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## Occurrence, human exposure, and risk of microplastics in the indoor environment

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Microplastics (MPs) are a group of emerging contaminants that have attracted increasing scientific and societal attention over the past decade due to their ubiquitous detection in all environmental compartments. So far, most studies on MPs focus on characterizing their occurrence, fate, and impact in the aquatic environment. Therefore, very little is known about the magnitude, patterns, and associated risks of human exposure to MPs, particularly indoors. This is a significant research gap given that people spend most of their time (up to 90%) indoors, which is exacerbated over the past year by COVID-19 lockdown measures. Critical evaluation of the existing literature revealed the presence of MPs at higher concentrations in indoor air and dust (from homes and offices) compared to outdoors. This was attributed to several factors including: indoor MPs sources (e.g. furniture, textiles), increased deposition of atmospheric MPs indoors, and less atmospheric mixing and dilution compared to outdoor air. Current understanding is that indoor human exposure to MPs occurs *via* a combination of inhalation, ingestion, and dermal contact. Dietary intake was considered the major pathway of human exposure to MPs until recent studies revealed potential high exposure *via* inhalation. Moreover, exposure *via* inadvertent dust ingestion and dermal contact cannot be neglected, particularly for young children. This is alarming due to the potential toxic implications of MPs exposure. Early toxicological evidence indicates that small MPs (<20  $\mu\text{m}$ ) can cause oxidative stress and inflammation, while particles <5  $\mu\text{m}$  can be engulfed by cells and translocated to accumulate in different organs. Also, there is increasing concern over potential leaching of toxic chemicals used as plastic additives (e.g. plasticizers and flame retardants) upon exposure to MPs due to their large surface area. However, MPs exposure and risk assessment in humans is still in its infancy and more research is necessary to provide the knowledge base required for regulations to protect human health and environment against MPs.

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### Environmental significance

So far, most studies on Microplastics (MPs) focus on characterizing their occurrence, fate, and impact in the aquatic environment. Therefore, very little is known about the magnitude, patterns, and associated risks of human exposure to MPs, particularly indoors. This is a significant research gap given that people spend up to 90% indoors, which is exacerbated over the past year by COVID-19 lockdown measures. Critical evaluation of existing literature revealed the presence of MPs at higher concentrations in indoor air and dust compared to outdoors. Dietary intake was considered the major pathway of human exposure to MPs until recent studies revealed potential high exposure *via* inhalation. Moreover, exposure *via* inadvertent dust ingestion and dermal contact cannot be neglected, particularly for young children. This is alarming due to the potential toxic implications of MPs exposure. However, MPs exposure and risk assessment in humans is still in its infancy and more research is necessary to provide the knowledge base required for regulations to protect human health and environment.

## 1 Introduction

Plastic contamination is considered a global threat to human and environmental health. The substantial increase in the worldwide annual production of plastics from 2 million tonnes in 1950 to over 300 million tonnes in 2018 has led to high levels of environmental plastic pollution.<sup>1</sup> This is mainly due to the ability of plastics to accumulate in various environmental media owing to their resistance to chemical and/or biological

degradation.<sup>2</sup> Several types of polymers have been identified as the main sources of plastic pollution in different environmental compartments, including: polypropylene (PP), polyethylene (PE), polyethylene terephthalate (PET), polystyrene (PS), polyurethane (PUR), polyvinyl chloride (PVC), and polycarbonate (PC).<sup>3</sup> While larger plastic waste items present an imminent visible risk to the environment and biota, there is increasing concern over the environmental and health impacts of smaller plastic fragments. Based on size, plastics can be classified into five major categories: “nanoplastic” (<0.03  $\mu\text{m}$ ), “microplastic” (<0.5  $\mu\text{m}$ ), “mesoplastic” (0.5–5  $\mu\text{m}$ ), “macroplastic” (5–50  $\mu\text{m}$ ), and “megaplastic” (>50  $\mu\text{m}$ ).<sup>4,5</sup> Thompson (2006) was the first

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author to use the term “Microplastics (MPs)” for plastic particles such as fragments, pellets and fibres.<sup>6</sup> MPs is inclusive of all types of plastic polymers in different shapes with a longest dimension < 5 mm, including nanoplastics, which are <0.1 mm.<sup>7</sup> To further distinguish MPs from nanoplastics; Frias and Nash (2019) defined MPs as “synthetic solid particles or polymeric matrices, with regular or irregular shape and with size ranging from 1 µm to 5 mm, of either primary or secondary manufacturing origin, which are insoluble in water”.<sup>8</sup> Accordingly, MPs can have various shapes, such as, pellets, films, foam, fragments, and microbeads. Also, MPs can be classified into “primary” and “secondary” based on their origin. Primary MPs are those manufactured or released to the environment in the “micro” size. This includes microbeads used in cosmetics, microfibrils shed from clothing and other textiles upon washing, as well as micronized particles emitted from the wear of rubber tyres.<sup>9</sup> Secondary MPs are produced from the breakdown of larger plastics in the environment as a result of natural weathering processes including photo-, chemical-, and biological degradation.<sup>10</sup>

MPs have become emerging pollutants of increasing global concern due to their ubiquitous detection in several environmental compartments including air, water, soil, sediment, and biota.<sup>5,11–13</sup> However, most studies on MPs so far are centering on characterizing their occurrence, fate, and impact in the aquatic environment. Studies that have focused on MPs in terrestrial outdoor and indoor environments are limited compared to those in the marine/freshwater environment.<sup>14,15</sup> Therefore, very little is known about the magnitude, patterns, and associated risks of human exposure to MPs in the terrestrial environment, particularly indoors.

Plastics were long considered inert materials due to the covalent-bonded polymer structure that renders them of high molecular weight, size, and hydrophobicity; thereby unavailable for absorption and readily excreted unchanged. However, recent studies revealed that MPs (*particularly those < 1 mm*) have the potential to cause adverse health effects to living organisms by: obstruction, inflammation, and/or accumulation in organs after translocation.<sup>14,16–18</sup> Moreover, there is further concern over the potential release of hazardous plastic chemical additives to the environment and biota upon exposure to MPs containing such additives. These chemicals are added to plastic polymers at varying concentrations (up to 70% by mass) to impart some desired physical (*e.g.* colour, strength) or performance properties (*e.g.* flame-retardancy, flexibility).<sup>19</sup> However, several classes of these plastic additives can cause serious adverse health effects (*e.g.* phthalates, bisphenols, organophosphates, biocides), as well as persistence and bioaccumulative properties (*e.g.* brominated flame retardants, chlorinated paraffins). This potential risk is aggravated by the high surface area to mass ratios of MPs, which may facilitate the leaching of these chemicals out of the plastic polymer upon human exposure to these particles.<sup>5,13,16</sup>

Against this backdrop, the present study aims to: (a) provide a critical review of the state-of-knowledge on the occurrence and concentrations of MPs in the indoor environment; (b) evaluate the existing literature on human exposure to MPs indoors *via*

different exposure pathways; (c) investigate the potential risk(s) arising from such exposure; and finally (d) identify major research gaps and provide recommendations for future research to assess the risk of human exposure to MPs in the indoor environment.

