Brian Garrison

Creation of plastics is one of the downstream products of the proposed methanol plant. The EIS does not account for the long-lasting and widespread environmental impacts of plastics.

Many plastics are embedded in products as one of many materials and not readily recyclable. Even when plastics could be easily recycled, rates are very low (30% in Europe, 9% in the US, see Scientific American article, "Solving Microplastic Pollution..." attached). Which means large quantities of the downstream products created from this methanol refinery would become part of the growing solid waste heaps.

Plastics made from fossil fuels do not readily break down. The resulting waste may sometimes degrade and crumble, but still continue to pollute as microplastics. These microplastics are a threat to human and animal health. The World Health Organization's (WHO) 2019 report, "Microplastics in freshwaters and drinking water: Critical review and assessment of data quality" (see attached) and the related information sheet (see attached) speak to the harms of microplastics. For example, "The potential hazards associated with microplastics come in three forms: physical particles, chemicals and microbial pathogens as part of biofilms." Though the facility offers hope through efficiency, We don't need efficient means of making plastics, we need materials that do not widely and permanently infest our clean water systems. For more on the effects to wildlife and humans, see the 2020 article from the International Journal of Environmental Research and Public Health and the other Scientific American article, "From Fish to Humans..." (attached).

Though it's possible to filter microplastics from water, we put human health at risk by becoming dependent on complex purification systems. Allowing plastics and microplastic pollution to proliferate also overlooks individuals and communities that do not have easy access to filtered water. Furthermore, the current systems in place are not keeping drinking water humans safe from microplastics. According to the same report, "Microplastics are ubiquitous in the environment and have been detected in a broad range of concentrations in marine water, wastewater, fresh water, food, air and drinking-water, both bottled and tap water." This EIS offers no means to mitigate the resulting pollution that would arise from the plastics manufactured using the facility's methanol.

To continue building infrastructure that pollutes in this manner is irresponsible and reckless. The plan for this facility fails to consider the impact on human health caused by the downstream plastic products. As a species, our survival depends on us making a hard transition away from "business as usual" and toward fundamentally different manufacturing systems. We cannot say that predicted demand is a sufficient reason to create supply, or we become trapped in a self-fulfilling prophecy. If you place a bowl of sugar in front of a baby, they will eat it (predicted demand causes the consumer to take the supply). If you teach responsible eating habits, then unhealthy behaviors and the appetite for sugar can be kept in check (demand for one product becomes demand for healthier alternatives).

By offering a readily available supply of plastic and the methanol that creates it, this facility enables business-as-usual, allows the continued pollution of our basic life-sustaining resources (water), and threatens human lives. I urge you to reject the proposed project.

In addition to the PDFs attached, articles cited are retrievable through the following links:

Scientific American, From Fish to Humans...
https://www.scientificamerican.com/article/from-fish-to-humans-a-microplastic-invasion-may-be-taking-a-toll/

Scientific American, Solving Microplastics Pollution...
https://www.scientificamerican.com/article/solving-microplastic-pollution-means-reducing-recycling-mdash-and-fundamental-rethinking1/'

WHO report
https://www.sciencedirect.com/science/article/pii/S0043135419301794

WHO information sheet
https://www.who.int/water_sanitation_health/water-quality/guidelines/microplastics-in-dw-information-sheet/en/

International Journal of Environmental Research and Public Health, A Detailed Review Study on Potential Effects of Microplastics and Additives of Concern on Human Health
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7068600/

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Review

Microplastics in freshwaters and drinking water: Critical review and assessment of data quality

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ABSTRACT

Microplastics have recently been detected in drinking water as well as in drinking water sources. This presence has triggered discussions on possible implications for human health. However, there have been questions regarding the quality of these occurrence studies since there are no standard sampling, extraction and identification methods for microplastics. Accordingly, we assessed the quality of fifty studies researching microplastics in drinking water and in its major freshwater sources. This includes an assessment of microplastic occurrence data from river and lake water, groundwater, tap water and bottled drinking water. Studies of occurrence in wastewater were also reviewed. We review and propose best practices to sample, extract and detect microplastics and provide a quantitative quality assessment of studies reporting microplastic concentrations. Further, we summarize the findings related to microplastic concentrations, polymer types and particle shapes. Microplastics are frequently present in freshwaters and drinking water, and number concentrations spanned ten orders of magnitude (1×10^{-2} to 10^{8} #/m^{3}) across individual samples and water types. However, only four out of 50 studies received positive scores for all proposed quality criteria, implying there is a significant need to improve quality assurance of microplastic sampling and analysis in water samples. The order in globally detected polymers in these studies is PE ≈ PP > PS > PVC > PET, which probably reflects the global plastic demand and a higher tendency for PVC and PET to settle as a result of their higher densities. Fragments, fibres, film, foam and pellets were the most frequently reported shapes. We conclude that more high quality data is needed on the occurrence of microplastics in drinking water, to better understand potential exposure and to inform human health risk assessments.

Contents

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1. Introduction

Microplastics are generally characterised as water-insoluble, solid polymer particles that are ≤5 mm in size (Bergmann et al., 2015). A formal definition for the lower size boundary does not exist, but particles below 1 μm are usually referred to as nanoplastics rather than microplastic (Koelmans et al., 2015). Although microplastics are often detected in the environment, the risks they pose are debated and largely unknown. One key challenge in assessing the risks of microplastics to humans and the environment relates to the variability of the physical and chemical properties, composition and concentration of the particles. Further, microplastics in the environment are difficult to identify and standardized methods do not exist (Mintenig et al., 2018). The dominant source of microplastics often is the fragmentation of larger plastics or product wear, however the rate of fragmentation under natural conditions is unknown (Eerkes-Medrano and Thompson, 2018). These challenges and unknowns hamper the prospective assessment of exposure and risk (Koelmans et al., 2017). In this uncertain field, regulatory efforts to examine microplastic safety have been raised (SAM, 2018a, b).

The presence of microplastics has been reported for air samples, food and drinking water (EFSA, 2016; Gasperi et al., 2018; Lusher et al., 2017; Van Cauwenberghe and Janssen, 2014; Wright and Kelly, 2017; Yang et al., 2015) and recently, the implications of microplastics for human health have been reviewed (Wright and Kelly, 2017). Although microplastic exposure via ingestion or inhalation could occur, the human health effects are still unknown. If inhaled or ingested, limited data from animal studies suggest that microplastics may accumulate and cause particle toxicity by inducing an immune response (Deng et al., 2017; Gasperi et al., 2018). Chemical toxicity could occur due to leaching of plastic-associated chemicals (additives as well as adsorbed toxins) (Diepens and Koelmans, 2018; SAPEA, 2019). Such effects are likely to be dose-dependent, however knowledge of exposure levels is currently lacking. Furthermore, biofilms growing on microplastics may be a source of microbial pathogens (GESAMP, 2016). Hence, although there are potential chemical, particle and microbial hazards associated with microplastics, current exposure levels, including through drinking water need to be assessed first.

The ubiquity of microplastics of all sizes in surface water, groundwater and wastewater (SAPEA, 2019), has raised the question if pollution of drinking water occurs. To date, there is only a limited number of studies that address this issue and they indeed reported the presence of microplastics in tap water and bottled water (Kosuth et al., 2018; Mason et al., 2018; Mintenig et al., 2019b; Schymanski et al., 2018). Some of these studies triggered a great deal of attention in the scientific community as well as the media, putting the issue of human exposure to microplastics via drinking water high on the agenda of public health agencies worldwide. More broadly, ensuring safe drinking water is high on the political agenda, with a dedicated target on safe and affordable drinking water under the Sustainable Development Goals (SDG 6) (WHO and UNICEF, 2017).

To date, about 50 studies exist that provide concentration data for microplastics in drinking water or its freshwater sources, i.e., surface water and groundwater, as well as (indirectly) wastewater. These studies provide data for specific types of water, but methods of sampling, isolating, purifying and identifying microplastics vary enormously among studies. A systematic review of methodologies used and study characteristics is currently lacking. There are several scoping reviews that emphasise the relevance of microplastics in freshwaters (Eerkes-Medrano and Thompson, 2018; Li et al., 2018; Wagner et al., 2014) or that specifically discuss processes or models in freshwaters (Kooi et al., 2018). We are aware of only a limited number of reviews that touch upon methodologies and concentration data (Eerkes-Medrano and Thompson, 2018; Li et al., 2018).

Besides variation in methodologies used and concentrations reported, existing studies are likely to vary with respect to the level of quality assurance deployed. The quality of microplastic research has been debated recently (Burton, 2017; Connors et al., 2017; Koelmans et al., 2016) and has been quantitatively assessed for studies on microplastic ingestion by biota (Hermsen et al., 2018). However, a critical review of studies reporting concentration data in freshwater and drinking water, which also evaluates the quality of applied sampling methods, microplastic extraction and identification steps, is currently lacking.

For chemical risk assessments in a regulatory context, quality criteria have been set in order to be able to evaluate the reliability of data from toxicological studies (Kase et al., 2016; Klimisch et al.,

1997; Schneider et al., 2009). Such criteria contribute to the harmonization of the hazard and risk assessments of chemicals across different regulatory frameworks. Recently, Hermsen et al. proposed a weight-of-evidence scoring method for studies of microplastic ingestion by marine biota (Hermsen et al., 2018). This method defined minimum quality criteria for various aspects of the analytical procedure, such as sampling, sample treatment, use of controls and polymer identification. It assigns a score for each aspect and provides a total reliability score for data reported in a study. Such a method can also be developed for the analysis of microplastics in freshwater samples, and can be applied to quantify the relative reliability of reported concentration data.

The aim of the present paper is to critically review the available literature on microplastics in drinking water and its freshwater sources, from a quality assurance perspective and by using a quantitative approach. Wastewater studies were also assessed as these are discharged into the environment. Further aims are to review data on concentration, polymer type, shape and size distribution data across studies. Guidance is provided to improve the quality of future occurrence studies.

Our paper is organised as follows. We first present the key areas that should be assessed to determine the reliability of studies. These areas are presented in separate sections and are: sampling method, sample size, sample processing and storage, laboratory preparation and clean air conditions, negative controls, positive controls, sample treatment and polymer identification. For each of these areas we discuss quality assurance aspects, considerations for scoring, and present the assessment scores for each of these criteria. Subsequently, the combined overall reliability scores are discussed, followed by a discussion on implications for human health risk assessments. In the section thereafter we discuss the outcomes of the reviewed studies. An overview of the concentrations, shapes and polymer types measured is provided and trends are discussed with respect to sample type, location or system characteristics. Finally, we provide recommendations to improve the analysis of microplastics in water samples and summarize the key conclusions.

2. Methods

2.1. Literature search

Fifty-five records from fifty studies reporting microplastic concentrations in drinking water (2 tap, 3 bottled water) or its freshwater sources (1 groundwater, 30 surface water, 18 wastewater) were reviewed. Some studies reported data on microplastics in more than one water type. Most papers were retrieved from the Scopus database. Search strings used were *microplastic AND (bottle OR surface OR tap OR wastewater OR groundwater).* Three studies were from the grey i.e. not peer-reviewed literature and were found via Google searches, using the same or similar key word combinations. Searches were performed until August 2018. Only those studies that reported original concentration data were reviewed.

2.2. Quantitative quality assessment

The reliability of data in studies was evaluated based on criteria originally developed for microplastic in biota samples by Hermsen et al. (2018), and surface water samples by Mintenig et al. (2019a, in prep.). The present approach further refines the method to different categories of water samples, including tap or bottled drinking water, surface water, groundwater and wastewater. The method uses nine crucial criteria, which are detailed below. Criteria relate to those that are common in analytical chemistry, such as reproducibility of described methods, precision, accuracy and sensitivity, which together determine the robustness of an applied method. Reproducibility does not imply that another researcher would obtain the same result, which is due to the variability in conditions inherent to nature. Reproducibility in the context of analytical chemistry refers to minimizing the contribution of random or systematic error to the total observed variability. For each criterion a value of 2 (reliable), 1 (reliable to a limited extent) or 0 (unreliable) is assigned. A 'Total Accumulated Score' (TAS) is calculated by adding scores for individual criteria (maximum 18 points) (Tables 1, S2, S3). For data to be considered sufficiently reliable, a study should preferably have no 'zero' values for any of the individual scores (Hermsen et al., 2018).

2.3. Study characteristics

For each study the following characteristics were summarized in tabular form (Table S1): Reference, Country (area), Source (water type), Treatment applied (for wastewater treatment plants (WWTP) or drinking water treatment plants (DWTP), bottled and tap water), Sampling date, Size/shape (of microplastics detected), Polymer types (of microplastics detected), Chemicals (analysed on microplastic), Value (of microplastics detected in water sample), Quality assurance applied (detection limit, positive controls, negative controls), Sampling method, Analysis method, Comments. Raw concentration data were pooled per water type: WWTP influent, WWTP effluent, lake, river, canal, groundwater, untreated and treated tap water, and bottled water, and analysed for means, ranges and significance of differences among the water types. As data were not normally distributed, the differences were assessed with the Mann-Whitney-Wilcoxon test with Bonferroni correction.

3. Results and discussion

3.1. Quality assessment of studies reporting data on microplastics in water samples

In this section, methodological aspects are reviewed in subsections and the final total quality scores are presented and discussed. Following Hermsen et al. (2018), for each aspect, scoring criteria are provided and each criterion is explained and justified (Table S2). Such a score based, quantitative evaluation does not result in an absolute judgment but is an indicator of the reliability of these studies for monitoring purposes and to inform risk assessments of microplastics in the drinking water supply chain. The quality criteria provided here are considered adequate for the present assessment, yet may develop over time with increased experience in sampling and analysing microplastics and better understanding of global concentrations. Here we review the general trends; for details on specific studies the reader is referred to Tables S1 and S3.

3.1.1. Sampling methods

Sampling methods were reviewed to understand the variety of approaches utilized, to assess whether sampling was described in sufficient detail, and to be able to define quality assessment criteria for sampling (Tables S1 and S2). Surface water is sampled by pumping, trawling or filling bottles or buckets, followed by sieving to isolate particles of the desired size range (Table S1) (Li et al., 2018). For wastewater, samples are either grabbed with bottles, pumped directly or collected with automatic composite samplers, then sieved, whereas tap and bottled water are directly sieved. Residues in nets or sieves are typically flushed into glass or metal jars or bottles. To obtain a maximum score of 2, the date, location and materials used should be reported. Specific further criteria were defined for wastewater, surface water, untreated and treated

tap water and bottled water. For wastewater, the applied treatment type should be mentioned as this can impact the microplastic concentrations and should be considered when assessing retention or removal efficiencies of individual technologies. For the same reason, this should be done when taking samples on DWTPs. For surface water, the depth of sampling should be reported, as this may affect concentration (Kooi et al., 2018). For tap water, when the aim is to assess concentration in general, running the tap before sampling is recommended (e.g. 1 min) in order to avoid incidental contamination from air (Wesch et al., 2017), unless it is specifically mentioned that the aim is to measure the first portion of the water, e.g., the first glass. Furthermore, flowrate and source of tap water (e.g., storage tank, groundwater, surface water) should be reported, as this may be relevant for data interpretation. For the same reason, for bottled drinking water, the source, batch production lot and bottled water type (sparkling vs still water) should be specified. To maximize particle recovery from the bottle, the sample should be shaken before filtration and the emptied bottle should be flushed three times with filtered water. A score of 1 was assigned if a study provided a subset of the required characteristics (e.g. date, location), but is still fairly reproducible. About half of the studies score 2 on this criterion whereas only three studies score 0.

3.1.2. Sample size

Different factors were considered when recommending an optimum water volume to be sampled. For microplastics, the limit of detection can be seen as the methods' capability of reliably detecting at least one particle with statistical rigor. A sample volume that is too low reduces the chance of finding particles, reduces the power of a study and increases the margin of error. This means that detection limits benefit from large sample volumes. Similar approaches i.e. sufficient sample size are used when analysing chemicals in environmental matrices (Einax et al., 2004). However, for samples with particles, samples should be small enough to prevent clogging of filters or sieves. This means that recommendations for sample sizes will differ for different water types. Because the actual concentration cannot be predicted, occurrence of non-detects or filter clogging can never be fully prevented.

Detection limits also depend on the particle size range aimed for in a study. Various studies have shown that smaller particles are more abundant (Cabernard et al., 2018), implying that smaller sample volumes are required when exclusively examining small microplastics that are analytically challenging to detect (e.g., <100–300 μm). However, if such a study would also aim to detect larger microplastics accurately, a large volume would still be required. Establishing sample volume recommendations for studies primarily aiming for larger (roughly > 300 μm) microplastics, should consider both expected microplastic concentrations for a given water type and practical considerations. Most studies reviewed belong to this category that aimed to detect also larger microplastics. In surface water, > 300 μm microplastic concentrations span a wide range of concentrations; roughly 1×10^{-3} to 10 particles per litre (Fig. 1). Because of the low concentrations and ease of obtaining large volumes from surface waters, we set 500 L as a minimum sample volume for surface water. However, given the often very low particle number concentrations in some lakes and rivers, a volume greater than 500 L is recommended for remote locations.

For tap water (range 1×10^{-4} to 100 particles per litre), a greater sample volume is proposed compared to surface water. We advise a minimum volume of 1000 L, because of the concentrations that can be very low (Mintenig et al., 2019b), uncertainties with the representativeness of this range given the low number of studies identified, and ease of sample collection. For bottled water, there were also a limited number of studies available. Yet they all demonstrate presence of at least several particles per litre, such that even a minimum of 1 L would be defensible in case a 1 L bottle would be the study unit and only very small particles (<100 μm) would be targeted. However, the study unit in such studies is often the brand or production lot, and also larger particles are targeted, in which case we recommend to sample >10 L for a more representative result. As bottled water usually is provided in volumes smaller than 10 L, this would imply the need to either analyse multiple bottles or to treat the total volume of multiple bottles as one sample. For WWTP influents where concentrations of particles are expected to be higher (Fig. 1), a sample volume of 1 L is considered sufficient. For WWTP effluent, a sample volume greater than 500 L is recommended, or a reported clogging of the sieve e.g. (Carr et al., 2016; Mintenig et al., 2017; Vollertsen and Hansen, 2017; Ziajahromi et al., 2017). These volumes mentioned would lead to roughly 5 to 500 particles detected, which is considered sufficiently representative if the detection limit would be 1 particle as mentioned above. Use of these volumes would receive a maximum score of 2. However in some cases lower volumes have been used with good reason and may still yield fair results. In these cases a score of 1 is assigned (Table S2). Studies that explicitly aim for only smaller particles can use smaller volumes as long as detection limits are met, and still receive the maximum score.

