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THE HEALTH IMPACT OF HUMAN EXPOSURE WITH MICROPLASTICS: A REVIEW

Anamaria-Iosefina TRIFU*, David DEBU*, Marius Alexandru MOGA and Mihaela BADEA

Faculty of Medicine, Transylvania University of Brasov, 56 – Nicolae Balcescu St, Brasov – 50019, Romania,
iosefinatrifu@gmail.com, daviddebu1@gmail.com, moga.og@gmail.com, mihaela.badea@unitbv.ro
**Both authors contributed equally to this paper*
Corresponding author: mihaela.badea@unitbv.ro

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Currently, plastics hold a crucial role in the production of various products such as packaging, construction materials, textiles, consumer goods, transportation components, electrical devices, and industrial machinery. However, in response to environmental concerns regarding pollution and post-consumer waste, there's a growing shift towards substituting plastics with recycled and biodegradable alternatives. Improper reuse or recycling of products can lead to the generation of micro- and nanoplastic particles. In this review, we initially provided a concise overview of the environmental pollution caused by micro- and nanoplastic particles (MNPs), subsequently exploring their potential health impacts on DNA, reproductive system, endocrine function, weight gain, insulin sensitivity, and possibly cancer. In addition, our review states that in recent studies there were MNPs found in the Danube River, which are carried in the Black Sea, concluding that the population of Romania is at risk of developing diseases and health issues if the problem is not addressed in the near future.

Keywords: microplastics, post-consumer waste, potential health impacts, Danube River, Black Sea.

INTRODUCTION

Microplastics (MPs) are particles characterized by a diameter of less than 5 mm, whereas nanoplastic particles (NPs) typically range between 1 and 100 or 1000 nm. They are found in water, soil and air, suggesting that humans can be exposed to them through consumption of polluted liquids and foods and also through inhalation[1].

These particles can be categorized into primary and secondary plastic debris. Primary plastic particles are intentionally manufactured at specific sizes, while secondary plastic debris is formed through fragmentation in the environment or during usage. Consequently, secondary MPs/MNPs may be found in diverse sizes and shapes, affecting their dispersion and distribution in both the environment and within living organisms. Furthermore, during the ageing process, secondary plastics may carry additional contaminants that contribute to the toxic effects of MPs/NPs[1].

To enhance the quality of human life and for the sake of convenience, plastics are integrated into a variety of items utilized by humans, including polyvinyl chloride (PVC) products, medical devices, and food packaging[2]. However, the lack of proper management has the consequence of the worldwide spreading of plastic pollution, with evident negative effects. Plastic production has witnessed a significant surge over the past 70 years, surging from 1.7 million tons in the 1950s to a remarkable 348 million tons by 2017[3]. While humans possess clearance mechanisms designed to safeguard them against potentially harmful substances, exposure to microplastics (MPs) still implies high risks. These include inflammation, oxidative stress, and DNA damage, which could potentially contribute to the development of cardiac and pulmonary diseases, as well as cancer, as determined in studies made *in vitro* and also *in vivo*[1.]

Moreover, Hou *et al*.[4] and Zhao *et al*.[5] stated in their studies that MPs have the potential to cause reproductive toxicity and can accumulate in the testes, adversely affecting the fertility of men. Various types of testicular cells were examined to support this assertion, along with elucidation of the involved mechanisms including excessive generation of reactive oxygen species (ROS), autophagy, and pyroptosis[3]. However, findings from animal experiments have uncovered significant evidence in this case.

Regarding the female reproductive system, there were MPs found in multiple tissues, bodily fluids and excreta, including blood, stool and placenta discovered by Yuan et al. in their study[6]. In addition, the damage is dose-dependent with an obvious disfunction of the hypothalamus-pituitary-gonadal axis. Since MPs and NPs can pass through the placental barrier, fetal development can be susceptible to abnormalities[6].

The discovery of microplastics (MPs) in the Danube River was first noted in a study examining fish larvae[7]. Following this, a separate study focused on microplastics developed a sampling tool and presented initial data on their transportation within the Danube River[8].

