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A REVIEW ON IMPACT OF MICRO PLASTICS IN HUMAN BEINGS

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ABSTRACT
Microplastics are ubiquitous in the global environment. As a typical emerging pollutant, their potential health hazards have become a significant concern. This brief paper introduces the sources, identification, toxicity, and health hazards of microplastics in humans. A review of the literature shows that microplastics are frequently detected in both environmental and human samples. Humans can be exposed to microplastics through oral intake, inhalation, and skin contact. We summarize the toxic effects of microplastics in experimental models, including cells, organoids, and animals. These effects include oxidative stress, DNA damage, organ dysfunction, metabolic disorders, immune responses, neurotoxicity, and reproductive and developmental toxicity. Additionally, epidemiological evidence suggests that a variety of chronic diseases may be related to microplastic exposure. Finally, we identify gaps in the toxicity research of microplastics and discuss their future development directions. This review will help improve the understanding of exposure risks and potential health hazards associated with microplastics.

KEYWORDS: Micro plastics, Placenta, Infertility.

INTRODUCTION
Plastic pollution significantly impacts environmental and human health. The extensive production and consumption of plastics, along with inadequate waste management, have resulted in billions of tons of plastic waste in ecosystems. Notably, 79% of plastic products are improperly treated, leading to plastic waste accumulations in landfills or natural environments. These plastics leach toxic chemicals, harm wildlife, and pose health risks to humans. Primary micro plastics, intentionally added to consumer products, such as cosmetics and detergents, paints, medications, nappies, and insecticides, contribute further to this issue. Human exposure to micro plastics occurs via ingestion of contaminated food and water, use of personal care products (toothpaste, face wash, scrubs, soap; also, dermal route), and inhalation, leading to bioaccumulation in various tissues, including the lungs, bloodstream, and placenta. The toxicological effects of micro plastics in cell cultures, organoids, and animal models include oxidative stress, DNA damage, altered metabolism, and neurotoxicity. The reproductive and developmental impacts of MPs are alarming, with potential intergenerational effects.

Many single use plastic products have a functional lifespan of minutes to hours, yet they may persist in the environment for hundreds of years. Plastic degradation is a very slow process, with fragmentation and degradation of plastic polymers occurring by physical forces, ultraviolet (UV) rays, temperature changes and biodegradation in the environment. The resulting breakdown products are smaller plastic fragments, known as micro and nano-plastics.

DEFINITION AND CHARECTERISTICS
Micro plastics are generated by the breakdown of larger plastic products. Micro plastics are omnipresent in our environment, being found in large quantities in oceans, rivers, ground water, sediments and soil environments, sewage, and even the air we breathe Most plastics in use have a strong resistance to biodegradation. However, they are susceptible to mechanical and photochemical processes that can break them down into micro and nanoscale particles. Plastics are made up of various

polymers, including polyethylene (PE), polypropylene (PP), polystyrene (PS), polyvinyl chloride (PVC), polyethylene terephthalate (PET), polycarbonate (PC), polymethacrylate (PMMA), and polyurethane (PU). However, polyethylene, polypropylene and polystyrene are the three most common occurring polymers.

Commercial plastics contain many additives that can leech out of plastic into the surrounding environment or tissue(s), as they are not covalently linked to the polymer matrix. A recent review estimated that over 10,000 unique chemicals are used at various stages in plastics manufacturing, of which roughly 2,400 have been identified as chemicals of regulatory concern. Toxicological studies on microplastics are increasing rapidly. Experiments show that the exposure to microplastics induces a variety of toxic effects, including oxidative stress, metabolic disorder, immune response, neurotoxicity, as well as reproductive and developmental toxicity.