3.1.3. Sample processing and storage

For the transfer of a primary sample (e.g. material in a net or sieve) to a storage bottle, or for preservation or storage of samples before reaching the laboratory, certain criteria need to be met. Some studies rinse jars, bottles or other materials with targeted water e.g. (Kosuth et al., 2018; Talvitie et al., 2015). However, particles from that rinsing water could easily stick to surfaces and remain, which thus would lead to contamination of the actual sample. Ideally, sample containers should be rinsed in the laboratory with filtered water before bringing them to the field. In general, samples should be stored shortly after sampling and further handling avoided before arriving in the laboratory. When sampling, use of plastic materials should be avoided as much as possible to again minimize contamination. Many studies use a fixative like ethanol, formalin or methyl aldehyde (Anderson et al., 2017; Baldwin et al., 2016; Eriksen et al., 2013; Fischer et al., 2016; Mason et al., 2016a; Su et al., 2016; Wang et al., 2018; Xiong et al., 2018; Zhang et al. 2015, 2017). However, the effects of the fixative on different types of plastic should be evaluated before application, or studies should report evidence from the literature (Hermsen et al., 2018). Ethanol and formalin for instance, have been shown not to affect polymer characteristics (Courtene-Jones et al., 2017). Some of the studies reviewed here used volunteers for sampling and sample processing (Christiansen, 2018; Kosuth et al., 2018). Citizen science (CS) approaches have been used in environmental monitoring and are increasingly being used in research on plastic debris (Liboiron et al., 2016; Syberg et al., 2018). It has been argued that this may improve risk perception within society and therefore improve the foundation for timely and efficient societal measures (Syberg et al., 2018). There is also an economic incentive to collect data with volunteers rather than by paid professionals, and some monitoring research would even be impracticable if data were not collected by volunteers (Brett, 2017). However, concerns with respect to the quality of CS have been raised, and validation studies have shown that the reliability of CS based data is highly uncertain (Brett, 2017). Other than for macroplastics, quality assurance for sampling and sample processing of microplastics is technically demanding and the error rate can be expected to be higher for volunteers than for professionals. Since no CS validation studies for microplastics sampling and analysis exist to date, it is not clear to what extent the quality of data is affected by having some of the crucial steps performed by non-professionals. Therefore, as scientific quality

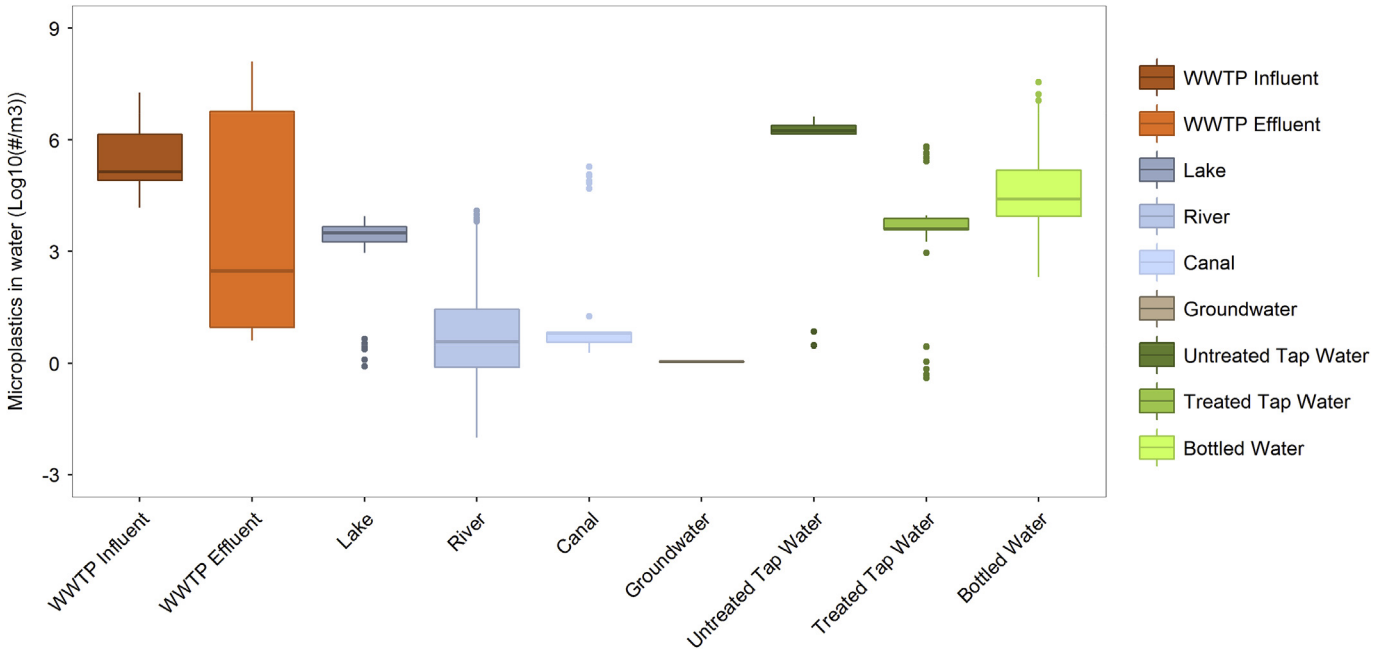

Fig. 1. Box and whisker plot showing median and variation in microplastic number concentrations in individual samples taken from different water types. Data relate to individual samples unless only means were reported, in which case the mean value was taken into account n times, with n being the number of samples which the mean was based on. References included: (Estahbanati and Fahrenfeld, 2016; Faure et al., 2015; Fischer et al., 2016; Hoellein et al., 2017; Kosuth et al., 2018; Leslie et al., 2017; Magnusson and Norén, 2014; Mason et al. 2016a, 2018; McCormick et al. 2014, 2016; Michielssen et al., 2016; Mintenig et al., 2019b; Oβmann et al., 2018; Pivokonsky et al., 2018; Rodrigues et al., 2018; Schymanski et al., 2018; Simon et al., 2018; Talvitie et al. 2015, 2017a, 2017b; Vollertsen and Hansen, 2017; Wang et al. 2017, 2018; Ziajahromi et al., 2017), with n = 27. For statistical significances of differences among water types, see Table S4.

assurance is the primary perspective of this paper, use of volunteers for major parts of the sampling work was considered less reliable, leading to a score of 1 in case of validation of the adequacy of the protocols, and 0 in all other cases for this criterion.

3.1.4. Laboratory preparation

Contamination of samples due to airborne polymer particles and fibres has been described as a major problem in microplastic analysis (Hermsen et al. 2017, 2018; Torre et al., 2016; Vandermeersch et al., 2015; Wesch et al., 2016). Therefore, to avoid contamination and prior to actual sample preparation and analysis, certain measures need to be taken. These include avoiding synthetic components in clothing, wearing of cotton lab coats, and pre-rinsing and cleaning of all materials used as well as laboratory (bench, laminar flow cabinet) surfaces. If precautions were not fully reported but sufficient blanks (i.e., three blanks, see section 'negative controls' below) were included to keep track of background contamination, then a score of 1 was assigned (Table S2).

3.1.5. Clean air conditions

To avoid contamination with airborne microplastic particles or fibres, sample handling should be performed in a laminar flow cabinet or in a clean air laboratory to receive the maximum score (Hermsen et al., 2018). Recent studies are increasingly using such conditions (Mason et al., 2018; Oβmann et al., 2018; Schymanski et al., 2018; Wang et al., 2018; Zhang et al., 2017). In case clean air conditions were not used but covering of samples and sufficient blanks were reported, a score of 1 was assigned (Cable et al., 2017; Dris et al. 2015, 2018b; Miller et al., 2017; Mintenig et al., 2019b; Pivokonsky et al., 2018).

3.1.6. Negative controls

To verify and correct for contamination or to demonstrate absence of contamination, replicated ($n \geq 3$) procedural blanks need to be analysed. All reviewed studies reported particles counts; if the variability of contamination was quantified, and if it was clearly indicated that actual sample results were corrected for blank values, a score of 2 was assigned. Some precautions are less reliable but still provide some useful information on the level of contamination, like the filtration of air, or the sole examination of petri dishes/soaked papers placed next to the samples (Cable et al., 2017; Dris et al. 2015, 2018b; Estahbanati and Fahrenfeld, 2016; Hendrickson et al., 2018; Lares et al., 2018; Mani et al., 2015; McCormick et al., 2016; Rodrigues et al., 2018; Simon et al., 2018; Ziajahromi et al., 2017). If these precautions were taken, a score of 1 was assigned.

3.1.7. Positive controls

Losses of particles may occur during various steps of sampling, sample preparation and analysis and it is recommended to quantify losses using positive controls. Estahbanati and Fahrenfeld (2016) assessed particle losses during sampling with nets, by adding plastic particles in distilled water. Subsequent sample handling in the laboratory often includes complex steps to remove organic matter from samples (see 'sample treatment' below), particularly from WWTP influent or effluent or surface waters. To verify a sufficiently high recovery of particles during filtration, digestion, transfer and analytical identification steps, representative replicated positive controls ($n \geq 3$) should be performed (Hermsen et al., 2018). If recoveries are low yet reproducible, the reported counts should be corrected for this incomplete recovery. Positive controls should be conducted for the targeted microplastics, covering different size classes and polymer types. Microplastic sizes span a wide range and it cannot be assumed that recoveries are constant across the range of sizes and polymer types. In practice, it is important to at least use small enough microplastics as controls, as these are more difficult to recover. In some cases, larger microplastics still require separate controls, especially when different

methods are applied. For instance, the method used by Mason et al. (2018) for particles smaller than 100 μm was different from that for particles larger than 100 μm, whereas positive controls were only performed for the smaller particles. Only three studies provided full data on positive controls (Simon et al., 2018; Vollertsen and Hansen, 2017; Wang et al., 2018) and received maximum scores, indicating that it is not yet a very common practice. Other studies conducted positive controls but with no or insufficient replicates (Di and Wang, 2018; Dyachenko et al., 2017; Hendrickson et al., 2018), or only for one step in the analysis (Rodrigues et al., 2018), or for part of the targeted size range (Mason et al., 2018) and received a score of 1.

3.1.8. Sample treatment

To assure the quality of visual inspection and subsequent polymer identification, which is especially critical for <300 μm particles and to enable the usage of more advanced identification techniques (see section 'polymer identification'), a sample digestion step should be performed for surface and WWTP water samples in order to score 2 points. Tap and bottled water do not require a digestion step and thus were always assigned 2 points on this criterion. Digestion should be done under conditions that do not affect the microplastics weights, counts or shapes. In the context of biota analysis, use of potassium hydroxide (KOH) or enzymes has been demonstrated to be acceptable (Catarino et al., 2016; Cole et al., 2014; Kühn et al., 2017; Munno et al., 2018). The reviewed studies here commonly used hydrogen peroxide (H_2O_2) which is known to affect some polymers (Hurley et al., 2018). However its effects have been demonstrated to be minimal within an exposure of 48 h (Löder et al., 2017) and was therefore deemed acceptable. Several studies kept the temperature around 35–45 °C, e.g. by using a cooling or ice bath (Simon et al., 2018), however sometimes higher temperatures up to 75 °C (Anderson et al., 2017; Baldwin et al., 2016; Estahbanati and Fahrenfeld, 2016; Hendrickson et al., 2018; Hoellein et al., 2017; Pivokonsky et al., 2018) or even 80 °C were used in some of the digestion steps (Vermaire et al., 2017), or even 90 °C for drying (Estahbanati and Fahrenfeld, 2016; Hendrickson et al., 2018; Ziajahromi et al., 2017). Effects of temperature in combination with various digestion chemicals were studied by Munno et al. (2018). Based on comparison of data on polymer mass losses during heating and digestion, the authors concluded it was best to stay below 60 °C. We set 50 °C as the safe upper limit, and as a criterion to assign a maximum score as a precautionary measure and since many of the reviewed studies were below 50 °C. Digestion without such considerations of mass losses was assigned a score of 1. A score of 1 was also assigned for surface water when it was reported to be very clear and clean even without digestion applied. Furthermore, studies that did not apply digestion but explicitly were aiming for the detection of ≥300 μm particles only, were assigned a score of 1 (Hermsen et al., 2018).

3.1.9. Polymer identification

To assure reliable assessment of plastic particles, the polymer identity needs to be confirmed, preferably by using (micro) FTIR or Raman spectroscopy, pyrolysis-GCMS or TGA-GCMS techniques (Hermsen et al., 2018; Löder and Gerdts, 2015; Mintenig et al., 2018). Although subsampling should be avoided, these techniques are so laborious that representative sub-sampling is often required. Best practice for subsampling and subsequent polymer identification will differ for different microplastic size classes and technologies applied (Mintenig et al., 2018). The manual sorting and subsequent identification of microplastics has a bias compared to the identification of particles enriched on filters with FTIR or Raman microscopy (i.e., avoid missing transparent or small particles), and is therefore discouraged when analysing particles <300 μm. For manually sorted particles, following Hermsen et al. (2018), we argue that analysis of all particles is feasible and therefore recommended if the numbers of pre-sorted particles *per study* are <100. For particle numbers >100, 50% should be identified, with a minimum of 100 particles. If polymer identities are reported on a *per sample* basis, we also advise to analyse all particles found, however with a minimum of 50. This minimum is considered reasonable to represent the variety of particle shapes and polymer types in environmental samples. Anyway, for such hand-picked representative subsets, studies generally still should describe how representativeness was assured. For smaller microplastics and when applying FTIR or Raman microscopy, the representativeness of subsampling (the area of a filter that was measured) is relatively easy to assess. Particularly when coupling a focal plane array detector to the microscope, many more particles (especially the small and transparent particles) can be assessed in one analysis. Although measurement times can be long, at least 25% of the filter needs to be analysed (Mintenig et al., 2017; Redondo-Hasselerharm et al., 2018). If these criteria for number of particles and/or percentage of the filter are met, a score of 2 is assigned. If polymers were identified for a too low number of particles or on a smaller part of the filter, a score of 1 was assigned. Also, if SEM-EDS or - EDX was applied to distinguish polymers from non-polymeric materials (Anderson et al., 2017; Cable et al., 2017; Mason et al., 2016b; Su et al., 2016), a score of 1 was assigned

3.1.10. Overall reliability of method aspects and studies

For each study, we assessed against all quality criteria and calculated a total accumulated score (TAS) (Table S3). Whereas the maximum achievable TAS score is 18, average (min − max) TAS scores were 13.7 (13–14) for bottled water, 11.5 (8–15) for treated tap water, 12.5 (11–14) for DWTP water, 7.9 (4–15) for surface water, and 7.3 (3–13) for waste water studies, respectively (Table 1). This ranking in average scores for the different water types probably reflects the relative ease of analysing these different water types. For instance, bottled and tap water require no digestion, which means that 2 points were always assigned to the sample digestion criteria. It should be noted though that the number of studies examining DWTP and treated tap water (each n = 2), and bottled water studies (n = 3) was very low, rendering the averages to be less rigorous. On average, studies were assigned roughly half (8.41/18) of the maximum score for data quality, a result which is very similar to the average score assigned to studies reporting data on ingestion of microplastic by biota (Hermsen et al., 2018).

Only four studies received non-zero scores for all criteria. These were the study on surface water by (Wang et al. 2018) (TAS = 15), the study on bottled water by Mason et al. (2018) (TAS = 14), and two studies on wastewater by Ziajahromi et al. (2017) (TAS = 12) and Hendrickson et al. (2018) (TAS = 11). For the ranking of such non-zero studies, a multiplied score X can be calculated (Hermsen et al., 2018), followed by a ^{2}Log X transformation in order to obtain a linear scale for a maximum score of 9. This would lead to a score of 6 for the data provided by Wang et al. (2018), a score of 5 for the data provided by Mason et al. (2018), a score of 3 by Ziajahromi et al. (2017), and a score of 2 for the data provided by Hendrickson et al. (2018). These four studies were published in the years 2017 or 2018, which may reflect recent progress in the quality of applied methods to analyse microplastics in environmental samples. With only four studies having all non-zero scores, it can be concluded that the majority of the reviewed studies (46 studies or 92%) cannot be considered fully complete or reliable on at least one crucial aspect of quality assurance. This does not mean that studies may not be useable or important as a more specific consideration of scores and study outcomes in hindsight, can still make a study very well fit for certain research questions.

Table 1
Overview of individual and accumulated scores[a] of papers reporting microplastic concentrations in surface water and drinking water.

Author	Type	Sampling methods	Sample size	Sample processing and storage	Lab preparation	Clean air conditions	Negative controls	Positive controls	Sample treatment	Polymer ID	Total Accumulated Score[b] (TAS, max = 18)
Mason et al. (2018)	**Bottle**	1	2	2	1	2	2	1	2	1	**14**
Schymanski et al. (2018)	**Bottle**	1	1	2	2	2	2	0	2	2	**14**
Oβmann et al. (2018)	**Bottle**	1	1	2	2	2	2	0	2	1	**13**
Mintenig et al. (2019b)	**Tap**	2	2	2	2	1	2	0	2	2	**15**
Kosuth et al. (2018)	**Tap**	0	0	0	2	2	2	0	2	0	**8**
Mintenig et al. (2019b)	**DWTP**	2	1	2	2	1	2	0	2	2	**14**
Pivokonsky et al. (2018)	**DWTP**	1	1	2	1	1	2	0	1	2	**11**
Mintenig et al. (2019b)	**Ground**	2	1	2	2	1	2	0	2	2	**14**
Wang et al. (2018)	**Surface**	2	1	1	2	2	2	2	2	1	**15**
Hendrickson et al. (2018)	**Surface**	2	1	2	1	1	1	1	1	1	**11**
Di and Wang (2018)	**Surface**	2	0	2	2	0	0	1	2	1	**10**
Mani et al. (2015)	**Surface**	2	2	1	1	1	1	0	1	1	**10**
Wang et al. (2017)	**Surface**	1	0	1	2	1	2	0	2	1	**10**
Baldwin et al. (2016)	**Surface**	2	1	1	1	1	2	0	1	0	**9**
Cable et al. (2017)	**Surface**	2	1	1	1	1	1	0	1	1	**9**
Dris et al. (2018a)	**Surface**	2	2	0	1	1	1	0	1	1	**9**
Lares et al. (2018)	**Surface**	1	0	1	2	1	2	0	1	1	**9**
Rodrigues et al. (2018)	**Surface**	2	2	1	1	0	1	0	1	1	**9**
Su et al. (2016)	**Surface**	2	1	1	1	1	1	0	1	1	**9**
Zhang et al. (2017)	**Surface**	2	1	1	1	2	0	0	0	2	**9**
Dris et al. (2015)	**Surface**	2	1	2	1	1	1	0	0	0	**8**
Estahbanati and Fahrenfeld (2016)	**Surface**	2	2	1	0	0	1	1	1	0	**8**
Hoellein et al. (2017)	**Surface**	2	1	2	0	0	1	0	1	1	**8**
Mason et al. (2016b)	**Surface**	2	1	1	0	0	2	0	1	1	**8**
Sighicelli et al. (2018)	**Surface**	2	2	1	0	0	0	0	2	1	**8**
Vermaire et al. (2017)	**Surface**	2	1	2	0	0	2	0	1	0	**8**
Xiong et al. (2018)	**Surface**	2	1	0	1	1	1	0	1	1	**8**
Anderson et al. (2017)	**Surface**	2	1	1	0	0	1	0	1	1	**7**
Faure et al. (2015)	**Surface**	1	2	1	1	0	0	0	1	1	**7**
McCormick et al. (2016)	**Surface**	1	1	1	0	0	2	0	1	1	**7**
Miller et al. (2017)	**Surface**	1	0	1	1	1	2	0	0	1	**7**
McCormick et al. (2014)	**Surface**	1	1	1	0	0	2	0	1	0	**6**
Fischer et al. (2016)	**Surface**	2	1	1	0	0	0	0	1	0	**5**
Free et al. (2014)	**Surface**	2	1	1	0	0	0	0	1	0	**5**
Lahens et al. (2018)	**Surface**	1	1	1	0	0	0	0	1	1	**5**
Leslie et al. (2017)	**Surface**	1	0	2	0	1	1	0	0	0	**5**
Eriksen et al. (2013)	**Surface**	2	1	1	0	0	0	0	0	0	**4**
Zhang et al. (2015)	**Surface**	2	1	0	0	0	0	0	0	1	**4**
Mintenig et al. (2017)	**WWTP**	2	2	2	1	1	2	0	1	2	**13**
Ziajahromi et al. (2017)	**WWTP**	2	2	1	1	1	1	1	1	2	**12**
Simon et al. (2018)	**WWTP**	1	1	0	1	1	2	2	2	1	**11**
Lares et al. (2018)	**WWTP**	2	0	1	2	1	2	0	1	1	**10**
Talvitie et al. (2017a)	**WWTP**	2	1	1	1	1	2	0	0	2	**10**
Murphy et al. (2016)	**WWTP**	1	1	2	2	1	1	0	0	1	**9**
Mason et al. (2016a)	**WWTP**	2	2	1	0	0	2	0	1	0	**8**
Vollertsen and Hansen (2017)	**WWTP**	0	2	1	0	0	0	2	1	1	**7**
Carr et al. (2016)	**WWTP**	2	2	1	0	0	0	0	0	1	**6**
Magnusson and Norén (2014)	**WWTP**	2	2	1	0	0	0	0	0	1	**6**
Michielssen et al. (2016)	**WWTP**	2	1	2	0	0	1	0	0	0	**6**
Talvitie et al. (2017b)	**WWTP**	2	0	1	0	0	2	0	0	1	**6**
Vermaire et al. (2017)	**WWTP**	1	0	2	0	0	2	0	1	0	**6**
Dyachenko et al. (2017)	**WWTP**	1	0	1	0	0	0	1	1	1	**5**
Leslie et al. (2017)	**WWTP**	1	0	2	0	1	1	0	0	0	**5**

Table 1 (*continued*)

Author	Type	Sampling methods	Sample size	Sample processing and storage	Lab preparation	Clean air conditions	Negative controls	Positive controls	Sample treatment	Polymer ID	Total Accumulated Score[b] (TAS, max = 18)
Dris et al. (2015)	**WWTP**	1	0	0	1	1	1	0	0	0	**4**
Talvitie et al. (2015)	**WWTP**	2	1	0	0	0	1	0	0	0	**4**
Browne et al. (2011)	**WWTP**	0	0	1	0	0	0	0	0	2	**3**
Average		**1.57**	**1.02**	**1.20**	**0.77**	**0.64**	**1.18**	**0.21**	**0.93**	**0.89**	**8.41**

[a] For the scoring criteria, the reader is referred to Table S2.
[b] TAS values are underlined when all underlying scores are non-zero.