Subsequent research has consistently reported both the presence and movement of significant quantities of plastic waste and microplastics towards the Black Sea, which is greatly impacted by the Danube River[9].

The European Commission's goal remains to enhance an accessible and also unified market for food products conforming with the EU regulations[10], aiming to uphold people’s health and safety while identifying and eliminating non-conforming products. Under this framework, every EU member state is required to submit information about its marketed food products to achieve a thorough grasp of their quality and safety standards. In Romania, the majority of studies have centred on evaluating the risk of potentially toxic elements (PTEs) to population health through the ingestion of vegetables, dairy products, wine, and drinking water[8]. Furthermore, research addressing human risk assessment concerning PTE ingestion from fish and seafood consumption primarily focuses on marine species.

The principal method by which microplastics enter the bodies of fish is through ingestion, with studies suggesting that approximately 80% of the top 10 marine fish species that were captured have consumed microplastics[11].

Because of their size, MPs enter the food chain directly through the gastrointestinal route. This has been illustrated by the ingestion of polluted algae by the planktonic crustacean- *Daphnia magna*, followed by ingestion by a secondary consumer fish, ultimately culminating in consumption by an end consumer fish[7].

Considering the aforementioned points, it becomes imperative to give particular consideration to the utilization of microplastics in our daily lives. Thus, this paper examines a review of the risks posed to human health and the environment by microplastics (MPs) and nanoplastics (NPs).

THE IMPACT OF MPs ON HUMAN HEALTH

The most frequent MPs and NPs that are ingested by humans are found in mussels, fish, commercially sold salt, sugar, as well as honey, tea bags and bottled drinking water. Contaminants can be found in plastic water bottles and containers.

Due to the involvement of multiple precise steps in human germ cell generation, the process is susceptible to the influence of various environmental factors, as Ge *et al*. mention in their paper[11].

It has been shown that exposure to microplastics results in testicular toxicity and decreased sperm production. Several cells were analyzed: germ cells, Sertoli cells, and Leydig cells[3].

In an experiment conducted on mice and documented by Zeng *et al*., it was observed that microplastic (MP) pollution adversely affected the viability of granulosa cells, leading to implications for the fertility of female mice. Furthermore, animal studies have determined that microplastics (MPs) impact the swimming performance of male sperm, resulting in decreased production of ATP, reduced sperm viability, and altered DNA integrity, ultimately contributing to infertility[3].

A recent study has also discovered that exogenous hydrogen sulfide (H_2S) mitigates the overactive autophagy and mitochondria-mediated apoptosis triggered by PS-NPs in the mouse spermatocyte cell line GC-2 by modulating the peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) and Nrf2 signalling pathways[3].

Hamza *et al*.’s research made a new connection and discovered that the injury inflicted on germ cells by PS-MPs/NPs involves significant roles of oxidative stress initiated by reactive oxygen species (ROS) and programmed germ cell death pathways, including apoptosis, autophagy, and necroptosis, along with inflammation and DNA fragmentation[12].

It is essential to mention that although we possess information regarding the dose-dependent effects of particles on human health and fertility, it remains unclear whether size-dependent effects also hold significance. Presently, it can only be affirmed that smaller particles can easily breach the barriers of the human body and enter cells.

Y. Zhang *et al*. in their study revealed that the ingestion of polyethylene microplastics (PE-MPs, 10–150 μm, 40 mg/kg/day) orally for 30 days was found to result in DNA damage, programmed cell death, oxidative stress, and mitochondrial dysfunction in the oocytes of Kunming female mice. After the germ cell impairments, reduced oocyte maturation, fertilization rate, and disrupted embryonic development were witnessed[13].

Additionally, Z. Liu *et al*. found that after 35 days of continuous exposure to polystyrene microplastics (PS-MPs), a decrease in the rate of first polar body extrusion and decreased survival rates of superovulated oocytes were noted in the mouse ovaries[14].

As a conclusion, in subsequent experiments, it was discovered that exposure to PS-MPs for 35 days triggered ovaritis, leading to diminished oocyte quality[14].

