

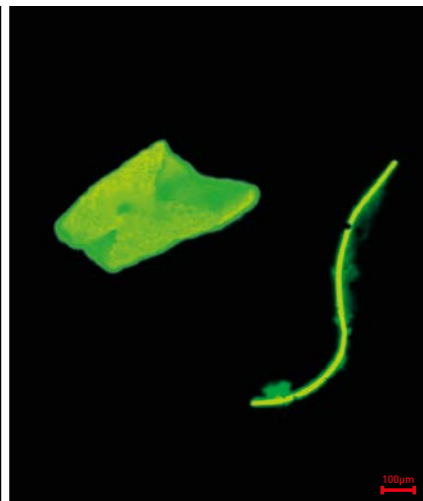
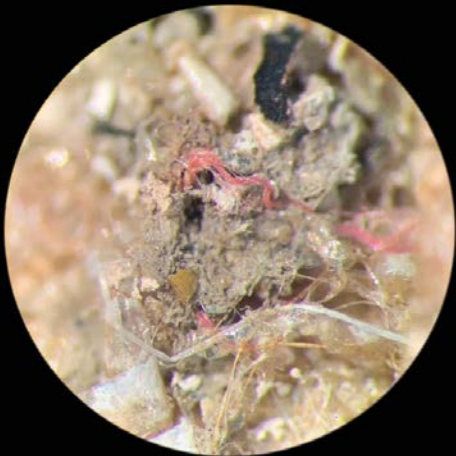


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MICROPLASTICS IN FOOD COMMODITIES A FOOD SAFETY REVIEW ON HUMAN EXPOSURE THROUGH DIETARY SOURCES

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FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS
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PREPARATION OF THIS DOCUMENT

This document was developed by Esther Garrido Gamarro and Violetta Costanzo, who co-wrote the initial draft. Their work was consolidated at the FAO Expert Meeting on Microplastics in Food, during which the experts outlined below had the opportunity to contribute to the document. Kennedy Bomfeh incorporated additional inputs from the expert group and the FAO Secretariat.

ABSTRACT

The contamination of the environment with whole plastics or pieces thereof (micro- and nanoplastics) is the subject of extensive discussion nowadays in academia and the media. In addition to environmental matrices, micro- and nanoplastics have been detected in fishery products and other important food commodities, with concerns over their impact on human health. Food consumption is considered one of most significant routes of human exposure to these small plastic particles. Such concerns may arise not only from the exposure to reactive monomers in the otherwise biologically inert polymer structure, but also from their associated contaminants. Many studies have reported neurotoxicity, oxidative stress and immunotoxicity among the main consequences of exposure to micro- and nanoplastics.

This document outlines the existing literature on the occurrence of microplastics and their associated contaminants in foods. It estimates the dietary exposure of consumers to these materials, highlights some knowledge gaps with respect to their relevance to public health, and offers some recommendations for future work on microplastic particles to support food safety governance.

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ABBREVIATIONS AND ACRONYMS

ABS	acrylonitrile butadiene styrene
AChE	acetylcholinesterase
ADI	acceptable daily intake
AhR	aryl hydrocarbon receptor
ATBC	acetyl tributyl citrate
BBP	butyl benzyl phthalate
BPA	bisphenol a
Casp3	caspase-3
CAT	catalase
Chg H	choriogenin
CP	cellophane
CYP450	cytochrome p450
DBP	di-n-butyl phthalate
DDD	dichlorodiphenyldichloroethane
DDE	dichlorodiphenyldichloroethylene
DDT	dichlorodiphenyltrichloroethane
DEHA	di(2-ethylhexyl)adipate
DEHP	di(2-ethylhexyl)phthalate
DEP	diethyl phthalates
DIDP	di-isodecyl phthalate
DINP	di-isononyl phthalate
DIOP	diisooctyl phthalate
DIPB	diisobutyl phthalate
DOA	dioctyl adipate
DPP	dipentyl phthalate
EDC	endocrine disrupting chemical
EFSA	European Food Safety Authority
EP	ethylphenol
EPS	expanded polystyrene
ERα	estrogenic receptor

ERK	extracellular signal-related kinase
EVA	ethylene-vinyl acetate
FCM	food-contact material
GIT	gastrointestinal tract
GOT	aspartate transaminase
GP	glutathione peroxidase
GPPS	general purpose polystyrene
GPT	alanine aminotransferase
GR	glutathione reductase
GSH	reduced glutathione
GST	glutathione-s-transferase
HBCDD	hexabromocyclododecane
HCH	hexachlorocyclohexane
HDL	high-density lipoprotein
HDPE	high density polyethylene
HMWPE	high molecular weight polyethylene
HIPS	high-impact polystyrene
IARC	International Agency for Research on Cancer
IDH	isocitrate dehydrogenase
IL1a	interleukin 1 alpha
IL1b	interleukin 1 beta
IFN	interferon
ITX	isopropylthioxanthone
JECFA	FAO and WHO Joint Expert Committee on Food Additives
JNK	c-jun n-terminal kinase
LDH	lactate dehydrogenase
LDPE	low density polyethylene
LLDPE	linear low-density polyethylene
MAPK	mitogen-activated protein-kinase
MCP-1	monocyte chemoattractant protein-1
MIP-2	macrophage inflammatory protein 2
MP	microplastic
NIAS	non intentionally added substances
NOAEL	no observed adverse effect level

NOEL	no observed effect level
NP	nonylphenol
Nrf2	nuclear factor erythroid 2-related factor 2
OML	overall migration limit
OPFR	organophosphorus flame retardant
OP	octylphenol
OTU	operational taxonomic units
PA	polyamides
PAH	polycyclic aromatic hydrocarbons
PAM	polyacrylamide
PAN	polyacrylonitrile
PARP	poly(adp-ribose)polymerase
PB	poly(1-butene)
PBA	polybutylacrylate
PBB	polybrominated biphenyl
PBDE	polybrominated diphenyl ether
PBTs	persistent bioaccumulative toxic substances
PC	polycarbonate
PCB	polychlorinated biphenyl
PE	polyethylene
PEST	polyester
PET	polyethylene terephthalate
PEVA	polyethylene vinyl acetate
PMMA	poly methyl methacrylate
PP	polypropylene
PPH	propylphenol
PPS	polyphenylene sulfide
PPTA	<i>p</i> phenylene terephthalamide
POPs	persistent organic pollutants
PS	polystyrene
PSU	poly aryl sulfone
PTDI	provisional tolerable daily intake
PTFE	polytetrafluoroethylene
PTT	polytrimethylene terephthalate

PU	polyurethane
PVA	polyvinyl alcohol
PVC	polyvinyl chloride
PVDC	polyvinylidene chloride
PYR	pyruvate
ROS	reactive oxygen species
RY	rayon
SAN	styrene acrylonitrile
SML	specific migration limit
SOD	superoxide dismutase
TBA	hepatic total bile acids
TBBA	tetrabromobisphenol a
T-CHO	total cholesterol
TDI	tolerable daily intake
TG	triglycerides
TNF-α	tumour necrosis factor alpha
VTG	vitellogenin
XPS	extruded polystyrene

EXECUTIVE SUMMARY

Over the last half-century, the volume of plastics produced every year has steadily increased. This points to a high demand for plastics, which can be seen in the wide range of applications for these materials in everyday life. The most common use of plastics is in packaging (circa 40 percent), followed by their use in construction, the automotive industry, electronics and household materials. Such usage is incentivized by their low cost and advantageous characteristics, including malleability, light weight and gas barrier properties (the latter feature notably also favours their use in the food industry). However, the same properties also make them less prone to degradation, thus enhancing their persistence in the environment, with potential consequences not only for environmental sustainability, but also for food safety and public health.

As a consequence of their inappropriate disposal, and the effects of human activities and nature, plastics may be broken down into smaller particles that are generally categorized by size as macro- (> 25 mm), meso- (25 mm–5 mm), micro- (5 mm–0.1 µm) and nanoplastics (< 0.1 µm). Of these size categories, microplastics and to a lesser extent nanoplastics have received considerable attention in food safety discussions: this is because of their potential transfer along the food chain and their subsequent probable impact on human health. Concerns about their potentially negative public health impact may arise in part from their chemical constituents. As plastics they are made of polymeric chains, which in turn consist of monomers, some of which may be present in an unreacted form and may thus interact with biological molecules upon ingestion. Concerns may also stem from the fact that some plastic polymer components (such as vinyl chloride) are known to be toxic. Residues of other (potentially) harmful chemicals used in the plastic manufacturing process (e.g. bisphenol A and phthalates) may also be found in the final product and their fragments. Additionally, microplastics are noted as having the potential to sorb and concentrate various food safety hazards from the surrounding environment.

A number of studies have, therefore, evaluated the occurrence of micro- and nanoplastics in foods, although more attention has been given to the former. For example, some studies have reported their occurrence in fishery products and other food commodities such as sugar, honey, beer and water. Reports in the scientific literature have also cited harmful health effects such as neurotoxicity, oxidative stress and immunotoxicity among the main consequences of exposure to microplastics.

This document outlines the knowledge currently available on the presence of microplastics in food commodities, which result from various contamination sources. It discusses the toxicity of the particles' components and provides the estimated exposure to microplastics in selected foods as an indicator of their public health relevance. It argues that although the reported levels of the hazards and their associated exposure levels are generally low, significant challenges such as data

paucity, knowledge gaps on the toxicity of micro- and nanoplastics, and a lack of standardized analytical methods hamper the formulation of definitive conclusions on the public health significance of these particles. It therefore recommends, among other things: the development, fine-tuning and harmonization of analytical techniques for (micro)plastics in food; ongoing investigations into the occurrence and toxicity of these substances in food value chains; and the evaluation of acute and chronic exposures to the (components of) (micro)plastics in various foods.

It is hoped that the information provided in this document, as well as actions taken based on this same, will support a clearer understanding of the food safety significance of (micro)plastics in food. It should also support future exposure assessments and aid the development of appropriate legislation and guidance documents on food production, processing, distribution and consumption, as these relate to (micro)plastic contamination.



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CHAPTER 1

INTRODUCTION

The term “plastic” includes a broad group of artificial compounds primarily generated through the polymerization reactions of monomers, which are typically derived from fossil and renewable biosources such as starch and castor oil (Plastic Europe, 2019). Presently, polymers are classified into three main families based on their response to heat and elasticity and other physical properties: thermosets (e.g. polyurethane, epoxy resins, silicone); thermoplastics (e.g. polyethylene (PE), polypropylene (PP), polyvinyl chloride (PVC), polyethylene terephthalate (PET), polystyrene (PS), polyamides (PA)); and elastomers (neoprene and rubber). Of these, only thermoplastics can be remoulded once heated (FAO, 2017; Plastic Europe, 2019).

The number of plastics produced every year has steadily increased over the last half-century. As of 2017, an estimated total of 8.3 billion tonnes of resins and fibres had been produced globally (Geyer *et al.*, 2017), with 360 million tonnes produced in 2018 alone (Plastic Europe, 2019). These large production volumes point to a correspondingly high demand for plastics, which is evident in the wide range of applications for these materials in everyday life. The most common use of plastics is in packaging (circa 40 percent), followed by their use in construction, the automotive industry, electronics and household materials (Plastics Europe, 2018). Their use is highly incentivized due to their low cost and advantageous physico-chemical characteristics such as their gas barrier properties (which favours their use in the food industry), malleability and light weight (Andrady, 2011). Nevertheless, the same properties also make them less prone to degradation, thus enhancing their persistence in the environment, with potential consequences not only for environmental sustainability but also for food safety and public health.

Pieces of plastic materials found in the environment are categorized by their sizes into macro- (> 25 mm), meso- (25 mm–5 mm), micro- (5 mm–0.1 µm) and nanoplastics (< 0.1 µm) (Arthur *et al.*, 2009; FAO, 2017; Koelmans *et al.*, 2015; Lee *et al.*, 2015; Thompson *et al.*, 2004). Aside from these size categorizations, there is significant debate in polymer science concerning a universal definition that encompasses all criteria describing the particles, especially for microplastics, e.g. shape, colour, solubility in water, etc. (Frais and Nash, 2019; Hartmann *et al.*, 2019). In this document, size distinctions are prioritized, and the above size definitions have been adopted.

Of the aforementioned size categories, microplastics and to a lesser extent nanoplastics have received attention in food safety discussions because of their potential transfer along the food chain and subsequent probable impact on human health. Typically, these two groups result from either a breakdown of macroplastics (e.g. through weathering), or occur in such sizes from manufacture. When resulting from the former they are referred to as secondary microplastics, and primary microplastics when occurring from the latter (Andrady, 2011; Andrady and Neal, 2009; Arthur *et al.*, 2009; de Sá *et al.*, 2018; FAO, 2017). Nanoplastics may result from the further fragmentation/breakdown of microplastics (Dawson *et al.*, 2018; Hasegawa and Nakaoka, 2021). Emphasis is placed on microplastics in this document because of the relatively larger body of literature on the same in relation to food safety.

The presence of microplastics in the environment was first reported in the 1970s (e.g. Carpenter and Smith, 1972 and Wong *et al.*, 1974). These particles are believed to enter the food chain and may ultimately be ingested by humans, as some evidence of trophic transfer has been reported (Farrell and Nelson, 2013; Santana *et al.*, 2016; Setälä *et al.*, 2014). Fisheries and aquaculture products have thus been studied extensively for contamination from microplastics. What is more, many studies have reported their occurrence in other food commodities such as salt, sugar, drinking water and vegetables.

Concerns about the potential negative public health impact of exposure to microplastics may arise in part from the chemical constituents of the polymeric chains, some of which may be present in an unreacted form and may therefore interact with biological molecules upon ingestion. The concern may also stem from the fact that some components of plastic polymers are known to be toxic. Moreover, residues of other (potentially) harmful chemicals used in the plastic manufacturing process may be found in the final product and their fragments. Microplastics also have the potential to sorb and potentially concentrate contaminants from the surrounding environment. For example, microplastics sampled from the North Pacific Central Gyre and along the Portuguese coast had polychlorinated biphenyls (PCBs) and polycyclic aromatic hydrocarbons (PAHs) at concentrations of 2 856 and 44 800 ng per gram, respectively (Antunes *et al.*, 2013; Rios *et al.*, 2010). Some PCBs and PAHs are carcinogenic. Microplastics may therefore pose risks to public health following human exposure on account of their inherent composition, because of the presence of manufacturing aid residues, or by virtue of the accumulation (adsorption/attachment) of harmful substances from the environment.

As with many substances of concern, the routes of human exposure for microplastics are oral (ingestion through food), dermal (skin contact) and inhalation (Prata *et al.*, 2020; Catarino *et al.*, 2018). Cox *et al.* (2019) estimated that the annual amount of microplastics ingested through food may be as high as 52 000 MP/year. This number reaches a maximum of 121 000 MP/year when inhalation is considered. It has also been reported that oral exposure may be higher in places where fish and shellfish consumption is high (Barboza *et al.*, 2020b; Cox *et al.*, 2019). Catarino *et al.* (2018) have suggested that a further contribution to dietary exposure comes from household dust settling on food; they concluded that this was potentially much greater (up to 68 415 MP/year) than exposure from the consumption of contaminated mussel tissues (4 620 MP/year).

Considering that everyday items that humans come into contact with, such as textiles and personal care products (e.g. toothpaste, cosmetics, facial scrubs and cleansers) may contain microplastics (Praveena *et al.*, 2018), some attention is being given to their evaluation as sources of microplastics for the various routes of exposure. Additionally, the plastic polymers used in making some medical devices and in pharmacological applications (e.g. the use of synthetic biodegradable polymers such as poly[lactic-co-glycolic] acid as carriers in drug delivery) may also constitute potential sources of exposure (Maitz, 2015; Kapoor *et al.*, 2015). Consequently, exposure to particles from plastic medical devices such as prosthetic replacements and implants, and their subsequent effects, have also attracted research interest (Sternschuss *et al.*, 2012).

With regard to oral exposure, the European Food Safety Authority (EFSA) and the Food and Agriculture Organization of the United Nations (FAO) conducted two case studies on dietary exposure to chemical substances from microplastics contained in seafood (EFSA, 2016; FAO, 2017). Those studies focused on the consumption of mussels (225 g) as these organisms are eaten with their viscera, where an accumulation of microplastics is expected. Using that worst-case scenario, both organizations concluded that the overall contribution of microplastics as part of human exposure to environmental contaminants and additives can be considered negligible. Nevertheless, it should be stressed that such a conclusion is valid only within the limits of the assumptions and limited data used.

Commercial aquatic species have also been widely investigated, as several publications have pointed to the ingestion of microplastics by fish, crustaceans and bivalves (Lusher *et al.*, 2013; Van Cauwenberghe and Janssen, 2014; Devriese *et al.*, 2015; Li *et al.*, 2016, 2015; Rummel *et al.*, 2016; Hossain *et al.*, 2020; Gedika *et al.*, 2022; Esposito *et al.*, 2022). Other food commodities such as table salt, sugar, honey, beer, water, edible fruits and vegetables have also been reported to contain microplastics (Renzi and Blašković, 2018; Liebezeit and Liebezeit, 2013, 2015; Oliveri Conti *et al.*, 2020).

In many cases, and particularly for water, the source of contamination was suggested as being the packaging material rather than environmental pollution (Mason *et al.*, 2018; Schymanski *et al.*, 2018; Hee *et al.*, 2022). The average global range of microplastic ingested (GARMI) per year has been estimated at 7.7–287 g per capita (or 0.1–5 g/week), whereas the estimated total average number of microplastics ingested (ANMP) was 102 527 MP/year. Drinking water was suggested as the source providing the highest contribution to the exposures (Senathirajah *et al.*, 2021).

The nature and extent of the adverse health effects of microplastics on the human body following exposure are controversial and still under investigation. Although considerable literature is available on the occurrence of microplastics, much less is known about their toxicity and the mechanisms of interaction with biota. For example, although microplastics might be absorbed from the intestine, factors such as hydrophilicity, surface chemical composition, charge and shape may also play a role in their subsequent systemic transport and toxicity. De Jong *et al.* (2008) and Samuelsen *et al.* (2009) suggest that microplastics may interact with biological

systems following entry. The form and impact of such interaction, however, remains to be firmly established. At the time of writing, only a few authors had reviewed the possible toxicological effects of microplastics on human health (Barboza *et al.*, 2018a; De-la-Torre, 2020; Prata *et al.*, 2020; Smith *et al.*, 2018; Wright and Kelly, 2017). Most studies had reported evidence of oxidative stress, immunological and metabolic alterations and neurotoxicity following exposure to secondary microplastics (Brown *et al.*, 2001; Canesi *et al.*, 2015; Chiu *et al.*, 2015; Choi *et al.*, 2018; Deng *et al.*, 2017; Espinosa *et al.*, 2018; Hwang *et al.*, 2019; Jeong *et al.*, 2017, 2016; Jin *et al.*, 2018; Lei *et al.*, 2018; Liu *et al.*, 2015; Lu *et al.*, 2016; Petit *et al.*, 2002; Samuelsen *et al.*, 2009; Schirinzi *et al.*, 2017; Veneman *et al.*, 2017; Yang *et al.*, 2019; Yu *et al.*, 2018, 2020).

As noted above, the potential toxicity (and thus food safety concern) of microplastics is mostly related to the polymer components (e.g. monomers, residual impurities, and physical damage) and the adverse effects induced by plastic additives. Furthermore, microplastics have the potential to concentrate substances such as persistent organic pollutants (POPs) and heavy metals, and also provide a favourable substrate for the adhesion of microorganisms (Endo *et al.*, 2005; Holmes *et al.*, 2014, 2012; Zettler *et al.*, 2013). These two aspects may add to the primary toxicity of polymers. For instance, Cedervall *et al.*, (2012) noted some alterations in the behaviour (delayed feeding time and motility) and fat metabolism (changes in serum triglycerides/cholesterol, weight loss, cholesterol distribution between muscle and liver) of fish (*Carassius auratus*) exposed to polystyrene nanoplastics (size: 24 nm) through trophic transfer. Alterations began appearing around the twenty-second day of the fish feeding on contaminated zooplankton. Barboza *et al.* (2020a) observed a correlation between the concentration of bisphenols in the liver and muscle of wild fish and the amount of microplastics ingested by the fish. However, the estimated daily intake for bisphenols from fish consumption in both children and adults was lower than the oral reference dose recommended by the EFSA. Despite this, the authors suggested that the consumption of fish contaminated with microplastics containing bisphenols may lead to a higher exposure to these chemicals than the consumption of fish not contaminated with the microplastics.

Food safety considerations of aquatic organisms typically involve those that are eaten whole, since plastic particles larger than 150 µm in size should generally not be absorbed by the intestine and are mostly retained in the digestive tract. Ragusa *et al.* (2021) reported the first evidence of microplastics (size 5–10 µm) in the human placenta on both the maternal and foetal sides, in addition to the chorioamniotic membrane. Leslie *et al.* (2022) also reported the occurrence of microplastics in human blood at levels of 1.6 µg/mL, providing pioneering evidence on the potential uptake of particles into the bloodstream.

The detection and quantitation of nanoplastics with current analytical techniques remains a challenge. At their longest, these particles measure less than 100 nm (Koelmans *et al.*, 2015). Such dimensions may facilitate particle uptake from the gut lumen, which has been seen in the haemolymph of mussels (Browne *et al.*, 2008; Pittura *et al.*, 2018), human placenta (Ragusa *et al.*, 2021; Wick *et al.*, 2010) and may be endocytosed and phagocytosed at sizes around 0.5 µm (Yoo *et al.*, 2011).

The human body is expected to eliminate more than 90 percent of micro- and nanoplastics ingested (EFSA, 2016). For example, Schwabl *et al.* (2019) found microplastics ranging in size from 50 to 500 μm in all human stool samples from eight volunteers, suggesting the oral ingestion and eventual elimination of (some of) the particles. The fate of microplastics in the gastrointestinal tract requires further investigation. When inhaled, microplastics are most likely eliminated from the upper airways and alveoli through mucociliary clearance or macrophages, respectively (Wright and Kelly, 2017).

This report presents the knowledge currently accessible on the presence of microplastics in food commodities as they result from various contamination sources, including plastic food packaging. The toxicity of plastic polymers and microplastics is also discussed, along with an estimated exposure to microplastics in selected foods. The exposure assessment is limited to the oral route, although dermal and inhalation exposures are briefly mentioned in parts of the report. Some knowledge gaps considered significant with respect to microplastics and public health are highlighted, and some recommendations are put forward concerning the food safety governance of same. Given the significant differences and current limitations in sampling, sample preparation and analytical methods for microplastics, data from the literature are presented as is. It is therefore expected that discussions of – and inferences from – such data may be less nuanced than ideal. Furthermore, the reader should note that many publications that assess the impact of microplastics on biological systems use pristine commercial polymeric particles (such as polystyrene) because of the challenges with sourcing microplastics from real-life scenarios. Differences may thus be expected in the actual behaviour of (mixtures of) microplastics from real-life sources.



CHAPTER 2

CHEMICAL COMPONENTS OF (MICRO)PLASTICS

In this section, the chemical constituents of plastics are discussed, with a focus on those components that may be inherently toxic. As far as food safety is concerned, the toxicity of the components discussed is linked to their potential transfer along the food chain in (association with) microplastics or, in some cases, to their transfer from food-contact materials to foods. Although toxicity arising from oral exposure remains the focus of the document, adverse effects from other exposure routes are briefly mentioned where necessary.