Besides insights in methodological differences among individual studies, the scores allow for a cross comparison of reliability differences per criterion (Table 1) (Hermsen et al., 2018). Average scores per criterion were all lower than 2, which means there is room for improvement of quality assurance in this field of research. The average scores per criterion across 55 records were lower than 1 for the criteria *sample treatment* (0.93), *polymer identification* (0.89), *laboratory preparation* (0.77), *clean air conditions* (0.64), and *positive controls* (0.21). Therefore, significant improvements are needed especially for these five out of nine quality aspects. Our analysis further illustrates that besides actual quality assurance, also full reportage of method details is important, to assure traceability and reproducibility of data. Reporting is a quality aspect in itself and some studies may have scored higher had they been reported better. In this respect we recommend to also include detection limits in terms of number and mass concentrations, but also in terms of minimum and maximum detectable particles sizes inherent to the applied methodology.

3.1.11. Implications of quality criteria and reliability of studies for human health risk assessment

Human health risks depend on exposure and it is well known that drinking water is an uptake pathway for microplastics. Consequently, quality in the analysis of microplastics in drinking water and its sources is very relevant to accurately assess risks to human health.

In this respect it should be mentioned that the proposed criteria are related to concentrations in the water, which however may not fully correlate with exposure. For instance, we recommended running the tap before sampling to avoid contamination of the first portion of water, to assure reproducibility of results and further, because many consumers would do this anyway. However, others may not do this and addressing this variability may be relevant for exposure assessment. Exposure to microplastics may also depend on the level of shaking of a bottle before drinking, whereas our criteria recommend shaking in order to maximize the chance that all particles are measured, and to assure reproducibility of the analysis. Exposure in drinking water can additionally be influenced by direct contamination of drinking water through contact with air, but to better understand contamination that is coming directly from the water supply and to support comparability and reproduciblity, we recommend procedures to prevent airborne contamination. Finally, exposure to microplastics would also include uptake via inhalation or food (Wright and Kelly, 2017), which is not covered in this paper that only addresses drinking water and its sources.

The fact that high quality data are limited also has implications for human health risk assessment, which considers both exposure as well as health effects. Only four out of 50 studies (which were published in 2017 and 2018) were of such a level of reliability (i.e. having no zero scores) that they could be used confidently for an exposure assessment. Importantly, of these four studies, the recent study on microplastic particles in bottled drinking water (Mason et al., 2018) would be highly relevant for human health risk assessment, based on the criteria used here, although the study only had maximum scores in 5 out of 9 criteria. Therefore, this uncertainty in the overall exposure data precludes the ability to conduct a robust risk assessment, whether related to particle toxicity, chemical toxicity or microbial toxicity. We therefore conclude that more high quality data is needed on the occurrence of microplastics in drinking water to more confidently assess potential exposure, as a critical piece for understanding the potential human health risks.

3.2. Microplastics in freshwater

3.2.1. Global microplastic concentrations in different water types

We reviewed the available literature on microplastics in drinking water, fresh water and wastewater. Monitoring has been conducted in multiple locations in Asia, Australia, Europe and North America. A selection of studies reporting particle number concentrations were used for a further analysis (Figs. 1 and 4), if they reported means and/or raw data on a volume basis. These microplastic concentrations, reported as number of particles, spanned ten orders of magnitude (1×10^{-2} to 10^{8} #/m^3) across all individual samples and water types, also when excluding wastewaters (Fig. 1). The number of microplastic particles in samples per water type was statistically different ($p < 0.05$) for all pairwise comparisons of water types, except for the comparisons between ground water and all other water types, WWTP effluent versus (untreated) DWTP and tap water, and WWTP influent versus (untreated) DWTP water (Fig. 1, Table S4). As these concentration data relate to numbers, they do not distinguish between particle size, shape or material type; differences that will be discussed in the sections below. Studies often do not mention a lower nor an upper size limit, or only mention the targeted size class. The data include particles *reported* as microplastics, that is, we did not take out suspect non-polymer particles as identified either by authors themselves or based on our quality assessment discussed above. The range for 50% of the data per water type (the boxes in Fig. 1) is 1–2 orders of magnitude, and quite similar for influent, effluent, lake, river and bottled water data. For canal and tap water only a few studies were available, which may have caused the variation to be much smaller. For bottled water, the number of studies was also low (Mason et al., 2018; Oβmann et al., 2018; Schymanski et al., 2018), however there were many samples (bottled water brands) for this water type available in these studies. The median concentrations per water type vary over four orders of magnitude.

Some general patterns exist in the concentration data (Fig. 1). Surface waters have the lowest concentrations of all water types, with, bottled water closer to the higher end. The lower concentrations observed in surface water, particularly compared to drinking water, is likely attributed to the fact that most surface water studies targeted only larger particles whereas smaller particles are more abundant (Cabernard et al., 2018). WWTP influent shows the highest concentrations based on the median and

interquartile range of reported concentrations (Fig. 1) although WWTP studies generally did not monitor small particles. The high concentrations therefore reflect direct domestic inputs and inputs from those diffuse land-based sources that are routed via waste water. WWTP effluent has a lower median compared to WWTP influent, which probably reflects the retention of microplastics in WWTPs. Similarly, untreated tap water has higher concentrations than treated tap water. Concentrations in bottled water are higher than in tap water, which may reflect the higher influx of airborne particles in the factories, which are inherently more locked in, wear

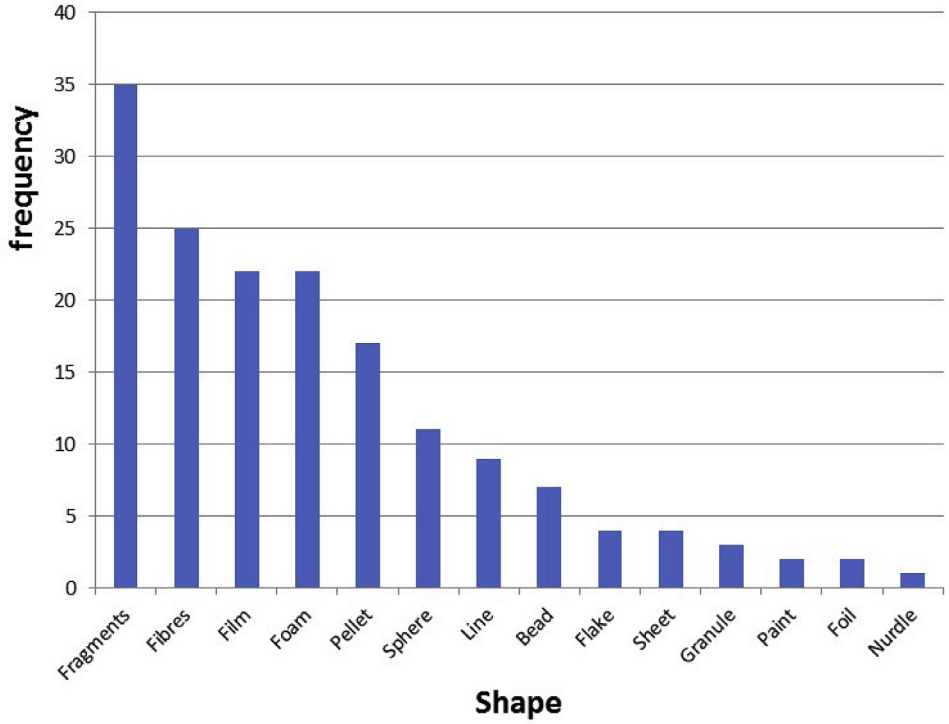

Fig. 2. Number of studies reporting a particular shape of microplastic particles (from a total of 55 records).

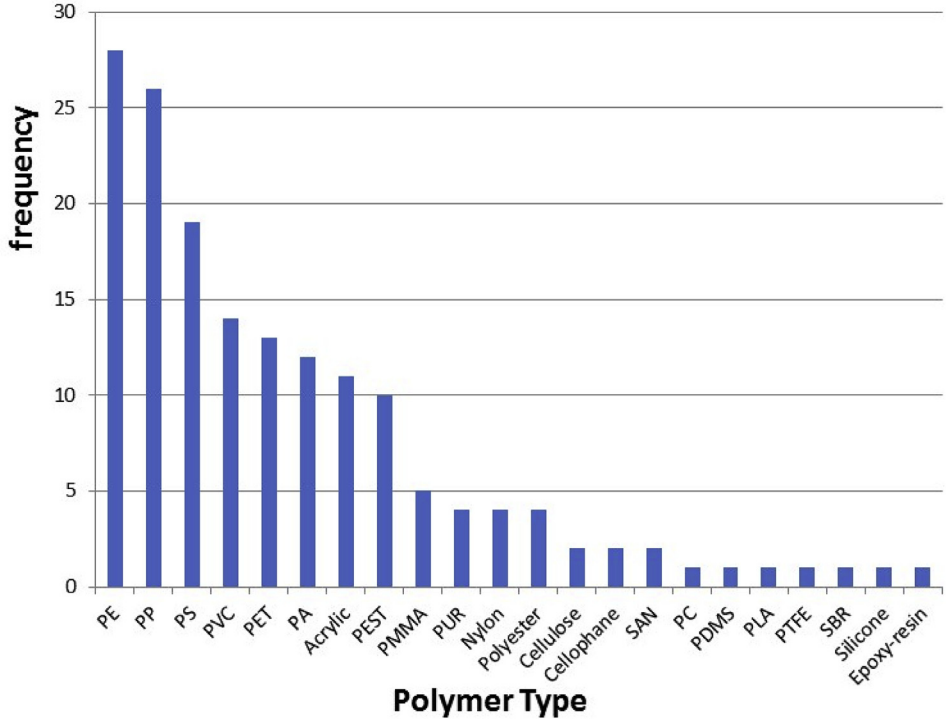

Fig. 3. Number of studies reporting a particular polymer type of microplastic particles (32 out of 55 records reported polymer type).

from caps or bottle walls after production, or the fact that these studies also included smaller sized particles. For instance, Schymanski et al. (2018) used Raman microscopy and was thus able to identify down to > 5 μm, which also explains the high number concentrations. The general trends observed here (Fig. 1) still remain when only the studies that received highest quality scores are taken into account (Fig. S1). Still, the generalities listed here should be interpreted with caution given the low number of bottled water (n=3), treated tap water (n = 2), (untreated) DWTP water (n = 2) and ground water studies (1), although as noted earlier, there were many bottled water samples available in the limited number of studies.

3.2.2. Microplastic shapes in global freshwaters

Microplastics of different shapes were reported. Several factors limit a potential quantitative analysis of reported data on the relative abundance of shapes among water types. First, many studies typically only analysed shapes of a subset of all isolated particles and it is not clear how representative these subsets were when it comes to particle shape. Second, studies targeted different size ranges which also limits their comparability. For instance, fibres are typically small (Cole, 2016), so easily missed when trawling. Third, studies differed in the extent their water samples were representative of the studied water systems or water type, which in turn is affected by spatial and temporal variability. Fourth, although some particles' shapes were quite well-defined and thus interpreted similarly across studies, some others are more ambiguous, like nurdle, pellet, pre-production pellet, sphere, resin or granule. Nevertheless, we can provide a relatively robust view of the relative importance of particle shapes by showing the frequency of shapes observed across studies (Fig. 2). The reviewed studies (n = 50) reported (in the order of decreasing reporting frequency): fragment, fibre, film, foam, pellet, sphere, line, bead, flake, sheet, granule, paint, foil and nurdle (Fig. 2). We argue that this order also reflects a relative order of importance of shapes, that is, the most frequent shapes detected in a high number of locations globally, as the reviewed studies concerned many different locations on the globe.

3.2.3. Polymer types reported in global studies on freshwater microplastics

For 32 out of 55 records, polymer types were assessed. Similar to particle shape as discussed above, and rather than discussing relative abundances per study, we consider the relative frequency of reported polymer types observed in water types on a global level. Often, relative abundances per study are not provided, or may not be considered accurate due to limited or biased subsets of particles used for the polymer identification. Most frequently observed polymer types across studies and records are PE ≈ PP > PS > PVC > PET, with

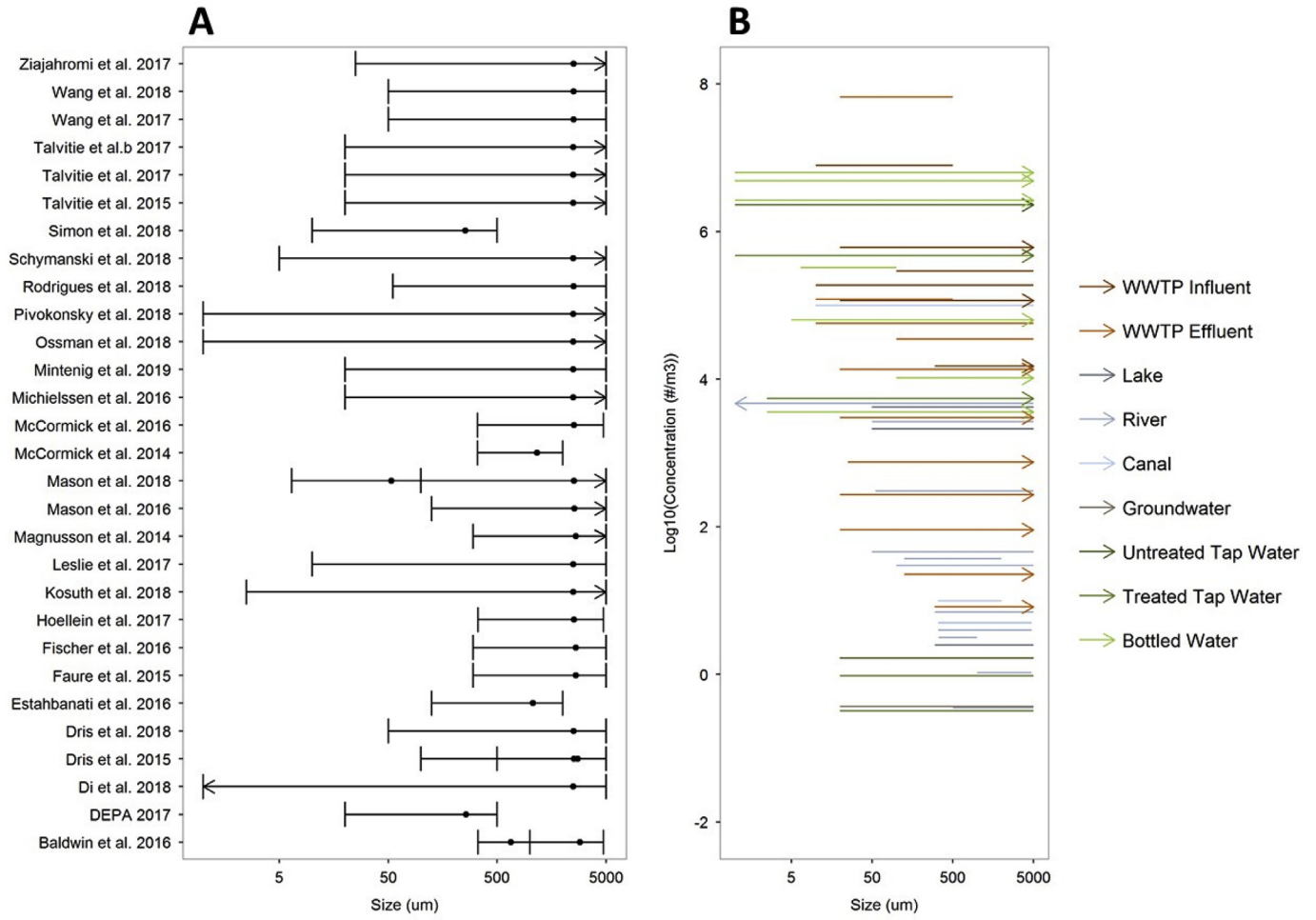

Fig. 4. Size ranges used (A) and number concentrations per size range reported (B) in studies on microplastics in drinking, surface and waste waters (referenced in Fig. 1). Arrows indicate that no upper or lower size limit was specified, in which case values of 5 mm or 1 μm were assigned, respectively. Panel A: Size ranges per study are ordered alphabetically per author name. Data points represent the average of the size range. Panel B: reported concentrations as a function of size range. Colours of arrows (Panel B) correspond to colours of the box and whiskers in Fig. 1. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Acrylic or acrylic-related compounds, PA, PEST and PMMA reported in five or more records (Fig. 3). The order of the five most abundant polymers can be roughly explained by two factors; global plastic demand and polymer density (Andrady, 2011; Bond et al., 2018). Global plastic demand would cause an order of PE > PP > PVC > PET > PS (Bond et al., 2018; Geyer et al., 2017). However, whereas PE and PP have densities below 1 g/cm^3 and are buoyant and PS has a density close to that of water, PVC and PET have densities of 1.3–1.7 g/cm^3. Therefore, a relatively high degree of settling could explain the lower abundances of PVC and PET in the surface water samples mostly assessed here. Specific subsets, i.e. Lakes/Rivers versus WWTP samples were checked for differences in relative abundances of polymer types, but no such differences were found. For a more detailed analysis of polymers reported in studies, the reader is referred to Table S1, which provides all observed polymers on an individual record basis. Recently, Bond et al. (2018) provided a review of polymer abundance data across environmental compartments in Europe, including 3 surface water and 5 WWTP studies. Instead of providing the reporting incidence across a large number of global studies, they averaged relative abundances reported across these 8 European studies, yet found the same order of abundances for the 5 most dominant polymers.

3.2.4. Sizes of microplastic particles

Studies generally did not report sizes or size distributions relating to individual particles, which precludes a meta-analysis of particle size across studies. However size classes were reported (Table S1) as well as the number of particles observed per size class. Still, this does not allow for a meaningful quantitative analysis, because the size bins vary widely across studies (Fig. 4A). Furthermore, often lower or upper size limits are not specified so that it is not clear to what size class reported number concentrations actually relate. Instead of plotting the reported size ranges across studies (Fig. 4A), reported ranges can be plotted against mean particle number concentrations (Fig. 4B). The latter graph clearly shows that studies aiming for smaller particles, like some of the bottled water and tap water studies, generally find the higher particle number concentrations.

