatic attachment of small MPs to the tip of the probe (Shim et al., 2017).

5.3.5.3 Focal plane array (FPA)-FTIR

The FPA-FTIR technique can be used to analyze and identify MPs below 20 *μ*m in size (Cai et al., 2019; Harrison et al., 2012; Löder & Gerdts, 2015). This technique allows scanning of all MP residues on filter paper simultaneously, providing a high degree of lateral resolution without the need for pre-sorting in the filter zone. As a result, it generates multiple spectra in a single measurement using a grid of detectors. This method enables the analysis of various small-sized MPs assays with a high degree of accuracy (Tagg et al., 2015). It has been successfully used to detect various types of MPs including nitrile, PU, PA, cellulose fibers, PVC, PET, low-density PE, high-density PE, and PS (Morais et al., 2020).

5.3.6 Near Infrared Spectroscopy (NIR)

The near-infrared ray can penetrate deeper into MPs than infrared (IR), making it the method of choice for accurately identifying the nature of MPs. Furthermore, MPs can be detected in bulk without the need for sample preparation, making the process easier. Small-sized MPs (with a size of 1 *μ*m) present in environmental samples can be easily detected using this technique. When MPs are exposed to near-infrared (NIR) radiation, they absorb the radiation and generate molecular overtone and combination vibrations. The resulting patterns of C-H, N-H, and C-O bands give an approximation of the types of molecules present in the MPs (Tirkey & Upadhyay, 2021).

One interesting example of using this method for MPs identification was conducted by Corradini et al. They found that soil polluted with MPs exhibited lower reflectance in the near and shortwave IR region in a concentration-dependent manner, as detected using a spectrophotometer (Corradini et al., 2019). Paul et al. were also able to detect several types of MPs present in soil at very low concentrations (1% by mass) using advanced high-throughput NIR spectroscopy coupled with chemometrics. They were able to characterize the detected MPs based on size, age, and concentration in the soil sample (Paul et al., 2019). Pakhomova et al. further used a Micro NIR spectrophotometer to identify MPs with a size smaller than 1 mm present in a marine sample, demonstrating the excellence of using this tool for MPs identification (Pakhomova et al., 2020).

5.3.7 NMR spectroscopy

Proton Nuclear Magnetic Resonance (^{1}H-NMR) is rarely used, yet it is a highly reliable method for analyzing MPs samples. It can be employed for both qualitative and quantitative analysis of MPs. The peak intensity of hydrogen (H) in NMR provides the basis for quantifying MPs in a sample. However, in this method, the MPs sample should be dissolved in an appropriate deuterated solvent before scanning (Tirkey & Upadhyay, 2021).

Peez et al. applied quantitative NMR (qNMR) and validated methods for the quantitative determination of MPs in samples using a calibration curve of standard MPs (Peez et al., 2019). Later, Peez and Imhof quantified some MP samples using Peak Fitting as an alternative method to integration and a calibration curve, demonstrating the quantitative potential of NMR for detecting MPs of various sizes, shapes, and polymer varieties (Peez & Imhof, 2020).

Different analytical methods commonly employed for MPs detection, quantification and characterization discussed above are summarized in the **Table 4** below.

Table 4: Comparison of different methods available in characterization of MPs (Lv et al., 2021; Peñalver et al., 2020; Sridhar et al., 2022; Tirkey & Upadhyay, 2021)

Analytical Method	**Advantages**	**Disadvantages/limitations**
Optical detection	● Simple, inexpensive and fast as performed by naked eyes ● Particle of greater than 500 μm can be detected ● Can be used with optical microscope as well	● Counting miscalculation and errors ● Small particle can't be visualized ● Transparent MPs can't be visualized ● Can't be used with complex mixture

		• Less reliability
SEM	• Gives high resolution images • Ideal for determining surface morphology • Can detect MPs and non-MPs rapidly when used with EDS detector	• Rigorous sample preparation needed • Incomplete chemical information • Can't be used for quantification of MPs
Thermal Methods	• Both qualitative and quantitative information about MPs can be achieved • Fast, Simple and easy to perform • Sample preparation is not needed • Range of selectivity and sensitivity can be achieved using different detection methods	• Destructive method • Signal overlapping might happen • Complex sample are difficult to analyze with some detectors
FTIR	• Gives an information about sample's chemical composition • Nondestructive methods • Can be performed with small samples • No need of sample preparation • Can detect very small particle of up to 10-20 μm • Gives information about size distribution of particles • ATR-FTIR can be used irrespective of thickness, shape and polymer type	• Instrument is expensive • Laborious work and takes long time for complete analysis • Signal overlapping happen due to contaminants and additives • Can't be performed when sample contain water
Raman Spectroscopy	• Gives information about chemical composition of sample • Ideal for MPs with non-polar functional group • Nondestructive method • Ideal for very small sample • No sample preparation needed • Very small particle of 1–2 μm size can also be detected • Can also give information about particle size distribution	• Expensive • Laborious and takes long times for identification • Signal overlapping from contaminants and additives • Comprehensive library of spectra is needed • Error due to fluorescent dye in MPs
NIR	• No sample pretreatment is needed	• Only few studies are available

	● Can detect particle of very small size <1 mm ● Can also give quantitative information	
^{1}H NMR	● Independent of size of MPs ● Gives both qualitative and quantitative information about the sample ● High accuracy (>98%)	● Sample needed to dissolve in deuterated solvent ● Very few databases available

6. Potential Impacts of Microplastics on Human health

Exposure to MPs can result in health hazards, either directly from the MPs or from the monomers and additives released during production. Additionally, due to the relatively extensive surface area of the MPs, several waterborne organic pollutants such as PCBs, polycyclic PAHs, heavy metals, and antibiotics can adhere to their surface, and subsequent leaching can further result in contamination and secondary hazardous effects (Cole et al., 2011). Due to the limited availability of data on the potential effects of MPs on human health, most of the investigations are based on *in vitro* and animal studies, with a comparable impact expected in humans. Some of the possible health effects that may arise from MP exposure to humans are discussed below (Figure 2).

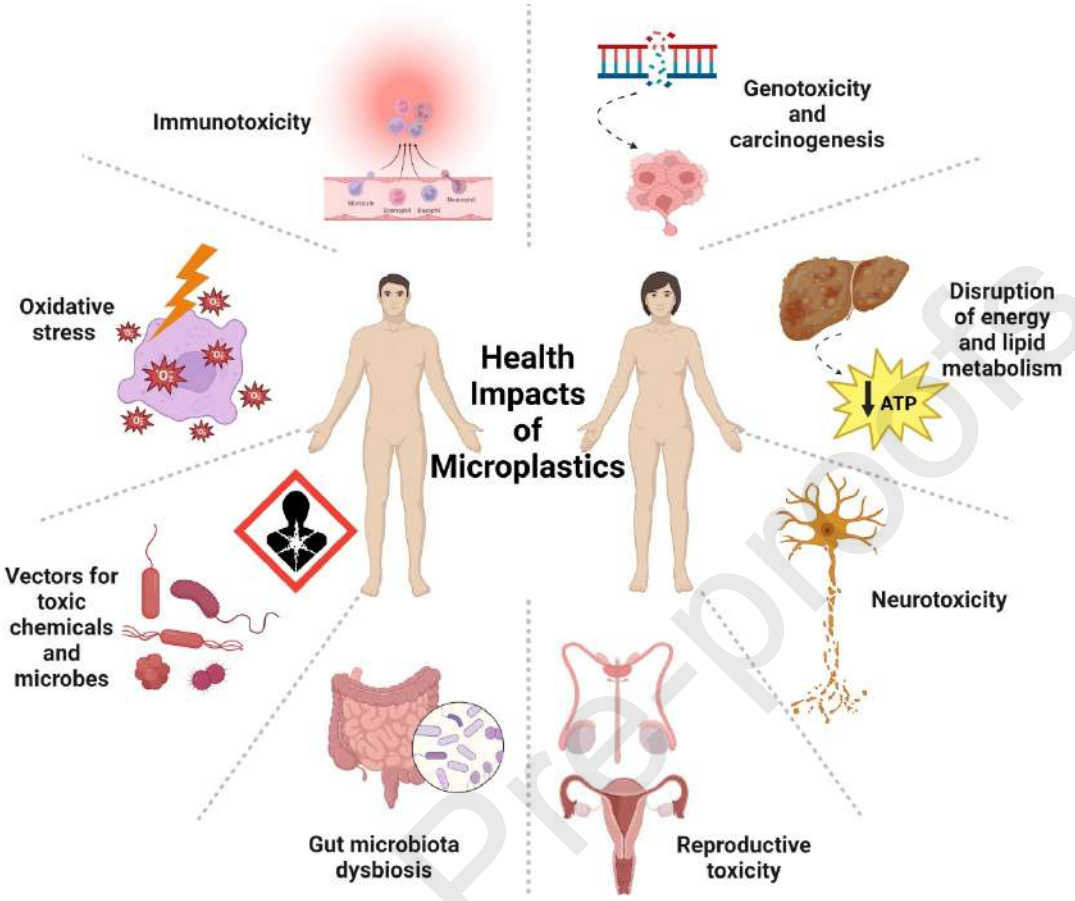

Figure 2. Graphical representation of various adverse effects of microplastics on human health

6.1 Oxidative stress and damage

Several *in vitro* and *in vivo* studies have shown that MPs can induce oxidative stress and apoptosis (An et al., 2021; Chiu et al., 2015; Qiao et al., 2019; Schirinzi et al., 2017). Study conducted by Chiu et al. revealed that cationic PS nanospheres to cause autophagic cell death due to the generation of reactive oxygen species (ROS) and endoplasmic reticulum stress in macrophages (RAW 264.7) and lung epithelial cells (BEAS-2B) (Chiu et al., 2015). Similar finding was also observed by Schirinzi et al. showing both polyethylene (PE) and PS-MPs to induce oxidative stress in cerebral (T98G) and human epithelial cells (HeLa) (Schirinzi et al., 2017). Another study on zebrafish also reported that the exposure to pristine PS-MP beads resulted in inflammation and oxidative damage in the gut of zebrafish (Qiao et al., 2019). Oxidative stress and apoptosis was also observed in the ovaries of rats exposed to PS-MPs, via the Wnt/*β*-Catenin signaling pathway (An et al., 2021). A study conducted by Deng et al. by exposing mice to MPs also found induction of apoptosis, and disruption of the endogenous antioxidant defense system (Deng et al., 2017). Moreover, PE-MPs are found to induce lipid peroxidation in the digestive glands of mussels (*Mytilus galloprovincialis*), even lower concentrations of 1 and 10

*μ*g/L. Whereas at higher concentration(100 and 1000 *μ*g/L), those MPs inactivated antioxidant enzymes (catalase and glutathione transferase), increasing oxidative stress (Abidli et al., 2021). Likewise, Mai et al. demonstrated that PE microspheres (27–32 *μ*m) and PET microfibers (200-400 *μ*m) induced mitochondrial pathway mediated apoptosis in gills and digestive gland of *Mytilus galloprovincialis* by inhibiting the AKT and ERK signaling pathway (Mai et al., 2023). Exposure of MPs to common species of European seabass (*Dicentrarchus labrax*) resulted in oxidative damage in the brain and muscle. Lipid peroxidation and inhibition of enzyme isocitrate dehydrogenase was thought to have contributed to oxidative stress (Barboza et al., 2018a). The oxidative stress triggered by MPs could be due to the release of oxidizing species like metals adsorbed on the surface of MPs (owing their large surface area) or as a result of ROS generated during an inflammatory reaction (Prata et al., 2020).