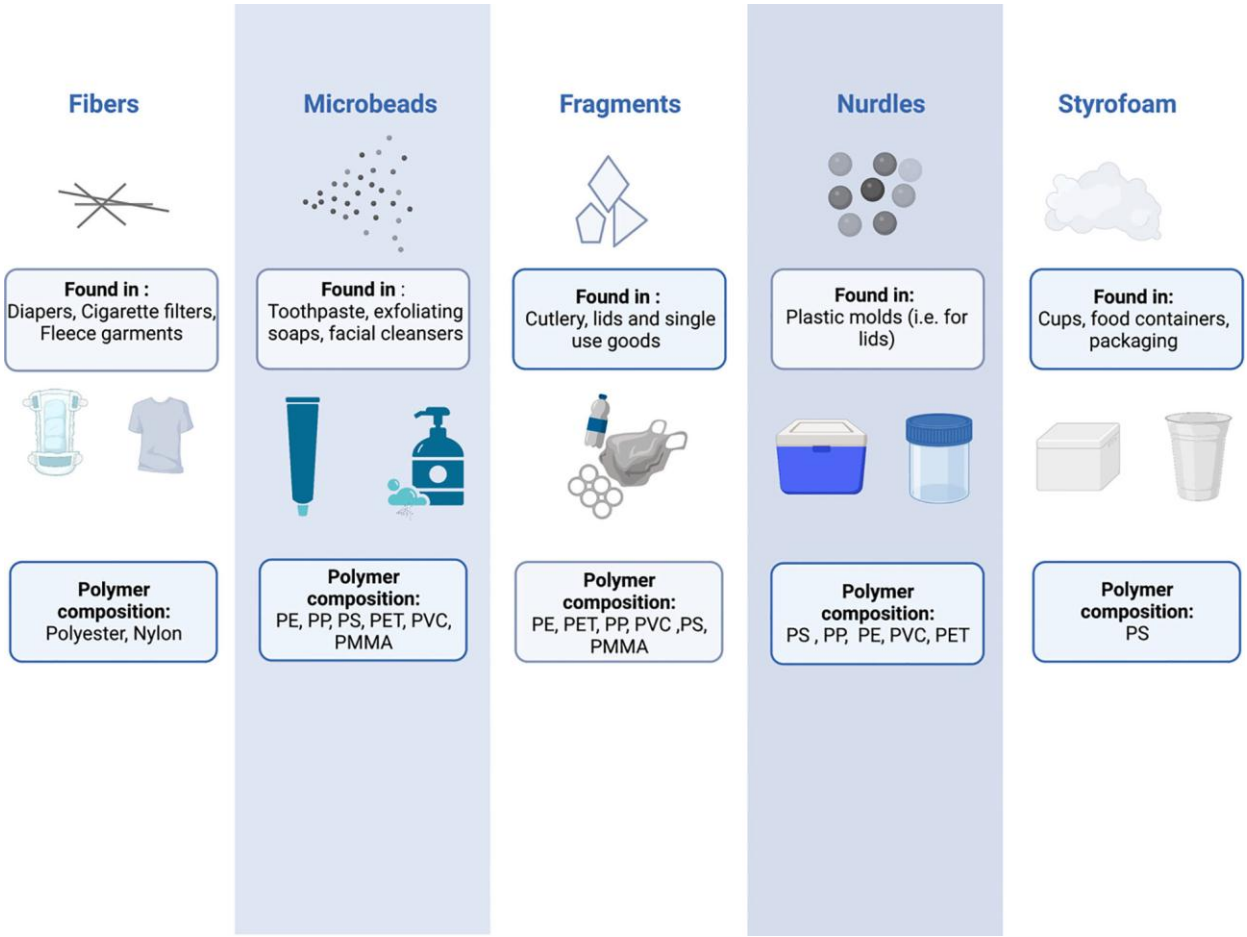


Figure: 1.

EXPOSURE TO HUMANS

There are three routes through which the human body is exposed to micro plastics are inhalation, ingestion and dermal contact. It is estimated that an individual will be exposed to approximately 74,000-121,000 MPs per year, with ingestion and inhalation considered the primary routes of exposure. In humans, MNPs have been found in a diverse range of biological samples, including blood, urine, sputum, feces and breast milk. Further, micro plastics accumulation has been identified in numerous organ systems including lung, colon and spleen. Microplastics have more recently been identified in human placenta tissue and meconium demonstrating direct exposure to the fetus and raising concerns for developmental toxicity and long-term health consequences for the offspring.

1. Oral intake

Micro plastics exist in our daily necessities like drinking water, bottled water, seafood, salt, sugar, tea bags, milk, and so on. Europeans are exposed to about 11,000 particles/person/year of micro plastics due to shellfish consumption, and according to food consumption, the intake of plastic particles in human body is 39,000−52,000 particles/person/year. Once micro plastics enter agricultural systems through sewage sludge, compost and plastic mulching, they will cause food pollution, which may increase the risk of human exposure.