4. Conclusions

We conclude that based on the limited number of high quality studies identified, standardization of microplastic analysis in water is needed. Quality assurance criteria that require the most improvements are sample treatment, polymer identification, laboratory preparation, clean air conditions and positive controls. In addition to ensuring that individual studies are of higher quality in order to achieve more confidence in study findings, standardized methods will allow reproducibility and comparability of results and will lead to the quality of data that are needed to conduct risk assessments. Among water types, reported microplastic concentrations differed widely, but the fact that studies target different size classes contributes to this variability. Despite the quality limitations, our analysis confirmed that microplastic is frequently present in freshwaters and drinking water. There is a high need to improve the analysis of very small microplastics, and to identify them in different water samples. Fragments, fibers, film, foam and pellets were the most frequently found microplastic shapes in surface water samples. Relative abundance of polymer types found across studies reflected plastic production and polymer densities. Conclusions on size comparisons among studies and water types are difficult to draw due to the aforementioned differences in targeted particle sizes. More studies are needed to better understand occurrence, shape, polymer types, and particle sizes, particularly for the small plastic particles.

Declarations of interest

None.

Conflicts of interest

There is no conflict of interest.

Author agreement

AAK and JDF designed the study. NHMN, EH, MK, SM and AAK performed the study. AAK wrote the article. NHMN, EH, MK, SM and JDF commented on draft versions of the article. All authors have approved the final article.

Disclaimer

The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the views, decisions or policies of the World Health Organization.

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Appendix A. Supplementary data

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World Health Organization

Microplastics in drinking-water

Key messages

- Microplastics are ubiquitous in the environment and have been detected in a broad range of concentrations in marine water, wastewater, fresh water, food, air and drinking-water, both bottled and tap water. The data on the occurrence of microplastics in drinking-water are limited at present, with few fully reliable studies using different methods and tools to sample and analyse microplastic particles.
- The potential hazards associated with microplastics come in three forms: physical particles, chemicals and microbial pathogens as part of biofilms. Based on the limited evidence available, chemicals and biofilms associated with microplastics in drinking-water pose a low concern for human health. Although there is insufficient information to draw firm conclusions on the toxicity related to the physical hazard of plastic particles, particularly for the nano size particles, no reliable information suggests it is a concern.
- Limited evidence suggests that key sources of microplastic pollution in fresh water sources are terrestrial run-off and wastewater effluent. However, optimized wastewater (and drinking-water) treatment can effectively remove most microplastics from the effluent. For the significant proportion of the population that is not covered by adequate sewage treatment, microbial pathogens and other chemicals will be a greater human health concern than microplastics.

Recommendations

- **Water suppliers and regulators** should continue to prioritize removing microbial pathogens and chemicals from drinking-water that are known significant risks to human health. As part of water safety planning, water suppliers should ensure that control measures are effective, including optimizing water treatment processes for particle removal and microbial safety, which will incidentally improve the removal of microplastic particles. Routine monitoring of microplastics in drinking-water is not necessary at this time.
- To better assess the human health risks and inform management actions, **researchers** should undertake targeted, well-designed and quality-controlled investigative studies to better understand the occurrence of microplastics in the water cycle and in drinking-water throughout the water supply chain, the sources of microplastic pollution and the uptake, fate and health effects of microplastics under relevant exposure scenarios.
- Irrespective of any human health risks posed by exposure to microplastics in drinking-water, measures should be taken by **policy makers and the public** to better manage plastics and reduce the use of plastics where possible, to minimize plastics released into the environment because these actions can confer other benefits to the environment and human well-being.

Key questions and answers

What are microplastics?

As a category, microplastics encompass a wide range of materials composed of different substances, with different densities, chemical compositions, shapes and sizes. There is no scientifically-agreed definition of microplastics, although they are frequently defined as plastic particles <5 mm in length. However, this is a rather arbitrary definition and is of limited value in the context of drinking-water since particles at the upper end of the size range are unlikely to be found in treated drinking-water. A subset of microplastics <1 µm in length are often referred to as nanoplastics.

How do microplastics get into drinking-water?

Microplastics may enter drinking-water sources in a number of ways: from surface run-off (e.g. after a rain event), to wastewater effluent (both treated and untreated), combined sewer overflows, industrial effluent, degraded plastic waste and atmospheric deposition. Surface run-off and wastewater effluent are recognized as the two main sources, but better data are required to quantify the sources and associate them with more specific plastic waste streams. Plastic bottles and caps that are used in bottled water may also be sources of microplastics in drinking-water.

How much microplastic has been found in drinking-water and drinking-water sources?

In freshwater studies, reported microplastic particle counts ranged from around 0 to 1000 particles/L. Only nine studies were identified that measured microplastics in drinking-water; these studies reported particle counts in individual samples from 0 to 10 000 particles/L and mean values from 10^{-3} to 1000 particles/L. A comparison of the data between fresh water and drinking-water studies should not be made because in most cases freshwater studies targeted larger particles, using filter sizes that were an order of magnitude larger than those used in drinking-water studies.

What kinds of microplastics are being found?

In fresh water a wide variety of particle shapes have been found while the polymers most frequently detected roughly correlates with plastic production volumes. In drinking-water, fragments and fibres were the predominant particle shapes and polyethylene terephthalate and polypropylene were the polymers most detected.

Can these studies be trusted?

A WHO-commissioned study concluded that most of these studies are not fully reliable because their methods lacked sufficient quality control. Results should therefore be interpreted with caution. The quality control areas requiring the most improvement included sample treatment, polymer identification, laboratory preparation, clean air conditions and positive controls. For example, in two drinking-water studies and for a subset of smaller particles in a third study, no spectroscopic analysis was conducted to confirm that the particles identified were plastic. Four of the 52 studies that scored highest for quality were published in 2017 and 2018, indicating some improvements in quality control.

What are the potential threats posed by microplastics in drinking-water?

The potential hazards associated with microplastics come in three forms: physical particles, chemicals and microbial pathogens that are part of biofilms. Particles may cause impacts in the body, depending on a range of physicochemical properties of the particle, including size, surface area and shape. However, the fate, transport and health impacts of microplastics following ingestion are not well studied, with no human studies on ingested microplastics. Although plastic polymers are generally considered to be of low toxicity, plastics and microplastics can contain unbound monomers and additives. Hydrophobic chemicals in the environment, including persistent organic pollutants, may also sorb to the plastic particle. Biofilms in drinking-water are formed when microorganisms grow on drinking-water distribution systems and other surfaces. Most microorganisms that are part of biofilms are non-pathogenic. However, some biofilms can include pathogens such as *Pseudomonas aeruginosa*, *Legionella* spp., non-tuberculosis *Mycobacterium* spp. and *Naegleria fowleri*.

The health risk from microplastics in drinking-water is a function of both hazard (potential to cause adverse effects) and exposure (dose). The same substance can have different effects at different doses, which depends on how much of the substance a person is exposed to and may also depend on the route by which the exposure occurs, e.g. ingestion, inhalation or injection. The risks associated with each hazard class are further described below.

What is the human health risk of ingesting microplastic particles through drinking-water?

Although there is insufficient information to draw firm conclusions on the toxicity of plastic particles and particularly the nano size particles, no reliable information suggests it is a concern. Studies on absorption indicate that microplastics >150 µm are likely to be excreted directly through faeces. Uptake of smaller particles is expected to be limited, although absorption and distribution of very small microplastic particles including nanoplastics may be higher. Toxicology studies in rats and mice reported some impacts including inflammation of the liver. However, these few studies are of questionable reliability and relevance, with findings reported at very high exposures that would not occur in drinking-water.

What is the human health risk from chemicals associated with microplastics in drinking-water?

Risk assessments have been conducted for many chemicals to determine the level at which no or limited adverse effects should occur (toxicological point of departure, POD). To assess health risks of chemicals associated with microplastics, a margin of exposure (MOE) assessment was conducted for the chemicals that have been detected in microplastics, are of toxicological concern and have adequate or accepted toxicological PODs. Since there are several orders of magnitude difference between estimated intakes from a very conservative exposure scenario and the PODs, chemicals associated with microplastics in drinking-water are a low concern.

What is the human health risk associated with biofilms that attach to microplastics in drinking-water?

Biofilms associated with microplastics are considered a low health concern considering the relative concentration of microplastics compared to other particles that pathogens can adhere to in fresh water. For microplastics that are not removed during drinking-water treatment, the relative significance of microplastic-associated biofilms is still likely negligible due to the larger mass of drinking-water distribution systems and their subsequent ability to support more biofilms, compared to microplastics. Disinfection, including in distribution systems can inactivate pathogens and control their growth.

How do the risks from microplastics stack up against other potential risks to drinking-water?

Microbial pathogens represent the most significant public health threat in drinking-water. In 2016, 485 000 diarrhoeal related deaths were attributed to microbially-contaminated drinking-water (Prüss-Ustün, 2019) and it is estimated that 2 billion people are drinking faecally contaminated water (WHO, UNICEF, 2017).

A significant source of faecal contamination in drinking-water is inadequately or untreated wastewater. About 20% of wastewater collected in sewers does not undergo at least secondary treatment and an even higher proportion of people lack access to sewage connections or other appropriate systems for collecting and treating wastewater. Therefore, although wastewater effluent is recognized as a key source of microplastic pollution in freshwater, pathogens and other chemicals associated with the lack of effective sewage treatment are of greater concern. By addressing the bigger problem of exposure to faecally contaminated water, communities can simultaneously address the smaller concern related to microplastics.

How can microplastics be removed from drinking-water?

Wastewater and drinking-water treatment systems—where they exist and are optimized—are considered highly effective in removing particles of similar characteristics and sizes as microplastics. According to available data, wastewater treatment can effectively remove more than 90% of microplastics from wastewater with the highest removals from tertiary treatment such as filtration. Drinking-water treatment has proven effective in removing far more particles of smaller size and at far higher concentrations than those of microplastics. Conventional treatment, when optimized to produce treated water of low turbidity, can remove particles smaller than a micrometre. Advanced treatment can remove even smaller particle; for example, nanofiltration can remove particles >0.001 µm while ultrafiltration can remove particles >0.01 µm.

Based on the conclusions of the report, should any actions be taken to minimize microplastic pollution in drinking-water? If so, what actions should be taken?

Irrespective of any human health risks posed by microplastics in drinking-water, policy-makers and the public should take action to minimize plastics released into the environment, since these actions will confer multiple other benefits for the environment and human well-being. Actions could include reducing the use of plastics where possible, improving recycling programmes, reducing littering, improving circular solutions and decreasing industrial waste inputs into the environment. Care must be taken, however, to select mitigating actions that do not create new problems.

Based on the conclusions of the report, what actions should be taken by water suppliers and drinking-water regulators?

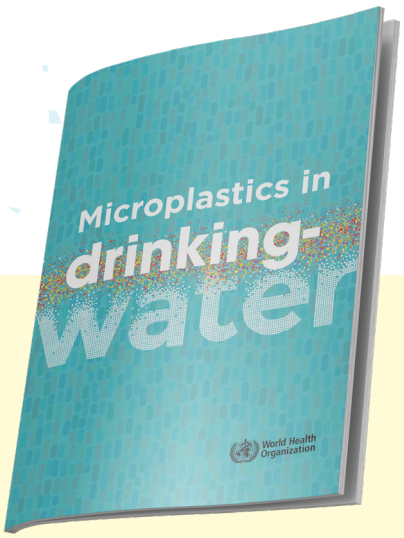
Water suppliers and regulators should continue to prioritize the removal of microorganisms and chemicals in drinking-water that pose a public health concern. As part of water safety planning, water suppliers should ensure that control measures are effective and should optimize water treatment processes for particle removal and microbial safety, which will incidentally improve the removal of microplastic particles. Routine monitoring of microplastics in drinking-water is not recommended at this time, as there is no evidence to indicate a human health concern.

What further research is needed?

A number of research gaps need to be filled to better assess the risk of microplastics in drinking-water and inform management actions. Targeted, well-designed and quality-controlled investigative studies should be carried out to better understand microplastics occurrence throughout the water supply chain, including the numbers, shapes, sizes, composition and sources of microplastics and to better characterize the effectiveness of water treatment. Research is also needed to understand the significance of treatment-related waste streams as contributors of microplastics to the environment. Quality-assured toxicological data are needed on the most common forms of plastic particles relevant for human health risk assessment. Further, a better understanding on the uptake and fate of microplastics and nanoplastics following ingestion is needed. Finally, given that humans can be exposed to microplastics through a variety of environmental media, including food and air, a better understanding of overall exposure to microplastics from the broader environment is needed.

Where will WHO direct its future research on the human-health effects of microplastics in the environment?

Given that humans can be exposed to microplastics through a variety of environmental media, WHO has initiated a broader assessment of microplastics in the environment. A future report will characterize the potential human health risks due to total microplastic exposure from the environment, including through food and air.



This information sheet summarizes key findings, recommendations and conclusions from the WHO technical report, Microplastics in drinking-water (WHO, 2019).

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ENVIRONMENT

Solving Microplastic Pollution Means Reducing, Recycling—and Fundamental Rethinking

New practices, and new chemistries, are needed to end the scourge

By Andrea Thompson on November 12, 2018

Rubbish left stranded by the tide on the River Thames. Credit: Anthony John West *Getty Images*

This is the third of a three-part series that examines our growing understanding of the scope and impacts of microplastics pollution.

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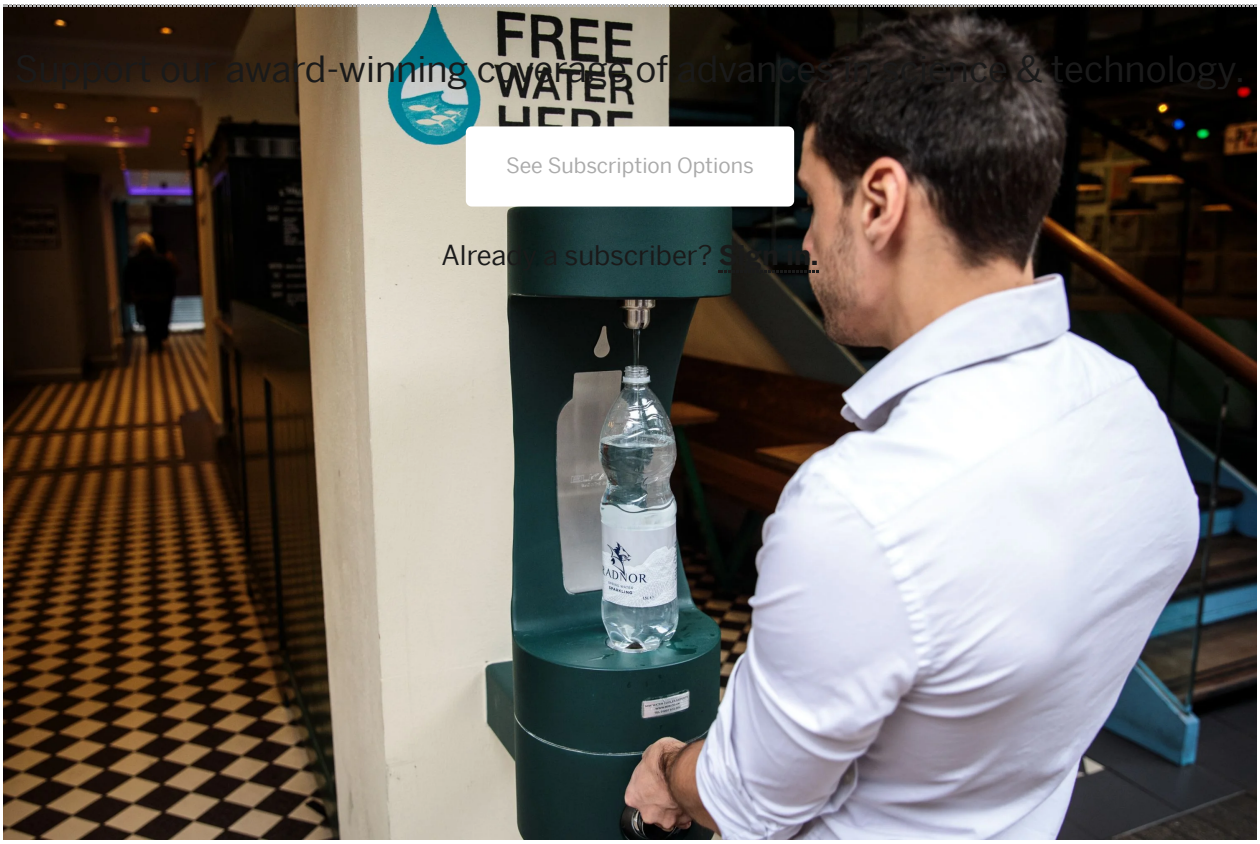
At several locations around London last winter and spring, researchers stalked the streets counting the number of discarded plastic water bottles they encountered, as if tallying species across a coral reef.

Their aim was to see if a new initiative to enlist businesses where people can refill empty bottles with tap water was making a dent in the trash littering the pavement, says marine biologist Heather Koldewey, who oversaw the research. Bottled water use has doubled in the U.K. in the past 15 years. And notably, plastic bottles are abundant along the banks of the River Thames, which carries them out to sea as they gradually break down into ever smaller fragments, tainting the river and the ocean with microplastics that can invade every level of the food chain.

Scientists have found these tiny bits of degraded plastic—along with fibers shed from synthetic fabric, and microbeads from cosmetics—lurking throughout the oceans, lakes, soil and even the air. Creatures from plankton to earthworms to humans are eating them, posing a potentially serious health threat to animals and ecosystems. The problem is only expected to balloon as plastic production increases exponentially—from a mere two million metric tons annually in 1950 to more than 300 million metric tons today, and a projected 33 billion metric tons each year by 2050.

Read more from this special report:

How Plastic Became a Plague



A man refills a plastic bottle at a new public water fountain in London, England. Credit: Jack Taylor *Getty Images*

To get the microplastics problem under control, the world has to take three primary steps, those who study the issue say. In the short term society needs to significantly curtail unnecessary single-use plastic items such as water bottles, plastic shopping bags, straws and utensils. In the medium term governments need to strengthen garbage collection and recycling systems to prevent waste from leaking into the environment between the trash can and the landfill, and to improve recycling rates. In the long run scientists need to devise ways to break plastic down into its most basic units, which can be rebuilt into new plastics or other materials. “There’s definitely no single solution,” says Koldewey, of the Zoological Society of London and a National Geographic Fellow.

REDUCE AND RECYCLE

An attractive, low-hanging target for tackling microplastic pollution is the drink bottles, utensils and bags that are called single-use plastics. Because they are used for convenience, not necessity, they are easier to do without, and the polymers used to make

becoming an increasingly popular way of curtailing their use, and limited evidence indicates they do reduce debris. But as Koldewey and others point out, governments that impose bans need to consider: whether such measures are cost-effective; what the environmental impacts of alternatives are; and what roadblocks such as, in the case of bottled water, a lack of places to fill up a reusable bottle might hamper the effectiveness of a ban.

Koldewey's own campaign to reduce the use of bottled water in London, called #OneLess, studied possible locations for placing refilling kiosks that would get the most use, such as public transportation hubs. The group also conducted surveys that found most residents would prefer to get water from the tap but were uncomfortable asking stores or restaurants for a free refill. The initiative to sign up businesses that would allow people to refill their bottles was aimed at overcoming that reluctance. Addressing such potential barriers is crucial to changing people's habits, Koldewey says.