2.1 POLYMERS

Polymers are the macrocomponents of plastics. They are the result of polymerization reactions occurring between single units called monomers. Polymers can be made of just one type of monomer (homopolymers) or from a mixture of monomers (copolymers). The most widely used commercial polymers are: polypropylene (PP), polyethylene (PE), high-density polyethylene (HDPE), low-density polyethylene (LDPE), linear low-density polyethylene (LLDPE), polyvinyl chloride (PVC), polyurethane (PU), polyethylene terephthalate (PET), polystyrene (PS), expanded polystyrene (EPS), extruded polystyrene (XPS), polycarbonate (PC), epoxy resin, acrylic, acrylonitrile butadiene styrene (ABS), polyamides (PA)(nylon), polyester (PEST), polyvinylidene chloride (PVDC)(Saran), poly methyl methacrylate (PMMA), poly aryl sulfone (PSU), polyacrylonitrile (PAN), polyvinyl alcohol (PVA) and polytetrafluoroethylene (PTFE, Teflon) (FAO, 2017; Plastic Europe, 2019). Polymers are not considered to be toxic per se; they are generally considered biologically inert, largely because of their size. Their monomeric units, however, may be toxic.

Polymerization reactions generally require the use of initiators, solvents and catalysts. These substances are typically added in concentrations below 2 percent of the polymer weight and should ordinarily not remain in the final products (Lithner *et al.*, 2011). When they persist in the final product they are considered impurities and need to be assessed for their toxicological properties.

2.2 MONOMERS

Monomers are the building blocks of polymers, and they react with each other to form macromolecular chains. They can make up 4–100 percent of the final polymer by weight (Lithner *et al.*, 2011). As indicated above, some monomers can be toxic. Therefore, although the polymers are generally too large to interact with tissue and result in adverse effects, an excessive amount of residual reactive monomers in the polymer may cause concern. Lithner *et al.* (2011) developed a hazard ranking of plastic polymers based on the toxicity of each of their components. According to that ranking, the most hazardous plastic polymer monomers for human health are vinyl chloride (in PVC), epichlorohydrin (in epoxy), acrylonitrile (in ABS), methylenedianiline (in epoxy), 1,3-butadiene, propylene oxide, ethylene oxide (in some PU) and acrylamide, in ascending order. Some of the most relevant monomers with potential adverse effects are described next.

2.2.1 STYRENE

Styrene is the main component of polystyrene (PS) and can make up to 100 percent of the polymer by weight. Some studies have investigated the adverse effects of exposure to styrene microparticles, such as the induction of immunological alterations at the cellular level (Hwang *et al.*, 2020). The majority of studies investigating styrene toxicity in humans focused on the effects on workers exposed through inhalation, a pathway which could allegedly cause inflammation and impair the functions of the respiratory tract (Meyer *et al.*, 2018). Moreover, the concentration of styrene in the blood of workers of both sexes from 17 different places was suggested as being positively related to serum prolactin levels (Luderer *et al.*, 2004). Exposure through styrene-contaminated water caused subjective symptoms related to irritation of the respiratory tract and abdominal pain (Arnedo-Pena *et al.*, 2003). There were also some suggestions of carcinogenicity, although it is still difficult to obtain sufficient evidence of the relationship between these effects and styrene exposure (Agency for Toxic Substances and Disease Registry, 2010).

2.2.2 VINYL CHLORIDE

Vinyl chloride is the main component of PVC and accounts for up to 100 percent of this polymer. This molecule is reported to be mutagenic, may have consequences on reproduction and is considered as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC, 2008). Its adverse effects are attributed to the interaction of the parent compound or derived metabolites with neural membranes or other targets in the human body. Metabolites are generally believed to be easily excreted in the urine following a two-phase detoxification pathway. However, the intermediate metabolites from the phase I detoxification step, namely chloroethylene oxide and chloroacetaldehyde, can interact with DNA to form adducts (Brandt-Rauf *et al.*, 2012). Acute toxicity mainly involves oxidative reactions such as lipid peroxidation, while chronic exposure can result in alterations of the connective tissue of the fingers and their bones (acro-osteolysis), liver cancer (angiosarcoma) and

hepatotoxicity (Agency for Toxic Substances and Disease Registry, 2002). Because of its observed toxicity on humans, the European Commission has established a threshold limit of 1 mg/kg of free or residual vinyl chloride in food-contact materials made of plastic (European Commission, 2011a).

2.2.3 BISPHENOL A

Bisphenol A (BPA) is an aromatic chemical belonging to the group of bisphenol compounds and is used as a monomer in the production of polycarbonate plastics (circa 50 percent of the polymer by weight) and epoxy resins (up to 67 percent by weight) (Lithner *et al.*, 2011). It is classified as a xenoestrogenic endocrine disruptive chemical (EDC) within the European Union Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) classification (BPA, CAS 80-05-7; EC/List 201-245-8), and is known to induce alterations and adverse effects on human cells even at low doses (Benachour and Aris, 2009; Fujiwara *et al.*, 2018). Li *et al.* (2010) observed a dose-dependent increase in sexual dysfunction in workers from BPA and epoxy resin manufacturers. The use of this chemical in commercial products and in food-contact materials is strictly regulated by international authorities such as the European Commission (European Commission, 2011b). The Food and Drug Authority of the United States (FDA), the Food and Agriculture Organization of the United Nations (FAO), and the World Health Organization of the United Nations (WHO) have also provided guidance through risk assessment exercises (WHO, 2010). In the European Union this compound can be used in food-contact materials and in food can coatings, and the specific migration limit (SML) into food in contact with these materials has been set at 0.05 mg/kg of food (European Commission, 2018). In 2015, the EFSA derived a temporary tolerable daily intake (TDI) of 4 µg per kilogram of body weight/day (EFSA, 2015), and in 2021 EFSA proposed to lower the TDI to 0.04 ng per kilogram of body weight/day (EFSA, 2021). In addition to its use as a monomer in water pipes and metal cans, BPA is also used as an additive during the manufacture of PP, PVC and PE (Rani *et al.*, 2015). In the United States of America, the FDA banned the use of BPA for baby feeding bottles and epoxy resin for packaging for infant formulas (FDA, 2014).

2.3 RESIDUES OF PRODUCTION AIDS

Production aids and reagents are commonly added in concentrations lower than 2 percent of the polymer by weight (Lithner *et al.*, 2011). When reaction by-products, oligomers and other impurities persist in the final product they are referred to as non-intentionally added substances (NIAS) whose identity is still largely unknown and may add to the toxicity of the final compound. Many chemicals can be used in the manufacturing of plastics: catalysts, surfactants, solvents, lubricants, chain stabilizers, chain transfer, exchange and stop agents, suspension aids and initiators are the most common, and are generally added in very small concentrations (Wiesinger *et al.*, 2021). Peroxides (e.g. benzoyl peroxide) and azo compounds (e.g. ammonium persulfate) are common initiators that can be used to induce the polymerization reaction, and

become part of the final polymer (Lithner *et al.*, 2011). On the other hand, catalysts, which are generally metal compounds such as zinc oxide and copper chloride, should not remain in the polymer, but they are still detected in some cases (Lithner *et al.*, 2011). Many other substances can also remain in traces, and it is not easy to identify all of them. This may lead to an underestimation of the toxicity of polymers and their possible harm to humans.

2.4 PLASTIC ADDITIVES

To give plastic materials their characteristics and properties, such as flexibility and resistance to heat and UV light, some substances must be added during manufacturing. These low molecular weight substances are called plastic additives and are generally included in plastics at concentrations of up to 4 percent (EFSA, 2016). Some polymers may require higher amounts to achieve their desired features. For instance, PVC is the plastic polymer that requires the largest number of substances to acquire its final features. Additives can be classified as antioxidants, plasticizers, heat and UV stabilizers, flame retardants, processing aids, colorants, fillers, surfactants and biocides (Andrady and Neal, 2009). These substances are not covalently bound to plastics, and can easily leach and become bioavailable after ingestion, leading to possible interactions with biological macromolecules and disruptive endocrine effects.

2.4.1 PHTHALATES AND NON-PHTHALATE PLASTICIZERS

Phthalates are hydrophobic compounds added to plastic materials to enhance their malleability and flexibility. The plasticizers most commonly used for the production of PVC are di(2-ethylhexyl)phthalate (DEHP) and di(2-ethylhexyl)adipate (DEHA). Phthalates can account for up to 80 percent of the total plasticizer volume in the final PVC (Bhunia *et al.*, 2013). Typical plasticizers for the production of PE are DEHA together with dipentyl phthalate (DPP), di-n-butyl phthalate (DBP), dioctyl adipate (DOA), diisobutyl phthalate and diethyl phthalates (DEP) (Bhunia *et al.*, 2013). Moreover, DBP, DEHP, butyl-benzyl-phthalate (BBP), di-isononyl phthalate (DINP) and di-isodecyl phthalate (DIDP) can be used in the production of food-contact materials. Humans are mainly exposed via food ingestion. Notable include are DEHA, which is added to PVC films in sizeable amounts (> 20 percent polymer weight) for food wrapping (Goulas *et al.*, 2000). Similarly, BBP has been used as a plasticizer in the PVC industry and the manufacturing of many other products worldwide, and it is expected to remain in the aquatic environment for decades (Herrero *et al.*, 2015). Epidemiological studies have shown a positive correlation between phthalate exposure and both human reproductive defects and breast cancer incidence (Lopez-Carrillo *et al.*, 2010). Benzyl butyl phthalate (BBP) has been found to activate the aryl hydrocarbon receptor in breast cancer cells to stimulate sphingosine kinase 1 (SPHK1)/sphingosine 1-phosphate (S1P)/sphingosine-1-phosphate receptor 3 (S1PR3) signalling and enhance formation of metastasis-initiating breast cancer stem cells (BCSCs) (Wang-Y.C *et al.*, 2016).

It has been suggested that some plasticizers may disrupt endocrine activity and induce adverse effects on fertility and reproduction (Buck Louis *et al.*, 2014; Grindler *et al.*, 2015; Oehlmann *et al.*, 2009; Zhang *et al.*, 2009). The use of DBP, BBP, DEHP, DINP and DIDP in plastic materials intended for food contact is authorized, and tolerable daily intake (TDI) levels have been identified (Silano *et al.*, 2019) (Table 1).

TABLE 1 TOLERABLE DAILY INTAKES (TDI) FOR PLASTIC ADDITIVES

ADDITIVE	TDI	REFERENCE
Bisphenol A (BPA)	4 µg/kg of body weight/day	EFSA, 2015
Nonylphenol (NP)	5 µg/kg of body weight/day	Nielsen <i>et al.</i> , 2000
Di-n-butyl phthalate (DBP), Butyl-benzyl-phthalate (BBP), Di(2-ethylhexyl) phthalate (DEHP) and Di-isononylphthalate (DINP)	50 µg/kg of body weight/day	Silano <i>et al.</i> , 2019
DIDP	150 µg/kg of body weight/day	Silano <i>et al.</i> , 2019
Di(2-ethylhexyl)adipate (DEHA)	0.3 mg/kg of body weight/day	EFSA, 2005

Source: Authors' own elaboration.

2.4.2 FLAME RETARDANTS

Flame retardants are a group of chemicals whose use in industrial manufacturing aims to decrease the flammability of the final products. They comprise different categories of compounds, such as polybrominated diphenyl ethers (PBDEs), hexabromocyclododecanes (HBCDDs), polybrominated biphenyls (PBBs) and tetrabromobisphenol A (TBBA). Many of these substances are no longer used because of evidence of their adverse biological effects, but residues can still be found in the environment because of their persistency. Organophosphorus flame retardants (OPFRs) are now widely used in their place, and some information on their toxicity and dynamics in food chains has already been provided. However, additional research must be conducted to better characterize their toxicological properties and behaviour in the food supply chain (reviewed by Du *et al.*, 2019).

2.4.3 ALKYLPHENOLS

Alkylphenols are a group of hydrophobic chemicals of varying chain length that include propylphenol (PPH), ethylphenol (EP), octylphenol (OP) and nonylphenol (NP) among others. The latter can be used in the production of antioxidants and non-ionic surfactants for plastics (USEPA, 2010). Alkylphenols are known xenoestrogens with capacity to disrupt endocrine function; they are able to interact with the nuclear estrogenic receptor (ER α), whose affinity increases along with chain length (Tabira *et al.*, 1999). The estrogenic activity of NP is three to six times lower than that of the natural compound (17 β -estradiol), but NP still appears able to induce vitellogenin production in female and male fish and reduce testicular weight (Bontje, D. *et al.*, 2004). Moreover, Kochukov *et al.*, (2009) reported non-genomic effects of alkylphenols, such as changes in intracellular Ca⁺⁺, and extracellular-regulated kinase phosphorylation and prolactin release in pituitary tumour cells,

which were more pronounced for the long-chained compounds. The Danish Institute for Safety and Toxicology estimated a tolerable daily intake (TDI) of 5 µg per kilogram of body weight for NP (Nielsen *et al.*, 2000) (Table 1).

CHAPTER 3

PLASTIC CONTAMINANTS FROM THE ENVIRONMENT

The incorrect disposal of household and industry plastics eventually leads to their deployment at sea. Microplastics in the marine environment may accumulate chemicals from surrounding areas because of their physico-chemical characteristics, among which hydrophobicity may be the most crucial. Many POPs are lipophilic and have a higher affinity for hydrophobic microplastics than seawater. For example, International Pellet Watch and many other research groups have investigated the amount of microplastics at sea and the concentration of metals and organic pollutants on their surface (Endo *et al.*, 2005; Ogata *et al.*, 2009; Teuten *et al.*, 2009). The ingestion of these microplastics was hypothesized to lead to the additional exposure to other chemicals whose toxicity has been widely studied. PCBs, DDT and HCHs are listed in Annexes A (elimination: PCBs, α , β , γ -HCH), B (restriction; DDT) and C (unintentional production; PCBs) of the Stockholm Convention, as they have recognized adverse effects on human health. Even though the contribution of microplastics to the total dietary uptake of these chemicals was estimated as negligible compared to other sources (EFSA, 2016; FAO, 2017), it is important to identify the potential risk posed by absorbed contaminants.

3.1 POLYCHLORINATED BIPHENYLS (PCBS)

Polychlorinated biphenyls (PCBs) are a class of persistent organic contaminants whose production and use have been banned since the 1970s. They can be categorized as dioxin-like and non-dioxin-like according to the position of the chlorine atoms on the two phenyl rings, which can influence the conformation of the molecule. The degree of toxicity and the biological action of dioxin-like PCBs is similar to that of dioxins, as they have a coplanar conformation that allows them to interact with the aryl hydrocarbon receptor (AhR) in the cell and induce the transcription of enzymes belonging to the cytochrome P450 (CYP450) superfamily. The International Agency for Research on Cancer (IARC) observed a correlation between the occurrence of these chemicals and cancer (Lauby-Secretan *et al.*, 2013). Concentrations of up to 2 856 ng of PCBs per gram of microplastics have been measured on pellets from

the North Pacific Central Gyre (Rios *et al.*, 2010). The tolerable daily intake (TDI) and no observed effect level (NOEL) of these contaminants are 20 ng per kilogram of body weight and 0.04 mg per kilogram of body weight (Faroon *et al.*, 2003; JECFA, 1990).

3.2 DICHLORODIPHENYLTRICHLOROETHANE (DDT)

Widely deployed as an insecticide from the 1940s onwards, DDT is an organic compound used to eradicate malaria and other diseases carried by insects. Its use was then prohibited from the 1970s in most countries as a result of its recognized toxicity and persistency. Nevertheless, there appears to be continued use of the compound in some countries in the Global South in indoor applications to cope with insect-borne diseases (WHO, 2011). Following its degradation in the environment, the two main metabolites are DDE and DDD, whose physico-chemical characteristics are basically the same as the parent compound. No clear evidence of adverse effects has been produced in humans so far, but it might have a role in the aetiology of some diseases, and the persistence of DDT and its metabolites in tissues seems relevant (ATSDR, 2002; Beard, 2006; IARC, 2018). Marine pellets have been reported to contain up to 1100 ng/g of DDT and 276 ng/g of DDE in California and Japan (Rios *et al.*, 2007; Teuten *et al.*, 2009). The provisional tolerable daily intake (PTDI) and no observed adverse effect level (NOAEL) for DDT have been set as equal to 0.01 mg per kilogram of body weight and 1 mg per kilogram of body weight/day, respectively (JECFA, 2001).

3.3 HEXACHLOROCYCLOHEXANES (HCHS)

Hexachlorocyclohexanes are a group of persistent organic compounds used as insecticides; HCH occurs as several stereoisomers, based on different stereochemistry of chlorine atoms along the cyclohexane ring. Although evidence of the toxicity of HCHs in humans is scarce, the IARC has suggested some of the isomers as possible carcinogens (IARC, 2018). Marine microplastics from the Bay of Maputo (Mozambique) were reported to have a maximum concentration of 37 ng/g of HCHs (Ogata *et al.*, 2009). The acceptable daily intake (ADI) and NOAEL for γ -HCH (lindane) are 0–0.005 mg per kilogram of body weight and 0.47 mg per kilogram of body weight/day (JECFA, 2002).

3.4 POLYBROMINATED BIPHENYLS (PBDES)

Polybrominated biphenyls are a group of 209 hydrophobic polyhalogenated compounds classified as persistent organic pollutants. They have been widely used as flame retardants in different fields, as well as additives in plastics, but their production is now restricted under the Stockholm Convention. They can be classified into lower and higher brominated congeners according to the number of bromine atoms on the molecule: congeners with one to four bromines are classified as lower brominated; molecules with five or more bromines are classified as higher brominated. Observations on model organisms have suggested that these chemicals might cause

neurotoxicity and endocrine disruption (reviewed by Costa and Giordano, 2011; Darnerud *et al.*, 2001). However, there is no current correlation with cancer in humans. Up to 9 909 ng/g of PBDEs were detected on microplastics from the Central Pacific Gyre (Hirai *et al.*, 2011). No TDI or NOAEL has been established.

3.5 POLYCYCLIC AROMATIC HYDROCARBONS (PAHS)

Polycyclic aromatic hydrocarbons are environmental pollutants whose source can either be anthropic or natural. They are mostly found in fossil fuels and can be generated following incomplete combustion (pyrolytic origin), the transformation of biogenic precursors following their deposition (diagenetic origin) and crude oil spillage (petrogenic origin). Their chemical structure is composed of several aromatic rings that assume a coplanar conformation. It is possible to trace their origin by calculating the ratio between low (2–4 rings) and high (4–6 rings) molecular weight PAHs. The latter are generally detected at higher concentrations on microplastics in the environment (Gauquie *et al.*, 2015; Rios *et al.*, 2007). These compounds are recognized mutagens and carcinogens; they have no established TDI. When analysing food contamination, benzo(a)pyrene can be used as a marker for their presence (JECFA, 2006), although the sum of two, four or eight PAHs has been suggested as a more suitable parameter for this purpose (EFSA, 2008). A concentration of 44 800 ng/g PAHs has been found in microplastics along the Portuguese coast (Antunes *et al.*, 2013).

3.6 MICROBIAL BIOFILMS

Microplastics present at sea provide a suitable substrate for microbial attachment, mostly because of their hydrophobicity that promotes biofilm formation. Bacterial communities on marine microplastics can be distinct from those in the surrounding seawater, thus creating an ecosystem of their own, also referred to as a “plastisphere” (Zettler *et al.*, 2013). As suggested by Oberbeckmann *et al.* (2018), environmental factors such as nutrient concentrations and salinity may play a role in the colonization. The same authors also pointed out the possible role of microplastics as substrates where horizontal gene transfer between antibiotic-resistant bacteria and other bacteria may occur. Bacteria belonging to the genus *Vibrio* – which also includes some pathogenic species – have been shown to be among the very first colonizers (yet short-term residents) of microplastics in marine environments, with correspondingly higher concentrations in proximity to major land cities (Kesy *et al.*, 2020). Based on 16S rRNA identification, the authors observed that the two most represented operational taxonomic units (OTUs) were seen to cluster close to the species *Vibrio anguillarum*, *Vibrio rumoiensis* and *Vibrio vulnificus*. They suggested that the concentration of nutrients in seawater could be another factor favouring the presence of these microorganisms, along with high temperatures and low salinity. For instance, a recent study observed a high abundance of *Vibrio* spp. on microplastics near a mariculture farm, possibly due not only to the high temperatures but also to the organic matter produced by the cultured shellfish (Sun *et al.*, 2020). The authors also noticed a time-dependent change in the

community of microorganisms on the microplastics, which revealed a preferential colonization and enrichment of *Vibrio* spp., *Pseudoalteromonas* spp. and *Alteromonas* spp. (carbohydrate metabolizing and infectious bacteria) compared to the surrounding water. In the North and Baltic Seas, *Vibrio parahaemolyticus* was identified on PE, PS and PP microplastics (Kirstein *et al.*, 2016). Moreover, in addition to *Vibrio* spp., which were present on microplastic samples in great abundance (up to 24 percent of the biofilm community in one PP sample), Zettler *et al.* (2013) identified the hydrocarbon-degrading bacteria that are likely to help with microplastics breakdown. Hydrocarbon-degrading bacteria were also detected in microplastic (LDPE) particles rapidly colonized in coastal sediments from a microcosm experiment (Harrison *et al.*, 2014). Some harmful algal species have also been detected on the surface of microplastic debris, which could then act as vectors for these organisms too (Masó *et al.*, 2003). Pham *et al.* (2021) reported that microplastics could serve as substrates of antibiotic-resistant bacterial biofilm.

CHAPTER 4

MICROPLASTIC CONTAMINATION IN THE FOOD VALUE CHAIN

Microplastic contamination has been seen to affect all environmental compartments, but the most widely studied is the hydrosphere. In general, the final point of deposit (also called the “ultimate/final sink”) of microplastics leave sediments in terrestrial, freshwater and marine environments. From this point, they may be introduced into the food value chain by anthropogenic activities (e.g. food production) and bioturbation (disturbance of sediments by living organisms causing microplastic displacement). In food production, microplastics can enter the food value chain at all the different stages, from primary production through processing, packaging transport/distribution, consumption and even disposal. Yates *et al.* (2021) have undertaken a comprehensive analysis of the current literature on seven widely used plastic polymers (HDPE, LDPE, PET, PS, PP, PVC and miscellaneous plastics) in food systems. The extent of microplastic contamination in the food value chain remains largely unknown as a result of the scarcity of published scientific data.

In terrestrial environments, the presence of microplastics in soil has been reported and may in fact be an underestimated and equally important sink that could influence human health and economy, given that agriculture and land use could be significantly impacted by the contamination. As noted above, the occurrence of microplastics in agricultural produce such as fruits and vegetables has been reported.

Several recent studies have also reported the occurrence of microplastics in foods of animal origin. The contamination could be related to the use of contaminated feed – fishmeal, for instance, which is made of raw fish, has been repeatedly reported as being contaminated with synthetic particles retained within the gastrointestinal tract.

The various contributions of soils, production waters, food-processing environments, distribution and the domestic environment to the introduction or transfer of microplastics in or along the food value chain are discussed next.

4.1 CONTAMINATION OF PLANT FOODS FROM SOILS

The uptake of microplastics by terrestrial plants has been reported recently. Reports suggest that microplastics could accumulate in a plant's roots before being transported to aerial parts such as leaves, flowers and fruits (Li *et al.*, 2020; Li *et al.*, 2021). Deposition on plant food surfaces has also been reported (Tympana *et al.*, 2021; Dong *et al.*, 2021; Silva *et al.*, 2021; Jia *et al.*, 2022).

