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Microplastics in Environmental Setting: A Review on Sources, Exposure Routes and Potential Toxicities on Human Health

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ABSTRACT. Microplastics are pervasive throughout various ecosystems, but the potential risk of exposure to humans remains uncertain. Microplastics are plastic particles measuring less than five millimeters, and they infiltrate ecosystems via soil, water, atmosphere and living organisms where they are potentially impacting human health. The sources, routes of exposure, and potential effects on human health are reviewed in the current paper. Microplastics are regularly identified in both environmental and human specimens. They can be found in roadside dust, indoor air, fresh and surface water, beverages, honey, sugar, and other dietary items. Microplastics can enter the human body through the skin, food, or inhalation and may have negative health impacts. A significant challenge in assessing the potential health risks posed by microplastics is the lack of data regarding human exposure. There is an urgent need for effective analytical instruments capable of sampling, isolating, detecting, quantifying, and characterizing microplastics. The objective of the paper is to summarize the literature on the sources, distribution, route of exposure and the potential toxicities of microplastics and to identify the research gap for the future work. We searched for hundreds of papers related to microplastics from 2013-2023. We then screened them for inclusion, evaluated the quality of the study, extracted the data and conducted the data analysis. We provide a summary of the harmful effects of microplastics on animals, organoids, and cell models used in experiments. Microplastics have been linked to immunotoxicity, neurotoxicity, metabolic disorders, and reproductive toxicity. Finally, we provide future perspectives on the prevalence, characterization, fate, and breakdown of microplastics as they are needed for gaining a comprehensive understanding of microplastics. This review provides a concise overview of the sources, pathways through which humans are exposed to microplastics and potential toxicity effects of microplastics.

Keywords: Microplastics, Sources, Exposure routes, Toxicity

INTRODUCTION

Plastics have a global presence, with the annual production of plastic products has experienced a substantial increase over the past approximately 65 years, resulting in the production of a staggering 6,300 million metric tons (Geyer et al., 2017). Polypropylene (PP), polyethylene (PE), polyethylene terephthalate (PET), polystyrene (PS), and polyvinyl chloride (PVC) are the principal polymers that are commercially accessible (Cheung et al., 2018). Due to their affordability, adaptability, long-lasting properties and robustness, plastics find extensive application in diverse fields, including automotive, construction, machinery, healthcare, aerospace, packaging, and agriculture (Hu et al., 2019). During their use, plastics undergo processes like crushing, splitting, and degradation, leading to the formation of small fragments or particles.

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Microplastics are tiny plastic fragments and particles that measure less than five millimeters in size. Meanwhile, nanoplastics are the term used for particles with a diameter smaller than 1 μm (Kasmuri et al., 2022; Li et al., 2021). Microplastics do, in fact, come in a variety of sizes, ranging from a few microns to a few millimeters. Microplastics can originate from various sources, and they can be categorized into two types: primary microplastics and secondary microplastics (Laskar & Kumar, 2019). Primary microplastics are tiny plastic particles that are intentionally produced and used in various products and applications (Wang et al., 2019). Primary microplastics are produced as tiny plastic particles or fibers for particular uses, in contrast to secondary microplastics, which are the byproduct of the breakdown of larger plastic objects. The presence of primary microplastics in the environment can have adverse effects on ecosystems and wildlife. Some common sources and examples of primary microplastics are microbeads (added to personal care and cosmetic products), microfibers (shed from synthetic textiles like polyester and nylon when they are washed), pellets or nurdles (raw material in the manufacturing of various plastic products) and powdered plastics (additives or fillers in products like paint, coatings, and automotive parts) (An et al., 2020; Gouin et al., 2015). Secondary microplastics are tiny plastic particles that result from the breakdown of larger plastic items, either through physical processes like weathering, fragmentation, and UV radiation or through chemical processes like degradation due to exposure to environmental conditions (Hale et al., 2020). These secondary microplastics are distinct from primary microplastics, which are manufactured as small plastic particles for specific purposes, such as microbeads in cosmetics or nurdles (pre-production plastic pellets). Secondary microplastics can originate from various sources such are tire wear particles, paint and coating erosion, microplastic fragmentation and synthetic fiber shedding (Hanun et al., 2021; Lusher et al., 2017). Figure 1 shows the sources of microplastics from primary and secondary types.

Microplastics can be distributed throughout various environmental compartments, including water bodies, soil, air, wildlife and organisms. Microplastics are commonly found in oceans, seas, rivers, lakes, and even in freshwater sources (Andrady, 2017; Peng et al., 2020). They can be transported by water currents and can accumulate in aquatic ecosystems, posing risks to marine life (Auta et al., 2017). Microplastics can also be found in soil, either directly from the application of plastic-based agricultural products or indirectly as they settle from the atmosphere (Campanale et al., 2022; Koutnik et al., 2021). Microplastics are also susceptible to entering both soil and water through processes like wind dispersal, rainfall, surface runoff, and atmospheric deposition where their environmental impact is extensive and significant (Bigalke et al., 2022; Kallenbach et al., 2022; Sa'adu & Farsang, 2023). Microplastics can become airborne and be transported through the atmosphere. They can settle in various terrestrial and aquatic environments, including urban areas (Bigalke et al., 2022; Sridharan et al., 2021). Furthermore, microplastics have been discovered in a wide range of organisms, from small zooplankton to larger marine animals, and even in the tissues of terrestrial animals (Issac & Kandasubramanian, 2021). This can occur through ingestion or through the transfer of microplastics up the food chain (Botterell et al., 2019).