Recycled product is displayed at a recycling facility in Ontario, Canada. Credit: James MacDonald *Getty Images*

Reducing single-use plastics will help the environment because the packaging sector more broadly is the biggest user of plastic polymers. But plastic, including some of the same polymers found in single-use packaging, is also used in construction, electronics and fabrics. The latter are the sou ch are proving to be one of the most ubiquitous forms of microplastic pollution. Scientists are concerned that focusing on single-use plastics will obscure more systemic issues around plastic that need to be addressed. “It’s a super-useful first step,” says Martin Wagner, an ecotoxicologist at Norwegian University of Science and Technology. “What I’m afraid of is that that will be it.”

His worry is well founded. In Europe only 30 percent of plastic is recycled, whereas in the U.S. it is a measly 9 percent. “Our waste management systems are good, our use of them is pretty lousy,” Koldewey says. The need to expand recycling capacity in places like the U.S. is becoming acute now that China—which has imported 45 percent of all plastic waste intended for recycling since 1992—has closed its doors, leaving many Western countries with nowhere but the landfill to ship their discarded plastic.

One key aspect of improving recycling, some experts say, is designing products so they are easier to recycle. Plastic is typically recycled by shredding it, melting it down and molding it into new plastics. But other chemicals added to improve product flexibility or durability, or to simply add color, make it difficult to recycle and reduce the quality of recycled plastics. “We’re taking some of what are potentially our most recyclable polymers and rendering them unrecyclable because of inadequate or inappropriate thought at the design stage,” says Richard Thompson, a marine biologist at the University of Plymouth. As an example of a potential remedy, he cites Japan, where all polyethylene terephthalate (PET), used in plastic bottles, is transparent. Clear PET is much easier to recycle than when coloring is added in. “It’s possible to do it,” he says.

RETHINKING PLASTIC AND RECYCLING

Curtailing the use of plastic and improving recycling and waste systems would put a

recyclable and some will still likely make their way into rivers, soil and seas. In the long term some scientists think changing the very nature of the material and the methods of recycling it could be the ultimate solution to the plastic problem. “We need a much more fundamental change in our appr

For years materials scientists have been trying to create plastics that will biodegrade. Today plastic that is labeled biodegradable can actually only be broken down in specialized facilities that heat it to high temperatures. “In an aquatic environment, in your backyard compost pile, that’s not going anywhere,” says Sherri Mason, a professor of chemistry at the State University of New York at Fredonia.

There is a fundamental tension to creating truly biodegradable plastic, because a polymer that will completely degrade into carbon, oxygen and other elements in a lake or soil would not be particularly useful as packaging, say for keeping food on a shelf for months. “There’s a central problem around what we want versus what’s realistic,” says Andrew Dove, a chemist at the University of Birmingham. Thompson thinks biodegradable plastic may need to be confined to products only needed for a short time that are then discarded, such as burger wrappers at sports stadiums or utensils at fast-food restaurants.

What Dove and a growing number of materials scientists envision to reshape our relationship with all plastics is to move from physically recycling plastics by grinding them up to chemically dismantling them to weed out all the impurities that taint recycled plastic. Such a method would take a PET bottle, for example, and break it down into its most basic molecules, separating out added chemicals to provide the building blocks to remake virgin polymers. In this way plastic would become its own perpetual

not just chemically broken down). “With some plastics, there’s no reason why you can’t infinitely recycle,” Dove says. “People just haven’t looked at it. It’s not been considered something that’s important.”

For the polymers that cannot be unraveled into their most basic molecules, Dove thinks it should be possible to at least chemically break them up into other small molecules that could be used for different purposes, such as fuel or pharmaceuticals. Ideally, scientists would devise chemical reactions that did not require too many harsh compounds and are not too expensive. That would give value to the plastic waste that currently has no, or very little, value. Currently, “it’s much cheaper to burn them or to throw them away in landfills, and that’s the core of the issue,” Wagner says.

Making discarded plastic valuable could also provide incentive for cleaning up the plastic waste already in the environment. “If we can create something high-value from cheap plastic waste, there might be an economic argument to go and dredge this out of the ocean,” Dove says. “We’re a long way from that, but that’s what we’d like to achieve.”

A few scientists have already begun to look at ways to clean up some of the microplastic waste, which could remain in the environment for at least several hundred years. Cleanup is difficult because the plastic particles are small and varied in nature, and the ecosystems in which they are embedded are vast. Researchers have found enzymes and bacteria that can break down certain types of plastic, but they need to figure out how these might be deployed without any potential negative side effects, such as producing greenhouse gases. Agroecologist Esperanza Huerta Lwanga, of Wageningen University in the Netherlands and the College of the Southern Frontier in Mexico, for example, hopes to test whether earthworms that possess plastic-munching bacteria in their guts might be able to remediate soil littered with plastic from the burning of trash.

While those methods are being developed, cutting off the flow of plastic is key. Doable steps need to be taken now. “The bottom line,” Thompson says, “really is that all of this [pollution] is avoidable.”

Part 1: Earth Has a Hidden Plastic Problem—Scientists Are Hunting It Down

Part 2: From Fish to Humans, a *May Be Taking a Toll*

ABOUT THE AUTHOR(S)

Andrea Thompson

, an associate editor at *Scientific American*, covers sustainability.

Credit: Nick Higgins

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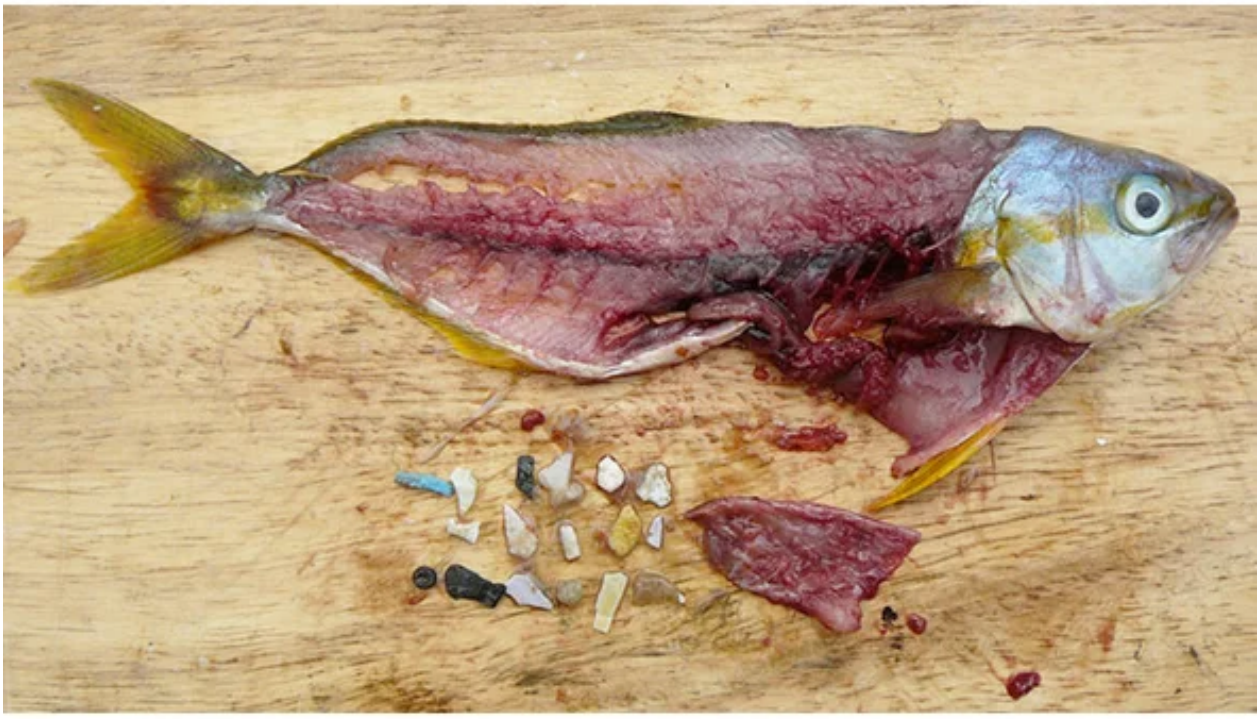
ENVIRONMENT

From Fish to Humans, A Microplastic Invasion May Be Taking a Toll

Tiny bits of plastic have seeped into soil, fish and air, posing a threat to animal and human health

By Andrea Thompson on September 4, 2018



A Rainbow Runner in the North Pacific Gyre that had ingested 18 pieces of plastic (2008). Credit: Dr. Marcus Eriksen *Gyres Institute*

This is the second of a three-part series that examines our growing understanding of the scope and impacts of microplastics pollution.

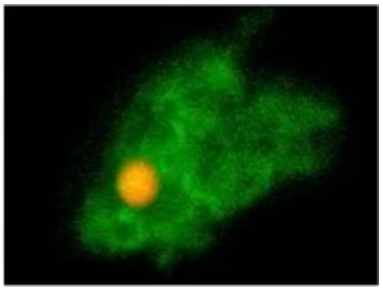
Mark Browne had a suspicion. He hoped the samples of dried blood taken from a blue mussel and placed under a special microscope would tell him if he was correct. As a fuzzy, three-dimensional image of the mussel's blood cells appeared, there they were, right in the middle—tiny specks of plastic.

Whereas photos of sea turtles eating plastic bags have become the poster child of the environmental harm wrought by humanity's plastic waste, research like Browne's illustrates the scope of the problem is far larger than the trash we can see. Tiny pieces of degraded plastic, synthetic fibers and plastic beads, collectively called microplastics, have turned up in every corner of the planet—from Florida beach sands to Arctic sea ice, from farm fields to urban air.

Their size—from about five millimeters, or the size of a grain of rice, down to microscopic—means they can be ingested by a wide range of creatures, from the plankton that form the basis of the marine food chain to humans. As Browne's 2008 study was one of the first to demonstrate, those plastic particles don't always pass harmlessly through the body. The finding "was one of those sort of bittersweet moments," the ecotoxicologist at the University of New South Wales in Sydney says. "You're pleased that some prediction you've made has come true—but then you're devastated" because of the potentially profound ecological implications.

Read more from this special report:

How Plastic Became a Plague



A particle of plastic in the blood cell of a blue mussel. Credit: Dr. Mark Anthony Browne

Ingested microplastic particles can physically damage organs and leach hazardous chemicals—from the hormone-disrupting bisphenol A (BPA) to pesticides—that can compromise immune function and stymie growth and reproduction. Both microplastics and these chemicals may accumulate up the food chain, potentially impacting whole ecosystems, including the health of soils in which we grow our food. Microplastics in the water we drink and the air we breathe can also hit humans directly.

Browne is one of dozens of scientists trying to sort out exactly what this widespread, motley assortment of microplastics pollution might be doing to animals and ecosystems. Tantalizing evidence is emerging, from the impaired reproduction of fish to altered soil microbe communities. As researchers accumulate more data, “we start realizing we’re just at the tip of the iceberg with the problem,” Browne says.

A THREAT TO ORGANS AND BLOODSTREAM

When Browne experimented with blue mussels back in 2008, many researchers thought animals would just excrete any microplastics they ate, like “unnatural fiber,” as Browne called it—but he wasn’t so sure. He tested the idea by placing mussels in water tanks spiked with fluorescent-tagged microplastic particles smaller than a human red blood cell, then moved them into clean water. For six weeks he harvested the shellfish to see if they had cleared the microplastics. “We actually ran out of mussels,” Browne says. The particles “were still in them at the end of those trials.”

The mere presence of microplastics in fish, earthworms and other species is unsettling, but the real harm is done if microplastics linger—especially if they move out of the gut and into the bloodstream and other organs. Scientists including Browne have observed

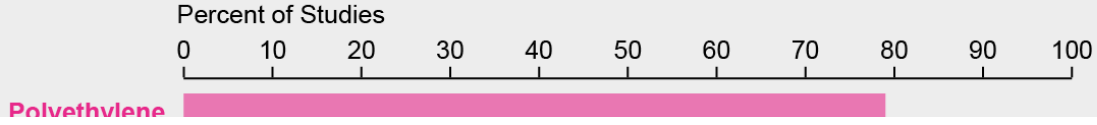
signs of physical damage, such as inflammation, caused by particles jabbing and rubbing against organ walls. Researchers have also found signs ingested microplastics can leach hazardous chemicals, both those added to polymers during production and environmental pollutants like pesticides that are attracted to the surface of plastic, leading to health effects such as liver damage. Marco Vighi, an ecotoxicologist at the IMDEA Water Institute in Spain, is one of several researchers running tests to see what types of pollutants different polymers pick up and whether they are released into the freshwater and terrestrial animals that eat them. The amount of microplastics in lakes and soils could rival the more than 15 trillion tons of particles thought to be floating in the ocean's surface alone.

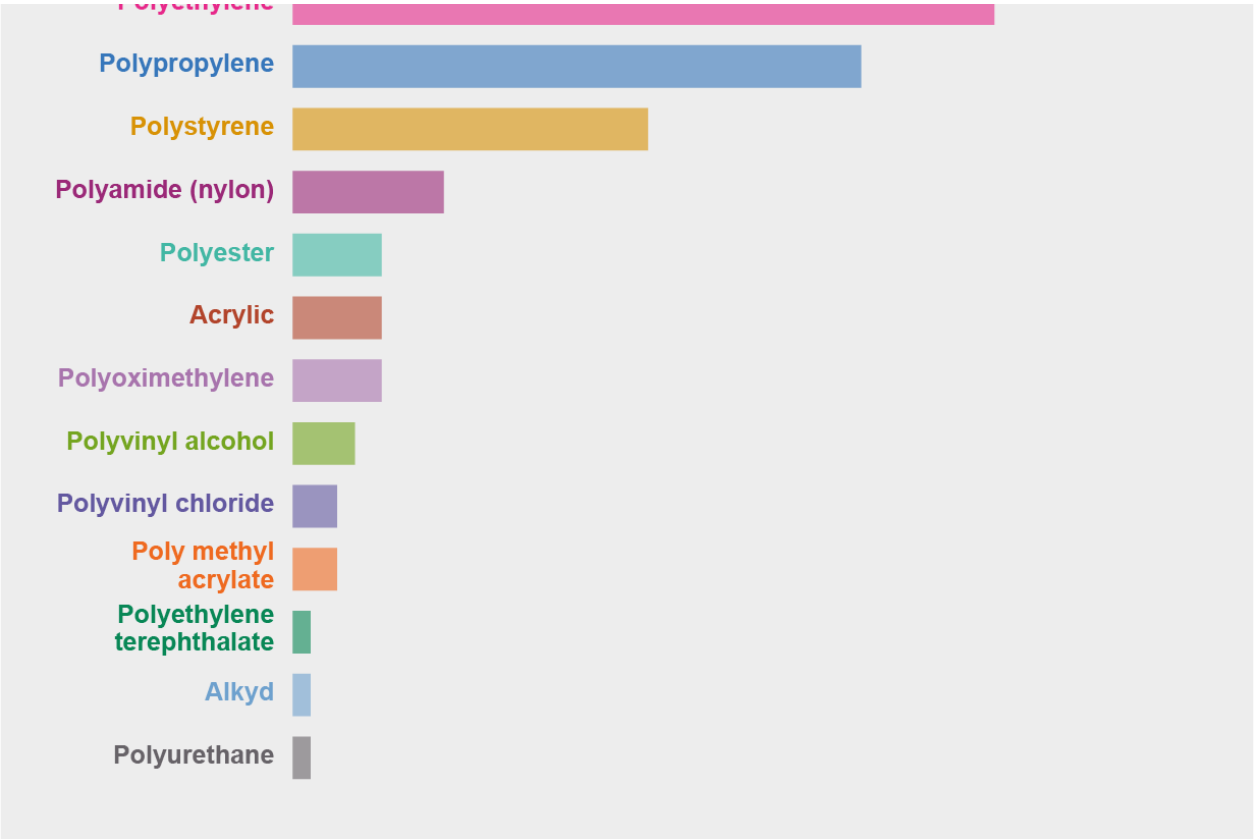
Plastics Permeate the Planet

Plastic polymers and the added chemicals that make them more durable and flexible have been used in thousands of combinations, found in everything from clothing to electronics to paint. One of the biggest categories is single-use packaging, such as plastic grocery bags and soft drink bottles. This prevalence is reflected in the polymers that show up most commonly in the microplastic debris found in the environment.

Common Polymers and Ways They Are Used

How Often Polymers Are Found in Marine Microplastic Debris





Credit: Amanda Montañez; Source: "Sources, Fate and Effects of Microplastics in the Marine Environment: A Global Assessment," edited by Peter J. Kershaw, (IMO/FAO/UNESCO-IOC/UNIDO/WMO/IAEA/UN/UNEP/UNDP Joint Group of Experts on the Scientific Aspects of Marine Environmental Protection), GESAMP Reports and Studies, No. 90; 2015

What matters most is whether these physical and chemical impacts ultimately affect an organism's growth, reproduction or susceptibility to illness. In a surprising study published in March, not only did fish exposed to microplastics reproduce less but their offspring, who weren't directly exposed to plastic particles, also had fewer young, suggesting the effects can linger into subsequent generations. Some organisms such as freshwater crustaceans called amphipods haven't yet exhibited any ill effects, perhaps because they can handle natural indigestible material like bits of rock, says Martin Wagner, an ecotoxicologist at Norwegian University of Science and Technology, who studied them. And some species have shown toxic effects from microplastics exposure from certain types of plastic, but not others, says Chelsea Rochman, a microplastics researcher at the University of Toronto.

Most work on microplastic impacts has been done in the lab for short stints, with only a single type of plastic, often with larger particles than some species tend to eat, and at higher concentrations than are found in the environment. The studies "won't tell us about long-term ecological consequences happening at low concentrations," Wagner

says. He is one of several researchers starting to bridge that gap by matching animals to the polymers and pollutants they are most likely to encounter and incorporating the intricacies of the real world where microplastics "won't be the only stressor," Wagner says. Microplastics could be a last straw for species subject to pressures as chemical pollutants, overfishing and climate change. "It's just damn complicated," Wagner says.

INVITING CHAOS

Messy, real-world conditions are the goal on the green lawn of a botanical garden in Frankfurt, Germany. A row of small, identical ponds stretch across the grass, exposed to the elements. Wagner spiked each one with different microplastic particles—some virgin polymers, some contaminated with pollutants—to see how freshwater insects and zooplankton fare. Although Wagner hasn't yet observed any overt impacts, he is investigating whether certain organisms exhibit more subtle signs of harm, which could have a ripple effect throughout an ecosystem's food web.

Such cascading impacts could happen even when individual species don't seem to suffer. Browne's mussels showed no short-term ill effects but he worries their accumulated microplastics could be transferred to animals that eat them. "They might not be so kind to the other organisms," he says.

Mesocosm pools at Goethe University in Frankfurt am Main, Germany, where Martin Wagner and his colleagues study the impacts of microplastics on different animals in semirealistic conditions. Credit: Martin Wagner

Like Wagner, Browne is venturing farther out into the real world. He has several freezers' worth of fish and other organisms plucked from Sydney Harbor that he will examine for ingested microplastics. His team will be linking those to the routes by which microplastics might be entering the harbor and looking for signs of ecological damage such as changes in population size. The approach means animals can behave normally and are exposed to typical environmental conditions such tides and storms, as well as a host of other stressors such as changing ocean temperatures and industrial pollutants. "We want a chaotic system because if something can cause an impact in that chaotic system, above those other stresses, we know that we really, really need to be worried about it," Browne says.

Matthias Rillig, a plant ecologist at Free University of Berlin, has shown how microplastics can affect organisms by altering their environments. In a recent study he co-authored, soil laden with polyester microfibers was much fluffier, retained more moisture and seemed to affect the activity of microbes that are crucial to the soil nutrient cycle. The finding is an early but concerning one, given that farmers around the world apply microfiber-rich treated sewage sludge as fertilizer to agricultural land. Rillig is also one of several scientists looking to see how microfibers in soils might be affecting crop growth.