6.2 Immunotoxicity

The extent of the immune response after exposure to foreign particles depends on their distribution and can range from local to systemic. However, in some conditions, exposure to MPs from the environment can result in autoimmune diseases or immunosuppression (Prata et al., 2020). Several studies have established a link between MP exposure and disruption of the immune system (Détrée & Gallardo-Escárate, 2018; Greven et al., 2016; Paul-Pont et al., 2016; Von Moos et al., 2012) .

For instance, a study on *Pimephales promelas*, a freshwater fish, exposed to PS nanoparticles (41 nm, 0.025 to 0.2 *μ*g/*μ*L) showed an elevation in myeloperoxidase activity and neutrophil extracellular trap release (Greven et al., 2016). Another study on mussels (*Mytilus galloprovincialis*) reported toxicity to blood cells, decreased phagocyte activity, and reduced integrity of the lysosomal membrane (Détrée & Gallardo-Escárate, 2018; Von Moos et al., 2012). Increased red blood cell death and ROS production were observed when mussels (*Mytilus* sp.) were exposed to PS microbeads (2 and 6 *μ*m; final concentration: 32 *μ*g L^{-1}) (Paul-Pont et al., 2016). Exposure to PS-MPs (5 *μ*m, 0.04 to 40 mg/mL) in crabs for 7, 14, or 21 days resulted in a substantial alteration of hemocyanin content and levels of various enzymes related to the immune system, particularly acid phosphatase, alkaline phosphatase, lysozyme, and phenoloxidase (Liu et al., 2019). In a recent study, Wang and colleagues confirmed that exposure to PS microbeads (5 *μ*m) in water for 4 weeks significantly suppressed mouse immunity, as indicated by a higher CD4+/CD8+ T-cell ratio and lower spleen weight (Wang et al., 2022). Further analysis using proteomics and bioinformatics revealed that pathways associated with asthma, mineral absorption, and the interleukin (IL)-17 signaling were the most significantly enriched in those mice. They also observed spleen damage and immune suppression which were primarily mediated by the downregulation of the S100A8 protein (involved in local inflammation and immune response), as observed by histochemistry staining. Moreover, another study on mouse splenocytes showed a modification of the serum IL-1*α*, and granulocyte colony-stimulating factor (G-CSF), a reduction in the number of regulatory T cells, and an increased proportion of Th17 when mice were exposed

to PE-MPs (10–150 *μ*m, 20 and 200 *μ*g/g) for 5 days (Li et al., 2020). These studies clearly indicate that MPs bring about a significant alteration of the immune system.

6.3 Genotoxicity and carcinogenesis

DNA damage is one of the major and concerning toxic effects of MPs exposure. Particles can induce genotoxicity through various mechanisms, such as direct contact with DNA, indirect generation of ROS in the cytoplasm, or impairment of DNA replication and/or repair machinery. These phenomena can lead to DNA lesions and mutations, and if they involve the genes that regulate the cell cycle, they can lead to carcinogenesis (Fadeel et al., 2017). Therefore, if MPs can induce DNA damage, they have the potential to initiate carcinogenesis. However, only a few studies have reported the genotoxic and carcinogenic effects of MPs exposure.

A study performed by Paget et al. in Calu-3 cells (human pulmonary epithelial cells) and THP-1 cells (human macrophage cells) using the *γ*-H2AX foci assay concluded that aminated PS nanobeads (50 nm) substantially increased DNA damage in both cell lines (Paget et al., 2015). Bonanomi and colleagues reported that exposure of PS particles (0.5 and 2 *μ*m) to the normal human colon cell line (CCD-18Co) led to the alteration of normal metabolic processes by inducing oxidative stress, increased glucose and glutamine metabolism, and decoupling of glucose and glutamine. Surprisingly, the metabolic shift was found to be similar when the cells were treated with a potent carcinogen, azoxymethane (AOM) in human colorectal cancer cell line (HCT15), which suggests that PS-MPs/NPs can induce carcinogenesis and could increase the risk of colon cancer (Bonanomi et al., 2022). Another study on the human fibroblast cell line (Hsp 27) using the micronucleus assay also showed that an exposure to PS-NPs (100 nm) resulted in a dose-dependent increase in DNA damage with increased formation of micronuclei and nuclear buds (Poma et al., 2019). Additionally, the authors observed an increase in ROS generation, which further results in DNA damage and hence has genotoxic potential. Similarly, Mai et al. reported that exposure to spherical PE (27–32 *μ*m) and fibrous PET (200-400 *μ*m) MPs on mussel (*Mytilus galloprovincialis*) resulted in increased DNA damage leading to induction of cellular apoptosis on the mussel digestive tubules and gill cells (Mai et al., 2023). An *in vitro* study on gastric cancer cell lines (AGS, MKN1, MKN45, NCI-N87, and KATOIII) showed that exposure of the cells to PS-MPs (9.5-11.5 *μ*m) resulted in a substantial increase in tumor cell proliferation, invasion, and migration in all cell lines (Kim et al., 2022). Moreover, the cell lines were resistant to commonly used anticancer drugs (bortezomib, cisplatin, paclitaxel, gefitinib, lapatinib, trastuzumab), which demonstrates the risk of multidrug resistance. Interestingly, in the same study, *in vivo* experiments on PS-exposed cell (NCI-N87) xenografted mice demonstrated that exposure to PS-MPs accelerated tumor growth, reduced survival, while showing multidrug resistance to chemotherapeutic agent including bortezomib, paclitaxel, gefitinib, lapatinib, and trastuzumab. RNA-sequencing showed elevated expression of asialoglycoprotein receptor 2 (ASGR2) that resulted in tumor growth, migration, and multidrug resistance in both cell culture and mice models.

Thus, MPs exposure has the potential to induce DNA damage, which could lead to the development of cancerous cells.

6.4 Disruption of energy and lipid metabolism

Zhao et al. reported that when mice were orally exposed to PS-MPs beads of 0.5 and 5 *μ*m sizes, it led to a dose-dependent increase in body fat, weight gain (indicating obesity), and hyperglycemia (Zhao et al., 2022). In particular, the smaller 0.5 *μ*m MP beads, administered at a higher concentration of 1 *μ*g/ml, resulted in more pronounced adiposity and hyperglycemia. The authors suggested that these increased obesity and hyperglycemia could be attributed to changes in Wnt signaling and alterations in gut microbiota, findings that align with previous research (DiBaise et al., 2008; Khan et al., 2016). Similarly, PS-MPs was found to disrupt energy metabolism in the liver of mice by decreasing ATP levels while increasing lactate dehydrogenase (LDH) activity in the liver (Deng et al., 2017). This disruption led to a reduction in the relative weight of the liver, and increased food intake. In the same study, the deposition of MPs in tissues resulted in a considerable reduction in total cholesterol and triglycerides, along with the accumulation of lipid droplets in the liver, suggesting an alteration in lipid metabolism. Similar findings were observed when marine fish (*Dicentrarchus labrax*) were exposed to PMMA NPs (45 nm), which interfered with lipid metabolism and disrupted energy mobilization by inducing genes (peroxisome proliferator-activated receptors; PPARs) involved in lipid metabolism (Brandts et al., 2018).

Another study performed by Lu and co-workers demonstrated that PS-MPs (0.5 and 50 *μ*m; oral exposure of 1000 *μ*g/L) decreased the levels of hepatic triglycerides and total cholesterol in mice (Lu et al., 2018). While, molecular studies showed the downregulation of hepatic PPAR*γ*, a major transcriptional factor with a key role in lipid metabolism and adipogenesis, together with downregulation of genes affecting triglyceride synthesis (Gpat, Dgat1, and Dgat2). Barboza and colleagues observed a significant induction of LDH in the muscles of European seabass (*Dicentrarchus labrax*) exposed to MPs, suggesting the upregulation of the anaerobic pathway for energy production and an alteration of energy metabolism (Barboza et al., 2018a). In comparison to the studies on marine fishes, high depletion of energy reserves by up to 50% was observed in marine worms (*Arenicola marina*) exposed to MPs, and the energy depletion was attributed mainly to decreased feeding activity, along with increased residence time of food in the gut and an increased inflammatory response (Wright et al., 2013). Likewise, other studies also showed reduced consumption of food, decreased energy available for growth, and reduced clearance rate after the ingestion of MPs (Watts et al., 2015; Xu et al., 2017). Furthermore, in an *in vitro* study on liver organoids, PS-MPs (1 *μ*m) were shown to disrupt lipid metabolism and decrease ATP levels in the liver, along with the downregulation of PPAR*α*, PPAR*γ,* and CPT1A (a marker for *β*-oxidation) (Cheng et al., 2022). These findings further support the fact that MPs induce lipid metabolism disorder by altering the expression of hepatic PPAR genes.

6.5 Neurotoxicity

Exposure to MPs contaminants has been linked to neurotoxicity and the potential development of neurodegenerative diseases. Murali and co-workers conducted *in vitro* studies on several neural cells and showed that, depending on the type of cells and concentration, exposure to 40-70 nm PS nanospheres could induce toxicity and modifications in metabolic activity. The toxicity was also observed to increase over time as a result of aggregation and the presence of biologically active substances after extended storage of PS (Murali et al., 2015). Similarly, 50 nm PS-NPs were shown to be internalized into the hCMEC/D3 cell line (human cerebral microvascular endothelial cell; a model for the blood-brain barrier), disrupting its tight junctions along with increased oxidative stress, nuclear factor kappa-B (NF-*κ*B) activation, tumor necrosis factor alpha (TNF-*α*) secretion, and necroptosis (Shan et al., 2022). Furthermore, in the same study the PS-NPs accumulated in murine microglial cells (BV2) with an upregulation of ROS, TNF-*α*, and IL-1*β*, suggesting microglial activation and neuronal damage.

As with *in vitro* studies, animal studies have also shown that exposure to particulate matter may lead to neurotoxicity due to oxidative stress and the activation of microglial cells in the brain. This could result from direct contact with transported particles or the action of proinflammatory cytokines from other sites of inflammation, causing harm to neurons (MohanKumar et al., 2008). Deng et al. reported that fluorescent PS-MPs, upon oral administration to mice, increased the activity of acetylcholinesterase (AChE), which may disrupt and decrease cholinergic neurotransmission (Deng et al., 2017). In addition, MPs exposure has also been shown to alter neuronal function and behavior. Gasper et al. reported that short-term exposure (3 weeks) of pristine PS-MPs to young and old mice resulted in retention of MP particles in several organs including brain and heart, and demonstrated an alteration in cognitive function which was more pronounced in old-aged mice (Gaspar et al., 2023). An *in vivo* study on the brains of widely consumed marine fish (*Dicentrarchus labrax*) showed that exposure to microspheres 1-5 *μ*m resulted in acetylcholinesterase (AChE) inhibition, oxidative damage, together with an increase in lipid peroxidation (Barboza et al., 2018a). Furthermore, the authors observed changes in lactate dehydrogenase (LDH) and isocitrate dehydrogenase (IDH), suggesting the upregulation of the anaerobic pathway for energy production and alteration of energy metabolism. In another study, MP exposure to the same species has been demonstrated to reduce swimming velocity and resistance time, along with changes in swimming behavior (Barboza et al., 2018b). Another study reported that PS-NPs (50 nm) could pass through the blood-brain barrier, accumulate in the brain in a dose-dependent manner, and induce neurotoxicity by activating microglial cells (Shan et al., 2022). Hence, it can be concluded that MPs exposure can impair neuronal cells via oxidative damage, which may lead to neurodegeneration.