Because of the possible effects on the ecosystem and human health, the spread of microplastics in the environment is a developing issue. The field of toxicological research on microplastics is growing quickly. According to experimental results, exposure to microplastics causes a wide range of detrimental consequences, including neurotoxicity, immune system reactions, metabolic disruptions, oxidative stress, and toxicity to the reproductive and developmental systems

(Li et al., 2023; Sangkham et al., 2022). However, due to limitations in existing technological methodologies, comprehensive study is lacking in understanding the absorption, metabolism, migration, transformation, and accumulation of microplastics. Thorough research is missing in understanding the absorption, metabolism, migration, transformation, and accumulation of microplastics due to limitations in current technical approaches. This review provides a concise overview of the sources, pathways through which humans are exposed to microplastics, health hazards and toxicity effects of microplastics.

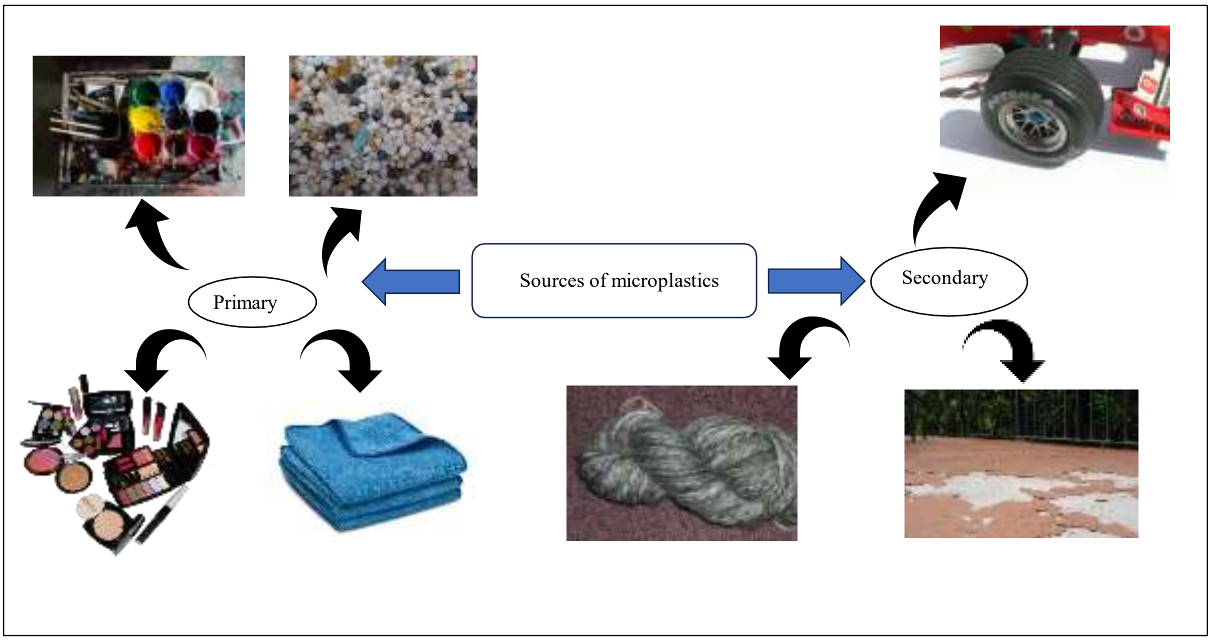

Figure 1. Sources of microplastics from primary and secondary types

SOURCES OF HUMAN EXPOSURE TO MICROPLASTICS

Table 1 compiles data from recent studies, summarizing the documented levels of microplastics found in diverse human exposure sources, including roadside dust, indoor air, fresh and surface water, beverages, honey, sugar, and other dietary items. In research conducted by Alam et al. (2019), microplastic distribution in surface water and sediment river around slum and industrial area were discovered. Analysis of river water samples revealed that the mean microplastic concentration, along with its standard deviation, stood at 5.85 ± 3.28 particles per liter of river water. Meanwhile, the average concentration of microplastics in sediment samples was 3.03 ± 1.59 microplastic particles per 100 g of dry sediment. A study by Yuan et al. (2019) indicated that the presence of microplastics in various environmental zones within Poyang Lake, which is China's largest freshwater lake. The findings revealed that microplastic abundance ranged from 5 to 34 items per liter in surface waters, 54 to 506 items per kilogram in sediments, and 0 to 18 items per individual in wild crucians (*Carassius auratus*). The spatial distribution of microplastics in Poyang Lake exhibited significant heterogeneity, with the greatest abundance observed in the central area of the lake for surface waters and in the northern region for sediments. Meanwhile, a study conducted in Lake Hovsgol, Mongolia by Free et al. (2014) indicated that there was pelagic microplastic pollution that came from consumer goods.