## 2 Microplastics in the indoor environment

The indoor environment is important to modern human life due to the large proportion of time (up to 90% or more) that people spend indoors (*e.g.*, homes, offices, transport *etc.*).<sup>20</sup> Subsequently, indoor environmental quality has substantial implications for human health and wellbeing. This is further exacerbated by the various lockdown measures taken by several countries around the world to limit the spread of COVID-19, which may contribute to elevated exposure to emerging contaminants, such as MPs, indoors.

The following sections will summarise the current state-of-knowledge on the concentrations of MPs in environmental media relevant to indoor exposure. This includes indoor environment media (*e.g.* dust and air), as well as other exposure media relevant for indoor exposure (*e.g.* food and drinking water).

### 2.1 Settled dust

Indoor dust is considered an important medium for human exposure to several pollutants such as, construction materials, painting products, microorganisms, heavy metals such as lead, and several organic chemical pollutants (*e.g.* flame retardants and plasticisers).<sup>21–23</sup> The occurrence of MPs at various concentrations, shapes, and sizes in indoor dust has been recently reported. A study on three different indoor sites in Paris including two private apartments and one office at the University of Paris-Est-Creteil pointed out that the number of MPs fibres in dust sampled from vacuum cleaner bags ranged from 1 to 60 fibres per m<sup>3</sup>. These concentrations exceeded those detected in outdoor dust (0.3 to 1.5 fibres per m<sup>3</sup>), indicating higher potential for human exposure to MPs *via* indoor than outdoor dust.<sup>24</sup> In a worldwide study on MPs in house dust from 12 different countries including China, Colombia, Greece, Japan, Kuwait, and Saudi Arabia. MPs were detected in all 286 dust samples, at concentrations of 38–120 000 µg g<sup>-1</sup> (median: 5900 µg g<sup>-1</sup>).<sup>25</sup>

A recent study investigated the presence of MPs in settled indoor dust collected from two offices, two schools, and two apartments in Surabaya, Indonesia. MP numbers measured in the two offices were: 334 particles on weekdays, 242 particles on a weekend (office 1); and 351 particles on weekdays, and 252 particles at the weekend (office 2). In schools they were: 290 particles on weekdays, and 239 particles at the weekend (school 1); and 321 particles on weekday, and 257 particles at the weekend (school 2), while in the apartments there were: 133 particles on weekdays, and 127 particles at the weekend (apartment 1); and 108 particles on weekdays, and 95 particles at the weekend (apartment 2). Despite the small sample size, it



was evident that the number of MPs collected at each location during weekdays exceeded that found at weekends. This was attributed to the greater occupancy levels of the studied indoor environments on weekdays, which contribute to increasing MPs numbers through increased human activity.<sup>26</sup>

Liu *et al.* (2019) investigated indoor and outdoor dust samples from 39 different cities of China to determine two types of MPs, *viz.* polyethylene terephthalate (PET) and polycarbonate (PC). The results found PET MPs in all samples at high concentrations of 1550–120 000 mg kg<sup>-1</sup> (indoor) and 212–9020 mg kg<sup>-1</sup> (outdoor). PC MPs were detected in 70% of the samples, with median concentrations of 4.6 mg kg<sup>-1</sup> (indoor) and 2.0 mg kg<sup>-1</sup> (outdoor).<sup>27</sup>

Peng *et al.*, (2020) developed a method to measure nylon MPs (polyamide, PA6, and PA66) in different environmental media including: indoor dust, sludge, marine sediment, freshwater sediment, and fishery sediment in China. The results revealed that PA6 and PA66 MPs in indoor dust were present at 0.431–86.3 and 3.10–92.9 mg kg<sup>-1</sup>, respectively. The authors also observed that the total concentrations of PA6 and PA66 MPs in indoor dust exceeded those in the other environmental matrices studied such as sludge, marine sediment, and freshwater sediment.<sup>28</sup>

## 2.2 Air

Generally, there are limited data on the levels and types of MPs in air compared to other environmental media.<sup>25,27,29</sup> The presence of MPs in indoor air was attributed to emission and distribution from various sources including, furniture, municipal litter, and construction materials.<sup>30</sup> Likewise, Webster *et al.*, (2009) identified several sources of MPs to indoor air such as: textiles (mats, clothing, curtains, mattresses), toys, rubber, kitchen items (plates, cups, utensils, bowls, bottles), electrical cables, electronics, indoor paint, and cleaning agents.<sup>31</sup>

Dris *et al.* (2017) measured atmospheric MPs concentrations at three different indoor sites including two private apartments and one office in Paris. The results showed the concentrations of indoor air fibres in the studied sites ranged from 4.0–59.4 fibres per m<sup>3</sup>. The highest concentrations were observed in the office (4.0–59.4 fibres per m<sup>3</sup>), followed by apartment A (2.5–18.2 fibres per m<sup>3</sup>) and finally apartment B (1.1–16.3 fibres per m<sup>3</sup>). The variation was attributed to differences in emission of MPs fibres from indoor sources like furniture and carpets as a result of daily usage and/or cleaning activities. Concentrations of MPs in indoor air from all 3 sites exceeded those measured in outdoor air (0.3–1.5 fibres per m<sup>3</sup>). This was explained by the existence of indoor sources of the MPs fibres detected, as well as greater atmospheric dilution of MPs outdoors compared to indoors.<sup>32</sup> Moreover, the rate of MPs deposition from air (also known as atmospheric fall out) in different indoor sites was reported to range from 1586 to 11 130 particles per m<sup>2</sup> per day.<sup>32,33</sup> These rates are substantially higher than those reported outdoors for a European metropolitan region (137–512 particles per m<sup>2</sup> per day)<sup>34</sup> and a remote conservation area in the United States (132 particles per m<sup>2</sup> per day).<sup>35</sup>