Similar to spermatogenesis, the maturation of eggs is a complex and continuous process. This raises the question of which phase of egg development in the ovaries could be impacted by exposure to microplastics/nanoplastics (MPs/NPs). Given the finite number of eggs in women from birth, there is a chance to develop personalized and precise drug treatment strategies for affected female patients grappling with infertility[3]. Additional research is required to provide treatment options and gain a better understanding of the stages of egg development.

In a study conducted by G. Zuri *et al*., a total of 91 studies were analyzed, and data was collected indicating the presence of MPs in various human tissue specimens, including blood, urine, lung tissue, breast milk, stool, semen, and placenta[15].

To prevent the passage across barriers and reaching target organs or tissues, and to prevent bioaccumulation, clearance mechanisms such as sneezing, coughing, the mucociliary escalator, macrophage phagocytosis, and lymphatic transport are activated[16].

Despite the robust protective mechanisms in humans, these particles have the potential to cause severe diseases such as cardiovascular and respiratory conditions, and ultimately, cancer.

On account of their compact size, humans can accidentally inhale airborne microplastics, potentially leading to discomfort resulting from an inflammatory response (production of cytokines, for example, IL-6, IL-1β, TNF-α, as well as TGF-β) in the respiratory tract and parenchyma[16]. Exposure to MPs harms the normal pulmonary functions of surfactants and destroys the alveolar structure. The airway barrier is affected as well. Even at low concentrations, individuals who are at risk can develop pulmonary lesions, as Atis et al. confirmed in their research[17]. Furthermore, it has been proven that microplastics can be deposited in the human respiratory system and it can cause much harm to patients who have asthma because of their inflammatory response.

Patients with associated respiratory diseases were found to have microplastics present in their lungs and sputum and there were hundreads of particles identified per 10 mL and around 21 types of MPs in the sputum. These included polyurethane (PU), polyester, chlorinated polyethylene and alkyd varnish which collectively accounted for 78.36% of the total of microplastics detected[16].

On the other hand, MPs fragments in the blood flow are carried through the circulatory system are leading to compromised angiogenesis and immunocompetence. There could also be seen an enhanced thrombosis and damaged vascular structure.

RBCs (red blood cells) are the most represented cells in the bloodstream with a life cycle of 120 days. The red blood cells which were treated with PS-NPs triggered the accumulation of aggregates and promoted endothelial cell adhesion. Because of this triggered adhesion, which is considered to be a cause of cardiovascular diseases, it was concluded that NPs might be a potential risk factor for cardiovascular disease in humans[17].

Another study made on RBCs focused on silica nanoparticles (sNPs) and their potential negative effects on RBCs. The study concluded that bigger sNPs fixed on the surface of red blood cells induced a local membrane deformation, meanwhile, smaller sNPs do not have the same effect. The greater the size of the sNPs, the higher haemolytic activity was observed and the internalization rate of the particles at both tested concentrations of 50 and 100 μg/mL. These findings suggest that the sizes of plastic particles have varying effects on cardiovascular cellular components[18].

In addition, studies that were made on mammals proved that exposure to nanoparticles promoted cardiotoxicity, compromised vascular function, and increased blood pressure, with a risk of developing myocardial infarction (Fig. 1). Since cardiovascular diseases remain a leading global cause of mortality, investigating the effects of plastic particles on mortality and morbidity has the potential to save lives.

Additionally, diabetes mellitus represents another health issue spread worldwide with a great impact on human life. In their study, C. Shi *et al*. analyzed the gut-liver axis metabolism which was exposed to MPs and reached the conclusion that the cross path between the liver and the gut led to insulin resistance and even type 2 diabetes- after they measured the levels of fasting blood glucose and fasting insulin. These levels were observed to be significantly elevated in mice exposed to contaminants[19].

