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HUMAN HEALTH EFFECTS OF ENVIRONMENTAL EXPOSURE TO MICROPLASTICS

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ENVIRONMENTAL EXPOSURE TO MICROPLASTICS: AN OVERVIEW ON POSSIBLE HUMAN HEALTH EFFECTS

Abstract

Microplastics are ubiquitous environmental contaminants leading to inevitable human exposure. Even so, little is known about the effects of microplastics in human health. Thus, in this work we review the evidence for potential negative effects of microplastics in the human body, focusing on pathways of exposure and toxicity. Exposure may occur by ingestion, inhalation and dermal contact due to the presence of microplastics in products, foodstuff and air. In all biological systems, microplastic exposure may cause particle toxicity, with oxidative stress, inflammatory lesions and increased uptake or translocation. The inability of the immune system to remove synthetic particles may lead to chronic inflammation and increase risk of neoplasia. Furthermore, microplastics may release their constituents, adsorbed contaminants and pathogenic organisms. Nonetheless, knowledge on microplastic toxicity is still limited and largely influenced by exposure concentration, particle properties, adsorbed contaminants, tissues involved and individual susceptibility, requiring further research.

Keywords: microplastics; nanoplastics; human health risks; marine litter; toxicology.

1. Introduction

Plastics play an important role on the general improvement of human health, for instance, by allowing the production of disposable medical equipment and the increase in food safety. However, mismanaged plastic entering the environment may have the opposite effect, such as, providing a breeding ground for disease-carrying mosquitoes or blocking water drainage, causing flooding and the spread of diseases (Pullin and Knight 2005). This lack of proper waste management has led to the accumulation of over 250,000 tons of plastic pieces floating in the oceans (Eriksen et al. 2014). It is estimated that costal countries released 4.8 to 12.7 million metric tons of plastic to the oceans in 2010 (Jambeck et al. 2015).

Plastics in the environment, often originating from incorrectly discarded consumer products, undergo slow degradation caused by photo and thermooxidative processes and to a lower extent by biodegradation, weakening material integrity which leads to fragmentation into pieces smaller than 5 mm, called secondary microplastics (Andrady 2011). When plastic particles of this size are intentionally produced to be used in products (e.g. cosmetics, such as exfoliants or toothpaste) or by industries (e.g. air blasting), they are called primary microplastics (Browne et al. 2011). Microplastics are already found in seawater in concentrations up to 102,000 particles m^{-3} (Nóren 2007), and are also reported to contaminate freshwater (Eriksen et al. 2013; Estahbanati and Fahrenfeld 2016; Rodrigues et al. 2018), sediment (Abidli et al. 2018; Reed et al. 2018), soil (Watteau et al. 2018; Zhang et al. 2018), air (Abbasi et al. 2019; Dris et al. 2016) and even foodstuff, such as beer, sea salt and tap water (Kosuth et al. 2018).

The ubiquitous nature of microplastics in the environment and in consumer products leads to the inevitable human exposure to these particles. However, the consequences of

this exposure are not yet well understood. In this work, the current evidence of the effects of environmental exposure to microplastics on human health is critically reviewed, presenting hypotheses for their routes of exposure and mechanisms of toxicity (**Figure 1**), hopefully providing a foundation for further research. Information on the impacts of microplastics in humans is limited due to ethical constrains, strict biosecurity measures to handle human samples, and limited detection techniques. Thus, discussion of exposure and toxicity also includes information gathered from tests in organism.

2. Routes of exposure

Microplastics are widespread contaminants. The human body is exposed to microplastics through ingestion of food containing microplastics, inhalation of microplastics in the air and by dermal contact of these particles, contained in products, textiles or in the dust (**Figure 1**; Revel et al. 2018). These routes of exposure are detailed in the following sections.

2.1. Ingestion

Ingestion is considered the major route of human exposure to microplastics (Galloway 2015). Based on the consumption of foodstuff, the estimated intake of microplastics is 39,000 to 52,000 particles person^{-1} year^{-1} (Cox et al. 2019). Particles may reach the gastrointestinal system through contaminated foodstuff or through the mucociliary clearance after inhalation, possibly leading to inflammatory response, increased permeability, and changes in gut microbe composition and metabolism (Salim et al.