Zhang *et al.*, (2020c) investigated concentrations of MPs in indoor air at three different indoor microenvironments,

namely: dormitory room, office, and a lecture building at East China Normal University. The results showed the highest average MPs abundance to be in the dormitory ( $9.9 \times 10^3$  MPs per m<sup>2</sup> per day), followed by the office ( $1.8 \times 10^3$  MPs per m<sup>2</sup> per day) then the corridor ( $1.5 \times 10^3$  MPs per m<sup>2</sup> per day). The measured MPs existed mostly in the form of fibres, which had similar polymer compositions to the textile products used in the studied microenvironments. This led to the conclusion that textile quantity in an indoor microenvironment is one of the main factors affecting MPs abundance in indoor air, whereas high airflow turbulence can increase abrasion of textile fibres and MPs migration in indoor environments.<sup>36</sup>

Another investigation of airborne MPs both indoors and outdoors in coastal California, showed higher concentrations of MPs in indoor air ( $3.3 \pm 2.9$  fibres and  $12.6 \pm 8.0$  fragments per m<sup>3</sup>) than in outdoor air ( $0.6 \pm 0.6$  fibres and  $5.6 \pm 3.2$  fragments per m<sup>3</sup>). Also, the results showed that indoor MP fragments ( $58.6 \pm 55$  µm) were smaller in size than outdoor MP fragments ( $104.8 \pm 64.9$  µm). The authors concluded that the risk of inhalation exposure to MPs indoors is higher than outdoors due to increased abundance and smaller size of MPs in indoor air.<sup>37</sup>

A recent investigation of indoor air MPs from 20 houses in Hull, UK revealed an average household MPs concentration of 1414 MPs per m<sup>2</sup> per day over a 6 month monitoring period. MP fibres (5–250 µm) were the most abundant shape of MPs (90%), while PET accounted for 62% of the identified MPs. Moreover, results suggested substantially higher human exposure to MPs (1–45 times) *via* inhalation indoors than outdoors.<sup>38</sup>

## 2.3 Drinking water

MPs were detected at varying concentrations in both tap water and bottled water.<sup>39,40</sup> Table 1 summarizes the current knowledge on the presence of MPs in drinking water. One of the potential reasons for presence of MPs in tap water is the possible erosion and/or degradation of the plastic components of distribution networks (*e.g.*, pipes, tubing) leading to fragments of MPs entering drinking water.<sup>41</sup> Also, using plastic bottles and caps as packaging for drinking water and potential degradation through the processes of manufacture, distribution, marketing, and repetitive use might be an important source of MPs in drinking water.<sup>42</sup>

## 2.4 Food

Fish and seafood are considered major sources of MPs in the human diet because of the relatively early detection of different types of MPs in various types of fish, shrimp, shellfish, and bivalves.<sup>43–45,130</sup> In addition, recent studies have reported the presence of MPs in different types of food and beverages such as sugar, honey, milk, table salt, soft drinks, and beer.<sup>46,47</sup> Table 2 summarises current knowledge on the presence of MPs in food and beverages. The extensive use of plastic materials in food packaging may be a reason for the presence of MPs in packaged food.<sup>48,49</sup> The extent of MP release from food wraps/packages to packaged food remains unknown, although it is thought high based on the findings that one plastic tea bag can release millions of MPs into one cup of the hot beverage.<sup>49</sup> Moreover,



Table 1 MPs in drinking water<sup>d</sup>

Sample number and description	Concentrations MPs per L		Detection frequency (%)	Polymer types	Size	Shape	Reference	
	Average	Range						
95	65 plastic bottles	140	N/A	100%	PET 28.4%, PE 24.2%, PP 18.1%, PA 7.2%, PVC 4.4%	6.5 to $\geq 50$ $\mu\text{m}$	Fibres and fragments	Kankanige and Babel, (2020) <sup>108</sup>
7	30 glass-bottles Tap water	52 0.7	0.3–1.6	100%	Rayon, PET, PE, PS, polyester, PAA, PMPS, PI	10–5000 $\mu\text{m}$	Fibres and fragments	Zhang <i>et al.</i> , (2020b) <sup>109</sup>
38	Tap water	440	0–1247	95%	PE 26.8%, PP 24.4%, co PE–PP 22.0%, PPS 7.3%, PS 6.5%, PET 3.3%	3–4453 $\mu\text{m}$	Fragments, fibres, and spheres	Tong <i>et al.</i> , (2020) <sup>110</sup>
15	Tap water	0.0007	0–0.0007	42%	Polyester 62%, PVC 14%, PA and epoxy resin 9%, PE 6%	>20 $\mu\text{m}$	Fragments	Mintenig <i>et al.</i> , (2019) <sup>111</sup>
20	10 still water 10 sparkling water	$5.42 \times 10^7$ $10^7$	$3.16 \times 10^7$ to $1.1 \times 10^8$	100%	N/A	0.5–10 $\mu\text{m}$	N/A	Zuccarello <i>et al.</i> , (2019) <sup>111</sup>
32	12 reusable plastic bottles 10 single use plastic bottles 10 glass bottles	4889 2649 6292	N/A	100%	PET, PP, PE	>5 $\mu\text{m}$	N/A	Oßmann <i>et al.</i> , (2018) <sup>134</sup>
259	253 plastic bottles 6 glass bottles	$10.4^a$	0–14	93%	PP 54%, nylon 16%	>100 $\mu\text{m}$	Fragments, fibres, pellets and films	Mason <i>et al.</i> , (2018) <sup>140</sup>
36 tap water from 3 WTPs <sup>b</sup>	12 WTP1 12 WTP2 12 WTP3	443 338 628	N/A	100%	PET 44%, PP PET 62%, PP PET 26%, PP, PE 24%	<10 $\mu\text{m}$	Fragments, fibres, and spheres	Pivokonsky <i>et al.</i> , (2018) <sup>112</sup>
17	9 houses 3 offices 5 public institutions	<0.58	N/A	24%	PP 50%, PS 25%, PET 25%	>100 $\mu\text{m}$	Fragments	Strand <i>et al.</i> , (2018) <sup>113</sup>
38 from mineral water	15 reusable plastic bottles 11 single use plastic bottles 3 beverage cartons 9 glass bottles	118 14 11 50	28–241 2–44 5–20 4–156	100%	PET 84%, PP 7%, PE 5%, PA 2%	50–500 $\mu\text{m}$	Fragments	Schymanski <i>et al.</i> , (2018) <sup>148</sup>
1	1 mineral water brand	1 in the sample <sup>c</sup>	N/A	100%	PET	N/A	Fibres	Wiesheu <i>et al.</i> , (2016) <sup>114</sup>

