REVIEW ARTICLE

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A comprehensive review of the impact of microplastics on the Respiratory, Digestive and Renal Systems – mechanisms of toxicity and health implications

Kompleksowy przegląd wpływu mikroplastików na układ oddechowy, pokarmowy i moczowy – mechanizmy toksyczności i implikacje zdrowotne

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Abstract

Introduction and Objective. In 2021, global plastic production reached 390.7 million tons and continues to increase annually. The accumulation of microplastic (MP) particles has been observed in all tissues and body fluids, with the respiratory tract, gastrointestinal tract and urinary system being particularly vulnerable to its toxic effects through direct contact.

Review Methods. The PubMed database was searched using various combinations of specific key words: 'microplastics', 'nanoplastics', 'lung diseases', 'intestinal diseases', 'renal diseases', and 'hepatic diseases'.

Brief description of the state of knowledge. In response to microplastic stimulation, disturbances in oxidative stress balance and increased free radical formation have been observed in lung parenchyma, along with inflammation development via activation of the NF-κB pathway dependent on p38 phosphorylation and the Wnt/β-catenin pathway. Similar changes were observed in the gastrointestinal tract where microplastic-induced activation of the ROS–NF-κB/NLRP3/IL-1β/MLCK stress pathway led to damage to the intestinal barrier, alterations in gut microbiota composition, and disruptions in microbial metabolism. In the kidney parenchyma, in addition to the activation of the prior-mentioned inflammatory mechanisms, microplastic exposure resulted in inhibited cell proliferation, intracellular accumulation of microplastics, and a decrease in the expression of genes encoding antioxidant enzymes. This reduced the cells ability to neutralize free radicals and intensified cytotoxic effects.

Summary. Understanding the health risks of daily microplastic exposure requires interdisciplinary studies that reflect real-world concentrations, emphasizing chronic effects, particle characteristics and their interactions with associated compounds.

Key words

microplastic, nanoplastic, environmental pollution, microplastic toxicity, respiratory diseases, renal diseases

Streszczenie

Wprowadzenie i cel pracy. Globalna produkcja plastiku w 2021 roku wynosiła 390,7 mln ton i liczba ta rokrocznie się zwiększa. Akumulację cząsteczek mikroplastiku (MP) zaobserwowano we wszystkich tkankach i płynach ustrojowych, a szczególnie narażone na jego toksyczne działanie – ze względu na bezpośredni kontakt z MP – są drogi oddechowe, przewód pokarmowy i układ moczowy.

Metody przeglądu. W celu przeprowadzenia przeglądu literatury przeszukano bazę PubMed przy użyciu różnych kombinacji konkretnych haseł: „microplastics", „nanoplastics", „lung diseases", „intestinal diseases", „renal diseases" i „hepatic diseases".

Opis stanu wiedzy. W odpowiedzi na stymulację mikroplastikiem w miąższu płucnym zaobserwowano zaburzenia równowagi stresu oksydacyjnego i wzrost powstawania wolnych rodników, rozwój zapalenia poprzez aktywację szlaku NF-κB zależnego od fosforylacji p38 oraz szlaku Wnt/β-katenina. Podobne zmiany dostrzeżono w przewodzie pokarmowym, gdzie z powodu aktywacji przez mikroplastik szlaku zależnego od stresu oksydacyjnego ROS–NF-κB/NLRP3/IL-1β/MLCK dochodziło do uszkodzenia bariery jelitowej oraz zaburzeń w składzie, a także w metabolizmie mikrobioty. W miąższu

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nerki pod wpływem działania MP oprócz aktywacji wspomnianych wyżej mechanizmów zapalnych wykazano również zahamowanie proliferacji komórek, gromadzenie się mikroplastiku w ich wnętrzu oraz spadek ekspresji genów kodujących enzymy antyoksydacyjne, co zmniejszało zdolność komórek do neutralizowania wolnych rodników i nasilało efekt cytotoksyczny.

Podsumowanie. Codzienna ekspozycja na mikroplastiki wymaga rzetelnej oceny zagrożenia poprzez interdyscyplinarne badania oparte na realistycznych stężeniach środowiskowych, uwzględniające długoterminowe skutki, właściwości fizykochemiczne cząstek oraz ich oddziaływania z innymi substancjami.

