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Review

From food-to-human microplastics and nanoplastics exposure and health effects: A review on food, animal and human monitoring data

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ABSTRACT

This review figures out the overall status on the presence of microplastics (MPs) and nanoplastics (NPs) in food and their bioaccumulation in animal and human tissues, providing critical insights into possible human health impacts. Data are discussed on both *in-vivo* and *ex-vivo* animal and human studies, and the role of physico-chemical properties in determining the biological fate and toxicological effects of MPs and NPs. Particular attention is given to dietary exposure assessments, specifically evaluating daily intake through the consumption of contaminated food items. The current limitations in the body of knowledge and some considerations for future assessments are also reported. Overall, there is a pressing need to establish more robust biomarker research and develop standardized methodologies, for a better understanding of MPs and NPs fate and associated effects in more realistic scenarios for their safe consumption. The review underscores the importance of integrating the human biomonitoring into monitoring programs and interdisciplinary research to ultimately inform on MPs and NPs real burden in the human body.

1. Introduction

Used by almost every industry in the world, from food packaging to space exploration, plastic is the ultimate commodity of convenience. Goods made of this material show many positive features, such as lightness and durability, and resistance to mechanical damage, corrosion, and weather conditions (Anik et al., 2021). Unfortunately, the popularity of such products has also its negative consequences. Studies indicate that about 79% of the plastic annually produced returned into the environment as waste (Geyer et al., 2017). In the long and slow process of decomposition, large plastic litters will most likely break down to mesoplastics (i.e., plastics fragments with size >5000μm) and microplastics (MPs, plastic particles with size of 1–5000μm) and even disintegrate into smaller nanoplastics (NPs, plastic particles ≤0.1μm) (Gigault et al., 2018). According to the European Chemicals Agency (ECHA), the terms MPs and NPs are applied for any solid-polymer-containing particles, to which additives or other substances may have been added, and where ≥1% w/w of particles have all dimensions between 1nm and 5mm or for fibers, a length between 3nm and 15mm and a length-to-diameter ratio >3 (Arthur et al., 2009; ECHA, 2020). The MPs and NPs can be in fragments, pellets, filaments, plastic films, foamed plastic, granules and styrofoam. Due to the small size, MPs

Abbreviations: PET, polyethylene terephthalate; PP, polypropylene; PE, polyethylene; PB, polybutylene; PS, polystyrene; PVC, polyvinyl chloride; CP, cellophane; PA, polyamide; PL, polyester; PAN, polyacrylonitrile; PMMA, polymethyl-methacrylate; PA-6, nylon or polyamide-6; PI, polyisoprene; PAM, polyacrylamide; PES, poly(ether sulfone); PSU, polysulfone; PU, polyurethane; PEA, poly(ester-amide); ABS, acrylonitrile-butadiene-styrene; SAC, styrene-acrylonitrile copolymer; EVA, ethylvinyl acetate; PC, polycarbonate; PVF, polyvinyl fluoride; PPS, polyphenylene sulfite; RY, rayon; PEST, polyester + polyethylene terephthalate; DBP, dibutyl phthalate; SBR, styrene butadiene rubber; PBD, polybutadiene; PDMS, polydimethylsiloxanes; PTFE, polytetrafluoroethylene; EPDM, ethylene propylene diene monomer; PEVA, poly(ethylene-vinyl acetate); POM, polyoxymethylene; PBT, poly(butylene terephthalate); AS, acrylonitrile-styrene; NC, nitrocellulose; CPE, chlorinated polyethylene; PEMA, poly(ethyl methacrylate); PLA, poly(lactic acid).

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and NPs can be of concerns for the following characteristics: i) transferring fast and far in the environment; ii) large surface for fast sorption and release of pollutants and/or plastic additives; iii) slow degradation process and iv) potential capacity to interact with a wide range of organisms, mainly in marine environment (Lehner et al., 2019; Stapleton, 2019; Kik et al., 2020). Compared with MPs, NPs are probably much more dangerous for humans due to their smaller particle size (more abundant and reactive) leading to potential capability to cross through cell membranes (Sharma et al., 2023). Sources of MPs and NPs can be the environment (agricultural soil, sediments, air, urban dust, etc.), diet (water and food) and consumer products (cosmetics, personal care products, textiles, etc.) (Anik et al., 2021). While it is widely accepted that the human exposure to MPs and NPs represents a potential health risk, the magnitude and variability of MPs and NPs exposure concentrations and intake rates are still on debate (Mohamed Nor et al., 2021).

Although human exposure to MPs and NPs may be through multiple routes, particular attention should be paid to MPs and NPs ingestion. Different data revealed the presence of these compounds in beverage and food items, and they were recently detected in human biological media like feces, breastmilk, placenta, blood, saliva, and urine (Pironti et al., 2022; Leslie et al., 2022; Ragusa et al., 2022; Abbasi and Turner, 2021; Schwabl et al., 2019; Zhang et al., 2021a; Zhang et al., 2021b). The potential toxicity and effects on human health arising from MPs and NPs exposure is a field poorly explored, although *in-vivo* studies have shown potential health risk including inflammatory effects, oxidative stress and metabolic disorders (Rahman et al., 2021; Powell et al., 2010). In addition, studies on human cell lines revealed the MPs capability to cause inflammatory responses, variation in cell morphology, inhibition of cell growth, and alterations in gut microbiota (Hwang et al., 2019; Choi et al., 2020).

At present there is no European Union (EU) legislation for MPs and NPs as contaminants in food and beverages but are a broad range of EU initiatives aimed at stimulating translational research and support European and national policies in relation to the MPs and NPs transfer through the food-web and their implication on human health. In this view, the implementation of human biomonitoring (HBM) studies - able to integrate the human exposure from all the potential sources – should represent a topic of priority matter.

This review explored the current evidence of the human exposure and possible health effects to MPs and NPs after their oral intake, and specifically it describes: i) the occurrence of MPs and NPs in foods and drinks; ii) the absorption, biodistribution, and bioaccumulation of MPs and NPs and biological adverse health effects after oral intake; iii) the role of physicochemical properties of MPs and NPs in affecting the MPs and NPs toxicological features; iv) the dietary exposure assessment in humans following MPs and NPs oral intake. To address these issues, only *in-vivo* and *ex-vivo* studies, including animal and human samples (organs, tissues and fluids) were taken into account. The final purpose was to promote HBM studies and data focused on this emerging type of contaminants to better understand their real burden in the human body.

2. Review methodology

The review was conducted to assess and understand the current state of knowledge on the human exposure and toxicological effects associated to MPs and NPs consumed *via* diet. Pubmed/Medline, Scopus and Web of Science databases were searched for studies published until 2023 addressing the following 5 main questions that provided guidance for the definition of appropriate search terms:

1) "**Occurrence and identification of MPs and NPs in the food chain**": identification of published studies that determined MPs and NPs in the food web using keywords as "drinking water", "fish", "vegetables", "salt", "honey", "milk", "meat", "beer", etc.
2) "**Uptake, biodistribution and bioaccumulation of MPs and NPs**": identification of published *in-vivo* and *ex-vivo* studies that assessed the MPs and NPs uptake, accumulation and distribution after oral exposure in different organs and tissues (such as intestine, liver, kidney, blood, spleen, brain, etc.), also including studies that reported the influence of physicochemical properties (size, shape, surface, chemical composition, weathering) on adsorption.
3) "**Biological health effects after oral exposure to MPs and NPs"**: identification of published *in-vivo* and *ex-vivo* studies that evaluated the toxicological effects after oral exposure by means of keywords as "toxicity", "inflammation", "oxidative stress", "nephrotoxicity", "hepatotoxicity", "reproductive effects", "neurotoxicity", etc., also including studies that reported the influence of physicochemical properties (size, shape, surface, chemical composition, weathering) on toxicity.
4) "**Level of MPs and NPs in human samples**": identification of published studies that assessed the human exposure through their direct quantification in human samples, including "stool", "blood", "urine", "breastmilk", "placenta", "meconium", "hair", "saliva", "brain".
5) "**Dietary exposure assessment to MPs and NPs in humans**": identification of published studies that quantified the potential dietary exposure assessment including keywords such as "average daily ingestion", "average daily intake" and "estimated daily intake".

More than one hundred and fifty studies were identified from the initial searches, and they were divided into folders according to the categorical searches and used to discuss the following sections. Additional studies were screened and added as discovered in a less systematic way during the development of the manuscript to describe specific processes. For each study the following characteristics were collected and included in Tables 1–3: country; type of food and drink; studied model (mice, rat, fish etc.); studied organ/tissue/fluid (e.g., stool, blood, liver, brain, etc.); polymer type; size range and/or mean size; shape; concentration range and/or mean concentration; major observations and/or toxicological notes.

3. Occurrence of MPs and NPs in the food chain

Microplastics and NPs may enter the human food chain in various ways, animals consuming them in their natural environment (Santillo et al., 2017), contamination during the food production processes (Karami et al., 2017), and/or through leaching from plastic packaging of foods and drinks (Mason et al., 2018). It has been reported that exposure to MPs and NPs by ingestion is mainly due to drinking water and basic foods including fish, fruits, vegetables, meat, cereals, and legumes (Mamun et al., 2023). According to the EFSA Panel on Contaminants in the Food Chain (CONTAM) MPs and NPs may originate from other sources than the food itself, e.g., processing aids, water, air or being release from machinery, equipment, and textiles. It is therefore possible that the number of NPs increases during processing (EFSA Panel on Contaminants in the Food Chain, 2016).

3.1. Drinking water

An overview of the recent studies on the occurrence and quantification of MPs and NPs in drinking water are reported in Table 1. In general, MPs and NPs were found in water from all bottle types (single-use, reusable, and glass bottles) and, in contrast to MPs only few data are available for NPs. In addition, most single-use and reusable plastic water bottles are composed of PET since this polymer is non-permeable to water, moisture, and bacteria. About 93% of the 259 bottled water sampled in 19 locations from USA, Indonesia, China, EU, and South America were found to be contaminated with particles between 6.5 and 100 μm in size, with a double amount of MPs in bottled than tap water (Mason et al., 2018). Micro-sized plastics were composed by PP, PS, PE and PEST and mainly in fibres form in tap water and fragments in bottled water. Data suggested the contamination is at least partially coming

Table 1
Occurrence and quantification of microplastics (MPs) and nanoplastics (NPs) in foods, drinks and beverages.