<sup>a</sup> Only particles  $\geq 100$   $\mu\text{m}$  were verified with FTIR. <sup>b</sup> Water treatment plant. <sup>c</sup> Only fibres counted. <sup>d</sup> (PP): polypropylene, (PVC): polyvinyl chloride, (PA): polyamide (nylon), (PE): polyethylene, (PET): polyethylene terephthalate, (PS): polystyrene, (PTT): poly trim ethylene terephthalate, (PPS): polyphenylene sulfide, (PAA): polyacrylic acid, (PMPS): poly (methyl phenyl siloxane), (PI): poly (isoprene), N/A: not reported.

the potential for ingesting MPs depositing from the atmosphere onto the surface of food items cannot be neglected as it has been estimated to lead to exposure in the range  $1.4\text{--}6.8 \times 10^4$  MPs per person per year.<sup>33</sup>

### 3 Human exposure to MPs

Currently, little is known about human exposure to MPs, especially indoors. This may be attributed to several reasons including the lack of standardized methods for quantitative analysis of MPs in different matrices relevant to human exposure (e.g. indoor dust, air, diet, water and personal care products). This is compounded by the reporting of results as number

of MPs in the majority of the few available studies, while most exposure assessment models require the exposure doses in mass units. Nevertheless, current understanding is that human exposure to MPs occurs *via* a combination of inhalation (air), ingestion (food, drinks, dust), and dermal contact (dust, fabrics, cosmetics).<sup>5,50</sup> Fig. 1 provides a schematic representation of the different pathways of human exposure to MPs and the risks associated with such exposure.

#### 3.1 Inhalation

Inhalation has recently emerged as an important route of human exposure to MPs; due to their consistent detection at



Table 2 MPs in food and beverages<sup>a</sup>

Food type	Sample number	MPs average content	Polymer types	Size	Shape	Reference
Fish	100	2.2 ± 0.89 MPs per individual	PET 55%, PP 33%, PEST 6%, PU 2%	<500 µm	Fibres, films, fragments, foams, and granules	Ghosh <i>et al.</i> , (2021) <sup>115</sup>
Fish	44	11.4 MPs items per fish (0.015 items per g wet weight)	N/A	<500 µm	Fibres, fragments, and beads	Taghizadeh Rahmat Abadi <i>et al.</i> , (2021) <sup>116</sup>
Fish	111	2.29 MPs per fish	N/A	0.5–4.75 mm	Fibres, fragments, film, and beads	Zakeri <i>et al.</i> , (2020) <sup>117</sup>
Bivalves	30	1.26 ± 0.39 to 1.56 ± 0.33 MPs per individual	PP, PA, PE, PS, PET, PVC, PAN	0.1–16.4 mm	Fibres, fragments, and films	Fang <i>et al.</i> , (2019) <sup>118</sup>
Red sea fishes	178	26 MPs per fish	PP 42%, PET 42%, PVC 8%, PS 4%, PAN 4%	2.39 ± 0.28 mm	Fibres, fragments, and films	Baalkhuyur <i>et al.</i> , (2018) <sup>119</sup>
Canned sardines and sprats	20	6 particles per item	PP 33.3%, PET 33.3%, PE 16.6%, PVC 16.6%	190–3800 µm	Fragments, filaments, and films	Karami <i>et al.</i> , (2018) <sup>120</sup>
Table salts	39	0–1674 particles per kg in sea salts 0–148 particles per kg in rock salt 28–462 particles per kg in lake salt	PP, PE, PS, PET, PVC, PA	100–5000 µm	Fragments, fibres, sheets, and spherules	Kim <i>et al.</i> , (2018) <sup>121</sup>
Mussels ( <i>Mytilus edulis</i> )	162	0.7–2.9 MPs items per g of tissue (wet weight)	PP, PEST, PET	0.005–5 mm	Fibres, fragments, spheres, and flakes	Li <i>et al.</i> , (2018) <sup>122</sup>
Molluscs	123	0.2–21.0 MPs particles per g of soft tissue (wet weight)	PE, PET, PA	10–5000 µm	Fragments, films, and pellets	Naji <i>et al.</i> , (2018) <sup>123</sup>
Mussels	20	6.2–7.2 MPs items per g of tissue	N/A	1150–2290 µm	Filaments	Renzi <i>et al.</i> , (2018) <sup>124</sup>
Sea salt	6 Italian brands (Italy)	1.57–8.23 items per g	N/A	4–2100 µm (Italian salts)	Fibres, films, fragments, granules, and foams	Renzi and Blašković, (2018) <sup>125</sup>
	5 Croatian brands (Croatia)	27.13–31.68 items per g		15–4628 µm (Croatian salts)		
Fish	212	1.56 ± 0.5 MPs per fish	N/A	0.38–3.1 mm	Fibres, spheres, films, and fragments	Bellas <i>et al.</i> , (2016) <sup>126</sup>
Fish	16	1–7 particles per fish	PE 40%, PA 22%, PP 13%, PS 10%, PET 5%, PU 5%, PEST 5%		N/A	Rummel <i>et al.</i> , (2016) <sup>43</sup>
Fish	64	2.3 pieces on average and up to 15 pieces per individual	PE 52%, PP 43.3%	150–1000 µm	Fragments and beads	Tanaka and Takada, (2016) <sup>127</sup>
Bivalves	9	2.1–10.5 particles per g	PE, PET, PA	5–5000 µm	Fibres, fragments, and pellets	Li <i>et al.</i> , (2015) <sup>128</sup>
Shrimp	165	0.68 ± 0.55 MPs per g wet weight	N/A		Fibres, film, spherule, and fragment	Devriese <i>et al.</i> , (2015) <sup>44</sup>
Fish	76	0–21 particles per individual fish	N/A	>500 µm	Fragments, foam, and film	Rochman <i>et al.</i> , (2015) <sup>129</sup>
Blue mussels ( <i>Mytilus edulis</i> )	36	0.36 ± 0.07 items per g	N/A	5–25 µm	N/A	Van Cauwenberghe <i>et al.</i> , (2015a) <sup>130</sup>
Table salt	15	550–681 particles per kg in sea salts 43–364 particles per kg in lake salts 7–204 particles per kg in rock/well salts	PET, PE, CP		Fragments and fibres	Yang <i>et al.</i> , (2015) <sup>131</sup>
Blue mussel ( <i>Mytilus edulis</i> )	30	2.6–5.1 fibres/10 g of mussel	N/A	200–1500 µm	Fibres	De Witte <i>et al.</i> , (2014) <sup>67</sup>
Honey	19	166 ± 147 fibres per kg 9 ± 9 fragments per kg	N/A	10–20 µm	Fragments and fibres	Liebezeit and Liebezeit, (2013) <sup>132</sup>
Sugar	5	217 ± 123 fibres per kg 32 ± 7 fragments per kg	N/A	10–20 µm	Fragments and fibres	Liebezeit and Liebezeit, (2013) <sup>132</sup>
Beer	24	0.025 fibres per mL 0.033 fragments per mL 0.017 granules per mL	N/A	10–20 µm	Fragments, fibres, and granules	Liebezeit and Liebezeit, (2014) <sup>133</sup>