6.6 Reproductive toxicity

Various studies have reported the harmful effects of MPs on the reproductive system (An et al., 2021; Hou et al., 2021; Liu et al., 2022; Xie et al., 2020). A study on rat ovaries illustrated that PS-MPs can enter granulosa cells in the ovaries and cause fibrosis and apoptosis through the Wnt/*β*-Catenin signaling pathway triggered by oxidative stress (An et al., 2021). Similarly, another study reported that PS-MPs could distribute widely in tissues, including the ovaries, and induced reproductive toxicity in mice by affecting follicular development and causing inflammation in the ovaries (Liu et al., 2022). Study conducted by Xie et al. also revealed decrease in the number of ovarian follicles and the size of the ovary, along with a reduction in the levels of serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) in female mice exposed to PS-MPs (Xie et al., 2020). Likewise, mice treated with MPs showed a reduction in pregnancy rate and fewer production of embryos (Wei et al., 2022). A recent study on female zebrafish (*Danio rerio*) treated with PS-MPs demonstrated impairment of reproductive system by induction of oxidative stress, apoptosis and hormonal imbalance through SIRT1/p53 signaling pathway (P. Gupta et al., 2023).

On the other hand, PS-MPs (5 *μ*m) affected spermatogenesis in male mice by reducing the number of viable sperm cells, inducing inflammation, testicular atrophy, and apoptosis of sperm cells via the Nrf2/ HO-1/NF-*κ*B signaling pathway (Hou et al., 2021). In an *in vivo* study on male mice exposed to PS-MPs, testicular follicles were disrupted, sperm viability decreased, and there was a decrease in serum testosterone, LH, and FSH. Further *in vitro* studies revealed that the MPs were internalized in Leydig cells and downregulated the LH receptor, steroidogenic enzymes, and steroidogenic acute regulatory protein (StAR) expression by inhibiting the AC/cAMP/PKA pathway (Jin et al., 2022). Similarly, Xie and colleagues demonstrated that PS-MPs resulted in a reduction in sperm count and motility, as well as a decrease in serum testosterone levels in male mice, via oxidative stress and activation of the p38 MAPK signaling pathway. In male mice, there was a reduction in serum testosterone, sperm count, and motility (Xie et al., 2020). Wei and colleagues observed that the accumulation of MPs and oxidative stress was greater in the ovaries than in the testes and concluded that female mice were more susceptible to MPs effects on reproduction and fertility than males (Wei et al., 2022). Additionally, a recent study indicated that exposure to PA-MPs resulted in greater decrease in testosterone bioavailability, sperm quality, and disruption of seminiferous tubule in comparison with PMMA-MPs which was attributed to reduced nuclear translocation of androgen receptors (P. Zhang et al., 2024).

6.7 Effects on gut epithelium and microbiota

Exposure to MPs can have adverse effects on intestinal epithelial cells and disrupt the gut microbiota. Stock et al. investigated the uptake and translocation of PS-MPs (1, 4, and 10 *μ*m) in three different *in vitro* systems, namely monoculture of human intestinal epithelial cells (Caco-2), co-culture of Caco-2 and HT29-MTX cells (representing goblet cells), Caco-2 and Raji B (representing M cells), and THP-1-derived macrophages (Stock et al., 2019). The authors

reported increased uptake of 4 μm MPs by the co-culture system in comparison to monocultures. However, in the same study, *in vivo* experiments on transgenic mouse models, very few particles were found in the intestinal cells with the absence of histologically significant adverse effects and no signs of toxicity (Stock et al., 2019). A study on zebrafish showed that MPs exposure can cause significant disruption in the gut metabolome and microbiome, which were linked to oxidative stress and inflammation (Qiao et al., 2019). Similarly, Lu and colleagues also demonstrated that oral exposure to PS-MPs (0.5 and 50 μm) to mice at a dose of 1000 μg/L for 5 weeks reduced mucus secretion in the colon and brought notable changes in the composition of gut microbiota together with dose-dependent increase in body fat, weight gain and hyperglycemia (Lu et al., 2018). Smaller-sized MP beads (0.5 μm) at a higher concentration (1 μg/ml) resulted in greater adiposity and hyperglycemia (Zhao et al., 2022). The authors concluded that increased obesity and hyperglycemia may have occurred due to alterations in Wnt signaling and changes in gut microbiota, which were consistent with previous findings (DiBaise et al., 2008; Khan et al., 2016). Similarly, another study also reported that exposure to PS-MPs (32–40 μm) in juvenile guppies (*Poecilia reticulata*) resulted in reduced activity of digestive enzymes in the intestine, stimulated the inflammatory immune response, and induced alterations in gut microbiota (Huang et al., 2020). Altogether, MPs exposure can cause significant alterations in gut function and may lead to gut microbiota dysbiosis.

6.8 Vectors for toxic substances and microorganisms

In addition to the hazards directly posed by MPs monomers and additives, plastics also absorb chemicals and microorganisms from their surroundings due to their high surface area. Consequently, such chemicals and microbes may leach out from the plastic polymers into the surrounding environment (Yee et al., 2021). MPs collected from the environment have been found to contain chemicals classified as persistent organic pollutants (POPs), including PAHs and PCBs. These substances have been shown to have various toxic effects (Crawford & Quinn, 2017b). For instance, exposure to PCBs can weaken the immune system, increase the likelihood of cancer by amplifying the effects of other carcinogenic substances, disrupt thyroid and reproductive function in both genders, and raise the risk of cardiovascular disease, liver disease, and diabetes. Additionally, PCBs exposure in mothers resulted in a greater risk of low birth weight in infants, and when exposed during fetal development and early life, it can lead to decreased IQ levels and altered behavior in children (Carpenter, 2006). PAHs are a category of organic pollutants that pose a significant threat to the environment and human health due to their toxic, genotoxic, mutagenic, and carcinogenic effects (D. Ghosal et al., 2016).

As discussed above, MPs contain several additives such as BPA, phthalates, and BFR. These additives are known for their endocrine-disrupting effects in humans if they are ingested or inhaled (Cingotti & Jensen, 2019). The surface of MPs may also be colonized by microorganisms such as *Vibrio* spp. (Kirstein et al., 2016) and may, therefore, serve as carriers, transmitting microorganisms to the body, which can cause tissue injury and increase the risk of infection.

Moreover, consuming a significant amount of MPs by humans can disrupt the gut microbiota, potentially leading to negative consequences such as the growth of harmful bacteria, increased gut permeability, and endotoxemia (West-Eberhard, 2019). Therefore, apart from the aforementioned direct impacts, MPs can have deleterious secondary effects by acting as carriers for harmful chemicals and microbes.

7. Control and Prevention of Microplastic Pollution

The aforementioned studies have clearly indicated the detrimental effects of MPs on the living organisms, therefore there is an urgent need to control global MP pollution. To address this issue, an integrative approach is recommended, incorporating source control and the principles of reduce, reuse, recycle, recover, and replace (5 Rs) (D. K. Gupta et al., 2023). Crucially, reducing plastic waste generation through strengthened legislation and industry shifts to plastic alternatives is paramount, which entails discouraging the use of single-use plastic items in households and industries. Several countries have already issued strict policies and regulations to minimize the production of plastic litter. For instance, the United States' Microbead-Free Waters Act 2015 prohibits the production and sale of plastic microbeads in cosmetics items and Nepal's Plastic Bag Regulation and Control Directive 2011 banned the production and use of plastics < 40 micron thickness (Lamichhane et al., 2023). The imposition of fines and taxes is proposed to reinforce regulatory measures, while public awareness campaigns are pivoital for educating the population about the health hazards associated with MPs. To control the MP pollution, replacing conventional petroleum-based plastics with eco-friendly alternatives like cellulose and polyolefin-based bioplastics is recommended (Ammala et al., 2011). Polybutylene succinate and polyactatide are suggested as biocompatible polymers to substitute non-degradable plastics (D. K. Gupta et al., 2023). Recycling plastic through centralized collection facilities, with collaboration between the government and stakeholders, is a key solution. However, emerging processes like solvent extraction and hydrothermal processing are effective for recycling mixed-plastic waste ((Reimonn et al., 2019). Bioremediation, employing organisms like *Ideonella sakaiensis* bacterium for PET breakdown and marine bacteria (*Exiguobacterium* and *Halomonas* species) for efficient PE degradation, offers novel approach to control MP contamination (Gao & Sun, 2021; Yoshida et al., 2016).

Moreover, fungi (*Aspergillus fumigatus, Fusarium* and *Monascus* species), seagrass (*Thalassia testudinum*), microalgae (*Fucus vesiculosus*) and marine invertebrates (*Mytilus edulis, Arenicola marina,* and *Apostichopus japonicus*) show promise in MP particle degradation and retention (Krishnan et al., 2023). Notably, earthworms demonstrate innovative MP bioremediation by fragmenting and depolymerizing certain plastics in their gut (Meng et al., 2023). The primary origin of MP is commonly attributed to wastewater treatment facilities, thereby removing the MPs from water effluents by utilizing advanced water treatment technologies can greatly decrease plastic pollution. Combining traditional methods (sedimentation, screening, filtration, flotation, and ion-

exchange) with newer approaches such as rapid sand filtration, membrane bioreactors, reverse osmosis, electrocoagulation, and photocatalytic degradation achieves over 99% MP removal efficiency (Krishnan et al., 2023). Innovative strategies, including intelligent visible-light-driven microrobots, also demonstrate efficient degradation of large plastic particles like polylactic acid and polycaprolactone (Lamichhane et al., 2023). Recognizing MP pollution as a global issue necessitates collaboration efforts among nations, emphasizing regional and global communication to exchange research-derived ideas and policy guidelines for effective control and prevention.