Country	Product (no.)	Polymer type	Size range or mean (% abundance)	Concentration range or mean	Major observations	Reference
Drinking water						
UK	Plastic bottle (no. 2)	PET	66 nm (16.1%) 433 nm (83.9%) 40 nm (64.8%) 605 nm (31.4%) 5 μm (3.8%)	nr	Spherical shape	Huang et al. (2022)
China	Tap water (no. 130)	PE, PP, PB, PS, PVC, PA	58–255 nm	1.67–2.08 μg/L	Plastic additives were identified	Li et al. (2022a)
Spain	Tap water (no. 42)	PE, PP, PI, PBD, PS, PA, PDMS	0.7–20 μm	9.143 ng/L (PI) 1.897 ng/L (PBD)	PE, PP, and PA the most detected polymers	Vega-Herrera et al. (2022)
Saudi Arabia	Plastic bottle (no. 24)	PE, PS, PET	25–500 μm	1.1–4.2 particles/L	MPs identified in 17/30 samples; PE (38%) > PS (25%) > PET (22%); upper bound exposure 0.247 ± 0.7 particles/kg bw day	Almaiman et al. (2021)
	Tap water (no. 2)			0.92–1.8 particles/L		
	Aluminium bottle (no. 2)			13-26 particles/L		
	Glass bottle (no. 2)			<1.3 particles/L		
Thailand	Plastic bottle (no. 65)	PET, PE, PP, PA, PVC	6.5–50 μm	140 particles/L	Fibres (62.8%) followed by fragments; rutile (TiO_2) detected in 11 samples	Kankanige and Babel (2020)
	Glass bottle (no. 30)			52 particles/L		
China	Tap water (no. 7)	RY, PET	10–5000 μm	0.3–1.6 particles/L	Fibres (99.2 %); human activities and atmospheric deposition contributed to the MPs in the water sources	Zhang et al. (2020a)
	Water source (no. 7)			0.2–0.7 particles/L		
China	Tap water (no. 38)	PE, PP, PE + PP, PPS, PS, PET	<50 μm (31.2–100%) 50–100 μm (1.5–31.2%) 100–300 μm (1.7–31.2%) 300–500 μm (1.2–7.7%) 500–5000 μm (1.7–11.8%)	0-1247 particles/L	Fragments (53.8–100%), fibres (1.18–30.77%); particle size percentage increased as size decreased	Tong et al. (2020)
Italy	Plastic bottle (no. 10)	nr	1.28–4.2 μm	3.16×10^7-1.1×10^8 particles/L	Daily exposure: 1,531,524 particles/kg/bw day (adults) and 3,350,208 particles/kg/bw day (children); contamination correlated with pH waters and plastic thickness	Zuccarello et al. (2019)
19 countries (USA, Indonesia, China, EU, South America)	Plastic bottle (no. 259)	PET, PP, PE, PEST	6.5–100 μm (93%) >100 μm (7%)	7-47 particles/L 0-14 particles/L	PP (54%) the most abundant, fragments (66%), fibres (13%), films (12%)	Mason et al. (2018)
14 countries (USA, Central America, UK, EU, Lebanon)	Tap water (no. 159)	nr	0.1–5 mm (81%)	0-61 particles/L	Fibers (98.3%); higher particles in developed than developing countries	Kosuth et al. (2018)
Germany	Reusable plastic bottle (no. 12)	PET	>1.5–5 μm (48.4%)	4889 ± 5432 particles/L	Higher amounts of PET in reusable bottles; pigment and additives particles detected in reusable bottles	Oβmann et al. (2018)
	Single use plastic bottle (no. 10)	PET	≤1.5 μm (53.6%)	2649 ± 2857 particles/L		
	Glass bottle (no. 10)	PE, PP	>1.5–5 μm (61.4%)	6292 ± 10521 particles/L		
Germany	Reusable bottle (no. 15)	PEST, PE, PP, PA	5–10 μm (56%)	28-241 particles/L	Low number of particles in still than sparkling water	Schymanski et al. (2018)
	Single use bottle (no. 11)	PEST, PE, PP, PA	5–10 μm (41%)	2-44 particles/L		
	Glass bottle (no. 9)	PEST, PE, PP, PA	5–10 μm (45%)	4-156 particles/L		
	Beverage carton (no. 3)	PEST, PE, PP	5–10 μm (39%)	5-20 particles/L		
Food and beverages						
Fish and mollusc						

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Table 1 (*continued*)

Country	Product (no.)	Polymer type	Size range or mean (% abundance)	Concentration range or mean	Major observations	Reference
Turkey	Mussel (no. 412)	PET, PE, PP, PA, PS, PAN, PVC, PBP, SAC, DBP, EVA, PC, PVF	<0.5 mm (19.34%) 0.5–1 mm (17%) 4.0–4.5 mm (13.79%)	0.11–4.58 particles/g	Fibres (81.16%) > fragments > films, and PET the most abundant polymer	Gedik et al. (2022)
India	Fish (no. 100)	PE, PP, PES, PU, EPDM, SBR	<500 μm (85%)	0.02–0.15 particles/g bw; 0.45–6.45 particles/g (gastrointestinal tract)	Fibres (53.4%), films (40%), fragments (3.3%), foam (1.9%), granules (1.4%). Species with large gastrointestinal tract contain a higher MPs	Ghosh et al. (2021)
Iran	Fish (no. 44)	nr	<500 μm (66%)	0.015 particles/g	Fibres (76%), fragments (12%), microbeads (12%). Presence of Al (~1%) and Si (~0.6–0.8%)	Taghizadeh Rahmat Abadi et al. (2021)
China	Fish (no. 20)	PET, PP, PAN, PA,	74–1500 μm (80–90%)	0.01-0.04 items/g	Fibres (97.3%)	Wu et al. (2020)
	Oyster (no. 15)	PET, PA	74–5000 μm (67%)	0.31 items/g		
	Clam (no. 15)	PET, PP, PA, PE	≤500 μm (80%)	0.21 items/g		
	Shrimp (no. 20)	PE	500–1000 μm (45%)	0.25 items/g		
Iran	Fish (no. 111)	PA	0.5–4.75 mm	2.29 particles/fish	Fibres (50%), fragments (30%)	Zakeri et al. (2020)
Iran	Fish meal (no. 4)	PP, PS, PE, PET, RY	158–810 μm	4.0–6.5 particles/g	Fragments > films > pellets > fibres; positive relationships between MPs levels in fish meal and cultured fish	Hanachi et al. (2019)
	Cultured fish (no. 150)	PP, PS, PE, PET, RY				
Malaysia	Canned fish (no. 129)	PP, PET, PE, PVC	190–3800 μm	nr	Fragments (46.6%), films (26.6%), and filaments (26.6%). Particles identified as additives were TiO_2 (rutile, 44.4%), Pc (33.3%) or a combination of both (22.2%)	Karami et al. (2018)
China	Oyster (no. 330)	PET, PP, PE, PS, CP, PVC, PA, EPS	<100 μm (75.6–89.7%)	1.5–7.2 particles/g	Fibres and fragments (82.5%–97.2%)	Li et al. (2018a)
UK	Mussel (no. 246)	PL, PP, PE	5–250 μm (50–80%)	0.7–2.9 particles/g	Fibres (50–90%), fragments (5–40%) 70 MPs ingested for 100 g mussel	Li et al. (2018b)
Italy	Fish (no. 533)	PVC, PP, PE, PL, PA	<100 μm 100–500 μm (50–85%)	1.64–1.73 particles/g	Fragments (72%), fibres (28%)	Pellini et al. (2018)
USA	Fish (no. 74)	nr	<1.5 mm (~80%)	10-13 particles/fish	Fibres (97–100%), fragments (2.5–3%)	McNeish et al. (2018)
Brazil	Fish (no. 189)	PA, PA-6, PE	0.38–4.16 mm	nr	Pellets (97.4%), films (1.3%), fragments (0.4%), fibers (0.9%)	Pegado et al. (2018)
China	Mussel (no. 390)	CP, PET, PL	<250 μm (17%–79%) >1 mm (1–34%)	0.9–4.6 particles/g	Fibres (>65%) and fragments (5–67%). Higher MPs in wild than farmed mussels	Li et al. (2016)
China	Bivalve (no. 144)	PE, PET, PA	<250 μm (33–84%)	2.1–10.5 particles/g	Fibres >50% in each species .	Li et al. (2015)
China	Mussel (no. nr)	nr	200–1500 μm	2.6–5.1 MPs fibres/10 g	Higher prevalence of orange fibres related to fisheries activities	De Witte et al. (2014)
Vegetables and fruits						
Turkey	Vegetables (no. 72) and fruits (no. 12)	PE, PP, PET	0.1 μm-1 mm (rate of 86.1%) and 1–5 mm	2.9 ± 1.6 particle/g in all samples with highest amount in tomato (3.63 ± 1.39 particle/g)	Children ingest more MPs through the consumption of fruits and vegetables than adults	Aydın et al. (2023)
Italy	Vegetables and fruits (no. 36)	nr	1.51 (carrots)-2.52 (lettuce) μm	52050-223000 particles/g	Apples the most contaminated fruits and carrots the most contaminated vegetables	Oliveri Conti et al. (2020)
Salt						
17 countries (Asia, EU, North and Central America, Oceania, Africa)	Salt (no. 39)	PE, PP, PET	<500 μm (47–61%)	<13629 particles/kg	Fragments (54–88%), fibres (11–45%), films (1–6%)	Kim et al. (2018)
Turkey	Salt (no. 16)	PE, PET, PU, PP, PMMA, PA-6, PVC	20 μm-5 mm	11.8–46.0 items/kg	Fibres (>70% and 128.3 particles/salt), fragments (24 particles/salt), films (19 particles/salt)	Gündoğdu (2018)
Italy	Italian salt (no. 6)	nr	4–2100 μm	1.57-8.23 items/g	Italian salts: fragments > fibres > granules > films;	Renzi and Blašković (2018)
Croatia	Croatian salt (no. 5)	nr	15–4628 μm	23.5–39.8 items/g	Croatian salts: fibres (>80%)	
Spain	Salt (no. 21)	PET, PE, PP	30 μm-3.5 mm	50-280 particles/kg	83.3% PET	Iñiguez et al. (2017)

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Table 1 (*continued*)

Country	Product (no.)	Polymer type	Size range or mean (% abundance)	Concentration range or mean	Major observations	Reference
8 countries (Oceania, EU, Africa)	Salt (no. 17)	PP, PE, PET, PS-PI, PAN, PA-6	160–980 μm (41.6%)	0-10 particles/kg	Fragments (63.8%), fibres (25.6%), films (10.6%); Pigments particles: Pc (82.3%), chrome yellow (5.88%), hostasol green (5.88%), and hostaperm blue (5.88%)	Karami et al. (2017)
China	Salt (no. 15)	PET, PL, PE, PB, PP, CP	45 μm-4.3 mm (84.9%)	7-681 particles/kg	MPs 3 times higher in sea than lake salts; MPs 7 times higher in sea than in rock/well salts; Fragments and fibres more prevalent shape	Yang et al. (2015)
Honey, sugar, beer and tea						
Bangladesh	Sugar (no. 5)	ABS, PVC, PET, EVA, CA, PTFE, PE, PC, PA	<300 μm	343.7 particles/kg	ABS and PVC (43%)	Afrin et al. (2022)
China and 15 countries	Tea (no. 4)	PE, PET	nr	200-500 particles/g	Fibers 5000 per 20 g tea	Li et al. (2022b)
	Beer (no. 15)	PS, PP		20-80 particles/mL	Fragments 929–9154 per 100 mL beer	
Mexico	Soft drink (no. 19)	PA, PEA, PET, ABS	0.1–2 mm (>90%)	0-7 particles/L	Fibres (>95%). Presence of S, Si. Al, Ca, Ti, K, Mg, Cl	Shruti et al. (2020)
	Energy drink (no. 8)		<1 mm (>70%)	0-6 particles/L		
	Cold tea (no. 4)		<1 mm (>80%)	1-6 particles/L		
	Beer (no. 26)		1–2 mm (>90%)	0-28 particles/L		
Canada	Tea (no. 4)	PA, PET	1–1000 nm 1–150 μm	11.6×10^9 MPs/cup 3.1×10^9 NPs/cup	~21% of particles are nano-sized (<100 nm)	Hernandez et al. (2019)
Germany	Beer (no. 24)	nr	nr	2-79 particles/L fibres 12-109 particles/L fragments 2-66 particles/L granules	High variability between samples from different production date	Liebezeit and Liebezeit (2014)
4 countries (Germany, France, Italy, Spain, Mexico)	Honey (no. 19)	nr	10–20 μm fragments 40 μm-9 mm fibers	4 ± 4 particles/500 g fragments 87 ± 73 particles/500 g fibres	Samples from Germany, Spain and Italy had highest content of fibers	Liebezeit and Liebezeit (2013)
	Sugar (no. 5)	nr	10–20 μm fragments 40 μm-6 mm fibres	32 ± 7 particles/kg fragments 217 ± 123 particles/kg fibres		
Milk and meat						
Turkey	Milk (no. 14)	EVA, PET, PP, PU, PA-6	500–1000 μm (99 particles) >1000 μm (87 particles) <500 μm (78 particles)	1-16 particles/L	EVA the most common type of polymer as fibres	Basaran et al. (2023)
France	Chicken packed (no. 4)	PS	130–450 μm	4.0–18.7 particles/kg	Meat products contaminated with MPs derived from packaging	Kedzierski et al. (2020)
Ecuador	Honey (no. 15) Milk (no. 10) Beer (no. 15) Soft drink (no. 14)	PP, PE, PAM	2.48–247.5 μm in fragments 13.5–6742 μm in films	10-100 particles/L	Higher content in honey and beer than beer and soft drink Lower presence in industrially treated than homemade products	Diaz-Basantes et al. (2020)
Mexico	Milk (no. 23)	PES, PSU	<0.5 mm (40%) 0.5–1 mm (28%) 1–2 mm (25%)	3-11 particles/L	Films (97.5%), fragments (2.5%); Presence of Si, Al, Ti, Pb, Mg, Na, Cl and Fe.	Kutralam-Muniasamy et al. (2020)

nr: not reported.

