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Review

Microplastics in aquatic environments: A review on occurrence, distribution, toxic effects, and implications for human health

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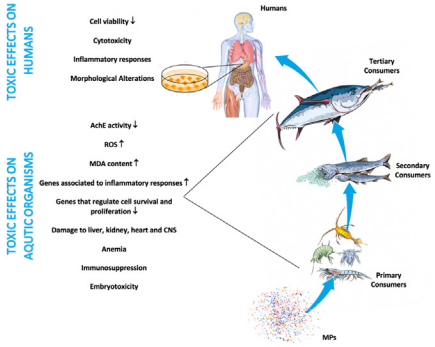
HIGHLIGHTS

- The inherent properties of microplastics affect their buoyancy and spatial distribution.
- Microplastics pose a potential risk to aquatic organisms and humans.
- Membranes with larger pore size lead to low concentrations of microplastics in table salt.
- Syncytiotrophoblast may regulate the microplastics transport across the human placenta.

GRAPHICAL ABSTRACT



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ABSTRACT

Microplastics (MPs) are fragments, fibers, granules, flakes and spheres with a diameter or length of less than 5 mm. These may eventually end up in the aquatic environment by the progressive breakdown of larger plastics or via domestic and industrial sewage spillage. In order to better understand the current knowledge in this field, we carried out and extensive literature research to retrieve articles mainly focusing on the occurrence and distribution of MPs in aquatic matrix as well as their impacts on aquatic organisms and human derived cells. Once in the environment, MPs may be transported via wind and water movement, affecting their spatial distribution. Furthermore, density may also affect the buoyancy and vertical distribution of these pollutants. Consequently, MPs are ubiquitously distributed in fresh- and marine- water systems, posing a real threat to aquatic organisms. Furthermore, trophic transfer and biomagnification processes represent a viable route for the input of MPs to humans. This paper focuses on (1) Outline the occurrence of MPs in worldwide aquatic ecosystems; (2) Investigate the factors affecting the abundance and distribution of MPs in aquatic ecosystems; (3) Provide an in-depth discussion about the harmful effects that MPs poses to aquatic organisms; (4) Summarizes the possible mechanisms by which MPs may induce toxic effects on humans.

Contents

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1. Introduction

Plastics are made of a large variety of polymers, which are derived from breaking down carbon based materials such as petroleum, natural gas, or coal. Given their cheapness, versatility, durability and strength, plastics are widely used in many strategic sectors, such as packing, building, transportation, agriculture and medicine. The large-scale use of plastic products, as well as their improper disposal and persistent nature make plastics a worldwide threat to aquatic ecosystems. It is estimated that an average of 5 to 13 million tons of plastic waste enters into the world's oceans each year and by 2050 the weight of marine plastics would exceed that of fish (Wang et al., 2019).

Once released into the environment, plastics are subjected to progressive breakdown under the action of environmental physicochemical and biotic factors that derive into so called secondary microplastics (MPs) (Barnes et al., 2009). Secondary MPs are fragments, fibers, granules, flakes and spheres with a diameter or length of less than 5 mm, and constitute the major source of MPs in the aquatic environment (Jiang, 2018). In addition to secondary MPs, plastics can also be manufactured in microscopic sizes, known as primary MPs, which are commonly found in medicines, textiles and personal care products (Browne, 2015). Primary MPs may eventually end up in the aquatic environment via surface run-off, domestic and industrial drainage systems, and waste water treatments plants discharge.

MPs may pose a risk to aquatic environments due to their ubiquity in freshwater and marine systems (Vermaire et al., 2017; Sighicelli et al., 2018; Rodrigues et al., 2018; Bucol et al., 2020). Furthermore, due to their similar size with plankton, MPs can be easily ingested by aquatic organisms from different trophic levels (Bessa et al., 2018; Li et al., 2018; Su et al., 2019). Thus, they can accumulate at higher trophic levels, enter the food chain, and poses a potential risk to and human health (Schirinzi et al., 2017; Hwang et al., 2019). Among the detrimental effects that MPs may induce on aquatic species include neurotoxicity and behavioral changes, histopathological damage, biochemical and hematological changes, and embryotoxicity (Chen et al., 2017; Yin et al., 2018; Lei et al., 2018a, 2018b; Hamed et al., 2019; Li et al., 2020).

This paper focuses on (1) Outline the occurrence of MPs in freshwater and marine systems on a global scale; (2) Investigate the factors affecting the abundance and spatial distribution of MPs in aquatic ecosystems; (3) Provide an in-depth discussion about the detrimental effects that MPs poses to aquatic organisms; (4) Determine the potential risk of MPs in food security and human health.

2. Method of literature review

An extensive literature review was conducted to retrieve articles on MPs in aquatic ecosystems and their toxic effects using the Scopus, ScienceDirect, Springer, Wiley, ACS and Google Scholar databases. Unpublished studies (such as theses, conference proceedings, book chapters or reports) were not included. A combination of keywords was applied as the criteria, such as “microplastics” OR “microplastic” AND “freshwater” OR “microplastics” AND “sediments” OR “microplastic” AND “ toxic effects”. From the results obtained, we selected a total of 151 publications, mainly from the last 10 years, which were further classified into several subtopics, such as occurrence and distribution, sampling and characterization, ecotoxicology, and human risk.

3. Results and discussion

3.1. Occurrence of MPs

The occurrence and spatial distribution of MPs in surface water and sediments are shown in Table 1. (See Tables 2 and 3.)

High concentrations of MPs have been reported at the sea surface, in the deep sea, in sea ice, on shorelines and in biota of several continents around the globe. (Sutton et al., 2016; Cincinelli et al., 2017; Güven et al., 2017; Gray et al., 2018; Khalik et al., 2018). However, the occurrence of MPs in fresh water systems has received less attention, with only few studies carried out on surface water and sediments of Europe, North America and Asia (Vermaire et al., 2017; Sighicelli et al., 2018; Jiang et al., 2018; Di and Wang, 2018). Thus, further research of MPs in several freshwater systems around the globe is still needed.

The occurrence and spatial distribution of MPs in aquatic systems it is affected by several factors. Hu et al. (2018), for instance found MPs reached a maximum concentration of 21.52 particles/L in various small waterbodies of China. Furthermore, they pointed out that these small water bodies reached greater concentrations of MPs than large-scale aquatic systems. This might be due to the small volume of water, which reduce the potential of dilution for contaminants. However, in disagreement with these results, Gray et al. (2018) found MPs reached concentrations of up 88 particles/L in various seawater samples. These differences could be explained due to the different environmental characteristics. For instance, in seawater, the amount of salt and dissolved solids may enhance the sorption of MPs, producing higher concentrations of these pollutants. Other key factors affecting the abundance and distribution of MPs are the wind and surface run-off, the inherent

Table 1
Occurrence of MPs in worldwide water bodies and sediments.

Country	Location	Surface water	Sediments	Method of quantification	Sieve size	MPs composition	Shape/Size of MPs	Source
North America								
Canada	Ottawa River and its tributaries	0.05–0.24 fragments/L	–	*Leica* stereomicroscope at 40× magnification	100 μm	–	Shape: red and blue microfibers and microbeads.	Vermaire et al., 2017
	Wascana Creek	0.5–9.7 particles/m^3	–	Dissection microscope	75 μm	–	Shape: fragments, fibers, beads.	Campbell et al., 2017
	East coast of Vancouver Island	139.01–1180.75 particles/m^3	<1.0–123.6 particles/kg	Dissection microscope at 40–50× magnification	100 μm	–	Shape: clear and blue fibers and fragments. Most abundant size: 100 μm - 500 μm.	Collicutt et al., 2019
US	Charleston Harbor & Winyah Bay	3–88 particles/L	33.7–1389.6 particles/m^2	Dissection microscope	63 μm	PE: 6–83% PA: 56% PP: 33–83%	Shape: black fragments, white foam, blue fibers, green spheres. Most abundant size: 150 μm - 499 μm.	Gray et al., 2018
Europe								
Czech Republic	WTP	1439–4102 particles/L	–	Vega high resolution scanning electron microscope	0.2 μm	PET PP PE	Shape: Fragments and fibers Most abundant size: <10 μm.	Pivokonsky et al., 2018
France	Gulf of Lion	6×10^3–1×10^6 items/km^2	–	ZooScan	125 μm	–	Size: 0.6–2.36 mm.	Schmidt et al., 2018
Italy	Southern subalpine lakes	1300–93,000 particles/km^2	–	Stereomicroscope	1 mm	PE: 41.3–48% PP: 5.4–21.8% EPS: 9.0–24.6%	Shape: fragments, filaments and sheets. Most abundant size: < 5 mm.	Sighicelli et al., 2018
Portugal	Antuã River	58–1265 items/m^3	18–629 items/kg	Stereomicroscope *Optika* at 1.2–1.5× magnification	55 μm	PE PP PS PET PVA EVA PTFE Cellulose	Shape: white, black, transparent and blue foams, fibers and fragments.	Rodrigues et al., 2018
Asia								
China	Xiangxi River	0.55×10^5–342×10^5 items/km^2	80–864 items/m^2	Stereomicroscope at 40× magnification	1 mm	PE PP PS PET	Shape: blue and red sheet, fragment, lines and foam. Most abundant size: 1-5 mm	Zhang et al., 2017
	Hanjiang River and Yangtze River	1020.9–10,561 n/m^3	–	*M165FC Leica* stereomicroscope at 160× magnification	0.45 μm	PET PP PE PA PS	Shape: transparent, blue, purple and red fiber, granule, film and pellet. Most abundant size: <2 mm	Wang et al., 2017
	Yangtze River Delta	0.48–21.52 items/L	35.76–3185.33 items/kg	Carl Zeiss Discovery V8 stereomicroscope	20 μm	PP	Shape: fibers and fragments Most abundant size: <0.5 mm	Hu et al., 2018
	Three Gorges Reservoir	1597–12,611 n/m^3	25–300 n/kg	*M165FC Leica* stereomicroscope at 160× magnification	0.45 μm	PS: 38.5% PP: 29.4% PE: 21%	Shape: transparent fibers. Most abundant size: <0.5 mm.	Di and Wang, 2018
	Dongting and Lake Hong Lake	900–4650 n/m^3	–	*M165FC Leica* stereomicroscope at 160× magnification	0.45 μm	PE PP PS PVC	Shape: transparent, blue, purple, black, red, and white fiber, granule and film Most abundant size: <330 μm	Wang et al., 2018
	West Dongting Lake & South Dongting Lake	433.33–2216.67 items/ m^3 366.67–2316.67 items/m^3	320–480 items/m^3 200–1150 items/m^3	*SZX7 Olympus* stereomicroscope	0.22 μm	PET: 40.13% PS: 21.02% PE: 15.92% PP:11.46% PVC: 4.46%	Shape: transparent, white, blue, black and green fibers, fragment, film and pellet. Most abundant size: <0.5 mm	Jiang et al., 2018
	Bohai Sea	0.4–5.2 pieces/L	0.2–256.3 pieces/kg	Nikon SMZ25	5 μm	PP PE PVC PS PET ABS	Shape: white, blue and black fibers Most abundant size: 100–3000 μm	Dai et al., 2018
	Wei River	3.67–10.7 items/L	360 to 1320 items/kg	*MV5000 R/TR Nanjing Jiangnan Novel Optics* metallographic microscope	0.45 μm	PE PVC PS	Shape: Fiber, films, fragments, foam, pellets Most abundant size: <0.5 mm	Ding et al., 2019
India	Vembanad	–	96–496	Compound microscope	5 mm	LDPE	Shape: film, foam, fragment,	Sruthy and