Take-out food containers made of common polymer materials (PP, PS, PE, PET) are used widely, from which micro plastics are found. It is estimated that people who order take-out food 4−7 times weekly may intake

12−203 pieces of micro plastics through containers. In addition, research demonstrates that the surface of silicone rubber baby teats degrades when they are sterilized by steam, during which micro plastic particles are released into the environment. It is estimated that the total number of micro plastic particles entering the baby's body during one year of normal bottle feeding reaches about 0.66 million.

Fig. 2.

2. Inhalation

Micro plastics in the air are mainly PE, PS, and PET particles and fibers with size ranges of 10−8000 μm. The largest source of micro plastics (84%) in the atmosphere comes from the road. It is estimated that annual micro plastics consumption ranges from 74,000 and 121,000 particles when both oral intake and inhalation are considered. The size of micro plastics detected in lung tissue is smaller than that in the atmosphere. This further confirms that humans can be exposed to micro plastics by inhalation and prompts attention to the potential harm to the human body.

3. Skin contact

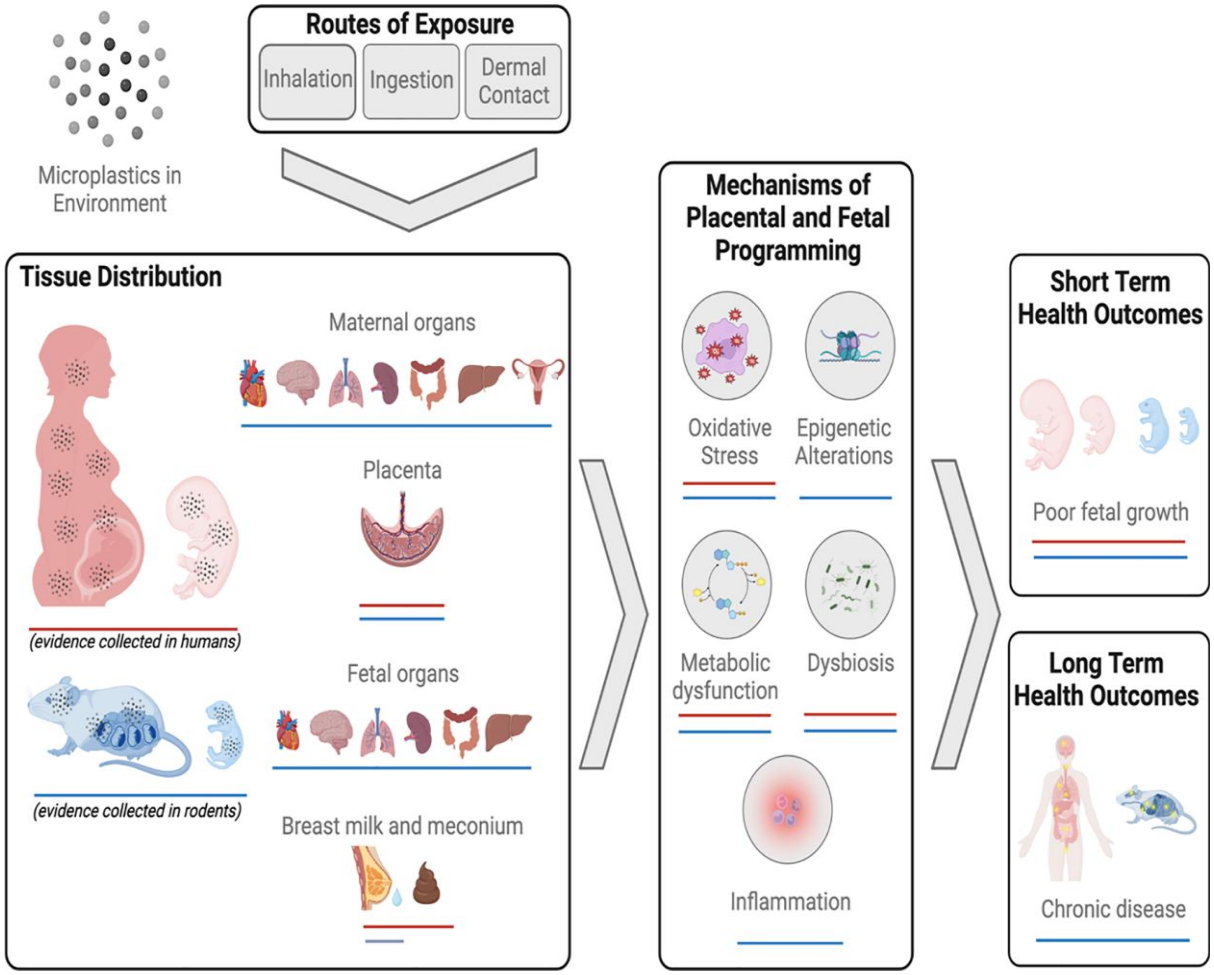
Micro plastics are usually considered not to pass through the skin barrier, but they can still increase exposure risk by depositing on the skin. For example, the use of consumer products containing micro plastics (such as face cream and facial cleanser) will increase the exposure risk of PE. The protective mobile phone cases (PMPCs) can generate micro plastics during use, which are transferred to human hands.