Research findings have documented the existence of microplastic particles in indoor air within urban environments and further enhanced by the detection of microplastics in street dust. The rise in the annual consumption of plastics for diverse applications has resulted in an uptick in the presence of microplastic particles in various settings, including indoor environments. High concentration of microplastics is present in indoor environment of buildings with different applications in Bushehr and Shiraz cities, Iran which pose high exposure risk to different age groups (Kashfi et al., 2022). Furthermore, microplastics were detected in the atmosphere, with indoor air (3.3 ± 2.9 fibers and 12.6 ± 8.0 fragments m^{-3}; mean $\pm$ 1 SD) containing double the amount found in outdoor air (0.6 ± 0.6 fibers and 5.6 ± 3.2 fragments m^{-3}) (Gaston et al., 2020). Indoor environments can accumulate microplastics from a variety of sources such as synthetic fabrics shedding fibers, microbeads in personal care products, dust from outdoor microplastic pollution being tracked inside, and even from the degradation of larger plastic items within the home. Plus, indoor air circulation can sometimes trap microplastics, leading to higher concentrations compared to outdoor environments where they can disperse more readily (Yang et al., 2021). Several other studies also indicated the abundance of microplastic in indoor dust (Abbasi et al., 2022; Aslam et al., 2022; Bahrina et al., 2020; Kacprzak & Tijing, 2022; Nematollahi et al., 2022; Peng et al., 2023; Zhu et al., 2022). Microplastic pollution in the road dust of Chennai was observed by Patchaiyappan et al. (2021) where the mean concentration of microplastic was calculated to be 227.94 ± 91.37 per one hundred grams of street dust sample which 92.46% of them were fragments. According to research done on roadside dust in rural and urban Victoria, Australia, the mean concentration of microplastic changed between two different seasons between 20.6 and 529.3 items per kilogram (based on dry weight), mostly made up of fibers and objects smaller than one millimeter. Cotton and cellulose were the most common non-plastic materials, making up 27%, while polyester and polypropylene were the most common polymer categories, making up 26% (Su et al., 2020).

The increasing accumulation of microplastics in the environment has raised substantial concerns regarding human exposure to these particles through food consumption. Microplastic presence was identified in nine out of eleven samples taken from commercial marine fish species in Malaysia. Among the detected plastic polymers, polyethylene is the most prevalent (Karbalaei et al., 2019). A study about microplastic contamination of packaged meat indicated that food products contain XPS microplastics (MP-XPS) at concentrations varying between 4.0 and 18.7 MP-XPS per kilogram of packaged meat. Based on analysis, it appears that the XPS trays are most likely the source of these microplastics. These particles can be cooked before eating because they are difficult to remove with common washing techniques. Nevertheless, it remains uncertain, based on current scientific literature, whether there exists a potential human health risk associated with the ingestion of MP-XPS (Kedzierski et al., 2020). The study of abundance of microplastic in mostly consumed fruits and vegetables from Turkey by Aydin et al. (2023) suggested that a collective count of 210 particles (with an average of 2.9 ± 1.6 particles per gram) was identified across all the samples. The samples are cucumber (*Cucumis sativus*), potatoes (*Solanum tuberosum*), tomato (*Solanum lycopersicum*), pear (*Pyrus communis*), apple (*Malus domestica*) and onion (*Allium cepa*). The investigation of microparticles in five brands of commercial sugars from different supermarkets in Dhaka, Bangladesh revealed that microplastics-like particles were identified in all analyzed samples (Afrin et al., 2022). On average, there were 343.7 ± 32.08 plastic particles per kilogram of sugar, with a notable trend indicating a higher occurrence of microplastics measuring less than 300 µm. In general, microfibers were the most common, and the primary colors observed among microplastics were black, pink, blue, and brown.

Table 1. Sources, chemical compositions, sizes and locations of commonly found microplastics