Table 2 (Contd.)

Food type	Sample number	MPs average content	Polymer types	Size	Shape	Reference
Milk	10	137 fibres per L 204 fragments per L	HDPE, LDPE 44%, PAAm 30%, PP 26%		Fragments and fibres	Diaz-Basantes <i>et al.</i> , (2020) <sup>47</sup>
Tea	4	~11.6 MPs per cup of the beverage	PA, PET	25 µm	N/A	Hernandez <i>et al.</i> , (2019) <sup>49</sup>

<sup>a</sup> (PP): polypropylene, (PA): polyamide (nylon), (PE): polyethylene, (PET): polyethylene terephthalate, (PS): polystyrene, (PEST): polyester, (CP): cellophane, (HDPE): high-density polyethylene, (LDPE): high-density polyethylene, (PAAm): polyacrylamide, (PU): polyurethane, (PVC): polyvinyl chloride, (PS): polystyrene, (PAN): polyacrylonitrile, N/A: not reported.

considerable concentrations in both indoor and outdoor air.<sup>36,51</sup> Cox *et al.* (2019) highlighted the significance of the inhalation pathway through a meta-analysis of 26 studies on human exposure to MPs with a particular focus on the American population. Using an average concentration of 9.8 MPs per m<sup>3</sup>, results revealed adult inhalation exposure of 170 and 132 MPs per day for males and females, respectively, while children were exposed to 110 and 97 MPs per day. These estimates constituted ~50% or more of the total daily exposure *via* all routes in the studied population groups indicating inhalation to be the major pathway of human exposure to MPs.<sup>46</sup> A more recent study of MPs in Australian homes reported a mean inhalation intake of 0.2 mg per kg bw per year (equivalent to 12 891 MPs fibres per year) with the highest intake in young children at 0.31 mg per kg bw per year.<sup>52</sup> Domenech and Marcos estimated a relatively low global human daily inhalation intake of 5.9 MPs per day based on average global airborne MPs concentration of 0.685 particles/m<sup>3</sup> and breathing rate of 8.64 m<sup>3</sup> per day.<sup>53</sup> In earlier studies, individual MPs inhalation exposure was estimated to be between 26 and 132 MPs per day,<sup>54</sup> while Vianello *et al.* reported mean inhalation of 272 MPs per day for average male adults doing light activity.<sup>55</sup> Interestingly, a recent study

highlighted the increased risk of MPs inhalation due to wearing different types of face masks during the COVID-19 pandemic. Fibres and spheres were the most abundant MP types detected, while activated carbon masks and N95 masks produced the highest and lowest levels of MPs inhalation, respectively.<sup>56</sup>

It is worth mentioning that meaningful comparison between the few available MPs inhalation exposure studies is difficult due to the different sampling, analysis and exposure assessment techniques. Such variation extends to the units for reporting concentrations of airborne MPs. Some studies report concentrations as number of MPs per m<sup>2</sup> (measured atmospheric fallout area), while others report number of MPs per m<sup>3</sup> (volume of air samples).<sup>57</sup> Therefore, development of standardised methods for analysis of MPs in air is crucial for accurate and comparable exposure assessment results.

Currently, very little is known about inhalation exposure to MPs *via* resuspension of settled indoor dust. Several studies have provided experimental evidence on the contribution of resuspended house dust to inhalable airborne particulate matter. Resuspension of indoor dust occurs when the previously settled particles are detached from surfaces (*e.g.* carpets, floor) to become re-entrained into indoor air by human



Fig. 1 Pathways of human exposure to MPs and associated risks.



activities such as walking, crawling and vacuuming.<sup>58–61</sup> Interestingly, toddlers were reported to experience higher inhalation exposure to contaminants in resuspended dust particles *via* crawling, compared to adult exposure *via* walking.<sup>58</sup> Several studies have assessed the inhalation intake of various resuspended particulate-phase contaminants in indoor dust (*e.g.* PM<sub>10</sub>, PM<sub>2.5</sub>, bacteria).<sup>62–64</sup> Resuspension of house dust was found to be equivalent to a PM<sub>2.5</sub> source strength ranging from 0.03 to 0.5 mg min<sup>-1</sup>. Moreover, resuspension from walking on carpets was reported as the most significant contributor to both PM<sub>2.5</sub> and PM<sub>10</sub> exposure in the personal cloud (*i.e.* personal breathing zone) of retirement centre inhabitants.<sup>60,65</sup> While MPs particles are expected to behave similarly, there exists no data on inhalation exposure to MPs *via* resuspension of settled indoor dust. This represents a significant knowledge gap suggesting that current reports of human inhalation exposure to MPs may be underestimated, particularly in toddlers.