Soil biota, such as earthworms, have been seen to influence and promote the transport of plastic particles down through the soil profile in a size-dependent manner (Huerta Lwanga *et al.*, 2017; Rillig *et al.*, 2017b). Agricultural activities such as ploughing and harvesting may also play an important role in the movement and incorporation of the polymers into the soil matrix (Rillig *et al.*, 2017a).

Recent research has shown a positive correlation between microplastics in soil and in the gastrointestinal tracts of fish in paddy co-culture systems, suggesting a possible contamination even in these farming systems (Lv *et al.*, 2019). Higher concentrations were observed during rice-planting periods, perhaps as a consequence of the use of organic fertilizers and fish feed in the agrofish system. Organic fertilizers could become an important entry route for microplastics into agricultural ecosystems, as sewage sludge is often used as a fertilizer in developed countries because it is inexpensive. Use of contaminated biosolids and sludge could eventually lead to an approximate annual release in soils of up to 850 tonnes of microplastics per million inhabitants (Nizzetto *et al.*, 2016).

Also, the proximity of agroecosystems to urban centres might affect the particle load in the ground. Cultured fields near suburban roads contained almost twice as many microplastics compared to those in residential areas further from roads in China. The main sources were identified as traffic (e.g. migration from tire marks on the road), household discharges, organic fertilizers, and the plastic nets and bags used in agricultural activities (Chen *et al.*, 2020).

The use of plastic materials in agriculture is a direct source of pollution, especially on plant surfaces. Plastic mulches, for example, are used to protect seedlings and crops, but they may also induce some alteration in the soil community and chemistry by changing the microclimatic conditions – this is in addition to the obvious plastic accumulation, especially of HDPE, LLDPE and LDPE (Steinmetz *et al.*, 2016). All of these factors can lead to a degradation in soil properties and quality (e.g. nutrient depletion), and much concern derives from the leaching of chemicals from plastics into soils and farm products. In China, phthalate concentrations in vegetables resulting from the use of plastic film in greenhouses were higher than in soil (2.38 mg/kg), with 5.84 mg/kg in pothead mustard, 3.62 mg/kg in celery and 3.49 mg/kg in lettuce. Levels of DEHP and DBP were above European Union limits for vegetables and the human risk was suggested to arise mainly from vegetable consumption (Wang *et al.*, 2015).

4.2 CONTAMINATION OF FOOD FROM PRODUCTION WATERS

Wastewater treatment plants (WWTP), depending on their effectiveness, may remove over 90 percent of microplastics from wastewater. However, particularly in the case of ineffective systems, a certain level of micro- and nanoparticles can easily be found in WWTP effluents, which will subsequently be used as water sources for purposes such as field irrigation (crops, flowers, vegetables, fodder crops) and for livestock drinking water (Kaur *et al.*, 2012). Moreover, when microplastics end up in surface water and in groundwater reservoirs, they can later enter the drinking water supply chain and be found in household taps. Plastics loading in drinking water can further increase through the abrasion and degradation of plastic materials that make up the supply system. Tap water contamination may arise from abrasion and following the leaching of chemicals and polymeric particles from the pipes (e.g. PVC, PE) and tanks in the water supply network: they may be coated with plastic films such as epoxy resins (Mintenig *et al.*, 2019; Strand *et al.*, 2018). Epoxy resin is in fact used to lessen the extent of corrosion in water tanks, while PA can be found as a fitting component in pipes (Mintenig *et al.*, 2019).

Finally, in the case of sea and lake salt, the main source of microplastics may be the source water, which has been seen to contain significant amounts of synthetic particles. Sea salt production is carried out by progressive crystallization from water, which is passed through different evaporation ponds to eventually obtain the final product (Yang *et al.*, 2015). The contamination of rock salt is more likely related to its processing.

4.3 CONTAMINATION OF FOOD FROM THE PROCESSING ENVIRONMENT

The use of machinery and technologies made of, or including, plastic materials could lead to the transfer of parts of the polymers to the foods they come into contact with. For example, the membranes used to process milk beverages were identified as the main source of plastic contamination, as most of the synthetic particles identified in the products were thermosulfones (Kutralam-Muniasamy *et al.*, 2020). In another study, substances used in the production process were cited as one possible cause of the presence of xenoestrogens in mineral water, though this could also have resulted from the use of treated groundwater that still contained some chemicals uneasy to filter (Wagner and Oehlmann, 2009). Fadare *et al.* (2021) hypothesized possible contamination sources from the production process or the use of contaminated water. Even in the case of honey, contamination from synthetic fragments and fibres was hypothesized as starting from the very first step of natural production: either bees transport it from contaminated wildflowers to the hive, or it originates from the plastic bags used to supply sugar to the bees (Liebezeit and Liebezeit, 2015, 2013). Renzi and Blašković (2018) attributed the presence of polypropylene fibres in salt to contamination from the clothes worn by production staff. Similarly, a clear change in phthalate concentration was noted in Japan, when the levels of phthalates detected in retail packed lunch meals substantially decreased after a ban on the use of PVC gloves containing DEHP during production and cooking processes (Tsumura *et al.*, 2001).

4.4 CONTAMINATION OF FOOD IN THE DOMESTIC ENVIRONMENT

Microplastics in the domestic environment may contaminate exposed food. For example, Liebezeit and Liebezeit, 2014, 2013 suggested that the deposition of microplastics (especially those from textile materials) from the atmospheric and indoor air may be one of the main causes of contamination in honey and beer. Catarino *et al.*, 2018 also reported that household dust accounted for up to 68 415 MP fibres on meals per year. Estimates of the atmospheric fallout of synthetic and semi-synthetic fibres indicated a daily deposition of between 2 and 355 MP/m² (Dris *et al.*, 2016).

CHAPTER 5

PLASTIC MIGRATION FROM FOOD-CONTACT MATERIALS AND PACKAGING

The need for plastic packaging arises from the necessity to protect food and avoid its chemical, physical or biological degradation, thus increasing its shelf-life (Lee, 2010). Plastics have been extensively used in this field because of their useful characteristics, which also enable international trade and improve the quality of foodstuffs. Approximately 40 percent of all produced plastics are used for packaging: PE (especially LDPE), PS (including high-impact polystyrene, HIPS and general-purpose polystyrene, GPPS), PP, PET, polycarbonates (PC), polyamide (PA 6, 6.6, 6.10, 10, 11), and the polyurethane (PU) used in adhesives, as well as PVC, are the leading polymers involved in this sector (Bhunia *et al.*, 2013; Plastic Europe, 2019). Some other polymers are polytetrafluoroethylene (PTFE or Teflon, used in cookware), polyvinylidene chloride (PVDC, used as barrier layer) and ethylene copolymers (Bhunia *et al.*, 2013).

Synthetic particles in bottled drinking water mostly derive from the packaging material, as the identified polymers are generally those that make up the bottle caps (e.g. PP, PE), labels, internal coating of cartons and bottles themselves (e.g. PET) (Mason *et al.*, 2018; Oßmann *et al.*, 2018; Schymanski *et al.*, 2018).

Besides the potential contamination with microplastics, the migration of leachable chemicals from plastic packaging into foods is a noted concern (Groh *et al.*, 2019). Although chemical migration is outside the scope of this report, some aspects are highlighted, such as the possibility of migration occurring from microplastics found in food.

5.1 FACTORS AFFECTING MIGRATION OF PLASTIC COMPONENTS

Most polymers used in packaging materials can undergo certain changes as a result of external conditions, and this can lead to the release of chemical components. Polymer-specific physico-chemical alterations occur after exposure to high temperatures, UV light and changes in pH (Bhunja *et al.*, 2013; Pilevar *et al.*, 2019). This could result in food safety issues for packaged goods and food, especially those imported from the Global South where there are availability and compliance challenges with regard to regulations on the limits of toxic substances.

Migration of plastic components depends not only on the quality of the plastic material, but also on the characteristics of the food and contact time. According to Bach *et al.* (2013), there was an increase in the migration of some components of PET bottles into water at 60 °C. They also reported an increase in the water concentration of two aldehydes and antimony (Sb), though no increase in the cytotoxicity, genotoxicity or estrogenic activity of water extracts in *in vitro* bioassays. A temperature-dependent release of heavy metals was also detected in food cooked in polyethylene bags, with a total migration of 7 percent, 16 percent, 8 percent and 48 percent for lead (Pb), cadmium (Cd), chromium (Cr) and cobalt (Co) respectively, resulting in food concentrations of up to 121, 12, 9.5 and 15 ppm after 5 hours of exposure at 95 °C, especially on the surface of the food (Musoke *et al.*, 2015).

Hernandez *et al.* (2019) also investigated the release of micro-sized particles from plastic teabags when these are immersed in water at 95 °C and estimated an overall exposure to approximately 11.6 and 3.1 billion micro- and nanoplastics per cup of tea, respectively. Renzi *et al.* (2018) observed that by cooking mussels, the amount of microplastics in the edible tissue decreased by up to 14 percent compared to raw tissues, with some smaller-sized fragments found in the surrounding cooking water. Other studies have also detected some plastic manufacturing aids (such as additives) in meat and dairy products, identifying a correlation between migration level and fat content (Goulas *et al.*, 2000; Guerreiro *et al.*, 2018; Khaksar and Ghazi-Khansari, 2009; Sanches Silva *et al.*, 2007; Tsumura *et al.*, 2002).

5.2 OCCURRENCE OF PLASTIC CHEMICALS COMING FROM FOOD PACKAGING MATERIALS

In plastics, additives are not covalently bound to the polymer and are thus free to move and migrate towards the food they are in contact with. Antioxidants from PET reusable bottles and pigmented particles have been found in bottled mineral water (Oßmann *et al.*, 2018). The chemical components of microplastics could either migrate into water before the consumption of the product or afterwards, once the consumer has ingested them. Titanium dioxide and other unidentified pigments have been observed in bottled water (Schymanski *et al.*, 2018). The pigments hostaperm blue, chromate yellow and phthalocyanine – dyes widely used in the plastics industry – were also detected in salt samples (Karami *et al.*, 2017b).

Fasano *et al.* (2012) measured specific migration limits (SML) well below the ones established by the European Union for plastic additives in cans, yoghurt packaging, baby bottles and other food-containing materials. Besides, the exposure to additives contained in plastic food-contact materials (FCM) would only be 0.003, 0.04 and 0.02 μg per kilogram of body weight/day for adults, infants and young children, which is well below the stated daily toxicity threshold limit (0.15 μg per capita in 60 kg adults; Welle and Franz, 2018). It is expected, therefore, that the migration of associated contaminants from microplastics would be much lower, with correspondingly lower exposure levels for consumers.

The concentration of plasticizers and antioxidants in foodstuffs has been measured, with the highest values found in corn and potato snacks (García Ibarra *et al.*, 2018). The authors detected the highest concentrations for the plasticizer ATBC (*O*-acetyl tributyl citrate), with up to 7.09, 0.56 and 2.33 $\mu\text{g}/\text{g}$ in corn snacks, cookies and cake, while DIPB was the most prominent in potato snacks (1.51 $\mu\text{g}/\text{g}$). The most frequently detected phthalate was DEP, together with DEHP. It is important to note that DEP and DIPB are not authorized in the production of food-contact materials. Moreover, DBP exceeded the set migration limit of 0.3 mg/g in part of the samples (European Commission, 2011a). Genualdi *et al.* (2014) measured the amount of styrene monomers that migrated into food, determining a concentration range of between 2.6 ng/g in raw chicken and 163 ng/g in sandwich cookies. The concentration in raw beef (5.6 ng/g), sandwich cookies and chocolate chip cookies (107 ng/g) were in the same range as that detected in a study by Fleming-Jones and Smith (2003) for the same commodities (max: 13 ng/g, 165 ng/g and 111 ng/g, respectively). The migration of dimers and trimers was found to be negligible.

Wang *et al.* (2020) demonstrated that BPA migration in animal feed is dependent on both contact time and the initial concentration in the packaging, ultimately reaching a maximum migration rate and concentration of 26.2 ng/cm² and 17.4 ng/g in corn powder. These values were lower than the specific migration limit (SML) of 0.05 mg/kg set for BPA in food (European Commission, 2018).

To summarize, migration of plastic monomers, oligomers, additives and NIAS is likely to occur, and concentrations will depend on the polymer's characteristics, contact and storage times, food composition, and food-packaging interactions. In spite of this, no significant concerns are expected to arise from the results presented in the majority of studies, which have indicated chemical diffusions into food lower than the chemicals' TDI. Accordingly, the potential migration of such components from microplastics in food may be of even less concern. This notwithstanding, it is important to highlight the current knowledge on the occurrence of (micro)plastic components in food commodities to guide research and regulatory efforts.

5.2.1 DAIRY PRODUCTS

Concentrations of DEHA exceeding the SML set by the European Union were detected on the surface layer of fatty cheese wrapped in PVC film after a contact interval of 240 hours (12.2 mg/dm², 18.9 mg/dm²; Goulas *et al.*, 2000). Penetration into deeper food layers was seen to be very limited.

Fat content, time and temperature-dependent migration of styrene monomers was also investigated in cups containing hot drinks. Styrene leaching occurred at a maximum of 0.05 percent of the cup content, and was found to be highest in general purpose polystyrene (GPPS) cups compared to high impact polystyrene (HIPS), with values of up to 8.15, 8.30 and 8.65 µg/L in tea, milk and cocoa milk (Khaksar and Ghazi-Khansari, 2009). Styrene concentration was also observed to reach higher levels in packaged Gorgonzola cheese (max: 803 ng/g) compared to unpackaged samples (max: 250 ng/g). Its presence was suggested as the likely result of both migration and production by *Penicillium roqueforti*, the fungal starter used in the production of this cheese (Chiesa et al., 2010). The values were however below the legislative limit established by the European Union (60 mg/kg; European Commission, 2011).

Along the dairy supply chain, microplastics can be introduced during the milking of cows at the farm, during downstream processing, or via the final packaging (Da Costa Filho *et al.*, 2021). Contamination levels of 14 MP/L have been reported; the source was suggested as being the membrane filters used during dairy processing (Kutralam-Muniasamy *et al.*, 2020).

5.2.2 WATER

Oßmann *et al.* (2018) measured an average concentration of 23 594 and 195 047 pigment particles per litre of water in reusable PET and glass bottles, which were the same as those in the labels, suggesting bottle cleaning as the possible contamination source. Microplastics were consistently more concentrated in plastic bottled water (1 410 MP/L) compared to glass bottles (204 MP/L) from the same source (Mason *et al.*, 2018).

In addition to this, Wagner and Oehlmann (2009) measured a xenoestrogenic activity in 60 percent of analysed glass, PET and Tetra Pak mineral water samples, with the highest 17 β-estradiol equivalent concentrations (EEQ) of 75.2 ng/L in a non-reusable PET bottle. Glass bottled water samples seemed to induce lower activities compared to PET and Tetra Pak. The authors suggested different possible sources of contamination with endocrine-disrupting compounds; these included contamination during the production process and migration from the bottles themselves. In a worst-case scenario, based on ingestion of 3 L of water per day, the daily intake of estrogenic compounds was measured as 226 ng EEQ.

A WHO study suggested that even at high concentrations, the exposure to microplastic-bound chemicals and biofilms in water did not present a significant health concern (WHO, 2019).

5.2.3 MEAT

Plastic for vacuum packaging contains several films. The chemical compounds used in their manufacture must be regulated to demonstrate the absence of adverse effects on the consumer and on the organoleptic properties of the food. Migration of diisooctyl phthalate (DIOP), polyethylene glycol, phthalic anhydride and stearamide was observed in vacuum-packed beef samples (Guerreiro *et al.*, 2018). Furthermore, the partitioning of a model substance from the LDPE packaging film was seen to be strictly and positively dependent on the contact time between plastic and food, temperature and fat content in pork and chicken (Sanches Silva *et al.*, 2007). Recently, Kedzierski *et al.* (2020) detected extruded polystyrene (XPS) microfibrils on the surface of packaged chicken meat ranging from 4 to 18.7 MP/kg of meat. This most likely came from the packaging process. Rinsing was not efficient in removing the fibrils, and the authors estimated a daily ingestion between 7 µg and 1.4 mg for high-density particles (1040 kg/m³) and meat consumption of 135 g/day.

5.2.4 ALCOHOLIC BEVERAGES

ATBC was detected at a concentration ranging from 2.61 to 7.30 µg/g in bottled *sake* (a Japanese beverage made from fermented rice), possibly after its migration from the gasket cap. This resulted in an exposure of 26.3 µg per kilogram of body weight/day (Tsumura *et al.*, 2002), still considerably lower than the NOAEL.



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CHAPTER 6

ANALYTICAL TECHNIQUES FOR THE DETERMINATION OF MICROPLASTICS AND ASSOCIATED CONTAMINANTS

Investigations into microplastics in a variety of environmental and consumable products have seen considerable methodological development over the last 10 years (Rist *et al.*, 2021). Most of the focus has been on the accuracy of the methods applied, such as analytical approaches to confirm suspected particles as plastic (e.g. by way of spectroscopy, which allows the generation and interpretation of a chemical signature) and the need to carefully ensure samples are not contaminated (e.g. from airborne fibres or from sampling and the analysis process) (Brander *et al.*, 2020). As this is a rapidly evolving field of research, some of the approaches applied 10 years ago are no longer recommended as standalone methods to confirm particles as plastic (Provencher *et al.*, 2020). Similarly, whereas researchers were often limited to larger-sized microplastics (e.g. > 300 µm), working with microscopes and visual inspection of particles alone, nowadays they can work with much smaller particles, albeit with more costly analytical instruments and stricter contamination control procedures.

Some methods are still in development (e.g. for nanoplastics), thus limiting their application on a broad geographical scale because of a lack of instrumentation and (human) capacity. Researchers have also begun to test their methods for accuracy through recovery tests and add procedural blanks to track sources of contamination. These approaches were not common in microplastics research prior to 2015 but are now recommended, if not mandatory (Cowger *et al.*, 2020). Moreover, the way researchers treat their data when they identify sources of procedural contamination in their samples can be vastly different, which can impact the final results and the conclusions drawn from them.

Given this caveat on the nascent character of methodologies in microplastics research, it is worth reiterating that literature cited in this report spans almost the entire lifespan of (micro)plastics studies, from seminal work in the 1970s, to reports published at the beginning of 2022. The research has also been conducted across different continents with an uneven distribution of, and accessibility to (quality) research infrastructure. For example, some of the investigations that identified microplastics in food products over the previous decade applied basic visual identification (e.g. Liebezeit and Liebezeit, 2013, 2014; Boerger *et al.*, 2010). Correcting such data in line with current research requirements is hardly possible. It is therefore important to keep methodological differences in mind when comparing and interpreting research outputs.

6.1 ANALYTICAL METHODS TO IDENTIFY MICROPLASTICS

As noted, the lack of standardized or, at least, comparable analytical methodologies makes it challenging to compare the results provided by different studies. Moreover, the lack of consensus on terminology (e.g. a universally accepted definition of micro- and nanoplastics) also detracts from research progress in the field.

Organisms to be tested are often collected from the environment, purchased at local supermarkets or bought directly from fishers. Depending on the type of organism sampled, different approaches may be employed for the extraction of microplastics. For example, studies investigating microplastic contamination in fish mainly focus on the analysis of gut content, removing the gastrointestinal tract (GIT) and either digesting it or simply opening for a visual identification of the particles. For example, the European Commission Decision 2010/477/European Union highlights the need to analyse stomach content when investigating litter contamination in fish. On the other hand, for mussels (and shellfish generally) the whole animal must be analysed, and tissue digestion is the first step. However, in some studies on crustaceans, either only the GIT was considered, or the animal was simply opened for visual detection (Andrade and Ovando, 2017; Horn *et al.*, 2019; Hossain *et al.*, 2020). The main extraction methods are performed through enzymatic tissue or chemical digestion of tissue. Chemical digestion includes the use of acids, hydroxides and peroxides and it is the technique most frequently used by researchers. It is important to note that in some cases the digestion solution can induce some chemical changes on plastic particles. For instance, hydrogen peroxide (H₂O₂) and nitric acid (HNO₃) could lead to alterations in particle size and the degradation of some polymers such as polyamide (PA) (Claessens *et al.*, 2013; Nuelle *et al.*, 2014). Moreover, nitric acid discolours PE particles (Phuong *et al.*, 2018).

After digestion, a density separation step is carried out in order to separate and collect the lighter microplastics from water, sediment or organic matter, usually through the use of saturated saline sodium chloride (NaCl) or sodium iodide (NaI) solutions. Phuong *et al.* (2018) have suggested that the use of potassium hydroxide (KOH) and potassium iodide (KI) – 10 percent for tissue digestion and 50 percent for sedimentation respectively – may be the best choice for a more complete and

efficient removal of organic matter. A reported benefit of KOH digestion is that it causes only minimal visual or molecular damage to microplastics (Bianchi *et al.*, 2017; Thiele *et al.*, 2019). Finally, the supernatant solution is filtered, and the polymeric particles are identified.

The identification step can be carried out with a microscope, using either Fourier Transformed Infrared spectroscopy (FTIR) or Raman spectroscopy. In this step, the best option may be the combination of two or more analytical approaches to give a better identification of microplastics of a broad size class range. This approach has previously been recommended by K  ppler *et al.* (2016) and Kumar *et al.* (2021): they suggested analysing MP particles larger than 50 μm by micro-FTIR, and those smaller than 50 μm MP by micro-Raman spectroscopy. Raman is also able to characterize the crystalline structure of the polymer. In some studies on beer, salt, water and honey, synthetic particles were detected using dyes such as Nile Red and Rose Bengal, which are not able to identify the polymer type, but enabled researchers to distinguish synthetic materials from organic matter (Kosuth *et al.*, 2018; Liebezeit and Liebezeit, 2015, 2014; Mason *et al.*, 2018). Recently, Huang *et al.* (2020) evaluated a new, faster method to analyse microplastic contamination in chicken meat using attenuated total reflection mid-infrared spectroscopy (ATR-MIR), which seems promising and could, following some improvements, have a significant role in this field. Table 2 summarizes some analytical techniques used for (micro)plastics in seafood.

