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Review Paper

Potential Biological and Health Effects of Nanoplastics

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Abstract

Due to the increased use of plastic products, environmental plastic pollution is rapidly increasing, leading to a rise in microplastic and subsequently nanoplastic pollution. In recent years, increase in nanoplastic load has become a serious concern toward the safety of the environment and human health, especially when the ecotoxicological effects of plastic nanomaterials are overwhelmingly unknown. The data obtained from a limited number of studies indicate that hydrophobic nanoplastics can pass through biological membranes and get accumulated in the cells and tissues of various organisms including humans. Studies also indicate that nanoplastics are capable of causing biological disfunctions, but with the insufficient data available, it is a daunting task to adequately address or assess the extent and severity of such disfunctions. Suspected biological effects of nanoplastics include the uptake of nanoplastics by a wide range of tissues, impaired cell signaling, altered metabolism, endocrine dysfunction, developmental defects and possible genotoxicity. Due to their extremely small size, it is enormously difficult to estimate the total volume of nanoplastics present in the environment, and although various studies indicate that these nanomaterials are hazardous, with the current state of insufficient experimental data, it is highly impractical to draw an inference on the ecological distribution, bioavailability, and toxicological effects of these nanoparticles.

Keywords: Plastic pollution, microplastics, nanoplastics, human ingestion, bioavailability, distribution, toxicity.

1.0 Introduction

Plastics are synthetic organic polymers and are widely used in packaging and various manufacturing industries to produce a wide range of consumer products. The use of plastic commodities results in about 79 percent of the produced plastics returning to the environment as waste (Rhodes, 2018). Plastics are not easily degradable substances and accumulate in the environment quite rapidly thus becoming a major polluter. The status of global plastic pollution is a crucial problem which demands an immediate global attention.

In our previous communications, we reviewed the impacts of plastic pollution on oceans and land, and the potential problems associated with the accumulation of plastic waste and microplastics in both aquatic and terrestrial environments (Zaman *et al.*, 2019a; 2019b). Gigault *et al.* (2018) have observed that nanoplastic particles range from 1-1000 nm, have colloidal behaviors, and are produced from the degradation and manufacturing of plastic objects. However, the upper size limit of "nanoplastics" is debated as other studies set the upper size limit at 100 nm or 1000 nm (Gigault *et al.*, 2018; Stapelton, 2019).

Naturally produced or "incidental" nanoplastics come in different shapes, sizes and compositions, while the manufactured or "engineered" nanoplastics that are produced for various commercial uses, such as personal care products, biomedical, agricultural, automobile components, and laboratory uses, are synthesized with the desired size, composition, and shape to make use of their physical and chemical properties (Stapelton, 2019).

The presence of nanoplastics is ubiquitous; however, the amount of nanoplastics in the environment is

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unknown. In recent years, the existence of nanoplastics in the environment and the concern with their potential ability to produce adverse biological and health effects, have attracted increased attention in the scientific community. Therefore, the exposure to nanoplastics and their biological and health effects are emerging research areas, and not enough information is currently available on the interactions of nanoplastics with biological structures and their toxicological effects. In this review, we will provide an overview of nanoplastics and their biological impacts based on currently available information.

2.0 Sources of Nanoplastics

As mentioned earlier, incidental nanoplastics are produced when microplastics are degraded by various environmental and biological factors. Usually, microplastic degradations occur when they are exposed to solar radiation, ocean salts, waves, hydrolytic (bond weakening) and other chemical or physical factors. Biodegradation of microplastics may occur by microbial actions. Extracellular enzymes produced by bacteria can break down polymer chains to produce nanoplastic materials (Shen *et al*., 2019).

When microplastics are broken down into nano-sized particles (nanoparticles), the physical and chemical characteristics may change significantly due to changes in surface area to volume ratios (Lehner *et al*., 2019). Since nanoparticles come in different shape, size and compositions, it is difficult to predict their physical or chemical properties and their interactions with the environment.

Engineered nanomaterials are commercially produced due to their demand by the consumer industry (Kessler, 2011; Stapelton, 2019). Commercial synthesis and use of various nanomaterials (such as copper, siver and gold) began in the 1980s (Kessler, 2011). Such nanomaterials are designed to deliver desired advantages with their physical, chemical, and biological properties in manufacturing consumer products. They are used in a wide range of products including agriculture, medicine, sunscreens, cosmetics, food packaging, dietary supplements, etc. (Kessler, 2011; Hernandez, 2017). Nanoplastics are hydrophobic in nature and due to their small sizes, nanoplastics can be transported into cells through the cell membrane, posing unique risks as they may have the potential to cause cellular toxicity (Yousefi and Tufenkji, 2016).