PET: polyethylene terephthalate; PE: polyethylene; PP: polypropylene; PB: polybutylene; PS: polystyrene; PVC: polyvinyl chloride; PA: polyamide; PI: polyisoprene; PBD: polybutadiene; PDMS: polydimethylsiloxanes; bw: body weight; RY: rayon; PPS: polyphenylene sulfite; PEST: polyester + polyethylene terephthalate; PA-6: polyamide-6; PAN: polyacrylonitrile; PBP: dibutyl phthalate; SAC: styrene-acrylonitrile copolymer; DBP: dibutyl phthalate; EVA: ethylvinyl acetate; PC: polycarbonate; PVF: polyvinyl fluoride; PES: polyethersulfone; PU: polyurethane; EPDM: ethylene propylene diene monomer; SBR: styrene butadiene rubber; Pc: phthalocyanine; CP: cellophane; EPS: expanded polystyrene; PL: polyester; PMMA: polymethyl-methacrylate; ABS: acrylonitrile-butadiene-styrene; PTFE: polytetrafluoroethylene; PEA: poly(ester-amide); PAM: polyacrylamide; PSU: polysulfone.

from the packaging and/or the bottling process itself (Mason et al., 2018). Similar outcomes were shown in 159 tap water samples from 14 different countries (i.e., USA, Central America, UK, EU, and Lebanon) which contained anthropogenic MPs; the majority were fibers between 0.1 and 5 mm in length (Kosuth et al., 2018). Interestingly, the number of particles in tap water from more developed countries (average density of 6.85 particles/L) was significantly higher than in tap water from developing countries (average density of 4.86 particles/L), suggesting water source, population density and water treatment processes as influencing factors of the MPs pollution (Kosuth et al., 2018). In bottled

Table 2
Biodistribution of microplastics (MPs) and nanoplastics (NPs) after ingestion *in-vivo* and *ex-vivo* models and potential health effects.

Polymer type	Studied model	Size range or mean	Biodistribution	**Major toxicological issues**	Reference
PS	Rat	25 nm	Accumulation in liver, kidney, heart, lung and brain fetal tissues	nr	Cary et al. (2023)
PS	Mice	50 nm	Accumulation in liver, lung, intestine and brain	Variation of community composition of intestinal microbiota and disruption of mucus secretion in intestine. No alterations in inflammatory or oxidative stress-related indicators in liver, lung, intestine and brain	Xiao et al. (2022)
PS	Mice	1 μm	No relevant accumulation	Oral ingestion did not promote microbiome alteration. A mild pro-inflammatory signature in the colon was observed	Rawle et al. (2022)
PS	Mice	5μm	Accumulation in liver	Hepatotoxicity with damages on liver structure and function (increased AST, ALT, AST/ALT, ALP, LDH). Activation of pyroptosis (increased IL-1β, IL-18), oxidative stress (increased MDA, GSH, SOD) and ferroptosis (activation of TFRC and inhibition of FTH1, xCT system, GPX4, ACSL4)	Mu et al. (2022)
PS	Mice	100 nm, 3 μm	Both particles enter the blood circulation and may be excreted *via* urine	nr	Sun et al. (2022)
PS	Mice	50 nm, 300 nm, 600 nm, 4 μm	Accumulation in kidney (600 nm aggregated, 4 μm appeared in kidney individually)	Nephrotoxicity through lipid peroxidation (increased MDA) and inflammation (increased TNF-α, IL-6, MCP-1, IL-10) in renal cells	Meng et al. (2022)
PS	Mice	50 nm	Accumulation in brain with dose-dependently behavior	Neurotoxicity by inducing activation of microglia and neuron damage	Shan et al. (2022)
PS	Mice	0.79 μm	Accumulation in heart, liver, spleen, lung, kidney, brain, large and small intestine, uterus, ovaries and blood	Reproductive toxic effects with inflammation and oxidative stress of ovaries (decreased GSH, MMP, ER calcium and increased ROS)	Luo et al. (2022)
PE	Mice	10–20 μm	Accumulation in brain	Exposure induced autism spectrum disorder-like traits during the different life stages (prenatal, puberty, adult)	Zaheer et al. (2022)
PS	Mice	80 nm, 5 μm, 10 μm	Accumulation in spleen	Hematopoietic injury manifested by disorder of bone marrow cell arrangement, reduction in colony-forming, self-renewal and differentiation capacity, and increased number of lymphocytes	Jing et al. (2022)
PS	Mice	50 nm	Accumulation in small intestine, liver, spleen and lymph nodes	Oral ingestion did not induce or promote intestinal inflammation and oxidative stress-related biomarkers in liver	Schwarzfischer et al. (2022)
PS	Mice	5 μm	Accumulation in testis tissue	Testicular toxicity with sperm deformity and abnormal sperm quality (increased pro-inflammatory molecule NF-κB, IL-1β and IL-6)	Hou et al. (2021)
PS	Mice	5 μm	Presence in abdomen and the limb bones	Hematotoxicity on gene expression and altered molecular and biological pathways in bone marrow cells	Sun et al. (2021)
PS	Human placental perfusion model	80 nm	PS transfer across the human placenta	Protein corona formed by human albumin induced the transfer of PS particles across the tissue	Gruber et al. (2020)
PS	Mice tissues (liver, lung, kidney)	40 nm, 50 nm, 200 nm	Accumulation in macrophages mainly in lung slices	Amino-modified PS at 50 nm induced toxicity on kidney and lung	Bartucci et al. (2020)
PS	Human whole-blood model	0.05–0.1 μm 0.04–0.9 μm	Highest internalization for monocytes, lowest for lymphocytes	Genotoxicity with DNA damage observed in monocytes and polymorphonuclear cells, but not in lymphocytes	Ballesteros et al. (2020)
PE	Mice	10–150 μm	Accumulation in gut	Small intestinal inflammation, higher secretion of IL-1α in serum, variation of the gut microbiota composition	Li et al. (2020a)
PS	Rat	0.5 μm	Accumulation in heart	Cardiovascular system impaired with structural damage and apoptosis of myocardium, causing collagen proliferation of heart (increased troponin I, CK-MB in serum)	Li et al. (2020b)
PS	Mice	5 μm	Accumulation in gut	Gut microbiota dysbiosis, intestinal barrier dysfunction and metabolic disorders	Jin et al. (2019)
PS	Mice	1 μm, 4 μm, 50 μm	No relevant accumulation	Absence of particle-induced oxidative stress and inflammation	Stock et al. (2019)
PS	Mice	5 μm	Accumulation in gut, liver and kidney	Changes in ATP synthesis and lipid metabolism. Particle size affect toxicological behavior (lipid metabolism and oxidative stress in liver)	Yang et al. (2019)
PS	Mice	0.5 μm	nr	Decrease of body, liver and fat weights, gut microbiota dysbiosis and hepatic lipid metabolism disorder (decreased TG, TCH)	Lu et al. (2018)
PS	Rat	25 nm, 50 nm	No relevant accumulation	No measurable neurobehavioral effects	Rafiee et al. (2018)
PE, PS	Mice	0.5–1.0 μm	Accumulation in gut and liver	Oxidative stress and neurotoxicity, impaired amino acid metabolism and energy metabolism (increased SOD, CAT, LDH, AChE)	Deng et al. (2018)
PS	Mice	5 μm 20 μm	Accumulation in gut (1.39 mg/g), kidney (0.95 mg/g) and liver (0.30 mg/g) Accumulation in gut, kidney and liver (0.76 mg/g)	Alteration of lipid metabolism and improper energy metabolism (reduction in ATP levels and higher LDH), and induction of oxidative stress pathways (increased GPX, SOD, CAT)	Deng et al. (2017)
PS	Fish	53 nm, 180 nm	Accumulation in brain (53 nm)	53 nm particles crossed the blood-to-brain barrier and produced morphological changes (higher weight loss and less	Mattsson et al. (2017)

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Table 2 (*continued*)

Polymer type	Studied model	Size range or mean	Biodistribution	**Major toxicological issues**	Reference
				water) and behavioural disorders, and neurotoxicity was dependent on the particle concentration	
PS	Rat	50 nm	Accumulation in kidney (37.4 μg/g), heart (52.8 μg/g), stomach (98.3 μg/g) and small intestine (94.4 μg/g)	Estimated bioavailability ranging from 0.2 to 1.7% of the administered dose (125 mg/kg bw)	Walczak et al. (2015a, 2015b)

nr: not reported.

PS: polystyrene; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; LDH: lactate dehydrogenase; IL: interleukin; MDA: malondialdehyde; GSH: glutathione; SOD: superoxide dismutase; TFRC: transferrin receptor; FTH1: ferritin heavy chain 1; GPX: glutathione peroxidase; ACSL4: acyl-CoA synthetase long-chain family member 4; TNF-α: tumor necrosis factor-α; MCP-1: monocyte chemoattractant protein-1; MMP: mitochondrial membrane potential; ER: endoplasmic reticulum; ROS: reactive oxygen species; PE: polyethylene; NF-κB; nuclear factor-κB; CK-MB: creatine kinase-MB; ATP: adenosine triphosphate; TG: hepatic triglyceride; TCH: total cholesterol; CAT: catalase; AChE: acetylcholinesterase; bw: body weight.

drinking water sampled in UK, the smallest detected particle size of PET at size of 40 nm (Huang et al., 2022). Plastic bottles are also one of the primary sources of MPs for infants. The release of these contaminants from infants feeding PP bottles was investigated and the average number of MPs per L of water amounted to 4 million while the maximum was 16.2 million (Li et al., 2020a). While in plastic bottles the predominant polymer type was PET, in glass bottles various polymers such as PE or styrene-butadiene-copolymer were found with the smallest analysed particle size of 1 μm (Oβmann et al., 2018). The presence of PET and other polyolefin (PP, PEST and PE) in water from beverage cartons and glass bottles was associated with the coating of the beverage cartons and the cap lubricants (Schymanski et al., 2018). For example, pigment commonly used to color bottle caps as TiO_2 rutile was detected in plastic-bottled water from Thailand (Kankanige and Babel, 2020). The number of MPs <10 μm found in plastic bottled mineral waters from Italy was strongly correlated to the pH of water and the plastic thickness of bottles; more deformable plastics and weakly alkaline pH might increase the number of smallest MPs (Zuccarello et al., 2019). In bottled drinking water in Saudi Arabia, MPs of PE, followed by PS and PET in the range between 25 and 500 μm were identified in 17 out of 30 samples (Almaiman et al., 2021). In a study conducted in China the abundance of MPs in water sources (0.2–0.7 particles/L) was linked to human activities and atmospheric deposition Zhang et al. (2020). Likewise, it was demonstrated that plastic pipes in household distribution systems of drinking water in China may cause MPs pollution with increased abundances of particles in tap water samples (Tong et al., 2020). Again, in China tap water samples showed particles of PE, PP, PB, PS, PVC, PA with size from 58 to 255 nm (Li et al., 2022a). The household tap water of the Barcelona Metropolitan Area was also contaminated with PE and PP particles sized between 0.7 and 20 μm (Vega-Herrera et al., 2022).