TABLE 2 ANALYTICAL METHODOLOGIES CURRENTLY IN USE TO ANALYSE THE OCCURRENCE OF PLASTICS IN SEAFOODS

FOOD	SAMPLE	EXTRACTION	SEPARATION	FILTER PORE SIZE	IDENTIFICATION	REFERENCE
Bivalves	Soft tissue	HNO ₃ (69%)		5 μm	μ -Raman	Van Cauwenberghe and Janssen, 2014
Bivalves	Soft tissue	H ₂ O ₂ (30%)	NaCl	0.8 μm	Microscope	Mathalon and Hill, 2014
Bivalves	Soft tissue	H ₂ O ₂ (30%)	NaCl	5 μm	μ -FTIR	Li <i>et al.</i> , 2015
Fish, bivalves	GIT, Soft tissue	KOH (10%)			Microscope	Rochman <i>et al.</i> , 2015
crustaceans	Whole, abdominal muscle	HNO ₃ : HClO ₄ (65% : 68%)		10-20 μm		Devriese <i>et al.</i> , 2015
Bivalves, annelida	Soft tissue	HNO ₃ (69%)		5 μm	μ -Raman	Van Cauwenberghe <i>et al.</i> , 2015
Bivalves	Soft tissue	H ₂ O ₂ (30%)	NaCl	5 μm	μ -FTIR	Li <i>et al.</i> , 2016
Bivalves	Soft tissue	HNO ₃ (22.5 M)		0.7 μm	Microscope	Santana <i>et al.</i> , 2016
Bivalves	Soft tissue	KOH (10%)	NaCl	20 μm	μ -FTIR	H. X. Li <i>et al.</i> , 2018
Crustaceans	GIT	H ₂ O ₂ (30%)	NaCl	45 μm	μ -FTIR	Hossain <i>et al.</i> , 2020
Bivalves	Soft tissue	HNO ₃ (69–71%)		1.2 μm	Microscope	Davidson and Dudas, 2016

TABLE 2 ANALYTICAL METHODOLOGIES CURRENTLY IN USE TO ANALYSE THE OCCURRENCE OF PLASTICS IN SEAFOODS (continued)

FOOD	SAMPLE	EXTRACTION	SEPARATION	FILTER PORE SIZE	IDENTIFICATION	REFERENCE
Bivalves, gastropods, crustaceans.	Whole	HNO ₃ (69%)		5 µm	Raman	Thushari <i>et al.</i> , 2017
Bivalves crustaceans, bivalves, gastropods	Soft tissue	HNO ₃ , NaOH, H ₂ O ₂ (30%)	NaOH	0.7 µm	Microscope	Leslie <i>et al.</i> , 2013
Bivalves	Soft tissue	HNO ₃ : HClO ₄ (65% : 68%)			Hot needle	De Witte <i>et al.</i> , 2014
Fish	GIT	KOH (10%)	NaI	0.45 µm	µ-FTIR	Zakeri <i>et al.</i> , 2020
Fish	GIT	KOH (10%)		1.2 µm	µ-FTIR	Bessa <i>et al.</i> , 2018
Fish	GIT	H ₂ O ₂ (30%)	NaCl	5 µm	µ-FTIR	Jabeen <i>et al.</i> , 2017
Fish	GIT	H ₂ O ₂ (35%)		26 µm	FTIR	Güven <i>et al.</i> , 2017
Fish	GIT	NaOH (1M)		200 µm	µ-FTIR	Baalkhuyur <i>et al.</i> , 2018
Fish	GIT			63 µm	Microscope	Silva-Cavalcanti <i>et al.</i> , 2017
Fish	Viscera and gills	KOH (10%)	NaI	149 µm, 8 µm	µ-Raman	Karbalaee <i>et al.</i> , 2019
Fish	Whole	KOH (10%)	NaI	149 µm, 8 µm	µ-Raman	Karami <i>et al.</i> , 2017a
Fish	Liver	NaClO (9%)		5 µm	Raman	Collard <i>et al.</i> , 2017
Fish	Muscle	KOH (10%)		<2 µm	Microscope	Akhbarizadeh <i>et al.</i> , 2018
Fish, bivalves	Digestive glands and gills GIT	H ₂ O ₂ (30%)		1.2 µm	FTIR	Digka <i>et al.</i> , 2018
Fish	GIT	KOH (10%)		200 µm	FTIR	Tanaka and Takada, 2016
Fish	GIT	H ₂ O ₂ (30%)	NaCl	11 µm	FTIR-UATR	Cheung <i>et al.</i> , 2018
Fish	Muscle, skin, gills, liver, GIT	H ₂ O ₂ (35%), KOH (4%), HClO ₄ (68%), HNO ₃ (65%)	NaI		Microscope	Abbasi <i>et al.</i> , 2018
Fish	Muscle, GIT, gills	KOH (10%)		1.2 µm	FTIR-ATR	Barboza <i>et al.</i> , 2020b
Bivalves	Soft tissue	KOH (10%)		20 µm	µ-FTIR-ATR	Cho <i>et al.</i> , 2019
Gastropods, bivalves	Soft tissue	H ₂ O ₂ (30%)		25 µm, 0.45 µm	µ-FTIR	Naji <i>et al.</i> , 2018
Bivalves	Soft tissue	KOH (10%)	KI	12 µm	µ-FTIR	Phuong <i>et al.</i> , 2018
Bivalves	Hepatopancreas, gills	H ₂ O ₂ (30%)		0.45 µm		Renzi <i>et al.</i> , 2018
Bivalves	Soft tissue	Enzymatic	NaCl	0.8 µm	µ-FTIR-MCT	Catarino <i>et al.</i> , 2018
Bivalves	Soft tissue	H ₂ O ₂ (30%)	NaCl	5 µm	µ-FTIR	J. Li <i>et al.</i> , 2018
Crustaceans, mollusc	Edible tissue	KOH (10%)		11 µm	FTIR	Daniel <i>et al.</i> , 2021
Mussels	Soft tissue	KOH (10%)		2.7 µm	µ-FTIR	Bråte <i>et al.</i> , 2018
Mussels	GIT, digestive glands	KOH (10%)		0.7 mm	µ-FT-IR	DING <i>et al.</i> , 2018

TABLE 2 ANALYTICAL METHODOLOGIES CURRENTLY IN USE TO ANALYSE THE OCCURRENCE OF PLASTICS IN SEAFOODS (continued)

FOOD	SAMPLE	EXTRACTION	SEPARATION	FILTER PORE SIZE	IDENTIFICATION	REFERENCE
Seaweed	Whole	Enzymatic, H ₂ O ₂ (30%)	NaCl	5 µm	µ-FTIR	Li <i>et al.</i> , 2020
Bivalves	Soft tissue	H ₂ O ₂ (30%)	NaCl	5 µm	Microscope, ATR	Qu <i>et al.</i> , 2018
Bivalves	Soft tissue	KOH (10%)		1 µm	Microscope, µ-FT-IR	Teng <i>et al.</i> , 2019
Fish	GIT	KOH (10%)		250 µm	Microscope	Lusher <i>et al.</i> , 2016
Honey, sugar		H ₂ O ₂ (30%)		0.8 µm, 40 µm	Fuchsin, Rose Bengal	Liebezeit and Liebezeit, 2013
Beer				0.8 µm, 40 µm	Rose Bengal	Liebezeit and Liebezeit, 2014
Honey		H ₂ O ₂ (30%)		0.8 µm, 40 µm	Rose Bengal	Liebezeit and Liebezeit, 2015
Salt		H ₂ O ₂ (30%)		5 µm	µ-FTIR	Yang <i>et al.</i> , 2015
Salt		KOH (10%)	NaI	150 µm	µ- Raman	Karami <i>et al.</i> , 2017b
Salt		H ₂ O ₂ (30%)		0.45 µm	FTIR	Seth and Shrivastav, 2018
Water, beer, salt				2.5 µm, 11 µm	Rose Bengal	Kosuth <i>et al.</i> , 2018
Salt		H ₂ O ₂ (30%)	NaI	0.2 µm	µ- Raman	Gündoğdu, 2018
Salt		H ₂ O ₂ (17.25%)		2.7 µm	FTIR-ATR	Kim <i>et al.</i> , 2018
Salt		H ₂ O ₂ (30%)		0.3 µm	SEM Microscope, FTIR	Fadare <i>et al.</i> , 2021
Salt				5 µm	FTIR	Itiniguez <i>et al.</i> , 2017
Water		H ₂ O ₂ (30%)		5 µm, 0.2 µm	µ-FTIR, µ-Raman	Pivokonsky <i>et al.</i> , 2018
Water				1.5 µm	Nile Red, FTIR-ATR	Mason <i>et al.</i> , 2018

Source: Authors' own elaboration.

6.2 ANALYTICAL METHODS FOR PLASTIC ADDITIVES AND CONTAMINANTS

Chemicals associated with microplastics are generally analysed and quantified through chemical separation techniques based on their molecular characteristics. First, the samples undergo an extraction process. Depending on the nature of the food analysed, different techniques can be used. For instance, Fierens *et al.* (2012) extracted phthalates from homogenized high-fat foods and low-fat foods with the use of a mixture (1:1) of acetone/*n*-hexane, followed by a clean-up operated through gel permeation chromatography with dichloromethane (DCM) as the mobile phase. Meanwhile, for aqueous-based beverages and packaging materials a liquid-liquid extraction with DCM or *n*-hexane was performed, without any further purification step. The authors then detected and quantified the single phthalates by gas chromatography, using low-resolution mass spectrometry coupled with electron impact ionization.

Other authors have used techniques such as solid phase microextraction (SPME), solid phase extraction (SPE) with acetonitrile, acetone, *n*-hexane, ethyl-acetate and *n*-hexane (1:2), ether and *n*-hexane to determine monomers or additives in foods and packaging (Chiesa *et al.*, 2010; Goulas *et al.*, 2000; Tsumura *et al.*, 2002). Guerreiro *et al.* (2018) used tetrahydrofuran and methanol in the extraction step to analyse concentrations in packaging materials and beef meat.

Following extraction, a chromatographic separation process is applied, which can be carried out through high-performance liquid chromatography (HPLC), ultra-performance liquid chromatography (UPLC), gas chromatography (GC) coupled with a single or double quadrupole mass spectrometer (MS, MS-MS) or high-resolution gas chromatography (HRMS). Most recently, a new technique using the matrix solid phase dispersion (MSPD) coupled with high-performance liquid chromatography has been implemented (Cañadas *et al.*, 2021). The obtained chromatogram from the separation step is used to check the identity of compounds and measure them by comparing their peaks with library spectral data.

CHAPTER 7

OCCURRENCE OF MICROPLASTICS IN FOOD COMMODITIES

7.1 OCCURRENCE OF MICROPLASTICS IN FISHERY AND AQUACULTURE PRODUCTS

Plastic materials are used extensively in the aquaculture industry and in fisheries. Many fishing gears and equipment such as buoys, nets and ropes are made of synthetic materials, which have already proven their resistance and durability. The composition of plastic polymers found in marine organisms generally reflect the types of plastic that are used in aquaculture or fishing gears, whether to breed or collect these organisms (Castro *et al.*, 2016; Wang *et al.*, 2018). Higher concentrations of microplastics have in fact been found in farmed mussels (Li *et al.*, 2015). Polypropylene (PP) and expanded polystyrene (EPS) have been detected in cultured mussels, and their presence is most probably related to the use of these polymers to make ropes for the line culture of mussels and buoys (Cho *et al.*, 2019; Mathalon and Hill, 2014). PA (nylon) and polyester (PEST) are also extensively used in this industry. What is more, the number of microplastics present in fish has been seen to increase together with the size of the animal (Akhbarizadeh *et al.*, 2018; Boerger *et al.*, 2010), its proximity to urbanized sites, and the concentration of plastic debris in seawater and sediment (Güven *et al.*, 2017; Qu *et al.*, 2018; Silva-Cavalcanti *et al.*, 2017).

A plethora of research has investigated the presence and quantity of microplastics in fish from all over the world, with a great number of papers focusing on the contamination of commercial marine and freshwater species (Table 3). The major polymer types commonly found in the marine environment are PE, PP, followed by PS, PA and PVC (Antunes *et al.*, 2013; Castro *et al.*, 2016; Endo *et al.*, 2005; Fok *et al.*, 2017; Frias *et al.*, 2010; Rios *et al.*, 2007; Wang *et al.*, 2018). As previously mentioned, no particular concerns should arise from the consumption of microplastic-contaminated fish, since most of the microplastics will be removed when the animal is eviscerated (except in small fish, which are typically eaten whole).

However, removal of the fish's gastrointestinal tract may not completely prevent the ingestion of microplastics, as some particles have been detected in the edible muscle tissues of fish, squid, crab and prawn (Abbasi *et al.*, 2018; Akhbarizadeh *et al.*, 2018; Barboza *et al.*, 2020b; Daniel *et al.*, 2021; Karami *et al.*, 2018, 2017a; Ahmadi *et al.*, 2022). These results suggest that considering the digestive tract the only reservoir of plastic could lead to an underestimation of the actual amount that may be ingested.

High-density plastics such as PVC or PET are more likely to sink and be less available to organisms that feed in the upper layers of the water column (Wright *et al.*, 2013). For this reason, it is thought that benthic species may be more impacted, although higher levels of microplastics have generally been found in pelagic species (Güven *et al.*, 2017; Rummel *et al.*, 2016). The reason for their presence in other tissues has made researchers consider other possible exposure mechanisms, such as translocation and adherence (Abbasi *et al.*, 2018; Collard *et al.*, 2017; Karami *et al.*, 2017a; Kolandhasamy *et al.*, 2018). For example, in canned fishery products, contamination could be the result of improper evisceration or processing (Karami *et al.*, 2018).

Seaweed is another important aquaculture product, but literature on the presence of microplastics is still scarce. One study observed between 0.9–3.0 MP/g dw and 1.0–2.8 MP/g dw on the thalli of packaged and processed nori intended for human consumption (Li *et al.*, 2020).

Studies suggest that the most abundant polymer types found in shellfish are polyethylenes (PE, LDPE, HDPE), followed by polyethylene terephthalate (PET), polypropylene (PP), polyamide (PA) and polystyrene (PS). In fish, the most common polymers are PE, PP, PA, PET and PS in descending order, while PE and PP seem to be dominant in fisheries and aquaculture products. Their widespread presence could be explained by their large use and production that reaches 36 percent and 21 percent for PE and PP respectively (Geyer *et al.*, 2017). Besides, PE and PA have been encountered in the surface layers of water close to a mariculture farm (Wang *et al.*, 2018).

Plastics are more frequently found in the shape of fibres or fragments, while other morphologies such as beads, film and pellets are less common. The great abundance of fibres suggests that the main sources of plastics may be fishing gears and aquaculture facilities in the case of PA and PP, while household disposal could be the origin of many textile polymers such as rayon (RY). It has been suggested that around 0.19 million tonnes of microplastic fibres from the production and normal use of synthetic textiles enter the marine environment alone annually (Henry *et al.*, 2019).

As can be seen in Table 3, the average number of microplastics found in the gastrointestinal tract of fish varied from 0.03 to 7.2 MP/individual, while the concentration of microplastics per gram ranged from 0.16 to 34.9 MP/g. In the edible tissue of shellfish, the concentration range of microplastics was between 0.04 and 12.8 MP/g. The concentration of particles detected in the muscle tissue of commercial fish in the northeast Atlantic Ocean and Persian Gulf ranged from 0.05 to 1.85 MP/g, respectively (Akhbarizadeh *et al.*, 2018; Barboza *et al.*, 2020b).

Studies have reported varying levels of contamination in fish species, including those targeted for human consumption (Table 3). As an example, some of the earliest work on fish identified between 2.4 and 33 percent of sampled fish as containing microplastics (Foekema *et al.*, 2013; Liboiron *et al.*, 2016). Barboza *et al.* (2020) also detected microplastics in 49 percent of 150 investigated commercial fish species from the northeastern Atlantic Ocean. The highest prevalence of contaminated fish was found in a river in northeast Brazil, with 83 percent of catfish (*Hoplosternum littorale*) showing evidence of having ingested plastic debris (Silva-Cavalcanti *et al.*, 2017), followed by anchovies (*Engraulis japonicas*) collected in Tokyo Bay, with 77 percent of the individuals containing microplastics (Tanaka and Takada, 2016). As for bivalves, microplastics were detected in 33 percent of Pacific oyster (*Crassostrea gigas*) samples from California, in 46 percent of mussels (*Mytilus galloprovincialis*) from the Ionian Sea and in 84 percent of oysters collected from farms along the Chinese coastline (Digka *et al.*, 2018; Rochman *et al.*, 2015; Teng *et al.*, 2019).

7.2 OCCURRENCE OF MICROPLASTICS IN OTHER FOOD COMMODITIES

Aquaculture and fisheries products are not the only food groups that may be contaminated with microplastics. Plastic polymers have also been detected in other foods such as salt, sugar, beer and honey. Since 2018, many studies have also developed an interest in the contamination of drinking water. In all the aforementioned commodities, plastic fibres and fragments are commonly detected shapes. However, the number of microplastics in these foods may be under- or overestimated, as not many studies used spectroscopic techniques to identify synthetic particles. Similarly, some studies used dye techniques that are unable to indicate the types of microplastics found.

7.2.1 SALT

Sea salt contamination most likely reflects the contamination of the seawater used to produce it. The most probable source of microplastics would therefore be fragments present in the water column. Salts can also be made from lake waters and mineral deposits, but the most common source is marine water. Sea salt is produced by way of a stepwise evaporation of water in successive ponds, resulting in the crystallization of salt. Salt brands from Asia, and especially Indonesia, were seen to contain higher levels of microplastics compared to other countries, likely reflecting the higher coastal (micro)plastic pollution levels in these countries (Kim *et al.*, 2018). For mineral salt, contamination may occur during industrial processing and manufacture. For instance, refining could influence the load of plastic in the product (Kim *et al.*, 2018).

Packaging is also likely to contribute, to a certain degree (Yang *et al.*, 2015). Renzi and Blašković (2018) found significant differences in fine iodized sea salt brands according to their price, with more expensive brands showing a lower quantity of plastics. The concentration of microplastics in Croatian table sea salt varied

TABLE 3 OCCURRENCE OF MICROPLASTICS IN AQUATIC SPECIES

SPECIES	SAMPLE NUMBER	PARTICLE AMOUNT	SAMPLING	SHAPE	PARTICLE SIZE	POLYMERS	LOCATION	REFERENCE
5 mesopelagic and 1 epipelagic fish species	670	1–83 MP/ fish (2.1 ± 5.78 MP/fish)	Manta trawl	Fragments, film, fishing line, ropes	1–2.79 mm		North Pacific Central Gyre	Boeger <i>et al.</i> , 2010
10 species of fish (5 pelagic, 5 demersal)	504	1–15 MP/fish (1.90 ± 0.10 items/fish)	Standard haul trawl	Fibres, fragments, beads	0.13 mm–14.3 mm	PA, LDPE, PS, RY, PEST	English Channel	Lusher <i>et al.</i> , 2013
<i>Mytilus edulis</i> <i>Crassostrea gigas</i>	72 21	0.36 ± 0.07 MP/g ww 0.47 ± 0.16 MP/g ww	Mussel farm, supermarket	Particles	5–10 µm 11–20 µm		North Sea, Atlantic Ocean	Van Cauwenberghe and Janssen, 2014
<i>Mytilus edulis</i>	45	Wild: 34 MP/ind 106–126 MP/ind Cultured: 75 MP/ind 178 MP/ind	Collection at low tide, grocery store	Fibres			Newfoundland, Nova Scotia, Canada	Mathalon and Hill, 2014
26 species of commercial fish	263	1.40 ± 0.66 MP/ fish or 0.27 ± 0.63 MP/fish	Stern trawlers	Fibres, fragments	0.217–4.81 mm	Alkyd resin, PE, PP, RY, PA 6, PEST, acrylic	Portuguese coast	Neves <i>et al.</i> , 2015
9 species of commercial bivalves	144	4.3–57.2 MP/ ind 2.1–10.5 MP/g ww	Shanghai fishery market	Fibres, fragments, pellets	5 µm–5 mm	PE, PET, PA	Coastal waters of China	Li <i>et al.</i> , 2015
Indonesia: 11 fish species United States of America: 12 fish species and <i>Crassostrea gigas</i>	152	Indonesia: 0–21 MP/ fish (1.4±3.7 MP/fish) United States of America: 0–10 MP/ fish, 0–2 MP/ oyster (0.5 ± 1.4 MP/ind)	Fish markets, fishers	Fibres, fragments, films, foams, Styrofoam, monofilaments	Indonesia: 3.5 ± 1.1 mm United States of America: 6.3 ± 6.7 mm (fish), 5.5 ± 5.8 mm (oysters)		Sulawesi (Indonesia) and California (United States of America)	Rochman <i>et al.</i> , 2015
<i>Crangon crangon</i>	165	0.68 ± 0.55 MP/ g ww Max: 1.92 ± 0.61 MP/g ww 1.23 ± 0.99 MP/ind	Shrimp trawl and beam trawl net	Fibres, granules, films	200–1000 µm		Channel area and Southern part of the North Sea (France, Belgium, Netherlands, United Kingdom)	Devriese <i>et al.</i> , 2015
<i>Mytilus edulis</i> <i>Arenicola marina</i>	n.s.	0.2 ± 0.3 MP/g ww Max 1.1 MP/g ww 1.2 ± 2.8 MP/g Max 11.3 MP/g ww	Randomly on breakwaters, bait-pump or shovel	Particles	20–90 µm 15–100 µm	LDPE, HDPE, PS	French, Belgian and Dutch North Sea coast	Van Cauwenberghe <i>et al.</i> , 2015
5 fish species (3 demersal and 2 pelagic)	290	0.03 ± 0.18 MP/fish 0.19 ± 0.61 MP/fish (pelagic)	Bottom/pelagic trawling	Particles	< 180 µm	PE, PA, PP, PS, PET, PEST, PU	North and Baltic Seas	Rummel <i>et al.</i> , 2016
<i>Mytilus edulis</i>	12–30 per 22 sites	1.5–7.6 MP/ind (4 MP/ ind) 0.9–4.6 MP/g ww (2.2 MP/g ww)	Tweezers at low tide, underwater with fishermen	Particles	< 250 µm Fibres: 33µm–4.7 mm	OP, PET, PEST	Coastline of China	Li <i>et al.</i> , 2016

TABLE 3 OCCURRENCE OF MICROPLASTICS IN AQUATIC SPECIES (continued)

SPECIES	SAMPLE NUMBER	PARTICLE AMOUNT	SAMPLING	SHAPE	PARTICLE SIZE	POLYMERS	LOCATION	REFERENCE
<i>Perna perna</i>	30	75% mussels contaminated with MPs	Byssus cut and removal	Fragments	< 5 000 µm		Santos's estuary, São Paulo, Brazil	Santana <i>et al.</i> , 2016
<i>Saccostrea cucullata</i>	≥30 samples per 11 sites	1.4–7.0 MP/ind 1.5–7.2 MP/g ww	Intertidal zone	Fibres, fragments, production pellets	20–5 000 µm (mostly < 100 µm)	PET, PP, PE, PS, CP, PVC, PA, EPS	Pearl River Estuary, South China	H. X. Li <i>et al.</i> , 2018
<i>Penaeus monodon</i>	100	6.60 ± 2 MP/ind 1.55–4.84 MP/g ww (3.40 ± 1.23 MP/g ww)	Offshore shrimp trawlers and bag net fishing	Fibres, fragments, particles	1–5 mm 250–500 µm	PA 6, RY	Northern Bay of Bengal, Bangladesh	Hossain <i>et al.</i> , 2020
<i>Metapenaeus monoceros</i>	50	7.80 ± 2 MP/ind 2.17–4.88 MP/g ww (3.87 ± 1.05 MP/g ww)						
<i>Venerupis philippinarum</i>	54	0.07–5.47 MP/g ww Wild: 8.4 ± 8.5 MP/ind Max 12.7 ± 13.0 MP/ind 0.9 ± 0.9 MP/g Farmed: 11.3 ± 6.6 MP/ind Max 15.4 ± 6.3 MP/ind 1.7 ± 1.2 MP/g (Max 2.2 ± 0.8 MP/g)	0.5 m × 0.5 m quadrat, from farmed sites	Fibres, films, fragments			Baynes Sound, British Columbia	Davidson and Dudas, 2016
<i>Emerita analoga</i>	5–15 crabs per 38 sites	0.65 ± 1.64 MP/ind Max 16 MP/ind	Shovel, sand-coring tool	Fibres, particles		PP, polyacrylate, PEST, PE	Pacific coast of California	Horn <i>et al.</i> , 2019
<i>Lithodes santolla</i>	30	1–3 MP/ind	Trap gears	Fibres	3–>20 mm	n.s.	Nassau Bay, Cape Horn, Chile	Antrade and Ovando, 2017
<i>Saccostrea forskalii</i>	15	0.37 ± 0.03 - 0.57 ± 0.22 MP/g ww	Intertidal zone at low tide	Fibres		PS, PET, PA	Upper Gulf of Thailand	Thushari <i>et al.</i> , 2017
<i>Littoraria</i> sp.	50	0.17 ± 0.08 - 0.23 ± 0.02 MP/g ww						
<i>Balanus amphitrite</i>	50	0.23 ± 0.10 - 0.43 ± 0.33 MP/g ww						
<i>Crassostrea gigas</i>	6	87 MP/g dw	From littoral zones	Fibres	1–5000 µm (Mostly 1–300 µm)		Dutch coast	Leslie <i>et al.</i> , 2013
<i>Gammarus</i> sp.	16	11 MP/g dw						
<i>Mytilus edulis</i>	20	105 MP/g dw						
<i>Littorina littorea</i>	10	20 MP/g dw						
<i>Mytilus edulis</i>	30	0.04–0.81 MP/g ww (0.37 MP/g ww)	Department stores, manual sampling at groynes and quayside	Fibres	200–1500 µm		Belgium, Netherlands	De Witte <i>et al.</i> , 2014
<i>Chelon aurata</i>	60	2.95 ± 1.98 MP/fish		Fibres, fragments	1.94 ± 0.71 mm 1.77 ± 0.53 mm	PA	Southern Caspian Sea	Zaheri <i>et al.</i> , 2020
<i>Rutilus kutum</i>	51	1.66 ± 1.23 MP/fish		Fibres, fragments				
<i>Platichthys flesus</i>	40	0.18 ± 0.55 MP/fish	Beam trawl	Fibres, fragments		PE, PP, PEST, PA-6, RY, PAN	Mondego estuary, Portugal	Bessa <i>et al.</i> , 2018
<i>Diplodus vulgaris</i>	40	3.14 ± 3.25 MP/fish						
<i>Dicentrarchus labrax</i>	40	0.30 ± 0.61 MP/fish						