(continued on next page)

Table 1 (*continued*)

Country	Location	Surface water	Sediments	Method of quantification	Sieve size	MPs composition	Shape/Size of MPs	Source
	Lake		particles/m^2	at 10× magnification		PS PP	fiber and pellets	Ramasamy, 2017
Indonesia	Jakarta Bay	–	18,405–38,790 particles/kg	Monocular microscope at 100× magnification	30 μm	PP	Shape: Fibers, fragments and pellets. Most abundant size: 100 μm - 500 μm	Manalu et al., 2017
	Submba water	19.41–68.59 n/m^3	–	*M205C Leica* microscope	0.45 μm	PE: 63.64% PS: 9.09% PA: 4.55% PP: 22.73%	Shape: Fibers and granule. Most abundant size: 300 - 1000 μm	Cordova and Hernawan, 2018
Malaysia	Kuala Nerus and Kuantan port	0.13–0.69 particles/L	–	*Olympus SZX7* stereomicroscope at 40× magnification	20 μm	PS PA PVC PE PP	Shape: filament, fragment, and irregular shape. Colors: black, blue, brown, gray, red, orange, yellow, transparent.	Khalik et al., 2018
Philippines	Negros Oriental	–	0.082 items/g	Stereomicroscope at 40× magnification	8 μm	Rayon PE PVC	Shape: fibers Most abundant size: 1 mm	Bucol et al., 2020
Turkey	Mediterranean Sea	16,339–520,213 particles/km^2	–	*Olympus SZX16* stereomicroscope at 30× magnification	26 μm	PTHC resin PS PA resin PE PP	Shape: fibers and hard plastic. Most abundant size: 0.1 and 2.5 mm	Güven et al., 2017
Africa Kenya	Indian Ocean	33.3–275 particles/m^3	–	*Optika* dissection microscope at 20× magnification	0.7 μm	PP LDPE	Shape: black, filaments, fragments granules and foams. Most abundant size: 0.25–1.0 mm	Kosore et al., 2018

PS: polystyrene PP: polypropylene; PE: polystyrene; PA: polyamide; PET: polyethylene terephthalate; EPS: expanded polystyrene; PVA: polyvinyl acetate; EVA: ethylene vinyl acetate; PTFE: Polytetrafluoroethylene; PVC: polyvinyl chloride; ABS: acrylonitrile-butadiene-styrene; LDPE: low density polyethylene; PTHC: poly(polytetrahydrofuran carbonate).

properties of MPs and population density, which will be discussed in following sections.

3.1.1. Factors affecting abundance of MPs

MPs in freshwater and marine environments can come from a wide variety of land- and marine-based sources. Nonetheless, it is known that 80% of marine debris originates from land-based sources, and the remainder from marine-based activity (Jang et al., 2020). Population density and proximity to urban centers have been considered the main factors that can influence the abundance of MPs in environment. Cable et al. (2017), for instance demonstrated that the highest concentration (2 million particles/km-2) of MPs in the Great lakes came from urban sites. Similarly, Jiang et al. (2019) finds that the abundance of MPs in the sediment near Lhasa, a touristic center of the Tibet Autonomous Region of China, is higher than in the sparsely populated areas. In addition, high MPs densities have been reported in the Rhine and Main rivers, China's Qinghai Lake, Lagoon of Venice, Jakarta Bay and the Ottawa river, where the rivers and lakes experience intensive industrial activity and tourism (Vianello et al., 2013; Klein et al., 2015; Manalu et al., 2017; Vermaire et al., 2017; Xiong et al., 2018).

Greater concentrations of MPs have been also associated with rainfall events. Studies carried out in surface waters of Swiss lakes and in sediments of Lake Ontario demonstrated MPs concentrations increased after rainfall events (Corcoran et al., 2015; Faure et al., 2015). One possible explanation for this is that the runoff after rainfall on land, where plastic production and the degradation rate of plastic debris is higher, could deliver these microplastics into the aquatic environments (Dris et al., 2016). Consequently, the greater the rainfall is, the stronger the erosion effect of surface runoff on land will be, and the more plastic debris will be transported. On the other hand, hydrodynamics have the ability to change the distribution of microplastics in water, and compared with surface water, sediments accumulate higher microplastic amounts (Zhang et al., 2018). Thus, the strengthened hydrodynamics during rainfall can lead to resuspension of microplastic debris in sediment, thereby facilitating the presence of microplastics in surface water. Since previous studies have reported that there are plenty of microplastics floating in the atmosphere (Klein and Fischer, 2019), another hypothesis is that these microplastics can adhere to raindrops and be directly transferred into lake water.

Domestic and industrial sewage spillage may also play an important source of MPs to marine and freshwater systems. However, the contribution of these sources remains controversial. Carr et al. (2016), for instance found that almost no MPs were detected in the effluents of a tertiary waste water treatment plant (WWTP). Furthermore, abundance of MPs in the discharge of a secondary WWTP was low (one plastic particle per 1.14 l of effluent). In disagreement with these results, Murphy et al. (2017) found that although a secondary WWTP in Scotland had a removal rate of 98.41%, 6.5 × 107 of MPs were still discharged daily. Thus, the different treatment techniques applied in each plant could lead to varied removal rates, and quantitative differences in size and type of MPs. Mintenig et al. (2019), for instance demonstrated MPs with a dimeter lower than 500 μm were more abundant (10 to 9000 particles/m3) than larger plastics particles (0 to 50 particles/m3) in 12 WWTPs of Germany. Moreover, PE was the most abundant polymer of both size, followed by polyester fiber with 90 to 1000 particles/m3.

Sampling techniques used in the gathering of environmental samples for MPs analysis, especially in the aquatic environments is vital to the overall estimation of its abundance (Alimi et al., 2020). Nonetheless, different sampling and analytical methods lead an underestimation or an overestimation of microplastics abundance. Manta trawl based sampling methods for instance, allow that large volumes of water can be sampled in a rather short time. However, the concentration of microplastics in the environment may be underestimated due to the limitation of the net's mesh size (300-500 μm) (Lindeque et al., 2020). Furthermore, sampling device itself, frames and connectors are

Table 2
MPs toxic effects on aquatic organisms.

Specie	MPs concentration	Time	Type of MPs	MPs shape/size	Uptake	Toxic effects	References
Fish							
Danio rerio	1 mg/L MPs + 2 μg/L & 20 μg/L EE2	120 h	PS	Shape: Size:50 nm & 45 μm	–	Larvae length↓ EE2 uptake ↓ mRNA gene expressions: zfrho & zfblue ↑ Biochemical changes: CAT & GPx activities ↑ AChE activity ↓	Chen et al., 2017
	Feed with 4% clean plastic	3w	LDPE	Shape: - Size: 125-250 μm	–	Histopathological changes: Livers had normal appearance.	Rainieri et al., 2018
	Feed with 2% plastic mixture with PCBs, BFRs, PFCs & methylmercury	3w				Histopathological changes: Livers showed white grain shaped formations & vacuolization mRNA gene expressions: β-actin, chrna1, cyp1a1, ef1α, esr2, gstp1, ngn1, prdx1 ↑	
	0.0001–10 mg/L	10d	PA PE PP PVC PS	Shape: - Size: 70 μm	–	Histopathological changes: Intestine: Cracking of villi and splitting of enterocytes	Lei et al., 2018a, 2018b
	0.1, 1, 10 ppm	120 h	PS	Shape: - Size: 20–100 nm	–	Heart rate↓ PS-NPs accumulated in the yolk sac (24 hpf) & migrated to the GIT; gallbladder, liver, pancreas, heart, & brain (48–120 hpf) Behavior changes: Swimming activity↓	Pitt et al., 2018
	100 & 1000 μg/L	14d	PS	Shape: spheres Size: 0.5 & 50 μm	–	Volume of mucus in the gut↑ Microbiome changes: Bacteroidetes & Proteobacteria abundance↓ Firmicutes abundance↑ mRNA gene expressions: il1a & il1b ↑	Jin et al., 2018
	20 - 200 μg/L MPs + 10 μg/L Cd	3w	PS	Shape: beads Size: 5 μm	–	Accumulation of Cd in gill, gut & liver ↑ Histopathological changes: Infiltration in hepatocyte, cilia defects in enterocyte & fuzzi structure in gill filaments cells Biochemical changes: SOD & GSH ↓ mRNA gene expressions: mt1, mt2, tnfa, il1b & ifng1↑ sod1, sod2 & nfe2l2↓	Lu et al., 2018
	20 mg/L	21d	PP PS	Shape: bead, fragment and fiber Size: 4 - 40 μm	At 7d in gut: Fibers: 8.0 μg/mg Fragments: 1.7 μg/mg Beads: 0.5 μg/mg	Body weight ↓ Gut microbiota dysbiosis Histopathological changes: Beads: slight vacuolization Fragments and fibers: increased vacuolization and cilia defects Biochemical changes: SOD↑, D-Lac↓, IL-1α↑	Qiao et al., 2019a, 2019b
	11, 110, 1100 particles/L	96 h	HDPE	Shape: red, blue, green, clear, yellow spheres. Size: 10 - 600 μm	–	Behavior observations: Erratic movement, seizure, tail bent upward/downward. mRNA gene expressions: cyp1a↑ (intestine) vtg1 ↑(liver)	Mak et al., 2019
	100 & 1000 μg/L	7d	PS	Shape: microspheres Size: 5 & 50 μm	–	Microbiome changes: Bacteroidetes, γ-Protobacteria, Sphaerotilus, Haliangium, Leptothrix & Pseudomonas abundance↓ Firmicutes, Methyloversatilis, Polynucleobacter, Legionella, Ottowia, Flectobacillus & Methylophilus abundance↑ Metabolomic alterations: PS-MPs induced changes in 121 metabolites including carbohydrates, fatty acids, amino acids, nucleic acid.	Wan et al., 2019