Sources	Location	Abundance	Size	References
Surface water	Ciwalengke River, Indonesia	5.85 ± 3.28 items/ L	50–100 µm	(Alam et al., 2019)
Freshwater	Lake Hovsgol, Mongolia	20,264 particles km^{-2}	0.333– 0.999 mm	(Free et al., 2014)
Coastal sediment	Macao	259 and 1,743 items/L	26 µm–11 mm	(Bashir et al., 2021)
Marine fish	Malaysian market	-	2600 ± 7.0 µm	(Karbalaei et al., 2019)
Street dust	India	227.94 ± 91.37/100 g	-	(Patchaiyappan et al., 2021)
Atmospheric fallout	Vietnam	1801.2 particles m^{-2}	-	(Thuong et al., 2020)
Roadside dust	Australia	20.6–529.3 items kg-1	-	(Su et al., 2020)
Indoor air	Shiraz, Iran	90.8 items/mg	100–1000 µm	(Kashfi et al., 2022)
Indoor air	California, USA	0.4 ± 20.6 n/m^3	641–810.7 µm	(Gaston et al., 2020)
Plastic packaging	Australia	0.46–250 MPs/cm	-	(Sobhani et al., 2020)
Packaged meat	France	0–18.7 MP-XPS/kg	300-450 µm	(Kedzierski et al., 2020)
Fruit and vegetable	Turkey	3.63 ± 1.39 particle g^{-1}	-	(Aydın et al., 2023)
Sugar	Dhaka, Bangladesh	343.7 ± 32.08 particle kg^{-1}	-	(Afrin et al., 2022)
Chicken meat	Pakistan	7.8 ± 12.1 MPs/crop	-	(Bilal et al., 2023)
Foodplain soils	German	0 - 55.5 mg kg^{-1}	-	(Weber et al., 2022)

ROUTE OF EXPOSURE TO MICROPLASTIC FOR HUMAN

Since microplastics are widely found in the environment and have been shown to have harmful effects, they pose a risk to human health. Understanding the potential pathways for human exposure to microplastics is critical. Common avenues of exposure include ingestion, inhalation, and skin contact (Yuan et al., 2022). Figure 2 shows the exposure routes of microplastics to get into the human body via inhalation, ingestion and dermal.

INGESTION

Microplastics have the potential to contaminate drinking water, build up within the food chain, and emit harmful chemicals that could be associated with health issues, including specific forms of cancer. Out of all the ways of exposure, the consumption of microplastics was considered the primary pathway (Sun & Wang, 2023). Because of the high concentration of microplastics in the ocean (reaching up to 102,000 particles per cubic meter), seafood has been identified as a significant source of microplastic ingestion (Rahman et al., 2021) . Despite a recent report from the World Health Organization (WHO) that did not find conclusive evidence of harmful effects caused by microplastics in drinking water, the long-term consequences of continuous exposure to tap water on human health required more attention (Praveena et al., 2022). Drinking water is regarded as a potential pathway for the introduction of microplastics into the human system, as indicated by Danopoulos et al. (2020). The confirmation of the existence of microplastics in human stool samples has been established recently (Schwabl et al., 2019).

Currently, the heightened focus on the potential risks posed by microplastics to human health has been driven by their widespread presence in various aspects of the human environment, including items like honey, milk, beer, seafood, table salt, drinking water, and even the air (Karami et al., 2017; Kutralam-Muniasamy et al., 2020; Li et al., 2018; Zhang et al., 2020a). Microplastics could have been extensively dispersed in soil, particularly within agricultural environments (Rillig & Lehmann, 2020). This is particularly concerning when they possess a negative charge, as they have the potential to infiltrate the plant's water transport system, subsequently migrating to its roots, stems, leaves, and ultimately its fruits (Schwabl et al., 2019). Food contamination may result from the entry of microplastics into agricultural systems through sewage sludge, compost, and plastic mulching, which may increase the risk of human exposure to these pollutants (Li et al., 2023). Another way gastrointestinal exposure to microplastics occurs is through the ingestion of dust, particularly when children put dirty toys and hands in their mouths (Ljung et al., 2006; Q. Zhang et al., 2020b).

INHALATION

Microplastics can become suspended in the atmosphere through mechanical processes, although it is not their primary source in the environment. The areas with high concentrations of microplastics in marine ecosystems serve as significant potential reservoirs of microplastics that can become aerosolized via wind or wave activity, similar to the formation of sea spray aerosols (Allen et al., 2020; Sebille et al., 2016). Owing to their reduced density and their upward movement facilitated by gas bubbles, non-soluble microplastics tend to aggregate in the vicinity of the mixed layer's surface. As a result, these particles are more easily transported into sea spray generated by wind or bubbles (Allen et al., 2020). Vehicle tires, brakes, and road surfaces contain plastic components that can undergo wear and tear and produce microplastics, subsequently released into the environment (Furuseth & Rødland, 2020; Mattsson et al., 2023; Napper & Abbott, 2020; Vogelsang et al., 2019). Of greater significance, the mechanical actions of vehicle tire rotation, the braking procedure, and the high turbulence created in the wake of vehicles provide these roadside plastics with enough mechanical energy to surpass inertial or cohesive forces, leading to their re-suspension into the atmosphere (Brahney et al., 2021). In human lungs, microplastic fibers that range from 8.12 to 16.8 µm and particles smaller than 5.5 µm are mostly made of PE and PP materials (Amato-Lourenço et al., 2021). It is noteworthy that the microplastics in lung tissues are smaller size than those in the environment. This underscores the possibility of human exposure to microplastics through inhalation, highlighting the need for increased vigilance regarding potential adverse effects on the human body (Li et al., 2023).