TABLE 3 OCCURRENCE OF MICROPLASTICS IN AQUATIC SPECIES (continued)

SPECIES	SAMPLE NUMBER	PARTICLE AMOUNT	SAMPLING	SHAPE	PARTICLE SIZE	POLYMERS	LOCATION	REFERENCE
21 species of marine fish, 6 species of freshwater fish	20-40 ind. per species	1.1 ± 0.3-7.2 ± 2.8 MP/fish 0.2 ± 0.1 - 17.2 ± 9.7 MP/g	Fishery markets, fishermen	Fibres, fragments, pellets	0.04-5 mm	OP, PET, PEST	Yangtze estuary, East China and South China Sea, Taihu Lake	Jabben <i>et al.</i> , 2017
<i>Boops boops</i>	337	2.47 ± 0.23-4.89 ± 0.45 MP/fish	Bottom trawl nets and purse seine	Filaments	1 mm-5 mm		Balearic Islands	Nadal <i>et al.</i> , 2016
6 marine fish species	1381	1.62 ± 1.58 - 2.96 ± 5.21 MP/fish (0-32 MP/fish)	Hook and line	Fibres, microbeads, fragments	< 5 mm		Texas Gulf Coast	Peters <i>et al.</i> , 2017
28 marine fish species	1337	2.36 MP/fish (1-35 MP/fish)	Trawl net	Fibres, hard plastic, nylon, rubber, miscellaneous plastic	656 ± 803 µm (Range: 9.07-12 074.11 µm)	Copolymers, alloys, PA, LDPE, PP, rubber	Mediterranean Coast of Turkey	Güven <i>et al.</i> , 2017
26 marine fish species	178	0-3 MP/fish	Tucker nets, fishermen	Fibres, film, fishing thread	2.39 ± 0.28 mm (range: 1-3 mm)	PP, PE, PS, PVC, PAN	Saudi Arabian Red Sea Coast	Baalkhuyur <i>et al.</i> , 2018
<i>Hoplosternum littorale</i>	48	3.6 MP/fish (1-24 MP/fish)	Fishers	Fibres, soft plastic, hard plastic	< 1-12 mm		Pajeru river, northeastern Brazil	Silva-Cavalcanti <i>et al.</i> , 2017
<i>Scomberomorus cavalla Rhizoprionodon lalandii</i>	32	2-6 MP/fish 1-3 MP/fish	Fishers	Resin pellets	2-5 mm 1-3 mm		Salvador, northeastern Brazil	Miranda and de Carvalho-Souza, 2016
<i>Rastrelliger kanagurta</i> <i>Stolephorus waitiei</i> <i>Chelon subviridis</i> <i>Johnius belangerii</i>	120	1-3 MP/fish	Local markets	Fragments, films, pellets		PP, PE, PS, PET, PA-6	Malaysia	Karami <i>et al.</i> , 2017a
<i>Alepes djedaba</i> <i>Epinephelus coioides</i> <i>Sphyrna tello</i> <i>Platycephalus indicus</i>	71	0.80 ± 0.12 MP/g muscle 0.78 ± 0.22 MP/g muscle 0.57 ± 0.17 MP/g muscle 1.85 ± 0.46 MP/g muscle	Fishmongers	Fibres, fragments, pellets	< 300 µm		Persian Gulf	Akbarizadeh <i>et al.</i> , 2018
<i>Mytilus galloprovincialis</i>	80	1.7 ± 0.2-2.0 ± 0.2 MP/ind 1.9 ± 0.2 MP/ind. 2.5 ± 0.3 - 5.3 ± 0.5 MP/g ww 1.8 ± 0.2 MP/fish 34.9 ± 7.9 MP/g ww 1.9 ± 0.2 MP/fish 27.8 ± 24.6 MP/g ww	Hand collection, trawling	Fragments, fibres	0.1-0.5 mm	PE, PP, PET, PS, PTFE	Northern Ionian Sea	Digka <i>et al.</i> , 2018 ¹
<i>Sardina pilchardus</i>	36							
<i>Pagellus erythrinus</i>	19							
<i>Mullus barbatus</i>	25	1.5 ± 0.3 MP/fish 11.2 ± 2.8 MP/g ww						

TABLE 3 OCCURRENCE OF MICROPLASTICS IN AQUATIC SPECIES (continued)

SPECIES	SAMPLE NUMBER	PARTICLE AMOUNT	SAMPLING	SHAPE	PARTICLE SIZE	POLYMERS	LOCATION	REFERENCE
<i>Engraulis japonicus</i>	64	2.3±2.5 MP/fish (0-15 MP/fish)	Fishing	Fragments, beads, filaments, foams	783 ± 1020 µm (150–6 830 µm)	PE, PP, PS, ethylene/propylene copolymer, ethylene/propylene/diene terpolymer	Tokyo Bay	Tanaka and Takada, 2016
<i>Mugil cephalus</i>	60	Wild: 4.3± 14.5 MP/fish Captive: 0.20 ± 0.48 MP/fish	Fish markets, fish ponds	Fibres, fragments, sheets	0.1- 12 mm	PP, PE, PEST, PET, PA, PTFE	East coast of China, Hong Kong SAR	Cheung <i>et al.</i> , 2018
<i>Platycephalus indicus</i> <i>Saurida tumbil</i> <i>Sillago sihama</i> <i>Cynoglossus a abbreviatus</i> <i>Penaeus semisulcatus</i>	56	0.16–1.5 MP/g	Trawl net	Fragments, fragments	< 100 µm– > 1000 µm		Musa Estuary, Persian Gulf	Abbasi <i>et al.</i> , 2018
<i>Crassostrea gigas</i> <i>Mytilus edulis</i> <i>Tapes philippinarum</i> <i>Patinopecten yessoensis</i>	60 (composite)	0.07 ± 0.06 MP/g (0–0.19 MP/g) 0.12 ± 0.11 MP/g (0–0.35 MP/g) 0.34 ± 0.31 MP/g (0.03–1.08 MP/g) 0.08 ± 0.08 MP/g (0.01–0.17 MP/g) Overall: 0–1.08 MP/g ww 0–2.8 MP/ind	Fishery markets	Fragments, fibres, films	100–200 µm	PE, PP, PS, PEST, silicon, PA, PEVA, PET, PU, acrylic, PTFE, PVC, PPS, PVA, PBT, polyethyl acrylate styrene, polyepoxides, styrene/styrene/acrylonitrile, and polystyrene ethylene butylene styrene	Seoul, Gwangju, Busan, Republic of Korea	Cho <i>et al.</i> , 2019
<i>Certhidea cingulata</i> <i>Thais mutabilis</i> <i>Amiantis umbonella</i> <i>Amiantis purpuratus</i> <i>Pinctada radiata</i>	123	Clams & oyster: 0.2–2.2 MP/g ww 3.9–6.9 MP/ind Snails: 12.8–20.0 MP/g ww 3.7–17.7 MP/ind	Intertidal zone at low tide	Fibres, fragments, films, pellets	10– > 5 000 µm	PE, PET, PA	Persian Gulf	Naji <i>et al.</i> , 2018
<i>Mytilus edulis</i>	120	0.23 ± 0.09 MP/g	Supermarket, collection from the wild	Fragments, fibres	30–200 µm	PP, PE, PEST, ABS	Region Pays de la Loire, market in Nantes	Phuong <i>et al.</i> , 2018
<i>Mytilus galloprovincialis</i>		8.33 ± 3.58 MP/g ww 3.6–12.4 MP/ind 4.4–11.4 MP/g ww	Local markets, collection from rocky bottom	Filaments	0.75–6.00 mm (Average: 1.15–2.29 mm)		Mediterranean Sea	Renzi <i>et al.</i> , 2018

TABLE 3 OCCURRENCE OF MICROPLASTICS IN AQUATIC SPECIES (continued)

SPECIES	SAMPLE NUMBER	PARTICLE AMOUNT	SAMPLING	SHAPE	PARTICLE SIZE	POLYMERS	LOCATION	REFERENCE
<i>Modiolus modiolus</i> <i>Mytilus</i> spp.	6 36	0.086 ± 0.031 MP/g ww 3.5 ± 1.29 MP/ind 3.0 ± 0.9 MP/g ww 3.2 ± 0.52 MP/ind	Scuba diving, collection at low tide	Fibres	0.2->2 mm	PET, PEST, poly (etherurethane)	Scottish coast, United Kingdom	Catano <i>et al.</i> , 2018
<i>Mytilus galloprovincialis</i> <i>Mytilus edulis</i>	61	0.04 ± 0.09-0.34 ± 0.33 MP/g ww (0.13 ± 0.14 items/g ww)	Hand collection, department stores	Fibres, particles			Europe	Vandemeersch <i>et al.</i> , 2015
<i>Pyropia</i> spp.		Packaged: 0.9-3.0 MP/g dw (1.8 ± 0.7 MP/g dw) Processed: 1.0-2.8 MP/g dw (1.8 ± 0.6 MP/g dw)	Local markets		Packaged: 0.11-4.97 mm Processed: 0.07-4.74 mm	PEST, RY, PP, PA, CP	China local markets, Yellow Sea	Li <i>et al.</i> , 2020
<i>Mytilus edulis</i>	162	0.7-2.9 MP/g ww 1.1-6.4 MP/ind	Collection from the coast	Fibres, fragments	8 µm-4.7 mm	PEST, PP, PE, RY	United Kingdom	J. Li <i>et al.</i> , 2018
<i>Mullus surmuletus</i>	417	0.04±0.04-1.07±0.26 MP/ ind	Bottom trawl and trammel	Filaments		PET, CP, polyacrylate	Western Mediterranean	Alomar <i>et al.</i> , 2017
<i>Ammodytes personatus</i> <i>Clupea pallasii</i>	734 205	1-9 MP/fish 5-27 MP/fish	Collected from rhinoceros auklets	Fibres	0.75mm-142.4mm	PEST, acrylic, RY, PP, PA, cotton, wool	British Columbia, Canada, and Washington State, United States of America	Hipfner <i>et al.</i> , 2018
<i>Mytilus edulis</i> <i>Perna viridis</i>	30 mussels/25 sites	1.52-5.36 MP/g ww 0.77-8.22 MP/ind	Tweezers at low tide	Fibres, fragments, beads	0.25-1 mm	PET, PE, RY, PVC, PP	Coastal waters of China	Qu <i>et al.</i> , 2018
10 species of mesopelagic fish	761	0-4 MP/fish 1.2 ± 0.54 MP/fish	Pelagic midwater trawling	Fibres, fragments	0.5-11.7 mm	n/a	Northeast Atlantic Ocean	Lusher <i>et al.</i> , 2016
<i>Mytilus</i> spp.	332	0-6.9 MP/ind (1.5 ± 2.3 MP/ind) 0-7.9 MP/g ww (0.97 ± 2.61 MP/g ww)	Hand collection, snorkeling, metal rake with net	Fibres, fragments, foams, films,	70-3 870 µm	PET, PP, PE, PA, epoxy resin, PVC, PAN, SAN, EVA, soloprene	Norway	Bråte <i>et al.</i> , 2018
<i>Mytilus galloprovincialis</i>	50 (markets) 15 (wild)	1.9-9.6 MP/ind 2.0-12.8 MP/g ww 5.2-19.4 MP/ind 3.2-7.1 MP/g ww	Fishery markets, coastal sampling	Fibres, fragments, granules	25 µm-5 mm	CP, PP, PTFE	China	DING <i>et al.</i> , 2018
<i>Chlamys farreri</i> <i>Dicentrarchus labrax</i> <i>Trachurus trachurus</i> <i>Scomber colias</i>	150	1.2 ± 2.0 MP/ind (GIT) 0.7±1.2 MP/ind (gills) 0.054±0.099 MP/g ww (muscle) Total mean: 1.2±2.0 MP/ind (GIT) 0.7±1.2 MP/ind (gills) 0.054±0.099 MP/g ww (muscle)	Trawls	Fibres, fragments, pellets	< 100-5 000 µm	PE, PEST, RY	Northeast Atlantic Ocean	Barboza <i>et al.</i> , 2020

TABLE 3 OCCURRENCE OF MICROPLASTICS IN AQUATIC SPECIES (continued)

SPECIES	SAMPLE NUMBER	PARTICLE AMOUNT	SAMPLING	SHAPE	PARTICLE SIZE	POLYMERS	LOCATION	REFERENCE
<i>Crassostrea gigas</i> <i>Crassostrea angulata</i> <i>Crassostrea hongkongensis</i> <i>Crassostrea sikamea</i>		0.11±0.10–2.35±1.39 MP/g ww 1.05±1.03–9.08±5.70 MP/md Total mean: 2.93 MP/md 0.62 MP/g ww	Purchased from farms	Fibres, fragments, films, pellets	20.3–4 807.2 µm	OP, PE, PET, PP, PA, PS, PC, PVC	Chinese coastline	Teng <i>et al.</i> , 2019
<i>Metapenaeus dobsoni</i> <i>Fenneropenaeus indicus</i> <i>Portunus pelagicus</i> <i>Urodeuthis (Photoligo) duvaucelii</i> <i>Temalosa ilista</i> <i>Penaeus indicus</i> <i>Macellicephalo affinis</i> <i>Penaeus semisulcatus</i>	50 50 30 50 12 12 151 103	n.d. n.d. 0.14 ± 0.44 MP/ind 0.003 ± 0.01 MP/g ww 0.18 ± 0.48 MP MP/ind 0.008 ± 0.02 MP/g ww 2.1 ± 0.81 MP/ind 0.41 ± 0.13 MP/g muscle 0.75 ± 0.5 MP/ind 0.11 ± 0.07 MP/g muscle 0.35 ± 0.46 MP/ind 0.45 ± 0.23 MP/g muscle 0.58 ± 0.61 MP/ind 0.62 ± 0.25 MP/g muscle 6 ± 7 MP/ind	Purchased from harbours	Fragments, fibres, sheets Fibre	100–300 µm < 100–1000 µm	PP, PE, PS n/a	Kerala, India Persian Gulf	Daniel <i>et al.</i> , 2021 Ahmadi <i>et al.</i> , 2022
3 fish species (<i>Cyprinus carpio</i>, <i>Mugil cephalus</i>, <i>Platichthys flesus</i>)	128	(Gastrointestinal tract) 0.5 ± 1.1 MP/ind (gills) 0.3 ± 0.7 MP/ind (liver) 0.6 ± 1.2 MP/ind(muscle) 0.3 ± 0.3 MP/g (Gastrointestinal tract) 0.6 ± 1.5 MP/g (gills) 0.7 ± 2.0 MP/g (liver) 0.1 ± 0.2 MP/g (muscle)	Fishers, beam trawl	Fibre Fragments	< 100–5 000 µm	36 Plastic polymers were identified (most common: Rayon, PE, PES, PP, polyacrylate, cellulose acetate)	Estuary of the Minho River	Guilhermino <i>et al.</i> , 2021
<i>Sardina pilchardus</i> <i>Engraulis encrasicolus</i> <i>Merluccius Merluccius</i> <i>Pegusa impar</i> <i>Mullus Surmuletus</i> <i>Gobius paganellus</i>	30 30 30 30 30 30	0.63 ± 1.10 MP/ind 0.033 ± 0.052 MP/g 0.47 ± 0.86 MP/ind 0.041 ± 0.077 MP/g 1.37 ± 1.56 MP/ind 0.011 ± 0.012 MP/g 2.47 ± 2.99 MP/ind 0.016 ± 0.018 MP/g 1.90 ± 1.81 MP/ind 0.048 ± 0.044 MP/g 0.93 ± 0.23 MP/ind 0.037 ± 0.065 MP/g	purchased from a hypermarket (*The origin labelling certified that these fish had been fished in the FAO sub-area 37.2.1 – Adriatic Sea).	Fibre Fragments	54–765 µm	PP, PE	North Adriatic Sea	Mistri <i>et al.</i> , 2022

¹ For individuals that ingested microplastics.

Note: ww = wet weight; ind = individual.

Source: Authors' own elaboration.

between 13 500 MP/kg to 19 800 MP/kg, with the great majority of them being polypropylene (PP) and polyethylene (PE) (Table 4). These polymers are among the main constituents of salt plastic packaging, together with PET (Yang *et al.*, 2015).

Environmental contamination of production water is also considered to be a plausible source of microplastic contamination (Iñiguez *et al.*, 2017; Kim *et al.*, 2018; Renzi and Blašković, 2018; Seth and Shriwastav, 2018; Yang *et al.*, 2015).

Compared to other exposure routes, the contribution of salt to total exposure is expected to be minimal (Kim *et al.*, 2018).

7.2.2 HONEY AND SUGAR

The most frequently detected shapes of plastics found in honey are fibres, followed by a lower number of fragments. Some studies have suggested that foraging bees are most likely to transport microplastics to the hive, which could be then incorporated into the honey (Liebezeit and Liebezeit, 2013). This suggests that airborne contamination, probably of flowers, may be an important transmission route. Besides, as already discussed, the harvesting, processing and packaging of the final product could contribute only minimally to contamination. The microplastics load in samples varied between 2–82 fragments/kg and 10–336 fibres/kg (Liebezeit and Liebezeit, 2015). Fibres were the most common, and most numerous, form of microplastics found in the product (Table 4).

Only one study (Liebezeit and Liebezeit (2013), was found on the occurrence of microplastics in sugar. The authors reported a greater number of synthetic particles in unrefined cane sugar (560 fibres/kg and 540 fragments/kg) compared to refined samples (388 fibres/kg sugar and 270 fragments/kg sugar; see Table 4).

7.2.3 BEER

Possible contamination sources cited for microplastics in beer are atmospheric deposition or direct contamination during production (Kosuth *et al.*, 2018; Liebezeit and Liebezeit, 2014). The most common plastic shapes found in beer samples are fibres and fragments. The microplastics load in commercial beer samples ranged from 12 to 109 fragments/L (Liebezeit and Liebezeit, 2014; see Table 4).

7.2.4 WATER

Water treatment plants generally remove up to 90 percent of microplastics (WHO, 2019; 2017). Pivokonsky *et al.* (2018) detected lower levels of microplastics in treated water (a maximum of 684 particles/L) compared to raw samples (a maximum of 4 464 particles/L). Not all studies were able to detect microplastics in water coming from waterworks, which suggests these materials were either absent or present in shapes or concentrations undetected by the method applied (Strand *et al.*, 2018; Uhl *et al.*, 2018).

The most frequently detected synthetic polymer residues in drinking water are usually the main components of the bottles used to contain it. Some studies have identified the packaging itself to be among the main sources of contamination (Mason *et al.*, 2018; Oßmann *et al.*, 2018; Schymanski *et al.*, 2018). Polyethylene terephthalate (PET) is generally used to make water bottles, while polypropylene (PP) and polyethylene (PE) make up the bottle caps. The latter is also used to cover the interior of beverage cartons. The presence of other plastic types such as PVC, polyester (PEST) and epoxy resin have also been detected, and their presence could be connected to the materials that make up tanks and pipes through which water flows before it is supplied to households (Mintenig *et al.*, 2019). Pivokonsky *et al.* (2018) observed that the main proportion of microplastics in water was that of particles smaller than 100 µm, with 40–60 percent of the particles from water treatment plants ranging from 1 to 5 µm in size.

For bottled water, a generally higher contribution to overall human exposure seems to be made by reusable plastic bottles, which have been seen to contain as much as ten times more microplastics compared to single-use bottles (Schymanski *et al.*, 2018). However, Oßmann *et al.* (2018) detected a higher concentration of microplastics in glass bottles ($6\,292 \pm 10\,521$ MP/L) compared to newer, returnable bottles (4889 ± 5432 MP/L). Older reusable PET bottles were the most contaminated (8339 ± 7043 MP/L). The production, cleaning and refilling of these bottles should be checked with greater attention, as they may cause stress and release of particles from the bottles. Finally, when compared to salt and beer, tap water causes the greatest exposure to microplastics, accounting for almost 88 percent of estimated total yearly exposure (Kosuth *et al.*, 2018).

7.2.5 FRUITS AND VEGETABLES

Oliveri Conti *et al.* (2020) reported the occurrence of microplastics in apples, pears, broccoli, lettuce and carrots (Table 4) The authors detected microplastics in the edible tissues of these food items, with higher average concentrations in fruits (apples: 195 500 MP/g; pears: 189 550 MP/g) compared to vegetables (broccoli: 126 150 MP/g; carrots: 101 950 MP/g; lettuce: 50 550 MP/g). This difference was supposedly related to diversity in life-length, pulp vascularization and root system.

Some occurrence data for microplastics in non-marine foods are provided in Table 4.