Słowa kluczowe

mikroplastik, nanoplastik, zanieczyszczenia środowiskowe, toksyczność mikroplastiku, choroby nerek, choroby układu oddechowego

INTRODUCTION

Plastic is a material composed of polymers that are either artificially synthesized or naturally occurring but modified through polymerization processes. Due to its physicochemical properties, such as lightness, water resistance and durability, it is a multifunctional and importantly, relatively inexpensive material. The direct benefits of its use for human health and the environment are undeniable as it helps extend the shelf life of perishable food products, reduces fuel consumption in the automotive industry due to its low weight, and enables medical procedures requiring sterility by being a key component of tools such as disposable gloves and catheters. However, increasing attention is being given to the problem of uncontrolled plastic leakage into the environment. This issue often arises from improper solid waste management and a lack of adequate infrastructure for its reduction and reuse, as currently, only 21% of plastic undergoes recycling. This situation poses a potential threat to the environment, entire ecosystems, and human health [1]. It is projected that global plastic production, which amounted to 390.7 million tons in 2021, will rise to as much as 590 million tons by 2050. This growth is particularly striking when compared to the early 1950s, when annual plastic production was approximately 1.7 million tons [2].

Microplastics are defined as plastic particles smaller than 5 mm, with those under 1 μm referred to as nanoplastics (NP). Among the polymers currently produced, the most dominant substances include polyethylene (28.5%), polypropylene (16.7%), polyvinyl chloride (9.1%), polyethylene terephthalate (8.1%), and polystyrene (6.1%) [3]. Key sources of microplastic accumulation in the environment and living organisms include textile fibres, cleaning agents and cosmetics, tyre wear, construction waste, and paints. Currently, the fragmentation of bigger plastic objects appears to be the primary source of pollution. However, it is important to recognize that in all cases, human activity is directly responsible for the accumulation of plastic particles in the environment. Newer sources of concern include plastic-coated fertilizers, agricultural films, mechanical plastic recycling, and the breakdown of marine ropes and fishing nets.

The exact rate at which macroplastics degrade into microplastics and subsequently into nanoparticles is not fully understood. Additionally, the precise time frame required for the complete mineralization of plastic remains undetermined. However, the rate of biodegradation appears to be significantly slower than the rate at which plastic accumulates in the environment. As a result, it is suggested that, except for plastic that has been incinerated, all conventional plastics ever produced still exist on Earth in a form too large to undergo biodegradation. A potential solution to this issue was the development of plastics with a shorter degradation time. However, incomplete degradation of these materials has proven to be another source of microplastics and may only be beneficial in specific scenarios [4].

Research conducted over the past decade has demonstrated that microplastic pollution is a global phenomenon and no environment remains free from its presence. Microplastics have been found in the gastrointestinal tracts of seahorses inhabiting the deepest regions of the Pacific Ocean, reaching depths of 10,890 meters [5], as well as in Antarctic freshwater reservoirs within the Antarctic Specially Protected Area on Byers Peninsula, where their presence had not been reported prior to 2020 [6].

It is estimated that approximately 7.6 million tons of macroplastic enter the oceans each year, while terrestrial environments receive three to ten times more. This amounts to a total of 10–40 million tons of plastic infiltrating ecosystems annually. Furthermore, due to the fragmentation of existing waste, even if plastic production were to cease entirely, the amount of microplastics in the environment would continue to increase. There is no doubt that, over time, the concentration of microplastics in the environment will rise, along with human exposure, which is already a growing concern and the subject of numerous studies [4]. According to a 2019 WHO report on the presence of microplastics in drinking water, the smallest detected particles measured 1 μm. This limitation likely resulted from the constraints of laboratory techniques available at the time, which were unable to detect smaller molecules. In surface water samples, the detected microplastic concentration ranged from $0–10^3$ particles/L, whereas in drinking water, where finer measurement filters were used, concentrations ranged from $0–10^4$ particles/L [1].

