

Hazard Effects and Mechanisms of Action of Microplastics on Health

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Received: July 19, 2024; Accepted: July 26, 2024; Published: July 30, 2024

ABSTRACT

Microplastics, particles smaller than five millimeters, have emerged as significant environmental pollutants, drawing attention due to their widespread distribution in the atmosphere, water, and soil. They enter organisms through ingestion, inhalation, and skin contact, inducing cytotoxicity, tissue damage, and compound health risks. This review systematically examines exposure pathways, health hazards, and mechanisms of microplastics, aiming to inform research on their environmental health impacts.

Keywords: Microplastics, Pollution, Health Effects, Toxic Effects

Introduction

Microplastics refer to particles in the environment smaller than 5 mm. Plastic fibers, particles, or films, the main components include polyethylene, polypropylene, polystyrene, polyvinyl chloride, polylactic acid and polyethylene terephthalate, etc. It is spread throughout the ocean, land and atmosphere, and is a “white pollution” [1]. Microplastics are high-molecular polymers that are difficult to degrade. Nano-scale microplastics can enter the circulatory system through the body’s physical barriers and accumulate in different tissues and organs, directly affecting the normal physiological functions of the body. At the same time, the surface of microplastics can absorb hydrophobic organic pollutants (such as polycyclic aromatic hydrocarbons, polychlorinated biphenyls, and bisphenols A) and metal chemical pollutants (such as heavy metals zinc, lead, nickel and cadmium, etc.), long-term intake can indirectly cause tissue damage such as liver, heart, bone, kidneys, ovary and testis [2-8]. This article discusses the exposure pathways, health hazards and effects of microplastics, the mechanism of action, and other aspects that are reviewed to provide reference for research on the environmental health hazards of microplastics.

Exposure Pathways of Microplastics

Microplastics are widely present in the environment and can enter through many ways the human body, mainly through gastrointestinal ingestion, respiratory inhalation and skin contact. The “Human Microplastics Consumption” report shows that adults consume food every year 39 000~52,000 particles of microplastics are inhaled into the respiratory tract, and the exposure can be as high as 74,000~121 000 particles, and vary according to age and gender [9,10]. Currently, microplastics have been detected in marine life, salt seasonings, and plastic products. It is estimated that the amount of microplastics ingested by Europeans through eating bivalves is approximately 11,000 particles/ (per person per year) [11]. The amounts of microplastics ingested by Europeans and Chinese through salt are respectively 37 particles/ (person-year) and 1000 particles/ (person-year) [12,13]. Microplastics can be released into the air through various ways and then enter the human respiratory system through the respiratory tract. Air sampling based on a human body model, anticipating light activity of a person of adult men inhaling 272 particles of microplastics. Properties such as particle size and density will affect the deposition of microplastics in the respiratory system [14]. Skin is the main physical barrier organ of the human body and was not considered to be the main exposure route to microplastics;

however, studies have found that less than 100nm microplastics can enter subcutaneous tissue through skin wrinkles and then be absorbed by the body, causing oxidative stress in epithelial cells. The toxicity produced should not be ignored [15]. The current understanding of the exposure pathways of microplastics is still very limited. Therefore, future research still needs to conduct a systematic assessment of the pathways and exposure levels of human exposure to microplastics.

Health Hazard Effects and Mechanisms of Action of Microplastics
Microplastic exposure can have toxic effects on the body. First, microplastics the material is not degradable, and their high specific surface area can cause cellular oxidative stress and metabolic disorders, ultimately leading to cell death. Secondly, microplastics, such as nanoparticles, can accumulate in different organs of the body, affecting the circulatory system, immune system and even the nervous system. Finally, microplastics, as carriers, will release various chemicals and microorganisms, indirectly causing health hazards (Figure 1).

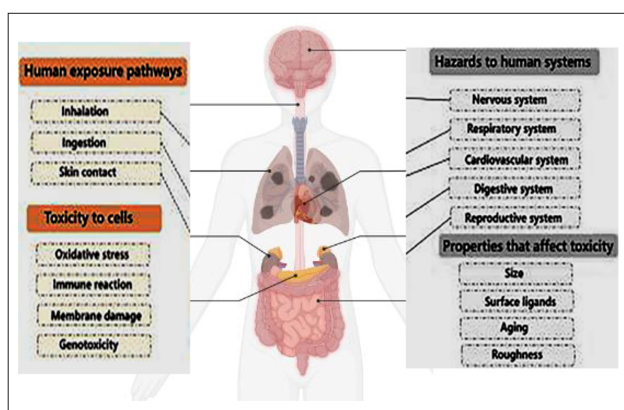


Figure 1: Microplastics accumulate in different organs of the body, and affecting the different body systems