TABLE 4 OCCURRENCE OF MICROPLASTICS IN HONEY, SUGAR, SALT AND WATER

COMMODITY	NUMBER OF SAMPLES	PARTICLE AMOUNT	SAMPLING	SHAPE	PARTICLE SIZE	POLYMERS	LOCATION	REFERENCE
Honey Sugar (refined) Cane sugar (unrefined)	19 5	—	Local producers, supermarkets	Fibres, fragments	40 µm–9 mm 10–20 µm		Germany, Italy, Spain, Mexico, France	Liebezeit and Liebezeit, 2013
Beer	24	2–79 fibres /L 12–109 fragm/L 2–66 granules/L	Supermarkets	Fibres, fragments, granules			Germany	Liebezeit and Liebezeit, 2014
Honey	47	10–336 fibres /kg 2–82 fragm/kg	Supermarkets, beekeepers	Fibres, fragments	1 µm–5 mm		Germany	Liebezeit and Liebezeit, 2015
Salt	15	Sea: 550–681 MP/kg Lake: 43–364 MP/kg Rock: 7–204 MP/kg	Supermarkets	Fragments, Fibres, pellets, sheets	45 µm–4.3 mm	PET, PEST, PE, PB, PP, CP	China	Yang <i>et al.</i> , 2015
Salt	16	1–10 MP/kg	Brands from Malaysian market	Fragments, filaments, films	160–980 µm	PP, PE, PET, PA-6, PS, PAN	Australia, Iran (Islamic Republic of), Japan, Malaysia, New Zealand, Portugal, South Africa	Karami <i>et al.</i> , 2017b
Salt	11	Italy: 22–594 MP/kg Croatia: 13 500–19 800 MP/kg	Supermarkets	Fragments, fibres, films, foams, granules	4–2100 µm 15–4628 µm	PP, PE	Italy, Croatia	Renzi and Blašković, 2018
Salt	8	56±49–103±39 MP/kg	Supermarket s, local markets	Fragments, fibres	200–7000 µm	PEST, PET, PS, PE, PA	India	Seth and Shrivastav, 2018
Salt Beer Tap water Bottled water	12 12 159 3	46.7±0.58 – 806±15.3 MP/kg 0–14.3 MP/L 0–61 MP/L 1.8–5.4 MP/L	Grocery stores, liquor stores	Fibres, fragments, films	28.8–5 mm		14 countries	Kosuth <i>et al.</i> , 2018
Bottled water	30	3.16x10 – 1.1x10 MP/L	Supermarkets		0.5–10 µm		Italy	Zuccarello <i>et al.</i> , 2019
Salt	16	Sea: 16–84 MP/kg Lake: 8–102 MP/kg Rock: 9–16 MP/kg	Supermarkets	Fibres, fragments, films	20 µm–5 mm	PE, PET, PU, PP, PMMA, PA-6, PVC	Türkiye	Gündođdu, 2018
Salt	39	Sea: 0–1674 MP/kg Lake: 28–462 MP/kg Rock: 0–148 MP/kg	Supermarkets	Fragments, fibres, sheets	> 100 µm	PE, PP, PET, PTFE	17 countries	Kim <i>et al.</i> , 2018
Water	24	0–0.007 MP/L	Groundwater wells, household taps	Fibres	50–150 µm	PE, PA, PEST, PVC, epoxy resin	Germany	Mintemig <i>et al.</i> , 2019

TABLE 4 OCCURRENCE OF MICROPLASTICS IN HONEY, SUGAR, SALT AND WATER (continued)

COMMODITY	NUMBER OF SAMPLES	PARTICLE AMOUNT	SAMPLING	SHAPE	PARTICLE SIZE	POLYMERS	LOCATION	REFERENCE
Water	12	Reusable: 118 ± 88 MP/L (28–241 MP/L) Single-use: 14 ± 14 MP/L (2–44 MP/L) Beverage cartons: 11 ± 8 MP/L (5–20 MP/L) Glass: 50 ± 52 MP/L (4–156 MP/L)	Supermarkets		5–1349 µm	PEST, PET, PE, PA, PP	Germany	Schymanski <i>et al.</i> , 2018
	10							
	3							
	9							
Water	27 L of raw water 27 L of treated water	Raw: 1383–4464 MP/L Treated: 243–684 MP/L	Drinking water treatment plants	Fragments, fibres	1–100 µm	PET, PP, PE, PS, PAM, PVC, PMMA, PPTA, PTT	Czechia	Pivokonsky <i>et al.</i> , 2018
Water	32	Reusable: 4889±5432 MP/L Single-use: 2649±2857 MP/L Glass: 6292±10521 MP/L Max: 35436 MP/L	Food stores		1–10 µm	PET, PE, PS, styrene-butadiene-copolymer	Germany	Oßmann <i>et al.</i> , 2018
Water	259	325 MP/L (0–10390 MP/L)	Purchase from different locations	Fragments, fibres, films	6.5–>100 µm	PP, PA, PE	9 countries	Mason <i>et al.</i> , 2018
Water	17	15.6 MP/50L (4–30 MP/50L)	Taps from households, institutions, workplaces	Fibres, fragments, films	10–100 µm	PET, PP, PS, ABS, PU	Denmark	Strand <i>et al.</i> , 2018
Salt	21	Well: 115–185 MP/kg Sea: 50±7–280±3 MP/kg	Supermarkets, salt producers	Fibres	30 µm–3.5 mm	PET, PP, PE	Spain	Iríiguez <i>et al.</i> , 2017
Salt	23 brands	0.67 ± 1.15 - 3.42 ± 4.94 MP/kg	Supermarkets, open markets	Fibres, particles	3.3–4660 µm	PVA, PP, PE	8 African countries	Fadare <i>et al.</i> , 2021
Salt	n/a	23–115 MP/g (200 g)	Supermarkets	Fragment, fibres, pellet, film	100–1000µm	PE, PVC, PS	Gujarat and Tamil Nadu, India Montreal, Canada	Vidyasakar <i>et al.</i> , 2021
Tea bags	4 plastic teabag	1.6 billion MPs/cup of tea or beverage	Grocery stores and coffee shops	Fibres	20 nm–270 µm	PET, Nylon		Hernandez <i>et al.</i> , 2019
Apples Pears Broccoli Lettuce Carrots	6 samples each	52600–307750 MP/g 98325–302250 MP/g 65025–201750 MP/g 26375–75425 MP/g 72175–130500 MP/g			1.56–3.19 µm 1.87–2.59 µm 1.86–2.95 µm 2.18–2.78 µm 1.36–2.00 µm		Italy	Oliveri Conti <i>et al.</i> , 2020

Source: Authors' own elaboration.



CHAPTER 8

DIETARY EXPOSURE TO MICROPLASTICS IN DIFFERENT FOOD COMMODITIES

Estimates of dietary exposure to substances can provide information on: (1) risks to human health through a comparison of exposure estimates to acceptable or tolerable levels; (2) the likely relative contributions of different foods to overall dietary exposure; and (3) the impact of risk management measures such as maximum limits on dietary exposure. At present, it is only possible to use estimates of dietary exposure to microplastics for purpose (2); that is, to determine which foods are likely to be the major contributors to overall dietary exposure to microplastics.

In this section, estimated dietary exposure to microplastics in selected foods is calculated based on the available data on contamination levels in the foods, and their respective consumption rates. The foods of interest were mussels, clams, shrimps and prawns (considered together), oysters, salt, honey, sugar and water.

8.1 MICROPLASTIC CONCENTRATIONS IN THE SELECTED FOODS USED IN DIETARY EXPOSURE ESTIMATES

Data on microplastic contamination in bivalve molluscs were taken for clams (*Scapharca subcrenata*), mussels (*Mytilus galloprovincialis*) and oysters (*Saccostrea cucullate*) from three studies on commercial species (Table 3). For these species, the highest plastic load was estimated to be 10.5, 12.8 and 7.2 MP/g of wet weight respectively (DING *et al.*, 2018; H. X. Li *et al.*, 2018; Li *et al.*, 2015). Contamination data on other foods considered in the exposure estimation are summarized in Table 5. In addition to these, information on concentration of MP in shrimp were drawn from a recent study, where up to 4.88 MP/g of tissue (wet weight) were found in commercial brown shrimp (*Metapenaeus monoceros*) (Hossain *et al.*, 2020; Table 3).

8.2 CONSUMPTION DATA ON THE SELECTED FOODS USED IN THE DIETARY EXPOSURE ESTIMATES

In order to determine the potential dietary exposure to microplastics for each of the foods considered, a high habitual consumption amount was used for each food. Food consumption data were taken from the WHO and FAO food safety collaborative platform (FAO/WHO 2022), which includes data from the Chronic Individual Food Consumption Database – Summary statistics (CIFOCOss). This database contains food consumption data from a range of developed and developing countries. For the current exercise, the food consumption metric used was the 95th percentile (P95) food consumption estimate, and only for consumers across the countries included in CIFOCOss. Consumers are the proportion of the total survey cohort who reported consuming the food of interest.

The food consumption values used in the current exercise and their origins are summarized in Table 5.

TABLE 5 MAXIMUM P95 CONSUMER FOOD CONSUMPTION FOR SELECTED FOODS (G/DAY)

FOOD	COUNTRY	AGE CLASS	MAX P95 (G/DAY) ¹
MUSSELS	China	Adults and elderly	250
CLAMS	Italy	Adults and elderly	162
SHRIMPS AND PRAWNS	Malaysia	Adults and elderly	162
OYSTERS	China	Children and adolescents	133
SALT	Burkina Faso	Adults and elderly	222
HONEY	China	Children and adolescents	83
SUGAR	Burkina Faso	Adults and elderly	168
WATER	Mexico	Adults and elderly	2669

¹ Estimates of the P95 food consumption level based on less than 20 consumers were not considered.
Sources: FAO/WHO, 2022.

8.3 CALCULATION OF ESTIMATED DIETARY EXPOSURE

The microplastic concentration and food consumption amounts identified in the previous sections were combined to give daily and annual estimates of dietary exposure to microplastics for a high (P95) consumer of each of the selected foods. Results are summarized in Table 6.

TABLE 6 ESTIMATES OF DIETARY EXPOSURE TO MICROPLASTICS FROM CONSUMPTION OF SELECTED FOODS

FOOD	MAXIMUM MICROPLASTIC CONCENTRATION (MP/G)	MAXIMUM P95 CONSUMER CONSUMPTION (G/DAY)	ESTIMATED DIETARY EXPOSURE	
			MP/DAY ¹	MP/YEAR ²
MUSSELS	12.8	250	3 200	1 168 000
CLAMS	10.5	162	1 701	620 865
SHRIMPS AND PRAWNS	4.88	162	791	288 554
OYSTERS	7.2	133	958	349 524
SALT	19.8	222	4 396	1 604 394
HONEY	0.66	83	55	19 995
SUGAR (REFINED)	0.39	168	66	23 915
WATER (TAP)	0.06	2669	160	58 451

¹ MP/day calculated as: Microplastic concentration (MP/g) x food consumption (g/day)

² MP/year calculated as: MP/day x 365

Source: Authors' own elaboration

8.4 OTHER ESTIMATES OF DIETARY EXPOSURE

The ingestion rates of microplastics from food commodities and their associated exposure levels have been evaluated in some studies and are presented in Table 7. Taken at face value, the exposures estimated in the present report (Table 6) are generally higher than those reported in earlier studies (Table 7). For example, whereas the estimated annual exposure to microplastics in mussels was 1 168 000 MP/year in this report, the highest estimate from the literature was 4 620 MP/year. This may be explained by differences in the sources, and magnitudes, of the contamination and consumption data used. Table 7 also reveals that the exposures are purposely reported in different units, as they appeared in the cited literature. This was done as some of the reported units could not readily be converted into a common unit (e.g. from $\mu\text{g}/\text{year}$ to MP/year). Furthermore, the studies reported in Table 7 appear to have been more interested in seeking a “no effect” level, rather than a dose–response relationship. These factors must be considered in any attempt to compare the exposures outlined in the two tables.

TABLE 7 ESTIMATES OF DIETARY EXPOSURE (DERIVED MP INTAKE) TO MICROPLASTICS (MP) IN SEAFOOD, VEGETABLES, WATER, SALT, FRUIT AND VEGETABLES

	CONSUMPTION	DERIVED MP INTAKE	COUNTRY	REFERENCE
MOLLUSCS	72.1 g/day (top consumers) 11.8 g/day (minor consumers)	11 000 MP/year (top consumers) 1 800 MP/year (minor consumers)	Europe	Van Cauwenberghe and Janssen, 2014
FISH MUSCLE	300 g/week (adults) 50 g/week (children)	169–555 MP/week (adults) 28–92 MP/week (children)	Iran (Islamic Republic of)	Akhbarizadeh <i>et al.</i> , 2018
FISH MUSCLE	2080 g/year 2600 g/year 10 400 g/year 15 600 g/year	112 MP/year (child 1 year old) 140 MP/year (child 2–6 years) 562 MP/year (child > 6 years) 842 MP/year (adults)	Europe	Barboza <i>et al.</i> , 2020b
FISH MUSCLE	9 600 g/year 47 700 g/year 31 100 g/year 21 400 g/year 57 000 g/year	518 MP/year/person 2 576 MP/year/person 1 679 MP/year/person 1 156 MP/year/person 3 078 MP/year/person	Brazil Spain Italy United States of America Portugal	Barboza <i>et al.</i> , 2020b
BIVALVES	3.01 g/day	212 MP/year	Republic of Korea	Cho <i>et al.</i> , 2019
SHELLFISH	4.03 g/day	283 MP/year	Republic of Korea	Cho <i>et al.</i> , 2019
MUSSELS	82 g/year	123 MP/year	United Kingdom	Catarino <i>et al.</i> , 2018
MUSSELS	3.08 kg/year	4 620 MP/year	Spain/France/ Belgium	Catarino <i>et al.</i> , 2018
MUSSELS	225 g	7 µg/day 0.1 µg/kg of body weight per day	Globally	EFSA, 2016; FAO, 2017
FISH	15.21 kg/year	31–8 323 MP/year	Globally	Danopoulos <i>et al.</i> , 2020
SHELLFISH	4.9 kg/year	13 MP/year	Globally	Daniel <i>et al.</i> , 2021
CRUSTACEANS MOLLUSCS	2.06 kg/year 2.65 kg/year	206–17716 MP/year 0–27825 MP/year	Globally Globally	Danopoulos <i>et al.</i> , 2020
WATER	2 L	85 µg/day 1.4 µg/kg of body weight per day	Globally	WHO, 2019
WATER	2.2 L/day (women) 3 L/day (men)	4 400 MP/year (women) 5 800 MP/year (men)	Globally	Kosuth <i>et al.</i> , 2018
SALT	5 g/day	1 000 MP/year	China	Yang <i>et al.</i> , 2015
SALT	3.95 g/day	37 MP/year	Globally	Karami <i>et al.</i> , 2017b
SALT	5 g/day	40.6–1085.2 MP/year	Italy	Renzi and Blašković, 2018
SALT	14.8–18.01 g/day	64–302 MP/year	Türkiye	Gündoğdu, 2018

TABLE 7 ESTIMATES OF DIETARY EXPOSURE (DERIVED MP INTAKE) TO MICROPLASTICS (MP) IN SEAFOOD, VEGETABLES, WATER, SALT, FRUIT AND VEGETABLES (continued)

	CONSUMPTION	DERIVED MP INTAKE	COUNTRY	REFERENCE
SALT	2.3 g/day	40–680 MP/year	Globally	Kosuth <i>et al.</i> , 2018
SALT	10.06 g/day	0–42600 MP/year (average 3000)	Globally	Kim <i>et al.</i> , 2018
SALT	5 g/day	510 MP/year	Spain	Iñiguez <i>et al.</i> , 2017
SALT	5 g/day	117 µg/year	India	Seth and Shrivastav, 2018
APPLES*	165.3 g/day	4.62x10 ⁵ MP/kg of body weight per day (adults)	Italy	Oliveri Conti <i>et al.</i> , 2020
	115.7 g/day			
PEARS*	165.3 g/day	1.41x10 ⁶ MP/kg of body weight per day (children)		
	115.7 g/day			
BROCCOLI*	53.0 g/day	4.48x10 ⁵ MP/kg of body weight per day (adults)		
	24.2 g/day			
LETTUCE*	53.0 g/day	1.37x10 ⁶ MP/kg of body weight per day (children)		
	24.2 g/day			
CARROTS*	20.3 g/day	9.55x10 ⁴ MP/kg of body weight per day (adults)		
	18.0 g/day	1.91x10 ⁵ MP/kg of body weight per day (children)		
		3.83x10 ⁴ MP/kg of body weight per day (adults)		
		7.65x10 ⁴ MP/kg of body weight per day (children)		
		2.96x10 ⁴ MP/kg of body weight per day (adults)		
		1.15x10 ⁵ MP/kg of body weight per day (children)		

Note: High exposure in the fruits and vegetables correspond to the reportedly high occurrence of the microplastics in those commodities, as per Oliveri Conti *et al.* (2020) (see Table 4). As mentioned in Section 1.0, published data are presented at face value.

Source: Authors' own elaboration



CHAPTER 9

TOXICITY OF MICRO- AND NANOPLASTICS

Model organisms and cell culture have generally been used to evaluate the biological alterations that can be induced following exposure to microplastics. Few studies have investigated the effects of plastic materials in humans, with most studies focusing on the effects of prostheses and cellular responses *in vitro*. In a study by Ormsby *et al.* (2016), it was observed that wear particles from ultra-high molecular weight polyethylene (UHMWPE) hip replacements can cause periacetabular bone loss, commonly leading to aseptic loosening and failure of the replacement. Liu *et al.* (2015) also identified particle size, shape and composition as the main factors driving osteolytic cytokine release in response to debris from the wearing of HMWPE implants. Polypropylene used as mesh in implants aimed at replacing damaged tissue in the human body could be considered inert, providing other substances such as stabilizers, plasticizers and antioxidants are not added during manufacture. However, where present, these chemicals can leach from the mesh once it starts to degrade. Meshes made of PP are extremely susceptible to oxidation, which usually occurs during inflammatory responses mediated by neutrophils and can lead to the production of free radicals and a loss of integrity (Sternschuss *et al.*, 2012).

Toxicological alterations exerted by (micro)plastics are likely to be dependent on particle size. A smaller size means an increase in the surface-to-volume ratio of a plastic particle, which subsequently leads to an increase in the body's bioavailability, accumulation and systemic exposure to these materials (Deng *et al.*, 2017; Lei *et al.*, 2018; Yang *et al.*, 2019). Many authors have provided evidence of higher immunological and oxidative stress responses from smaller (micro)plastics (Brown *et al.*, 2001; Hwang *et al.*, 2019; Jeong *et al.*, 2017, 2016; Schirinzi *et al.*, 2017).

As regards the immunotoxicology of micro- and nanoplastics, the available scientific literature points to gut deposition and the excretion of larger micro- and macroplastics, while smaller microplastics and nanoplastics can potentially pass through intestinal barriers and end up in the blood stream, potentially resulting in immunotoxicity. Occurrence and human exposure data are limited for these materials from food consumption. However, data is available on the immunotoxicity of nanomaterials, especially polymeric nanoparticles, which can be considered

in designing experiments for nanoplastics. Physical and chemical properties such as particle size, shape, surface chemistry, surface charge, hydrophobicity/hydrophilicity, as well as the composition of nanoplastics all play a significant role in immunotoxicity (Dobrovolskaia and McNeil, 2016). For this reason, it is inappropriate to extrapolate immunotoxicology data from pristine commercial particles (such as polystyrene), since the real-life particle properties and surface functionalities resulting from bulk plastic degradation/oxidation and trophic transfer may be different. Protein corona formation on these particles may also be different for the same reason. Appropriate studies utilizing real-life particles and mixtures should be considered for a thorough assessment of the potential immunotoxicity of micro- and nanoplastic mixtures.

9.1 TRANSLOCATION

As presented earlier in this report, ingestion and inhalation are two of the three means of microplastic exposure in humans. Once in the body, the systemic movement (translocation) of micro- and nanoparticles largely depends on their size. In the gut, these materials can either be eliminated from the body, or absorbed from the intestine. Absorption is strictly restricted to extremely small particles – typically in the nano range (0.1 μm – to pass through the gut epithelium and reach the portal circulation), while particles bigger than that size range will most likely be eliminated from the gut. After ingestion of 0.05, 0.5 and 6 μm polystyrene microbeads, only the smallest beads were retained and distributed throughout the body, while the larger beads were mostly concentrated in the digestive tract (Jeong *et al.*, 2017). Van Cauwenberghe and Janssen (2014) noted that the only microplastics present after gut depuration in mussels were those in the size range below 20 μm , suggesting a possible absorption into the circulatory system. Transport to other tissues via this system was also hypothesized for mice, a model mammal (Deng *et al.*, 2017). The most reliable route of microparticle entrance into the circulatory system is thought to be their uptake by the microfold cells (M cells) in Peyer's patches in the ileum, ultimately reaching the gut-associated lymphatic system and liver before being excreted (Galloway, 2015).

Other possible uptake mechanisms will also depend on particle size and may include endocytosis (< 0.5 μm) and phagocytosis (> 0.5 μm) (Monti *et al.*, 2015; Yoo *et al.*, 2011). Some have also suggested a paracellular uptake pathway, whereby particles pass through the tight junctions between cells (Powell *et al.*, 2010). It is assumed that very small particles could eventually end up being filtered through the spleen (> 0.2 μm) or kidney (< 10 nm) and then be eliminated (Yoo *et al.*, 2011). Forte *et al.* (2016) observed a higher and faster intake of 44 nm compared to 100 nm polystyrene particles in human gastric adenocarcinoma cells, which were also shown to affect cell morphology, viability and immunological responses. These synthetic particles were internalized in cells via clathrin-mediated endocytosis along with some other possible energy-dependent mechanisms. Their uptake seemed to be influenced by exposure concentration, time, and particle size. Nevertheless, information on their distribution in environmental matrices and in biota is poor, as detection techniques and methodologies are not yet able to identify and measure them.

When nanoparticles enter biological media, they likely associate with biomolecules such as proteins, which create a corona structure on their surface. The corona is highly specific, and its structure can be influenced by the type of nanoparticles, and especially their surface properties (e.g. hydrophobicity) and size, as was seen for PS nanoparticles in human plasma (size: 50 nm, 100 nm; Lundqvist *et al.*, 2008). This association could play a role in the transport of the nanoparticles. Under laboratory conditions, Cedervall *et al.*, (2012) observed in fish blood, in vitro, the binding of 24 nm polystyrene nanoparticles to the apolipoprotein A, an important protein in the mobilization of fat resources. The authors hypothesized that, once absorbed through the gut wall, the nanoparticles could have been transported through the blood to other organs thanks to this molecule and high-density lipoproteins (HDL). Chae *et al.*, (2018) also observed the presence of nanosized PS particles in the yolk sac of fish embryos, which could have plausibly entered the embryonic membrane and interacted with the lipids by virtue of their lipophilic nature. An investigation of the toxicity of polylactic acid microparticles showed that these do not have a substantial impact on the viability of human intestinal Caco-2 cells after 24 hours and 48 hours, with minor effects only seen at concentrations of 500 µg/mL (Shopova *et al.*, 2020).

9.2 OXIDATIVE STRESS

Most studies have noted that oxidative stress might be the main and most common biological response after exposure to microplastics. Microplastics are known to contain a variable number of reactive oxygen species (ROS), deriving in part from their manufacturing (e.g. polymerization reactions). Microplastics can thus play a role in the induction of oxidative stress, beginning with the production and accumulation of ROS in the cells (Choi *et al.*, 2018), which may induce and activate response pathways that could lead to inflammation and apoptosis (Cheng *et al.*, 2015). Levels of intracellular ROS have been correlated with the induction of signalling pathways such as the mitogen-activated protein-kinase (MAPK), involved in the regulation of cellular functions and oxidative stress responses (Jeong *et al.*, 2017, 2016). A size-dependent antioxidant enzyme induction was seen in the marine copepod *Paracyclopsina nana* exposed to PS microbeads, with 0.05 µm particles leading to significant increases of ROS and antioxidant enzyme activities (Jeong *et al.*, 2017). Similar size-dependent, intracellular ROS increases and MAPK activation were also observed in the rotifer *Brachionus koreanus*, with the ultimate activation of antioxidant enzymes superoxide dismutase (SOD), glutathione peroxidases (GPx), glutathione reductase (GR) and glutathione-S-transferase (GST) (Jeong *et al.*, 2016). Induction of antioxidant enzymes has been measured by many authors (Table 6). An increase in SOD and GPx and high levels of GSH were also detected after the exposure of juvenile crabs to PS microspheres at concentrations of 40 and 400 µg/L. At the highest tested concentrations (4 000 and 40 000 µg/L) decreases in the activity of these enzymes was observed, possibly as a result of the organism's inability to bear the high-energy cost of the antioxidant response (Yu *et al.*, 2018). The same authors also reported an induction of the MPAK pathway and a concentration-dependent lipid peroxidation.