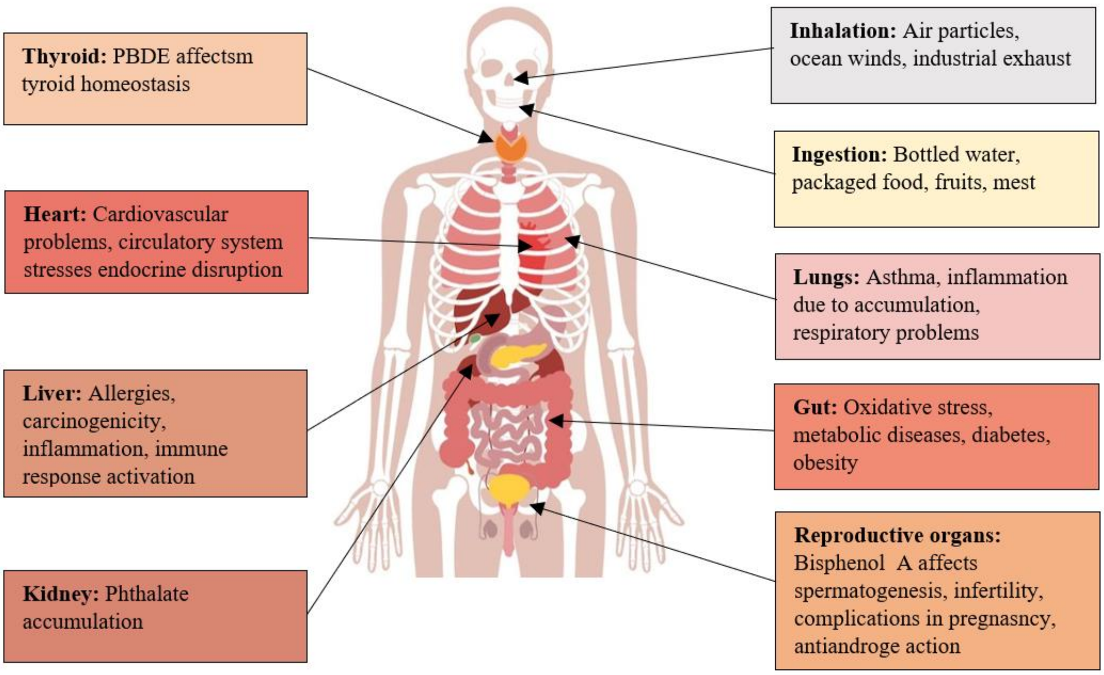

Figure 1. The impact of MPs on human health.

Insulin resistance is an abnormal response to insulin stimulation of tissues, such as muscle, liver and adipose tissue. It is a cellular defect, that reduces glucose disposal, leading to hyperinsulinemia. In time, it will promote hyperglycemia, type 2 diabetes mellitus and metabolic syndrome[19].

Insulin resistance can be evaluated through two main methods: direct and also indirect measurement of insulin sensitivity. The gold standard for proving insulin resistance is HEC (hyperinsulinemic-euglycemic glucose camp), described by Matthewset *et. al*[20]. This procedure consists in giving a non-diabetic patient a constant dose of insulin infusion to maintain insulin levels as well as infused glucose to keep an euglycemic state of the blood glucose. However, direct methods are still quite invasive and non-practical to this day[20].

The indirect methods are used not only to assess cell resistance to insulin, but also to determine the function of pancreatic beta cells.

There are some specific contaminants which are believed to induce insulin resistance, such as BPA[21], bisphenol[22] and phtalates[23]. These chemicals produce polyvinyl chloride, which makes contaminants flexible, more durable and transparent[17]. However, this is a recent study and more information is needed in this case.

Further studies should be conducted to verify the negative impact that microplastics hold, the diseases they produce on humans and also useful methods people can use to reduce pollution and direct contact with MPs. This matter should raise awareness, considering the systemic effect MPs have.

THE IMPACT OF MICROPLASTICS IN ROMANIA

When it comes to MPs spread, Romania is no exception, as they can be found in the Black Sea, carried by the Danube River.

Long half-life pollutants that are released into the environment, for example, plastic materials, can accumulate in the marine basins. As a result, this matter became a general concern for the future of humans, oceans and wildlife.

The Danube, Europe's largest river, contributes to an average of 4.2 tons of plastics to the Black Sea, which passes through many European countries, including Romania. As a consequence, the Black Sea's wildlife is affected. In contrast, the Black Sea provides a large scale of facilities for both humans and the environment[24].