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Table 2 (*continued*)

Specie	MPs concentration	Time	Type of MPs	MPs shape/size	Uptake	Toxic effects	References
						mRNA gene expressions: Pepckc, Gk, Acc1. SREBP1α, Fas, Apo & PPARγ ↑ PK, HK1, Aco, Cpt1, Fabp6 & Dgat ↓ Biochemical changes: GSH & CAT ↓	
	50 & 500 μg/L	21d	PS	Shape: beads Size: 5 μm	–	Histopathological changes: Intestine: Thinning of the bowel wall and congestive inflammation. Biochemical changes: CAT, SOD & D-lactate activities↑ DAO activity↓ Metabolomic alterations: PS-MPs induced changes in 36 metabolites Microbiome changes: Proteobacteria abundance↓ Fusobacteria abundance↑	Qiao et al., 2019a, 2019b
Oreochromis niloticus	1, 10, 100 μg/L	14d	PS	Shape: beads Size: 0.1 μm	At 14d: Gut: 23.3–174.6X10^{4}μg/kg Liver: 12–37.6X10^{4}μg/kg Gills: 17.8 - 81X10^{4}μg/kg Brain: 10–41.1X10^{4}μg/kg	Biochemical changes: AChE, activity↓ SOD & EROD activities↑	Ding et al., 2018
	1, 10, 100 mg/L	15d	–	Shape: irregular Size: >100 nm	–	Biochemical changes: GPT, GOT, glucose, creatinine, uric acid, cholesterol, total protein, albumin, globulin & A/G ratio↑ Hematological changes: RBC's, Hb, Ht, MCHC, platelets, WBC's & monocytes↓ MCV & MCH↑	Hamed et al., 2019
	1, 10, 100 μg/L MPs + 50 μg/L ROX	14d	PS	Shape: microspheres Size: 0.1 μm	At 14d: Gut: 145.7–477.22X10^{3}μg/kg Gills: 97–316.2X10^{3}μg/kg Brain: 49.6–158.9X10^{3}μg/kg Liver: 10.4–37.2X10^{3}μg/kg	Bioaccumulation of ROX in fish ↑ Biochemical changes: AChE activity ↓ EROD & SOD activities ↑	Zhang et al., 2019
Dicentrarchus labrax	0.26 & 0.69 mgL MPs + 0.010 & 0.016 mg/L Hg	96 h	–	Shape: microspheres Size: 1 - 5 μm	–	Swimming velocity & resistance time↓ Lethargic and erratic swimming behavior (swimming upside down, erratic jumping, loss of swimming control, sings of rapid fatigue)	Barboza et al., 2018a
	0.26 & 0.69 mg/L MPs + 0.010 & 0.016 mg/L Hg	96 h	–	Shape: spherical Size: 1 - 5 μm	–	Bioaccumulation of mercury↑ AChE, ChE (muscle) & IDH (muscle) activities ↓ LPO levels (brain & muscle) & LDH activity↑	Barboza et al., 2018b
Cyprinus carpio	1 - 2 mgL 1- 2 mg/L MPs + 0.2–0.4 mg/L PQ	21d 21d	PE	Shape: - Size: -	–	Biochemical changes: ALP, CPK activities↑ Total protein, globulin, cholesterol, creatinine triglyceride & albumin levels & γ-glutamyl transferase activity↓ Biochemical changes: GOT, GPT, LDH, ALP, CPK activities & glucose, creatine & albumin levels↑ Total protein, globulin, cholesterol, triglyceride levels & γ-glutamyl transferase activity↓	Haghi and Banaee, 2017
Carassius auratus	0.96, 1.36, 1.94 & 3.81% (g (food+MPs)/g ww fish)	6w	PS PA	Shape: fibers, fragments, pellets. Size: <5 mm	–	Weight ↓ Histopathological changes: Jaws: severe breakage of the dermal layer with hemorrhages Liver: dilated sinusoids, inflammation, infiltration and microgranuloma. Intestine: inflammation, hypertrophic goblet cells.	Jabeen et al., 2018
Cyprinodon variegatus	50 & 250 mg/L	4d	PE	Shape: microspheres	–	Movement (in the dark), distance travelled & maximum velocity↓	Choi et al., 2018

Table 2 (*continued*)

Specie	MPs concentration	Time	Type of MPs	MPs shape/size	Uptake	Toxic effects	References
				& irregular Size: 150 -180 μm & 300 - 355 μm		Intestinal distention mRNA gene expression: Cyp1a1 ↓ CAT, Sod3, Cxcr5, Tnfsf13b, Casp3, Tp53 ↑	
Sebastes schlegelii	1×10^6 microspheres/L	14d	PS	Shape: microspheres Size: 15 μm	–	After 7 days, PS-MPs still exist in intestine and gills of fish.	Yin et al., 2018
						Behavior changes: Feeding time & foraging time ↑ Swimming speed ↓ Histopathological changes: Bile became black Hyperaemia in liver	
Oryzias latipes	0.01, 0.1 & 1% *w*/w in fish food	30d	PE PP PS	Shape: - Size: 16.4–962.2 μm	–	Larvae growth & head/body ratios ↓ CYP1A inhibition EROD activity & DNA breaks ↑	Pannetier et al., 2020
Pimephales promelas	20 & 2000-part/mL	5d	PS	Shape: microspheres Size: 6 μm		Null translocation Trophic transfer: 2.82–695.5 particles (mean number of MPs particles in each FHM after exposure) BAF: 0.057–0.256	Elizalde-Velázquez et al., 2020
Mussels							
Corbicula fluminea	0.2 & 0.7 mg/L MPs + 1.8 & 7.1 mg/L florfenicol	96 h	–	Shape: microspheres Size: 1 - 5 μm	–	MPs were found in the gut, lumen of the digestive gland, connective tissue, hemolymphatic sinuses & gills. Feeding↓ Biochemical changes: ChE & IDH activities↓ LPO levels & GST activity↑	Guilhermino et al., 2018
Perna perna	0.125 g/L	90d	PVC	Shape: 0.1–1.0 μm Size:	–	Feces of exposed organisms were highly contaminated with PVC. However, all physiological responses showed nonsignificant effects.	Santana et al., 2018
Scrobicularia plana	1 mg/L	14d	PS	Shape: - Size: 20 μm	–	Biochemical changes: AChE activity ↓ Gills: SOD, CAT, GPx & GST activities ↑ Digestive gland: SOD activity & LPO levels↑ CAT & GPx activities↓	Ribeiro et al., 2017
Crustaceans							
Daphnia magna	0.1 mg/L	TG	Pristine	Shape: microspheres Size: 1 - 5 μm	–	F_0: Females: growth, total offspring, mobile juveniles & population growth↓ F_1: B_1 Females: All died before starting to reproduce. B_3 Females: 20% of mortality & all juveniles produced were immobile juveniles growth, total offspring & number of broods↓ F_2 & F_3: Recovery was found. However, population growth rate was significantly lower than in the control.	Martins and Guilhermino, 2018
	20 & 2000-part/mL	4 h	PS	Shape: microspheres Size: 6 μm		Null translocation Trophic transfer: 0.64–73.16 particles (mean number of MPs particles in each Daphnia after exposure) BCF: 0.020–0.039	Elizalde-Velázquez et al., 2020
Eriocheir sinensis	40–40,000 μg/L	21d	PS	Shape: microspheres Size: 5 μm	At 7d: Gill: 0.077 μg/mg Liver: 1.66 μg/mg Gut: 0.81 μg/mg	SGR and HSIs↓ Biochemical changes: AChE, GPT, CAT, GOT, SOD, GSH, & GPx activities↓ mRNA gene expressions: p38 ↑ ERK, AKT, MEK ↓	Yu et al., 2018
Nematodes							
Caenorhabditis elegans	1 mg/L	3d	PS	Shape: - Size: 1.0–5.0 μm	–	Survival rate, body length & average lifespan ↓ Locomotor behavior changes: Number of head thrashes, body bends &	Lei et al., 2018a, 2018b

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Table 2 (*continued*)

Specie	MPs concentration	Time	Type of MPs	MPs shape/size	Uptake	Toxic effects	References
						crawling speed ↑ mRNA gene expressions: gst-4 ↑	
Hydroids *Hydra attenuata*	0.01, 0.02, 0.04, 0.08 g/mL	60 min	PE	Shape: flakes Size: <400 ím	–	Feeding rate, hydra morphological scores & hydranth number↓	Murphy and Quinn, 2018