Further evidence of the induction of lipid peroxidation in the brain and muscle was seen in European bass (*Dicentrarchus labrax*) (Barboza *et al.*, 2018b). Barboza *et al.* (2020) also observed higher peroxidation levels (up to twofold) in the gills, brain and muscle lipids of wild fish species that had ingested microplastics when compared to those specimens that had not been exposed. In the nematode species *Caenorhabditis elegans*, oxidative alterations (increase in cellular ROS, expression of oxidative-stress-related genes and lipofuscin accumulation) were only observed when nematodes were exposed to the highest concentration of PS microparticles (100 µg/L; Yu *et al.*, 2020). Moreover, Schirinzi *et al.* (2017) observed a higher production of ROS in human cell cultures exposed to PS compared to PE, possibly because of the smaller size of the investigated particles.

9.3 IMMUNOLOGICAL RESPONSES

Micro- and nanoplastics can be recognized by the immune system. The injection of 700 nm PS particles in zebrafish embryos at different stages of development showed that macrophage and neutrophils co-localized themselves around these xenobiotic materials, and there was also an induction of the innate immune system via the expression of genes belonging to the alternative complement pathway (Veneman *et al.*, 2017). Samuelsen *et al.* (2009) demonstrated the activation of the innate immune system and inflammatory responses in mouse lungs exposed to micro- and nano-sized PS particles, with higher responses induced by coarse particles, plausibly because they are more easily phagocytosed. This is an important defence system against pathogens and foreign materials. In the size range of 0.5 µm, PS were seen to induce inflammation, with the upregulation of the interleukin genes IL1a, IL1b and IFN, and the concentration of their proteins in the gut of zebrafish (*Danio rerio*) (Jin *et al.*, 2018). The authors also hypothesized that this response could have been the consequence of exposure to microplastics, inducing an alteration in the diversity of gut microbiota.

Concentrations of PVC and PE particles higher than those found in the environment were seen to impair immunological defences in an in vitro assay using head-kidney leukocytes from two fish species; this caused a decrease in phagocytosis and an increase in respiratory burst (Espinosa *et al.*, 2018). In this case, the authors suggested that phagocytosis was most probably hindered by the size of microplastics (40–150 µm), which was bigger than the investigated fish leukocytes. Longer exposure times enhanced the inflammatory response, evidenced by the formation of granulocytomas engulfing the foreign HDPE particles and disruption of the stability of lysosomal membranes in the digestive tubules of blue mussels (*Mytilus edulis*) (Von Moos *et al.*, 2012).

9.4 GASTROINTESTINAL ALTERATIONS

Among the many effects, intestinal hyperpermeability and damage, with alterations in the regulation of genes involved in its development, was observed in the nematode *Caenorhabditis elegans* (Yu *et al.*, 2020). Gut barrier functioning in mice can be

negatively affected by exposure to PS microplastics, because of decreased mucus secretion, as reported by Jin *et al.* (2019) and Lu *et al.* (2018). On the contrary, mucus production increased in the gut of adult zebrafish, where dysbiosis (a change in gut microflora) was also observed (Jin *et al.*, 2018). Microplastics exposure was able to cause damage to villi and enterocytes in the intestine of zebrafish, as well as moderate-to-severe alterations in the distal part of the intestine of European seabass; severity increased with exposure time, thus compromising intestinal function (Lei *et al.*, 2018; Pedà *et al.*, 2016).

9.5 LIVER DAMAGE

Microplastics have been reported to damage liver cells and organelles in crabs (*Eriocheir sinensis*), leading to an alteration in the activities of aspartate transaminase (GOT) and alanine aminotransferase (GPT) enzymes (Yu *et al.*, 2018). Moreover, a decrease in triglyceride (TG) and total cholesterol (T-CHO) levels and in the expression of genes involved in lipogenesis was measured in the livers of mice, suggesting that micro-PS could induce metabolic alterations in hepatic fats (Lu *et al.*, 2018). The authors also hypothesized that this change could have been the result of alterations in gut microbiota. The exposure to high concentrations of microscale PS particles (70 nm–5µm) caused lipid accumulation and liver inflammation in zebrafish (*Danio rerio*), which showed signs of vacuolation, infiltration and necrosis of hepatocytes (Lu *et al.*, 2016). Disruption in lipid and energy metabolism, possibly because of food malabsorption caused by microplastics has also been reported (Deng *et al.*, 2017; Lu *et al.*, 2018, 2016). Under high exposure conditions, hepatocytes breakdown and liver histopathological alterations were seen in rice fish (*Oryzias sinensis*) and dark chub (*Zacco temminckii*) (Chae *et al.*, 2018). The extent to which these changes could occur in humans remains to be investigated.

9.6 NEUROTOXICITY

The most widely analysed marker of neurotoxicity is the activity of the enzyme acetylcholine esterase (AChE). Although Deng *et al.* (2017) observed an increase in AChE activity and in the serum levels of threonine, taurine and aspartate, AChE inhibition is maybe the most common signal detected in microplastics toxicity assays (Barboza *et al.*, 2018b; Yu *et al.*, 2018). An increased brain AChE activity observed in microplastic-contaminated wild fish was reported in a recent study, indicating that AChE induction may also occur under long-term exposure to low concentrations of environmental contaminants like microplastics (Barboza *et al.*, 2020b).

9.7 APICAL ENDPOINTS

In model organisms, microplastic exposure has been observed to lead to rapidly identifiable *in vivo* endpoints. Effects on body growth, size and length, reproduction, motility and lifespan seem to be most common (Chae *et al.*, 2018; Choi *et al.*, 2018; Jeong *et al.*, 2017, 2016; Lei *et al.*, 2018; Yu *et al.*, 2018, 2020). A reduction in body size and growth has been suggested as a consequence of decreased nutrition and

malabsorption, as the ingestion of microplastics results in an insufficient, if not null, uptake of nutrients (Jeong *et al.*, 2016; Yu *et al.*, 2018). Choi *et al.* (2018) demonstrated that the shape of microplastics was another factor that influenced swimming behaviour in sheepshead minnow (*Cyprinodon variegatus*), with a significant decrease caused by irregular fragments. Reproductive toxicity could arise from the endocrine-disrupting effects of plastic polymers and their associated contaminants. For instance, exposure to both virgin (manufactured) and marine-deployed plastic pellets led to down-regulation of the estrogen receptor (ER α), vitellogenin (VTG I) and choriogenin (Chg H) genes in female rice fish (*Oryzias latipes*) (Rochman *et al.*, 2014). Cedervall *et al.* (2012) also noticed that polystyrene nanoparticles transported through the food chain were able to affect the feeding time of fish, which was consistently delayed, in addition to their motility and hunting behaviour.

Table 8 shows a summary of the information found on adverse effects of the exposure to micro- and nanoplastics.

TABLE 8 ADVERSE EFFECTS OF THE EXPOSURE TO MICRO- AND NANOPLASTICS

ORGANISM	CONCENTRATION OF MP	EXPOSURE TIME	POLYMER	SIZE	EFFECTS	APPLICABLE TO HUMAN HEALTH TOXICITY	REFERENCE
<i>Mullus surmuletus</i>	n.s.	Field study	PET, CP, polyacrylate, PAN	n.s.	<ul style="list-style-type: none"> • Activation of detoxification system (increase of GST activity) 		Alomar <i>et al.</i> , 2017
<i>Dicentrarchus labrax</i>	0.1% of diet	30, 60, 90 days	PVC	< 0.3 mm	<ul style="list-style-type: none"> • Histopathological alterations of the distal intestine (vacuolation of enterocytes, shortening, swelling and fusion of villi, lamina propria widening, increase and hyperplasia of goblet cells) • Reduction of perivisceral fat 		Peda <i>et al.</i> , 2016
<i>Danio rerio</i>	20, 200, 2000 µg/L	4h, 12h, 1 day, 2 days, 7 days, 3 weeks	PS	70 nm, 5 µm, 20 µm	<ul style="list-style-type: none"> • Liver inflammation and lipid accumulation (vacuolation, infiltration, necrosis) • Oxidative stress (Increase in SOD and CAT activities) • Alteration of lipid and energy metabolism 		Lu <i>et al.</i> , 2016
<i>Mus musculus</i>	0.01, 0.1, 0.5 mg/day	4 weeks	PS	5 µm, 20 µm	<ul style="list-style-type: none"> • Accumulation in liver, kidney and gut • Decreased liver weight, inflammation and lipid accumulation (lipid droplets) • Alteration of energy (decrease in ATP level, increase in LDH) and decreased lipid metabolism (lower T-CHO and TG levels) • Oxidative stress (induction of SOD and GPx, decreased CAT activity) • Neurotoxicity (increased AChE activity) 	YES	Deng <i>et al.</i> , 2017
Mouse macrophage cells (RAW 264.7) <ul style="list-style-type: none"> • Human bronchial epithelial cells (BEAS-2B) 	5, 10, 20, 40 µg/mL	2, 4, 6, 8, 16, 24 h	PS NH2-PS COOH-PS	60 nm	<ul style="list-style-type: none"> • Oxidative stress (ROS formation) • Alterations in protein folding • Endoplasmic reticulum stress • Induction of autophagic cell death 	YES	Chiu <i>et al.</i> , 2015
<ul style="list-style-type: none"> • Chinese hamster cells (V79) • Human lymphoblastoid cells (TK6) 	50 µL	6, 24 h	Marine plastic debris	≤ 1 mm	<ul style="list-style-type: none"> • Cytotoxicity 		Furukuma and Fuji, 2016
Mouse	100, 1000 µg/L	6 weeks	PS	5 µm	<ul style="list-style-type: none"> • Accumulation in the gut • Decreased intestinal mucus and intestinal barrier dysfunction • Dysbiosis (changes in gut microbiota: decreased abundance of Actinobacteria) • Increased hepatic total bile acids (TBA) levels • Increase in serum pyruvate, decrease in TG and T-CHO • Alteration of bile acid metabolites 	YES	Jin <i>et al.</i> , 2019

TABLE 8 ADVERSE EFFECTS OF THE EXPOSURE TO MICRO- AND NANOPLASTICS (continued)

ORGANISM	CONCENTRATION OF MP	EXPOSURE TIME	POLYMER	SIZE	EFFECTS	APPLICABLE TO HUMAN HEALTH TOXICITY	REFERENCE
Mouse macrophages J774	25, 125, 250 particles/macrophage	0–24 h	UHMWPE	0.5–2 µm	<ul style="list-style-type: none"> Immunological response (induction of TNF-α release) Apoptosis (proteolytic PARP cleavage) 		Petit <i>et al.</i> , 2002
<ul style="list-style-type: none"> Human brain cells (T98G) Epithelial cells (HeLa) 	0.05, 0.1, 1, 10 mg/mL 10 ng/mL–10 µg/mL	24, 48 h	PE PS	3, 16 µm, 100, 600 nm 10 µm, 40, 250 nm	<ul style="list-style-type: none"> Oxidative stress (ROS production) 	YES	Schirmer <i>et al.</i> , 2017
Mouse	1 mg/mL	4, 24 h	PS	64, 202 nm 1.1, 4.7 µm	<ul style="list-style-type: none"> Activation of the innate immune system (accumulation and activation of phagocytes) Inflammatory responses (TNF-α, IL-1β, MIP-2, MCP-1) 		Samuelsen <i>et al.</i> , 2009
Human cell lines: PBMCs, RAW 264.7, HDF, HMC-1	10, 50, 100, 250, 300, 500, 1000, 1 500, 4 500 µg/mL	6 h, 12 h, 48 h, 72 h or 4 days	PP	~20, 25, 200 µm	<ul style="list-style-type: none"> Oxidative stress (ROS production) Histamine release Stimulation of the immune system (inflammation, release of cytokines TNF-α and IL-6) 	YES	Hwang <i>et al.</i> , 2019
<i>Mytilus galloprovincialis</i> haemocytes	1, 5, 50 µg/mL	30 min to 4 hours	NH2-PS	50 nm	<ul style="list-style-type: none"> Lysosomal membrane destabilization Oxidative stress (ROS and NO production) Induction of apoptosis Inflammatory responses (decreased phagocytosis and increased lysozyme activity) 	YES	Canesi <i>et al.</i> , 2015
Rat	125 µg, 1 mg	24 h	PS	64, 202, 535 nm	<ul style="list-style-type: none"> Lung inflammation (IL-8 gene expression and release) Increased entry of extracellular Ca⁺⁺ Oxidative stress 		Brown <i>et al.</i> , 2001
Human cells (PBMM)	100 µm ³	12 h, 24 h	UHMWPE, PS	0.1, 1, 10 µm 20 nm, 40 nm, 200 nm, 1 µm	<ul style="list-style-type: none"> Increased activity of osteoclasts (osteolytic cytokine release: TNF-α, IL-1β, IL-6, IL-8) 	YES	Liu <i>et al.</i> , 2015
<i>Daphnia magna</i>	50, 5, 0.5%	24 h, 48 h	Teabag leachates PET, nylon-6,6	102 nm, 52 µm	<ul style="list-style-type: none"> Accumulation inside the organism Impaired carapace development Immobility 		Hernandez <i>et al.</i> , 2019
<i>Oryzias latipes</i>	Diet with 10% plastics by weight	1, 2 months	PE	<0.5 mm	<ul style="list-style-type: none"> Endocrine disruption (down-regulation of Chg H gene expression) Germ cells proliferation in males 		Rochman <i>et al.</i> , 2014
<i>Mytilus edulis</i>	0.1, 0.2, 0.3 g/L	8 h	PS	30 nm	<ul style="list-style-type: none"> Triggered pseudofaeces production Reduced filtering activity (feeding) 		Wegner <i>et al.</i> , 2012
<i>Mytilus edulis</i>	2.5 g/L	3, 6, 12, 24, 48, 96 h	HDPE	0–80 µm	<ul style="list-style-type: none"> Lysosomal membrane destabilization Inflammatory response (granulocytomas) 		Von Moos <i>et al.</i> , 2012

TABLE 8 ADVERSE EFFECTS OF THE EXPOSURE TO MICRO- AND NANOPLASTICS (continued)

ORGANISM	CONCENTRATION OF MP	EXPOSURE TIME	POLYMER	SIZE	EFFECTS	APPLICABLE TO HUMAN HEALTH TOXICITY	REFERENCE
Human renal cortical epithelial cells (HRCE)	2.5–40 µg/mL	1, 4, 24, 48, 72, 168 h	PS	44 nm	<ul style="list-style-type: none"> Internalization by energy-dependent (endocytosis) and energy-independent pathways Accumulation in the perinuclear region 	YES	Monti <i>et al.</i> , 2015
<i>Paracyclopsina nana</i>	0.1, 1, 10, 20 µg/mL	24 h	PS	0.05, 0.5, 6 µm	<ul style="list-style-type: none"> Oxidative stress (ROS production and SOD, GPx, GR, GST activation, GSH increase) MAPK (activation of p-ERK, p-p38, Nrf2) 		Jeong <i>et al.</i> , 2017
<i>Sparus aurata</i> , <i>Dicentrarchus labrax</i> Head Kidney Leukocytes (HKL)	1, 10, 100 mg/mL	1, 24 h	PVC, PE	40–150 µm	<ul style="list-style-type: none"> Modulation of innate immune parameters (decreased phagocytosis, increased respiratory burst) Oxidative stress (expression of the nrf2 gene) 		Espinosa <i>et al.</i> , 2018
<i>Danio rerio</i>	100, 1000 µg/L	14 days	PS	0.5, 50 µm	<ul style="list-style-type: none"> Increased volume of intestinal mucus Gut inflammation (expression of il1α, il1β, ifn genes and accumulation of proteins) Dysbiosis (changes in gut microbiota: decreased Bacteroidetes, γ-Proteobacteria and β-Proteobacteria, increase in Firmicutes abundance) 		Jin <i>et al.</i> , 2018
<i>Danio rerio</i> , <i>Caenorhabditis elegans</i>	0.001, 0.01, 0.1, 1, 10 mg/L 0.5, 1, 5, 10 mg/m ²	10 days 2 days	PA, PE, PP, PVC, PS	~70, 0.1, 1.0, 5.0 µm	<ul style="list-style-type: none"> Intestinal damage (cracking of villi, enterocytes splitting) in fish PS MP size and dose-dependent decreased survival rate (nematodes) Reduction of mean body length and reproductive capacity (brood size, embryo number) (nematodes) Decreased intestinal Ca⁺⁺ levels (nematodes) Oxidative stress (increased expression of gst-4) in nematodes 	YES	Lei <i>et al.</i> , 2018
<i>Mus musculus</i>	100, 1000 µg/L	5 weeks	PS	0.5, 50 µm	<ul style="list-style-type: none"> Decrease in body, liver and fat weight Alteration of the hepatic lipid metabolism (decrease in serum and hepatic TG and T-CHO levels, increase in hepatic PYR levels) Decreased mucus production in the colon Changes in gut microbiota (decreased abundances of Firmicutes, Bacteroidetes and α-Proteobacteria) 	YES	Lu <i>et al.</i> , 2018
<i>Cyprinodon variegatus</i>	50, 250 mg/L	96 h	PE	150, 180 µm	<ul style="list-style-type: none"> MP accumulation in the intestine Oxidative stress (ROS production, up-regulation of cat and sod3) Detoxification (up-regulation of cyp1a1) Apoptosis (up-regulation of casp3, tp53) Immune response (increased expression of ccr5 and Trnfs13b) 		Choi <i>et al.</i> , 2018
<i>Caenorhabditis elegans</i>	0.1, 1, 10, 100 µg/L	72 h	PS	1 µm	<ul style="list-style-type: none"> Oxidative stress (ROS generation, lipofuscin accumulation, expression of oxidative-stress-related genes) Intestinal damage (hyperpermeability of the intestinal barrier, disruption and expression of intestinal development genes) 		Yu <i>et al.</i> , 2020

TABLE 8 ADVERSE EFFECTS OF THE EXPOSURE TO MICRO- AND NANOPLASTICS (continued)

ORGANISM	CONCENTRATION OF MP	EXPOSURE TIME	POLYMER	SIZE	EFFECTS	APPLICABLE TO HUMAN HEALTH TOXICITY	REFERENCE
<i>Eriocheir sinensis</i>	40, 400, 4000, 40000 µg/L	4, 12, 24, 48, 168 h 21 days	PS	5 µm	<ul style="list-style-type: none"> MP accumulation in gill, liver and gut Decreased weight gain (WG), specific growth rate (SGR) and hepatosomatic index (HSI) Neurotoxicity (inhibition of AChE activity) Hepatic damage (inhibition of GPT and GOT activities) Oxidative stress and lipid peroxidation (modulation of CAT, SOD, GPx, GST and their genes, change in GSH and MDA levels) MAPK (increased expression of p38, inhibition of ERK, down-regulation of AKT, MEK) 		Yu <i>et al.</i> , 2018
<i>Danio rerio</i>	5 mg/mL	1, 3, 4, 5 days	PS	700 nm	<ul style="list-style-type: none"> Immune response (activation of the complement system, recognition by neutrophils and macrophages) Oxidative stress 	YES	Veneman <i>et al.</i> , 2017
<i>Brachionus koreanus</i>	0.1, 1, 10, 20 µg/mL	24 h 12 days	PS	0.05, 0.5, 6 µm	<ul style="list-style-type: none"> Growth inhibition, reduced fecundity, shortened lifespan Oxidative stress (ROS production, induction of GPx, GR, SOD, GST) MAPK (activation of JNK, p38) 		Jeong <i>et al.</i> , 2016
<i>Mus musculus</i>	0.2 mg/mL 0.01, 0.1, 0.5 mg/day	1, 2, 4, 7, 14, 21, 28 days	PS	5, 20 µm	<ul style="list-style-type: none"> Disruption of lipid and energy metabolism (inhibition of TG and ATP) Oxidative stress (CAT inhibition, SOD increment) 	YES	Yang <i>et al.</i> , 2019
<i>Daphnia magna</i> , <i>Oryzias sinensis</i> (eggs), <i>Zacco temminckii</i> , <i>Chlamydomonas reinhardtii</i>	0, 2, 4, 6, 8, 10 mg/L, 5 mg/L, 5 mg/L, 0, 20, 40, 60, 80, 100 mg/L	7 days 24h	PS	~ 51 nm	<ul style="list-style-type: none"> Intestinal alterations (damaged gut microvilli in <i>Daphnia magna</i>) Liver damage (vacuolization, cellular breakdown, alteration of lipid metabolism) in <i>Zacco temminckii</i> Yolk accumulation of Ps in <i>Oryzias sinensis</i>, embryos Decreased fish motility 		Chae <i>et al.</i> , 2018

Source: Authors' own elaboration.

CHAPTER 10

COMBINED EFFECTS OF MICROPLASTICS AND ENVIRONMENTAL CONTAMINANTS

Despite the many laboratory tests involving virgin polymers, this may not be indicative of actual environmental exposure. Organisms are exposed to a mixture of microplastics, plastic additives and environmental contaminants in the natural environment. This means that, when consuming an organism that has ingested microplastics from the environment, humans could also be exposed to any number of combinations of polymers and associated contaminants (additives or sorbed environmental contaminants). Some researchers have evaluated the combined effects of the exposure to microplastics and other contaminants, observing in some cases that the presence of microplastics can enhance the accumulation and uptake of some contaminants in living organisms (Table 7). For instance, Zhou *et al.* (2020) observed a more intense bioaccumulation of two antimicrobials in the blood clam (*Tegillarca granosa*) when the exposure was combined with microplastics, even though the target hazard quotient (THQ) was substantially lower than the safe limit. The authors hypothesized that consumption of clams containing the observed concentrations of antimicrobials could induce antimicrobial resistance (AMR) in the human body.

An increase in triclosan and roxithromycin uptake was also observed in green-lipped mussels (*Perna canaliculus*) and Nile tilapia (*Oreochromis niloticus*) exposed to a mixture of these antimicrobial agents and microplastics (Webb *et al.*, 2020; S. Zhang *et al.*, 2019). A mixture of microplastics and mercury also led to a higher bioaccumulation of the metal in European bass (*Dicentrarchus labrax*), with a significant increase in lipid peroxidation in muscle and brain and AChE inhibition (Barboza *et al.*, 2018b). AChE inhibition was also seen in freshwater clams (*Corbicula fluminea*) co-exposed to a mixture of microplastics and the antimicrobial florfenicol (Guilhermino *et al.*, 2018), with an additional increase

in bile pyrene metabolites in common goby (*Pomatoschistus microps*) juveniles exposed to microplastics and pyrene (Oliveira *et al.*, 2013). The authors suggested this could be a possible consequence of the modulation of the biotransformation mechanisms, and alteration of the activity of an enzyme belonging to the energy production pathway.

The consequences of combined exposure to microplastics and pharmaceuticals were reviewed by Santos *et al.* (2021), who provided three main possible consequences: an alleviation, an enhancement or no alteration in the toxicity of pharmaceuticals. Chronic oral exposure to contaminated PVC microparticles led to most severe histopathological alterations in the distal part of the intestine of European bass (*Dicentrarchus labrax*) in a time-dependent way (Pedà *et al.*, 2016). Male rice fish (*Oryzias latipes*) exposed to microplastic pellets deployed at sea showed an increase in germ cell proliferation and a decrease in the genetic expression of choriogenin, possibly caused by the mixture's endocrine-disruptive activity (Rochman *et al.*, 2014). Unfortunately, the information on the biological responses to combined exposures of microplastics and associated contaminants is poor, and the many variables and external factors involved in these interactions make it quite difficult to provide clear interpretations of the results. Finally, Tang *et al.*, (2020) observed immunological alterations exerted by the co-exposure to microplastics, benzo(a) pyrene and estradiol, noticing a size dependency in the effects, one probably caused by a size-dependent interaction of the two pollutants with the plastic microparticles.