FULL CIRCLE

Microplastics may threaten people more directly. A study published in April found particles and microfibers in packaged sea salt, beer, bottled water and tap water, making it virtually certain we are ingesting microplastics. In bottled beverages microplastics could be infiltrating during the bottling process; microfibers could be falling from the atmosphere into the reservoirs that supply tap water. Even for researchers steeped in the field, “it still comes as a shock,” Rochman says. “It just shows that the mismanagement of our waste is coming back to us.”

Because it is unethical to intentionally feed doses of microplastic particles to humans, some researchers, like Browne, have turned to medical studies that use particles to deliver precise amounts of drugs to specific areas of the body to get a better sense of how easily microplastics might move through humans. If particles are small enough, they might migrate through the body and potentially accumulate in places like the bloodstream. A study of hamsters injected with microplastics suggests such particles can lead to blood clots.

A close-up of one of the mesocosm pools, where insects and other species under study live among the plants and sediment they would in the real world to get a better understanding of how microplastics might affect them in their natural habitat. Credit: Martin Wagner

Humans could also be inhaling microfibers as they fall from the sky—everywhere from the heart of Paris to the remote Arctic. Small airborne particles are known to lodge deep in the lungs where they can cause various diseases, including cancer. Factory workers who handle nylon and polyester have shown evidence of lung irritation and reduced capacity (although not cancer), but they are exposed to much higher levels than the average person. Stephanie Wright, a research associate at King's College London, is trying to better understand how much microfiber humans are actually exposed to and whether airborne microplastics might penetrate the lungs. She is also teaming up with the university's toxicology unit to examine their lung tissue collection for signs of microfibers and related damage.

Some scientists say the focus on microplastics in humans might be missing a larger point: People are continually exposed to plastic food and beverage containers, which

could be a much bigger source of at least the chemicals added to plastics such as the endocrine disruptor BPA. The potential exposure to microplastics hasn't stopped Rochman from eating seafood, however. "To the best of my knowledge the benefits outweigh the costs," she says. It could be that, as with many pollutants, there is a threshold beyond which microplastics become toxic to humans or other species. "We just need to try to understand what that threshold is," she notes.

Experts say the sheer ubiquity of the contaminant combined with the harm that has already been observed is enough for humanity to start to clean up its act. "There are always questions to be answered," Rochman says, but we have reached the point where "it's enough information to act toward solutions."

Part 3: Solving Microplastic Pollution Means Reducing, Recycling—And Fundamental Rethinking

ABOUT THE AUTHOR(S)

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Review

A Detailed Review Study on Potential Effects of Microplastics and Additives of Concern on Human Health

Claudia Campanale *, Carmine Massarelli, Ilaria Savino, Vito Locaputo and Vito Felice Uricchio

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Abstract: The distribution and abundance of microplastics into the world are so extensive that many scientists use them as key indicators of the recent and contemporary period defining a new historical epoch: The Plasticene. However, the implications of microplastics are not yet thoroughly understood. There is considerable complexity involved to understand their impact due to different physical–chemical properties that make microplastics multifaceted stressors. If, on the one hand, microplastics carry toxic chemicals in the ecosystems, thus serving as vectors of transport, they are themselves, on the other hand, a cocktail of hazardous chemicals that are added voluntarily during their production as additives to increase polymer properties and prolong their life. To date, there is a considerable lack of knowledge on the major additives of concern that are used in the plastic industry, on their fate once microplastics dispose into the environment, and on their consequent effects on human health when associated with micro and nanoplastics. The present study emphasizes the most toxic and dangerous chemical substances that are contained in all plastic products to describe the effects and implications of these hazardous chemicals on human health, providing a detailed overview of studies that have investigated their abundance on microplastics. In the present work, we conducted a capillary review of the literature on micro and nanoplastic exposure pathways and their potential risk to human health to summarize current knowledge with the intention of better focus future research in this area and fill knowledge gaps.

Keywords: microplastics; additives; human health; nanoplastics

1. The Plasticene

In the last 70 years, we have abetted an increasing growth in the worldwide plastics production, which has consequently spread into the environment to such a point that we can say to live in a plastic world [1,2]. These synthetic polymers are environmental pollutants themselves and act as vectors of transport of various kind of chemicals [3], but they are also considered valid indicators of the recent and contemporary period, generally after the middle of the 20th century [4].

Nowadays, microplastic particles have been ubiquitously detected in a broad range of shapes, polymers, sizes and concentrations in the environments of marine water, freshwater [5], agroecosystems [6], atmosphere [7], food [8] and drinking-water [9], biota [10], and other remote locations [11].

They can be as thin as small veils and be carried away by the wind from miles away, or they can be hard and compact like rocks [12].

Their worldwide distribution is so vast that many scientists use it as a key geological indicator of the Anthropocene [4].

Plastic materials can be used as stratigraphic markers in the archaeological field by considering them as recent and precise indicators of earth deposits.

Some authors identify the period from 1945 onwards as a moment of a significant increase in plastics deposition, to the point that they have used this stratigraphic marker as an excellent indicator [13].

Figure 1 shows a famous picture taken by Spanish students during a university trip. In the photo, the flood level river in the canyon bed is well-recorded thanks to the deposition of plastic micro-fragments that by now have been well-mixed with the sedimentary curly making up the canyon.

We found a similar situation in Southern Italy; indeed, in Figures 2 and 3, it is possible to observe that plastics were even used to fill the road surface, probably to obtain a double advantage: no disposal costs for materials and no costs for the use of suitable materials (excavated rocks).

Figure 1. Appearance of the deposition and stratification of plastic materials in a Spanish canyon (Source: [16]).

Figure 2. Layering of plastic materials in an area of Southern Italy.

Figure 3. Detail of the plastic stratigraphy.

According to the layers, once accumulated and stratified, the sediment, which consists of fragments of various plastic sizes, can have a good conservation potential that is comparable to that one of recalcitrant organic fossils. Such synthetic fossil-based materials are so abundant and widespread on Earth that we can consider them "technofossils" as they will constitute a perennial proof of the existence of humans on Earth [4] to the point of being able to define this historical epoch as the Plasticene [14,15].

2. Plastics and Co-Contaminants

Microplastics (MPs) are defined by [17] as "synthetic solid particles or polymeric matrices, with regular or irregular shape and with size ranging from 1 μm to 5 mm, of either primary or secondary manufacturing origin, which are insoluble in water.".

A key concern of microplastics pollution is whether they represent a risk to ecosystems and human health. However, there is much uncertainty associated with this issue. Data on the exposure and effect levels of microplastics are therefore required to evaluate the risk of microplastics to environments and human health. The adverse effects on organisms that are exposed to microplastics can be separated into two categories: physical effects and chemical effects. The former is related to the particle size, shape, and concentration of microplastics, and the latter is related to hazardous chemicals that are associated with microplastics. Though data on microplastic exposure levels in environments and organisms have rapidly increased in recent decades, limited information is available on the chemicals that are associated with microplastics.

Microplastics can contain two types of chemicals: (i) additives and polymeric raw materials (e.g., monomers or oligomers) originating from the plastics, and (ii) chemicals absorbed from the surrounding ambience.

Additives are chemicals intentionally added during plastic production to give plastic qualities like color and transparency and to enhance the performance of plastic products to improve both the resistance to degradation by ozone, temperature, light radiation, mold, bacteria and humidity, and mechanical, thermal and electrical resistance [18].

They include inert or reinforcing fillers, plasticizers, antioxidants, UV stabilizers, lubricants, dyes and flame-retardants [18].

Among the charges, wood and rock flour, clay, kaolin, graphite, glass fibers, cotton flakes, jute or linen, cellulose pulp, etc. are used [18]. According to the definitions proposed by the American Society for Testing and Materials (ASTM-D-883), inert fillers are materials that are used to modify the strength, working and flow properties, and shrinkage of plastics, while the reinforcing ones, also called fillers, are defined as those with some strength properties that are significantly superior to those of the base resin [19]. These fillers (such as carbon black in rubber), which are mixed in with the polymer, result in an interface volume that is generated at the filler-resin contact surface. It is the superior properties of this interface layer that obtain increased modulus and mechanical properties such as impact strength or tensile strength in the composite polymer. As the effect is surface-related, the smaller particle sizes of fillers generally yield a better reinforcing effect. There are clays, silica, glass, chalk, talc, asbestos, alumina, rutile, carbon black, and carbon nanotubes [20].

Plasticizers are complex chemical products that have low vapor pressure, are insoluble in liquids, are chemically stable, and which are inserted between molecular chains to reduce their forces of physical attraction and increase their mobility, workability or distensibility. In this way, the flexibility and plasticity of a resin that is processed and the impact resistance of the product during use are increased [21].

Because plastics are particularly sensitive to the degrading action of light, UV radiation and heat, the stabilizers, have the function of preventing the thermal decomposition during the processing, as well as the oxidation and the consequent breaking of the polymeric chains (using phenols and aromatic amines). They mainly consist of organic or inorganic cadmium, barium, or lead salts [22].

Soluble or insoluble dyes are organic or inorganic substances in the form of fine powders that give the polymer the desired color; the soluble dyes maintain the transparency of the plastic, while the insoluble ones (pigments) cover it to make it opaque. Many inorganic pigments contain heavy metals, while organic pigments include various chromophoric families like azo pigments, phthalocyanine pigments, anthraquinone chromophores, and various other chromophores [23].

Lubricants and anti-adhesives are substances that facilitate the processing of plastic materials, improving their flow characteristics. They consist of calcium or magnesium stearates [24].

Flame retardants have the function of cooling or protecting a material in the event of a fire by preventing the oxidation of flammable gases or by forming a layer of ash. They are products that contain, for example, chlorine and bromine, which release by the action of the flame; phosphorus, which favours the transformation into coal; and aluminium hydroxide, which generates water vapour and CO_2 at 200 °C [24].

The additives, in almost all cases, are not chemically bound to the plastic polymer; only some flame retardants are polymerized with plastic molecules, becoming part of the polymeric chain [18].

Though these additives improve the properties of polymeric products, many of them are toxic, and their potential for the contamination of soil, air and water is high [18]. Studies on their impact on aquatic organisms with which they come into contact through macro and microplastics ingestion are still ongoing [25,26].

The combination of various kind of polymers of different sizes and shapes that are joined to the action of a large amount of additives that originate from plastics results in a cocktail of contaminants that not only alter the nature of plastic but can leach into the air, water, food, and, potentially, human body tissue during their use or their disposal, thus exposing us to several chemicals together.

2.1. Additives of Concern

Many substances that are classified as hazardous according to the EU regulation on classification and labelling [27] are present in everyday products as regular ingredients.

The toxicity of a substance is its ability to cause harmful effects. These effects can strike a single cell, a group of cells, an organ system, or the entire body. Chemicals that are considered most harmful are those that cause cancer, mutations to DNA, have toxic reproductive effects, are recalcitrant into the environment, are capable of building up in the food chain or bodies, and other harmful properties, such as disrupting hormones [28,29]. The internal organs that are most commonly affected are the liver, the kidneys, the heart, the nervous system (including the brain) and the reproductive system [29,30].

Among these chemicals, many routinely used to make plastics are dangerous. Bisphenol A (BPA), phthalates, as well as some of the brominated flame retardants, that are used to make household products and food packaging, have been proven to be endocrine disruptors that can damage human health if ingested or inhaled [30].

Endocrine-disrupting chemicals (EDCs), identified as substances that are exogenous to the human or animal organism, have hormonal activity that alters the homeostasis of the endocrine system, so they are of particular concern. These compounds interfere with the development of the endocrine system and affect the functioning of organs that respond to hormonal signals. The endocrinal and reproductive effects of endocrine disruptors may be a consequence of their ability to: (a) mimic natural hormones, (b) antagonize their action, (c) alter their pattern of synthesis and metabolism, or (d) modify the expressions of specific receptors [31–33].

Recent science has associated EDCs with various diseases and conditions, such as hormonal cancers (breast, prostate, testes), reproductive problems (genital malformations, infertility), metabolic disorders (diabetes, obesity), asthma, and neurodevelopmental conditions (learning disorders, autism spectrum disorders). Alongside the already shown scientific evidence, concern exists because of the rising levels of many diseases in Europe and worldwide. Additionally, the public is widely exposed to these chemicals from various sources [30].

2.1.1. BPA

BPA is a carbon-based synthetic compound with formula $C_{15}H_{16}O_2$ and a structure that contains two 4-hydroxyphenyl groups, which give to it a mild phenolic odor. It was first synthesized in the 1890s by the condensation of acetone with two equivalents of phenol [33].

BPA is a common plasticizer that is used in industry, especially in polycarbonate plastics manufacturing processes and food packaging [34,35].

BPA-based polycarbonate plastics are robust and stable because they can endure exposure to high temperatures and sustain high-impact collisions. These characteristics make them valuable as components of safety equipment and food packaging as they withstand heating in microwave ovens. Because it is a component of epoxy resins in protective coatings, such as the insides of aluminum and metal cans (as well as the lid closures of glass jars and bottles), BPA helps to extend the shelf life of food and beverage products [35,36]. Even if the compound is highly persistent, its instability within plastic products facilitates leaching, thus reporting a high prevalence in aquatic environments, particularly in landfill leachates [37,38].

In the early 1930s, Dodds and Lawson discovered that BPA was estrogenic [39], and, recently, the General Court of the EU confirmed that it is a 'substance of serious concern' for its hormonal disrupting properties on the human body. The Court upheld a previous decision by the European Chemicals Agency (ECHA) to identify the substances that are used in the manufacture of plastic products such as water bottles, food containers and receipts. It has been confirmed in several studies to be associated with obesity, cardiovascular disease, reproductive disorder, and breast cancer [30,40–42], and so it has gained increasing attention over the last decade, especially in terms of human safety. The contamination of food from BPA has been estimated to be responsible for 12,404 cases of childhood obesity and 33,863 cases of newly incident coronary heart disease in 2008. Another study estimated that BPA in

food contact materials and thermal paper was likely responsible for 42,400 obese four-year-olds in Europe (with health costs of 1.54 billion euros per year) [30]. It is still under discussion if microplastics are relevant pollutant vectors for uptake into organisms in comparison to further uptake pathways, e.g., via water or sediment particles, even if studies regarding the level of bisphenol A adhered on microplastics surface are very limited.

The first study that investigated the presence of BPA on microplastics sampled from the remote, open ocean and urban beaches from America and Europe, reported concentrations ranging from 1 to 729.9 ng/g [42]. In most locations, including urban coasts, only trace concentrations (<1 ng/g) of BPA were detected. Due to its lower hydrophobicity (log n-Octanol/Water Partition Coefficient (Kow) = 3.40), the sorption of significant concentrations of BPA to marine plastics is unlikely. Indeed, in plastic fragments from remote coasts (730 ng/g) and open ocean fragments (283 ng/g), sporadic high concentrations of BPA were detected. Its utilization explains these higher BPA concentrations because it is a component of the plastic products and an additive. Indeed, BPA is a constituent monomer of polycarbonate plastic and epoxy resin and unreacted monomers in the plastics and resin and, degradation products from the polymers, can leach to the environment. Moreover, BPA is also used as additive to some plastics, and the leaching of BPA from commercial plastic products and dumped plastics can occur [42].

In the study of [43], the authors analyzed how the presence of non-suspended microplastics (polyamide particles (PA), which aggregated at the water surface or settled) modifies the acute effects of the environmental pollutant BPA on freshwater zooplankton (*Daphnia magna*). Daphnids are exposed to PA particles and BPA alone in a first step, and they are combined in a second step with a fixed concentration of PA and varying concentrations of BPA. All BPA concentrations used in the experiment greatly exceeded concentrations of the BPA that has been detected in rivers and lakes. The concentration of the PA particles used was also above the expected values in freshwater environments. There were two possible uptake pathways for BPA included in the experiments: direct uptake by BPA that was dissolved in water and vector-based uptake by the ingestion of PA particles that were loaded with BPA. The immobilization of daphnids was analyzed as an experimental endpoint to directly determine the influence of microplastics on pollutant toxicity. The results showed grazing by daphnids on settled PA particles from the bottom of the test beakers with high uptake rates that ensured the availability of PA particles, which could then potentially act as vectors for BPA. The analytical measurements showed that PA particles alone did not induce adverse effects, while the effects of BPA alone followed a typical dose-dependent manner. The sorption of BPA to PA particles before exposure led to a reduction of BPA in the aqueous phase. The combination of BPA and PA led to decreased immobilization, although the daphnids ingested PA particles that were loaded with BPA. These results showed the lower BPA body burden of daphnids in the presence of PA particles.

Another study [44] evaluated the retention of polyvinyl chloride (PVC) microplastics in sewage sludge during wastewater treatment. A model-based analysis indicated that PVC microplastics influenced the methane production from the anaerobic digestion of waste-activated sludge (WAS).

The presence of PVC microplastics (1-mm 20, 40, and 60 particles/g) inhibited methane production from WAS during anaerobic digestion to 90.6 ± 0.3%, 80.5 ± 0.1%, and 75.8 ± 0.2% of the control, respectively. Bisphenol A (BPA) leaching from PVC microplastics was the primary reason for the decreased methane production, causing significant (p = 0.037, 0.01, and 0.004) inhibitory effects on the hydrolysis–acidification process. The results of relevant enzyme activities also confirmed this.

2.1.2. Phthalates

Phthalates are esters of phthalic acid (1,2-benzene dicarboxylic acid) on which there are two carbon chains of different lengths. Phthalates are a class of compounds that are produced in high quantities; they are the largest class of synthetic chemicals when considering production volume [45]. The authors of [46] reported that approximately 6,000,000 t/year phthalates are produced throughout the world. This production has remained quite constant for the past 20 years.

Their primary use is as plasticizers that are added to basic plastic material to impart specific qualities such as flexibility, pliability, and elasticity to plastic polymers [47].

They are colorless, odorless, oily liquids with low volatility and low water solubility [48]. Some phthalates have proven to be of concern due to their adverse effects to humans and ecosystems. Indeed, many phthalates are documented endocrine disruptors, and they are suspected of being endocrine disruptors, of affecting the reproduction of human beings, animals, or o being carcinogenic [49–51].

The problem is enhanced by the fact that several phthalates have similar modes of action, and that the overall risk, therefore, could increase when people and the environment are exposed to the different phthalates. Therefore, it is necessary to take the possible combination effects as a result of exposure to other phthalates and other substances into account [52]. There are many different types of phthalates, and there are indications that these do not have the same effects on the environment and human health.

Since 2007, there has been a ban in the EU on di(2-Ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP) and butyl-benzyl-phthalate (BBP) in all toys and childcare articles in concentrations above 0.1% (entry 51 of Annex XVII of the Regulation of the European Union (REACH) [53], as well as bans on diisononyl phthalate (DINP), diisodecyl phthalate (DIDP) and di-n-octyl phthalate (DNOP) in toys and childcare articles that can be placed in the mouth in concentrations above 0.1% [52,53]. DEHP is classified as reprotoxic category two and as T (toxic), while DBP is well-documented as having toxic effects on reproduction, as well as prenatal and postnatal development, in animals, and it is classified as reprotoxic category 3, as T (toxic), and as N (dangerous for the environment) [54]. DBP and diethyl phthalate (DEP) are the most widely used phthalates in medicinal products, even if toxicological effects have been observed in animals; as it cannot be ruled out that these findings have clinical relevance, the European Medicines Agency (EMA) is in the process of preparing limits for the use of DBP in medicines. Furthermore, the agency will probably also establish limits for the use of DEP and polyvinyl acetate phthalate (PVAP) in medicines [52].

Because of the potential risk of DEHP and DBP [55–58] and the potential hazard of the other phthalates, this group is considered as a hazard category [59].

With the publication of the new regulation [60] (EU) No. 2018/2005, which modifies Annex XVII of the REACH, the European Commission reinforces the limitations that are related to the presence of some phthalates in consumer products.