Recent studies have suggested that the uptake of microplastics through inhalation may surpass their uptake through dietary consumption (Cox et al., 2019; Zhang et al., 2020a; Zhu et al., 2021). One *in vitro* research, for example, showed that polyvinyl chloride (PVC) displayed a low level of cytotoxicity in human pulmonary cells, but human alveolar cells could absorb polystyrene (PS) nanoparticles, which caused severe inflammation and death (Xu et al., 2019). The fact that airborne microplastics may be absorbed into the respiratory system and may cause buildup, irritation, and blockage was further confirmed by research on animals (Fournier et al., 2020; Tiotiu et al., 2020; Wang et al., 2016). Furthermore, these particles have the ability to go from the mother's lungs, cross the placenta, and enter the fetal tissue, which may lead to a smaller fetus and slower growth (Wang et al., 2016). However, the actual risk posed by exposure to airborne microplastics to human health remains unclear. Accurately assessing the exposure of the respiratory tract to microplastics in humans is crucial before investigating the dose-response connection between inhalation exposure to microplastics and detrimental health consequences (Abbasi et al., 2019; Alimba & Faggio, 2019; Auta et al., 2017; Dris et al., 2017; Zhang et al., 2020b).

DERMAL

Despite the widespread belief that microplastics cannot pass through the skin barrier, their ability to stick to the skin's surface can nonetheless raise the risk of exposure (Prata, 2018; Schneider et al., 2009). For example, using consumer goods that contain microplastics—like cleansers and face creams—can increase the chance of being exposed to PE (Hernandez et al., 2017). Furthermore, when mobile phone covers intended for protection are used, they may produce microplastics that end up in users' hands. When kids play or crawl, they could come into touch with microplastics that are prevalent on the ground. Certain popular plastic additives, like triclosan (TCS), bisphenols (BPs), brominated flame retardants (BFRs), and phthalates, have the potential to be absorbed by the skin after dermal exposure to microplastics (Wu et al., 2022).

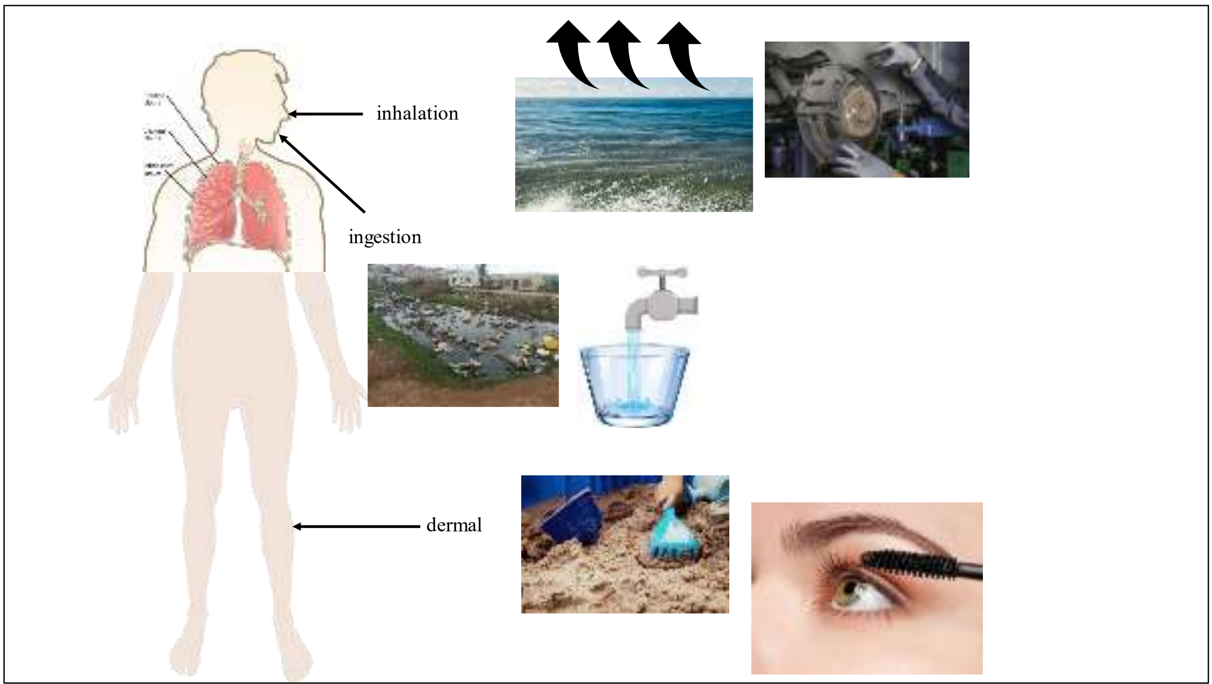

Figure 2. Route of exposure of microplastics to human body

POTENTIAL TOXICITY OF MICROPLASTICS ON HUMAN HEALTH

Significant concerns have arisen regarding microplastics toxicity on human health because they have been extensively identified in different human tissues and they have the ability to move around inside the human body. In order to evaluate the possible negative impact of microplastics on human health, human-derived cell lines and laboratory rats have been frequently used as experimental models (Sun & Wang, 2023). The occurrence of toxic effects from microplastics is a multifaceted process influenced by numerous factors, such as their physical and chemical characteristics, duration of exposure, additives and more (Niu et al., 2023). Microplastics not only possess inherent toxicity but also serve as vehicles for various pollutants to infiltrate biological tissues and organs (Li et al., 2023). While microplastics pose their own set of challenges, it's worth noting that the organic contaminants adhering to microplastics can also present issue (Wang et al., 2017). Recent research on microplastic toxicity has started to address the concept of combined toxicity with other substances (Park & Park, 2021). Figure 3 summarizes the potential toxicities of microplastics based on human and animal experiment.