SOD: superoxide dismutase; D-Lac: d-lactate;IL-1α: interleukin-1α;SGR: specific growth rate; HSIs: hepatosomatic index; AChE: acetylcholinesterase; GOT: aspartate transaminase; GSH: glutathione; GPx: glutathione peroxidase: CAT: catalase; GPT: alanine aminotransferase; ERK: extracellular signal-regulated kinase; AKT: protein kinase B; MEK: mitogen-activated protein kinase; cyp1a: cytochrome P450 enzyme 1a; vtg1: vitellogenin 1; RBC's: erythrocytes count; Hb: hemoglobin concentration; Ht: hematocrit; MCHC: mean corpuscular hemoglobin concentration; WBC's: total white blood cells count; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; PCBs: polychlorinated biphenyls; BFRs: brominated flame retardants; PFCs: perfluorochemicals; chrna1: neuronal acetylcholine receptor subunit α-1; ef1α: elongation factor 1-α; esr2: estrogen receptor 2; gstp1: glutathione-S-transferase Pi 1; ngn1: neurogenin 1; prdx1: peroxiredoxin-1; PQ: paraquat; ALP: alkaline phosphatase; CPK: creatine phosphokinase; LDH: lactate deshydrogenase; Pepckc: cytosolic phosphoenol pyruvate carboxykinase; Gk: glucokinase; PK: pyruvate kinasa; HK1: hexokinase1; Aco: acyl-CoA oxidase; Cpt1: carnitine palmitoyltransferase1; Fabp6: fatty acid binding protein 6; Dgat: diacylgycerol acyltransferase; Acc1: acetyl-CoA carboxylase1; SREBP1α: sterol regularotry element binding protein 1α; Fas: fatty acid synthase; Apo: apolipoprotein; PPARγ: proliferator-activated receptor γ; EROD: ethoxyresorufin-O-deethylase; mt1: metallothionein 1; mt2: metallothionein 2; tnfa: tumor necoris factor α; il1b: interleukin 1 β; ifng1: interferon γ-1; ROX: roxithromycin; sod1: superoxide dismutase 1; sod2: superoxide dismutase 2; nfe2l2: nuclear factor erythroid 2-related factor 2; gst-4: glutathione S-transferase 4; ChE: cholinesterase; IDH: isocitrate dehydrogenase; LPO: lipid peroxidation; il1a: interleukin 1 α; EE2: α-ethynylestradiol; zfrho: rhodopsin; zfblue: blue opsin; sod3: superoxide dismutase 3; Cxcr5: chemokine (C-X-C motif) receptor 5; Tnfsf13b: tumor necrosis factor ligand superfamily member 13b; Casp3: caspase 3; TG: transgenerational; GST: glutathione-S-transferase.

made up of a variety of plastic polymers (polyamide, polyethylene, polypropylene, or polyvinyl chloride), which may cause contamination of the sample.

Before characterizations being carried out, isolation and extraction processes are needed because organic matters and other impurities are mixed with MPs samples. Filtering or sieving is the most frequent method in separation of microplastics from water samples and for the supernatant containing plastics from density separation of sediment samples (Manalu et al., 2017; Sruthy and Ramasamy, 2017; Khalik et al., 2018; Kosore et al., 2018; Pivokonsky et al., 2018; Schmidt et al., 2018; Collicutt et al., 2019; Ding et al., 2019; Bucol et al., 2020). It can be performed with only one sieve or with a series of sieves. The number of sieves used, and their mesh sizes depend on the sieving goal, such as selection of a specific MP size range. Smaller pore or mesh size can cause organic and mineral clogging. Meanwhile, larger pore or meshes can lose small sized microplastics, leading to an underestimation of the abundance of microplastics. Thus, a standardized pore or mesh size should be defined to allow comparison between works, even though this is sometimes dependent on protocol constrains. For their quantification, visual identification is one of the most used and widely available methods, even if followed by chemical characterization (Vermaire et al., 2017; Gray et al., 2018; Sighicelli et al., 2018; Di and Wang, 2018; Khalik et al., 2018; Bucol et al., 2020). However, there are many disadvantages with this method, such as wide variations between observers, high time consuming and low reliability (Lavers et al., 2016). Therefore, visual identification is not accurate enough and it may cause underestimation (e.g. white fragments) or overestimation (e.g. biologic material confused for black fragments) of microplastics abundance.

3.1.2. Factors affecting dispersal of MPs

Their inherent properties, such as small size and low density, let MPs be transported over long distances, via wind and water movement. However, these physical forces differ according to spatial scale. For example, it is suggested that on large scales, wind-driven currents and geostrophic circulation can influence the movement of MPs in marine areas (Ballent et al., 2012; Cózar et al., 2014). Meanwhile, at smaller spatial scales, experiments have shown that wind-driven mixing affects the spatial distribution of MPs (Kukulka et al., 2012; Eerkes-Medrano et al., 2015).

In freshwater environments, density may also affect the buoyancy and vertical distribution of MPs. Overall, it is suggested that low-density MPs tend to be found in the surface, while high-density MPs tend to appear in deep seas and benthic organisms (Eerkes-Medrano et al., 2015). However, their distribution and diffusion can be affected if particle density is altered by adsorption of other contaminants, biological fouling, or by the exchange of particles from high-salinity to lower-salinity waters due to overflow tidal. Shape and texture may also influence the MPs transport. For example, fibers are more likely to experiment biofouling, so these particles spend less time in surface waters than spherical particles, which tend to increase settling velocity.

The driving factors affecting the migration and diffusion of MPs are not only related to their inherent characteristics but also by environmental

Table 3
Uptake of MPs in commercial marine seafood included in FAO List-2016.

Commercial specie	Samples containing MPs	MPs concentration (items/individual)	MPs composition	MPs shape	MP size range (μm)
Clupea harengus	2%	4	PE, PP, PET & styrene acrylate	Fibers & fragments	>1000
Decapteru smacrosoma	29%	0–21	–	Fragments & styrofoam	>500
Decapterus muroadsi	80%	1–5	PE	Fragments	5000
Engraulis japonicus	77%	15	PE & PP	Fragments, bead, filaments & foam	10–500
Gadus morhua	1.4% - 18.8%	0–2	PE, PS, PU PP, PET & styrene acrylate	Fiber, fragments & film	1000 - >20,000
Micromesistius poutassou	51.9%	1.8–2	PA, PS, LDPE, rayon & acrylic	Fibers, fragments & beads	1000–2000
Sardinella longiceps	60%	–	–	Fragments	500–3000
Sardina pilchardus	19%	0.81–2.75	PE, PET, PS, PVC, nylon & PP	Fragments, pellets & film	10–5000
Scomberomorus cavalla	62.5%	2–6	Resin	Pellets	1000–5000
Scomberj japonicas	3.3%–71%	0.03–10.25	PP, PE & alkyd resin	Fibers, fragments & hard plastic	9.07–4810
Scomber scombrus	31% - 30.8%	0.32–4	PP, PE & alkyd resin	Fibers, fragments & film	217–5000
Sprattus sprattus	6% - 52%	0.26–0.68	–	Fibers & fragments	100 - >5000

(Data source: Foekema et al., 2013; Lusher et al., 2013; Sulochanan et al., 2014; Avio et al., 2015; Rochman et al., 2015; Neves et al., 2015; Liboiron et al., 2016; Miranda and de Carvalho-Souza, 2016; Tanaka and Takada, 2016; Bråte et al., 2016; Rummel et al., 2016; Ory et al., 2017; Güven et al., 2017; Ory et al., 2018; Beer et al., 2018).

factors such flow velocity, matrix type and seasonal variability. For example, decreased flow velocity makes MPs to settle, producing an increase in the concentration of plastic particles in the area (Castañeda et al., 2014; Ding et al., 2019). River morphology as well as vegetation is some environmental factors that may affect flow velocities and therefore influence the transport of microplastics. Corcoran et al. (2019) for instance, demonstrated that the sediment samples collected along the straight river channel contained less microplastics than those collected from the inner and outer bends. On the other hand, riparian or aquatic vegetation helps to capture suspended particles from the water and hold sediments by the roots, reducing the mobility of microplastics, and leading to their settlement in the water column (Wu et al., 2020).

Regarding seasonal variability, Ben-David et al. (2021) studied the influence of seasonal variation in the MP distribution in a domestic wastewater treatment plant. According to their results, the variations in MP particles and fibers abundances between different seasons may reflect the higher contribution of terrestrial runoff during the winter season, while the lower rainfall in other seasons means domestic MPs sources dominate the raw wastewater. Another study that also demonstrated the seasonal variability is the one carried out by Hitchcock (2020). They showed that upstream sites had a higher abundance on microplastics on the day of the storm compared to the downstream sites. However, in the days after the storm microplastic abundance was higher at the downstream sites. These differences may be due differences in particle residence between sites during the storm. Likewise, Veerasingam et al. (2016) and James et al. (2021) demonstrated that the strong monsoon winds, from June to September and from October to November, of the Indian coastal play a crucial role in the transport and deposition of microplastics. Thus, it is suggested that a substantial component of microplastic input to the world's ocean occurs specifically during rain and storm events.

Matrix type may also influence the abundance and distribution of MPs. For examples, it is believed that the concentration of MPs in urban water bodies is higher than in any other water bodies. However, recent studies have revealed that the concentration of microplastics on glaciers or snow is surprisingly higher than even urban water bodies, even though microplastics are not directly used or produced near glaciers (Bergmann et al., 2019; Kelly et al., 2020). This may be attributed to a net accumulation of microplastic during snow deposition with limited opportunity to be washed off. In contrast, in urban locations, MPs can be accumulated and washed off by surface runoff. A higher concentration of microplastics in glaciers indicates that transport via wind is a significant pathway to distribute microplastics in the environment. Thus, future studies should examine the mechanism of wind-driven transport of microplastics in remote locations and their impact on the glacier ecology.

3.2. Toxic effects of MPs

3.2.1. Neurotoxicity and behavioral changes

MPs have shown to induce a lethargic swimming and feeding behavior in fish, mussels and nematodes, under severe overload situations. Chen et al. (2017) for instance demonstrated that the catalytic capacity of acetylcholinesterase (AChE) on zebrafish larvae was suppressed, after an exposure to 1 mg/L of PS-MPs. AChE enzymes are essential to cholinergic neurotransmission in neuromuscular junctions and cholinergic brain synapses. Thus, the inhibition of AChE activity may cause a significant increase and accumulation of ACh in the synaptic cleft, which results in over-stimulation of receptors and ultimately to paralysis and death. Although, this AChE activity inhibition has been also reported in other aquatic organisms, such as *Oreochromis niloticus, Artemia franciscana, Dicentrarchus labrax*. Ferreira et al. (2016) reported that MPs did not induced any significant effects on the catalytic capacity of AChE in common goby exposed to 184 μg/L of PE-MPs for 96 h. They suggested the absence of AChE inhibition to the large size of the fish, proposing that MPs effects on AChE are grater in smaller fish. Future works should elucidate the influence of body size, age and other potential factors that could influence the effects of MPs on AChE activity on aquatic organisms.

In addition to the inhibition of AChE, MPs can also increase cellular oxidative stress by affecting antioxidant defense responses and consequently leading to lipid peroxidation (LPO). LPO in the brain can induce the disruption of membranes of presynaptic vesicles triggering an important increase levels of neurotransmitters into synaptic cleft (Hilfiker et al., 1999). LPO damage in gill, liver and muscles has been widely documented in several fish species (Ferreira et al., 2016; Wen et al., 2018) and other aquatic species (Yu et al., 2018; Oliveira et al., 2018; Guilhermino et al., 2018). However, it should be mentioned that only Barboza et al. (2018a, 2018b) have reported the LPO damage in the brain of one fish (*Dicentrarchus labrax*) exposed to a mixture of MPs (0.26 and 0.69 mg/L) and Hg (0.010 & 0.016 mg/L) for 96 h. Further works should evaluate LPO damage in the brain with other aquatic species and under realistic conditions.