TOXICOLOGICAL PROFILE ON MICRO PLASTICS

Microplastics have been found to have adverse effects on the environment and living organisms, including humans. Numerous studies have investigated the toxic effects of microplastics, including both in vitro studies and in vivo studies, primarily in marine organisms and a few on rodents. Moreover, studies have investigated the accumulation of microplastics from human samples in a clinical setting, including stool, colectomy samples, human placenta, and meconium. In the absence of epidemiological data, various in vitro studies have utilized different types of human cells to evaluate the effects of microplastics on humans. The types of human cells used include human lung epithelial cells, human adeno carcinoma cell line, human dermal fibroblasts, peripheral blood mononuclear cells, with a total of ten different types of human cells being used.

Effects of micro plastics exposure on Mammalian fertility

Several adverse reproductive effects are observed in male mammals following oral exposure to MNPs of various size and with varying duration. For example, male rodents' oral exposure to PS-MNP leads to accumulation within the testis, coupled to disruption of the seminiferous epithelium, evidence of localized oxidative stress and mitochondrial dysfunction, and over-expression of pro-inflammatory cytokines in the testis. This same exposure is associated with disruption of the blood-testis barrier, with in vitro studies demonstrating oxidative stress, endoplasmic reticulum stress and misfolding/degradation of tight junctional proteins in Sertoli cells. There are clear functional consequences of these exposures, as MNP exposure in rodent models leads to reduced sperm quantity and quality in addition to reduced testicular androgen production and circulating levels of testosterone and luteinizing hormone (LH), suggesting that MNP exposure may have important implications in the pituitary gonadotropin endocrine signaling pathways, testis function and sperm quality in male mammals.