3.0 Routes of Exposure

Because of their nano-size, it is difficult to measure the quantity of nanoplastics in the environment. Studies suggest that the main exposures of living organisms to nanoplastic materials occur through the food chains (Cedervall *et al*., 2012; Alimi, 2018; Kovats, 2019). Waterbodies such as rivers and oceans contain a huge load of plastic contaminants. As a result, nanoplastics are widely distributed in the aquatic environment. Due to their minute size, nanoplastics are ingested and bioaccumulated in aquatic organisms (Bhattacharjee *et al*., 2014; Bhargava, 2018), causing biological damage to affected organisms. This opens the possibility of incorporating and tropic transferring nanoplastic materials to higher organisms through the food web (Cedervall *et al*., 2012; Alimi, 2018). Cedervall *et al*. (2012) reported that commercially manufactured polystyrene nanoparticles could be transported from algae to zooplankton and fish, supporting the view that microplastics could be transported through aquatic food chains.

Principal sources of human exposures to micro and nanoparticles could include: contaminated food, drinking water, and inhalation (Van Cauwenberghe and Janssen, 2014; Santillo *et al*., 2017; Gasperi *et al*., 2018; Revel *et al*., 2018; Cox *et al*., 2019; Koelmans *et al*., 2019; Williams, 2019). Food and water packaging industries, wastewater and water treatment plants have the potential to contribute significantly to such nanoplastic exposures (Cotruvo, 2020). Cosmetic and skin care products also may provide significant exposure to nanoplastic materials (Hernandez *et al*., 2017) (Figure 1).

4.0 Biological Significances of Nanoplastics and Human Health

Risk assessment criteria for a hazardous substance includes: (1) Exposure Assessment: which evaluates the risk associated with the exposure to the substance, (2) Hazard Identification: which evaluates the toxic effects posed by the substance, (3) Hazard

Characterization: which evaluates the dose-response in relation to toxicity, and (4) Risk Characterization: which evaluates the relationship between the hazardous dose and exposure (Meek *et al*., 2011). The science of nanoplastics is in its early stages of development, with more unknowns than knowns. Therefore, not enough data is available to adequately evaluate these risk assessment benchmarks. How these nanomaterials interact with biological molecules is subject to further intense investigations, and with so inadequate current information on the formation, bioavailability and toxicological effects of nanoplastic materials and their route to living organisms, it is extremely challenging to accurately assess their impacts on biological systems (Figure 1).

Miao *et al*. (2019) studied the effects of polystyrene nanoplastics on freshwater biofilms, which are vital for production and nutrient cycling in aquatic ecosystems. They observed that in high concentration nanoplastics significantly decreased chlorophyll content and some enzyme activities, suggesting a negative effect on carbon and nitrogen cycles of biofilms. Bhattacharya *et al*. (2010) studied physical adsorption of polystyrene nanosized plastic beads into *Chlorella* and *Scenedesmus*. They observed that the positively charged nanoplastics bind more strongly to algae as compared to negatively charged nanoplastics and affected algal photosynthesis significantly more. Ng *et al*. (2018) reported the accumulation and ingestion of nanoplastics in plants with the possibility that nano-size nanoplastic could cross the biological membrane barriers.

Studies with various organisms indicated that nanoplastics can pass through the cell membrane and invade vital organs. Kashiwada (2006) reported tissue uptake and distribution of nanoplastics in medaka. Nanoplastics were detected in yolk, gills, blood, gallbladder, liver, testis and brain, suggesting that nanoplastics are capable of crossing the blood-brain-barrier. Kashiwada also reported that in high concentrations nanoplastic particles exerted lethal toxicity in medaka. Cedervall *et al*. (2012) demonstrated that microplastic accumulation in fish caused several metabolic disfunctions including weight loss, disrupted fat metabolism, imbalanced blood triglyceride and cholesterol ratio, altered cholesterol distribution in muscle and liver tissues, and an alteration of feeding behavior in affected fish. Nanoplastic particles were reported to be accumulated in brain tissues of fish that feed on zooplankton and triggered toxicological effects (Kovats, 2019). Della Torre *et al*. (2014) reported developmental defects in sea urchin embryos exposed to polystyrene nanoparticles. Presence of