Lei et al. (2018a, 2018b) evaluated the expression of unc-1, unc-47 and dat-1, genes involved in motor modulation, and concluded that MPs may induce a selective neurodegeneration on *Caenorhabditis elegans* after 3d of exposure to 1 mg/L of PS. This because MPs significantly damage cholinergic and GABAergic neurons, but no changes were found in dopaminergic neurons. As, nematodes lack of blood brain barrier (BBB) and MPs have more chances to interact with neurons, more mechanisms of neurotoxicity need further research.

Finally, Yin et al. (2018) suggested MPs could induce abnormal behaviors in fish due to the accumulation of MPs in the GI tract. The continuous ingestion of MPs may cause a lumen distention of the intestine, eventually leading to an intestinal blockage. Thus, long-term exposure to microplastics in the environment could affect the health and growth of the fishes by influencing their nutrition. Considering the possibility that differences in morphology and physiology may influence the MPs accumulation in the GI tract of aquatic organisms, more complete tests including a final plastic-free period should be conducted to examine the elimination of MPs in freshwater fish in future works.

3.2.2. Histopathological damage, inflammation and oxidative stress

Rainieri et al. (2018) demonstrated that LDPE rounded plastic particles alone did not produce any significant effect on zebrafish adults fed with this MP for 3 weeks. Results that are in agreement with previous studies. Karami et al. (2017b) for instance, demonstrated zebrafish larvae did not show any significant change on oxidative stress biomarkers, after an exposure to 5, 50 or 500 μg/L of LD-PE fragments for 20 days. Analogously, no histopathological changes and no significant differences on oxidative stress bio markers were found in the bivalves (*Corbicula fluminea*) exposed to a mixture of florfenicol (1.8 and 7.1 mg/L) and MPs (0.2 and 0.7 mg/L) for 96 h (Guilhermino et al., 2018). However, all these studies are not in agreement with the results reported by other authors. Lu et al. (2018) for instance, demonstrated that the sub-chronic exposure of adult zebrafish to a mixture of PS-MPs (20 - 200 μg/L) and Cd (10 μg/L), promoted the generation of reactive oxygen species (ROS), producing a significant decrease in the activity of GSH and SOD. Furthermore, functional genes related to oxidative stress (sod1, sod2 and nfe212) were down regulated. Similar results, were described on juvenile *Eriocheir sinesis*, in which a subchronic exposure to PS microspheres (40–40,000 μg/L) inhibited the activities of SOD, CAT, GST, GSH and GP and increased the malondialdehyde (MDA) content in the hepatopancreas (Yu et al., 2018). The increase in MDA content suggest PS microspheres may be a potent inducer of reactive oxygen species (ROS), and that antioxidant enzymes in fish such as SOD are insufficient to counter against oxidative stress.

Previous studies have pointed out that discrepancies between these studies may be due to the different MPs chemical composition. However, Lei et al. (2018a, 2018b) investigated the toxic effects of five

common types of MPs (PA, PE, PP, PVC and PS) and discovered that chemical composition was not the key factor on the damage produced in zebrafish. Instead, they suggest toxic effects of MPs may be size-dependent, as a result of particles ability to go across the cell membranes. Thus, it is suggested that smaller-sized particles would be more toxic than larger-sized particles. However, the arguments for this assumption still remain inconclusive. For example, Lei et al. (2018a, 2018b) studied the effects that PS particles of different diameter sizes, in nanoscale (100 and 500 nm) and microscale (1.0, 2.0, 5.0 μm), may induce in *Caenorhabditis elegans* exposed to 1 mg/L of this MP. According to their results, 1.0 μm PS particles produced the biggest toxicity damage in Caenorhabditis elegans. Similarly, Lu et al. (2016) demonstrated larger-sized MPs (5 μm) induced higher activities of SOD and CAT than smaller-sized (70 nm) particles in adult zebrafish exposed to 20 mg/L of PS-MPs for 7d. On contrary, Elizalde-Velázquez et al. (2020) assessed the tissue translocation of PS-MPs in *Daphnia magna* exposed to 20 and 2000 particles/mL of this plastic, and found that 6 μm PS particles did not translocate to other organs. This is surprising, because previous studies have reported translocation of plastic particles in *Daphnia magna* tissues (Cui et al., 2017; Chae et al., 2018). However, these studies used plastic particles with sizes around 0.02–0.06 μm. This can be explained by the gut structure of arthropods, which contains a chitinous layer that is only permeable to particles with a diameter no larger than 300 nm (Elizalde-Velázquez et al., 2020). Taken together, all this information suggests plastic particles size is an important feature for the production of toxic effects on the different organisms. However, the tissue structure and anatomy of each organisms play and important role in the severity of the damage that these particles can produce.

Another crucial feature that influence the toxic effects produced by plastic particles is the shape. According to Kooi and Koelmans (2019), the most abundant shape of MPs in water and sediment is fibers (48.5%) followed by fragments (31%), beads (6.5%), films (5.5%) and foam (3.5%). Nevertheless, most of the studies have been carried out with beads, which are not readily found in aquatic ecosystems. Although some studies have not found differences in ROS generation between spherical and irregular MPs (Choi et al., 2018), other authors have pointed out fibers induce more severe toxic effects than fragments and beads. Qiao et al. (2019a, 2019b) for instance, demonstrated fibers caused higher SOD activity in the gut of zebrafish than beads and fragments. They suggested this may be due to the longer residence time, higher accumulation and larger physical damage produced by fibers. In addition, Jabeen et al. (2018) demonstrated fibers were the only plastics particles ingested by Carassius auratus, inducing several damage in the intestinal lining of goldfish. Meanwhile, fragment and pellet plastic particles were chewed and expelled by fish, producing different impacts on jaws. Thus, it can be suggested that smaller particles are passively ingested by fish and can be transferred to other organs, while larger particles with hard and sharp edges are not ingested. However, further works should make an effort to perform toxicological characterization of the different types of plastic considering all their inherent features, as well as the environmental conditions in which they can be found.

ROS can cause adverse effects in a variety of organic molecules, such as lipids, proteins, and nucleic acids, triggering an inflammatory process and subsequently the cell death by necrosis or apoptosis. Lu et al. (2018) demonstrated that PS-MPs may up-regulate the expression of nfa, il1b and ifng1–2, genes associated with inflammatory responses, on different tissues (livers, guts and gills) of zebrafish, exposed to a mixture of MPs (20 - 200 μg/L) and Cd (10 μg/L) for 3 weeks. Additionally, Choi et al. (2018) showed that the exposure of sheepshead minnow (*Cyprinodon variegatus*) to 50 and 250 mg/L of PE irregular MPs increased the transcriptional levels of Casp3 and Tp53. Similarly, Chinese mitten crabs exposed to several concentrations of PS (40–40,000 μg/L) for 21 days, showed a significant increase in the expression of p38, as well as a significant down-regulation in AKT and MEK (Yu et al., 2018). Casp3, Tp53, p38, AKT and MEK are important genes that regulate cell survival and proliferation (Cheng et al., 2015). Furthermore, p38 is one of the main components of the MAPK signaling pathway, which also plays important roles in cellular responses to extracellular stimuli (Cargnello and Roux, 2011). Thus, it is suggested MPs are likely to accelerate cell apoptosis by mediating the MAPK signaling pathway. However, future studies are needed to identify the effects of MPs on this signaling pathway.

Under inflammatory conditions, oxidative stress leads to the opening of inter-endothelial junctions and promotes the migration of inflammatory cells across the endothelial barrier. Inflammatory cells not only help in the clearance of pathogens and foreign particles but also lead to tissue injury (Mittal et al., 2014). Since MPs induce oxidative stress and antioxidant enzymes in aquatic organisms are insufficient to counter against it, MPs are likely to produce histopathological damage. Lei et al. (2018a, 2018b) for instance demonstrated that a 10 d exposure to several concentrations (0.0001–10 mg/L) of PA, PE, PP and PVC particles induced intestinal damage on zebrafish, mainly characterized by cracking of villi and splitting of enterocytes. In agreement with these results, Qiao et al. (2019a, 2019b) pointed out that three different shapes of MPs produced diverse histopathological changes in the gut of zebrafish, including vacuolization, cilia defects and mast cells. Furthermore, they concluded fibers lead to more serious intestinal epithelial cell necrosis than fragments and beads.

Until now we have only discussed about the toxicity induced by MPs as plastic particles alone. However, MPs raise wide concerns not only as particles per se but also as a vector for other contaminants in aquatic environments. It has been demonstrated that due to their small particle size, large specific surface area, and hydrophobicity, MPs can sorb and interact with other common environmental contaminants. Thus, MPs may affect the absorption, distribution, metabolism and excretion of these organic pollutants in aquatic organisms, which may result in unpredictable ecological risks. For example, Zhang et al. (2019) demonstrated that a co-exposure of MPs (1, 10, 100 μg/L) and roxithromycin (ROX; 50 μg/ L) during 14 days may result in alleviation of oxidative damage to *Oreochromis niloticus*. On contrary, a MPs (0.26 and 0.69 mg/L) co-exposure with mercury (0.010 and 0.016 mg/L) during 96 h caused a significant increase of LPO levels in brain and muscle (Barboza et al., 2018b). However, these effects were not induced in a concentration-dependent manner. In agreement with these results, Guilhermino et al. (2018) concluded that the magnitude and diversity of effects induced by mixtures containing the lowest or the highest concentrations of MPs and florfenicol were different. Although the importance of combined MPs and traditional organic pollution has been emphasized, information on the interactive effects between MPs and emerging contaminants, is still limited. More knowledge on such interactions is needed to assess the risks and increase the safety in the use and management of microplastics and other common environmental contaminants.