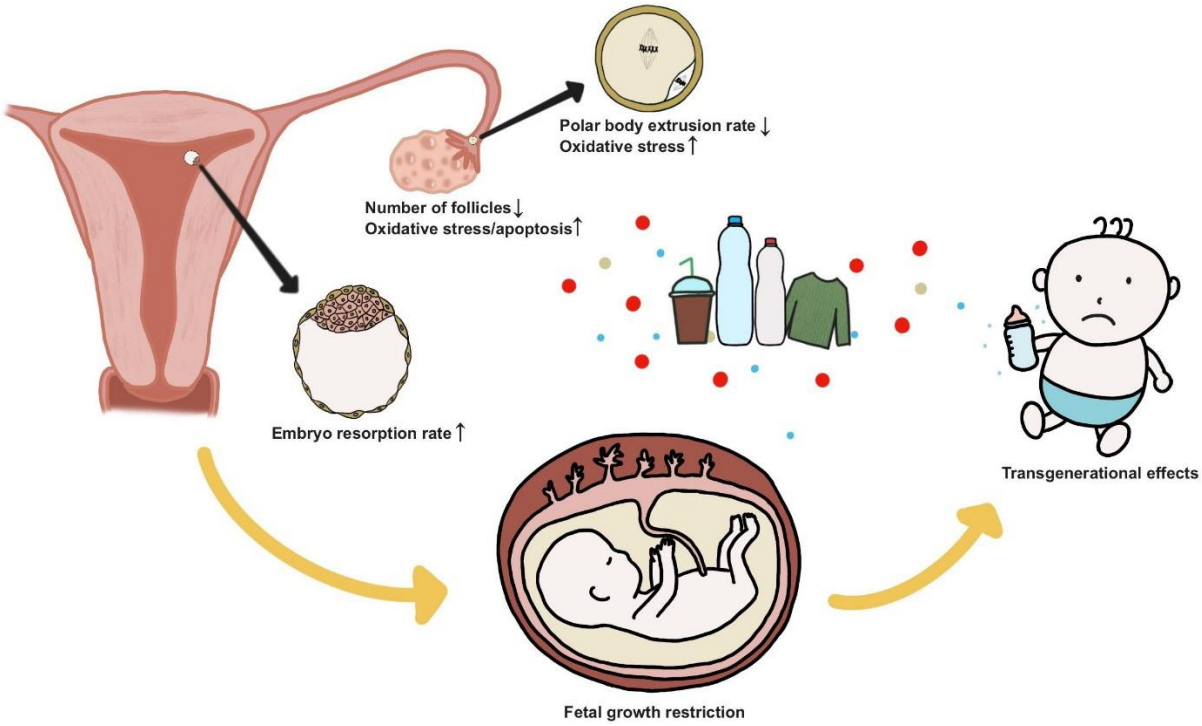


Male fertility, fetal health and the long-term health of offspring are dependent on the epigenetic programming events that occur during spermatogenesis, events that can be adversely disrupted by exposures to various testicular toxicants. Epigenetic modifications play a crucial role in regulating gene expression and developmental processes, including germ cell differentiation and sperm production.

Similar associations have been observed in human populations, with several studies demonstrating a correlation between urine phthalate and/or BPA metabolite concentrations and differential methylation patterns in the sperm, often in promoter regions of genes related to cellular growth and development, coupled to poor sperm quality and fertility outcomes. Furthermore, the intergenerational and transgenerational effects of phthalates and BPA on germ cell epigenetic marks have been observed, indicating the potential for long-lasting impacts on future generations.

Fertility effects in female

In both a rat and mouse model, oral exposure to micro plastics results in the accumulation of these particles within uterine tissue and in various ovarian compartments, including within growing follicles. Ovaries of these exposed rodents have reduced weight, decreased expression of cytoskeletal proteins, and demonstrated altered follicle dynamics, with a reduction in the number of growing and mature follicles and increased atretic and cystic follicles. In parallel, distinct changes in reproductive hormone signalling are observed, with reductions in the circulating concentrations of estradiol (E2) and anti-mullerian hormone (AMH), and increased concentrations of LH, follicle stimulating hormone (FSH) and testosterone. Exposed rodents demonstrate functional/fecundity consequences of this MNP exposure, with measurable changes in estrous cycle duration, decreased ovarian reserve, lower embryo implantation rates and smaller litter sizes. The mechanistic underpinning of this reproductive dysfunction is thought to be in large part driven by MNP-induced oxidative stress.



Micro plastics exposure in Pregnancy

Micro plastics can be transported across the placenta, potentially impacting pregnancy outcomes and resulting in reproductive toxicity. Human and animal studies have shown that micro plastics are able to affect placental development at any stage, resulting in placental insufficiency and FGR. For instance, in studies of maternal exposure to micro and nano plastics in mouse models of pregnancy, they were detected in the placenta and found to be transferred across the placental barrier into the fetus. This resulted in abnormal fetal and placental weights and detrimental effects on postnatal development (Aghaei *et al*., 2022). Trichloroethylene (TCE) is a common environmental contaminant and an industrial solvent, that was reported to cross the placenta of pregnant women and result in FGR (Elkin *et al*., 2020). While the effects of many environmental toxicants on placental development have been illustrated in available reports, how exposure to microplastics and nanoplastics impacts placental and fetal development is unknown.

DETECTION OF MICRO PLASTICS IN ORGANISMS AND HUMANS

Microplastics are found in animals. They pose a great threat to aquatic organisms, like fish and marine mussels. Microplastic fibers are the most frequent microplastic type ingested. For wild coastal animals, microplastics are found in their intestine, stomach, liver, and muscle. PET is also detected in the feces of pets, such as cats (<2300−340,000 ng/g) and dogs (7700−190,000 ng/g). Microplastics also exist in plants and algae.