2013). Microplastics have been reported in food items, such as mussels (Li et al. 2016), commercial fish (Neves et al. 2015), as well as table salt (Karami et al. 2017), sugar (Liebezeit and Liebezeit 2013), and bottled water (Oßmann et al. 2018), so their ingestion is likely. Exposure of Europeans through the consumption of bivalves has been estimated to be 11,000 microplastics person^{-1} year^{-1} (Van Cauwenberghe and Janssen 2014). Furthermore, the ingestion of microplastics in table salt has been calculated as 37 and 100 microplastics person^{-1} year^{-1}, in Europe (Karami et al. 2017) and China (Yang et al. 2015), respectively. However, Catarino et al. (2018) predicts that the settling of dust on plates during mealtime may be even more important than microplastics already present in food. Rist et al. (2018) also highlights disproportionate concern about environmental contamination of consumed organisms compared to the likely contamination by packaging and plastic containers. After ingestion, particles could be adsorbed in the intestine by specialized M-cells, covering an intestinal lymphoid tissue – Peyer's patches, depending also on adherence to the gastrointestinal mucus, where high adherence increases particle clearance rate (Ensign et al. 2012). Insoluble particles may penetrate the intestinal mucus through the increase in solubility due to the adsorption of a "corona" of intestinal contents (Powell et al. 2007) or due to their small sizes, as was demonstrated for 14 and 415 nm polystyrene (PS) latex particles in rat intestinal sections but not for larger sizes of 1.09 μm (Szentkuti 1997). Another possible mechanism of internalization of particles is persorption, the paracellular transfer of particles through the single layer of the intestinal epithelium (Volkheimer 1977). Microplastics could be subjected to these same mechanisms as their translocation to the circulatory system after oral administration has been demonstrated *in vivo*. For instance, in rats, 6% of PS (0.87 μm) reached the circulation within 15 minutes after oral administration (Eyles et al. 1995) whereas oral exposure to 1.25 mg

kg^{-1} of PS sizing 50 nm lead to 34% of absorption, possibly transported through the mesentery lymph to reach the circulatory system and accumulate preferentially in the liver (Jani et al. 1990). Furthermore, 44 nm PS nanospheres were internalized and released by human colon fibroblasts through passive translocation across the cell membrane (Fiorentino et al. 2015). When internalized by human gastric adenocarcinoma cells, 44 nm PS affected gene expression, inhibited cell viability, and induced pro-inflammatory responses and morphological changes (Forte et al. 2016). Human exposure through ingestion is very likely since our food and environment are contaminated with microplastics. However, the risk of ingesting microplastics is not known since little research has been conducted on estimating the overall human exposure and its effects.

2.2. Inhalation

Microplastics are released to the air by numerous sources, including synthetic textiles, abrasion of materials (e.g. car tires, buildings) and resuspension of microplastics in surfaces. One of the first determinations of microplastics in the air refers to outdoor concentrations of 0.3 – 1.5 particles m^{-3} and indoor concentrations of 0.4 – 56.5 particles m^{-3} (33% of polymers), including inhalable sizes (Dris et al. 2017). Individual inhalation has been estimated to be 26 to 130 airborne microplastics day^{-1} (Prata 2018). Based on the air sampling using a mannequin, it is expected that a male person with light activity inhales 272 microplastics per day (Vianello et al. 2019). Different estimations are dependent on sampling methodologies as well as space use factors, such as cleaning schedule, activities, furniture materials and season. Particle properties, such as size and density, will influence their deposition on the respiratory system, with less