Table 1. Average daily intake of microplastics in MP/kg body weight per day for adults, infants, and newborns

Parameter	Adult	Infants	Newborn
Inhaled Dose	114	190	362
Dust Ingestion	0.21	3.4	N/A
Estimated Daily Intake	96	N/A	96
Total Daily Intake	210	193	458

Source: [7] N/A- No data available

Microplastics enter the human body through inhalation, ingestion, or direct skin contact. Limited data suggest that only a small fraction of these polymers can cross epithelial barriers in the alveoli or intestines, with permeability increasing as particle size decreases. Although the amount of microplastics entering the body appears to be minimal,

long-term exposure and potential accumulation are significant concerns, requiring further investigation and understanding [4]. Additionally, microplastics are suspected of acting as vectors for opportunistic bacteria, biomolecules, and other substances adhering to their biofilm, facilitating their entry into the body.

The respiratory tract, with a total surface area exceeding 100 m^2, represents the largest interface between the human body and the external environment. Constantly exposed to airborne particles, it is considered the primary route of microplastic entry and accumulation [1]. Microplastics have been detected in all human tissues and body fluids, suggesting they are actively absorbed, transported throughout the body, and subsequently either accumulated or eliminated. A study conducted by Zhu et al. using laser spectroscopy analyzed the presence of microplastic particles larger than 20 μm in human tissues. The highest concentrations were found in lung parenchyma, averaging 14.19 ± 14.57 particles per gram, followed by the small intestine (9.45 ± 13.13), large intestine (7.91 ± 7.00), and tonsils (6.03 ± 7.37 particles per gram). Polyvinyl chloride was the most dominant polymer, and plastic accumulation was significantly higher in women than in men [8]. Laser spectroscopy has also been used to examine microplastic presence in placental tissues, where polymers were detected in every collected sample. The average concentration was 2.70 ± 2.65 particles per gram, with particle sizes ranging from 20.34–307.29 μm, approximately 90% of which were smaller than 100 μm. Polyvinyl chloride was again the most prevalent polymer, followed by polypropylene and polybutylene [9].

MATERIALS AND METHOD

To conduct this literature review the PubMed database was searched using various combinations of specific key words: 'microplastics', 'nanoplastics', 'lung diseases', 'intestinal diseases', 'renal diseases', and 'hepatic diseases'. After an initial review of the abstracts, publications unrelated to the topic of the article or focused on oncogenesis were excluded. Ultimately, 30 studies published between 2019–2025 were analyzed to ensure the review›s relevance and up-to-date coverage.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Microplastic-mediated respiratory diseases. The respiratory system is the first to directly interact with microplastic particles, making it particularly vulnerable to damage caused by their toxic effects. Currently, well-defined mechanisms of MP-induced harm include endoplasmic reticulum stress, inflammation, and oxidative stress imbalance which may exacerbate or contribute to respiratory diseases such as pulmonary fibrosis, asthma, chronic obstructive pulmonary disease (COPD) and even cancers [10]. The impact of plastic nanoparticles appears to depend on their size, with smaller particles tending to elicit a stronger inflammatory response; however, this is not a universal rule. Inflammation may also be triggered by the absorption of chemical substances associated with MP particles [11]. A major challenge remains in determining the duration and intensity of exposure required to cause significant damage. A study by Bengali et al. observed moderate acute toxicity *in vitro,* with effects becoming noticeable only after prolonged exposure to high concentrations of MP (100 μg/ml for more than 48 h). Additionally, subtoxic effects, such as cytoskeletal remodeling and genotoxicity, were detected, likely resulting from surface interactions and cellular uptake of MP particles. This suggests the potential for chronic adverse clinical implications due to the persistence of insoluble microplastics in lung tissues [12].