### 3.2 Ingestion

Until recently, ingestion was widely considered as the main route of human exposure to MPs.<sup>66</sup> This was led by a few early studies that identified MPs in various food items, particularly fish and seafood.<sup>67,68</sup> Moreover, evidence has now emerged of potential human exposure to MPs *via* inadvertent ingestion of indoor dust.<sup>25</sup>

**3.2.1 Diet.** Several studies have identified MPs at varying concentrations in different food items including fish, seafood, table salt, sugar, honey, milk, and beer (Table 2). This will inevitably lead to human exposure to these MPs *via* diet. However, few studies have estimated such dietary exposure. Cox *et al.*, (2019) estimated the dietary consumption of MPs by American male adults, female adults, male children, and female children to be 142, 113, 126, and 106 particles per day, respectively.<sup>46</sup> Another study estimated European adult exposure to MPs *via* consumption of table salt to range between 37 to 100 MPs per person per year.<sup>69</sup> Elsewhere, the measured concentrations of MPs in fish and shellfish samples from Iran could contribute to an average daily adult exposure of 5 particles per day.<sup>70</sup>

The current state-of-knowledge on dietary exposure to MPs is far from comprehensive due to the lack of knowledge on MPs in major food groups (*e.g.* meat, vegetables, oil, dairy products *etc.*). This research gap was highlighted in a report by SAPEA (Science Advice for Policy by European Academies), which called for more comprehensive dietary studies to better characterise the risk associated with human dietary exposure to MPs.<sup>13</sup> Another pertinent factor that requires further investigation is the release of MPs from plastic packaging to food and beverages which may result in elevated exposure. A study of hot beverages raised concern by reporting that brewing one plastic teabag at 95 °C releases approximately 11.6 billion MPs into a single cup of the beverage.<sup>49</sup> Although the methods and techniques applied in this study leading to such high estimate of MPs was questioned,<sup>71</sup> the potential release of MPs from plastic teabags has been confirmed. Another alarming study showed that polypropylene infant feeding bottles may release MPs resulting

in concentrations as high as 16 million particles per litre due to repeated sterilisation and exposure to high-temperature water. The resulting exposure estimates ranged from 14 600–4 550 000 particles per capita per day, which demonstrated that infant exposure to MPs may be higher than previously recognised.<sup>72</sup> A recent study provided evidence of the contamination of meat products with MPs from polystyrene packaging trays at concentrations of 4–18.7 MPs per kg of packaged meat. These particles were difficult to remove by rinsing and are probably cooked before consumption.<sup>73</sup> Similarly, low concentrations of MPs (1–14 MPs per litre) were detected in branded milk packages from Mexico, likely as a result of leaching from the thermoplastic sulfone membrane filters used during the manufacturing process.<sup>74</sup> Moreover, mechanical stress was identified as a factor that may influence human exposure to MPs *via* bottled drinks. Winkler *et al.* reported the frequent opening/closing of plastic bottles increases the number of MPs released into the bottled water *via* degradation; thereby increasing the chances of ingesting MPs.<sup>42</sup>

Collectively, these studies provide clear evidence on human exposure to MPs *via* diet in different countries and in different age groups from nursing infants to adults. There is even evidence on prenatal exposure to MPs *via* the placenta.<sup>75</sup> However, more comprehensive, large scale studies are required for further understanding of the magnitude, profiles and associated risk of human dietary exposure to MPs.

**3.2.2 Dust.** The role of indoor dust as an important matrix for human exposure to various groups of hazardous chemicals has been extensively highlighted over the past 2 decades. This has spurred some recent studies to investigate potential human exposure to MPs *via* unintentional ingestion of indoor dust. A study on polyethylene terephthalate (PET) and polycarbonate (PC) MPs in both indoor and outdoor dust samples from 39 cities in China reported the estimated daily intake (EDI) for different age groups to fall between 6500–89 700 ng per kg bw per day. Children were the highest exposed age group with a mean EDI of 17 300 ng per kg bw per day, while the mean EDIs of PET MPs in teenagers and adults were 7270 and 6500 ng per kg bw per day, respectively. Comparison between indoor and outdoor dust through EDI of PET MPs in all the studied age groups revealed higher exposure (almost double) *via* indoor dust.<sup>51</sup> The ubiquity of human exposure to MPs *via* indoor dust, combined with higher intake and subsequent risk in younger age groups was confirmed by another study of MPs in house dust from 12 different countries. High concentrations of MPs (38–120 000 µg g<sup>-1</sup>) were detected; resulting in median EDI values of 4000–150 000 ng per kg bw per day for infants. Adults were less exposed with median EDI values of 360–12 000 ng per kg bw per day, which was mainly attributed to a combination of higher dust ingestion rate and lower body weight in infants.<sup>25</sup> Similar findings were reported by a recent study on MPs in indoor dust from 32 Australian homes with estimated mean ingestion rates of 6.1 mg per kg bw per year (EDI = 16 712 ng per kg bw per day) for children and 0.5 mg per kg bw per year (EDI = 1370 ng per kg bw per day) for adults.<sup>52</sup>

Despite the small number of studies, it can be concluded that human exposure to MPs *via* ingestion of indoor dust and



the potential risk of such exposure cannot be neglected, especially for children. More research is needed to understand the spatial and temporal variability of such exposure and the impact of individuals' time-activity patterns (*e.g.* the proportion of time spent in homes, offices, outdoors, cars, schools, and other types of microenvironments) on the overall daily exposure to MPs *via* dust ingestion in different age groups.

### 3.3 Dermal contact

To date, there are no available studies assessing human dermal exposure to MPs and its associated risks. However, with the ubiquitous occurrence of MPs in indoor dust, atmospheric deposition from both indoor and outdoor air, as well as wide application of microbeads in cosmetics and continuous degradation of microfibrils from textiles; it is reasonable to consider dermal contact as a pathway of human exposure to MPs.<sup>53</sup> Microplastic beads (microbeads, generally < 1 mm in diameter) have been widely applied in dermal exfoliation and cleansing products, as well as in toothpaste and denture fillings.<sup>76</sup> Few studies have attempted estimation of per capita consumption of microbeads through the use of specific personal care products. A study on UK facial scrubs from different brands revealed a MPs content of 10–100 g L<sup>-1</sup> resulting in per capita consumption of 40.5–215 mg per day.<sup>77</sup> Gouin *et al.* estimated an average consumption of 2.4 mg MPs per day per capita for the US population through the use of liquid soap.<sup>78</sup>

While these few studies fall short of providing a comprehensive understanding on human dermal exposure to MPs, they provide evidence that the dermal route cannot be ignored. Although human skin can act as an efficient barrier against penetration of large particles and studies suggest that only particles <100 nm (*i.e.* nanoplastics) can directly cross the dermal barrier,<sup>50</sup> there are other possible routes for transdermal penetration of larger particles through hair follicles, sweat gland, or open skin injuries.<sup>79</sup> Moreover, skin damage as a result of inflammation and oxidative stress has been associated with dermal exposure to MPs.<sup>80</sup> Therefore, more research is required to assess human dermal exposure to MPs *via* contact with cosmetics, settled dust particles, fabric fibres *etc.*, as well as evaluating the significance of this exposure pathway and the associated health risk.