Table 9 shows a summary of the information found on the combined effects of (micro)plastics and environmental pollutants.

TABLE 9 SUMMARY OF THE LITERATURE ON THE COMBINED EFFECTS OF PLASTICS PARTICLES AND ENVIRONMENTAL POLLUTANTS

ORGANISM	EXPOSURE TIME	POLYMER	SIZE	POLYMER CONCENTRATION	POLLUTANT	POLLUTANT CONCENTRATION	EFFECTS	REFERENCE
<i>Mytilus galloprovincialis</i>	7 days	PE, PS	< 100 µm	1.5 g/L,xyzspiked with 200–260 ng/g pyrene	Pyrene	50 µg/L	<ul style="list-style-type: none"> Accumulation of MP in gills, haemolymph and digestive glandsxyzAccumulation of pyrene in digestive glands and gillsxyzNeurotoxicity (reduced AChE activity in gills)xyzImmunological responses (lower granulocytes/hyalinocytes ratio, lysosomal membrane destabilization)xyzOxidative stress (inhibition of GPs and CAT)xyzDNA damage (micronuclei, up-regulation of repair genes) 	Avio <i>et al.</i> , 2015
<i>Danio rerio</i>	4, 24 h	PE	10–106 µm	10, 100, 1000 particles/mL,xyzspiked with 1 µg Ag	Ag	1 µg/L	<ul style="list-style-type: none"> Decreased Ag uptake 	Khan <i>et al.</i> , 2015
<i>Tetraselmis chuii</i>	24, 48, 72, 96 h	PE	1–5 µm	0.184 mg/L	Cu	0.02, 0.04, 0.08, 0.16, 0.32, 0.64 mg/L	<ul style="list-style-type: none"> No significant influence of MPs on copper toxicity 	Davarpanah and Guilhermino, 2015
<i>Mytilus</i> spp.	7 days + 6 days depuration	PS	2, 6 µm	32 µg/L	Fluoranthene	30 µg/L	<ul style="list-style-type: none"> Alteration of detoxification mechanismsxyzHaemocytes mortalityxyzHistopathological damagesxyzOxidative stress (increase of GR, GST, SOD and decrease of CAT activities) 	Paul-Pont <i>et al.</i> , 2016
<i>Perna viridis</i>	44 days (2h/day), 91 days	PVC	1–50 µm		Fluoranthene		<ul style="list-style-type: none"> Decreased clearance rate, respiration and byssus productionxyzMortality 	Rist <i>et al.</i> , 2016
<i>Pomatoschistus microps</i>	96 h	PE	1–5 µm	18.4, 184 µg/L	Pyrene	20, 200 µg/L	<ul style="list-style-type: none"> Neurotoxicity (reduction of AChE activity)xyzLethargy and abnormal swimming behaviourxyzDisruption of energy metabolism (inhibition of IDH)xyzDelayed mortalityxyzIncreased bile concentration of pyrene metabolites 	Oliveira <i>et al.</i> , 2013
<i>Arenicola marina</i>	10 days	PVC	230 µm		Phenanthrene, nonylphenol, triclosan, PBDEs		<ul style="list-style-type: none"> Immune alteration (reduced phagocytic activity of coelomocytes)xyzAccumulation of NP and Phe into tissuesxyzReduced bioengineer activityxyzMortality 	Browne <i>et al.</i> , 2013

TABLE 9 SUMMARY OF THE LITERATURE ON THE COMBINED EFFECTS OF PLASTICS PARTICLES AND ENVIRONMENTAL POLLUTANTS (continued)

ORGANISM	EXPOSURE TIME	POLYMER	SIZE	POLYMER CONCENTRATION	POLLUTANT	POLLUTANT CONCENTRATION	EFFECTS	REFERENCE
<i>Oryzias latipes</i>	1, 2 months	LDPE	< 0.5 mm		Σ6 PAHs, Σ10 PCBs, Σ7 PBDEs		<ul style="list-style-type: none"> Accumulation of PBTs concentration in tissues Hepatic stress (glycogen depletion, fatty acids vacuolation, cell necrosis) 	Rochman <i>et al.</i> , 2013
<i>Oryzias latipes</i>	2 months	PE	< 0.5 mm		Deployed at sea		<ul style="list-style-type: none"> Endocrine disruption (lower Chg H, ERα and VTG l level) Abnormal growth and early proliferation of germ cells in males 	Rochman <i>et al.</i> , 2014
<i>Danio rerio</i>	3 weeks	LDPE	125–250 µm		PFCA, PCBs, α-HBCD, Me-Hg, 2,4,6-TBP, PBDEs		<ul style="list-style-type: none"> Hepatic stress (vacuolization, accumulation of contaminants) Overexpression of genes for oxidative stress and detoxification (cyp1a1, proxl and gsp1) 	Rainieri <i>et al.</i> , 2018
<i>Arenicola marina</i>	28 days	PS	400–1 300 µm	7.4% dw in sediment	PCBs	1.84 ± 0.22 µg/kg in sediment	<ul style="list-style-type: none"> Decrease in feeding activity and weight loss Increased PCB bioaccumulation at lowest plastic dose 	Besseling <i>et al.</i> , 2013
<i>Daphnia magna</i>	14 days	PS	50, 500 nm, 5, 10, 15 µm		Phenanthrene		<ul style="list-style-type: none"> Immobilization (physical body attachment and damage) Increased Phe bioaccumulation Decreased Phe dissipation 	Ma <i>et al.</i> , 2016
<i>Mytilus galloprovincialis</i>	4 weeks	LDPE	20–25 µm	10 mg/L, spiked with 15 µg/g benzo(a)pyrene	Benzo(a)pyrene		<ul style="list-style-type: none"> Accumulation of PE in gills, haemolymph and digestive glands Marked bioaccumulation of BaP in digestive glands and gills Somatosomal membrane destabilization DNA damage (micronuclei) Immune response (decreased phagocytosis) Increased neutral lipids (lipidosis) in digestive glands 	Pittura <i>et al.</i> , 2018
<i>Dicentrarchus labrax</i>	96 h	Fluorescence red polymer	1–5 µm	0.26, 0.69 mg/L	Hg	0.01, 0.016 mg/L	<ul style="list-style-type: none"> Neurotoxicity (Inhibition of AChE and muscle ChE) Oxidative stress (increased LPO levels in brain and muscle; induction of antioxidant enzymatic activity in gills (SOD, CAT, GST) and liver (SOD, CAT, GST, GPx, GR)) Modulation of anaerobic energy production (LDH, IDH) 	Barboza <i>et al.</i> , 2018a; 2018b

TABLE 9 SUMMARY OF THE LITERATURE ON THE COMBINED EFFECTS OF PLASTICS PARTICLES AND ENVIRONMENTAL POLLUTANTS (continued)

ORGANISM	EXPOSURE TIME	POLYMER	SIZE	POLYMER CONCENTRATION	POLLUTANT	POLLUTANT CONCENTRATION	EFFECTS	REFERENCE
<i>Mytilus galloprovincialis</i>	96 h	PS	110 ± 6.9 nm	0.05 mg/L	Carbamazepine	6.3 µg/L	<ul style="list-style-type: none"> • Oxidative stress • Genotoxicity and altered gene expression 	Brandts <i>et al.</i> , 2018
<i>Corbicula fluminea</i>	96 h	n.s.	1–5 µm,	0.2, 0.7 mg/L	Flufenicol	1.8, 7.1 mg/L	<ul style="list-style-type: none"> • Feeding inhibition • Neurotoxicity (AChE inhibition) • Oxidative stress (lipid peroxidation, increased GST, GR activity) • Disruption of energy metabolism (inhibition of IDH) 	Guilhermino <i>et al.</i> , 2018
<i>Tegillarca granosa</i>	28 days	PS	500 nm,	0.26 mg/L	Oxytetracycline, florfenicol	270 ng/L, 42 ng/L	<ul style="list-style-type: none"> • Enhanced bioaccumulation of the two antibiotics • Decreased GST activity • Downregulation of detoxification genes expression (<i>gst</i>, <i>cyp1a2</i>, <i>cyp2u1</i>, <i>mrp2</i>, <i>ugt</i>) 	Zhou <i>et al.</i> , 2020
<i>Perna canaliculus</i>	48 h	PE	38–45 µm,	0.5 g/L, spiked with 0.36 mg/g triclosan	Triclosan	50 mg/L (in methanol)	<ul style="list-style-type: none"> • Decreased oxygen uptake • Decreased byssus production • Oxidative stress (increased SOD activity, lipid peroxidation) • Increased triclosan uptake 	Webb <i>et al.</i> , 2020
<i>Oreochromis niloticus</i>	14 days	PS	100 nm	1, 10, 100 µg/L	Roxithromycin	50 µg/L	<ul style="list-style-type: none"> • Enhanced roxithromycin accumulation • MPs alleviated the oxidative stress (increased SOD activity, decreased lipid peroxidation) • Neurotoxicity caused by roxithromycin alone 	S. Zhang <i>et al.</i> , 2019
<i>Tegillarca granosa</i>	4 days	PS	30 µm, 500 nm	1 mg/L	Benzol(a) pyrene, 17β-estradiol	5, 50 µg/L, 1 µg/L	<ul style="list-style-type: none"> • Deleterious effects after exposure to nano-sized and mitigation with micro-sized particles • Immunotoxicity (inhibited expression of immune-related genes, alteration of phagocytosis and haematocyte count, lysozyme activity, Ca⁺⁺ concentration) • Oxidative stress (ROS production) 	Tang <i>et al.</i> , 2020
<i>Mytilus edulis</i>	96 h	PE	10, 90 µm	100, 1000 MP/mL	Fluoranthene	50, 100 µg/L	<ul style="list-style-type: none"> • Oxidative stress (alteration of antioxidant enzymes activity and total GSH levels) • No synergistic effects 	Magara <i>et al.</i> , 2018

TABLE 9 SUMMARY OF THE LITERATURE ON THE COMBINED EFFECTS OF PLASTICS PARTICLES AND ENVIRONMENTAL POLLUTANTS (continued)

ORGANISM	EXPOSURE TIME	POLYMER	SIZE	POLYMER CONCENTRATION	POLLUTANT	POLLUTANT CONCENTRATION	EFFECTS	REFERENCE
<i>Dicentrarchus labrax</i>	40 days	LDPE	125, 250 µm	2% of feed composition	Me-Hg, PFOS, α-HBCD, BFRs, PBDEs, PCBs, 2,4,6-tribromophenol		<ul style="list-style-type: none"> Enhanced accumulation of PCBs and BFRs Decreased capacity to eliminate contaminants from the body Alteration of liver metabolism (lipid mobilization) Oxidative stress (inhibition of detoxification processes through down-regulation of <i>cyp1a1</i> and <i>gstα</i> genes) Immune alterations (down-regulation of <i>il1β</i> gene) 	Granby <i>et al.</i> , 2018
<i>Daphnia magna</i>	48 h	PS	1, 10 µm	0.1 mg/L	Roxithromycin	0.01 mg/L	<ul style="list-style-type: none"> Oxidative stress (increased SOD activity, lower GST and GPx activity) Stress exacerbation under co-exposure 	P. Zhang <i>et al.</i> , 2019

Source: Authors' own elaboration.

CHAPTER 11

INTERNATIONAL STANDARDS AND RELEVANT REGULATIONS

Currently, there is no legislation that specifically regulates the presence of microplastics in foodstuffs and food safety, as according to current knowledge the ingestion of these synthetic particles per se is not considered a significant threat to human health. Data on their occurrence in foods is still scarce and mainly concerns aquatic products. What could pose a much higher concern is the exposure to their associated contaminants, some of which have been scientifically proven to induce some biological alterations and adverse effects in animals and humans. Some regulatory measures exist concerning the migration of plastic components from packaging and food-contact materials.

The European Commission Directive 2002/72/EC provides a list of all the monomers, additives and other substances that can be used in the manufacturing of food-contact materials (FCM) made of plastics. This list includes their migration limits into food. In order to establish the safety of packaged foods, specific migration limits (SML) in food-contact materials have been established for all those compounds of uncertain toxicity, or known toxic compounds. These parameters are calculated by considering the daily consumption of 1 kg of packaged food by an adult with average weight of 60 kg and are listed in Commission Regulation (European Union) No 10/2011 for all the authorized chemicals used in food-contact materials and plastic items. This document also establishes guidelines for migration testing using food simulants, classifying all foods as aqueous, alcohol, acidic, fatty or dry. The Commission Regulation, or Union list, does not include many NIAS, whose presence in foodstuffs is not permitted; however, it establishes a maximum migration level of 0.010 mg/kg for non-authorized substances in food (except for substances that are mutagenic, carcinogenic or toxic to reproduction), which migrate through the functional barrier in multilayer packaging. This limit was exceeded by two oligomers contained in some baby food samples in contact with multilayer material, with the majority of NIAS potentially migrating from the PU layer (Bauer *et al.*, 2019). When no information on a substance's SML is provided, a generic migration limit of 10 mg/dm² should apply (alternatively expressed as 60 mg/kg).

This quantity also coincides with the overall migration limit (OML) permitted for the total leaching of plastic constituents into foodstuffs and for FCM used in food intended for young children and infants (European Commission, 2011a). Standard good manufacture should create a product in order to make the release of substances lower than the limit of 10 mg/1 dm² of food contact surface (European Commission, 2011a). Migration from these plastics is higher for low-molecular-weight substances (< 1000 Da) such as monomers; hypothetically, these may contain up to one hundred times the number of contaminants found in other sources of contamination (Grob *et al.*, 2006). Estimates have indicated an approximate concentration of 10 mg of plastic-migrated substances per kg of food. Plastic additives are generally given a SML of 50 µg per kg of food, or even higher. Nevertheless, as pointed out by Welle and Franz (2018), the exposure to substances transferred from plastics in food should be negligible, mostly because of poor absorption in the body. However, in recent years multiple plastic layers bonded together by PU adhesives have been developed to create food-contact materials. These have an additional barrier to prevent migration, the limit for which has been suggested as 0.01 mg/kg (European Commission, 2011a). It is worth noting that the OML only gives information about the inertness of plastic food-contact materials, while the SML is a safety limit for specific substances extrapolated from toxicological studies.

The release of plastic components into foodstuffs that are in direct contact with packaging and coating is likely to occur but, as stated in commission regulation 1935/2004, materials in contact with food should be manufactured in a way that does not deteriorate the composition and organoleptic properties of commodities and endanger human health (European Commission, 2004). The quantity of migration and final concentration of these substances in food is, in any event, very low, as some studies have pointed out. However, no precise considerations can be outlined on this topic, as information on the identity and toxicity of the chemical components of plastic packaging is mostly lacking. The number of unknown and unregulated substances is still high. As an example, García Ibarra *et al.* (2018) were able to detect 48 compounds in packaging materials, of which only 19 were regulated by the current legislation.

Some countries have brought forward legislation which, while it does not directly address food safety, may be considered to affect exposure to microplastics in food. For example, under its Waste Minimisation Act of 2008, New Zealand is working towards phasing out certain types of plastic, including those that rapidly degrade to microplastics. Moreover, the Waste Minimisation (Microbeads) Regulations 2017 prohibit the inclusion of plastic microbeads in certain products. Microbeads are plastics which are typically 5 mm or smaller in size, which are used in the manufacture of health and beauty products. Concerns have been raised over their potential transfer to aquatic environments where they may be ingested by organisms and potentially passed along the food chain. Similar regulations have been introduced in the United States of America (The Microbead-Free Waters Act, and in China, where the National Development and Reform Commission indicated that the production of cosmetics containing plastic microbeads would be banned by the end of 2020, and the sale of cosmetics containing plastic microbeads would be banned by the end of 2022 .

CHAPTER 12

CONCLUSIONS

Although it is generally believed that micro- and nanoplastics may potentially raise concerns for public health, there is a scarcity of data on their occurrence and exposure in foods. Most of the limited scientific literature available focuses on fishery products, while much less is known about the occurrence of microplastics in other food commodities. A few studies have investigated contamination levels in salt, water, beer, honey and sugar. In general, the available evidence suggests considerably low concentrations of micro- and nanoplastics in foods.

Information on the toxicity and toxic dynamics of microplastics is not readily available. Most studies focus on model organisms and attempt to use these to extrapolate plausible effects in humans. These limitations make it rather difficult to establish more definitive conclusions on the public health implications of microplastic exposure. Based on the literature reviewed, some adverse effects such as the activation and impairment of the immunological system, oxidative stress and metabolic alterations were observed, albeit in experimental settings where the levels of microplastics considered significantly exceeded the real-life exposure of humans to the particles. This discrepancy may severely limit the applicability of these studies' results to humans.

At present, the methodologies for sampling, sample preparation and analysis of microplastics in foods are neither harmonized nor standardized. Furthermore, a consensus is yet to be reached with respect to the terminology employed in research on the subject, which hampers the interpretation, comparison, and valorization of research findings.

On the basis of the available occurrence and ingestion data, it appears that human exposure to micro- and nanoplastics may not be a significant public health concern per se. However, chemical components of known toxicity may occur in (micro) plastics and may migrate into foods and potentially raise health concerns. The extent to which either of these may be the case needs to be established.

The information provided in this document could be used to support future exposure assessments, as well as the development of appropriate legislation and guidance documents on food production, processing, distribution and consumption in relation to microplastic contamination.



CHAPTER 13

RESEARCH GAPS

One fundamental requirement for progress in our understanding of the nature and potential health effects of micro- and nanoplastics is that generated data be reliable, interpretable, reproducible and comparable. The development of harmonized (and eventually standardized) analytical methods on sampling, sample preparation, analysis (detection and quantitation) and the reporting of results (e.g. numbers vs. size) should therefore be considered of primary importance to enhancing the usability of collected data. It is also vital that the following (knowledge gaps) are addressed:

- > The occurrence of microplastics in edible tissues of fish and shellfish (i.e. muscle) should receive continued attention in future research, to improve the exposure assessment
- > More studies should investigate the contamination of food commodities other than seafood, which could give an important contribution to microplastics exposure
- > The contribution of the inhalation route of exposure to microplastics should be assessed in detail
- > Information on the composition of plastic packaging materials and the toxicity of its components should be more accessible for future risk estimates
- > Methodologies for the identification of non-intentionally added substances (NIAS) should be developed/refined
- > Risk assessment for compounds used in plastic food-contact materials (FCM) should be performed
- > Considering that knowledge on the toxicity of microplastics is limited, it is important that researchers keep carrying on experiments and analyses on the biological consequences of these chemicals on model organisms to better illustrate their action.

To support the formulation of legislation and food production guidance documents on microplastics, the following should be considered:

- > Evaluation of the toxicological effects induced by exposure to microplastics both in vivo and in vitro

- > Evaluation of the toxicological dynamics in biological systems through suitable (in silico) models when information cannot be obtained by experimental analyses
- > Assessment of size-dependent micro- and nanoplastics transport across cells and tissues as well as the mechanisms of absorption and accumulation of micro- and nanoplastics on different tissues
- > Assessment of the feasibility of establishing NOELs and NOAELs applicable to micro- and nanoplastics
- > Estimation of acute and chronic exposure for different microplastics to better characterize risks from different polymers
- > Use of concentration levels that mimic real-life conditions to identify any possible harm caused by realistic exposure scenarios
- > Evaluation of the impact of microplastics and contaminant mixtures to clearly identify possible interactions
- > Testing of more polymer types, shapes and sizes for toxicity
- > Evaluation of the impact of the potential effects of microplastics on (gut) microbiome
- > Evaluation of the impact of compositional differences in food-contact materials on the release of microplastics

CHAPTER 14

RECOMMENDATIONS

The following recommendations are offered as guidance for national and international authorities and food safety management stakeholders:

- > Increase the amount and transparency of information provided to consumers on plastic-packaged food commodities, both to allay unfounded fears and prevent plausible adverse health effects.
- > Recognize the impact of packaging and food-contact materials on the quality of food products, including their potential impact on organoleptic properties.
- > Evaluate and identify additional/novel routes of microplastics entry into the human food value chain.

Despite the poor information currently available on the toxicity of microplastics, it is vital that authorities, stakeholders and legislative bodies find a way to tackle the issue. Where necessary, limits on human exposure to these substances should be introduced by implementing suitable precautionary measures as needed. Some suggestions include:

- > identifying an adequate limit for certain food commodities, in order to limit the exposure and intake of microplastics through diet;
- > monitoring the intake of microplastics via food consumption, in order to produce up-to-date estimates of intake and give management bodies the instruments to evaluate risk mitigation options;
- > considering appropriate methods to improve the plastic circular economy and increase the use of biodegradable plastics.



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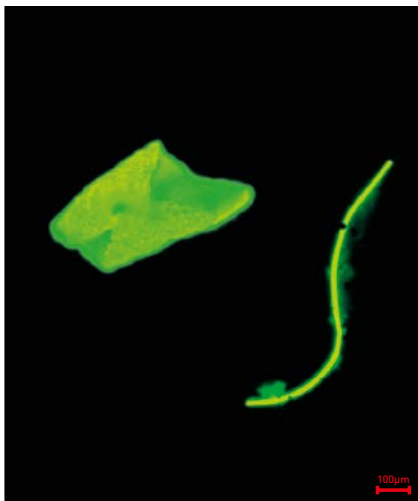
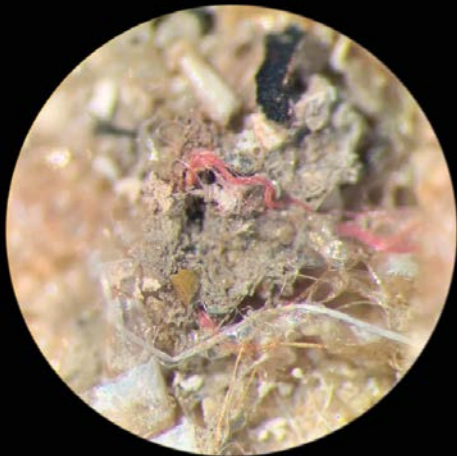
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MICROPLASTICS IN FOOD COMMODITIES

A FOOD SAFETY REVIEW ON HUMAN EXPOSURE THROUGH DIETARY SOURCES

Plastic contamination in the environment is one of the most currently discussed topics. In addition to environmental matrices, microplastics have been detected in fisheries and aquaculture species, but also in other important food commodities. Food consumption is considered as one of the main and most important pathways of human exposure to microplastics. Concerns might arise not only from the exposure to the plastic polymer itself which, although generally considered as biologically inert, might still contain some reactive monomers in its structure, but also to associated chemicals. Many researchers have reported oxidative stress and immunotoxicity among the main consequences of exposure to virgin micro and nanoplastic particles, with the least having a longer retention time within the organism. Moreover, many studies have also reported information on the individual toxicity of many plastic additives and components (e.g. flame retardants, plasticizers, monomers), in addition to the possible adverse effects elicited by the environmental pollutants sorbed to the microplastics. This document gathers and illustrates what is already known and the knowledge gaps on the presence of microplastics and plastic associated chemicals in food commodities, performing an exposure assessment on the dietary exposure to these synthetic materials and providing information on their possible biological effects on humans.

The report was consolidated by a group of selected experts, and sets up the basis for future risk assessment exercises and the information can be used for the provision of risk management options.

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