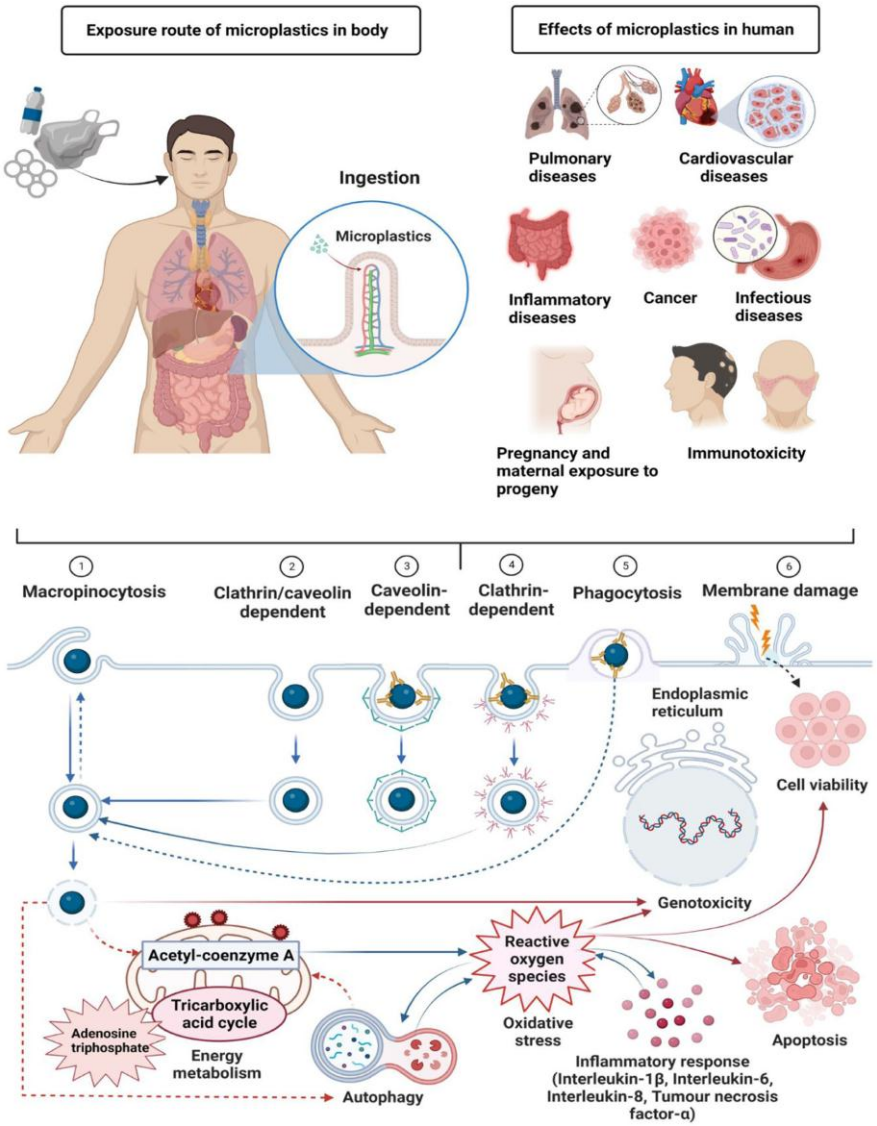
It is generally believed that after entering the human body, microplastics will be excreted out through the gastrointestinal tract and biliary tract. However, researchers detect the existence of microplastics in human blood. People begin to reconsider the harm of microplastics to human health. The intake, distribution, accumulation, and metabolism of microplastics in the human body are attracting more and more attention. Understanding the concentration of microplastics in the human body is an important prerequisite for exploring their potential harmful effects. A recent review indicates that microplastics are transported to the whole body through blood circulation, and the existence of microplastics are found in 15 human biological components, such as the spleen, liver, colon, lung, feces, placenta, breastmilk, etc. The organs with high content are the colon (28.1 particles/g) and liver (4.6 particles/g). The main types of microplastics detected include PE, PET, PP, PS, PVC, and PC.

