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Review Article

TOXIC EFFECTS OF MICRO-NANO-PLASTICS ON HUMAN HEALTH

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***Abstract:** Plastic pollution, particularly in the form of microplastics (MPs) and nano-plastics (NPs), poses a significant threat to human health. These tiny particles result from the degradation of larger plastic items or are intentionally manufacturedare ubiquitous in the environment and can enter the human body through one or all three modes ingestion, inhalation, and skin contact. MPs and NPs are linked to a range of adverse health effects, including inflammation, oxidative stress, and disruption of normal organ functions. Studies have shown that these particles can accumulate in various tissues, including the gastrointestinal tract, cardiovascular system, and reproductive organs, leading to conditions such as inflammatory bowel disease (IBD), cardiovascular disease, impaired fertility and cancer. This review highlights the mechanisms of toxicity of MPs and NPs, their routes of exposure, and their impact on human health, underscoring the urgent need for further research and global action to reduce plastic waste, improve waste management, and regulate plastic exposure to safeguard public health.*

Keywords: Plastic pollution,

INTRODUCTION

One of the biggest problems of the twenty-first century is plastic pollution [1]. Environmental and health issues have arisen as a result of the global biosphere's high concentration of plastic particles. Microplastics (MPs) are generally defined as plastic particles no smaller than 5 mm, while there isn't a single, widely recognized definition. Globally, there are six billion tonnes of plastic. In 2019, 353 million tons of plastic waste were generated; by 2060, that figure is predicted to triple to more than one billion tonnes [2,3].

A different term for it is "engineered nanomaterials."t There are around 10,000 compounds found in plastics, including carcinogens and endocrine disruptors [3]. Microplastic pollution, which is caused by the enormous increase in plastic trash, is present in all soil habitats, including floodplain, coastal, industrial, greenhouse, and agricultural/ farmland soils. MP mostly enter biological systems by touch and ingestion.

A recent investigation has revealed that microplastics are present in the majority of fruits and vegetables consumed, thereby promoting their movement within the food chain [7]. The analysis revealed the presence of various polymers, including polypropylene (PP), polyethylene (PE), polyethylene terephthalate (PET), polystyrene (PS), polyvinyl chloride (PVC), polycarbonate (PC), polyoxymethylene (POM), and acrylic. This indicates that ingestion and/or inhalation may serve as pathways for exposure to environmental microplastics. The breakdown of plastics can be sped up by UV light, as well as wind and wave action.

Plastic pollution represents a widespread and escalating issue. In 2022, global plastic production reached an astonishing 400.1 million tons, with more than 80% of this material being disposed of inadequately, thereby polluting ecosystems across land, water bodies, and the atmosphere [3,7]. Moreover, MP are airborne particles that can traverse extensive distances prior to being inhaled by land-dwelling organisms, including humans [3,6,7].

Furthermore, the presence of plastic-contaminated food is significant for human health, as these materials can penetrate cell membranes, enter lymphatic and blood circulation, and accumulate in various tissues and organs [8,10]. Plankton, whales, and other aquatic creatures unintentionally ingest these particles, which can subsequently move up the food chain and end up in human diets.

The widespread presence of microplastics (MP) has been associated with a rise in health issues, capturing the interest of researchers. Investigations have highlighted the physical and chemical effects of MP on human health, such as inflammatory reactions and possible toxic effects.

Microplastic toxicity is influenced by several factors, including the properties of the polymer, the size and shape of the particles, their concentration, the duration of exposure, the presence of additives, surface modifications, and hydrophobic Additionally, the concentration of microplastics, the length of exposure, and the presence of additives further affect toxicity levels. Recent studies have also identified the presence of micro/nano-plastics in various human tissues and organs [7,10]. Here, we discussed the impact of microplastic on various systems of human health.

2. Effects of Micro-nanoparticles (MNPs) on Inflammatory Bowel Disease (IBD: Inflammatory bowel disease (IBD) represents a significant public health concern in numerous nations, with a rising prevalence of individuals suffering from chronic or acute forms of the condition, such as Crohn's disease and ulcerative colitis (UC). Current statistics indicate that over 6.8 million individuals globally have received a diagnosis of IBD [11].

MP exposure resulted in a more noticeable reduction in colon length, worsened inflammation and histopathological damage, reduced mucus secretion, and increased colonic permeability.[12] This occurrence presents serious questions about their capacity to cause negative health outcomes, including inflammation, oxidative stress, and disruption of the makeup of the gut microbiota, all of which may have a substantial impact on general health and wellbeing [12,13].