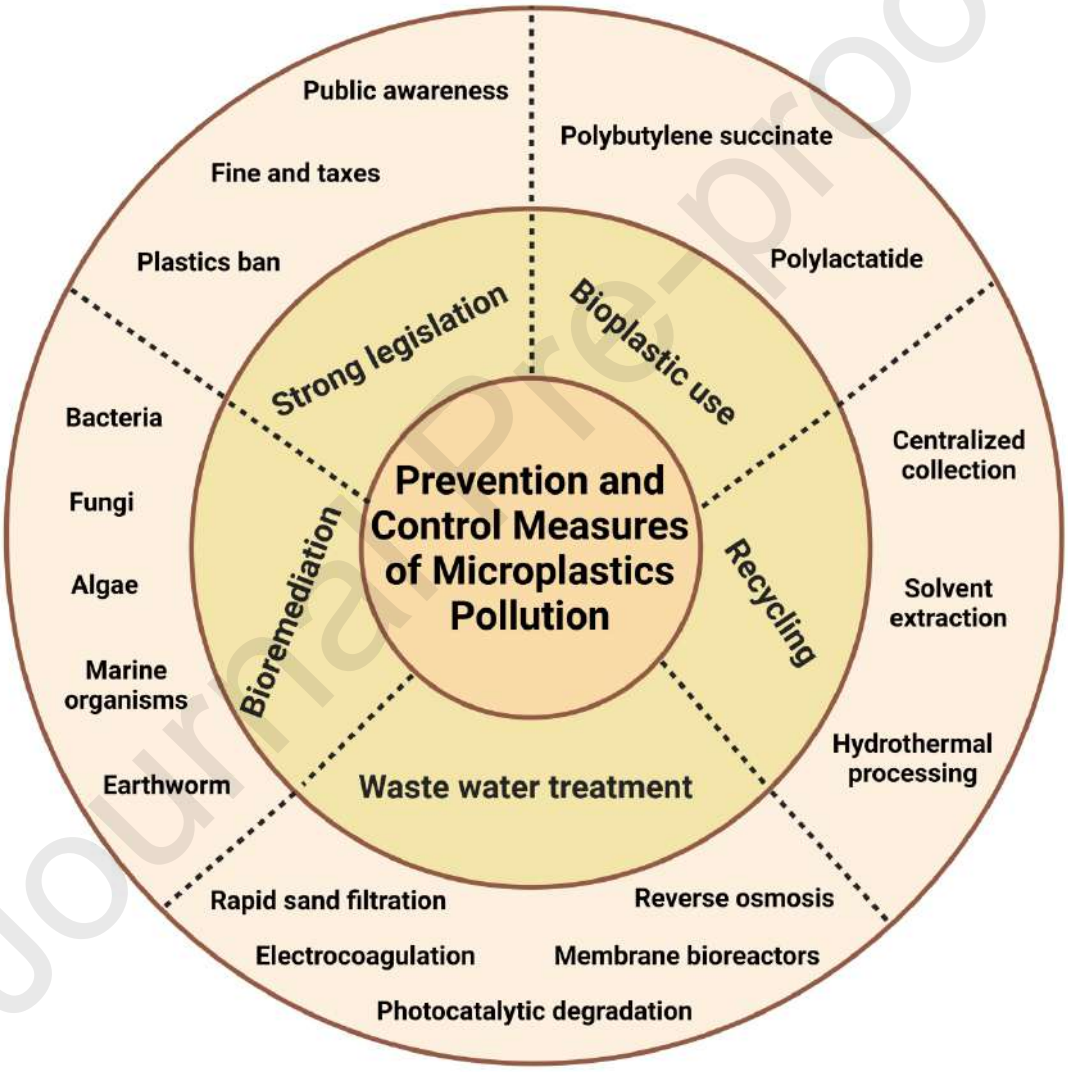

Figure 3. Control measures of microplastic pollution. Key strategies include: implementing strong laws and regulations (via raising public awareness, fines and taxes, and ban on plastics); substituting conventional plastic polymers with biodegradable or bioplastics (e.g. polybutylene succinate, polylactatide); promoting plastic recycling (through centralized collection services,

adopting novel recycling methods like solvent extraction and hydrothermal processing); using advanced waste water treatment technologies (rapid sand filtration, reverse osmosis, electrocoagulation, membrane bioreactors, and photocatalytic degradation); bioremediation (by using various species of bacteria, fungi, algae, marine organisms, and earthworm).

8. Future Research Direction and Recommendations

Based on the literature mentioned above, we can identify certain gaps and limitations. Additionally, we can offer recommendations to guide future studies on MPs. Currently, there is a lack of validated and standardized analytical methods for sample collection, separation, and detection of MPs. This deficiency can impact the accuracy of human exposure assessment because these techniques exhibit varying degrees of sensitivity and specificity. Therefore, upcoming studies should prioritize the development of specific methods and protocols for sampling and characterization along with focusing on precise measurements of MPs' exposure in human tissues and fluids. Moreover, the majority of toxicological studies related to MPs exposure are conducted *in vitro* or using animal models, making it challenging to accurately correlate the findings to their impact on humans. Furthermore, these studies tend to be acute and short-term toxicity assessments, with controlled exposure to MPs. Consequently, there is a pressing need for long-term, longitudinal, and cohort research into the specific health effects of both acute and chronic MP exposure. These investigations should delve deep into understanding the fate and mechanisms of toxicity in humans.

Despite polyolefins (e.g., PE and PP), PS, and PU being the most commonly used commercially available plastic materials, most published research relies heavily on PS-MPs. This preference is primarily due to their easy availability and simplicity in transforming them into the desired size. However, the size and composition of plastics used in experiments may significantly differ from those encountered in environmental and dietary exposures. Hence, it's imperative to study the effects of other relevant MP particles. Furthermore, as MPs can act as carriers for other pollutants, their combined effects may not simply synergize. Thus, additional research on the combined effects of MPs and other vectors is necessary. So far, studies have primarily concentrated on the dietary exposure of MPs, particularly in food products like seafood, plant-based items, and other consumables. There is limited data available regarding the impact of cooking and processing these food items at high temperatures on the fate of MPs and human toxicity. This could also be a potential area for future research.

Based on these findings, it becomes evident that MP contamination of food products is a global concern that necessitates a worldwide response. Given the relative chemical stability of MPs and the global increase in their production, it is imperative that strict national policies and regulations aim to reduce MP pollution. Raising public awareness about MP pollution and its health implications along with initiatives such as recycling of plastics, use of alternative biodegradable

polymers as a plastic substitute can significantly reduce plastic consumption and generation of plastic waste. Future studies should be encouraged on plastic recycling, biocompatible or bioplastics, and plastic bioremediation for wastewater treatment together with technological innovations for minimizing environmental MP pollution. For a comprehensive understanding of the impact of MPs on human health, a multidisciplinary research collaboration involving environmental scientists, toxicologists, medical professionals, and policymakers is an effective strategy. Therefore, global collaboration is essential to gain a comprehensive understanding of the impact of MPs on human health and formulate strategies to reduce human exposure.

9. Conclusions

The issue of MP contamination in food products has gained significant attention due to its potential impact on human health. Studies in both laboratory experiments and animal models have indicated that MPs exposure can lead to diverse toxicological effects mainly oxidative stress, inflammation, carcinogenesis, neurodegeneration, altered immune system and energy metabolism, and other adverse effects. However, the full extent of the impact on human health remains an active area of research, necessitating standardized detection methods, risk assessments, and long-term studies. Future research should focus on comprehensively evaluating the risks associated with MP exposure, including their size, composition, mechanisms of toxicity and combined effects with other toxicants. It is also crucial to establish effective regulations, promote public awareness on plastic recycling and plastic alternatives, and foster global collaboration to mitigate MP contamination in our food and protect human health. In a world grappling with plastic pollution, understanding and addressing the MP-food-human health nexus is an urgent and evolving challenge.

10. Abbreviations

ABS	Acrylonitrile-butadiene-styrene
ATR-FTIR	Attenuated Total Reflection-Fourier transform infrared spectroscopy
BFR	Brominated flame retardants
BPA	Bisphenol A
CA	Cellulose acetate
CP	Cellophane
EDS	Energy dispersive spectroscopy

EDX	Energy-dispersive X-ray spectroscopy
EVA	Ethylene-vinyl acetate
FTIR	Fourier-transform infrared spectroscopy
IL	Interleukin
MP	Microplastic
NF-κB	Nuclear factor kappa B
NP	Nanoplastic
PA	Polyamide
PA-6	Polyamide-6
PAH	Polycyclic aromatic hydrocarbons
PAN	Polyacrylonitrile
PB	Poly(1-butene)
PBDE	Polybrominated diphenyl ethers
PC	Polycarbonate
PCB	Polychlorinated biphenyls
PE	Polyethylene
PE/PEA	Poly (ethylene-co-ethyl acrylate)
PE/PP	Poly (ethylene-co-propylene)
PEA	Poly(ester-amide)
PEP	Polyethylene:polypropylene copolymer
PEPD	Polyethylene:polypropylene:dien
PES	Polyester
PET	Polyethylene terephthalate

PI-PS	Polyisoprene/polystyrene
PMMA	Poly methyl methacrylate
PP	Polypropylene
PPAR	Peroxisome proliferator-activated receptor
PPS	Polyphenylene sulfite
PS	Polystyrene
PTFE	Polytetrafluoroethylene
PU	Polyurethane
PVA	Polyvinyl alcohol
PVC	Polyvinylchloride
PVCA	Vinyl chloride/Vinyl acetate copolymer
SEM	Scanning electron microscopy
TD-GC/MS	Thermal desorption-gas chromatography-mass spectrometry
TEM	Transmission electron microscopy
TGA	Thermogravimetry
TNF-α	Tumor necrosis factor alpha

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13. Conflict of interest

Author have no conflict to declare.

14. References

Abidli, S., Pinheiro, M., Lahbib, Y., Neuparth, T., Santos, M. M., & Trigui El Menif, N. (2021). Effects of environmentally relevant levels of polyethylene microplastic on Mytilus galloprovincialis (Mollusca: Bivalvia): Filtration rate and oxidative stress. *Environmental Science and Pollution Research*, *28*(21), 26643–26652.

Afrin, S., Rahman, M. M., Hossain, M. N., Uddin, M. K., & Malafaia, G. (2022). Are there plastic particles in my sugar? A pioneering study on the characterization of microplastics in commercial sugars and risk assessment. *Science of The Total Environment*, *837*(Journal Article), 155849.

Akhbarizadeh, R., Moore, F., & Keshavarzi, B. (2018). Investigating a probable relationship between microplastics and potentially toxic elements in fish muscles from northeast of Persian Gulf. *Environmental Pollution*, *232*(Journal Article), 154–163.

Akoueson, F., Sheldon, L. M., Danopoulos, E., Morris, S., Hotten, J., Chapman, E., Li, J., & Rotchell, J. M. (2020). A preliminary analysis of microplastics in edible versus non-edible tissues from seafood samples. *Environmental Pollution*, *263*(Journal Article), 114452.

Almaiman, L., Aljomah, A., Bineid, M., Aljeldah, F. M., Aldawsari, F., Liebmann, B., Lomako, I., Sexlinger, K., & Alarfaj, R. The occurrence and dietary intake related to the presence of microplastics in drinking water in Saudi Arabia. *Environmental Monitoring and Assessment*, *193*(7), 390–399. https://doi.org/10.1007/s10661-021-09132-9

Alvarez-Román, R., Naik, A., Kalia, Y. N., Guy, R. H., & Fessi, H. (2004). Skin penetration and distribution of polymeric nanoparticles. *Journal of Controlled Release*, *99*(1), 53–62.

Ammala, A., Bateman, S., Dean, K., Petinakis, E., Sangwan, P., Wong, S., Yuan, Q., Yu, L., Patrick, C., & Leong, K. H. (2011). An overview of degradable and biodegradable polyolefins. *Progress in Polymer Science*, *36*(8), 1015–1049.

An, R., Wang, X., Yang, L., Zhang, J., Wang, N., Xu, F., Hou, Y., Zhang, H., & Zhang, L. (2021). Polystyrene microplastics cause granulosa cells apoptosis and fibrosis in ovary through oxidative stress in rats. *Toxicology*, *449*(Journal Article), 152665.

Andrady, A. L. (2017). The plastic in microplastics: A review. *Marine Pollution Bulletin*, *119*(1), 12–22.

Araujo, C. F., Nolasco, M. M., Ribeiro, A. M., & Ribeiro-Claro, P. J. (2018). Identification of microplastics using Raman spectroscopy: Latest developments and future prospects. *Water Research*, *142*(Journal Article), 426–440.

Aydın, R. B., Yozukmaz, A., Şener, İ., Temiz, F., & Giannetto, D. (2023). Occurrence of Microplastics in Most Consumed Fruits and Vegetables from Turkey and Public Risk Assessment for Consumers. *Life*, *13*(8), 1686.

Bai, C.-L., Liu, L.-Y., Guo, J.-L., Zeng, L.-X., & Guo, Y. (2022). Microplastics in take-out food: Are we over taking it? *Environmental Research*, *215*(Journal Article), 114390. https://doi.org/10.1016/j.envres.2022.114390

Barboza, L. G. A., Vieira, L. R., Branco, V., Figueiredo, N., Carvalho, F., Carvalho, C., & Guilhermino, L. (2018). Microplastics cause neurotoxicity, oxidative damage and energy-related changes and interact with the bioaccumulation of mercury in the European seabass, Dicentrarchus labrax (Linnaeus, 1758). *Aquatic Toxicology*, *195*(Journal Article), 49–57.