dense and smaller particles reaching deeper in the lungs. After deposition, clearance by macrophages or migration to the circulation or lymphatic system may lead to particle translocation. However, the large surface area of small particles in the respiratory system may induce an intense release of chemotactic factors that prevent macrophage migration and increase permeability leading to chronic inflammation, known as dust overload (Donaldson et al. 2000). Indeed, PS nanospheres (64 nm) lead to neutrophil influx and inflammation in rat's lungs and proinflammatory gene expression in epithelial cells, due to the confirmed high oxidant activity caused by the large surface area (Brown et al. 2001). *In vitro*, PVC (2 μm) produced by emulsion polymerization induced significant cytotoxicity and hemolysis in rat and human pulmonary cells (Xu et al. 2002). Respiratory symptoms associated with the development of airway and interstitial lung disease are found in occupational exposure to airborne microplastics in workers of the synthetic textile, flock and the vinyl chloride or polyvinyl chloride industries, with lesions successfully replicated *in vivo* (Atis et al. 2005; Agarwal et al. 1978; Pimentel et al. 1975; Porter et al. 1999; Xu et al. 2004). Fibers of 250 μm have also been detected in human lung biopsies, including in cancer biopsies even though causation has not yet been proven (Pauly et al. 1998). Thus, it is likely that under conditions of high concentration or high individual susceptibility, airborne microplastics could cause lesions to the respiratory system.

2.3. Dermal contact

Dermal contact with microplastics is considered a less significant route of exposure, although it has been speculated that nanoplastics (<100 nm) could transverse the dermal barrier (Revel et al. 2018). This route is more often associated with the exposure to

monomers and additives of plastics, such as the endocrine disruptors bisphenol A and phthalates, from daily use of common appliances. Nonetheless, the possibility that nanoplastics can cross the dermal barrier and cause toxicity should not be abandoned without proof. In medicine, plastics are known to induce low inflammatory reactions and a foreign body reaction, with fibrous encapsulation. For instance, surgical sutures using braided polyester and monofilament polypropylene resulted in lower inflammatory reaction than silk and fibrous encapsulation after 21 days (Salthouse and Matlaga 1975). In mice, an *in vivo* subcutaneous introduction of <10 mm plastics disks revealed that, after 98 days, PE disks induced encapsulation with minimum inflammation whereas polyvinyl chloride (PVC) containing organo-tin or plasticizers induced encapsulation with inflammatory infiltrate and moderate degeneration and necrosis, possibly due to leachate toxicity (Van Tienhoven et al. 2006). Even though micro and nanoplastics could also induce inflammation and foreign body reactions, differences in surface properties could also lead to distinct outcomes. Human epithelial cells suffer oxidative stress from exposure to micro and nanoplastics as well (Schirinzi et al. 2017). Thus, the potential adverse effects of nanoplastics and the widespread dermal exposure to plastic particles (i.e. from dust, synthetic fibers, and microbeads in cosmetics) support the need for further research in this area.

3. Pathways of microplastic toxicity

Once regarded as inert particles without toxicity, microplastics are now seen as potentially harmful to organisms (Anbymani and Kakkar 2018; Galloway 2015), depending on exposure and susceptibility. The high surface area of microplastics may lead to oxidative stress, cytotoxicity and translocation to other tissues, while their

persistent nature limits their removal from the organism, leading to chronic inflammation, which increases the risk of cancer. On the other hand, microplastics, as part of particulate matter, may also be involved in the increasing incidence of immune or neurodegenerative diseases. Furthermore, microplastics may release chemicals, from their matrixes or adsorbed from the environment (Crawford and Quinn 2017), or act as vectors for dangerous microorganisms (Kirstein et al. 2016).

3.1. Oxidative stress and cytotoxicity

Overwhelming of antioxidant responses may result in oxidative stress. Microplastics may be at the origin of this oxidative stress, caused by their high surface area, release of oxidizing species adsorbed to their surface (e.g. metals) or due to reactive oxygen species released during the inflammatory response (Kelly and Fussel 2012; Valavanidis et al. 2013). For instance, oxidative stress after exposure to microplastics has been reported in zebrafish (*Danio rerio*) (Lu et al. 2016) and mice (Deng et al. 2017). In polypropylene (PP) prothesis, after insertion acute inflammatory response culminates with the release of oxidants (e.g. hydrogen peroxide, hypochlorous acid) inducing degradation, hydrolysis, cracking and additive leaching of the polymer, producing a positive feedback loop of free radical production and revealing potential mechanisms of plastic removal from the organism (Sternschuss et al. 2012).