Limits on the presence of some phthalates were already present in the European legislation for the protection of consumers, but they were limited to "childcare articles," that is "intended to reconcile the sleep or relaxation of children, their hygiene and their nutrients chin or sucking; " these include teats, pacifiers, baby bottles, food containers and cutlery for children, and teethers for babies.

The new regulation extends the limitation to the following four phthalates (DEHP, DBP, BBP, and diisobutyl phthalate (DIBP)) also to other product and user groups. In particular, these four phthalates cannot be present in an amount higher than 0.1% of the plastic material (the limit applies to the sum, not only to the single phthalates) or in any article realized (in whole or in part) in a plasticized material—that is, in one or more of the following six materials:

- polyvinyl chloride (PVC),
- polyvinylidene chloride (PVDC),
- polyvinyl acetate (PVA),
- polyurethanes
- any other polymer (including polymeric foams and rubber) except silicone rubber and natural latex coatings;
- surface coatings, non-slip coatings, finishing products, decals, prints;
- adhesives, sealants, inks and paints.

The limitations provided by the regulation will come into force from 7 July 2020, but with some exceptions, as specified in Annex I of the regulation.

The consultation of the European Union rapid alert system for product safety (RAPEX) showed that in 14 years (from 2005 to 2018), 1591 cases of harmful phthalates were reported in various products (of which about the 89% of Chinese origin), mostly toys 94% [61]. In 2018 alone, there were 206 reported cases of toys that contained harmful phthalates [62].

If we then consider the cases that were related to food containers (detected by the Rapid Alert System for Food and Feed (RASFF), which is similar to RAPEX but reserved for the food sector), we find that from 2007 to 2018, there were as many as 108 cases of phthalate-contamination in food containers, an issue which came with the risk of ingestion through food products [63].

A study conducted in 2011 in Harbin and Shanghai (China) [64] analyzed the presence of nine phthalate esters in eight categories of foodstuffs. DEHP was the primary compound that was found in most of the food samples, with concentrations that ranged from below the limit of quantification (LOQ) to 762 ng/g wet weight.

Among the more frequently mentioned endocrine disruptors (EDCs), phthalates are of particular concern due to their ubiquity and to the higher levels found in the environment compared to other EDCs [65–68]. The detection of phthalates in purely domestic wastewater (the waste of plastic households) has also highlighted the leaching of phthalates from plastic during use into the environment [67–69].

Due to the high octanol–water partition coefficients, the strong sorption of phthalate esters (PAEs) by soil and sediment organic matters, biochar, and other carbonaceous sorbents has been reported [70,71]. However, the sorption behavior of PAEs on microplastics has not been studied systematically. Considering the hydrophobic surface of microplastics, they may have high sorption capacity for PAEs, which may pose a high environmental threat [72].

Recently, the authors of [73] investigated the sorption behavior of two PAEs, diethyl phthalate (DEP) and dibutyl phthalate (DBP), on three types of microplastics with particle sizes of less than 75 µm (PVC: polyvinyl chloride; PE: polyethene; and PS: polystyrene), and they demonstrated that hydrophobic interaction governed the partition mechanism. The sorption of the two PAEs on the three microplastics followed the order of PS > PE > PVC. For each kind of microplastics, the sorption of DBP was almost 100 times higher than that of DEP, demonstrating that the hydrophobic interaction dominated the partition. The results indicated too that the physical properties of microplastics did not play an essential role in their sorption behaviors. Moreover, on the one hand, solution pH (in the range of 2.0–7.0) and natural organic matter had no significant impact on the PAEs' sorption by microplastics, thus indicating that microplastics could accumulate hazardous PAEs in different aquatic environments. On the other hand, the presence of NaCl (0–600 mM) and CaCl2 (0–300 mM) enhanced the sorption of both DEP and DBP on microplastics because of the salting-out effect.

The authors of [74] investigated organophosphorus esters (OPEs) and phthalic acid esters (PAEs) in beached microplastics that were collected from 28 coastal beaches of the Bohai and the Yellow Sea in north China. The analyzed microplastics included polyethene (PE) pellets and fragments, polypropylene (PP) flakes and fragments, and polystyrene (PS) foams. Tris-(2-chloroethyl)-phosphate (TCEP), tris (1-chloro-2-propyl) phosphate (TCPP), and di-(2-ethylhexyl) phthalate (DEHP) were the three most predominant compounds found. The maximum Σ4 OPEs concentration found was 84,595.9 ng/g^{-1}, almost three orders of magnitude higher than the maximum Σ9 PAEs concentration observed. The PP flakes and PS foams contained the highest concentrations of the additives in contrast to the PE pellets, which contained the lowest concentrations. Moreover, the authors found that the spatial differences and compositional variation of the additives among the different microplastics suggested different origins and residence times in the coastal environment. These differences indicated that the characteristics of chemical additives might be a useful approach when tracing sources of microplastics in the environment.

2.1.3. Heavy Metals

Heavy metals are natural elements that have a relatively high atomic mass and a rather high density compared to water. Commonly, a density of at least 5 g/cm^{-3} defines a heavy metal and differentiates it from other "light" metals. Other, broader definitions for "heavy metals" require an atomic mass higher than 23 or an atomic number exceeding 20 [75–77]. However, these definitions are confusing and misleading due to the fact that they cause the inclusion of non-metals.

Therefore, some authors [78] have suggested that is better define "heavy metals" when referring to (1) transition elements; (2) rare earth elements, which can be subdivided into the lanthanides and the actinides, including La and Ac themselves; and (3) a heterogeneous group including the metal Bi, the elements that form amphoteric oxides (Al, Ga, In, Tl, Sn, Pb, Sb and Po), and the metalloids Ge, As and Te.

Even though heavy metals are naturally present in our environment (e.g., in the atmosphere, lithosphere, hydrosphere, and biosphere), their environmental contamination and their exposure to humans have mainly originated from various anthropogenic activities [77].

One of their primary uses is as additives in polymer products (e.g., colorants, flame-retardants, fillers, and stabilizers) (Table 1) during the production process to increase the properties of plastics.

Antimony oxide, aluminum oxide, and zinc borate are, for example, well-known flame retardants, as well as compounds that contain Cl and Br [18].

Metals such as Zn, Pb, Cr, Co, Cd and Ti are instead used as inorganic pigment-based colorants [22,79]; among these, colorants that contain cadmium and lead are used for all kinds of colored polymers, lending a coloration that goes from yellow to red. Chromium is mostly used for polymers such as PVC, polyethene and polypropylene, whereas cobalt acetate is used in blue paints, particularly in the production of bottles that are made of polyethene terephthalate.

Additionally, the presence of Ti in plastic products works as a TiO_2 indicator that is used both as a white pigment and as a UV stabilizer [80–82].

As part of the additives category, the stabilizers are generally used to prevent plastic degradation due to high temperatures, UV radiation, oxygen, and other kinds of atmospheric agents in order to lengthen product life. Among them, we again find compounds based on lead and cadmium, antimony trioxide and compounds based on Sn, which are mostly used in the making of doors and windows made of polyvinyl chloride.

Finally, although synthetic polymers are usually resistant to microbial attacks, some microorganisms can use some additives as sources of energy in the presence of water. This phenomenon can be prevented by adding, during the production of the polymer, biocides such as As, Sb and Sn [22].

According to the United States Environmental Protection Agency (USEPA) and the International Agency for Research on Cancer (IARC), arsenic, cadmium, chromium, lead and mercury are classified as "known" or "probable" human carcinogens based on evidences of epidemiological and experimental studies that have shown a correlation between exposure to those elements and cancer incidence on humans and animals [83].

Their toxicity depends on many different factors like dosage, how the subject is exposed to the element, and chemical species, as well as age, sex, genetics and the nutritional state of the exposed subject. A high concentration of heavy metals causes cellular and tissue damage, leading to a variety of adverse effects and human diseases [84–89]. Among metals, Al, Sb, As, Ba, Cd, Cr (II), Co, Cu, Pb, Hg, Ni, Se, Sn and V are defined metal–estrogens showing high affinity to estrogen receptors because they can mimic estrogen activation; for this reason, they are considered harmful and potentially linked with breast cancer [89–91].

Table 1. Main use of heavy metals as additives in polymer products and their effects on human health.

Heavy Metals	Additives	Type of Polymers	Effects on Human Health	References
Antimony (Sb)	Flame retardants and biocides	Various plastics	Metal–estrogen; breast cancer	[18,22,90]
Aluminum (Al)	Stabilizers, inorganic pigments and flame retardants.	PBT, PET, PE, PVC	Metal–estrogen; breast cancer	[18,22,90]
Zinc (Zn)	Heat stabilizers, flame retardants, anti-slip agents and inorganic pigments.	PVC, PE, PP	-	[18,22]
Bromine (Br)	Flame retardants	PBT, PE, PS, PP	Apoptosis and genotoxicity	[18,88]
Cadmium (Cd)	Heat stabilizers, UV stabilizers and inorganic pigments	PVC	Changes in metabolism of calcium, phosphorus and bone; osteomalacia and bone fractures in postmenopausal women; lipid peroxidation and in the promotion of carcinogenesis; cellular apoptosis; DNA methylation.	[18,22,77,79,92,93]
Copper (Cu)	Biocides	-	Formation of reactive oxygen species (ROS); inducing DNA strand breaks and oxidation.	[18,22,77]
Mercury (Hg)	Biocides	PU	Mutagen or carcinogen; induction of the disruption of DNA molecular structure and brain damage.	[11,22,77,95]
Arsenic (As)	Biocides	PVC, LDPE and polyesters	Congenital disabilities; Carcinogen: lung, skin, liver, bladder, kidneys; gastrointestinal damage; death.	[18,22,93]
Tin (Sn)	UV stabilizers and biocides	PU foam and PVC	Metal–estrogen; breast cancer; skin rashes; stomach complaints; nausea; vomiting, diarrhea; abdominal pain; headache and palpitations; potential clastogen.	[18,22,87,90]
Lead (Pb)	Heat stabilizers, UV stabilizers and inorganic pigments	PVC and all types of plastics, where red pigments are used	Anemia (less Hb); hypertension; miscarriages; disruption of nervous Systems; brain damage; infertility; oxidative stress and cell damage.	[18,22,77,79,90,93]
Titanium (Ti)	UV stabilizers and inorganic pigments	PVC	Cytotoxicity on human epithelial lung and colon cells.	[18,80,94]
Cobalt (Co)	Inorganic pigments	PET bottles	Formation of reactive oxygen species (ROS); neurological (e.g., hearing and visual impairment); cardiovascular and endocrine deficits.	[22,77,86]
Chrome (Cr)	Inorganic pigments	PVC, PE, PP	Allergic reactions to the body; nasal septum ulcer; severe cardiovascular, respiratory, hematological, gastrointestinal, renal, hepatic, and neurological effects and possibly death.	[77,79]
Barium (Ba)	Inorganic pigments and UV stabilizers	PVC	Metal–estrogen, breast cancer; cardiovascular and kidney diseases; metabolic, neurological, and mental disorders	[18,22,85,90]
Manganese (Mn)	Inorganic pigments	-	Neurodegenerative disorder	[18,84]

Cadmium has been suggested to take part in the promotion of cellular apoptosis and DNA methylation, in providing oxidative stress, in causing damage to DNA, in increasing bone fractures in postmenopausal women, and in lipid peroxidation [77,92,93].

Titanium oxide, for example, which is used as an additive in many plastics products, has been shown to generate cytotoxicity on human epithelial lung and colon cells [94]. Lead is responsible for a variety of consequences on human health such as affecting the DNA reparation system, producing ROS (reactive oxygen species), modifying the genes that are responsible for the cellular tumor regulation, and various effects on the central nervous system, including the damage of motor and cognitive functions, convulsions, coma, and death. Arsenic contamination could cause cancer to the urinary bladder, lungs, liver and kidneys. As for mercury, it affects two target organs: the central nervous system and the kidney. The toxicity of the elemental mercury is due to mercuric mercury. Inflated elemental mercury vapors promptly pass through the blood–brain barrier, and the consequent oxidation in mercuric mercury starts a connection with brain macromolecules [95].

The exposure of living organisms to such inorganic pollutants is ever increasing if we consider the interactions of microplastics, vectors themselves of metals, with biota [3,96].

Though polymers were considered to be inert towards metals in the past [97], great attention has recently been paid to better understanding the interaction between heavy metals and microplastics [98–108].

In this regard, earlies studies such as [98] investigated the ability of virgin and aged microplastics to adsorb metals. Plastic production pellets were collected from beaches and sediment flats of south-west England and revealed variable concentrations of trace metals (Cr, Co, Ni, Cu, Zn, Cd and Pb) that, in some cases, exceeded the concentrations that were reported for local estuarine sediments. The same authors studied the rates and mechanisms of metals that were associated with virgin and beached polyethene pellets in a laboratory-scale experiment. Trace metals were shown to adsorb to both virgin and beached pellets but with a higher rate on aged pellets. Presumably, metal adsorption proceeds through interactions between divalent cations (e.g., Cu^{2+}, Cd^{2+}, and Pb^{2+}) and oxyanions (e.g., $Cr_2O_4^{2-}$) with charged or polar regions of the plastic surface (effected by imperfections and the presence of charged contaminants and additives, for example), and via non-specific interactions between neutral metalorganic complexes and the hydrophobic surface of the bulk plastic medium. Aged beached pellets accumulate trace metals to a significantly greater extent, with equilibrium partition coefficients ranging from about 4 mL/g^{-1} (Co) to 220 mL/g^{-1} (Cr). Its reactivity is enhanced by changes to the polymer itself, as well as the presence of biofilms and chemical precipitates that enhance the critical role of plastic as a vehicle for the transport of metals in the marine environment.

In the study of [101], the authors examined, over the 14 days of the experiment, the adsorption of two heavy metals, copper (Cu) and zinc (Zn), that were leached from an antifouling paint to virgin polystyrene (PS) beads and aged polyvinyl chloride (PVC) fragments in seawater. They demonstrated that heavy metals were released from the antifouling paint to the water, and both microplastic types adsorbed the two heavy metals. The adsorption of Cu was significantly higher in PVC fragments than in PS, probably due to higher surface area and polarity of PVC. The concentrations of Cu and Zn increased significantly on PVC and PS throughout the experiment except for Zn on PS.

However, the absorption/desorption processes that can occur naturally in the environment are quite complex and present a high variability [109]. Indeed, several factors and variables can influence the interaction between metals and microplastics, such as the alteration of the plastic surface exposed to atmospheric agents, the increased roughness of aged particles compared to virgin materials, and the faster decomposition of darker particles [5]. All these components accelerate the degradation processes of microplastics, creating anionic and active sites that increase the interaction of particles with heavy metals [110].

Other significant variables to be considered responsible for increasing the interaction between microplastics and inorganic pollutants are related to pH, salinity variations, photo-oxidative erosion, the formation of biogenic biofilm, enhanced polymer polarity and plastic porosity [98,99,109,111,112].

The authors of [111] observed the Pb absorption capacity on nanoplastics (particles that are unintentionally produced within the size range from 1 to 1000 nm [113]) that were produced from microplastics that were collected on a beach exposed to the North Atlantic Gyre. Lead (II) adsorption kinetics, isotherm, and pH-edge analyses were carried out. The sorption reached a steady-state after around 200 min. The maximum sorption capacity varied between 97% and 78.5% for both tested Pb concentrations. Chemical reactions controlled lead (II) adsorption kinetics with the nanoplastics surface and to a lesser extent by intraparticle diffusion. Adsorption isotherm modelling demonstrated that nanoplastics were strong adsorbents that were equivalent to hydrous ferric oxides such as ferrihydrite. The adsorption was dependent on pH in response to the Pb(II) adsorption by the oxygenated binding sites that were developed on the account of the surface UV oxidation under environmental conditions. They could be able to compete with Fe or humic colloids for Pb binding, due to their amounts and specific areas, becoming efficient vectors of Pb and probably of many other metals.

Therefore, microplastics, once spread into the environment, with their load of intrinsic (additives) and extrinsic (environmental) heavy metals, can be conveyed into the food web to reach aquatic organisms [114–119] and then humans [120–122].

In this regard, the study of [123] pointed out the potential ability of metals that are present on marine microplastics in determining the co-selection of antibiotic-resistant human pathogens, representing a severe threat to humans that are exposed to the marine environment or even to seafood. Metals such as mercury, lead, zinc, copper and cadmium are accumulating to critical concentration in the environment and triggering the co-selection of antibiotic resistance in bacteria. In the marine environment, persistent pollutants like microplastics are recognized as a vector for the proliferation of metal/antibiotics, and human pathogens and horizontal gene transference between the phylogenetically distinct microbes that are present on microplastics are much faster than free-living microbes. Therefore, microplastics are an emerging global health threat [112].

However, studies on the impact of microplastics on human health are all in the early stages and need to be further developed [117,124].

2.1.4. Flame-Retardants

Flame retardants (FRs) are chemical compounds (Figure 4) that are capable of raising the flashpoint of the materials in which they are added. The main function of these molecules is, therefore, to prevent fires [125]. Flame retardants are divided into reactive and additive flame retardants according to their use. On the one hand, reactive chemicals are covalently bonded to polymers and are therefore less likely to reach the environment until the product is decomposed or burnt. The additive compounds, on the other hand, are only mixed with or dissolved in the material and can more easily migrate out of the product. Recently, over one hundred and forty types of flame retardants were counted, of which approximately seventy were found to belong to the brominated flame retardant (BFR) category. A first classification can be made based on their chemical nature—that is, organic or inorganic flame retardants:

- **Inorganic Flame Retardants:**

  Antimony Trioxide
  Aluminum Hydroxide

- **Organic Flame Retardants:**

  Tris (2,3-dibromopropyl) phosphate
  Short-chain chlorinated paraffin (10–13 carbon atoms) (SCCPs)
  Medium-chain chlorinated paraffin (14–17 carbon atoms) (MCCPs)
  Long-chain chlorinated paraffin (> 18 carbon atoms) (LCCPs)
  Polybrominated diphenyl (PBB)
  Polybrominated diphenyl Ethers (PBDEs)

Hexabromocyclododecanes (HBrCDs)
Tetrabromobisphenol_A (TBrBP_A)

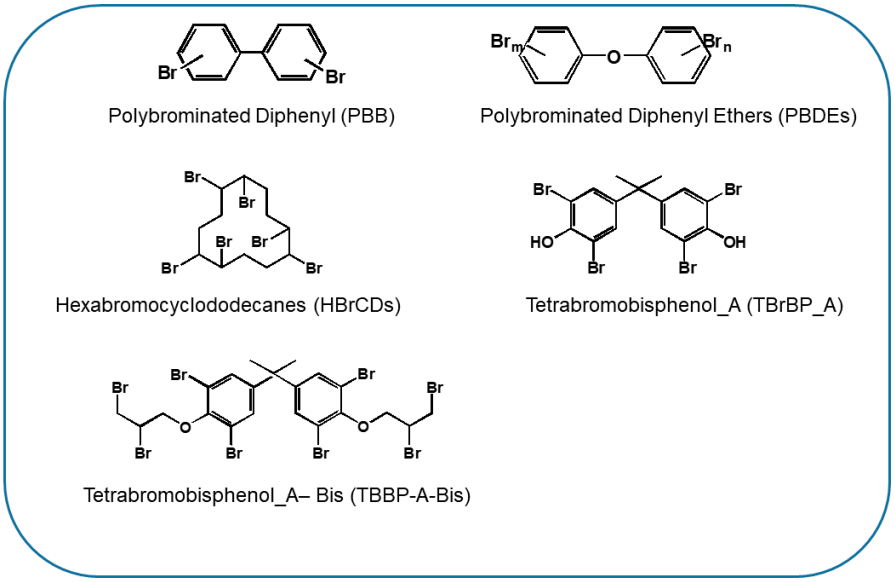

Figure 4. Chemical structure of some classes of halogenated flame retardants.