Barboza, L. G. A., Vieira, L. R., & Guilhermino, L. (2018). Single and combined effects of microplastics and mercury on juveniles of the European seabass (Dicentrarchus labrax): Changes in behavioural responses and reduction of swimming velocity and resistance time. *Environmental Pollution*, *236*(Journal Article), 1014–1019.

Bergmann, M., Gutow, L., & Klages, M. (2015). *Marine anthropogenic litter*. Springer Nature.

Biniek, K., Levi, K., & Dauskardt, R. H. (2012). Solar UV radiation reduces the barrier function of human skin. *Proceedings of the National Academy of Sciences*, *109*(42), 17111–17116.

Blair, R. M., Waldron, S., Phoenix, V., & Gauchotte-Lindsay, C. (2018). *Secondary microplastics were prevalent in sediment in a freshwater UK urban river*. *Journal Article*.

Bonanomi, M., Salmistraro, N., Porro, D., Pinsino, A., Colangelo, A. M., & Gaglio, D. (2022). Polystyrene micro and nano-particles induce metabolic rewiring in normal human colon cells: A risk factor for human health. *Chemosphere*, *Journal Article*, 134947.

Bouwstra, J., Pilgram, G., Gooris, G., Koerten, H., & Ponec, M. (2001). New aspects of the skin barrier organization. *Skin Pharmacology and Physiology*, *14*(Suppl. 1), 52–62.

Brandts, I., Teles, M., Tvarijonaviciute, A., Pereira, M. L., Martins, M. A., Tort, L., & Oliveira, M. (2018). Effects of polymethylmethacrylate nanoplastics on Dicentrarchus labrax. *Genomics*, *110*(6), 435–441.

Brown, D. M., Wilson, M. R., MacNee, W., Stone, V., & Donaldson, K. (2001). Size-dependent proinflammatory effects of ultrafine polystyrene particles: A role for surface area and oxidative stress in the enhanced activity of ultrafines. *Toxicology and Applied Pharmacology*, *175*(3), 191–199.

Browne, M. A. (2015). Sources and pathways of microplastics to habitats. *Marine Anthropogenic Litter*, *Journal Article*, 229–244.

Büchtemann, A. (1993). Spectroscopy of polymers. By Jack L. Koenig. An ACS Professional Reference Book. ISBN 0-8412-1924-9. American Chemical Society, Washington, DC, 1992, xvi, 328 p., soft cover, large size, US $49.95. *Acta Polymerica*, *44*(1), 57.

Cai, H., Du, F., Li, L., Li, B., Li, J., & Shi, H. (2019). A practical approach based on FT-IR spectroscopy for identification of semi-synthetic and natural celluloses in microplastic investigation. *Science of the Total Environment*, *669*(Journal Article), 692–701.

Campanale, C., Massarelli, C., Savino, I., Locaputo, V., & Uricchio, V. F. (2020). A detailed review study on potential effects of microplastics and additives of concern on human health. *International Journal of Environmental Research and Public Health*, *17*(4), 1212.

Campbell, C. S., Contreras-Rojas, L. R., Delgado-Charro, M. B., & Guy, R. H. (2012). Objective assessment of nanoparticle disposition in mammalian skin after topical exposure. *Journal of Controlled Release*, *162*(1), 201–207.

Canha, N., Jafarova, M., Grifoni, L., Gamelas, C. A., Alves, L. C., Almeida, S. M., & Loppi, S. (2023). Microplastic contamination of lettuces grown in urban vegetable gardens in Lisbon (Portugal). *Scientific Reports*, *13*(1), 14278.

Carpenter, D. O. (2006). Polychlorinated biphenyls (PCBs): Routes of exposure and effects on human health. *Reviews on Environmental Health*, *21*(1), 1–24.

Carr, K. E., Smyth, S. H., McCullough, M. T., Morris, J. F., & Moyes, S. M. (2012). Morphological aspects of interactions between microparticles and mammalian cells: Intestinal uptake and onward movement. *Progress in Histochemistry and Cytochemistry*, *46*(4), 185–252.

Cheng, W., Li, X., Zhou, Y., Yu, H., Xie, Y., Guo, H., Wang, H., Li, Y., Feng, Y., & Wang, Y. (2022). Polystyrene microplastics induce hepatotoxicity and disrupt lipid metabolism in the liver organoids. *Science of The Total Environment*, *806*(Journal Article), 150328.

Chiu, H.-W., Xia, T., Lee, Y.-H., Chen, C.-W., Tsai, J.-C., & Wang, Y.-J. (2015). Cationic polystyrene nanospheres induce autophagic cell death through the induction of endoplasmic reticulum stress. *Nanoscale*, *7*(2), 736–746.

Cincinelli, A., Martellini, T., Guerranti, C., Scopetani, C., Chelazzi, D., & Giarrizzo, T. (2019). A potpourri of microplastics in the sea surface and water column of the Mediterranean Sea. *TrAC Trends in Analytical Chemistry*, *110*(Journal Article), 321–326.

Cingotti, N., & Jensen, G. K. (2019). Health and Environment Alliance (HEAL). Food contact materials and chemical contamination. *Health and Environment Alliance: Brussels, Belgium*, *Journal Article*.

Cole, M., Lindeque, P., Halsband, C., & Galloway, T. S. (2011). Microplastics as contaminants in the marine environment: A review. *Marine Pollution Bulletin*, *62*(12), 2588–2597.

CONTAM. (2016). Presence of microplastics and nanoplastics in food, with particular focus on seafood. *Efsa Journal*, *14*(6), e04501.

Conti, G. O., Ferrante, M., Banni, M., Favara, C., Nicolosi, I., Cristaldi, A., Fiore, M., & Zuccarello, P. (2020). Micro-and nano-plastics in edible fruit and vegetables. The first diet risks assessment for the general population. *Environmental Research*, *187*(Journal Article), 109677.

Cooper, D. A., & Corcoran, P. L. (2010). Effects of mechanical and chemical processes on the degradation of plastic beach debris on the island of Kauai, Hawaii. *Marine Pollution Bulletin*, *60*(5), 650–654.

Corradini, F., Bartholomeus, H., Lwanga, E. H., Gertsen, H., & Geissen, V. (2019). Predicting soil microplastic concentration using vis-NIR spectroscopy. *Science of the Total Environment*, *650*(Journal Article), 922–932.

Cox, K. D., Covernton, G. A., Davies, H. L., Dower, J. F., Juanes, F., & Dudas, S. E. (2019). Human consumption of microplastics. *Environmental Science & Technology*, *53*(12), 7068–7074.

Crawford, C. B., & Quinn, B. (2017a). Microplastic collection techniques. *Microplastic Pollutants*, *Journal Article*, 179–202.

Crawford, C. B., & Quinn, B. (2017b). The interactions of microplastics and chemical pollutants. *Microplastic Pollutants*, *Journal Article*, 131–157.

Davidson, K., & Dudas, S. E. (2016). Microplastic ingestion by wild and cultured Manila clams (Venerupis philippinarum) from Baynes Sound, British Columbia. *Archives of Environmental Contamination and Toxicology*, *71*(Journal Article), 147–156.

Deng, Y., Zhang, Y., Lemos, B., & Ren, H. (2017). Tissue accumulation of microplastics in mice and biomarker responses suggest widespread health risks of exposure. *Scientific Reports*, *7*(1), 1–10.

Détrée, C., & Gallardo-Escárate, C. (2018). Single and repetitive microplastics exposures induce immune system modulation and homeostasis alteration in the edible mussel Mytilus galloprovincialis. *Fish & Shellfish Immunology*, *83*(Journal Article), 52–60.

Diaz-Basantes, M. F., Conesa, J. A., & Fullana, A. (2020). Microplastics in honey, beer, milk and refreshments in Ecuador as emerging contaminants. *Sustainability*, *12*(14), 5514.

DiBaise, J. K., Zhang, H., Crowell, M. D., Krajmalnik-Brown, R., Decker, G. A., & Rittmann, B. E. (2008). Gut Microbiota and Its Possible Relationship With Obesity. *Mayo Clinic Proceedings*, *83*(4), 460–469. https://doi.org/10.4065/83.4.460

Digka, N., Tsangaris, C., Torre, M., Anastasopoulou, A., & Zeri, C. (2018). Microplastics in mussels and fish from the Northern Ionian Sea. *Marine Pollution Bulletin*, *135*(Journal Article), 30–40.

Dong, C.-D., Chen, C.-W., Chen, Y.-C., Chen, H.-H., Lee, J.-S., & Lin, C.-H. (2020). Polystyrene microplastic particles: In vitro pulmonary toxicity assessment. *Journal of Hazardous Materials*, *385*(Journal Article), 121575.

Dong, Y., Gao, M., Qiu, W., & Song, Z. (2021). Uptake of microplastics by carrots in presence of As (III): Combined toxic effects. *Journal of Hazardous Materials*, *411*(Journal Article), 125055.

Dowarah, K., Patchaiyappan, A., Thirunavukkarasu, C., Jayakumar, S., & Devipriya, S. P. (2020). Quantification of microplastics using Nile Red in two bivalve species Perna viridis and Meretrix meretrix from three estuaries in Pondicherry, India and microplastic uptake by local communities through bivalve diet. *Marine Pollution Bulletin*, *153*(Journal Article), 110982.

Fadeel, B., Pietroiusti, A., & Shvedova, A. A. (2017). *Adverse effects of engineered nanomaterials: Exposure, toxicology, and impact on human health*. Academic Press.

Galloway, T. S. (2015). Micro-and nano-plastics and human health. *Marine Anthropogenic Litter*, *Journal Article*, 343–366.

Gao, R., & Sun, C. (2021). A marine bacterial community capable of degrading poly (ethylene terephthalate) and polyethylene. *Journal of Hazardous Materials*, *416*, 125928.

Gaspar, L., Bartman, S., Coppotelli, G., & Ross, J. M. (2023). Acute Exposure to Microplastics Induced Changes in Behavior and Inflammation in Young and Old Mice. *International Journal of Molecular Sciences*, *24*(15), 12308.

Ghosal, D., Ghosh, S., Dutta, T. K., & Ahn, Y. (2016). Current state of knowledge in microbial degradation of polycyclic aromatic hydrocarbons (PAHs): A review. *Frontiers in Microbiology*, *Journal Article*, 1369.

Ghosal, S., Chen, M., Wagner, J., Wang, Z.-M., & Wall, S. (2018). Molecular identification of polymers and anthropogenic particles extracted from oceanic water and fish stomach–A Raman micro-spectroscopy study. *Environmental Pollution*, *233*(Journal Article), 1113–1124.

Gong, W., Zhang, W., Jiang, M., Li, S., Liang, G., Bu, Q., Xu, L., Zhu, H., & Lu, A. (2021). Species-dependent response of food crops to polystyrene nanoplastics and microplastics. *Science of the Total Environment*, *796*(Journal Article), 148750.

Greven, A., Merk, T., Karagöz, F., Mohr, K., Klapper, M., Jovanović, B., & Palić, D. (2016). Polycarbonate and polystyrene nanoplastic particles act as stressors to the innate immune system of fathead minnow (Pimephales promelas). *Environmental Toxicology and Chemistry*, *35*(12), 3093–3100.

Gündoğdu, S. (2018). Contamination of table salts from Turkey with microplastics. *Food Additives & Contaminants: Part A*, *35*(5), 1006–1014.

Gupta, D. K., Choudhary, D., Vishwakarma, A., Mudgal, M., Srivastava, A. K., & Singh, A. (2023). Microplastics in freshwater environment: Occurrence, analysis, impact, control measures and challenges. *International Journal of Environmental Science and Technology*, *20*(6), 6865–6896.