3.2. Foods and beverages

Regarding foods and beverages, the presence of MPs and NPs was observed in many studies as reported in Table 1. Most investigations analysed the presence of plastic particles in fish and mollusc although other types of food items such salt, honey, beer, tea, milk, meat, vegetables and fruits were also explored.

3.2.1. Fish and molluscs

The occurrence of plastic pollution in marine ecosystem may lead to bioaccumulation and biomagnification in the aquatic food chain; an important issue related to human health since the fish-based food consumption is a meaningful pathway of MPs and NPs exposure (Barboza et al., 2020). Microplastics and NPs were detected both in a large variety of zooplanktonic organisms, in invertebrates (crustacean, molluscs) and vertebrates (fishes, lobsters, mussels, oysters) in which the gastrointestinal tract (GIT) is the main target of MPs and NPs accumulation. For humans, this imply that a source of dietary exposure might occur only when entirely organisms including GIT - such as molluscs - are consumed (Ghosh et al., 2021). Large MPs and NPs pollution was found in marine organism from Asia. In Chinese mussels, high amounts of PE, PET and PA as fibers, fragments and pellets sized <250 μm were found in 9 species of commercial bivalves (Li et al., 2015). Similarly in a Chinese aquaculture site, accumulation of cellulose, PA, PE, PP and PET fibres, ranging ≤500–1000 μm, was observed in fish, bivalve and shrimps (Wu et al., 2020), whilst PET, PP, PE and PS as fibers sized 20–5000 μm (83.9% of which less than 100 μm) were found in Chinese wild oysters (*Saccostrea cucullate)* (Li et al., 2018a). In the same area, higher abundance of MPs was found in wild than farmed mussels (Li et al., 2016), while in commercial fish species from the coast of Bangladesh the number of MPs found was directly related to the size of GIT (Ghosh et al., 2021). In wild mussels collected in the coastal area of Turkey, PET was the most abundant polymer and fiber smaller than 1 mm the most abundant shape (Gedik et al., 2022). In UK, the predicted ingestion of 70 MPs items (i.e, PL, PP and PE ranged 5–250 μm) in 100 g of processed mussels was assessed (Li et al., 2018b), while an abundance of 2.6–5.1 MPs fibres/10 g of mussel was quantified in commercial and wild mussels from Belgium (De Witte et al., 2014). Microplastic litters at two dimensions (<100 and 100–500 μm) of PVC, PP, PE, PL, and PA (72% as fragments and 28% as fibers) was found in the GIT of sole (*Solea solea*) in Adriatic Sea (Pellini et al., 2018). In USA and Brazil, MPs contamination of water reservoirs and in fish species connected to these was assessed by some authors (McNeish et al., 2018; Pegado et al., 2018). Another study showed a correlation between PP, PS, PE, PET and rayon particles with different shapes such as fragment, film, pellet and fiber in fish feeds and the uptake and ingestion of MPs in common cultured carp (*C. Carpio*) (Hanachi et al., 2019). Also processed seafood products might show contamination by MPs. Karami et al. (2018) investigated the MPs loading in canned sardines and sprats from 13 countries finding PP and PET as the most abundant polymers (an average ± SD size of 1149 ± 936 μm) (Karami et al., 2018).

3.2.2. Vegetables, fruits, and cereals

Agricultural soils are widely prone to MPs contamination mainly due to the use of fertilizers originating from sewage sludge. Biosolid application to the farmlands caused the release of more than 20,000 tonnes of MPs annually to agricultural soils in EU, USA, China, Canada, and Australia (Mohajerani and Karabatak, 2020). This imply that the amount accumulated in plant tissues may be transferred to the consumer through diet. The transfer of MPs from the environment to foods was reported with MPs concentration that increased from soil (0.87 particles/g) to earthworm casts (14.8 particles/g) and to chicken feces (129.8 particles/g) (Huerta Lwanga et al., 2017). According to the results obtained by Aydın et al. (2023), a total of 2.9 ± 1.6 particle/g were detected in all fruits and vegetable samples purchased from different markets in Turkey, and the maximum average amount of MPs was determined in tomato samples (3.63 ± 1.39 particle/g). In an Italian study on the presence of MPs (<10 μm) in vegetables and fruits, apples were the most contaminated fruits and carrots the most contaminated vegetables. The smallest size was found in the carrots (1.51 μm), while the biggest one in lettuce (2.52 μm) (Oliveri Conti et al., 2020).

Table 3
Occurrence and quantification of microplastics (MPs) and nanoplastics (NPs) in human samples.

Country	Samples (no.)	Polymer type	Size range or mean	Concentration range or mean	Major observations	Reference
Italy	Urine (no. 6 healthy adults)	PP, PE, PVC, PEVA	4–15 μm	nr	PEVA, PVC, PP and PE in fragments	Pironti et al. (2022)
Germany	Kidney, liver and spleen (no. 5 healthy adults and no. 6 patients with cirrhosis)	PS, PVC, PET, PMMA, POM, PP	4–30 μm	Kidney: 0.0 particles/g Spleen: 1.1 particles/g Liver: 1.0 particles/g (healthy) Liver: 8.3 particles/g (patients)	In cirrhotic liver tissues: PS, PVC and PET polymers ranging 3.0–29.5 μm	Horvatits et al. (2022)
Hong Kong	Stool (no. 8 healthy adults)	PS, PP, PE, PET, PVC	30–1800 μm	20.4–138.9 particles/g	PS, PP, PE, PET the most abundant type at 30–100 μm; PS, PP, PE, PVC in fragments; PET in fibres	Ho et al. (2022)
China	Stool (no. 50 healthy adults and no. 52 IBD patients)	PET, PA, PP, PE, PC, PVC, POM, PTFE, EVA, PS, PMMA, PBT, AS, PES, PU	1->300 μm Healthy: 4.4–333.2 μm IBD: 1.7–393.8 μm	healthy: 28.0 items/g IBD: 41.8 items/g	PET, PA, PE the most abundant with different frequency between IBD and healthy; PET higher in IBD (34.0%) than healthy (22.3%). Similar shape in both groups (sheets for PET and fibers for PA)	Yan et al. (2022)
Italy	Breastmilk (no. 34 healthy adults)	NC, CPE, PE, PP, PVC, ABS, PL, PEMA, PA	2–12 μm	0.17–2.72 particles/g	The most abundant PE (38%), PVC (21%), PP (17%)	Ragusa et al. (2022)
China	Placenta (no. 18 healthy adults) Meconium (no. 12 healthy neonates)	PA, PU, PE, PET, PP, PVC, POM, EVA, PTFE, CPE, PBD, PC, PS, PMMA, PLA, PSU	20–500 μm	Placenta: PU (5.5 particles/g) > PA (4.5 particles/g) > PE (2.0 particles/g) > PET (1.1 particles/g) > PC (0.7 particles/g) Meconium: PA (24.9 particles/g) > PU (10.7 particles/g) > PVC (2.2 particles/g) > PTFE (2.1 particles/g) > PET (1.3 particles/g)	PA, PU, PE and PET the most abundant particles in both samples and 20–50 μm the most abundant size PA higher in meconium than in placenta	Luo et al. (2022)
Netherlands	Blood (no. 22 healthy adults)	PMMA, PP, PS, PE, PET	700 e 500,000 nm	1.6 μg/mL PET: 2.4 μg/mL (max) PS: 4.8 μg/mL (max) PE: 7.1 μg/mL (max)	PET (50%), PS (36%), PE (23%), PMMA (5%)	Leslie et al. (2022)
Iran	Hair, hands, face skin, saliva (no. 2000 healthy adults)	PE, PET, PP, PVC, PS	<100 μm (hair: 40%; hand and face skin: 60%; saliva: 76–94%)	Hair: >3.5 particles individual/day Saliva: 0.33 particles individual/day	MPs were mainly fibers; MPs higher in urbanized regions (range 4000–6000 individual/day) than in the village (<800 individual/day); MPs more abundant in males than females	Abbasi and Turner (2021)
USA	Stool (no. 10 healthy adults and no. 6 healthy infants) Meconium (no. 3 healthy neonates)	PET, PC	nr	Adult stool: PET: 2.2–16 μg/g PC: 0.037–0.62 μg/g Infant stool: PET: 5.7–82 μg/g; PC: 0.049–2.1 μg/g Meconium: PET: 12 and 3.2 μg/g PC: 0.11 μg/g	Higher MPs in infant feces than adult. EDI in infants: PET: 83 mg/kg bw/day PC: 0.86 mg/kg bw/day EDI in adults: PET: 5.8 mg/kg bw/day PC: 0.2 mg/kg bw/day	Zhang et al. (2021a)
China	Stool (no. 23 healthy adults)	PP, PET, PS, PE, PVC, PC, PA, PU	20–800 μm	1-36 particles/g (0.01–14.6 mg)	PP, PET and PS the most abundant; associations between packaged water and beverages intake and MPs abundance in feces	Zhang et al. (2021b)
Indonesia	Stool (no. 11 healthy adults)	HDPE, LDPE, LLDPE, PP, PS, PET	nr	3.33–13.9 μg/g	HPDE (average concentration 9.195 μg/g) > PS (average concentration 9.885 μg/g)	Luqman et al. (2021)
Indonesia	Stool (no.11 healthy)	PET, PS, PP, PE, HDPE, LDPE	nr	6.94–16.5 μg/g	PP the most abundant followed by PE, PS, and PET	Wibowo et al. (2021)
Malaysia	Colon tissue (no. 11 colorectal malignancies patients)	PC, PA, PP	nr	28.1 particles/g	PC > PA > PP in filament shape (96.1%)	Ibrahim et al. (2021)
Italy	Placenta (no. 6 healthy adults)	PP	5–10 μm	12 particles in 4 placentas	3 particles were of PP. In all of them identified pigments of FeO(OH), Cu-Pc, Fe_2O_3, Cu_2-pigment, and Al-pigment used for plastic staining, cosmetic and personal care products	Ragusa et al. (2021)
Germany	Placenta, meconium and stool (no. 2 mothe-infant pair)	PE, PP, PVC, PS, PET, PA, PU, PC, PMMA, POM	>50 μm	nr	PP, PE, PU in placenta; PE in meconium (although possible	Braun et al. (2021)

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Table 3 (*continued*)

Country	Samples (no.)	Polymer type	Size range or mean	Concentration range or mean	Major observations	Reference
					contamination occurred); PS and PE in stool	
8 countries (Japan, Russia, Netherlands, UK, Italy, Poland, Finland, Austria)	Stool (no. 8 healthy adults)	PE, PP, PVC, PS, PET, PA, PU, PC, POM	50–500 μm	0.8–41.6 particles/g	PP (62.8%) and PET (17.0%) in all samples; average excretion rate of 20 MPs per 10 g of stool; fragments and film > sphere and fibres	Schwabl et al. (2019)

nr: not reported.
PP: polypropylene; PE: polyethylene; PVC: polyvinyl chloride; PEVA: poly(ethylene-vinyl acetate); PS: polystyrene; PET: polyethylene terephthalate; PMMA: polymethyl methacrylate; POM: polyoxymethylene; IBD: inflammatory bowel disease; PA: polyamide; PC: polycarbonate; PTFE: polytetrafluoroethylene; EVA: ethylene vinyl acetate; PBT: poly(butylene terephthalate); AS: acrylonitrile-styrene; PES: poly(ether sulfone); PU: polyurethane; NC: nitrocellulose; CPE: chlorinated polyethylene; ABS: acrylonitrile-butadiene-styrene; PL: polyester; PEMA: poly(ethyl methacrylate); PBD: polybutadiene; PLA: poly(lactic acid); PSU: polysulfone; EDI: Estimated daily intake; bw: body weight; HDPE: high-density polyethylene; LDPE: low-density polyethylene; LLDPE: linear low-density polyethylene; Pc: phthalocyanine.