Cytotoxicity is a result of particle toxicity, oxidative stress and inflammation. Cellular internalization of microplastic has been described for PS in cell cultures, including macrophages, erythrocytes (Geiser et al. 2005) and rat alveolar epithelial cells (Yacobi et al. 2008). Inside the cell, microplastics are not membrane bound, potentially interacting with intercellular structures (Geiser et al. 2005). *In vitro* testing has been

able to show cytotoxicity caused by plastic particles collected from the environment (Furukuma and Fuji 2016). On the other hand, exposure to 0.05 – 10 mg L^{-1} of PS and polyethylene in cerebral and epithelial human cells was not able to induce cytolysis but increased reactive oxygen species (ROS) to high concentrations, contributing to cytotoxicity (Schirinzi et al. 2017). Furthermore, exposure of macrophage and lung epithelial cell cultures to PS (60 μm) caused ROS and endoplasmic reticulum stress (caused by the aggregation of misfolded proteins) leading to autophagic cell death (Chiu et al. 2015). Thus, cytotoxicity and oxidative stress may be important mechanisms of microplastic toxicity.

3.2. Disruption of the energy homeostasis and metabolism

Energy homeostasis is influenced by the balance between available energy, from intake and reserves, and expenditure. Several studies have shown that microplastics may have impacts on energy homeostasis. For instance, microplastics may reduce energy intake due to: (a) decreased feeding activity (e.g. in marine worms, crabs and clams) (Xu et al. 2017; Watts e al 2015; Wright et al. 2013); (b) reduced predatory performance, possibly resulting from neurotoxicity (e.g. in fish) (Wen et al. 2018); (c) deficit in digestive capacities through the modulation of digestive enzyme activities, with resultant decrease in nutrient intake (e.g. increase in amylase and decrease in trypsin activities in fish)(Wen et al. 2018). On the other hand, microplastics may have an opposite effect, increasing food intake as a response to increasing energy demand or decreasing absorption efficiency, as observed in mice (Deng et al. 2017). Furthermore, microplastics may lead to negative energy balance due to increased energy consumption. In *in vivo* studies on microplastics, increased energy consumption has

been observed as resulting from: (a) energy demanding inflammatory reactions; (b) increased gut residence time with higher energy costs (Wright et al. 2013); (c) increased excretion mechanisms, such as ammonia excretion or the production of fecal pellets or pseudofeces (Xu et al. 2017; Watts et al. 2015). Indeed, depletion of 50% in energy reserves in marine worms (Wright et al. 2013) and remarkable decrease in liver weight in mice (Deng et al. 2017) have been observed secondary to microplastic exposure. Microplastics may cause metabolic changes as well, directly or secondary to their effects, such as the negative energy balance. For instance, exposure of fish and mice to microplastics resulted in an increase in lactate dehydrogenase (LDH), an anaerobic enzyme (Deng et al. 2017; Wen et al. 2018). In fish (*Dicentrarchus labrax*), 45 nm polymethylmethacrylate particles induced modulation of RNA of peroxisome proliferator-activated receptors related to lipid metabolism, potentially interfering the mobilization of energy reserves (Brandts et al. 2018). Moreover, in mice livers it also led to a decrease in ATP levels and decreased lipid metabolism (Deng et al. 2017). In human, microplastics may have similar effects, by increasing energy expenditure, decreasing nutrient intake or modulation of metabolism. However, observation of these effects may be limited considering the low exposure concentrations and higher energy needs of humans compared to tested organisms.