Gupta, P., Mahapatra, A., Suman, A., Ray, S. S., Malafaia, G., & Singh, R. K. (2023). Polystyrene microplastics disrupt female reproductive health and fertility via sirt1 modulation in zebrafish (Danio rerio). *Journal of Hazardous Materials*, *460*, 132359.

Hahladakis, J. N., Velis, C. A., Weber, R., Iacovidou, E., & Purnell, P. (2018). An overview of chemical additives present in plastics: Migration, release, fate and environmental impact during their use, disposal and recycling. *Journal of Hazardous Materials*, *344*(Journal Article), 179–199.

Harrison, J. P., Ojeda, J. J., & Romero-González, M., E. (2012). The applicability of reflectance micro-Fourier-transform infrared spectroscopy for the detection of synthetic microplastics in marine sediments. *Science of the Total Environment*, *416*(Journal Article), 455–463.

Hidalgo-Ruz, V., Gutow, L., Thompson, R. C., & Thiel, M. (2012). Microplastics in the marine environment: A review of the methods used for identification and quantification. *Environmental Science & Technology*, *46*(6), 3060–3075.

Hou, B., Wang, F., Liu, T., & Wang, Z. (2021). Reproductive toxicity of polystyrene microplastics: In vivo experimental study on testicular toxicity in mice. *Journal of Hazardous Materials*, *405*(Journal Article), 124028.

Huang, J.-N., Wen, B., Zhu, J.-G., Zhang, Y.-S., Gao, J.-Z., & Chen, Z.-Z. (2020). Exposure to microplastics impairs digestive performance, stimulates immune response and induces microbiota dysbiosis in the gut of juvenile guppy (Poecilia reticulata). *Science of the Total Environment*, *733*(Journal Article), 138929.

Huang, Y., Wong, K. K., Li, W., Zhao, H., Wang, T., Stanescu, S., Boult, S., van Dongen, B., Mativenga, P., & Li, L. (2022). Characteristics of nano-plastics in bottled drinking water. *Journal of Hazardous Materials*, *424*(Journal Article), 127404.

Iñiguez, M. E., Conesa, J. A., & Fullana, A. (2017). Microplastics in Spanish table salt. *Scientific Reports*, *7*(1), 8620.

Jabeen, K., Su, L., Li, J., Yang, D., Tong, C., Mu, J., & Shi, H. (2017). Microplastics and mesoplastics in fish from coastal and fresh waters of China. *Environmental Pollution*, *221*(Journal Article), 141–149.

Jambeck, J. R., Geyer, R., Wilcox, C., Siegler, T. R., Perryman, M., Andrady, A., Narayan, R., & Law, K. L. (2015). Plastic waste inputs from land into the ocean. *Science*, *347*(6223), 768–771.

Jatana, S., Callahan, L. M., Pentland, A. P., & DeLouise, L. A. (2016). Impact of cosmetic lotions on nanoparticle penetration through ex vivo C57BL/6 hairless mouse and human skin: A comparison study. *Cosmetics*, *3*(1), 6.

Jin, H., Yan, M., Pan, C., Liu, Z., Sha, X., Jiang, C., Li, L., Pan, M., Li, D., & Han, X. (2022). Chronic exposure to polystyrene microplastics induced male reproductive toxicity and decreased testosterone levels via the LH-mediated LHR/cAMP/PKA/StAR pathway. *Particle and Fibre Toxicology*, *19*(1), 1–17.

Jin, M., Wang, X., Ren, T., Wang, J., & Shan, J. (2021). Microplastics contamination in food and beverages: Direct exposure to humans. *Journal of Food Science*, *86*(7), 2816–2837.

Kadac-Czapska, K., Trzebiatowska, P. J., Mazurkiewicz, M., Kowalczyk, P., Knez, E., Behrendt, M., Mahlik, S., Zaleska-Medynska, A., & Grembecka, M. (2023). Isolation and identification of microplastics in infant formulas–A potential health risk for children. *Food Chemistry*, 138246.

Kankanige, D., & Babel, S. (2020). Smaller-sized micro-plastics (MPs) contamination in single-use PET-bottled water in Thailand. *Science of the Total Environment*, *717*(Journal Article), 137232.

Käppler, A., Fischer, D., Oberbeckmann, S., Schernewski, G., Labrenz, M., Eichhorn, K.-J., & Voit, B. (2016). Analysis of environmental microplastics by vibrational microspectroscopy: FTIR, Raman or both? *Analytical and Bioanalytical Chemistry*, *408*(Journal Article), 8377–8391.

Kapukotuwa, R. W. M. G. K., Jayasena, N., Weerakoon, K. C., Abayasekara, C. L., & Rajakaruna, R. S. (2022). High levels of microplastics in commercial salt and industrial salterns in Sri Lanka. *Marine Pollution Bulletin*, *174*(Journal Article), 113239. https://doi.org/10.1016/j.marpolbul.2021.113239

Karami, A., Golieskardi, A., Keong Choo, C., Larat, V., Galloway, T. S., & Salamatinia, B. (2017). The presence of microplastics in commercial salts from different countries. *Scientific Reports*, *7*(1), 46173.

Karlsson, T. M., Vethaak, A. D., Almroth, B. C., Ariese, F., van Velzen, M., Hassellöv, M., & Leslie, H. A. (2017). Screening for microplastics in sediment, water, marine invertebrates and fish: Method development and microplastic accumulation. *Marine Pollution Bulletin*, *122*(1–2), 403–408.

Khan, M. J., Gerasimidis, K., Edwards, C. A., & Shaikh, M. G. (2016). Role of gut microbiota in the aetiology of obesity: Proposed mechanisms and review of the literature. *Journal of Obesity*, *2016*(Journal Article).

Kim, H., Zaheer, J., Choi, E.-J., & Kim, J. S. (2022). Enhanced ASGR2 by microplastic exposure leads to resistance to therapy in gastric cancer. *Theranostics*, *12*(7), 3217.

Kirstein, I. V., Kirmizi, S., Wichels, A., Garin-Fernandez, A., Erler, R., Löder, M., & Gerdts, G. (2016). Dangerous hitchhikers? Evidence for potentially pathogenic Vibrio spp. On microplastic particles. *Marine Environmental Research*, *120*(Journal Article), 1–8.

Kılıç, E. (2022). Microplastic ingestion evidence by economically important farmed fish species from Turkey. *Marine Pollution Bulletin*, *183*(Journal Article), 114097.

Krishnan, R. Y., Manikandan, S., Subbaiya, R., Karmegam, N., Kim, W., & Govarthanan, M. (2023). Recent approaches and advanced wastewater treatment technologies for mitigating emerging microplastics contamination–A critical review. *Science of The Total Environment*, *858*, 159681.

Lamichhane, G., Acharya, A., Marahatha, R., Modi, B., Paudel, R., Adhikari, A., Raut, B. K., Aryal, S., & Parajuli, N. (2023). Microplastics in environment: Global concern, challenges, and controlling measures. *International Journal of Environmental Science and Technology*, *20*(4), 4673–4694.

Lehner, R., Weder, C., Petri-Fink, A., & Rothen-Rutishauser, B. (2019). Emergence of nanoplastic in the environment and possible impact on human health. *Environmental Science & Technology*, *53*(4), 1748–1765.

Leslie, H. A., Van Velzen, M. J., Brandsma, S. H., Vethaak, A. D., Garcia-Vallejo, J. J., & Lamoree, M. H. (2022). Discovery and quantification of plastic particle pollution in human blood. *Environment International*, *163*, 107199.

Li, B., Ding, Y., Cheng, X., Sheng, D., Xu, Z., Rong, Q., Wu, Y., Zhao, H., Ji, X., & Zhang, Y. (2020). Polyethylene microplastics affect the distribution of gut microbiota and inflammation development in mice. *Chemosphere*, *244*(Journal Article), 125492.

Li, J., Green, C., Reynolds, A., Shi, H., & Rotchell, J. M. (2018). Microplastics in mussels sampled from coastal waters and supermarkets in the United Kingdom. *Environmental Pollution*, *241*(Journal Article), 35–44.

Li, J., Yang, D., Li, L., Jabeen, K., & Shi, H. (2015). Microplastics in commercial bivalves from China. *Environmental Pollution*, *207*(Journal Article), 190–195.

Liebezeit, G., & Liebezeit, E. (2013). Non-pollen particulates in honey and sugar. *Food Additives & Contaminants: Part A*, *30*(12), 2136–2140.

Liebezeit, G., & Liebezeit, E. (2015). Origin of synthetic particles in honeys. *Polish Journal of Food and Nutrition Sciences*, *65*(2).

Liu, Z., Yu, P., Cai, M., Wu, D., Zhang, M., Chen, M., & Zhao, Y. (2019). Effects of microplastics on the innate immunity and intestinal microflora of juvenile Eriocheir sinensis. *Science of the Total Environment*, *685*(Journal Article), 836–846.

Liu, Z., Zhuan, Q., Zhang, L., Meng, L., Fu, X., & Hou, Y. (2022). Polystyrene microplastics induced female reproductive toxicity in mice. *Journal of Hazardous Materials*, *424*(Journal Article), 127629.

Löder, M., G. J., & Gerdts, G. (2015). Methodology used for the detection and identification of microplastics—A critical appraisal. *Marine Anthropogenic Litter*, *Journal Article*, 201–227.

Lu, L., Wan, Z., Luo, T., Fu, Z., & Jin, Y. (2018). Polystyrene microplastics induce gut microbiota dysbiosis and hepatic lipid metabolism disorder in mice. *Science of the Total Environment*, *631*(Journal Article), 449–458.

Lusher, A., Hollman, P., & Mendoza-Hill, J. (2017). *Microplastics in fisheries and aquaculture: Status of knowledge on their occurrence and implications for aquatic organisms and food safety*. FAO.

Lusher, A. L., Mchugh, M., & Thompson, R. C. (2013). Occurrence of microplastics in the gastrointestinal tract of pelagic and demersal fish from the English Channel. *Marine Pollution Bulletin*, *67*(1–2), 94–99.

Lv, L., Yan, X., Feng, L., Jiang, S., Lu, Z., Xie, H., Sun, S., Chen, J., & Li, C. (2021). Challenge for the detection of microplastics in the environment. *Water Environment Research*, *93*(1), 5–15.

Mai, N. T. Q., Batjargal, U., Kim, W.-S., Kim, J.-H., Park, J.-W., Kwak, I.-S., & Moon, B.-S. (2023). Microplastic induces mitochondrial pathway mediated cellular apoptosis in mussel (Mytilus galloprovincialis) via inhibition of the AKT and ERK signaling pathway. *Cell Death Discovery*, *9*(1), 442.

Meng, K., Lwanga, E. H., van der Zee, M., Munhoz, D. R., & Geissen, V. (2023). Fragmentation and depolymerization of microplastics in the earthworm gut: A potential for microplastic bioremediation? *Journal of Hazardous Materials*, *447*, 130765.

Milne, M. H., De Frond, H., Rochman, C. M., Mallos, N. J., Leonard, G. H., & Baechler, B. R. (2023). Exposure of US adults to microplastics from commonly-consumed proteins. *Environmental Pollution*, 123233.

MohanKumar, S. M., Campbell, A., Block, M., & Veronesi, B. (2008). Particulate matter, oxidative stress and neurotoxicity. *Neurotoxicology*, *29*(3), 479–488.