Several authors claim that exposure to MP results in mild to moderate colon inflammation, which is typified by increased expression of pro-inflammatory cytokines, activation of pro-inflammatory signaling pathways, and weak inflammatory infiltration of the mucosa. The intestinal epithelial barrier is harmed by MP [12,13]. Additionally, microplastics tend to accumulate in the digestive system, potentially causing physical irritation and blockages [1].

Approximately 20 mouse-based experimental investigations assessing the impact of MP on colon shape and function have been reported to date.[12] The capacity of micro- and nano-plastics to concentrate in the gastrointestinal tract has been clarified by many investigations; some particles have been shown to go over intestinal epithelial barriers and enter the systemic circulation [13].

A disturbance in the gut ora has been observed in human *in vitro* gut models, Studies conducted both *in vitro* and *in vivo* have demonstrated that PE MPs negatively impact the gut microbiota and epithelial barrier [13,14]. According to certain research MPs and NPs can cause toxicity, persistent inflammation, and an elevated risk of neoplasms [13]. According to *in vivo* research, MPs and NPs are both absorbed and built up in tissues, changing how organs and systems should work [1]. Higher levels of microplastics were also found in the faeces of individuals with inflammatory bowel disease (IBD) compared to healthy individuals, suggesting a possible connection between microplastics and the onset or progression of IBD [1].

3. Cardiovascular effects: Heart health and MNPs: Circulating MNPs may activate red blood cells and monocytes, which interact with endothelial cells, thereby contributing to circulatory disorders and atherosclerosis [1]. Current *in vitro* studies suggest that MNPs can infiltrate human cells and initiate various pathophysiological pathways and mechanisms associated with the onset of cardiovascular disease (CVD) [1]. Furthermore, animal research supports the role of MNPs in alterations to heart rate, deterioration of cardiac function, myocardial fibrosis, and endothelial dysfunction [17,18].

A study identified nine distinct types of micro/nano-sized particles MNPsin both cardiac tissues and blood samples, with sizes reaching up to 469 μm in diameter [1]. MNPs have been associated with the development of pericardial edema, which is a prevalent indicator of general cardiovascular toxicity [17,19].

In *vitro* studies suggest that specific MNPs can trigger oxidative stress, inflammation, and apoptosis in endothelial and various vascular cells. However, the clinical implications of these findings remain unclear [1]. Two investigations examined the presence of MNPs in thrombi obtained from various vascular regions, indicating that MNPs may have a tendency to accumulate in areas with vascular lesions. Furthermore, their presence in carotid plaques is linked to an increased risk of cardiovascular events or mortality [18,19]. Additionally, animal studies corroborate the involvement of MNPs in changes to heart rate, impairment of cardiac function, myocardial fibrosis, and endothelial dysfunction. Nevertheless, the clinical significance of these observations remains uncertain[20].

4. Impact on Sperm and Reproductive Health: Likun Gao et al. [21] suggested that the reduction of sperm viability and the rise in the rate of sperm abnormalities was significantly greater in the group exposed to microplastics.Microplastic exposure has been identified within the male reproductive system, and its toxic effects have been validated through in vitro studies [22,23]. Accumulating studies have revealed that MP/NP exposure exerts deleterious effects on male reproductive function [23].

Spermatogenesis, the process through which sperm is generated from spermatogonia stem cells (SSCs), is a highly intricate and ongoing phenomenon. ²t Over the past 80 years, there has been a notable decline in semen quality among men, with sperm concentration decreasing to roughly one-seventh of its initial level [2].

Exposure to microplastics and nano plastics has been extensively documented to affect gonadal structure and reduce both the quantity and quality of gametes in male and female representatives of aquatic and terrestrial species [2]. Microplastics are present in every ecosystem, and the detrimental impact of microplastic pollution on reproductive health poses a significant challenge [22]. The damage caused by Microplastic to the male reproductive system may lead to reproductive dysfunction and lower fertility [2]. MPs have been shown to diminish the activities of succinate dehydrogenase and lactate dehydrogenase in oysters during spermatogenesis, suggesting that these pollutants can disrupt the energy supply necessary for spermatogenesis and subsequently impair sperm quality [21].

Existing research indicates that microplastics have the potential to compromise the blood-testis barrier and negatively affect sperm quality in animal studies. For instance, mice that were exposed to polystyrene (PS) microplastics exhibited a decrease in the quantity of spermatogenic cells, disorganization of seminiferous tubules, an increase in the prevalence of abnormal sperm, and diminished activity of sperm metabolism enzymes [2].