In a study by Woo et al., mice exposed to polypropylene showed lung parenchyma damage, including pneumocyte hypertrophy, foam macrophage aggregation and infiltration of the parenchyma by inflammatory cells. In *in vitro* conditions, it was observed that the mechanism behind the damage, and ultimately the death, of respiratory epithelial cells is mitochondrial dysfunction caused by their depolarization and ATP level reduction, as well as directly through cytotoxicity, increased production of free radicals and pro-inflammatory cytokines (TNF-α, IL-1β, and IL-6). This suggests that stimulation with polypropylene may contribute to the development of inflammation through the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway, dependent on p38 phosphorylation, resulting from mitochondrial damage [13]. Similar effects were observed in response to stimulation with polystyrene, where lung damage was caused by the activation of intracellular oxidative stress dependent on free radicals, and the toxic effect of microplastics was reduced after the application of ROS inhibitors (reactive oxygen species), such as N-acetylcysteine [14]. In another study using low concentrations of microplastics, such as 0.0125 mg/mL, which corresponds to levels found in the environment, no massive cell death was observed. However, electron microscopy analysis showed that nanoparticles could penetrate cells and cause mitochondrial damage, which was confirmed by the overproduction of reactive oxygen species in mitochondria, changes in mitochondrial membrane potential, and inhibition of mitochondrial respiration [15]. An interesting observation was made in a study conducted by Tomonaga et al., where they analyzed the composition of bronchoalveolar lavage fluid and lung parenchyma fragments in rats for 6 months, who were intratracheally administered polystyrene particles in doses of 0.2 mg and 0.1 mg. In the experimental group, a significant increase in the number of inflammatory cells was observed up to 1 week after exposure to a high dose, along with an increase in lactate dehydrogenase (LDH) activity up to 3 days after exposure, but not in the chronic phase. Histopathological preparations showed an influx of inflammatory cells into the alveolar space lasting up to 1 week, but after a longer time, no signs of inflammation and fibrosis were found in the lung tissue, suggesting that these reactions are limited to the acute phase. Polystyrene modified with the amine group caused greater oxidative stress compared to the group modified with the carboxyl group and the unmodified one [16].

Among the diseases resulting from intensive or prolonged exposure to microplastics, pulmonary fibrosis is included. Identifying microplastics as a potential factor contributing to the development of interstitial lung disease is significant because it is a disease with a progressive and chronic course, poor prognosis, and a short median survival time. In a study by Li et al. on mice inhaled with high doses of MP (6.25 mg/kg for 3 weeks), it was shown that polystyrene induces lung fibrosis in a dose-dependent manner [17]. The mechanism

behind this process involves the activation of oxidative stress and the Wnt/β-catenin signalling pathway. This pathway regulates the differentiation of epithelial cells and fibroblasts and exposure to microplastics was found to increase the levels of fibroblast markers such as vimentin, α-smooth muscle actin (α-SMA) and collagen I. Inhibition of this pathway may be a potential method for preventing lung fibrosis [18].

There is insufficient evidence to categorically confirm a relationship between microplastics and the occurrence or progression of chronic obstructive pulmonary disease (COPD). Smoking is considered the leading risk factor and MP particles sized 20–500 μm are present in cigarette smoke. However, it is difficult to attribute the disease's progression solely to their impact. Two *in vitro* studies have shown that exposure to high concentrations of polystyrene leads to a decrease in the expression of the glycoprotein α1-antitrypsin, the deficiency of which is a recognized risk factor for the development of COPD [19, 20].

Despite the well-known correlation between air pollution and the development of asthma, the potential role of microplastics in this mechanism is not obvious. In *in vitro* studies using an allergic asthma model with ovalbumin, exposure to MP particles at a concentration of 5 mg/kg body weight for 28 days, had a minimal impact on inflammation in the airways and bronchial hyperreactivity. However, simultaneous exposure to MP and di-(2-ethylhexyl) phthalate (DEHP) resulted in increased oxidative stress, a stronger Th2-type response, and enhanced activation of the transient receptor potential ankyrin 1 (TRPA1) pathway, as well as mitogen-activated protein kinase 38 (p38 MAPK) [21]. Chen et al., analyzing the presence of MP in bronchoalveolar lavage fluid in Chinese children, found no significant differences in MP levels between patients suffering from asthma and those with community-acquired pneumonia. However, in the group with severe pneumonia, significantly higher MP concentrations were recorded compared to the milder form. This suggests that the relationship between microplastic inhalation and the development of lung diseases in the paediatric population is a complex issue [22].

Microplastic-mediated intestinal and hepatic diseases. The annual intake of microplastics is estimated to be around 39,000–52,000 particles per person, resulting from the direct ingestion of plastics through food or via the mucociliary clearance mechanism. It is believed that particles larger than 150 μm are not absorbed, but can still negatively affect the digestive system by increasing intestinal permeability or interacting with the microbiota. Since they come into direct contact with enterocytes, they may provoke a local inflammatory response. Particles smaller than 150 μm can be absorbed, although particle size alone is not necessarily the rule, as it also depends on the surface properties of the microplastics. Although their overall absorption is low, it can lead to systemic toxicity, as nanoparticles are transported throughout the body and penetrate into deep layers of organs [23].