3.2.3. Salt

According to statistics of EFSA, MPs content in European table salts vary between 0.007 and 0.68 particles/g (EFSA Panel on Contaminants in the Food Chain, 2016). Microplastics extracted from Chinese commercial salts (i.e., sea, lake and rock/well salts) were mainly fragments and fibres of PET, PE and CP sized 45–4300 μm (those <200 μm accounted for 55% of the total) (Yang et al., 2015). Similar outcome was assessed by Kim et al. (2018) on 39 different salts from worldwide regions (i.e., Asia, EU, North and Central America, Oceania, and Africa). Particles <500 μm of PE, PP, and PET polymers accounted for 47% in sea salts, 61% in rock salts, and 55% in lake salts. The highest number of MPs was found in salt produced in coastal Asian regions and the MPs level was defined as useful indicator of the magnitude of plastic pollution in the surrounding marine environment (Kim et al., 2018). In Europe, MPs abundance was higher in salts from Croatia (27-1-31.7 items/g) than from Italy (1.57–8.23 items/g) with size within 15–4628 μm and 4–2100 μm, respectively (Renzi and Blašković, 2018). In Spain, Iñiguez et al. (2017) found polymers of PET (83%), PP (6.7%), and PE (3.3%) ranged from 30 μm to 3500 μm in sea and well salts with no significant differences among samples (Iñiguez et al., 2017). In Turkey commercial salts, particles abundance was 16–84 item/kg in sea salt, 8–102 item/kg in lake salt and 9–16 item/kg in rock salt and the most common plastic polymers were PE (22.9%), PP (19.2%), PUR (17.5%), and PET (14.5%) followed by PVC (11.6%), PA-6 (8.7%), and PMMA (5.7%) ranging between 20 μm and 5 mm (Gündoğdu, 2018). In 17 salt brands originating from 8 different countries, MPs of PP (40.0%), PET (6.66%), PE (33.3%), PS-PI (6.66%), PA-6 (3.33%), PAN (10.0%) in the range 160–980 μm were assessed (Karami et al., 2017).

3.2.4. Honey, sugar, beer and tea

In honey and sugar samples of different origin, mostly from Germany, MPs as fragments and fibres were found; in both types of samples fragments sized 10–20 μm (Liebezeit and Liebezeit, 2013). Similar findings were lately observed in commercial sugar from Bangladesh, whose contamination (higher frequency of MPs <300 μm) reached a human intake of 343.7 plastic particles/kg sugar (Afrin et al., 2022). In a recent study in Ecuador, the major amount of MPs was found in craft and industrial honeys, and lower in industrial beer, milk and soft drinks. In all samples presence of fibers constituted by PP and low and high-density PE (LDPE/HDPE) and fragments of PAM was assessed (Diaz-Basantes et al., 2020). The average amount of MPs reported by EFSA for honey was 0.166 fibres/g and 0.009 fragments/g, whilst in beer, fibres, fragments and granules were found at the following amounts 0.025, 0.033 and 0.017 per mL, respectively (EFSA Panel on Contaminants in the Food Chain, 2016). Contamination from MPs was found on 24 German beer brands with a high variability between samples also depending on the different production dates (Liebezeit and Liebezeit, 2014). Microparticles as PA, PEA, ABS and PET were detected in commercial beverages as soft drinks, energy drinks, cold tea and beer and the contamination had probably a packaging origin (Shruti et al., 2020). Likewise, the use of teabags might cause the release of billions of nylon, PE and PET at micro and nanoscale range providing another source of exposure for human being (Hernandez et al., 2019; Li et al., 2022b).

3.2.5. Milk and meat

Results on MPs extracted from 23 milk samples confirmed the ubiquity of secondary MPs with an overall average of 6.5 ± 2.3 MP/L and with a variety of colours (blue, brown, red and pink), shapes (fibers and fragments) and sizes (0.1–5 mm) (Kutralam-Muniasamy et al., 2020). Also in 14 packaged milk of various brands sold in the Türkiye market MPs at mean of 6 ± 5 particles/L and in fiber and fragment shapes composed by EVA, PET, PP, PU, and nylon-6 were found (Basaran et al., 2023).

Microplatics in the range from 4.0 to 18.7 MP/kg and mainly in the form of fibers was found on the surface of commercial poultry meat from Turkey. The authors speculated that particles come from the PS trays used for fresh meat packaging and they cannot be removed by rinsing and so they were present when the food is cooked (Kedzierski et al., 2020).

4. Uptake, biodistribution and bioaccumulation of MPs and NPs after oral exposure

Once the MPs and NPs enter the human body, they may cross the primary GIT tissues barrier and transported, *via* vascular systems like blood and lymph circulation, towards the secondary tissues barriers and/or target organs (Zarus et al., 2021). The capability of MPs and NPs to bind the surface of erythrocytes by van der Waals, electrostatic, hydrogen bonding, and hydrophobic forces and, hence, their circulation through the bloodstream, was reported for carboxylated PS NPs (Chambers and Mitragotri, 2004; Anselmo et al., 2013). Several studies evaluated MP and NP biodistribution and potentially toxicological health concern through experimental mammalian models at relatively high doses. Furthermore, most of the mammalian model used PS particles as a benchmark material for more complex MPs and NPs (Jin et al., 2019; Stock et al., 2019; Lu et al., 2018; Rafiee et al., 2018; Deng et al., 2017; Walczak et al., 2015a; Yang et al., 2019; Mattsson et al., 2017; Liu et al., 2022b), and only a few considered the biodistribution of other plastic types as PE (Li et al., 2020b; Deng et al., 2018).

In Table 2 an overview of the *in-vivo* and *ex-vivo* studies that explored the uptake, biodistribution and bioaccumulation of MPs and NPs after their oral administration, is reported. Most of the oral studies revealed gut, kidney and liver accumulation after plastic exposure. In details, PS MPs at 5 and 20 μm were found in liver, kidney and gut of exposed mice with increased doses by oral gavage (doses at 0.01–0.5 mg/day). For

both particle sizes tested, a steady-state MPs concentration was reached within 14 days with maximal tissue concentrations in kidney and gut for the smaller 5 μm MP and similar for the larger ones (20 μm) and suggesting the bioaccumulation in mice tissues as size-dependent process (Deng et al., 2017). Similarly, gut was the target organ of PS at 5 μm in mice exposed to them with a residence time of ~17 days (Yang et al., 2019). Another research confirmed that in mouse exposed to 0.5 μm and 50 μm of PS MPs *via* drinking water, the gut and liver were the target organs (Lu et al., 2018). In rats orally exposed to a single acute dose of differently charged (neutral, positive and negative) PS at size 50 nm, the biodistribution from the GIT to different organs was shown within 6 h. The highest amounts were measured in the stomach and intestinal walls, although particles were also detected in lung, testis, spleen, kidney and heart. The authors concluded that the NPs were systemically available (Walczak et al., 2015a). In the study conducted by Schwarzfischer et al. (2022), mice were supplemented with spherical PS NPs (~50 nm) with daily consumption of ca. 0.2 mg NPs per mouse. Results showed that NPs bioaccumulated in the small intestine and organs including the spleen and liver, distant from the GIT (Schwarzfischer et al., 2022). The gut was also the major target organ for MPs of PE at 10–150 μm in mice exposed by contaminated feed for 5 weeks (Li et al., 2020b). According to Liu et al. (2022b), female mice exposed to PS NPs (0.79 μm in diameter) for 35 days showed bioaccumulation of particles in various organs as the heart, liver, spleen, lung, kidney, brain, large intestine, small intestine, uterus, ovary, and blood (Liu et al., 2022b). However controversy existed, considering that no biodistribution in any of the organs of mice treated by oral gavage with a mixture of PS at 1, 4, and 10 μm at the acute dose (10 ml/kg/bw) was observed (Stock et al., 2019), and same result was observed in rats orally exposed to pristine PS at 25 and 50 nm using four test doses (1, 3, 6, and 10 mg/kg/bw) for 5 weeks (Rafiee et al., 2018). These inconsistent results indicated a need for accurate methods to detect and quantify the presence of MPs and NPs in biological matrices. Anyway, studies indicated that the absorption *via* intestinal tracts in rodent models was low, ranging from 0.2 to 1.7% of the administered dose (Walczak et al., 2015a), and that absorption rates varied greatly across different intestinal models, and accordingly to the size and chemical structure of the plastic particles.

Researchers found that PS (size of 50 nm, 300 nm, 600 nm and 4 μm) bioaccumulated in the kidney when treated with 5 mg/day MPs solution for 4 weeks (Meng et al., 2022). In *ex-vivo* model, tissue slices from the different organs of mice (liver, lung and kidney) were exposed to silica, carboxylated (40 nm and 200 nm) and amino-modified PS NPs (50 nm) (Bartucci et al., 2020). Results showed the uptake of particles in all slices with preferential accumulation in the macrophages of the lung slices. Among the particles tested, those amino modified at 50 nm induced toxicity on kidney and lung tissues. Applying whole blood samples from different donors, Ballesteros et al. (2020) exposed *ex-vivo* blood to PS sized 0.05–0.9 μm. The internalization of MPs varied from different cell lineages with the maximum shown in monocytes and minimum in lymphocytes (Ballesteros et al., 2020).

Bioaccumulation of MPs in the brain was recently evidenced. A study on NPs obtained through the food chain showed that PS at 52 nm cross the blood–brain barrier in *Daphnia magna* (Mattsson et al., 2017). Zaheer et al. (2022) identified that PE transited into the brain after feeding mice with 100 ppm/100 μL of PE sized between 10 and 20 μm. The particles detected in brain were smaller (4 μm) than those detected in gut (20 μm); thus, the authors hypothesized that the particles were digested in the stomach, deposited into the gut and only smaller PE fragments transitioned into the brain and accumulated there (Zaheer et al., 2022). Also, Shan et al. (2022) fed mice with four different doses (0.5, 2.5, 10, and 50 mg/kg body weight) of fluorescent PS with a mean diameter of 42 nm for seven days before using immunofluorescence and immunohistochemistry to investigate whether particles had passed into the brain and in which amounts. This study found that PS NPs significantly induced the increase of permeability of the blood-brain barrier and dose-dependently accumulation in the brain (Shan et al., 2022).

Placental and fetal translocation of ingested carboxylated PS spheres (25 nm) in pregnant rats was recently explored. Hyperspectral imaging identified abundant PS particles within the placenta and in all fetal tissues examined, including liver, kidney, heart, lung and brain, where they appeared in 10–25 μm clusters (Cary et al., 2023). Furthermore, PS particles with size up to 140 nm were able to cross the placental-barrier through passive diffusion using an *ex-vivo* human placental perfusion model (Gruber et al., 2020).