TOXIC EFFECTS IN HUMAN EXPERIMENTS

The most recent development in *in vitro* modeling is represented by human organoids, which have become unique platforms for evaluating exposure to newly discovered pollutants such as microplastics. In contrast to cell cultures and animal models, human organoids offer a more accurate reflection of the potential harm microplastics can pose to the human body. A study by Winkler et al. (2022) suggested that human airway organoids are a suitable model for testing effects of airborne pollutants although their utilization for assessing the biological effects linked to exposure to microplastics has been overlooked until this point. They investigated assessment of microplastic fibers (MPFs) released from a household dryer's exhaust filter where they observed a notable decrease in the expression of the SCGB1A1 gene, which is associated with club cell functionality. Furthermore, cell growth exhibited a distinct polarization along the fibers. The MPFs did not induce significant inflammation or oxidative stress; however, they became enveloped by a cellular layer, leading to their incorporation into the organoid structure. This phenomenon could have potential long-term implications for lung epithelial cells during the repair process.

An investigation conducted by Hua et al. (2022) revealed that short-term exposure to microplastics lead to an increase in cell proliferation and elevated gene expression levels of Nestin, PAX6, ATF4, HOXB4, and SOD2. However, when exposed to microplastics for an extended duration, they noticed a decline in cell viability. Moreover, differences in the quantity and size of polystyrene microplastics (PS-MPs) affected the expression of genes linked to DNA damage and the formation of brain tissue patterns. Notably, as compared to the untreated control group, the PS-MP-treated conditions showed lower expression of the genes for β-tubulin III, Nestin, and TBR1/TBR2. The findings from this research indicate that exposure to PS-MPs can have detrimental effects on the development of tissue that resembles the embryonic brain in forebrain cerebral spheroids, and these effects appear to be dependent on the size and concentration of the microplastics. This study holds significance in the evaluation of environmental factors contributing to neurotoxicity and degenerative processes in humans.

An experiment conducted by Hou et al. (2022) involved human intestinal organoids exposed to polystyrene nanoplastics (PS-NPs). The measuring approximately 50 nm in size, at concentrations of 10 and 100 µg/mL. The study shows that these PS-NPs accumulate differently in different types of intestinal organoids' cells, which causes apoptosis and an inflammatory reactionFurthermore, our results demonstrate that co-exposure with chlorpromazine, an inhibitor of clathrin-mediated endocytosis, can effectively reduce the accumulation of PS-NPs in secretory cells. This demonstrates how crucial active endocytosis is to enterocyte cells' absorption of PS-NPs. Other study conducted by Cheng et al. (2023) made use of liver organoids (LOs), a novel 3D in vitro model made from human pluripotent stem cells. They employed this alternative model to the human liver. The aim was to investigate the adverse biological effects of 1 µm polystyrene-MP (PS-MP) microbeads using a dynamic exposure method. It was discovered that PS-MP increased hepatic CYP2E1 and HNF4A expression. These findings prompted the identification of plausible adverse outcome pathways (AOPs) connected to PS-MP, indicating possible dangers for cancer, fibrosis, and liver steatosis.

TOXICITY EFFECTS ON LABORATORY RODENTS

Immunotoxicity

Microplastics may trigger the immune system of the body. Microplastics have the capability to infiltrate lymphatic vessels, potentially crossing cell membranes, thereby posing a threat to the lymphatic and circulatory systems. They may accumulate in secondary organs, adversely affecting the immune system and overall cellular health (Yuan et al., 2023). The purpose of the study was to determine whether exposure to different PE-MP doses (1, 10, 100, and 1000 µg/mL) in adult zebrafish (*Danio rerio*) would disrupt the intestinal microbiota for a duration of 7 days, could potentially trigger the activation of the intestinal immune network. In summary, by altering the predominant intestinal microbiota's phylum-level makeup, PE-MPs increase the risk of infection within the intestinal mucosa. Mucosal immunoglobulins are produced as a result of the intestinal immune network pathway being activated by exposure to PE-MPs., notably at concentrations of 100 or 1000 μg/mL over a 7-day period (Yuan et al., 2023).