In a study by Yan et al., it was observed that among patients suffering from inflammatory bowel diseases, the concentration of microplastics in faeces was significantly higher compared to healthy individuals (41.8 particles/g dry matter vs. 28.0 particles/g dry matter). Furthermore, a positive correlation was found between the number of particles and the severity of the disease [24]. It is believed that dysfunction of the intestinal barrier results from the activation of the oxidative stress-dependent ROS–NF-κB/NLRP3/IL-1β/MLCK pathway by microplastics. In mice exposed to polystyrene at 1 mg/kg body weight for 28 days, increased permeability of the colon epithelium was observed due to a decrease in the expression of tight junction proteins (e.g., occludin, zonula occludens), reduced mucus production, increased expression of pro-inflammatory cytokines, and infiltration of inflammatory cells into the colon. Particles larger than 5 μm caused more severe damage. Impairment of the intestinal barrier due to plastics means that an even greater amount of microplastics can be absorbed, leading to the accumulation of negative effects of exposure [25]. Microplastics, through their toxic effects on the structure and function of enterocytes, also contribute to the flattening of villi and reduction of the active surface area for nutrient absorption, changes in the metabolism of lipids, amino acids, and glucose, thereby leading to malabsorption and digestive disorders [26].

Although there is a lack of sufficient human studies, data from animal models suggest that microplastics (MP) influence the composition of the gastrointestinal microbiota through their pro-inflammatory properties and direct induction of structural and functional changes in the mucosal membrane. An increase in the abundance of bacteria, such as *Firmicutes, Proteobacteria, Chlamydiae,* and a simultaneous reduction in the populations of *Bacteroidetes, Actinobacteria, Bifidobacterium, Ruminococcus* and *Halomonas,* have been observed. Changes in gut microbiota metabolism were also noted, including a decrease in the activity of pathways related to sulphur and pyruvate metabolism, tyrosine, vitamin B6, and fatty acid biosynthesis, as well as the degradation of fluorobenzoates and polycyclic aromatic hydrocarbons. However, an increase in activity was observed in pathways regulating mineral absorption, nitrogen metabolism, and the synthesis of isoflavonoids and carotenoids. It is also worth mentioning that MP increase the expression of genes responsible for antibiotic resistance, including tetracyclines, beta-lactams, aminoglycosides, and multidrug resistance [27].

It should be emphasized that the concentrations and shapes of nanoparticles to which experimental models were exposed do not necessarily correspond to actual environmental conditions, as well as the fact that the biological implications of MP exposure have been studied in zebrafish and mice, which, despite their genetic similarities to humans, will differ from human metabolism. In an observational study conducted by Zhang et al., the gastrointestinal and nasal microbiota of 20 workers from a Chinese plastic factory in Chengdu was analyzed and compared to the gut microbiota of 20 volunteers from areas with non-contaminated environments. Among individuals with high exposure to plastics, a statistically significant increase in the abundance of *Bifidobacterium, Streptococcus* and *Sphingomonas* bacteria was observed, which are known to correlate with gastrointestinal diseases, as well as a simultaneous reduction in the number of bacteria with health-promoting properties, including *Ruminococcus Torques Group, Dorea, Fusobacterium* and *Coprococcus*. The MP content in faeces in the high-exposure group was significantly higher than in the less exposed population ($p<0.001$), with polyurethane being the dominant material, constituting 37.30% of MP in the high-exposure group and 29.09% in the low-exposure group [28].