Morais, L. M. S., Sarti, F., Chelazzi, D., Cincinelli, A., Giarrizzo, T., & Martinelli Filho, J. E. (2020). The sea anemone Bunodosoma cangicum as a potential biomonitor for microplastics contamination on the Brazilian Amazon coast. *Environmental Pollution*, *265*(Journal Article), 114817.

Murali, K., Li, Y., Demeter, K., Környei, Z., & Madarász, E. (2015). Uptake and bio-reactivity of polystyrene nanoparticles is affected by surface modifications, ageing and LPS adsorption: In vitro studies on neural tissue cells. *Nanoscale*, *7*(9), 4199–4210.

Naji, A., Nuri, M., & Vethaak, A. D. (2018). Microplastics contamination in molluscs from the northern part of the Persian Gulf. *Environmental Pollution*, *235*(Journal Article), 113–120.

Neves, D., Sobral, P., Ferreira, J. L., & Pereira, T. (2015). Ingestion of microplastics by commercial fish off the Portuguese coast. *Marine Pollution Bulletin*, *101*(1), 119–126.

Oßmann, B. E., Sarau, G., Holtmannspötter, H., Pischetsrieder, M., Christiansen, S. H., & Dicke, W. (2018). Small-sized microplastics and pigmented particles in bottled mineral water. *Water Research*, *141*(Journal Article), 307–316.

Paget, V., Dekali, S., Kortulewski, T., Grall, R., Gamez, C., Blazy, K., Aguerre-Chariol, O., Chevillard, S., Braun, A., & Rat, P. (2015). Specific uptake and genotoxicity induced by polystyrene nanobeads with distinct surface chemistry on human lung epithelial cells and macrophages. *PloS One*, *10*(4), e0123297.

Pakhomova, S., Zhdanov, I., & van Bavel, B. (2020). Polymer type identification of marine plastic litter using a miniature near-infrared spectrometer (MicroNIR). *Applied Sciences*, *10*(23), 8707.

Pan, Z., Guo, H., Chen, H., Wang, S., Sun, X., Zou, Q., Zhang, Y., Lin, H., Cai, S., & Huang, J. (2019). Microplastics in the Northwestern Pacific: Abundance, distribution, and characteristics. *Science of the Total Environment*, *650*(Journal Article), 1913–1922.

Park, T.-J., Lee, S.-H., Lee, M.-S., Lee, J.-K., Lee, S.-H., & Zoh, K.-D. (2020). Occurrence of microplastics in the Han River and riverine fish in South Korea. *Science of the Total Environment*, *708*(Journal Article), 134535.

Paul, A., Wander, L., Becker, R., Goedecke, C., & Braun, U. (2019). High-throughput NIR spectroscopic (NIRS) detection of microplastics in soil. *Environmental Science and Pollution Research*, *26*, 7364–7374.

Paul-Pont, I., Lacroix, C., Fernández, C. G., Hégaret, H., Lambert, C., Le Goïc, N., Frère, L., Cassone, A.-L., Sussarellu, R., & Fabioux, C. (2016). Exposure of marine mussels Mytilus spp. To polystyrene microplastics: Toxicity and influence on fluoranthene bioaccumulation. *Environmental Pollution*, *216*(Journal Article), 724–737.

Peez, N., Becker, J., Ehlers, S. M., Fritz, M., Fischer, C. B., Koop, J. H. E., Winkelmann, C., & Imhof, W. (2019). Quantitative analysis of PET microplastics in environmental model samples using quantitative 1 H-NMR spectroscopy: Validation of an optimized and consistent sample clean-up method. *Analytical and Bioanalytical Chemistry*, *411*(Journal Article), 7409–7418.

Peez, N., & Imhof, W. (2020). Quantitative 1 H-NMR spectroscopy as an efficient method for identification and quantification of PVC, ABS and PA microparticles. *Analyst*, *145*(15), 5363–5371.

Peñalver, R., Arroyo-Manzanares, N., López-García, I., & Hernández-Córdoba, M. (2020). An overview of microplastics characterization by thermal analysis. *Chemosphere*, *242*(Journal Article), 125170.

Phillips, M. B., & Bonner, T. H. (2015). Occurrence and amount of microplastic ingested by fishes in watersheds of the Gulf of Mexico. *Marine Pollution Bulletin*, *100*(1), 264–269.

Pittroff, M., Müller, Y. K., Witzig, C. S., Scheurer, M., Storck, F. R., & Zumbülte, N. (2021). Microplastic analysis in drinking water based on fractionated filtration sampling and Raman microspectroscopy. *Environmental Science and Pollution Research*, *28*(42), 59439–59451.

Plastics—The Facts 2022 • Plastics Europe. (n.d.). *Plastics Europe*, *Online Discussion Forum/Blogs*. https://plasticseurope.org/knowledge-hub/plastics-the-facts-2022/

Poma, A., Vecchiotti, G., Colafarina, S., Zarivi, O., Aloisi, M., Arrizza, L., Chichiriccò, G., & Di Carlo, P. (2019). In vitro genotoxicity of polystyrene nanoparticles on the human fibroblast Hs27 cell line. *Nanomaterials*, *9*(9), 1299.

Powell, J. J., Thoree, V., & Pele, L. C. (2007). Dietary microparticles and their impact on tolerance and immune responsiveness of the gastrointestinal tract. *British Journal of Nutrition*, *98*(S1), S59–S63.

Prata, J. C. (2018). Airborne microplastics: Consequences to human health? *Environmental Pollution*, *234*(Journal Article), 115–126.

Prata, J. C., da Costa, J. P., Lopes, I., Duarte, A. C., & Rocha-Santos, T. (2020). Environmental exposure to microplastics: An overview on possible human health effects. *Science of the Total Environment*, *702*(Journal Article), 134455.

Protyusha, G. B., Kavitha, B., Robin, R. S., Nithin, A., Ineyathendral, T. R., Shivani, S. S., Anandavelu, I., Sivasamy, S., Samuel, V. D., & Purvaja, R. (2023). Microplastics in oral healthcare products (OHPs) and their environmental health risks and mitigation measures. *Environmental Pollution*, 123118.

Qian, N., Gao, X., Lang, X., Deng, H., Bratu, T. M., Chen, Q., Stapleton, P., Yan, B., & Min, W. (2024). Rapid single-particle chemical imaging of nanoplastics by SRS microscopy. *Proceedings of the National Academy of Sciences*, *121*(3), e2300582121. https://doi.org/10.1073/pnas.2300582121

Qiao, R., Sheng, C., Lu, Y., Zhang, Y., Ren, H., & Lemos, B. (2019). Microplastics induce intestinal inflammation, oxidative stress, and disorders of metabolome and microbiome in zebrafish. *Science of the Total Environment*, *662*(Journal Article), 246–253.

Ragusa, A., Notarstefano, V., Svelato, A., Belloni, A., Gioacchini, G., Blondeel, C., Zucchelli, E., De Luca, C., D'Avino, S., & Gulotta, A. (2022). Raman microspectroscopy detection and characterisation of microplastics in human breastmilk. *Polymers*, *14*(13), 2700.

Reimonn, G., Lu, T., Gandhi, N., & Chen, W.-T. (2019). Review of microplastic pollution in the environment and emerging recycling solutions. *Journal of Renewable Materials*, *7*(12), 1251–1268.

Renzi, M., Grazioli, E., Bertacchini, E., & Blašković, A. (2019). Microparticles in table salt: Levels and chemical composition of the smallest dimensional fraction. *Journal of Marine Science and Engineering*, *7*(9), 310.

Revel, M., Châtel, A., & Mouneyrac, C. (2018). Micro (nano) plastics: A threat to human health? *Current Opinion in Environmental Science & Health*, *1*(Journal Article), 17–23.

Roch, S., Walter, T., Ittner, L. D., Friedrich, C., & Brinker, A. (2019). A systematic study of the microplastic burden in freshwater fishes of south-western Germany-Are we searching at the right scale? *Science of the Total Environment*, *689*(Journal Article), 1001–1011.

Salim, S. Y., Kaplan, G. G., & Madsen, K. L. (2014). Air pollution effects on the gut microbiota: A link between exposure and inflammatory disease. *Gut Microbes*, *5*(2), 215–219.

Schirinzi, G. F., Pérez-Pomeda, I., Sanchís, J., Rossini, C., Farré, M., & Barceló, D. (2017). Cytotoxic effects of commonly used nanomaterials and microplastics on cerebral and epithelial human cells. *Environmental Research*, *159*(Journal Article), 579–587.

Schmid, K., Winemiller, K. O., Chelazzi, D., Cincinelli, A., Dei, L., & Giarrizzo, T. (2018). First evidence of microplastic ingestion by fishes from the Amazon River estuary. *Marine Pollution Bulletin*, *133*(Journal Article), 814–821.

Schneider, M., Stracke, F., Hansen, S., & Schaefer, U. F. (2009). Nanoparticles and their interactions with the dermal barrier. *Dermato-Endocrinology*, *1*(4), 197–206.

Schwabl, P., Köppel, S., Königshofer, P., Bucsics, T., Trauner, M., Reiberger, T., & Liebmann, B. (2019). Detection of various microplastics in human stool: A prospective case series. *Annals of Internal Medicine*, *171*(7), 453–457.

Schwaferts, C., Niessner, R., Elsner, M., & Ivleva, N. P. (2019). Methods for the analysis of submicrometer-and nanoplastic particles in the environment. *TrAC Trends in Analytical Chemistry*, *112*(Journal Article), 52–65.

Schymanski, D., Goldbeck, C., Humpf, H.-U., & Fürst, P. (2018). Analysis of microplastics in water by micro-Raman spectroscopy: Release of plastic particles from different packaging into mineral water. *Water Research*, *129*(Journal Article), 154–162. https://doi.org/10.1016/j.watres.2017.11.011

Seth, C. K., & Shriwastav, A. (2018). Contamination of Indian sea salts with microplastics and a potential prevention strategy. *Environmental Science and Pollution Research*, *25*(Journal Article), 30122–30131.

Shan, S., Zhang, Y., Zhao, H., Zeng, T., & Zhao, X. (2022). Polystyrene nanoplastics penetrate across the blood-brain barrier and induce activation of microglia in the brain of mice. *Chemosphere*, *298*(Journal Article), 134261.

Shim, W. J., Hong, S. H., & Eo, S. E. (2017). Identification methods in microplastic analysis: A review. *Analytical Methods*, *9*(9), 1384–1391.

Shruti, V. C., Kutralam-Muniasamy, G., Pérez-Guevara, F., Roy, P. D., & Elizalde-Martínez, I. (2022). First evidence of microplastic contamination in ready-to-use packaged food ice cubes. *Environmental Pollution*, *Journal Article*, 120905.

Shruti, V. C., Pérez-Guevara, F., Elizalde-Martínez, I., & Kutralam-Muniasamy, G. (2020). First study of its kind on the microplastic contamination of soft drinks, cold tea and energy drinks-Future research and environmental considerations. *Science of the Total Environment*, *726*(Journal Article), 138580.

Sobhani, Z., Amin, A., Naidu, R., Megharaj, M., & Fang, C. (2019). Identification and visualisation of microplastics by Raman mapping. *Analytica Chimica Acta*, *1077*(Journal Article), 191–199.

Song, Y. K., Hong, S. H., Jang, M., Han, G. M., Rani, M., Lee, J., & Shim, W. J. (2015). A comparison of microscopic and spectroscopic identification methods for analysis of microplastics in environmental samples. *Marine Pollution Bulletin*, *93*(1–2), 202–209.

Sridhar, A., Kannan, D., Kapoor, A., & Prabhakar, S. (2022). Extraction and detection methods of microplastics in food and marine systems: A critical review. *Chemosphere*, *286*(Journal Article), 131653.