## 4 Microplastics risk to human health

Toxicological understanding of the potential impacts of MPs exposure on human health is still in its infancy.<sup>13</sup> This may be attributed in part to the lack of accurate, sensitive and standardized analytical methods for determination of MPs in different human tissues (*e.g.* blood, milk) and exposure-relevant matrices (*e.g.* food, air). On the other hand, very little is known about toxicological endpoints of MPs and how they relate to environmentally-relevant human exposure doses.<sup>81</sup> It is also not clear if the sizes, shapes, and chemical composition of the wide variety of environmental MPs available for human exposure *via* different pathways will impact on their toxicity in humans.<sup>82</sup> Nevertheless, human internal exposure to MPs has been

recently confirmed through the detection of MPs in human stool<sup>83</sup> and placenta.<sup>75</sup> This has spurred more research into the potential toxic implications of human exposure to MPs. Current understanding is that adverse health effects from MPs may be associated with particle toxicity and/or toxicity from associated chemicals (*e.g.* plasticisers, flame retardants, colourants *etc.*).<sup>84,85</sup>

### 4.1 MPs particle toxicity

Evidence on the toxicological impacts of airborne MPs in human is sparse. It is widely thought that MPs fibres <20 µm are predominant in air.<sup>13,86</sup> Therefore, entry of such MPs into the airway is possible, although not as yet quantified. Larger MPs might be deposited in airways or trapped by the lung lining fluid and cleared out. However, smaller MPs may be engulfed by macrophages and epithelial cells.<sup>87</sup> Accumulation of MPs fibres in human pulmonary tissue has been previously reported.<sup>88</sup> Such accumulation of inhaled MPs in human airways may cause interstitial lung inflammatory and/or immune responses, and even cancer, although no large scale epidemiological associations or toxicological endpoints have been estimated for these adverse effects in humans.<sup>89</sup> Moreover, small MPs (<2.5–5 µm) were reported to be capable of entering the systemic circulation through endocytosis and can be translocated to mesenteric lymph nodes, blood circulation, liver, and spleen.<sup>90</sup> Increased permeability of the epithelial membrane due to inflammation was suggested as a plausible mechanism for this translocation of small MPs.<sup>91</sup> This was supported by the observed increased haemolysis and subsequent release of histamine, a pro-inflammatory chemical, from human cell lines exposed to polypropylene MPs (20–200 µm).<sup>92</sup> Another potential toxicological impact may be caused by inhalation of MPs carrying microbial colonisation. Pathogenic *Vibrio* spp. colonies were identified on a number of MPs particles (*e.g.* polyethylene, polypropylene and polystyrene) from North/Baltic sea.<sup>93</sup> In addition to the risk of pathogenic species infections, inhaled MPs with microbial colonisation could cause a shift in the microbial community structure in the lung.<sup>13</sup>

Similar to inhaled MPs, current understanding is that intestinal absorption of ingested MPs is generally low with 90% or more of ingested particles excreted in faeces, depending on the particle size and shape.<sup>94</sup> While an early study showed the mucus layer in the gut to present an effective barrier against the diffusion of 500 nm latex microbeads,<sup>95</sup> more recent studies in human cell lines and lab animals indicate that MPs <10 µm can cross the gastrointestinal barrier and be translocated *via* the blood circulation to other organs (*e.g.* liver and kidney).<sup>96</sup>

Controlled laboratory studies in human cell lines and laboratory animals have revealed several potential toxic implications as a result of MPs exposure. Cytotoxicity of MPs on cerebral and epithelial human cell lines was attributed to oxidative stress caused by increased reactive oxygen species to high concentrations.<sup>97</sup> This should be interpreted carefully though, because in other human cell lines (Caco-2), no significant cytotoxic effects were observed upon exposure to polystyrene MPs, even at high exposure doses.<sup>98,99</sup> Other studies investigating the toxicity of



MPs as particulate matter in air and water have reported on a range of potential toxicological impacts in animal models including immunosuppression and links to autoimmune diseases such as lupus erythematosus and autoimmune rheumatic disease.<sup>91</sup> Other studies suggested possible neurotoxic effects due to increased activity of acetylcholinesterase enzyme in the brain and altered serum neurotransmitters levels in fish and mice.<sup>100,101</sup> Exposure to MPs has been linked to obesity based on the increased food intake in mice as a response to higher energy demands or lower absorption efficiency associated with an observed decrease in liver weight and size.<sup>101</sup> Prata (2018) suggested that chronic exposure to airborne MPs might be linked with cancer due to DNA damage caused by chronic inflammation and interstitial irritation.<sup>54</sup>

It is worth noting that extrapolating results from these controlled laboratory animal studies to humans should be done carefully and interpreted with caution due to inter-species variability, more complex and sophisticated immune and nervous systems, as well as the differences in MPs exposure levels and pathways in humans.

#### 4.2 Toxicity from associated chemicals

A wide range of chemical additives are often incorporated into plastic polymers during manufacture at typical concentrations around 20% by weight (but can be up to 70% w/w) to impart specific properties or enhance the physical characteristics/appearance of the final product.<sup>19</sup>

Most of these additive chemicals (Table 3), particularly those used as flame retardants and/or plasticisers, have been well-documented to cause adverse health effects in humans including: endocrine disruption, reproductive toxicity, neurotoxicity, hepatotoxicity, and cancer.<sup>16,81,86</sup> In the case of MPs, the concern over exposure to these toxic chemical additives is exacerbated by the small particle size and large surface area of MPs. This is likely to allow more surface area for these additive chemicals to leach out from the plastic polymer to human body fluids (*e.g.* sweat, gastric, intestinal and lung fluids) upon exposure (*i.e.* higher bioaccessibility).<sup>91</sup> While the plethora of evidence on the potential adverse effects associated with exposure to MPs additive chemicals is concerning, very little is known about the leaching potential of these different chemical

groups from various polymer types and consequently their potential toxicological impacts in humans.