3.3. Translocation of microplastics to the circulatory system and distant tissues

After exposure, microplastics may act locally or translocate, leading to exposure of distant tissues. Translocation is especially likely during inflammation, due to the increased permeability of epithelial barriers. The gastrointestinal mucosa may also have increased permeability as result of malnutrition and in diets rich in saturated fats and

high-fructose sugars (through changes in the intestinal microbiome) (West-Eberhard 2019). Translocation of microplastics has been reported in rats after inhalation and ingestion of microplastics, reaching the circulation and distant tissues, such as the liver or spleen (Eyles et al. 2001; Jani et al. 1990). In humans, a perfusion model of the placenta has shown that 240 nm PS are able to cross the placental barrier (Wick et al. 2010). Internalization of negatively charged PS nanospheres up to 1 μm has been confirmed in cell cultures (Zauner et al. 2001). Microplastics in circulation could cause inflammation, pulmonary hypertension (Zargorski et al., 2003), vascular occlusions (Jones et al. 2003), increased coagulability (Churg and Brauer, 2000) and blood cell cytotoxicity (Canesi et al. 2015). Indeed, *in vitro*, PS (≤243 nm) led to the aggregation and endothelial adhesion of red blood cells (Barshtein et al. 2016), whereas 20 μm and 25-200 μm PP increased hemolysis and led to the release of histamine (Hwang et al. 2019).Microplastics in circulation could also reach the liver and kidney, responsible for the metabolism and excretion of xenobiotics. Tissue distribution in mice after oral administration of fluorescence 5 and 20 μm PS, in concentrations in the range of 10^6 and 10^4 respectively, lead to accumulation in the liver, kidney and gut, with evidence of oxidative stress, energy balance disturbance, and neurotoxicity (Deng et al. 2017). Smaller particles (5 μm) accumulated mainly in the gut, whereas larger particles accumulated consistently across tissues (20 μm). In human renal cortical epithelial cells, PS (44 nm) were internalized by both endocytosis and diffusion, without effects on cell viability, metabolism, or cell cycle progression, but accumulating in the perinuclear region and without signs of clearance in up to 90 minutes (Monti et al. 2015). After a threshold, continuous accumulation of particles in renal cells could lead to significant impairment in renal function. In distant tissues, the mechanisms described in the previous sections apply, also leading to adverse effects, inflammation, and increased

risk of neoplastic lesions. For instance, when reaching the bone, PE and PS particles may be responsible for bone loss due to an increased activity of osteoclasts, the cells responsible for bone reabsorption (Liu et al. 2015; Ormsby et al. 2016). Toxicity-based-toxicokinetic/toxicodynamic modeling of rats of 5 and 20 μm PS predicts higher accumulation bioaccumulation in the liver, and the overall estimated human threshold concentrations in the range of 53.3 to 5.1 mg g^{-1} of body weight, for the lower and larger size correspondingly (Yang et al. 2019).

3.4. Disruption of immune function

After exposure, particles may cause local or systemic immune responses, dependent on their dissemination. However, in some cases (e.g. genetic susceptibility) environmental exposure is enough to disrupt the immune function, favoring autoimmune diseases or immunosuppression. Autoimmune diseases may be caused by the inhalation of particulate matter through mechanisms of particle translocation, oxidative stress, release of immune modulators and activation of immune cells, resulting in exposure to self-antigens and production of autoantibodies (Farhat et al. 2011). For instance, exposure to particulate matter seems to be related to systemic autoimmune rheumatic disease (Bernatsky et al. 2016) and systemic lupus erythematosus (Fernandes et al. 2015). On the other hand, temporary immunosuppression has been reported *in vivo* after early-life exposure to combustion-derived particulate matter in mice as a result of lower activation of dendritic cells, production of IL-10 (anti-inflammatory cytokine) and suppression of T-helper type 2 responses with impartment of T-effector cell production (Saravia et al. 2014). Microplastics, as particulate matter in the air, could also contribute to this disruption of immune function, even though this has not yet been found on humans.

Nonetheless, mussels *Mytilus spp.* show immunosuppression (Canesi et al. 2015) and tissue dependent modulation of immune response (Détrée and Gallardo-Escárate 2018) after exposure to microplastics. Thus, further investigation of microplastic effects on the immune system are needed.