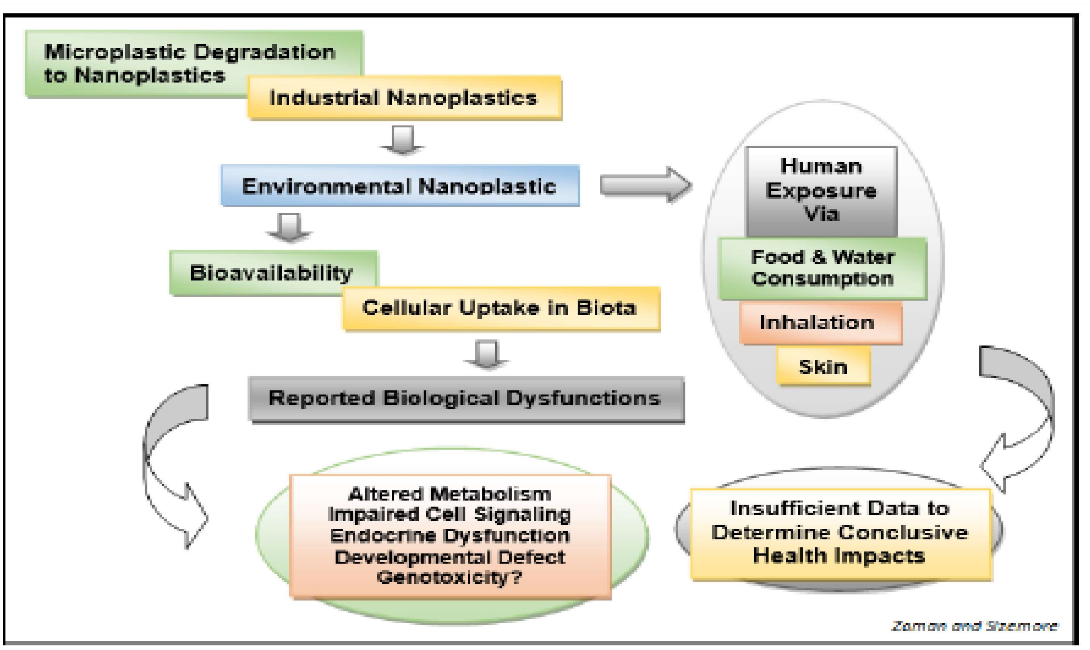

Figure 1: Source, distribution, and pathway of nanoplastic particles in the environment, their toxicity, and possible routes to human body.

nanoplastics also have been identified in the embryonic tissues of zebrafish (Parenti *et al*., 2019; Lu *et al*., 2016). Genotoxic effects of nanoplastics have been reported in brine shrimp (Mishra *et al*., 2019) and daphnia (Zhang *et al*., 2019), indicating exposure to higher doses of nanoplastics could cause mutagenesis.

Chronic exposure to nanoplastic particles is generally considered to be a major concern in that there is a probable cumulative effect from exposure (Wright and Kelly, 2017). In a recent article, Campananle *et al*. (2020) noted that the ingestion of nanoparticles via the intestinal tract could enter the mucosal lymphoid tissue and the circulatory system. The persistence of the nanoplastic particles would induce an inflammatory response that could then cause toxicity. They also noted that inhalation of nanoplastics could also lead to inflammatory results in the lungs, resulting in respiratory distress and even autoimmune disorders.

In *in vitro* studies, nanoparticles particles were shown to impair human lung cell metabolism (Lim *et al*., 2019), increase oxidative stress in human epithelial and cerebral cells (Schirinzi *et al*., 2017) and cause cellular stress and apoptosis in human cells (Della Torre *et al*., (2014). Gopinath *et al*. (2019) reported that proteins in the blood, including albumins and globulins, were absorbed to the surface of nanoplasics causing aggregation of these plastic and protein complexes. Besides blocking blood flow, these complexes could create a toxic effect on both leukocytes and erythrocytes. Since immunoglobulins (antibodies) are in the globulin fraction, the potential interference with antibody-mediated events could be an effect although the authors did not address this point.

5.0 Discussion and Conclusion

Pollution due to large platic products (macroplastics) is more visible and has therefore garnered more attention around the world. However, the breakdown of macroplastics and other plastic commodities via physical or chemical means could result in the transfer of nanoplastic particles to humans. Nanoplasics could be present in everything from toothpaste, shampoo, lipstick, mascara, bottled water and sea food. It is also thought that nanoplastics could be inhaled (Jain, 2019). The effects of nanoplasitcs in other species has indicated gastrointestinal, liver and reproductive toxicity along with neurotoxicity (Chang *et al*. 2020). Although the effects of nanoplastics on human health have not been intensely studied, several other direct or circumstantial evidence suggests that it could be a serious problem.

To extend improved products to the consumers, the chemical and physical properties of plastic materials are often being modified. Such modifications are often achieved by using various additives such as, bisphenol, ethers, phthalates, metals and metalloids. These additives are now considered to be health hazardous and may be responsible for producing carcinogenic and endocrine dysfunctional effects (Ravel *et al*., 2018). Therefore, in evaluating health effects of micro and nanoplastic materials, the effects of such additives should be seriously considered.

Although it is established that nanoplastic particles can cross cell membranes, the cellular or systemic toxicity of these particles is yet to be established. Further studies need to be conducted to determine the ecotoxicological safety of various additives such as Bisphenol S (BPS) and Bisphenol F (BPF) that have replaced Bisphenol A (an endocrine disrupting and possibly a carcinogenic compound used in polycarbonate plastics) and are being widely used in consumer products. Ecotoxicological safety of BPS and BPF are still controversial (Usman *et al*., 2019, Pelch *et al*., 2019).

Studies with the occurrence of nanoplastics in the human food production chain and their potential health effects suggested that the limited amount of available data was not sufficient to predict the potential human toxicity of various organic pollutants absorbed in nanoplastics or from the leaching of their additives (Bouwmeester *et al*. 2015). Other household objects such as cosmetics can also house nanoplastics (Jain, 2020). The gradual accumulation of nanoplastics in the human body is another area that has not been fully addressed. We suggest that studies examining potential toxic effects of nanoplasics on human health should remain a priority to prevent potentially serious consequences in the future.

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