Researchers looked at the less-than-fatal consequences of microplastic particles and cadmium chloride ($CdCl_2$) on common carp (*Cyprinus carpio*). The findings of this study suggest that fish are toxically affected by both separate exposure to Cd and microplastics, resulting in alterations to their metabolic and immunological markers. Furthermore, when Cd and microplastics are combined, these alterations are exacerbated, suggesting synergistic effects that enhance the toxicity of Cd, and vice versa (Banaee et al., 2019). Airborne microplastics may also impact the digestive tract and immune system. It is known that the smallest particles among airborne contaminants, specifically those in the inhalable fraction, are absorbed through the pulmonary epithelium (Asgharian et al., 2001). These particles enter the systemic circulation and can influence the immune response along the gut-lung axis (Enaud et al., 2020). Therefore, depending on their size, both ingested and inhaled plastics can interact with intestinal tissues, enter the bloodstream, and potentially disrupt the immune system's functioning (Tang et al., 2020).

Reproductive toxicity

The effect of microplastics on reproduction through ingestion pathways, such as intake of tainted food and drink sources, was another major area of concern. These particles can infiltrate the body primarily through ingestion, inhalation, and contact with the skin, selectively affecting the reproductive system in a manner that depends on their size, disrupting both germ cell and other somatic cell development (Hong et al., 2023). Exposure to microplastics resulted in reproductive degradation in male mice, characterized by reduced testosterone levels, a decrease in the quantity and motility of viable sperm, as well as an increase in deformities, atrophy, and apoptosis of sperm cells (Chen et al., 2017). In a study by Jin et al. (2021), it is revealed that PS-MPs have toxic effects on the male reproductive system in mice. The sperm quality and testosterone levels in mice exhibited a noticeable decline following a 28-day exposure to 0.5 μm, 4 μm, and 10 μm PS-MPs. Moreover, PS-MPs damaged the blood-testis barrier and caused inflammation in the testicles. According to recent study, female infertility may be influenced by microplastic exposure, which has been shown to have deleterious effects on the ovaries. These findings offer fresh perspectives on the toxicity of microplastics concerning female reproductive health (Hou et al., 2021). An experiment conducted by Xie et al. (2020) suggested that exposure to microplastics (micro-PS) led to a substantial reduction in both the quantity and mobility of sperm, as well as a notable increase in sperm deformity rates. Furthermore, a reduction in the activity of enzymes linked to sperm metabolism, specifically lactate dehydrogenase (LDH) and succinate dehydrogenase (SDH), was noted in the group exposed to microplastics. Additionally, there was a drop in blood testosterone levels.

Neurotoxicity

Research into the neurotoxicity of microplastics was relatively nascent, although there were some investigations concentrating on their impact on the brain. In experiments where microplastics were administered through a gastric tube, mice exhibited decreased locomotor activity, which was correlated with heightened anxiety and behavioral deficits (da Costa Araújo & Malafaia, 2021). Microplastics also exhibit toxicity towards neural development. The most frequently reported neurotoxic effect following exposure to microplastics is the inhibition of acetylcholinesterase (AchE) activity (Prüst et al., 2020). Microplastics induced neurotoxicity by inhibiting acetylcholinesterase (AChE), increasing lipid oxidation (LPO) in the brain and muscle, and altering the activities of energy-related enzymes such as lactate dehydrogenase (LDH) and isocitrate dehydrogenase (IDH) (Barboza et al., 2018). A study carried out by Yang et al. (2020) suggested that at elevated concentrations, microplastics had the potential to trigger oxidative stress, disrupt the integrity of the intestine, liver, and gill tissues, elevate heart rate, and impede the growth and swimming speed of the goldfish larvae. It is discovered that nanoplastistics (nMPs) were capable of infiltrating the muscle tissue by passing through the larvae's epidermis. This infiltration led to muscle tissue damage, nerve fiber disruption, the inhibition of acetylcholinase (AchE) activity, and exerted more pronounced adverse effects on larval mobility compared to microplastics (mMPs). Exposure to PS-MPs has the potential to result in impairments in learning and memory, as well as the induction of neurotoxic effects in mice. These findings carry significant implications for the general public concerning the possible hazards associated with microplastics (Jin et al., 2022).

Metabolic disorder

A research conducted by Kang et al. (2021) investigated how nanoplastics and microplastics impact the oxidative status and gut microbiota of the marine medaka *Oryzias melastigma*. The exposure to microplastics exhibited signs of intestinal damage, such as an elevated mucus ratio, along with notable modifications in the gut microbiota. Specifically, microplastics led to more substantial changes in the composition of microbiota, affecting both phylum and genus levels (Kang et al., 2021). A study carried out by Jin et al. (2019) revealed that the presence of polystyrene microplastics in the mice's gastrointestinal tracts, and their presence was associated with a decrease in intestinal mucus secretion and the impairment of intestinal barrier function. They suggested that polystyrene microplastics were responsible for metabolic disruptions and triggered imbalances in gut microbiota, dysfunction of the intestinal barrier, and metabolic disorders in mice. In a research on microplastics where five types of microplastics were employed, including polystyrene, polyethylene terephthalate, polyethylene, polyvinyl chloride, and poly(lactic-co-glycolic acid) (at a concentration of 80 mg/L in the small intestine), it is revealed that microplastics were markedly inhibited lipid digestion within the in vitro gastrointestinal system (Tan et al., 2020).