Undigested MPs would be largely excreted though fecal matter, but smaller NPs could potentially enter the circulation. In male mice after a single administration of fluorescent PS beads (100 nm and 3 μm), both MPs and NPs enter the blood circulation through digestive and respiratory pathways and may be excreted through urine (Sun et al., 2022).

5. Adverse health effects after oral exposure to MPs and NPs

Toxicological health effects arising from ingestion of MPs and NPs in animal models are reported in Table 2. In particular, the adverse health effects on the gut microbiota reserved great attention. In mice model, the oral administration of PS at 50 nm at doses of 0, 0.2, 1 and 10 mg/kg for 30 days disrupted the mucus secretion in the intestine and altered the community composition of intestinal microbiota (Lu et al., 2019; Xiao et al., 2022). On the contrary, the same particles at lower dose (80 μg/kg/day) and higher size (1 μm) administered for 4 weeks *via* drinking water did not produce any microbial change and only a mild pro-inflammatory signature in the colon was induced (Rawle et al., 2022). Another study observed gut microbiota dysbiosis and intestinal inflammation (i.e., increased levels of interleukin-1α in serum) in mice exposed *via* feeding to 2, 20, and 200 μg/g of PE MPs (10–150 μm) for 5 consecutive weeks, and effects increased dose-dependently (Li et al., 2020b). Similar outcomes like gut microbiota dysbiosis, intestinal barrier dysfunction and metabolic disorders were observed in mice exposed for 6 weeks to PS MPs sized 5 μm at the concentrations of 100 and 1000 μg/L (Jin et al., 2019). These results suggested that gut microbiota was altered after MPs exposure and that effects can increase at high doses, although all the studies observed the effects after the ingestion of very high quantities of MPs (mg/kg) and were focused on long-term exposure (4–6 weeks). In any case, the results can be helpful in understanding the differences in the gut microbial community between the control group and the MP-treatment group.

Beyond the impact on the gut microbiome, several studies showed the capability of plastic particles to surpass the intestinal barrier producing health effects in organs such liver (i.e., hepatoxicity) and kidney (i.e., nephrotoxicity). In mouse exposed to 1000 μg/L of 0.5 μm and 50 μm of PS *via* drinking water, gut microbiota dysbiosis and hepatic lipid metabolism disorder were observed (Lu et al., 2018). Polystyrene particles induced liver injury in mice intragastrically inoculated with 5 μm MP at concentrations of 0.1, 0.5, and 1 mg/mL for 4 weeks. Treatment also induced pyroptosis accompanied by intense oxidative stress and lipid peroxidation damage that, in turn, may activate the expression of ferroptosis related proteins, amino acid metabolism and lipid metabolism (Mu et al., 2022; Yang et al., 2019). Likewise, the exposure to PS particles at 5 and 20 μm in mice induced impairment of energy metabolism and increased oxidative stress biomarkers (Deng et al., 2017). Regarding the kidney, Meng et al. (2022) found that PS from nano-to micro-sized range (size of 50 nm, 300 nm, 600 nm, 4 μm) induced nephrotoxicity through oxidative stress and inflammation. Additionally, mice weight loss and increased death rate were also observed (Meng et al., 2022).

Neurotoxicity was observed in *Daphnia magna* exposed to PS NPs at 53 nm with morphological changes (i.e., higher weight loss and less water in the brains of exposed fish) and behavioural disorders; this research speculated that plastic NPs can be transferred up through a food chain, enter the brain of the top consumer and affect its behaviour (Mattsson et al., 2017). In mice model, the neurotoxicity caused by of organophosphorus flame retardants (OPFRs) was exacerbated by the

presence of PE and PS at 0.5–1.0 μm in the treated group (Deng et al., 2018). Also, Shan et al. (2022) in feeding mice with four different doses (0.5, 2.5, 10, and 50 mg/kg body weight) of fluorescent PS NPs with a mean diameter of 42 nm for 7 days showed microglia activation and neuronal damage (Shan et al., 2022). Zaheer et al. (2022) demonstrated a link between PE-MPs (size of 10–20 μm) exposure during the prenatal and early postnatal periods in mice and the development of autism spectrum disorder (ASD). By contrast, a study revealed no significant neurobehavioral effects in rats administrated orally (dosages: 1, 3, 6, and 10 mg/kg/bw) for 5 weeks with PS particles at 25 and 50 nm (Rafiee et al., 2018).

Impact on the hematopoietic system was recently reported. Hematotoxicity was observed in mice treated by oral gavage for 28 days with 0.1 and 0.5 mg of 5 μm PS MPs where impact on gene expression and altered molecular and biological pathways in mouse bone marrow cells were reported (Sun et al., 2021). Recently, exposed mice to PS both at nanosize (80 nm) and microsize range (5 μm and 10 μm) at 60 μg dose for 42 days by intragastric administration showed disorder of bone marrow cell arrangement, the decrease in colony-forming, self-renewal and differentiation capacity, and increased proportion of lymphocytes (Jing et al., 2022). Also, cardiovascular system may be affected in rat model after exposure to 0.5 μm PS particles at 0.5, 5 and 50 mg/L for 90 days (Li et al., 2020c). Reproductive toxic effects were also reported. In female mice exposed to PS NPs (0.79 μm in diameter) for 35 days inflammation of ovaries and reduction of quality of oocytes (Liu et al., 2022b). Testicular toxicity was evidenced in mice treated with PS sized 5 μm at concentrations of 100 μg/L, 1000 μg/L, and 10 mg/L *via* drinking water. In this study effects on spermatogenesis as sperm deformity and abnormal sperm quality were observed (Hou et al., 2021). The uptake of PS with diameters ranged 0.05–0.9 μm from different cell lineages of whole blood caused genotoxicity with major toxicological effects observed in monocytes and leukocytes (Ballesteros et al., 2020).

In general, the available studies indeed highlighted the adverse impacts of MPs and NPs on various systems, but the experiments often use high doses and prolonged exposure times that may not accurately reflect typical environmental exposure levels. While high doses can cause significant harm, the risks at lower levels might not be as severe, and it's crucial to continue studying this to fully understand the implications on human health.

6. Role of physicochemical properties on cellular internalization and toxicological effects

The physicochemical properties of MPs and NPs play a key role in the uptake, biodistribution and bioaccumulation of such particles, and thus in their toxicological effects. Microplastics and NPs can enter the cells *via* different routes and the efficiency of their uptake depends on several factors, including the type of tissue and the physicochemical properties of the particles. Size, surface chemistry, shape and polymer type play crucial roles in the interactions of MPs and NPs with cellular membranes and thus determine their cellular entry pathways and toxicological effects (Fig. 1). For instance, in primary mammalian cell cultures (e.g., human colon fibroblast), Fiorentino et al. (2015) found that PS NPs at 44 nm can be taken up by cells through a clathrin-independent endocytotic mechanism (Fiorentino et al., 2015), whilst, for the same NPs, Rossi et al. (2014) described the easily permeation of the lipid membranes bilayer. For the red blood cells (RBCs) a passive diffusion of PS less than 200 nm was suggested by Rothen-Rutishauser et al. (2006). The quantity of MPs and NPs that are absorbed and subsequently react with cells depends on several factors, such as their size, shape, surface functional groups and coating, surface charge, chemical composition, and weathering process. The current knowledge of the role of these factors on the toxicological features of the MPs and NPs were reviewed below.

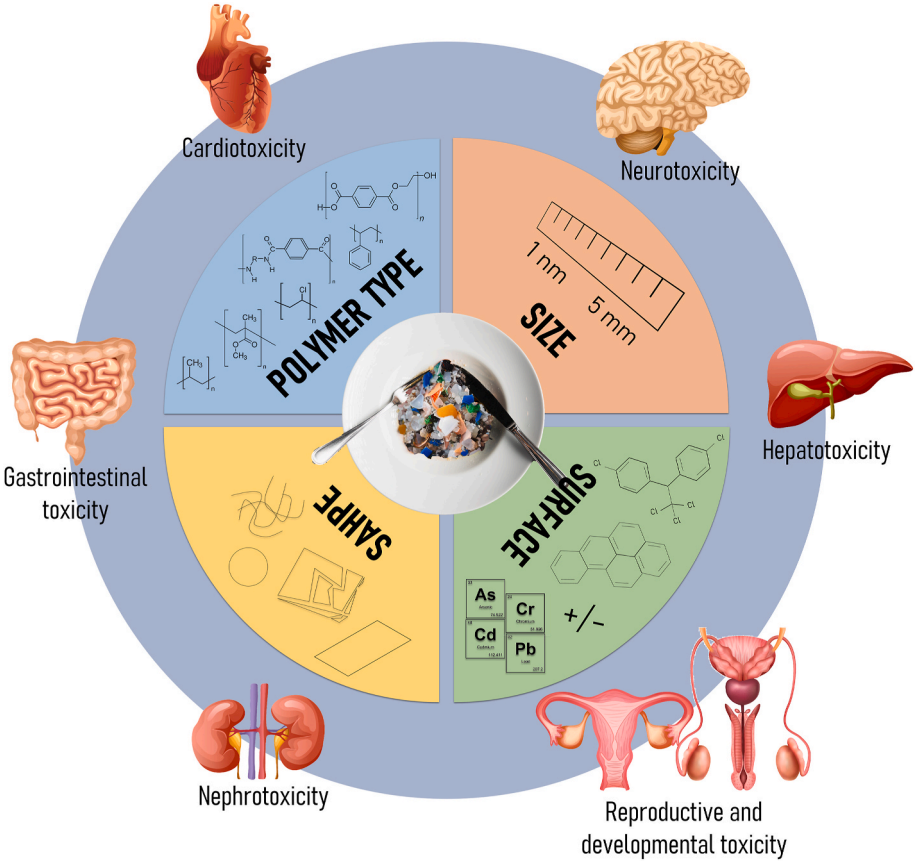

Fig. 1. Schematic representation of the key physicochemical properties affecting cellular uptake and subsequent toxicological effects.

6.1. Size

Size is one of the most important determinants of the uptake pathways, because many critical *in-vivo* functions, such as circulation time, targeting, internalization and clearance, depend on this parameter. By decreasing of size, the surface area of the particles increases, and higher surface area facilitates the diffusion of NPs into cells (Salatin et al., 2015). Walczak et al. (2015b) reported the size- and surface chemistry-dependent uptake of PS NPs in *in-vitro* intestinal cell models. The oral bioavailability level of 50 nm PS NPs was ten to one hundred times greater than the level of MPs (2–7%) (Walczak et al., 2015b). Likewise, it was found that 25 nm, but not 100 or 1000 nm, carboxylated PS MPs were readily taken up by and translocated across an *in-vitro* triculture small-intestinal epithelium (DeLoid et al., 2021). In addition, 10 μm spherical PS accumulated in the circulatory system of mussels (Browne et al., 2008), while spherical PS sized 5 μm were present in liver of zebrafish (Lu et al., 2016). In Deng et al. (2017) study, gut and kidney accumulated more 5 μm sizes, while liver accumulated more 20 μm sizes. In a recent study, Wang et al. (2020) confirmed that larger particles of PS (1 μm and 3 μm) were less likely to enter Caco-2 cells than smaller particles (300 nm, 500 nm, and 1 μm) at concentration of 120 μg/ml. Interestingly, they also found that cytotoxicity was size-based event, with significantly decreased cell viability for the PS in the nanosize range (300 nm, 500 nm, and 1 μm) than those in the microsize range (1 μm and 3 μm) (Wang et al., 2020). In general, smaller sizes seem to enhance the ability of the particle to translocate and to be biodistributed, entailing a real risk for the health of exposed populations (EFSA Panel on Contaminants in the Food Chain, 2016).