3.2.3. Biochemical and hematological changes

Although there are many evidences about hematological responses of fish exposed to environmental pollutants, the data about the effects of MPs on blood system of fish is still limited. Haghi and Banaee (2017) demonstrated that the activity of creatine phosphokinase (CPK) and alkaline phosphatase (ALP) was increased in *Cyprinus carpio,* after an exposure to 1 and 2 mg/L of PE-MPs for 21 days. Furthermore, gamma-glutamyl transpeptidase (GGT) activity, and blood levels of total protein, albumin, globulin, cholesterol and triglycerides were significantly decreased in fish. Similarly, Hamed et al. (2019) demonstrated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities, as well as glucose, creatine and uric acid levels were significantly increased in the blood of Nile tilapia after 15 days of exposure to 1, 10 and 100 mg/L of MPs particles.

AST, ALT, ALP, and CPK are intracellular enzymes found in different organs of fish. The release of these enzymes into the blood stream and their increased levels, suggest MPs induce damage to liver, muscle, kidney, heart and severe damage to central nervous system of fish.

Furthermore, alterations in biochemical parameters such as glucose, total protein, albumin, globulin, creatinine, cholesterol, and triglyceride are indices of physiological functions in different organs of fish. Thus, it is suggested that changes in these clinical parameters induced physiological disorders in fish exposed to MPs.

In addition to the biochemical parameters, hematological variables have become promising biomarkers in measuring the effects of aquatic pollution in fish. Hamed et al. (2019) for instance, demonstrated that several concentration of MPs (1, 10 and 100 mg/L) significantly reduced erythrocytes count, blood hemoglobin concentration (Hb), hematocrit (Ht), mean corpuscular hemoglobin concentration (MCHC), platelets and total white blood cells counts (WBCS), and percent of monocytes in Oreochromis niloticus after 15 days of exposure. Together these results suggest high concentrations of MPs may induce anemia and affect the immune system of fish, producing an important impact in animal health and defense. Anemia may be attributed to RBCs lysis and/or suppression of erythropoiesis owing to hematopoietic tissue damage (Wintrobe, 1978). Meanwhile, the decrease of total white blood cells counts (WBCs) may be due to the negative impact of MPs on lymphoid tissues of the exposed fish (Alkaladi et al., 2015). Furthermore, it has been pointed out that the immune system may be affected due to either the chemical substances that MPs might contain, absorb or release, which may be toxic (Rochman et al., 2013) or physically blocking the digestive organs, which decreases the absorption of nutrients and produces impairment of energy allocation (Cole et al., 2011). However, further research is needed to comprehensively understand the mechanisms by which these plastic particles induce physiological disorders, anemia and alterations in the immune system of fish. Furthermore, more biochemical and hematological studies are needed to predict possible chemical toxicity in human beings. This, because human hematopoietic cell renewal systems are similar in their principal structure and function to those of laboratory animals (Fliedner and Graessle, 2008).

3.2.4. Embryotoxicity

Scarce studies have been done to assess the effects of MPs on developmental life stages of fish. Originally, Manabe et al. (2011) pointed out that MPs of 50 to 500 nm of diameter might penetrate the chorion of *Oryzias latipes*, after their embryos were exposed to 10 mg/L of fluorescent plastic particles. Few years later, in disagreement with these results, Van Pomeren et al. (2017) reported that concentrations of 25 and 50 mg/L of PS-NPs larger than 50 nm of diameter were not capable of pass through the chorion of developing zebrafish. Nonetheless, they found MPs were capable to be distributed through the intestine after exposure of embryos via the dermal + oral route(while the mouth was open). Thus, it is suggested that the most likely exposure route is the gastrointestinal tract as direct dermal exposure induced no uptake of these particles. Finally, several concentrations of green fluorescence PS-NPs (0.1, 1, and 10 ppm) were used to evaluate the uptake and distribution of these particles in zebrafish embryos and early larval stages. Results provided strong evidence that PS-NPs of 51 nm of diameter are taken up by developing zebrafish to be subsequently accumulated in the yolk sac, and then migrate to gastrointestinal tract, gallbladder, liver, pancreas, heart and brain (Pitt et al., 2018). In agreement with these results, Li et al. (2020) revealed that multiple concentrations of fluorescent MPs (0, 2, 20, 200 μg/L) with a diameter of 10 μm gradually accumulated on the egg shells of *Oryzias melastigma*, and reached a plateau during 5–10 days after exposure. This may be due to the adsorption of MPs on the sticky chorion reached a saturation point.

Since MPs were shown to be taken up by zebrafish embryos, it was expected that plastic particles might exert toxic effects on these aquatic organisms. However, Pitt et al. (2017) demonstrated PS-NPs had no significant effect on mortality, hatching success, deformities, or pericardial area of zebrafish. Instead zebrafish embryos exposed to PS-NPs only exhibited bradycardia and hypoactivity, after 120 h of exposure. Until now, it is suggested MPs are localized into cells and are not membrane bound, creating potential for interactions with cardiac sarcomeres, leading to an abnormal heart rate. However, future studies are needed to determine the mechanism by which MPs reduce heart rate. Similar results were found on marine medaka, in which MPs significantly decreased the heart rate of embryos at 10 days post fecundation (Li et al., 2020). However, in this study, MPs were also able to reduce the hatching rate and delayed the hatching time of embryos. This may be due to the adsorption of MPs on egg shells could reduce the intake of oxygen and nutrients by blocking the spiracles and channels.

3.3. Major food sources polluted with MPs

One of the major MPs entry points into the human system is represented by the ingestion of contaminated food, with an estimated intake of 39,000 to 52,000 items/person/year, of which 37 to 1000 are from sea salt, 4000 are from tap water and 11,000 are from shellfish (Prata et al., 2020).

3.3.1. Table salt

Sea salt represents the main source of MPs to table salt due to the high level of MP pollution in coastal zones. However, MPs may also be introduced in table salt during collection, transportation, drying, or packing processes (Yang et al., 2015). Therefore, more attention should be paid to food production, because other commercial foods may also be produced and packed in a similar manner as that for table salt.

MPs have been widely documented in table salt from several brands all over the world, reaching concentrations of up to 2.0×10^4 items/kg (Fig. 1) (Iñiguez et al., 2017; Renzi and Blašković, 2018; Gündoğdu, 2018; Seth and Shriwastav, 2018; Lee et al., 2019). However, the differences in analytical method used, extraction reagent, and filter pore size lead to low comparability of the results among different studies. Australia, France Iran, Japan, Malaysia, Zealand, Portugal and Africa, for instance reported lower abundance of MPs in table salt. This could be explained by the usage of filters with larger pore size (149 μm), allowing smaller-sized MPs to escape in the filtration process and resulting in underestimated MP abundances (Karami et al., 2017a). Furthermore, some authors have pointed out that larger salt samples may also clog membranes by excessive impurities, such as soil and organic matter (Gündoğdu, 2018; Karami et al., 2017a). Thus, there is an urgent need to standardize an analytical method for the quantification of MPs in table salt. (See Figs. 2–4.)

Among the reviewed works, 8 studies used μ-FTIR spectroscopy as the identification method (Yang et al., 2015; Iñiguez et al., 2017; Kosuth et al., 2018; Kim et al., 2018; Renzi and Blašković, 2018; Seth and Shriwastav, 2018; Lee et al., 2019; Renzi et al., 2019) while only 2 studies used μ-Raman spectroscopy (Karami et al., 2017c; Gündoğdu, 2018). Raman spectroscopy allows the characterization of microplastics of <20 μm, but may be limited by weak signals and fluorescence interference, dependent on material characteristics such as color, biofouling and degradation. Meanwhile, micro-FTIR detects MPs between to 20 to 300 μm and provide high-resolution map without a preselection step (Shim et al., 2017; Prata et al., 2019). Since different studies have used diverse membranes with pores size ranging from 0.2 to 149 μm, we suggest the use of a membrane with a pore size of 5 μm, followed by identification using μ-Raman spectroscopy, which allows the identification of MPs of up to 1 μM, considered as the lower size limit of MPs as per definition (Käppler et al., 2016).

In order to achieve the standardization of microplastics detection methods in table salt, several factors must be taken into account. First, the sample quantity as well as the brand type. Based on the results of several studies, 100–250 g of salts per sample and three or more brands are recommended to prevent either overestimation or underestimation of MP abundances in salt from a region (Yang et al., 2015; Renzi and Blašković, 2018). Second, the exclusion of the digestion process and the density separation step. Although, some studies have used H2O2 to digest organic matter and/or NaI to isolate MPs from table salt samples (Kim et al., 2018; Gündoğdu, 2018; Seth and Shriwastav, 2018), some others have suggested that the number of organic particles and impurities in

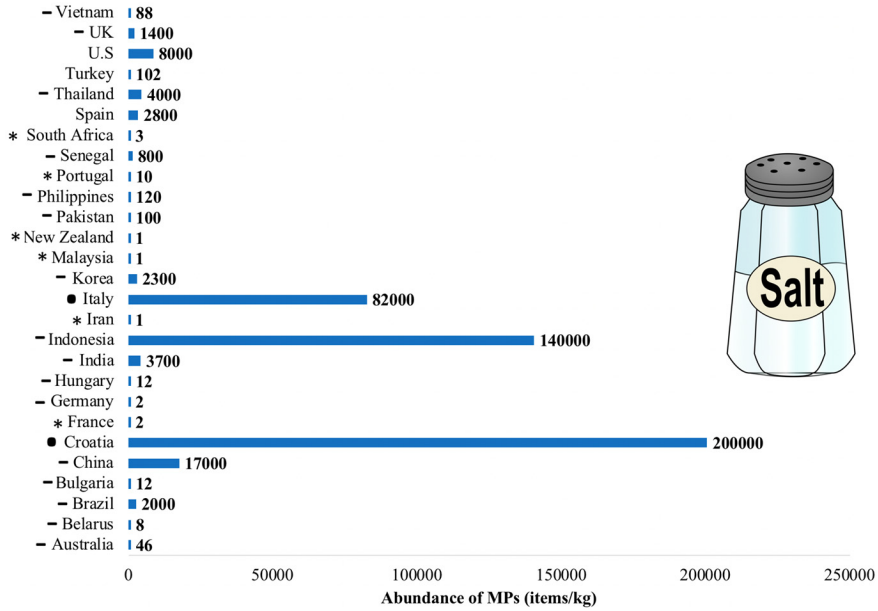

Fig. 1. Maximum concentration of MPs (items/kg) reported in table salt by country. * countries that used membranes with a pore size of 149 μm; — countries that used membranes with a pore size of 2.7 μm; • countries that used membranes with a pore size of 0.45 μm. U.S and Spain used membranes with a pore size of 11 μm and 5 μm, respectively. (Data source: Yang et al., 2015; Karami et al., 2017c; Iñiguez et al., 2017; Kosuth et al., 2018; Kim et al., 2018; Renzi and Blašković, 2018; Seth and Shriwastav, 2018; Gündoğdu, 2018; Lee et al., 2019; Renzi et al., 2019).

table salt is relatively low (Karami et al., 2017c). Furthermore, the use of these reagents may interfere with MPs identification. Therefore, the priority option is to filter all solutions after salt sample dissolution.