Pregnant women and infants are sensitive people exposed to microplastics. The concentration of PET in infant feces (5700−82,000 ng/g, median: 36,000 ng/g) is ten times higher than that in adults (2200−16,000 ng/g, median: 2600 ng/g), indicating that the exposure level of microplastics in infants may be much higher than adults. Twelve microplastic fragments, ranging from 5 to 10 μm, are detected in human placenta and then they first detect PVC and PP microplastics with a size of 2−12 μm in human breastmilk. Since then, more studies also detect microplastics in placenta, meconium, and breastmilk. More than 74% of microplastics are 20−50 μm in size. The appearance of microplastics in human placenta further emphasizes that these nondegradable chemicals have potential intergenerational influence on the human body and may affect the developing fetus. Therefore, more attention should be paid to the potential impact of early exposure of infants and early development of embryos.

FUTURE PROSPECTIVES

1. **Lack of Homogeneous and Well-Characterized Microplastics for Studies**: There's a notable scarcity of standardized, well-characterized microplastics in sufficient quantities for meaningful toxicological studies. Most research has relied on polystyrene (PS) micro- and nano-plastics (MNP), but this does not reflect the diversity of microplastic pollution in the environment, where there are a variety of polymers, shapes, and sizes. The variability of MNPs in the real world needs to be better represented in studies to fully understand their impact.
2. **High Exposure Rates in Rodent Studies**: Many rodent studies use exposure levels that are far higher than what might be encountered in the real world. These high doses of MNPs (tens of millions per kilogram of body weight) are often much more than humans or animals would experience in natural environments. The real-world exposure is likely much lower, and the effects at these more realistic levels should be more closely examined to understand the actual risks.
3. **Chemical Additives and Their Potential Toxicity**: Chemical additives that are often present in MNPs may contribute significantly to toxicity. These additives could potentially bypass the body's defense mechanisms, reaching vulnerable tissues and causing harm. This aspect is often underexplored in current research.
4. **Need for Further Research on Polymer Types and Additives**: Since different polymers and additives may behave differently in biological systems, more research is needed to evaluate the specific health risks posed by various types of microplastics, as well as how the additives might contribute to toxicity.

In summary, to improve our understanding of the health impacts of microplastic pollution, studies need to focus on more realistic exposure scenarios, use diverse types of MNPs that better mirror environmental pollution, and investigate the roles of polymer types and chemical additives. This would help clarify the real hazards of microplastics on reproduction and overall health.



CONCLUSION

Humans are exposed to microplastics by oral intake, inhalation, and skin contact. Microplastics have been found in a variety of organisms and multiple parts of the human body. We emphasize the potential impact of microplastics on the early exposure of infants and the early development of embryos. At present, the toxicity research on microplastics show that the exposure will cause intestinal injury, liver infection, flora imbalance, lipid accumulation, and then lead to metabolic disorder. In addition, the microplastic exposure increases the expression of inflammatory factors, inhibits the activity of acetylcholinesterase, reduces the quality of germ cells, and affects embryo development. At present, the commonly used analytical means can detect microplastics only at the micron level, and it is difficult to effectively analyze microplastics with smaller size (nanoplastics) and greater potential harm, which brings great challenges to accurately reveal the possible health risks of microplastics. In addition, there is still a lack of effective dynamic tracing means. Therefore, how to precisely identify, accurately quantify, and dynamically trace the microplastics in organisms is the primary problem. It may be improved by comprehensively utilizing existing imaging and analysis technologies, such as SEM, CLSM, Raman spectroscopy, and so on.

Several research gaps and issues require further examination and exploration in future studies related to microplastics. These include the need for more research on the impacts of microplastics on human health, identifying specific mechanisms underlying their harmful effects, exploring potential risk factors affecting human exposure, and developing effective mitigation strategies to promote public health. Further research is also needed to understand acute and chronic microplastic toxic effects on humans and animals and to develop suitable alternatives to single-use face masks and medical industry plastic waste.

Microplastics must be converted into valuable by-products, improve their separation from other pollutants, and determine their environmental fate. Identifying suitable alternatives to single- use face masks is crucial while developing recycling and reuse methods for medical industry plastic waste. Furthermore, efforts should be made to improve the quality and efficiency of plastic alternatives, such as bioplastics, and to integrate microplastic treatment technologies to enhance their removal efficiency and minimize negative impacts. Finally, selecting a strategy to reduce plastic use should consider factors such as infrastructure, economic conditions, types of microplastics released, alternative options, and public readiness to transition to a non-plastic dependent economy.

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