6.2. Shape

The shape has high effect on the circulation time, biodistribution and residency time of particles inside the cells. Elongated particles have a higher surface area that facilitate the interaction with cell surface compared to ones that are more spherical. As a result, the elongated particles exhibit a greater uptake than the spherical ones with similar dimension (Dasgupta et al., 2014).

In *in-vitro* study conducted on different human-derived cells (i.e., peripheral blood mononuclear cells, KATO III cells, HeLa cells and human dermal fibroblasts), the higher the roughness of PS MPs the higher the cell toxicity. Irregularly shaped particles increased the production of ROS, and cell death of fibroblasts and cancer cells. In red blood cells, roughness PS MPs induced damage on cell membrane leading to LDH and hemoglobin release in the cytosol (Choi et al., 2020).

6.3. Surface chemistry and biocorona

Surface chemistry (charge and hydrophobicity) is a crucial parameter that influences the interaction between particles and cells. This parameter was defined the major property determining cellular uptake efficiency by Jeon et al. (2018), that explored its role on phagocytic differentiated THP-1 cells or nonphagocytic A549 cells and found a positive correlation between the amount of internalized particles and the zeta potential (Jeon et al., 2018). Surface charge affects primarily the efficiency of internalization due to the charge of biomolecules that form an adsorption layer or "biocorona" around the MPs and NPs that, in turn, affects the endocytosis pattern (Oh and Park, 2014). The biocorona layer formation is driven by the biological exposure media, other than by the physico-chemical properties of the particle itself (Gopinath et al., 2019). This imply that biocorona may vary according to the biological media to which the particles come in contact, and, somehow, it represents the effective biological unit at cell–particle interface that modulates the biological fates and patho-biological effects of MPs and NPs. On the other hand, biocorona composition may exhibit dynamic change over time when a specific MP and NP crosses from one biological compartment to another (Tenzer et al., 2013). For instance, in macrophage-like cells the presence of serum protein decreased the cytotoxicity of different size of carboxylated PS beads (20 nm and 200 nm), being higher for the smaller ones (Clift et al., 2010). In *in-vitro* GIT studies, Walczak et al. (2015b) showed that the PS NPs protein corona complexes resulted in an increased translocation across the intestinal barrier (Walczak et al., 2015b), or increased cellular uptake and toxicity in *in-vivo* study on gut of *Daphnia magna* (Nasser and Lynch, 2016). Other research on PS NPs reported that protein corona reduces the RBC agglutination compared to the pristine ones (Pan et al., 2016), and that the complex PS NPs-RBC can determine particles accumulation in liver, kidney, and gut in mice model (Mohr et al., 2014; Deng et al., 2017).

6.4. Sorption of other pollutants and weathering process

Plastic particles can adsorb contaminants of organic as well inorganic nature, providing an additional transport vector for these contaminants in animal tissues. During the weathering process, many features like the mechanical strength, thermal stability, and crystallinity of MPs continuously decreased (Pflugmacher et al., 2021). Hence, the interface reaction between MPs and other contaminants (e.g., heavy metal, organic compounds, and pathogenic microorganisms, etc.) may vary with the properties of MPs (i.e., particle size, specific surface area, crystallinity, and polarity of MPs), since these properties may affect the adsorption capacity and biodistribution of contaminants (Mattsson et al., 2018). For instance, weathering process lead to degradation of MPs to smaller particle sizes and adds more surface area to sorb contaminants, which includes persistent organic pollutants (POPs), such as polychlorinated biphenyls (PBTs), polybrominated diphenyl ethers (PBDEs), dichlorodiphenyltrichloroethane (DDT), polycyclic aromatic hydrocarbons (PAHs) and other petroleum hydrocarbons, that can interact with animals and/or be a pathway for transfer of contaminants into their tissues (Galloway et al., 2017). Other pollutants known to sorb onto plastic debris include heavy metals such as Pb, Cd, Zn and Ni (Rochman et al., 2014) and organic contaminants such as pharmaceuticals (Guilhermino et al., 2018). Significant release of Mn, Zn, As, Cr, Cu, and Ni from the MP surface in NaCl solution and Mn, Zn, As, Cr, Cu, Pb, and Ni in GIT solutions was found (Chen et al., 2022). After oral exposure to MPs, dangerous substances as PAHs and polychlorinated biphenyl (PCB) may appear in the GIT tract (Kumar et al., 2022). Current studies of MPs and associated contaminants, as bisphenol A (BPA), detected concentrations of these compounds in the intestine, gills, liver, and brain of zebrafish (Chen et al., 2017; Rainieri et al., 2018), but none of them measured the concentration of these pollutants in the edible part such as the muscle. The toxic contaminant benzo[*a*]pyrene (BAP) accumulated on MPs and was found in adult zebrafish gills and could be also transferred to the next generation (Batel et al., 2018). In addition, certain tissue temperatures and physiological conditions may increase the potential transfer of contaminants to humans. In this regard, the potential for POPs such as DDT, perfluorooctanoic acid (PFOA), and di-2-ethylhexyl phthalate (DEHP) to desorb from MPs of PVC and PE under simulated physiological conditions was studied. Desorption rates were enhanced up to 30 times compared to seawater at lower pH and higher temperatures, in conditions simulating the physiological conditions of warm organisms (38 °C and pH 4) (Bakir et al., 2014). From toxicological perspective, the association between MPs and organic/inorganic pollutants may cause synergistic toxicity in animal tissues. For instance, the effect of MPs with adsorbed perfluorinated compounds such as PFOA, perfluorononanoic acid (PFNA), heptadecafluorooctane sulfonic acid (PFOS) on zebrafish liver was greater than that of MPs and perfluorinated compounds alone (Rainieri et al., 2018). In mice co-exposed to PE and PS beads (at size of 0.5–1.0 μm) and organophosphorus flame-retardants (OPFRs), a higher level of plastic particles in liver and gut in co-exposed compared with those exposed only with OPFRs was assessed. This implied a great influence of MPs on OPFRs toxicological effects (e.g., greater oxidative stress and neurotoxicity) (Deng et al., 2018). Therefore, it should be considered how the

interaction of contaminants and MPs can affect the absolute bioavailability of these contaminants that are transferred to biota, and this pathway of human exposure needs to be addressed.

7. Level of MPs and NPs in human samples by HBM studies

Microplastics and NPs occurrence and recognition in the human body (tissues and fluids) is a very poorly investigated field. HBM initiatives (i.e., cross-sectional or follow-up studies with significantly number of enrolled subjects) were not yet designed and performed within the scientific community, and, up to date, only small case-study reports were available. This fact is related to analytical and methodological concerns regarding: i) appropriate and reliable biomarkers of exposure which allow the detection of MPs and NPs in biological samples; ii) standardized protocols for collection, identification, and analytical quantification even at low levels; iii) the availability of certified reference materials (CRMs) to produce reliable data (i.e., suitable quality assurance and quality control measures). All these features explain the difficulty to obtain a real estimation of the internal dose of MPs and NPs in the human bodies. An overview of the investigations that deal with the occurrence of MPs and NPs in human samples is reported in Table 3.

Although pioneering reports on workers daily exposed to MPs through inhalation were carried out (Pauly et al., 1998; Prata, 2018), the GIT burden in the general population was investigated for the first time in 2019 by Schwabl et al. (2019). This study quantified MPs in human stool samples from 8 residents in Europe and Asia (with different dietary patterns), demonstrating the presence of 20 pieces of MPs - sized 50–500 μm and mainly PP (62.8%) and PET (17%) - per 10 g of stool as a result of food-based consumption. Other subsequent studies used human fecal specimens as reliable samples to provide the magnitude of human exposure through food and beverages intake. Zhang et al. (2021a) demonstrated 10 times higher concentration of PET and PC in infant feces than adult samples due to the extensive use of plastics articles (e.g., baby feeding bottles, sippy cups) and clothing, and the MPs release from packaged plastic containers used for processed baby foods (Zhang et al., 2021a). Similarly, associations between packaged water and beverages consumption and MPs abundance (mainly of PP, PET, and PS polymers) in feces were assessed in 23 healthy students living in the urban city of Beijing (China) (Zhang et al., 2021b). In feces of Hong Kong residents, the major frequency of PS polymers (55%) followed by PP (22.9%), PE (12.1%) and PET (9.5%) was linked to the widespread use of PS takeaway containers in this country (Ho et al., 2022). Particularly interesting is the fact that MPs pollution was found also in people living in rural areas demonstrating the far-reaching extent of MPs pollution beyond urban areas. For example, in Indonesia an average concentration of 9.159 μg/g of HPDE and 9.885 μg/g of PS in human stool from a fisherman community (Luqman et al., 2021), as well an average concentration of 10.19 μg/g of PP in human stool from a farming community were reported (Wibowo et al., 2021). In humans, the integrity of intestinal mucosa barrier has a critical role on the plastic particles absorption since patients with increased intestinal permeability, due for example to inflammatory bowel disease (IBD), might be more susceptible to absorption and consequently to more potential damage (Schmidt et al., 2013; Lomer et al., 2002). Another investigation showed higher fecal level of PET (34.0%) in IBD patients compared to healthy (22.3%) subjects, confirming that some diseases can exacerbate the retention of MPs arising from plastic packaging of drinking water, food and environmental dust exposure (Yan et al., 2022). Similarly, hepatic accumulation of PS, PVC and PET polymers ranging from 3.3 to 21 μm was observed in patient with liver cirrhosis likely due to the impaired intestinal barrier function (Horvatits et al., 2022). Likewise in patients with colorectal malignancies the presence of PC, PA, and PP polymers in their colon tissue (28.1 particles/g on average) demonstrated the capability of plastic particles to travel into human colon (Ibrahim et al., 2021).

Other studies used different human specimens like breastmilk, placenta, saliva, head hair, blood, and urine for quantifying the plastic burdens in human bodies. Pregnancy and infancy are vulnerable time windows to harmful exposure and the occurrence of PP particles (ranged from 5 to 10 μm in size) in human placenta and PE, PVC, and PP (ranged from 2 to 12 μm) in human breastmilk further highlighted the transgenerational potential health effects of these pollutants, as well the breastfeeding as a potential pathway of exposure for newborns (Ragusa et al., 2021, 2022). Similarly, human placenta samples were screened positive for PE, PP, and PS with size >50 μm by Braun et al. (2021), and the higher median concentration of total MPs observed in meconium (54.1 particles/g) than in placenta (18.0 particles/g) was linked to the accumulation of meconium in the human fetus (Liu et al., 2023). It is scientifically reasonable that plastic particles may be transported to organs *via* bloodstreams, since the plastic particles detected in blood are likely to be *via* mucosal contact (either ingestion or inhalation). Further supporting evidence from drug delivery field revealed the capability of nano-sized carriers to cross the blood-brain barrier, providing the quantification of plastic materials in blood a promising biomarker of exposure (Han et al., 2018). In a recent investigation PET, PE and polymers of styrene (a sum parameter of PS, expanded PS, acetonitrile butadiene styrene etc.) - at range between 0.7 and 500 μm was found in human blood of 22 healthy individuals by Leslie et al. (2022), although accidental contamination and other critical analytical issues of the used protocol should be carefully considered (Kuhlman, 2022). In addition, the presence of MPs in urine samples of six volunteers from different cities in the south of Italy was newly investigated and fragments (4–15 μm size), with irregular shapes, were found, and polymers composition included PVA, PVC, PP, and PE (Pironti et al., 2022). A human cohort from different regions of Iran were tested for MPs exposure by counting particles associated with or accumulated by various receptors (head hair, hands, faces and saliva). In contrast to the relatively high abundance of MPs in other human samples, limited MPs were measured in human head hair, hands, face skin, and saliva at 0.33–3.5 items per individual per day, with head hair returning the most samples (>7000, or, on average, >3.5 MPs per individual per day), saliva returning the least samples (about 650, or on average 0.33 MPs per individual). The majority were fine (length of <100 μm) fibres constructed of PE, PET, and PP that appear to be derived from both textiles (clothing and furnishings) (Abbasi and Turner, 2021).