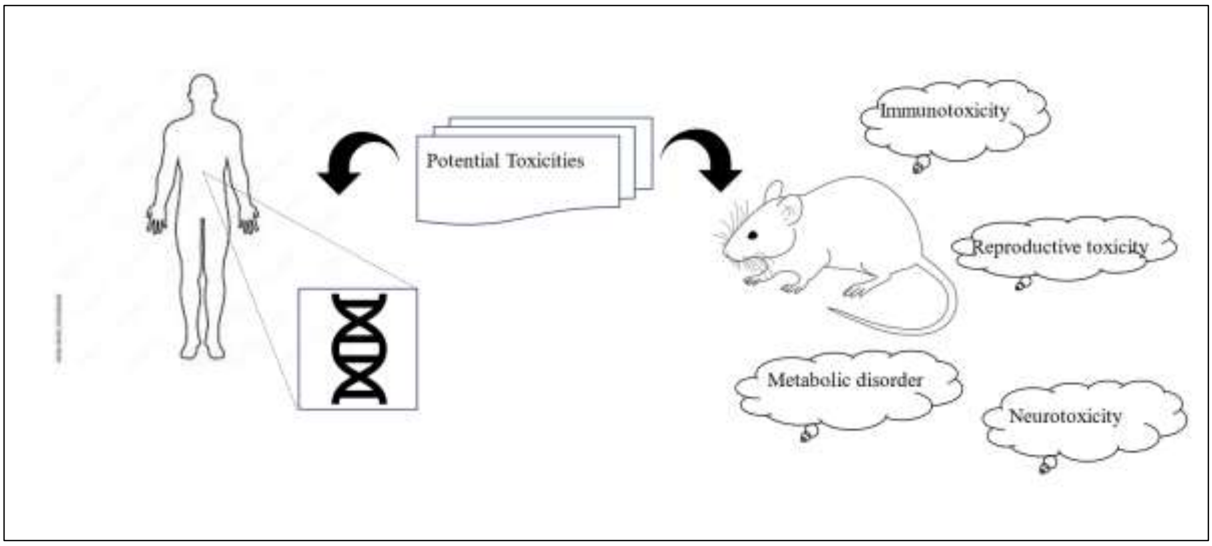

Figure 3. Potential toxicities posed by microplastics via human and animal experiment

CONCLUSIONS AND FUTURE PERSPECTIVES

Since microplastics are extensively dispersed throughout the environment, human exposure to them is unavoidable. Our review summarizes the current progress of the study of microplastic pollution, including occurrence, distribution, and potential toxicities on human health of microplastics. Since microplastics tend to collect in a variety of bodily tissues, it is crucial to look into any potential negative impacts on human health. Numerous studies using human-derived cells and lab animals have been conducted to identify the toxicity targets and fundamental processes of microplastics. In order to enhance our comprehension of potential harm to humans, the following suggestions for experimental designs are put forward.

This study reported abundance of sources of microplastics from different environmental settings. Additional investigation into the prevalence, characterization, fate, and breakdown of microplastics is needed for gaining a comprehensive understanding of and addressing the impacts of microplastics effectively. Other suggested research is to study the origins and destinations of plastics, the compartments they affect, and the mechanism of their transportation is essential. By possessing suitable analytical tools, we can enhance our understanding of where microplastics come from, the routes they follow, and where they accumulate in terrestrial, aquatic, and atmospheric settings. Any estimations made, whether they pertain to specific layers, size categories, polymer or forms (like pellets, fragments, or fibers) should be qualified to prevent any potential confusion.

The potential toxicities on human health of microplastics is being discovered in this review. To fully comprehend the cellular and molecular mechanisms behind microplastic toxicity and the ensuing health problems, further study is, nonetheless, desperately needed. Microplastics and a number of chemicals associated with plastics are substances that cause obesity. Further investigation is essential to elucidate the intricacies of these mechanisms and explore potential strategies for mitigating their effects. Research on critical technologies is essential for accurate microplastic detection, thorough characterisation at various sizes, and accurate quantitative and dynamic tracking of microplastics within living things. Because current analytical methods can only identify microplastics at the micron scale, it is difficult to evaluate nanoplastics, which are smaller microplastics that may be more harmful. The substantial variation in environmentally significant microplastics could complicate the interpretation of toxicological studies. Consequently, employing appropriate methods for identification and categorization would aid in the examination of the crucial factors of microplastics that influence their toxicity outcomes. Furthermore, a prolonged epidemiological investigation is necessary for a specific human population characterized as being highly susceptible to concurrent exposure to both microplastics and conventional pollutants.

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Nor Azura Sulong is responsible for research idea and write the original draft. **Fazni Susila Abdul Ghani** is responsible for editing, checking language and grammar. **Noradila Binti Mohamed** is responsible for checking the content of the introduction and conclusion. **Ahmad Hanafi Bin Sulong** is responsible for data analysis and curation.

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The authors declare that there are no competing interests.

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