Among the negative effects of exposure to microplastics (MP), liver dysfunction is also mentioned. As the primary detoxifying organ in the body, the liver is particularly vulnerable to their harmful effects, although the extent and severity of the issue are not yet fully understood. Studies show that prolonged contact with MP not only results in their accumulation in the liver but, more importantly, leads to the occurrence of inflammatory responses, oxidative stress, lipid metabolism disorders and liver fibrosis. A meta-analysis conducted by Zhang et al., which included 70 studies using animal models, showed that exposure to MP was associated with a significant increase in liver enzyme levels (ALT and AST), oxidative stress markers (MDA), and pro-inflammatory cytokines (IL-6 and TNF-alpha). Moreover, a significant reduction in antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), and glutathione peroxidase (GPx), which are involved in antioxidant processes, was observed [29]. Zhang et al. also identified oxidative stress and intracellular toxicity as the most significant mechanisms of plastic-induced hepatotoxicity. In a meta-analysis using data from 118 studies on vertebrates, they observed that organisms exposed for longer periods, to higher concentrations, smaller plastic particles, and younger organisms, were more susceptible to the harmful effects of MP. The potential pathogenicity of synthetic polymers may also stem from their complex interactions with heavy metals and xenobiotics which they carry, meaning that the true toxicity of microplastics may be either underestimated or overestimated [30].

In most experimental studies, models were subjected to short and intense exposure to microplastics, it is therefore worth comparing them with a 2025 study by Shi et al., where the observation time was significantly longer – lasting 6 months. Mice were exposed to polystyrene at a dose of 10 mg/L administered in drinking water, which led to the development of non-alcoholic fatty liver disease (NAFLD). Additionally, positively-charged polystyrene particles caused a greater toxic effect than unmodified ones. It was found that MP activated the HO-1/Nrf2 pathway, leading to ferroptosis, manifested by intense lipid peroxidation, excessive iron accumulation, and an increase in markers associated with ferroptosis [31]. Wang et al. also observed lipid deposition in the liver of mice exposed to polystyrene. Rodents were given water containing MP at concentrations of 100 μg/L or 1,000 μg/L for 8 weeks, which resulted in disturbances in the liver lipid profile, shown by increased levels of free fatty acids. Compared to the control group, the increase in the low-dose and high-dose groups was 20.2% and 26.4%, respectively. Moreover, in the high-exposure group, impaired glucose tolerance was observed, but there was no increase in body weight or serum triglyceride levels. Altered expression profiles were visible in genes encoding fatty acid degradation pathways, arachidonic acid metabolism and unsaturated fatty acid biosynthesis [32].

The accumulation of microplastics in the liver may also be significantly influenced by comorbidities. Furthermore, the results of a study conducted by Horvatits et al. on 11 German patients suggest that pre-existing liver cirrhosis could be crucial for the accumulation of plastics in organs. Using fluorescence microscopy and Raman spectroscopy, 6 samples from patients with liver cirrhosis who had undergone organ transplants were compared with 5 samples from autopsies of non-affected patients. It was shown that in healthy patients, the concentration of microplastics in tissues was below the detection level of 3.0282 (mean + 3 standard deviations), with the highest concentrations ranging from 0.3–1.9 particles per gram, whereas in patients with cirrhosis, the highest concentrations ranged from 4.6–11.9 particles per gram of tissue. The polymer concentrations in liver samples from cirrhosis patients were significantly higher than in control samples ($p = 0.009$). Therefore, it is not at all clear whether the accumulation of MP contributes to the development of fibrosis, or whether it is a consequence of portal hypertension and liver failure [33].

It is suspected that MP may also contribute to the formation of gallstones. In a study by Zhang et al., the composition of 16 gallstones from patients who underwent laparoscopic cholecystectomy was analyzed and microplastic particles were detected in all the collected materials, with significantly higher content in individuals under 50-years-old. This correlation was later confirmed in a study on mice, which, being on a high-cholesterol diet and simultaneously exposed to microplastics, developed a more severe form of gallstone formation. It is believed that MP have the ability to form large heteroaggregates with cholesterol particles [34]. Additionally, exposure to polystyrene further exacerbated glucose metabolism disorders caused by a high-fat diet and caused changes in the microbiota, particularly the proliferation of bacteria such as *Ileibacterium* and *Bifidobacterium* ($p < 0.05$). No correlation, however, was observed between exposure to microplastics and blood glucose levels in the regular diet group [35].