3.5. Neurotoxicity and the increasing incidence of neurodegenerative diseases

Exposure to contaminants may lead to neurotoxicity, which is related to neurodegenerative diseases. Neurotoxicity has been reported *in vivo* after exposure to particulate matter, possibly due to oxidative stress and the activation of the microglia in the brain (immune cells) due to direct contact with translocated particles or through the action of circulating pro-inflammatory cytokines (from other inflammation sites), resulting in damage to neurons (MohanKumar et al. 2008). Indeed, exposure to traffic pollution, including particulate matter, has been associated with mild cognitive impairment in the elderly, increasing the risk of Alzheimer's disease development (Ranft et al. 2009), and higher incidence of dementia (Chen et al. 2017). Through the same mechanisms, and depending on individual susceptibility, microplastics could contribute to the increasing incidence of neurodegenerative diseases. Indeed, *in vivo* toxicity testing have shown that microplastics can impact neuronal function and behavior. In the brain of European seabass (*Dicentrarchus labrax*), microplastics are reported to cause inhibition of acetylcholinesterase (AChE), oxidative stress with increase in lipid peroxidation levels and an increase in anaerobic pathway of energy production (Barboza et al. 2018a). In the same species, exposure to microplastics has been shown to impact swimming performance, a behavioral indicator (Barboza et al. 2018b). Exposure to PS has also been reported to cause adverse effects on

neurotransmission in mice, such as increased activity of AChE and changes in serum neurotransmitters (Deng et al. 2017). *In vitro* studies using neural cell types, 40 - 70 nm PS nanospheres were also able to induce toxicity and changes in metabolic activity, dependent on cell-type and concentration, with increased toxicity after long in-shelf storage periods of PS due to increased aggregation and presence of bioactive compounds (Murali et al. 2015). Due to the evidence of neurotoxicity when testing microplastics in organism or cells and resulting from human exposure to particulate matter, which microplastics are a part of, there is a need to understand how microplastics could be involved in neurotoxicity in humans, contributing to an increased risk of neurodegenerative disease development.

3.6. Microplastics as vectors of microorganisms and potentially toxic chemicals

Besides particle toxicity, microplastics could also present chemical and biological risk. Monomer and additives may leach from the microplastics matrix inside the organism, exposing the tissues to chemicals such as phthalates and bisphenol A, that are known as endocrine disruptors – substances that even in very low concentrations interfere with endogenous hormones (Cole et al. 2011). Besides their constituents, the high surface area of microplastics makes them prone to work as vectors to microorganism or chemicals they come in contact with. For instance, persistent organic pollutants (POPs) have been identified in microplastics recovered from the environment, including polycyclic aromatic hydrocarbons (PAHs) and polychlorinated biphenyls (PCBs) (Crawford and Quinn 2017; Frias et al. 2010). When ingested, microplastics could expose organisms to higher concentrations of these potentially toxic chemicals or even potentiate their toxicity. However, contribution of microplastics to the exposure to POPs

seems negligible when compared to the intake from food and water (Bakir et al. 2016). Nonetheless, human health impacts of monomers, additives and degradation products migrating from plastics and microplastics should be further explored (Rodrigues et al. In Press).

Microorganisms may also colonize the surface of microplastics, including *Vibrio* spp. (Kirstein et al. 2016). In this case, microplastics could act as vectors, delivering microorganisms to the tissues, protecting them from the immune system and creating tissue damage that may favor infection. Furthermore, microplastics altered and increased the diversity of the gut microbiome in soil organisms (*Folsomia candida*) (Zhu et al. 2018). The same effect could happen in human after ingestion of a significant amount of microplastics. Alterations to the gut microbiome could lead to adverse effects, such as the proliferation of harmful species, increase in intestinal permeability, and endotoxemia (West-Eberhard 2019). Nonetheless, negative effects from the release of chemicals or microorganisms adsorbed to microplastics will be highly dependent on the types associated with ingested particles, the clearance time and translocation of vector microplastics, the release rate and extent of the contaminant, and its translocation and noxious effects in human tissues.