Inorganic flame retardants act through different chemical and physical mechanisms [126]. With the application of heat, they can release water, they can release fire retardant gases that suffocate the flames, or, in other cases, they can form a protective film that protects the material in which they are inserted. Most often, inorganic flame retardants are used as adjuvants of organic ones. This is the case of antimony trioxide, which is used together with brominated flame retardants and acts as a catalyst in the decomposition reactions of BFRs [127]. Phosphorus-based flame retardants act in the solid phase [128]. With the application of heat, they form a polymer of phosphoric acid that carbonizes the material, blocking the pyrolysis process [128]. Though with some difference, the mechanism of action of organic flame retardants is the same. With the application of heat, they decompose even before the matrix that contains them, thus preventing the formation of flammable gases. In more detail, the halogens that are released by said molecules can react with the radicals H and OH, removing them from the chain reactions that are triggered during the combustion processes [129]. The critical factor that determines the goodness of the preventive action of these additives is their thermal stability, within the material that hosts them. If a retardant decomposes or evaporates too above or below the combustion temperature of the host material, its action will be ineffective. The brominated flame retardants decompose at a temperature of approximately 50 °C below the combustion temperature of the matrices to which they are inserted, therefore making them particularly useful for fire prevention [130].

The use of chemical additives to make materials fireproof is not a recent phenomenon. The ancient Egyptians used hydrated potassium aluminum sulphate ($KAl(SO_4)_2 12H_2O$) to treat wood [131]. Following, Gay Lussac described a technique to protect theatre fabrics from fire through treatments with mixes of ammonium phosphate, ammonium chloride, and borax [132]. Today, the main fields of use of flame retardants concern the production of electrical materials, electronic materials, construction, textiles and transport (Figure 5). The massive growth in the production of plastic polymers has led to a substantial increase in the production of flame retardants. For example, in 1965, only 10% of bromine was used for the production of brominated flame retardants; this percentage became 40% in 1996 [133]. The global production of BFRs (as in the sum of Europe, Asia and the United States) increased from 106,000 metric tons in 1989 to 2,035,000 metric tons in 1999 [134].

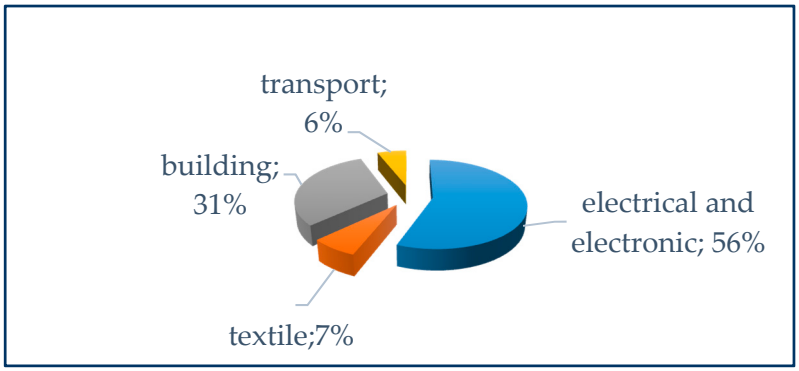

Figure 5. Greater fields of use of brominated flame retardants (BFRs) (Source data: [135]).

The high concentrations of FRs that are found in plastic products are because these molecules (distinctly lipophilic) not only adsorb onto the surface of plastics and microplastics but also are present inside them because they are added as additives during the plastic production process [135].

Given the chemical inertia and marked lipophilicity of flame retardants, it is easy to intuit their rapid bioaccumulation. Different concentrations of PBDEs have been detected in various matrices including human milk, article glaciers, domestic dust, and, obviously, in sludge that is derived from water purification plants [136]. The considerable accumulation in this sludge deserves special attention if one thinks of the common practice of reusing it as an organic soil improver in agriculture. Another widespread practice of sludge disposal is its incineration. Several authors have already shown that the incomplete combustion of PBDEs leads to the formation of highly toxic species such as polybromodibenzofuranes (PBDF) and polybromodibenzodioxins (PBDD) [137]. In this regard, BFRs have been classified as "persisting organic pollutants" (POPs). The risk assessment made by the European community has shown that some of these molecules are toxic, suspected to be carcinogenic, and actively act on the endocrine system (endocrine disruptor).

Regarding PBDEs, the European community has banned the use of pentaBDE and octaBDE. This ban is because they are classified as toxic for reproduction [138]. DecaBDE will not be classified as a dangerous substance according to the European Directive 67/548/EEC because it is not toxic to human health or the environment. Several papers [139] have highlighted the immunotoxic effect of tetrabromobisphenol A (TBBP_A). Regarding HBrCDs, there is evidence [140] that they interfere with thyroid hormones.

Just like many other hydrophobic contaminants, evidence of attachment of PBDEs onto microplastics from marine environment has been highlighted in recent years [42,141,142], and the assimilation of these pollutants by organisms that ingest microplastics is highly probable [141,143,144]. Different levels of PBDE concentrations on microplastic samples have been observed based on polymer type and local anthropogenic activities. For example, the study of [42] underlined the presence of a much higher concentration of total-PBDEs that were analyzed on PP microplastics (9909 ng/g) than on PE samples (0.3 ng/g), with the most significant values being reported in open seas areas compared to remote locations. BDE-209 is one common PBDE congener that usually occurs in very high concentrations, and its low diffusion coefficient in LDPE implies a consideration when taking into account the risk that is posed by microplastic particle ingestion by marine organisms [42].

Indeed, amphipods have demonstrated the ability to assimilate PBDEs that are derived from microplastics and have shown a greater uptake for higher-brominated congeners (BDE-154 and -153 compared to BDE-28 and -47) [143]. In the cited study, amphipods (*Allorchestes compressa*) that were exposed to microplastics that were isolated from a commercial facial cleansing soap ingested ≤45 particles per animal and evacuated them within 36 h. Amphipods were exposed to polybrominated diphenyl ether (PBDEs) congeners (BDE-28, -47, -99, -100, -153, -154, and -183) in the presence or absence of microplastics. The results demonstrated that PBDEs that were derived from microplastics

could be assimilated into the tissue of a marine amphipod. Microplastics reduced PBDE uptake compared to controls, but they caused a greater proportional uptake of higher-brominated congeners such as BDE-154 and -153, as compared to BDE-28 and -47. The study demonstrated that microplastics could transfer PBDEs into a marine organism by acting as a vector for the assimilation of POPs into marine organisms; thus, they pose a risk of contaminating aquatic food chains.

Another study [145] analyzed the feed of a typical commercial fish, the seabass, based on their absorption of microplastic-containing contaminants (PCBs and PBDEs). The study investigated how combinations of halogenated contaminants and microplastics that are associated with feed can alter toxicokinetics in European seabass and therefore affect the fish. Microplastic particles (2%) were added to the feed either with sorbed contaminants or as a mixture of clean microplastics and chemical contaminants, and they were then compared to a feed that contained contaminants without microplastics. For the contaminated microplastic diet, the accumulation of polychlorinated biphenyls (PCBs) and brominated flame retardants (BFRs) in fish were significantly higher, increasing up to 40 days of accumulation and then reversing to values that were comparable to the other diets at the end of accumulation.

The significant gene expression results of the liver (cyp1a, il1β, and gstα) after 40 days of exposure indicated that microplastics might indeed worsen the toxic effects (liver metabolism, immune system, oxidative stress) of some chemical contaminants that are sorbed to microplastics.

Moreover, on the one hand, at the end of the accumulation period, microplastics increased the bioavailability of the sorbed contaminants, showing a quadratic accumulation of all the 12 contaminants that were present on the microplastics. On the other hand, the metabolism of BDE99 to BDE47 (by debromination) in seabass was rather fast, and unlike other pollutants, this metabolism was unaffected by the presence of microplastics.

3. Effects of Micro and Nanoplastics on Human Health

A recent report from the "World Health Organization" [146] emphasized the ubiquitous microplastics presence in the environment and aroused great concern regarding the exposition and effects of nano and microplastics on human health [122,147–150]. One of the major nano and microplastic entry points into the human system is represented by the ingestion of contaminated food [8,151–153]. In a recent study conducted by [154], 0.44 MPs/g of nano and microplastics were found in sugar, 0.11 MPs/g were found in salt, 0.03 MPs/g were found in alcohol, and 0.09 MPs/g were found in bottled water. Humans could also assume an estimated intake of 80 g per day of microplastics via plants (fruits and vegetable) that accumulate MPs through uptake from polluted soil [155].

The presence of microplastics in marine species for human consumption (fish, bivalves and crustaceans) is now well-known [156]. As an example, in *Mytilus edulis* and *Mytilus galloprovincialis* of five European countries, the microplastic number has been found to fluctuate from 3 to 5 fibers per 10 g of mussels [116].

Therefore, following exposure via diet, uptake in humans is plausible, as evidenced by the capacity for synthetic particles smaller than 150 µm to cross the gastrointestinal epithelium in mammalian bodies, which causes systemic exposure. However, scientists speculate that only 0.3% of these particles are expected to be absorbed, while a lower fraction (0.1%) that contains particles that are bigger than 10 µm should be capable of reaching both organs and cellular membranes and passing through the blood–brain barrier and placenta [117]. Exposure concentrations are predicted to be low, although data about micro and nanoplastics into the environment are still limited due to the analytical and technical complications to extract, characterize, and quantify them from environmental matrices [157].

Once ingested, particles smaller than 2.5 µm can enter the gastrointestinal tract (Figure 6) through endocytosis by M cells (specialized epithelial cells of the mucosa-associated lymphoid tissues) of Peyer's patches. M cells transport particles from the intestinal lumen to the mucosal lymphoid tissues or through the paracellular persorption. Persorption consists of mechanical kneading of solid particles through gaps that are located in the single-layer epithelium at the villus tips of the gastrointestinal

tract (desquamation zones) and into the circulatory system. The resulting toxicity is via inflammation due to the persistent nature of microplastics, as well as their unique properties such as hydrophobicity and chemical composition, and it is supposed to have an accumulative effect that is dependent on dose [151]. This assumption, regarding levels of microplastics in men at a gastro-intestinal level, was further confirmed by the finding of microplastics into human stools: Twenty plastic particles, mostly PE and PP (ranging in size between 5 and 500 mm), were found for every 10 g of stool [158,159]. Indeed, the human excretory system should be responsible for removing up to 90% of micro and nanoplastics ingested [156].

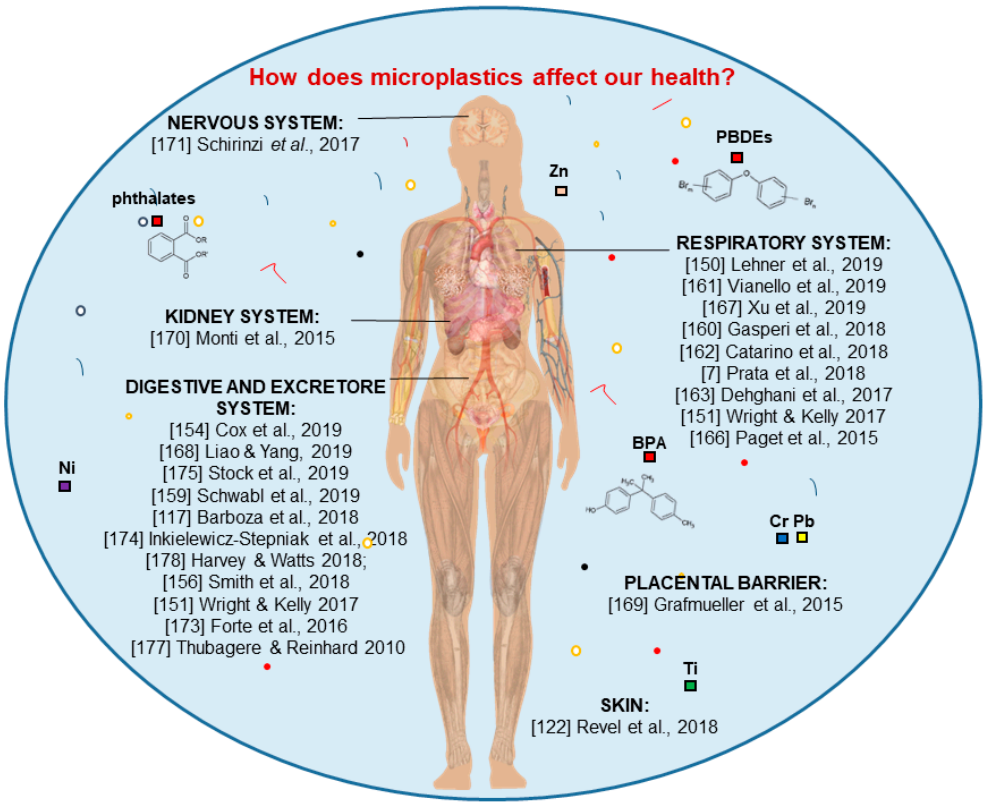

Figure 6. Overview of scientific studies focused on the effects of micro and nanoplastics on human health. Colored squares represent pollutants (organic and inorganic) that could be present in environmental matrices (free or associated with micro and nanoplastics) and that could enter into the human body through different entry routes.

Another microplastics entry point to the human body is the aerial one (Figure 6) through inhalation [160,161]. The authors of [162] showed how the ingestion of synthetic fibers from mussel consumption is less than that of the ones that are inhaled from domestic dust during the same meal. The authors of [151] reported finding 18 fibers and four fragments/L of rain during precipitation events. Microplastics are carried by the wind or from atmospheric depositions and could also result from the erosion of agricultural and fertilized lands, dried sludges, and products from wastewater treatment, synthetic clothes fabric, industrial emissions, road-dust, marine aerosol. This spread could lead to respiratory distress, cytotoxic and inflammatory effects, and autoimmune diseases in men [7,128,131,135,163–165]. Moreover, the human lung has a quite wide alveolation surface of ca. 150 m^2, with a very thin tissue barrier that is smaller than 1 µm and which could allow nanoparticles to penetrate the bloodstream and all human body [150]. Polystyrene particles of the size 50 nm have led to genotoxic and cytotoxic effects on pulmonary epithelial cells and macrophages (Calu-3 and THP-1) [166]. More widely, the response to inhaled particles, depending on differences on individual

metabolism and susceptibility, may be expressed as immediate bronchial reactions (asthma-like), diffuse interstitial fibrosis and granulomas with fiber inclusions (extrinsic allergic alveolitis, chronic pneumonia), inflammatory and fibrotic changes in the bronchial and peribronchial tissue (chronic bronchitis), and interalveolar septa lesions (pneumothorax) [7]. For example, similar effects have been registered in workers of the textile industry in close contact to nylon, polyester, polyolefin and acrylic fibers. The low deterioration of microfibers has been found in patients suffering from pulmonary cancer as a confirmation of the bio-persistence of these synthetic particles. In addition to bio-persistence, fiber size has an impact in their toxicity [151]; for example, fibers of 15-20 µm cannot be successfully removed from macrophages to the lungs. Additionally, in [167], the toxicity of smaller-sized polystyrene nanoparticles (25 nm in diameter), which induced lower cell viability, cell cycle arrest in the S phase, the transcription of the activated inflammatory gene, and changed protein expression that was associated with the cell cycle and pro-apoptosis, was demonstrated. Not to be overlooked is the potential transmission of microorganisms through the microplastics that are present in the air. By attaching to microplastic surfaces in order to be protected from UV radiations, microorganisms could reach the lung and become another threat of infections to human health [7].

The last exposure pathway of microplastics to the human body could be skin contact (Figure 6) through water while washing or while using scrubs and cosmetics that contain micro and nanoplastics.

However, the penetration of the corneous layer is limited to particles lower than 100 nm, so it is unlikely that microplastics absorption could occur through the skin; on the contrary, nanoplastics absorption is more probable [122].

Though plastic is considered an inert material, there is a broad range of properties that characterize microplastics, such as size, shape, chemical composition, and hydrophobicity, that could cause harm and influence the cytotoxicity of particles to cells and tissues [151].

The increased surface area/volume ratio of microplastics, combined with their hydrophobicity, translates to a high affinity to a broad range of hydrophobic and persistent organic pollutants, antibiotics, and heavy metals that could be introduced in the human body by microplastics uptake.

In regard to heavy metals, an in-vitro study was conducted about chromium (Cr) absorption/desorption behavior in the human digestive system considering non-degradable MP types (polyethene (PE), polypropylene (PP), polyvinylchloride (PVC), and polystyrene (PS)) and degradable MPs (polylactic, PLA). The results showed the ability to release Cr (VI) and Cr (III) from MPs into the digestive-gastric phase thanks to stomach acid conditions that stimulated the process [168].

The interactions between microplastics/nanoplastics and other human organs are still being tested, but their possible effects can be assessed based on human absorption models of nanomaterials that are produced by various industrial production processes. In the studies of [169,170], the ability of nanoparticles in polystyrene to cross the placental barrier and the primary human renal cortical epithelial (HRCE) cells was demonstrated.

The use of metal nanoparticles (NPs) (AgNP and AuNP, ZrO_2NPs, CeO_2NPs, TiO_2NPs, and Al_2O_3NPs), carbon nanomaterials (C60 fullerene, graphene) and polyethene (PE) and polystyrene (PS) microplastics has demonstrated that cytotoxic effects are induced on T98G and HeLa cell lines (human brain and epithelial cells) [171]. Additionally, the use of polypropylene (PP) particles has shown different but harmful effects on various cell lines, based on the size (~20 µm and 25–200 µm) and the different concentrations used in the various tests. Therefore, the interaction of microplastics with humans can produce cytotoxicity, hypersensitivity, unwanted immune responses, and acute responses like hemolysis, thus representing a potential risk to human health [172].

Recent in-vitro studies about effects of plastics on the human body have mostly used engineered nanoplastics that can influence their absorption and also the translocation and production of ROS due to their dimension, charge and shape [148,150,173–176]. In fact, in the study [174], the interaction between positively-charged nanoparticles of polystyrene (60 nm) and the secretion film of the gastrointestinal epithelium (first physical barrier after digestion) was analyzed. Nanoplastics showed a strong ability to interact with the secretion film, to influence cellular vitality, and to induce apoptosis in the intestinal

epithelial cell lines LS174T, HT-29 and Caco-2. Those cytotoxic effects were already observed in the study of [177], which was carried out on adenocarcinoma colon–rectal human differentiated cells, Caco-2, by using polystyrene nanoparticles of 20 and 40 nm.

4. Conclusions

The intake of microplastics by humans is by now quite evident. The entry point may be through ingestion (through contaminated food or via trophic transfer), through inhalation, or through skin contact.

Following the intake of microplastics into the human body, their fate and effects are still controversial and not well known. Only microplastics smaller than 20 µm should be able to penetrate organs, and those with a size of about 10 µm should be able to access all organs, cross cell membranes, cross the blood–brain barrier, and enter the placenta, assuming that a distribution of particles in secondary tissues, such as the liver, muscles, and the brain is possible. Not enough information is available to fully understand the implications of microplastics for human health; however, effects may potentially be due to their physical properties (size, shape, and length), chemical properties (presence of additives and polymer type), concentration, or microbial biofilm growth.

How toxic chemicals adsorb/desorb onto/from microplastics is not well known, but plausible mechanisms include hydrophobic interactions, pH variations, the ageing of particles, and polymer composition. Furthermore, not enough studies have fully explained the primary sources of pollutants that are present on microplastics and whether their origin is extrinsic from the surrounding ambient space, intrinsic from the plastic itself, or, more probably, from a combination of both and from a continuous and dynamic process of absorption and desorption that is related to the spread of the particles into the environment and to their consequent exposure to weathering.

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