Another toxicological concern over MPs and associated chemicals is the so called “Trojan Horse effect”, which refers to the potential for accumulation of hazardous environmental chemical pollutants on the surface of MPs (aided by their large surface area) and this will lead to an increase in the chemical toxicity within the organism as the chemicals are then released when the plastic is ingested and or inhaled.<sup>102,103</sup> While recent studies have demonstrated the potential for increased toxicity of polycyclic aromatic hydrocarbons (PAHs) in zebrafish<sup>102</sup> and heavy metals in *Daphnia*,<sup>104</sup> the Trojan Horse theory still needs verification in humans and higher trophic level animals. It is also possible that adsorption of chemical pollutants to MPs can reduce their bioaccessibility in organisms, through a reduced concentration in biological fluids, if the chemical co-pollutant is strongly bound to the MP and not desorbed easily, as reported in Northern Fulmars.<sup>105</sup>

## 5 Conclusion and future outlook

The extensive research on the identification and characterisation of MPs over the past decade has established their ubiquitous distribution in all environmental matrices. While the majority of this research was focused in the aquatic environment, few recent studies have raised concern over the existence of MPs in the indoor environment at concentrations relevant to human exposure. Current understanding is that human exposure to MPs in the indoor environment can occur through a combination of inhalation, ingestion, and dermal contact. The detection of MPs in indoor air and atmospheric deposition samples indicate inhalation as a significant exposure route, while the presence of MPs in indoor dust, food items, and beverages renders exposure *via* ingestion inevitable. Moreover, the use of MPs in cosmetics and personal care products, as well their release *via* the degradation of microfibrils from domestic fabrics means the dermal exposure pathway cannot be neglected. This is alarming due to the fact that people spend up to 90% or more of their time indoors, recently exacerbated by COVID-19 pandemic lockdown measures. Critical evaluation of existing literature in the present review has revealed the paucity of information on human exposure to MPs

Table 3 Common chemical groups used as plastic additives

Category	Group	Examples
Functional additives	Plasticizers	Phthalates, bisphenols, organophosphate esters
	Flame retardants	Brominated flame retardants, organophosphate flame retardants, chlorinated paraffins
	Stabilizers	Nonylphenols, cadmium and lead compounds
	Biocides	Triclosan, triclocarban
	Anti-static agents	Quaternary ammonium compounds, alkylsulfonates, and alkylphosphates
	Slip agents	Metallic stearates, fatty acid amides and waxes
Colourants	Soluble pigments	Azo dyes, anthraquinones
	Organic pigments	Cobalt diacetate
	Inorganic pigment	Cadmium, zinc and chromium salts
Reinforcements	Fibres	Carbon fibres, glass fibres
Fillers		Zinc oxide, talk, clay, calcium carbonate



indoors and the risk associated with it. The increasing public concern over MPs pollution and its potential detrimental effects on human health and the environment is escalating the pressure on regulators and policy makers to take decisive actions to mitigate such harmful effects. The knowledge base required for such informed decisions to protect public health against MPs pollution is still lacking. Significant research gaps exist in the current knowledge on both the sources and magnitude of human exposure to MPs, as well as the relative contribution of different exposure pathways to human body burdens of MPs. The few studies available on the indoor environment mainly originate from developed countries, while very little is known about human exposure to MPs in low and middle income countries (LMIC) and the impact of different climates (e.g. less time spent indoors in tropical and subtropical regions) and cultures on such exposure (e.g. consumption of plastic packaged takeaway food and beverages). Therefore, the following topics are recommended for prioritisation in MPs research:

(a) There is an urgent need for validated, standardised methods for quantifying concentrations of MPs in indoor air and dust samples. It is also essential to reach a consensus on the units for reporting these concentrations on a mass basis suitable for exposure assessment models. Of particular importance is the harmonisation of units used for reporting airborne concentrations of MPs. The discrepancy between studies reporting concentrations as MPs per m<sup>2</sup> (measured atmospheric fallout area) and those reporting MPs per m<sup>3</sup> (volume of air samples) in the existing literature is hindering comparability between various studies. Moreover, the use of atmospheric fallout data (MPs per unit area) to assess human inhalational exposure is challenging because existing exposure models are based on inhalation rates in volume (m<sup>3</sup>) of air.

(b) Despite the few studies reporting MPs concentrations in human exposure-relevant media (e.g. air, dust and diet), very little is known about the magnitude of this exposure under real-life scenarios and for different age/sex groups. Therefore, comprehensive human exposure assessment studies are crucially required to estimate individual- and population-level exposure to MPs *via* total diet studies, market basket studies, dermal contact scenarios, and/or time-activity patterns (*i.e.* time spent in homes, offices, schools, nurseries, cars, outdoor exercise *etc.*) for different age groups in various countries.

(c) There is paucity of data on some sources and pathways that may contribute substantially to human exposure to MPs. More research is required to assess the resuspension of MPs particles from settled indoor dust to the personal cloud of adults and toddlers; thereby assessing its contribution to human inhalation exposure of MPs. Studies should also address the factors influencing this exposure source, such as: personal activity (e.g. walking adult, crawling toddler), indoor features (e.g. carpeted *vs.* wooden floors), rate of vacuuming, temperature and ventilation.

(d) While few recent studies assessed human exposure to MPs *via* food items (mainly seafood), very little is known on the contribution of food packaging and food-contact materials on human intake of MPs. Future studies should investigate the contribution of packaging (e.g. plastic boxes, films, covers,

plates and utensils) on MPs concentrations in food and subsequent intake by different age groups in different cultures. Similarly, more research is required to understand the contribution of plastic bottles and caps to MPs exposure *via* drinking and the impact of beverage composition (e.g. probiotic drinks, multivitamin drinks) and temperature (e.g. hot coffee *vs.* cold juice) on the leaching of MPs from the bottle and consequent human exposure *via* drinking these beverages.

(e) Risk is assessed based on knowledge of both exposure and hazard. Recent studies have proposed risk assessment approaches for MPS in humans including probabilistic lifetime exposure models<sup>106</sup> and multi-compartment exposure frameworks.<sup>107</sup> However, more information on the toxicological implications and endpoints of MPs in humans (*i.e.* hazard) is essential to assess the risk arising from their exposure. In particular, more research is required on the particle-induced toxicity of MPs in human at exposure-relevant concentrations and MPs particle size ranges. Similarly, studies on the potential leaching and bioavailability of toxic chemical additives from human ingested/inhaled MPs are urgently required. These studies should preferably be conducted in human cell-lines and tissues, or pertinent mammalian laboratory animals due to the large inter-species variation that precludes meaningful extrapolation of toxicological endpoints from species like zebrafish and daphnia to humans.

## Conflicts of interest

There are no conflicts to declare.

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