4. Future directions of research on microplastics in human health.

Even though there is currently no evidence of widespread human health risk, there is a need to understand human exposure, specially to smaller microplastics (<10 μm) (SAPEA 2019). Modelling of polystyrene behavior leads to the estimation of human threshold concentrations in the range of 5.1 to 53.3 mg g^{-1} of body weight (Yang et al. 2019), corresponding to an estimated minimum human exposure to induce effects in the

most sensitive biomarkers of more than 7.7 g, considering the average human liver, or to 357 g, considering the average adult (70 kg), unlikely to occur. This conclusion is also supported by other reports, where ingestion of microplastics is put in perspective regarding environmental exposure to other (more abundant) additives and contaminants and the need for further research is stated based on the current lack of information for risk assessment (SAM 2018, Group of Chief Scientific Advisors 2018). Risk assessment is also being restricted by the complexity of microplastic toxicology, their interaction with other contaminants (e.g. metals) or the inclusion of their health effects in other contaminant categories (e.g. particulate matter). Furthermore, plastics used in toxicology assays are often very different from their environmental counterparts in terms of surface properties, weathering and adsorbed chemicals and organisms, leading to inaccurate conclusions. Thus, the risks of microplastics to public health must be further explored, including testing not only environmentally relevant concentrations but also environmentally relevant microplastics properties.

Humans are exposed to microplastics by inhalation, ingestion and dermal contact, potentially leading to chronic inflammatory lesions (**Figure 2**). Human exposure to microplastics can be determined by estimations, such as those provided for the inhalation (Prata 2018; Vianello et al. 2019) and ingestion of microplastics (Cox et al. 2019). Determination of human exposure can also be achieved, with higher precision, by adaptation of typical diagnostic procedures. Gastrointestinal exposure may be determined by analyzing stool samples, while bronchial lavages may provide information on the respiratory system. Biopsies, tissues obtained from autopsies and blood may be used in the histological determination of microplastics. However, development of methods of identifying plastics in these samples are still required, possibly involving the digestion of tissues or staining of histological sections. These

methods will always be limited by the tissue availability, as well as the potential contamination of the samples (such as the widespread use of plastic materials in medicine). Human health effects of microplastics may be determined by studies in animal models, such as mice or rats, or in cell cultures, also considering different endpoints. Observational studies relating exposure with negative outcomes may be attempted but will possibly require large samples and careful consideration for cofounder effects.

5. Conclusion

Growing consumption of plastic, allied to its persistent nature, is leading to the increasing exposure of humans to microplastics. Under conditions of high concentration or high individual susceptibility, microplastics may cause inflammatory lesions, originating from the potential of their surface to interact with the tissues. The increasing incidence of neurodegenerative diseases, immune disorders and cancers may also be related to the increased exposure to environmental contaminants, including microplastics. However, knowledge on the effects of environmental exposure to microplastics on human health is limited, leading to high uncertainties that should not be translated in alarmism even when applying the precautionary principle. With the predicted increase of these synthetic materials in our environment, more studies are needed to fully understand the risk of microplastics to human health, requiring knowledge on human exposure, pathogenesis and effects.

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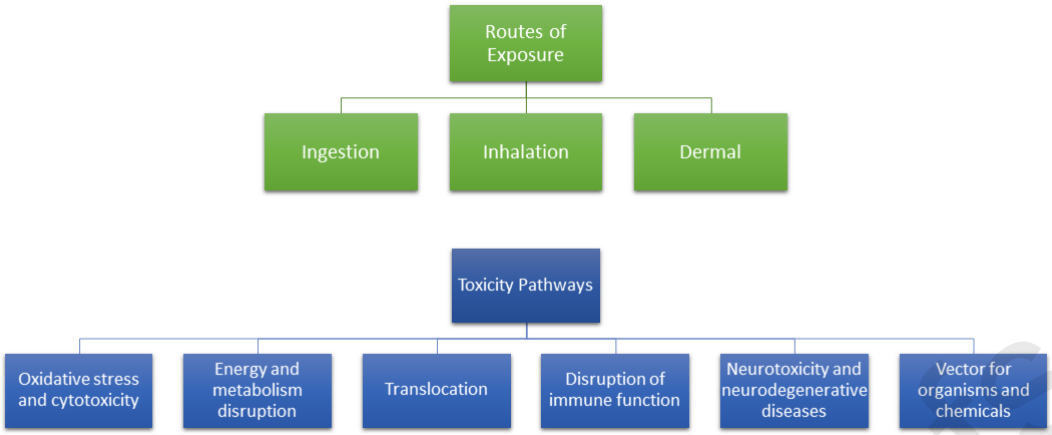

Figure 1. Potential routes of exposure and toxicity pathways for microplastics in the human body.