Microplastic-mediated renal diseases. The urinary system, being one of the last systems in contact with microplastics entering the bloodstream, can be a site for the accumulation of these particles. Once MP enter the urinary system, like in other organs, they induce oxidative stress [36]. Oxidative stress, caused by the excessive production of reactive oxygen species, leads to impaired kidney function. Exposure to microplastics additionally affects the altered expression of antioxidant marker genes. Studies have observed a decrease in the levels of SOD2, CAT, and the glycolysis marker glyceraldehyde-3-phosphate dehydrogenase (GAPDH) [37, 38].

The reactive oxygen species produced as a result of MP exposure can damage the endoplasmic reticulum. In 2021, Wang et al. conducted studies on male mice kidney tubular cells *in vivo*, using polystyrene particles of 2 μm in size. The results showed not only an increased ROS concentration, but also a rise in the levels of mitochondrial protein Bad, which is associated with mitochondria-dependent apoptosis. However, another protein involved in this process, Bax, was not significantly elevated after exposing the cells to MP. In response to endoplasmic reticulum stress, an increased expression of ATF6 was also recorded, leading to the activation of genes responsible for repairing damaged proteins in the endoplasmic reticulum. Additionally, MP exposure caused an increase in the concentration of inositol-requiring enzyme 1α (IRE1α) in the cells exposed to MP for 24 hours. The IRE1α protein initiates repair functions or apoptosis in cases of excessive endoplasmic reticulum stress [38]. Moreover, endoplasmic reticulum stress leads to the release of arachidonic acid, which is then converted into prostaglandin E2, activating the NF-κB pathway. Endoplasmic reticulum damage is part of the pathomechanism behind diseases such

as diabetic nephropathy, acute kidney injury, and primary glomerular kidney damage [35]. Oxidative stress also triggers necroptosis, as demonstrated in a 2022 study by Meng et al., which was conducted on chicks exposed to polystyrene microplastics at concentrations of 1, 10, and 100 mg/L for 6 weeks. Necroptosis resulted from the activation of the RIP1/RIP3/MLK pathway. The results showed a dose-dependent relationship between the administered dose and the degree of kidney damage in the chicks [38].

Goodman et al. (2022), in addition to analyzing the effect of polystyrene on oxidative stress in human HEK 293 kidney cells, also investigated the impact of exposing these cells to polystyrene microplastics of 1 μm size for 24, 48, and 72 hours. The researchers observed the internalization of MP by living cells and a significant reduction in cell proliferation after 48 hours, compared to the control group. Furthermore, there was a notable decrease in the metabolic activity of kidney cells, which dropped by 61%, compared to cells that were not exposed to MP. Additionally, the expression of genes encoding antioxidant enzymes, such as superoxide dismutase and catalase, was reduced 37. However, no significant difference in cell viability was observed between cells exposed and not exposed to microplastics [37, 39]. The nephrotoxicity of MP is also linked to the inflammatory response they induce. Microplastics activate the NF-κB p65 pathway, which leads to an increase in pro-inflammatory factors in the kidneys, such as TNF-α, iNOS, IL-1β and IL-6. As mentioned earlier, this response is exacerbated by endoplasmic reticulum stress, ultimately leading to glomerular fibrosis and the worsening of kidney function [38].

CONCLUSIONS

Every day, we are exposed to a wide range of particles resulting from the degradation of plastics; however, the scale of this phenomenon has not been precisely determined. It is important to use the latest technologies to detect microplastic levels in air, soil, food and drinking water in order to realistically assess the threat. The impact of MP on intracellular metabolism, tissue structure and function has been extensively studied, identifying potential cytotoxicity mechanisms using cell lines *in vitro*, zebrafish, mouse models and human-derived material. However, the problem in interpreting these results is the fact that the MP doses used in most studies were significantly higher than the concentrations naturally occurring in the environment. This led to the induction of acute toxic reactions, whereas in the context of daily, long-term exposure and its pathogenicity, chronic complications should be analyzed. Large-scale studies are needed, involving researchers from the medical sector, environmental sciences, biotechnology and plastics experts to determine the actual health risks associated with continuous exposure to microplastics. When designing further studies, attention should be paid to the concentration of substances, ensuring that they correspond to those naturally occurring in the environment, as well as to the duration of exposure, the type of substance, its size, shape, and surface properties, as well as other associated chemicals, including proteins, toxins or biofilm-forming opportunistic bacterial colonies.

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