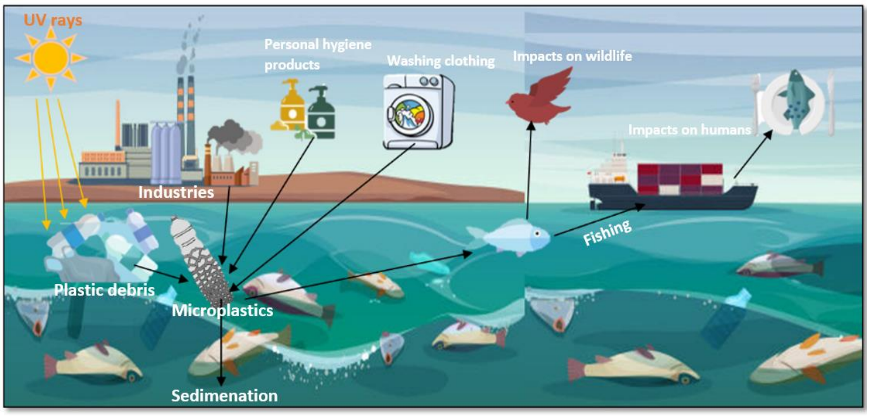

Figure 2. Accumulation of microplastics in the marine environment.

Studies show that MPs pollution in this specific region is secondary to the small continental shelf connecting the urban waters and the ropes and nets used while fishing (Fig.2).

The sole study confirming the existence of MPs in the Danube River was conducted by the University of Vienna between 2010 and 2012, focusing on a stretch of the river between Vienna and Bratislava, according to AGPRES. The findings revealed that approximately 4.2 tons of MPs reach Romania daily[25].

Based on the research conducted thus far

regarding the dispersion of plastic in flowing waters, over 98% of the debris is found within a depth of less than one meter from the surface, with the majority of it concentrated in the first half meter[25].

Between April 10–19th, 2022, "With Clean Waters" Caravan crossed, for 10 days, the Danube River from the confluence of the river with Jiul to Galati, according to AGPRES. The caravan travelled 531 km of water and mapped the waste areas along the Danube[25].

A critical situation was observed on the banks of the Borcea branch, where the waste floats on tens of kilometers. Problems with abandoned garbage on the banks of the Danube are also in the areas of Zimnicea, Giurgiu and Oltenita.

According to a report made by AGPRES on the situation of waste management in the Danube counties carried out by the ”Mai Mult Verde” Association, together with the Federation of Intercommunity Development Associations, tens of thousands of tons of uncollected waste remain annually in 5 counties[25] (Fig. 3). (Full on www.agpres.ro).

Source: AGPRES www.agpres.ro

Figure 3. MPs sampling areas.

To reduce the quantity of MPs, anti-pollution measures were recently taken in Romania, focusing on recycling household waste, such as plastic bottles, tin cans, paper and more.

It is important to acknowledge the impact that pollution has on Romanian's rivers and the food chain. The Black Sea is an important source of food and transportation for our country and its health should be conserved. Further studies should be conducted to analyze microplastics and particles that affect the wildlife and the fish species. Furthermore, there should be promoted a greener lifestyle, including recycling and preventing the discharge of plastic waste into the rivers.

CONCLUSIONS

In conclusion, our paper states that MPs have negative impacts on humans, affecting their health (triggering cardiovascular diseases, diabetes mellitus, asthma, and cancer) and fertility.

Moreover, it has been demonstrated that smaller particles are more easily inhalable, leading to the initiation of the inflammatory cascade. However, the diverse sizes of plastic particles exert differing impacts on cardiovascular cellular components. As the size of the sNPs increased, a corresponding rise in hemolytic activity and internalization rate of the particles was observed.

Regarding pollution in Romania, approximately 4.2 tons of plastics are estimated to enter the Black Sea from the Danube, Europe's largest river, traversing several European countries, including ours. This is a real concern for the population of Romania since MPs are jeopardizing our food and transportation resources, having a great impact on people's health and wildlife, as well.

Additional research is needed to examine the impact of microplastics and particles on wildlife and fish species. Efforts should be made to encourage a more environmentally friendly lifestyle, which includes promoting recycling and preventing the release of plastic waste into rivers.

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