8. Dietary exposure of MPs and NPs in humans

The dietary exposure assessment in humans following MPs and NPs oral intake *via* specific foods was reported in some of the studies. Fang et al. (2022) suggested an atmospheric MPs ingestion from deposition during dining/drinking activities greater than the amount directly ingested from food, reaching an intake of 1 million/year. Following oral intake, human daily exposure to plastic particles was frequently calculated using the EDI (Estimated Daily Intake). For Italian adults and children, EDIs due to mineral water consumption were 40.1 mg/kg body weight/day and 87.8 mg/kg body weight/day, respectively (Zuccarello et al., 2019). Oliveri Conti et al. (2020) assessed the EDIs (as particles/kg day) from fruit and vegetables ingestion and found that the amount of MPs <10 μm ingested was highest for apple (adults: 4.62×10^5; children: 1.41×10^6), and lowest for carrots (adults: 2.96×10^4; children: 1.15×10^5) (Oliveri Conti et al., 2020). From human stool samples, the average daily exposure doses *via* dietary sources to PET and PC MPs were estimated as 83 and 0.86 mg/kg body weight/day in one-year-old infants and 5.8 and 0.2 mg/kg body weight/day in adults (Zhang et al., 2021a). Similarly, from adult human stool PET exposure at a rate of 0.16 particles/kg body weight/day and PC exposure at a rate of 0.0063 particles/kg body weight/day were reported by Schwabl et al. (2019).

Other studies evaluated the number of particles ingested from water and specific beverage and food items. From water consumption, the average intake of MPs was 246 particles/day for the US population, with

those originated from bottled water (94 particles/day) 22-fold higher than those from tap water (4 particles/day) (Cox et al., 2019), while a daily exposure of 1.7–1.9 particles/kg bw were assessed in Saudi Arabia water consumers (Almaiman et al., 2021). Based on the recommended water intake by WHO (2 L for adults and 1 L for children), the highest daily exposures were calculated in Europe at 1260 MPs (adults) and 628 MPs (children) for tap water (Pivokonsky et al., 2018) and 9800 MPs (adults) and 4900 MPs (children) for bottled water (Oβmann et al., 2018). For Asian consumers a lower intake than for European consumers were assessed both for tap water (values up to 880 MPs for adults and to 440 MPs for children) (Tong et al., 2020) and bottled water (values up to 280 MPs for adults and to 140 MPs for children) (Kankanige and Babel, 2020). Based on the recommended water intake for infants (0.75 L), the results of Mason et al., (2018) revealed a major daily intake (471 MPs from tap water and 3667 MPs from bottled water) in European infants than Asian infants (330 MPs from tap water and 105 MPs from bottled water) (Mason et al., 2018). Microplastic exposure through milk consumption by individuals (in the age ranges of 15 - >65 years) varies between male and female, averaging 2×10^{-3}–6×10^{-3} particles/g body weight/day and 2×10^{-3}–7×10^{-3} particles/g body weight/day. (Basaran et al., 2023).

From seafood consumption, data for UK population, Li et al. (2018b) predicted an ingestion of 70 MPs per 100 g of mussel whilst Catarino et al. (2018) assessed an ingestion up to 123 particles per year in the UK and an individual exposure up to 4620 particles per year in countries with a higher shellfish consumption. Based on EFSA recommendation for fish intake by adults, human consumers of different wild fish (i.e., *Dicentrachus labrax*, *Trachurus trachurus*, *Scomber colias*) may intake 842 MP/year (Barboza et al., 2020) whilst values up to 11,000 MP/year were estimated for European shellfish consumers (Van Cauwenberghe and Janssen, 2014). Similarly high values (from 1267 to 5828 MPs ingested per year) were also derived for Scottish consumers of scallops and plaice (Akoueson et al., 2020).

Concerning salt intake, a negligible health risks associated with salt consumption was observed by Karami et al. (2017) that derived a particle intake of a maximum of 37 particles (sized <149 μm) per year from different salt brands (Karami et al., 2017). Microplastic individual intakes *via* salt consumption ranged from 0 to 117 particles/day (with an average of 3000 particles/year) depending on the brand consumed and population investigated (Kim et al., 2018). Although the general agreement was the higher exposures for the consumers of salts produced in Asia (Yang et al., 2015).

Recent evidence indicated that simple tasks in daily lives (scissoring with scissors, tearing with hands, cutting with knives, opening plastics containers/bags/tapes/caps) are able to generate about 0.46–250 MP/cm (Sobhani et al., 2020). Takeaway containers made from popular polymer materials (PP, PS, PE, and PET) were subjected to investigation (Du et al., 2020). MPs quantity ranged from 3 to 29 pieces/container in the analysed products, with the highest amount observed in PS containers. Consequently, the production of PS-based packaging for foods and beverages has been restricted by a decision of the European Parliament in 2021 (Du et al., 2020).

In addition, food preparation and cooking can influence the average MPs concentrations in meals. It has been estimated that 100–300 MP/mm are formed on a plastic cutting board during food preparation (Luo et al., 2022). Plastic particles can be also released from the surface of food containers when exposed to microwave or oven heating (Marazuela et al., 2022). It was found that soaking in water at approximately 100 °C released 1.07, 1.44, 2.24, and 1.57 million particles/ml from plastic packaging, cups, transparent boxes, and expandable boxes, respectively (Liu et al., 2022a).

Another study reported the mean size of MPs in the raw meat was 1279.2 ± 835.0 μm, but decreased when the meat was cooked or fried. Washing of the meat for 3 min helped decrease the MPs count to 0.07 particles/g meat (Habib et al., 2022). Similarly, washing the rice with water significantly reduced PE, PP and PET contamination, whilst instant pre-cooked rice contained 4 times higher levels of plastics (Dessì et al., 2021). Thus, the comparison between raw foods and final meals is required to assess human exposure to MPs through the diet.

Although the aforementioned studies estimated quantitatively the number of plastic particles consumed by humans from specific items, the mass of aggregate exposure to MPs and NPs is not well-defined. Only few studies performed the human exposure assessments to plastic particles, considering the total intake from different routes. For instance, the MPs body burden at the end of the human lifetime would be reached up to nearly 0.025 μg/L, with a median intake of MPs of 553 particles/capita/day for children and 883 particles/capita/day for adults (Mohamed Nor et al., 2021), while Cox et al. (2019) assessed a rate of human exposure from different routes between 74,000 and 121,000 per year. Likewise, exposure doses of 0.1–5 g weekly through multiple pathways was assessed by Senathirajah et al. (2021) or in the range of tens to billions of particles daily depending on the sources and pathways by Zarus et al. (2021). Therefore, the available exposure assessment data are highly heterogeneous since a wide range of exposure doses from very low to very high were reported through different empirical and probabilistic exposure models.

9. Current limitations and challenges

This review recognizes some major constraints in designing experiments to identify both the human exposure and potential adverse health effects to MPs and NPs *via* their oral intake. The reviewed animal and human studies showed different results in terms of particles uptake, biodistribution and bioaccumulation and potential toxicological effects. Many toxicological studies often use higher doses than what humans would typically encounter in real-life scenarios. This can sometimes lead to results that may not accurately reflect the true risk to human health. For a more accurate assessment, it's crucial to conduct studies at doses that mimic real-life exposure levels. In addition, the inconsistencies in experimental conditions such as varying doses, time frames, and biological models, can lead to significant variability in outcomes. This variability makes it challenging to compare results across different studies and draw reliable conclusions.

Moreover, most of the studies so far focused on MPs (size >1 μm) primarily due to the limited availability of reference NPs particles and the complexity of analytical methods required for their characterization. Thus it remains highly questionable whether exposure and effects observed with MPs can be extrapolated to NPs. Purchased particles are often spherical but this does not fully represent the complex and irregular shapes found in natural environments, and almost all the experiments are carried out by using PS models. Other polymers like PP, PE and PET that are heavily present in the human daily exposure were poorly investigated, and any extrapolations made from existing data to other polymers should be approached with caution. Another limitation is the lack of studies that consider the adsorbed contaminants on plastic materials and thus it's important to conduct more studies on the co-exposure to better understand their additive impact on human health.

Regarding the human exposure assessment to MPs and NPs, most of the studies focused their attention on the quantification of MPs and NPs in fecal specimen as reliable sample to provide the magnitude of exposure through food and drink intakes. More recently there is also evidence that MPs is making its way in human blood, placenta, meconium, breastmilk and urine, although very few studies have looked for them in these matrices. The presence of MPs in meconium and breast milk further highlighted the transgenerational potential health effects of these pollutants. For other tissues like brain tissue, the presence of MPs was demonstrated in fish and mice, but it remains to be shown if the plastic particles may be found in the human brain. Concerning health effects after ingestion, they were observed mainly on organs such liver, kidney and gut and were influenced by the administered concentration and size. In general, smaller sizes seem to enhance the ability of the particle to translocate and to be biodistributed, entailing a real risk for

the health of exposed populations.

Finally, based on the levels of MPs and NPs detected in human diets, studies reported the EDI or the number of particles per day from consumption of specific items, whilst the aggregate exposure to MPs and NPs trough the different foods and beverages is not well-defined. Hence, a major number of studies should be performed on the human risk assessment to plastic particles considering the total intake from different oral routes.

All these features suggest that the approach used in estimating human exposure and effects may lead to great variability on the final risk evaluation and further investigation to provide more quality data is required for effective pollution prevention and control of MPs and NPs.

10. Recommendations for future research

The identification of reliable biomarkers of exposure and effect to MPs and NPs becomes a priority for the future research. This requires the development and standardization of analytical methods to assess their presence, identity and to quantify their amount in food, animal and human samples. Furthermore, quality assurance should be in place and demonstrated, and data for the smaller sized particles, the different polymers and the low MPs and NPs concentration should be generated.

To assess the real adsorption of MPs and NPs and potential human health consequences at chronic low unavoidable levels exposure, HBM studies should be mandatory to better understand the degree of internal exposure to MPs and NPs and assess their real burdens in the human body. A HBM study is expected to contribute to the: i) choice of reliable exposure and effect biomarkers in human samples; ii) identification of subjects at risk and evaluation of their direct and indirect exposure; iii) assessment of the human health risk arising from MPs and NPs exposure in general population, vulnerable sub-groups, and workers. Thus, HBM studies focused on this emerging type of contamination are required.

CRediT authorship contribution statement

Flavia Ruggieri: Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Beatrice Battistini:** Writing – review & editing, Writing – original draft, Methodology, Data curation. **Angela Sorbo:** Methodology, Data curation. **Marta Senofonte:** Methodology, Data curation. **Veruscka Leso:** Writing – review & editing, Methodology, Data curation. **Ivo Iavicoli:** Visualization, Validation, Supervision, Conceptualization. **Beatrice Bocca:** Visualization, Validation, Supervision, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

No data was used for the research described in the article.

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