Cytotoxic Effects

Microplastics can enter cells. Because they have a high specific surface area, they can easily interact with substructures inside cells, disrupt cell homeostasis, and cause cytotoxic effects. Microplastics affect the structure and function of cell membranes: Polyethylene microplastics can bind to the hydrophobic core of lipid bilayers to form a network of untangled single polymer chains, thereby changing the structure of cell membranes [16-18]. Microplastics can also inhibit the activity of adenosine triphosphate-binding cassette transporters on cell membranes, leading to abnormal cell material transport functions [19]. Current research suggests that microplastics mainly enter cells through the clathrin-mediated endocytosis pathway, so low temperature or clathrin inhibitors can significantly inhibit their entry into cells [20]. When microplastics enter cells, they will affect the normal physiological functions of the cells. Oxidative stress caused by microplastics is the main cause of decreased cell viability. For example, 10µm Polystyrene microplastics can lead to increased levels of reactive oxygen species in human glioma cells and cervical cancer cells; 25µm Polyethylene microplastics can lead to a significant increase in reactive oxygen species in human glioma cells; 25µm Polypropylene microplastics lead to increased levels of reactive oxygen species in human dermal fibroblasts. Similar to other toxic microparticles, the smaller the particle size of microplastics, the more oxygen the higher the level of chemical stress and cytotoxicity. Microplastics can

cause abnormal expression of intracellular genes. For example, microplastics can up-regulate inflammatory factors. Daughter interleukin-6, interleukin-8 and tumor necrosis factor- α levels but the regulatory mechanism remains unclear [21,22]. Some studies believe 64nm polystyrene microplastics can regulate interleukin-8 equal gene expression levels, but further research is needed to confirm. Microplastics can alter intracellular metabolic water flow. The Microplastic exposure significantly changes the intracellular metabolic profiles of zebrafish and mouse livers in a dose-dependent manner mainly because micro Plastic affects metabolism-related pathways, such as reducing intracellular adenosine triphosphate levels, increasing lactate dehydrogenase activity, and reducing catalase activity [23-25]. In addition, microplastics can also lead to excessive autophagy by inducing endoplasmic reticulum stress (caused by the accumulation of misfolded proteins). Degree, and changes in cell morphology, etc. In summary, microplastics can cause abnormalities in cell structure and function through various pathways, which can then trigger a series of subsequent biological effects.

Tissue and Organ Damage

After exposure, microplastics tend to accumulate in organs such as the intestines, liver, and lymphoid tissues. As the particle size decreases, they enter the circulation system and exert toxic effects on the body. Mice exposed to microplastics of different particle sizes 4 4 after weeks, microplastics accumulate in the intestines, liver, and kidneys, and 5µm the accumulation level is significantly higher than the 20µm accumulation level [26-29]. In experiments on rats exposed to polystyrene microplastics, polystyrene microplastics were detected in the lungs, testicles, spleen, kidneys and heart, in addition to the gastrointestinal tract. Microplastics can also affect the neurobehavioral of *Caenorhabditis elegans* and rats, suggesting that they may be present in the nervous system [30-32]. The damage caused by microplastics to tissues and organs depends on various factors such as their type, size and charge, and the toxic effects produced are relatively complex.

The gastrointestinal tract, as the main organ exposed to microplastics, can exhibit multiple toxic effects. Microplastics can cause intestinal flora imbalance. Microplastics exposure alters the structure and abundance of gut microbiota in subjects across multiple research models, such as reducing the abundance of Firmicutes and increasing the abundance of Proteobacteria and Actinobacteria [33-35]. Microplastics can cause intestinal histological damage. Microplastics cause intestinal villi breakage and intestinal epithelial cell death in zebrafish Death [36]. In experimental studies in mice, it was also observed that microplastics inhibit the gene mucin secretion related to mucin and Kruppel the expression of similar factors leads to the reduction of colonic mucin secretion, thereby causing damage to intestinal barrier function, and damage to the gastrointestinal barrier function will lead to a series of subsequent pathological processes.

Microplastics can cause vascular occlusion after entering the circulatory system, increase blood coagulation and hematotoxicity and then reach different organs to produce toxic effects. Exposure to microplastics can cause metabolic disorders in the body [37-39]. The liver, as the main metabolic organ of the human body, is also one of the main accumulation organs

of environmental pollutants [4,40,41]. Microplastics cause histological liver damage outside, and can also cause changes in liver metabolic profile, including increased fatty acid metabolism and decreased amino acid metabolism, causing a decrease in triacylglycerol and total cholesterol and an increase in pyruvate, by altering bile acid synthesis genes for cholesterol 7 α -Levels of hydroxylase and transporter genes bile salt efflux pump protein up regulate total bile acids. The kidney, as the main excretory organ of the human body, is also another major accumulation organ of microplastics. Studies have shown that polystyrene microplastics enter renal cortical cells through endocytosis and diffusion, accumulate around the nucleus, affect cell viability, cell metabolism, and cell cycle, and ultimately lead to renal function damage [42-44]. Microplastics currently the effects of exposure on renal function are still poorly studied at the in vivo level.