Studies on plastic particles and human tissue are rare. However, results from animal experiments have revealed some important evidence. The calculated minimal human equivalent MP dose causing a reduced semen quality is 0.016 mg/kg/day, The sperm swimming performance, including ATP production, sperm viability, and DNA integrity, is reduced by MP [2]. Polytetrafluoroethylene (PTFE) exposure and the number of microplastic exposure types were significantly associated with reduced sperm count and motility, suggesting that microplastic pollution may pose reproductive health risks [22,24].

5. Microplastics as a drive for cancer: Microplastics may disrupt the mucus layer of the intestinal lining, increasing the risk of colorectal cancer. Exposure to plasticizers has been linked to changes in the expression of oncogenic microRNAs (miRNAs), such as let-7g, let-7f, miR-134, miR-125b, miR-22, miR-146a, miR-222, miR-192, miR-26b, miR-26a, miR-296, miR-27b, miR-335, miR-324, miR-122, miR-200, miR-23b, miR-21, and miR-29a, which are involved in cancer development [2]. The relationship between human exposure to plastic products and cancer has been suggested, but definitive proof has not yet been established. The study mentioned suggests that long-term consumption of microplastics could contribute to cancer through chronic inflammation and irritation, which may lead to DNA damage Additionally, the study notes that exposure to nano plastics induces oxidative stress and ongoing irritation, with signs of pro-inflammatory agents [2]. Human breast cancer cells may react differently to physical contact or stimuli when polypropylene microplastics interact with the cell membrane or are inserted between cells, leading to an increased secretion of pro-inflammatory cytokines like IL-6, which could promote cancer progression, cell proliferation, and resistance to apoptosis [30].

Toxins in microplastics: Phthalate esters, bisphenol A (BPA), and brominated fire retardants are among numerous plastic added substances known as harmful mixtures for organic entities when exposed into the climate. BPA is a purported xenoestrogen, which shows chemical-like properties, impersonating the impacts of estrogen. Cancer and changes in behavioral improvement are different impacts of added substances in plastics [31].

The research findings observed that testosterone levels in guys diminished and estradiol levels in females expanded because of variety in BPA levels [32]. This harm results from oxidative pressure, irritation, cell passing in the testicles, strange cell processes, and hormonal pivot disturbance. In females, MNPs cause irregularities in ovarian and uterine construction, upset hormonal equilibrium, prompt cell demise in granulosa cells, disturb the hypothalamic-pituitary-ovary hub, and lead to tissue fibrosis/ [33]

Molecular simulation study proposes that BPA cooperates with atomic receptors of cells by means of H-security and hydrophobic associations. BPA was found to have stable interactions with 3 atomic receptors in particular by human estrogen receptorα, human estrogen-related receptor γ and human peroxisome proliferator-activated receptor γ.[34] Poisonous heavy metals in colors and stabilizers, e.g., cadmium, chromium, lead and mercury, are other unsafe added substances in a few plastic things.[31] It leaves cell receptors in dynamic compliances, hence upsetting ordinary endocrine elements of the cell [34].

According to human epidemiological research, exposure to phthalates is significantly linked to poor reproductive outcomes in both men and women, including type II diabetes and insulin resistance, obesity, allergies, and asthma [35}.

Exposure to phthalates causes changes in structures that are androgen dependent, which lowers testosterone biosynthesis in the fetuses, according to a number of studies that used rats as model. Cell aggregates and deformed seminiferous cords were also observed in the fetal testes. It was also observed that some structures, including the prostate and seminal vesicles, were malformed [36].

CONCLUSION

The growing body of evidence highlighting the presence and toxicity of micro and nano plastics in human tissues and organs calls for urgent action to address plastic pollution. Exposure to these particles, which are prevalent in the environment, poses significant health risks, including inflammation, oxidative stress, gastrointestinal and cardiovascular disorders, and reproductive health problems. While further research is necessary to fully understand the long-term implications of microplastic exposure, the current evidence underscores the importance of reducing plastic waste and minimizing human exposure to these harmful pollutants. Moreover, strategies to mitigate plastic pollution and improve waste management practices are critical to safeguarding both environmental and human health in the future.

The Following needs to be done:

Prevention: Reducing the use of plastics, improving waste management, and advancing recycling technologies can help limit MNP contaminatio.

Regulation: Regulatory agencies should consider setting limits on MNP exposure and promoting research into safer alternatives to plastics.

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