3.3.2. Drinking water

Since MPs have been widely found in freshwater bodies, it is believed that MPs in drinking water originate from polluted freshwater resources, such as lakes, rivers, canals and groundwater. However, Koelmans et al. (2019) found groundwater has lower concentrations of MPs compared with tap water and bottled water, suggesting that MPs found in drinking water derived from packing process. In agreement with these results, Schymanski et al. (2018) demonstrated that the majority types of MPs in drinking water were PET and PS which may be derived from the bottles. Thus, packing processes could be an important source of MPs for bottled water.

Few studies have reported the abundance of MPs in drinking water (Mason et al., 2018; Ossmann et al., 2018; Mintenig et al., 2019) and as same as in table salt, concentrations varied due to use of membranes with different pore sizes. For example, in two studies carried out in bottled water from Germany, MPs abundances were much higher ($2.6–6.3 \times 10^3$ items/L) with 0.4 μm pore size membranes, than those ($0.1–1.2 \times 10^3$ items/L) using 3 μm pore size membranes (Ossmann et al., 2018; Schymanski et al., 2018). In addition to pore size of filter membranes, the use of different identification methods is another factor affecting the abundances of detected MPs. For instance, MPs in tap water have been often analyzed by μ-FTIR, detecting MPs of 20 μm or higher, whereas MPs in bottled water have been normally examined

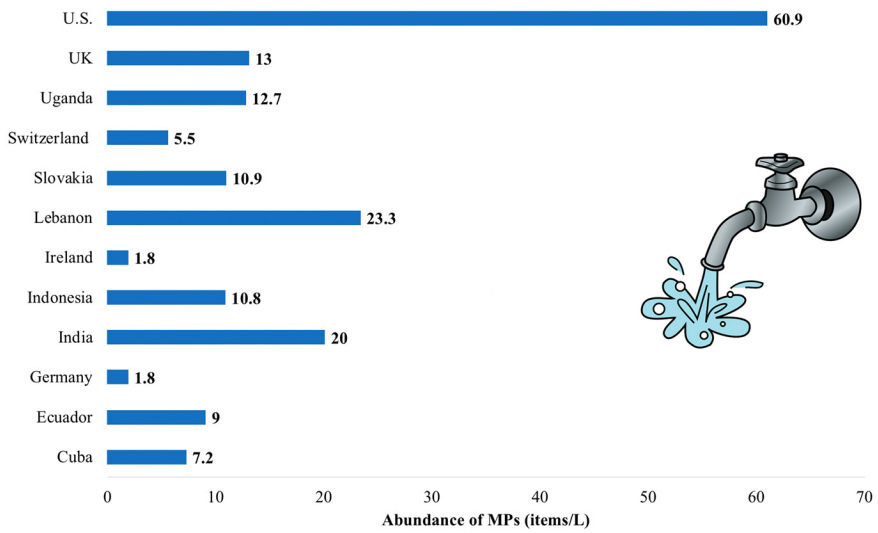

Fig. 2. Maximum concentration of MPs (items/L) reported in tap water by country. All countries used membranes with a pore size of 2.5 μm and μ-FTIR as identification method. (Data source: Kosuth et al., 2018).

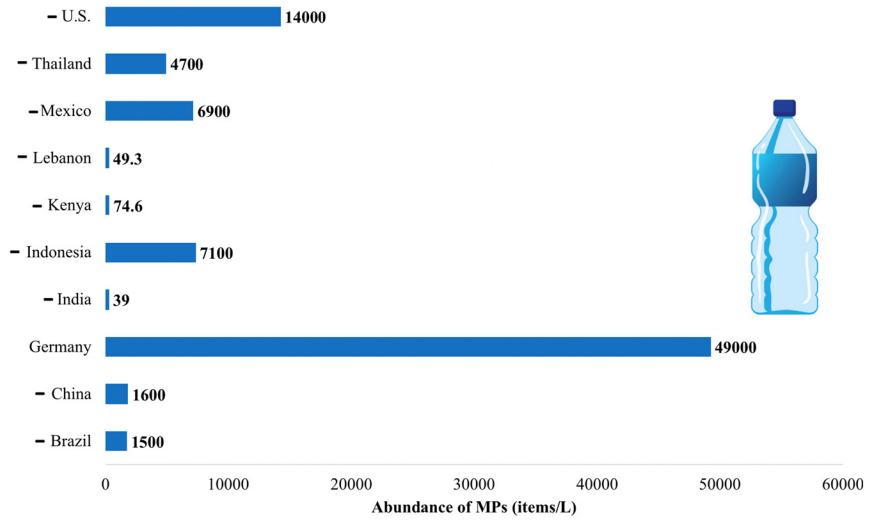

Fig. 3. Maximum concentration of MPs (items/L) reported in bottled water by country. - countries that used membranes with a pore size of 1.5 μm and μ-FTIR spectroscopy as identification method. Germany used membranes with a pore size of 0.4 μm and 3.0 μm, and μ-Raman as identification method. Italy reached a maximum concentration of 5.4×10^7 items/L so could not be graphed. (Data source: Ossmann et al., 2018; Mason et al., 2018; Schymanski et al., 2018; Zuccarello et al., 2019).

by μ-Raman, sensing smaller MPs. Thus, MPs abundance in samples where μ-FTIR was used can be underrated due to the instrumental incapability of detecting smaller MPs.

The sampling and treatment methods used for MP detection in drinking water are similar and have been elaborated by Koelmans et al. (2019). Following we will review some considerations and precautions that should be taken into account. Unlike surface water, for tap water a greater sample volume is proposed, with a minimum volume of 1000 L, while for drinking water the minimum volume vary from 1 L to 10 L, depending on the large of the plastic particles to analyze. As bottled water usually is provided in volumes smaller than 10 L, this would imply the need to either analyze multiple bottles

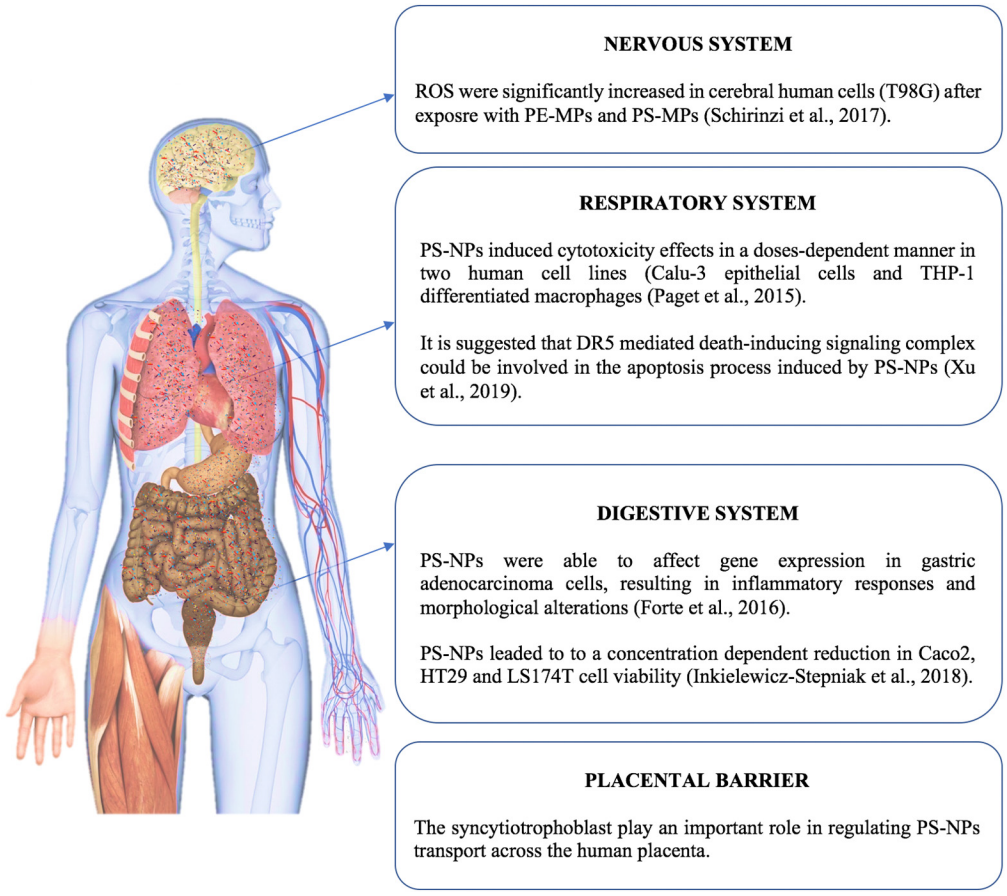

Fig. 4. Overview of the toxic effects that MPs and NPs may induce on different human derived cells.

(Mason et al., 2018; Schymanski et al., 2018; Zuccarello et al., 2019) or to treat the total volume of multiple bottles as one sample (Ossmann et al., 2018). In the specific case of tap water, some studies rinse jars, bottles or other materials with targeted water before their transfer or storage (Kosuth et al., 2018). However, particles from that rinsing water could easily stick to surfaces and remain, which thus would lead to contamination of the actual sample.

For surface water, sediments and WWTPs samples a digestion step should be performed to assure the quality of visual inspection and subsequent polymer identification. Nonetheless, tap and bottled water do not require a digestion step and thus next step is sieving or filtration. In the reviewed works, the pore size for membranes used in bottle water samples varied from 0.4 μm to 3.0 μm, which was evidenced by the enormous differences in MP concentration among samples. Since most of the MPs had a smaller size than 1.5 μm (Ossmann et al., 2018), most small MPs may be lost if the solution is filtered with 3 μm pore size filters. Therefore, standardization of membrane pore sizes are necessary for meaningful assessment of MP abundances.

3.3.3. Sea food

The occurrence and the type of ingested MPs, as well as their distribution along the trophic levels of the marine food chain depend on feeding strategies of each organism.