Stock, V., Böhmert, L., Lisicki, E., Block, R., Cara-Carmona, J., Pack, L. K., Selb, R., Lichtenstein, D., Voss, L., & Henderson, C. J. (2019). Uptake and effects of orally ingested polystyrene microplastic particles in vitro and in vivo. *Archives of Toxicology*, *93*(7), 1817–1833.

Su, L., Deng, H., Li, B., Chen, Q., Pettigrove, V., Wu, C., & Shi, H. (2019). The occurrence of microplastic in specific organs in commercially caught fishes from coast and estuary area of east China. *Journal of Hazardous Materials*, *365*(Journal Article), 716–724.

Tagg, A. S., Sapp, M., Harrison, J. P., & Ojeda, J. J. (2015). Identification and quantification of microplastics in wastewater using focal plane array-based reflectance micro-FT-IR imaging. *Analytical Chemistry*, *87*(12), 6032–6040.

Tirkey, A., & Upadhyay, L. S. B. (2021). Microplastics: An overview on separation, identification and characterization of microplastics. *Marine Pollution Bulletin*, *170*(Journal Article), 112604.

Tong, H., Jiang, Q., Hu, X., & Zhong, X. (2020). Occurrence and identification of microplastics in tap water from China. *Chemosphere*, *252*(Journal Article), 126493. https://doi.org/10.1016/j.chemosphere.2020.126493

Trasande, L., Krithivasan, R., Park, K., Obsekov, V., & Belliveau, M. (2024). Chemicals Used in Plastic Materials: An Estimate of the Attributable Disease Burden and Costs in the United States. *Journal of the Endocrine Society*, *8*(2), bvad163.

Tutaroğlu, S., Uslu, L., & Gündoğdu, S. (2023). Microplastic contamination of packaged spirulina products. *Environmental Science and Pollution Research*, 1–13.

Tympa, L.-E., Katsara, K., Moschou, P. N., Kenanakis, G., & Papadakis, V. M. (2021). Do microplastics enter our food chain via root vegetables? A raman based spectroscopic study on Raphanus sativus. *Materials*, *14*(9), 2329.

Udovicki, B., Andjelkovic, M., Cirkovic-Velickovic, T., & Rajkovic, A. (2022). Microplastics in food: Scoping review on health effects, occurrence, and human exposure. *International Journal of Food Contamination*, *9*(1), 1–16.

Van Cauwenberghe, L., Claessens, M., Vandegehuchte, M. B., & Janssen, C. R. (2015). Microplastics are taken up by mussels (Mytilus edulis) and lugworms (Arenicola marina) living in natural habitats. *Environmental Pollution*, *199*(Journal Article), 10–17.

Van Cauwenberghe, L., & Janssen, C. R. (2014). Microplastics in bivalves cultured for human consumption. *Environmental Pollution*, *193*(Journal Article), 65–70.

Van Tienhoven, E., Korbee, D., Schipper, L., Verharen, H. W., & De Jong, W. H. (2006). In vitro and in vivo (cyto) toxicity assays using PVC and LDPE as model materials. *Journal of Biomedical Materials Research Part A: An Official Journal of The Society for Biomaterials, The Japanese Society for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials*, *78*(1), 175–182.

Vianello, A., Jensen, R. L., Liu, L., & Vollertsen, J. (2019). Simulating human exposure to indoor airborne microplastics using a Breathing Thermal Manikin. *Scientific Reports*, *9*(1), 1–11.

Von Moos, N., Burkhardt-Holm, P., & Köhler, A. (2012). Uptake and effects of microplastics on cells and tissue of the blue mussel Mytilus edulis L. after an experimental exposure. *Environmental Science & Technology*, *46*(20), 11327–11335.

Wagner, J., Wang, Z.-M., Ghosal, S., Rochman, C., Gassel, M., & Wall, S. (2017). Novel method for the extraction and identification of microplastics in ocean trawl and fish gut matrices. *Analytical Methods*, *9*(9), 1479–1490.

WANG, J., WANG, X., ZHANG, C., & ZHOU, X. (2022). Microplastics induce immune suppression via S100A8 downregulation. *Ecotoxicology and Environmental Safety*, *242*(Journal Article), 113905. https://doi.org/10.1016/j.ecoenv.2022.113905

Watts, A. J., Urbina, M. A., Corr, S., Lewis, C., & Galloway, T. S. (2015). Ingestion of plastic microfibers by the crab Carcinus maenas and its effect on food consumption and energy balance. *Environmental Science & Technology*, *49*(24), 14597–14604.

Wei, Z., Wang, Y., Wang, S., Xie, J., Han, Q., & Chen, M. (2022). Comparing the effects of polystyrene microplastics exposure on reproduction and fertility in male and female mice. *Toxicology*, *465*(Journal Article), 153059.

West-Eberhard, M. J. (2019). Nutrition, the visceral immune system, and the evolutionary origins of pathogenic obesity. *Proceedings of the National Academy of Sciences*, *116*(3), 723–731.

WHO. (2019). No title. *Microplastics in Drinking Water*, *Journal Article*.

Wright, S. L., Rowe, D., Thompson, R. C., & Galloway, T. S. (2013). Microplastic ingestion decreases energy reserves in marine worms. *Current Biology*, *23*(23), R1031–R1033. https://doi.org/10.1016/j.cub.2013.10.068

Xie, X., Deng, T., Duan, J., Xie, J., Yuan, J., & Chen, M. (2020). Exposure to polystyrene microplastics causes reproductive toxicity through oxidative stress and activation of the p38 MAPK signaling pathway. *Ecotoxicology and Environmental Safety*, *190*(Journal Article), 110133.

Xu, X. Y., Lee, W. T., Chan, A., Lo, H. S., Shin, P., & Cheung, S. G. (2017). Microplastic ingestion reduces energy intake in the clam Atactodea striata. *Marine Pollution Bulletin*, *124*(2), 798–802.

Yan, Z., Liu, Y., Zhang, T., Zhang, F., Ren, H., & Zhang, Y. (2021). Analysis of microplastics in human feces reveals a correlation between fecal microplastics and inflammatory bowel disease status. *Environmental Science & Technology*, *56*(1), 414–421.

Yang, D., Shi, H., Li, L., Li, J., Jabeen, K., & Kolandhasamy, P. (2015). Microplastic pollution in table salts from China. *Environmental Science & Technology*, *49*(22), 13622–13627.

Yee, M. S.-L., Hii, L.-W., Looi, C. K., Lim, W.-M., Wong, S.-F., Kok, Y.-Y., Tan, B.-K., Wong, C.-Y., & Leong, C.-O. (2021). Impact of microplastics and nanoplastics on human health. *Nanomaterials*, *11*(2), 496.

Yoshida, S., Hiraga, K., Takehana, T., Taniguchi, I., Yamaji, H., Maeda, Y., Toyohara, K., Miyamoto, K., Kimura, Y., & Oda, K. (2016). A bacterium that degrades and assimilates poly (ethylene terephthalate). *Science*, *351*(6278), 1196–1199.

Zhang, P., Zhang, Y., Li, P., Tu, D., & Zheng, X. (2024). Effects of the adsorption behavior of polyamide microplastics on male reproductive health by reduction of testosterone bioavailability. *Ecotoxicology and Environmental Safety*, *269*, 115747.

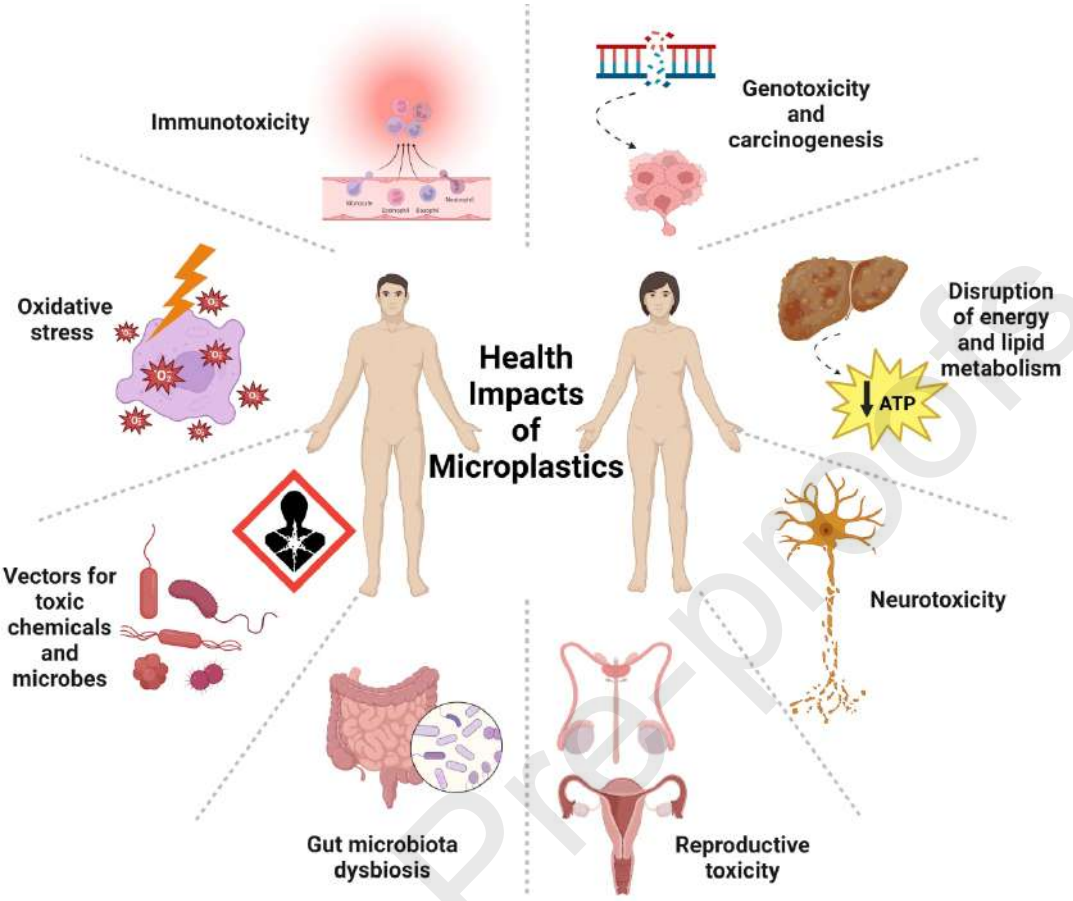
Zhang, Q., He, Y., Cheng, R., Li, Q., Qian, Z., & Lin, X. (2022). Recent advances in toxicological research and potential health impact of microplastics and nanoplastics in vivo. *Environmental Science and Pollution Research*, *Journal Article*, 1–34.

Zhao, J., Gomes, D., Jin, L., Mathis, S. P., Li, X., Rouchka, E. C., Bodduluri, H., Conklin, D. J., & O'Toole, T. E. (2022). Polystyrene bead ingestion promotes adiposity and cardiometabolic disease in mice. *Ecotoxicology and Environmental Safety*, *232*(Journal Article), 113239. https://doi.org/10.1016/j.ecoenv.2022.113239

Zhu, L., Zhu, J., Zuo, R., Xu, Q., Qian, Y., & Lihui, A. N. (2023). Identification of microplastics in human placenta using laser direct infrared spectroscopy. *Science of the Total Environment*, *856*, 159060.

Highlights

- Widespread use of plastics has led to environmental contamination including presence of MPs in daily food items.
- Ingestion, inhalation and dermal exposure are the common routes of exposure.
- MPs pose diverse health implications.
- Limitations in the existing analytical methods hinders human exposure assessment of MPs.



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