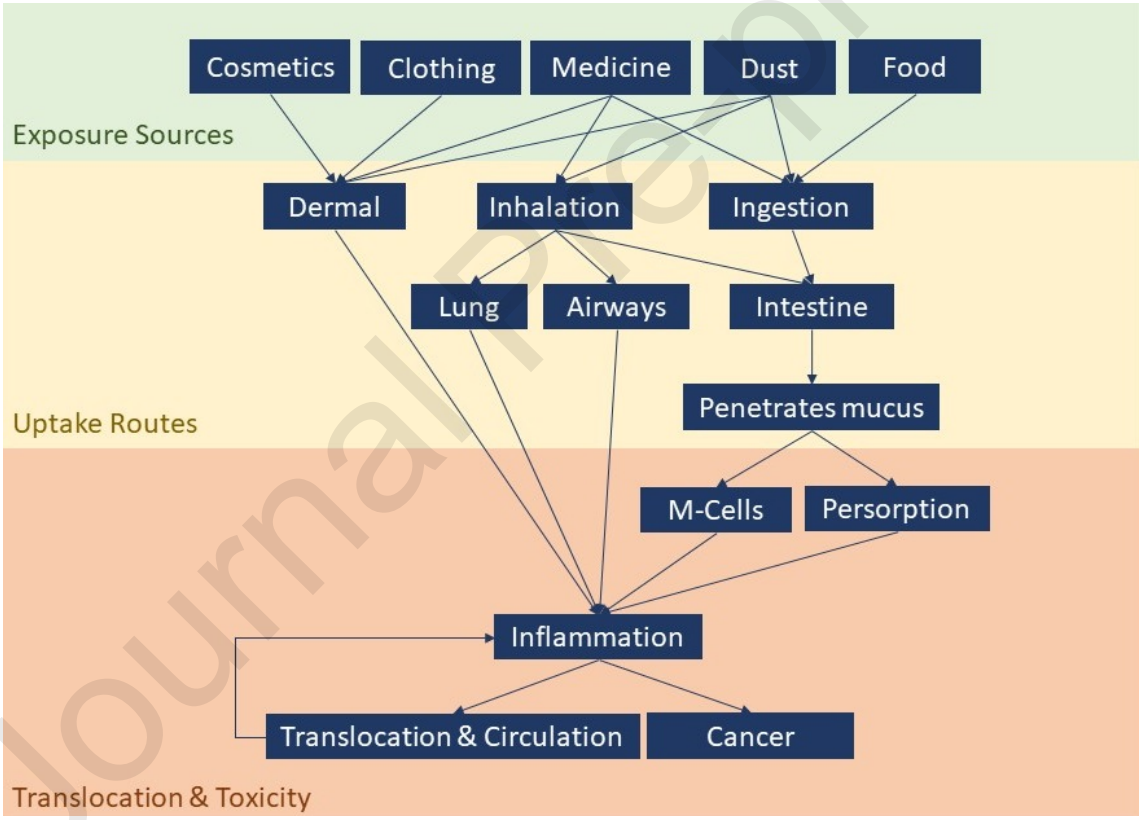

Figure 2. Potential pathways of exposure and particle toxicity for microplastics in the human body.

- Human are environmentally exposed to microplastics
- Routes of exposure include ingestion, inhalation and dermal contact
- Toxicity may result from particle toxicity, oxidative stress and inflammation
- Inflammation may lead to neoplasia and increased translocation of particles
- Microplastic may be involved in the disruption of immune function and neurotoxicity