3.3.3.1. Fish. Influenced by their feeding strategies, some fish have a highly selective diet and only rarely may eat plastics, while other may hunt and feed on a wide variety of prey making them more exposed to the ingestion of MPs. Anchovies, for instance are selective feeders, while sardines are unable to select the ingested particles. Consequently, sardines, during the spawning period, may indiscriminately ingest small planktonic organisms and floating MPs migrating toward surface water (Renzi et al., 2019). In addition, feeding strategies may be influenced by seasons. For example, Scomberomorus cavalla and *Rhizoprionodon lalandii* showed a greater MP intake in October than March (Barboza et al., 2018c).

3.3.3.2. Bivalves. Commercial invertebrates may filter and retain MPs depending on plastic particle concentrations and size (Bouwmeester et al., 2015). Scallops, for instance retain large, long and dense MPs, whereas mussels and oysters excrete all or part of the ingested MPs, allowing their use as a depuration treatment. Although, there are no significant differences in MP content between wild and cultured mussels, wild mussels may also be exposed to MPs through the use of plastic ropes and nets (Santillo et al., 2017). In china, MPs concentrations in commercial bivalves varied from 2 to 11 items/g and from 4 to 57 items/bivalve.

3.3.3.3. Crustaceans. MPs uptake in crustaceans may be both accidental and also related to the active collection during feeding. Copepods and tiny shrimps, for instance may be exposed to MPs through plankton and suspended material, whereas lobsters and crabs are active hunters and may ingest MPs when they are fed with fish polluted with plastic strands (Bouwmeester et al., 2015).

3.4. Potential toxic effects of MPs on human health

Upon their ingestion, MPs may enter the gastrointestinal tract through endocytosis by M cells, translocate in tissue through paracellular transport and subsequently determine a systemic exposure (Cox et al., 2019a, 2019b).

There is evidence that synthetic particles smaller than 150 μm may cross the mammalian gastrointestinal epithelium. However, it is speculated that only 0.3% of these particles are absorbed, and only 0.1% of particles that are bigger than 10 μm should be capable of reaching both organs and cellular membranes (Barboza et al., 2018c).

Although none study has reported about toxic effects of MPs in the human body, several studies have suggested that high concentrations of these pollutants may induce toxic effects in different in vitro systems. Following, we describe some of the toxic effects that MPs may induce at different levels:

3.4.1. Digestive system

In a study carried out in gastric adenocarcinoma cells, Forte et al. (2016) demonstrated that 44 nm and 100 nm unmodified polystyrene nanoparticles are internalized by a clathrin-mediated endocytosis. Furthermore, after internalized, PS-NPs at a concentration of 10 μg/L were able to up-regulate the expression of IL-6 and IL-8 genes, resulting in inflammatory responses and morphological alterations, especially when smaller size are used. In agreement with these results, Inkielewicz-Stepniak et al. (2018) demonstrated that co-incubation of positively charged PS-NPs (20, 50 and 100 μg/L) with cell lines lead to a concentration dependent reduction in Caco2, HT29 and LS174T cell viability. These results were corroborated by optical microscopy where the morphology of cells appeared completely distorted. Thus, it is suggested that high concentrations of PS-NPs may cause cell death through apoptotic mechanisms involving caspase −3,-7 and − 9-mediated cytotoxicity (Bexiga et al., 2011).

Using two cell viability assays, CBT and MTT, Stock et al. (2019) demonstrated that high concentrations of 1 μm of diameter PS-MPs increased the cytotoxicity in three different in vitro systems (Caco-2, M-cells and goblet cells). However, they also carried out an in vivo study with mice, where these did not show any histologically detectable lesion and/or any inflammatory response, even though they were treated three times per week by oral gavage with a mixture of PS-MPs (1 μm, 4 μm and 10 μm) at a volume of 10 mL/kg/bw. Therefore, future studies are needed to elucidate in vivo MPs exposure in more detail.

3.4.2. Respiratory system

The effects of three perfectly characterized PS-NPs were investigated in two human cell lines (Calu-3 epithelial cells and THP-1 differentiated macrophages) using concentrations from 1 to 100 μg/ml (Paget et al., 2015). According to their results, only positively charged PS-NPs induced cytotoxicity in a doses-dependent manner, reaching a LC50 of 31 μg/mL for Calu-3 cells and 75 μg/mL for THP-1 macrophages. They explained that cytotoxicity effects may be due to the capacity of PS-NPs to induce DNA double strand breaks and/or the high depletion of GSH in both Calu-3 cells and THP-1 macrophages. Similarly, Xu et al. (2019) used A549 cells as a representative of and extracorporeal model to study the effects of PS-NPs on the viability and function of human lung cells. Their results demonstrated PS-NPs are internalized by non-specific phagocytosis. Furthermore, it is suggested that when A549 cells.

become saturated by internalized PS-NPs, a release process may be activated. Regarding cell viability, they demonstrated that at high concentrations, PS-NPs inhibit cell viability in a dose-dependent manner, while at lower concentrations the cell viability is affected in a size-dependent manner. This results is consistent with other reports of size-dependent effects for both PS-NPs and non-PS-NPs (Johnston et al., 2010). Since PS-NPs up-regulate the expression of DR5, as well as the expression of downstream apoptotic proteins of DR5 such as caspase-8, caspase-3, and caspase-9, it is suggested that DR5 mediated death-inducing signaling complex could be involved in the apoptosis process induced by PS-NPs (Xu et al., 2019). Together these results suggest that PS-NPs can cause definite damage and functional disturbance to human and mammalian respiratory system. However, more studies are needed to determine the risk factors associated with PS-NPs uptake. It is suggested to perform studies with co-culture exposures to better mimic the in vivo pulmonary barrier.

3.4.3. Nervous system

In order to better understand the cytotoxicity of MPs at cell level in terms of oxidative stress and cell viability, cerebral human cells (T98G) were exposed to several concentrations (50 μg/mL to 10 mg/L) of PE-MPs and PS-MPs (Schirinzi et al., 2017). According to their results,

none of the MPs lead to a significant reduction of cell viability, suggesting cytolysis was not produced. However, reactive oxygen species were significantly increased in T98G cells after exposure with both types of MPs. These results suggest oxidative stress may be an important mechanism by which MPs exert their toxicity at cell level.

3.4.4. Placental barrier

Although MPs toxicity in utero might not be a major concern yet, this must become more important as MPs may cross the human placental barrier. Grafmueller et al. (2015) used the ex vivo human placental perfusion model to analyze the transport mechanisms underlie the placental transfer of PS-NPs (50 to 300 nm). Their results demonstrated that PS-NPs accumulated in the syncytiotrophoblast of placental tissue. Thus, it is suggested that the syncytiotrophoblast is the key player in regulating PS-NPs transport across the human placenta. Furthermore, the main mechanism underlying this translocation may be based on an energy-dependent transport pathway. These results highlight the necessity of further studies that help to comprehensively understand the transport mechanism of NPs across the placental barrier, as NPs may induce embryotoxicity.

Overall, high concentrations of MPs are capable to increase the production of ROS on different human derived cells, leading to an inflammatory response and finally result in an apoptotic process. Nonetheless, these results can be misleading due to the influence of several factors, such as the intrinsic chemical composition of MPs. Lithner et al. (2011) for instance, produced a comprehensive hazard ranking of plastic polymers, based upon internationally agreed criteria for identifying physical, environmental, and health risks factors. According to that classification, polyurethanes, polyvinylchloride, epoxy resins, and styrene-containing polymers such as PS, were placed in the highest positions of the ranking. Meanwhile PE, polyvinyl acetate (PVA), and PP were classified as potentially less hazardous. Apart from the chemical nature, there are other factors inherent to the polymers which might also influence toxicity. Wright and Kelly (2017) for instance, pointed out that during the polymerization process, and subsequent processing of plastics, free radical are generated, acting as a common factor to promote the production of ROS. Furthermore, these free radicals readily increase their concentration in the particles due to dissociation of the C — H bonds induced by light exposure or interaction with transition metals during the weathering process (Gewert et al., 2015). Therefore, it is worthwhile noting that environmental photodegradation and biodegradation produces surface changes affecting their functional groups (e.g., -COOH, -NH2), which alter the toxicological profiles (Andrady, 2011). Other particle properties such as shape or surface charge, among others, were also identified as potential toxicity factors of MPs (Kim et al., 2016).

4. Conclusions

MPs are widely spread in the aquatic environments, thereby poising a real threat to freshwater and seawater organisms. Furthermore, trophic transfer and biomagnification processes represent a viable route for the input of MPs into the human body. Therefore, it is necessary to expand our knowledge about the risk that MPs pose to aquatic ecosystems and humans.

Although the studies regarding MPs occurrence in rivers, lakes, and reservoirs has increased in the past few years, the factors affecting abundance and distribution of MPs in freshwater environments remain very scare, especially in sediments. Thus, the external forces driving the MPs transport and diffusion in freshwater systems need to be further studied. Additionally, as there are still some inconsistencies in the description and comparison of MPs abundance, standardization of methods for sampling and measurement of MPs in aquatic environments are needed.

Since the distribution and abundance of MPs in aquatic systems are likely to increase with the growing input of plastic into the environment, future studies should be directed toward the treatment and prevention of MPs pollution. For example, the process that transform primary MPs into secondary MPs as well as the methods that prevent their decomposition and diffusion need to be further understood. Furthermore, further research thus is needed to assess the capacity of depuration from *Perna perna* as a tool for the removal of MPs from the environment.

Until now, it has been reported that, under overload situations, MPs may induce an abnormal and lethargic behavior, to promote the production of ROS, to induce anemia and affect the immune system of fish. However, further research is need in order to comprehensively understand the mechanisms by which MPs induce these toxic responses. In addition, as most of the studies have been carried out under extremely high exposure scenarios, more research about MPs toxic effects under realistic exposure scenarios are needed.

Finally, cytotoxicity of MPs on human derived cells has been assessed with PE and PS polymers. However, other polymers such as PET, PVC, PP and PA have been also found in various food and drinks of human consumption. Therefore, it is needed these polymers to be monitored and evaluated in the future. Furthermore, in order to better mimic the real exposure conditions humans to these pollutants, MPs particles collected from surface water and drinking water should be also evaluated in human derived cells, and/or use concentrations that better resemble real-life conditions.

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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