Microplastics can cause local or systemic immune responses in the human body. Microplastics as particulate matter in the air, materials may cause auto antigen exposure and antibody production, leading to autoimmune diseases by inducing cellular oxidative stress, releasing immune factors, and activating immune cells [45-48]. Studies have shown that exposure to microplastics can cause immune suppression in the mussels system and tissue-dependent immune responses [49]. In mouse models, researchers also observed that microplastic exposure resulted in low activation of dendritic cells, helper T lymphocyte suppression and effector Lymphocytes produced, thereby producing an immunosuppressive effect [50]. However, these effects have not yet been verified in humans. Microplastic exposure affects neuronal function, linked to neurodegeneration the occurrence and development of the disease are closely related. Researchers evaluated the neurotoxicity of microplastics to *Caenorhabditis elegans* from different angles, the results show that exposure to microplastics will accelerate the frequency of head movements and body bending of nematodes, and increase the crawling speed, suggesting that it may cause excitotoxicity to the locomotors behavior of organisms; microplastics can damage cholinergic neurons and γ -amino butyric acid neuron, but does not cause changes in dopamine neurons, suggesting possible biological toxicity of selective neurodegeneration. Exposure to microplastics reduces acetylcholinesterase activity in the brain of European sea bass, causing oxidative stress, increasing lipid peroxidation levels, and increasing anaerobic respiratory supply microplastics also reduce their swimming speed [51,52]. Furthermore, exposure to polystyrene microplastics produced adverse effects on neurotransmission in mice, including increased acetylcholinesterase activity and altered serum neurotransmitters. Although the results of microplastics changing acetylcholinesterase activity in sea bass and mouse models are inconsistent, they both indicate that microplastics can affect the body's neurotransmission process. In vitro experiments using neuronal cells as research subjects have shown that 40~70nm Polystyrene microplastics can induce cell type, concentration and time-dependent changes in cytotoxicity and metabolic activity [53]. These exposure experiments on model organisms or neuronal cells show that microplastics are one of the causes of the occurrence and development of neurodegenerative diseases, but the reasons require further study. Microplastics are reproductively toxic. In the *Caenorhabditis elegans* reproductive model, microplastic

exposure reduces embryo number and size. Polyvinyl chloride microplastics can be distributed in the reproductive system of rats fed a high-fat diet after ingestion system, causing estradiol levels to increase in female mice and decrease in male mice, as well as causing compensatory enlargement of the gonads in male rats. The in vitro placental perfusion model shows that 240 nm polystyrene microplastics can pass through the placenta barrier and be passed between mother and baby [54-56]. Experiments on microplastic exposure in pregnant and lactating female mice demonstrated that the impact of microplastics on mice has intergenerational effects [57,58]. However, differences in types of microplastics and model organisms will affect microplastics. However, current research supports that microplastics can cause toxic effects on tissues and organs, ultimately leading to the occurrence and development of various diseases.

Compound Exposure Effect

In addition to particle toxicity, microplastics also have compound exposure health hazard effects. The microplastic matrix contains phthalates and bisphenols A and endocrine disruptors, which can interfere with the production of endogenous hormones. The high specific surface area of microplastics makes it easy to become a carrier of microorganisms or chemical substances exposing the body to microplastics and other toxic substances at the same time, resulting in compound exposure toxicity, and the resulting health hazard effects are highly dependent on the characteristics of microplastics, including the amount of particles ingested, the removal time and displacement of carrier microplastics, and the release of pollutants rate and extent, as well as the translocation and toxic effects of microplastics in tissues [59-61]. Of course, the harmful effects of microplastics as carriers are insignificant compared to the toxic effects of microorganisms or chemicals [62-64]. Nonetheless, the effects on human health of monomers, additives and degradation products attached to the surface of microplastics still need to be further explored [65,66].

Problems and Prospects

The growing consumption of plastics and the persistent nature of plastics have led to there are increasing opportunities for humans to be exposed to microplastics. Although there is currently no direct evidence that microplastics pose widespread harm to human health, it is necessary to understand their potential toxicity. The "Scientific Advice Mechanism" released by the European Union in 2017 pointed out that there are limitations in the quality and methods of research on microplastics on human health. It is necessary to understand the exposure dose and accumulation site of microplastics in human models to better conduct a toxicological effect assessment [67]. The complexity of the toxicological effects of microplastics themselves and the compound effects of other pollutants have limited research on their health effects. In addition, the surface characteristics, weathering degree, adsorbed chemicals and organisms of microplastics used in toxicological testing are often very different from the microplastics exposed to the real environment, leading to inaccurate conclusions. In the future, it is still necessary to comprehensively and accurately evaluate the harm of microplastics to human health in real environments.

Although the impact of microplastics on human health can be explored through toxicological research methods such as its molecular structure in vitro experiments, in vivo animal

experiments or disease models, these studies have limitations and cannot be directly extrapolated to the human body. Most of the studies reviewed in this article are experimental articles, and the final impact on human health requires epidemiological investigation in population cohorts. In short, research on the harmful effects of microplastics in the environment on human health is still in its infancy, and more comprehensive and systematic research is still needed.

Credit Authorship Contribution Statement

Funding: Funding not available.

Declaration of Competing Interest: The authors declare that there are no conflicts of interest

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