OPEN ACCESS PEER REVIEW

DOI: https://doi.org/10.52756/boesd.2023.e02.016

Chapter- 16

The Invisible Threat: Understanding Effects of Micro- and Nano-Plastics on Human Health and Environment

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Keywords: Micro-plastics, Nano-plastics, Environmental exposure, Human exposure.

Abstract:

Micro- and nano-plastic (MNPs) pollution has now become a global environmental threat that has persisted for the past few decades. Although large-scale experimental research evidence is still lacking, it has been found from a few research works that micro- and nano-plastic (MNPs) pollution has a significant negative impact not only on the environment but also on human health and well-being. This review aims to understand three main routes of human exposure to MNPs: ingestion, inhalation, and dermal contact. It further demonstrates the potential routes through which these MNPs are translocated to different tissues such as the lungs, intestines, and skin, damaging these organ systems. This correlation is significant with the studies conducted on both *in vivo* animal models and *in vitro* human-derived cell culture methods. Long-term exposure to MNPs could cause respiratory, excretory, immunogenic, gastrointestinal, and endocrine disruption. Some available reports also suggest that prolonged exposure to MNPs in humans could lead to oxidative stress, cytotoxicity, reproductive problems, congenital deformities of embryos, and even some forms of cancers. Although direct evidence supporting all of these effects of MNPs on human health and wellness is very limited, extensive research works are still needed not only to support these claims quantitatively but also to assess the potential threats for the future that might endanger human health and civilization.

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Shubhadeep Roychoudhury, Tanmay Sanyal, Koushik Sen & Sudipa Mukherjee Sanyal (eds.), A Basic Overview of Environment and Sustainable Development [Volume: 2]. ISBN: 978-81-962683-8-1; pp. 244-260; Published online: 17th December, 2023

Introduction:

Normally micro-plastics (MPs) are fragments with a diameter of ≤ 5 mm in size, while nano-plastics (NPs) have a particle size of ≤ 1 μm in size (Prata et al., 2020). Plastic pollution is found everywhere in this world, such as in oceans, rivers, soils, sediments, and the atmosphere, and also in animal biomass (Lau et al., 2020; Bandyopadhyay et al., 2023). The presence of micro-plastics (MPs) has also been reported in marine ecosystems, contaminating various edible items such as drinking water, marine fishes, and edible salts obtained from marine sources (Schymanski et al., 2018; Iniguez et al., 2017; Karthik et al.,2018). According to some research works, it has been found that different forms of micro-plastics (MPs) found in oceans, contaminating even zooplanktons and deep-sea organisms of this world (Taylor et al., 2016; Sun et al., 2018; Issac & Kandasubramanian, 2021; Lim, 2021). Several studies have indicated that microplastics (MPs) often enter the human body through the food web due to their very small and irregular size and shape disturbing the internal homeostasis of the human body (Murray & Cowie, 2011; Farrell & Nelson, 2013; Banerjee et al., 2021). Various cosmetic products and abrasives are produced from plastic pellets and plastic particles owing to the production of primary MPs in large quantities (GESAMP, 2015). Normally MPs are composed of polypropylene, polyethylene (PE), terephthalate, polymethyl methacrylate, and nylon. Among these, polyethylene (PE) alone is responsible for almost 93% of the MP production in the environment (Gouin et al., 2015; Das & Das, 2021). Generally, these are added directly into cosmetic products to enhance their cleansing and exfoliating activity. Apart from cosmetics, they have also been used in soaps and toothpaste for decades (Zitko & Hanlon, 1991). Other products used in daily life such as eyeliner, lip-gloss, deodorant, shampoo, etc may also contain MPs which may contribute to the global production of large amounts of MPs regularly (Leslie, 2014). On the other hand, nanoplastics (NPs) have been considered much more dangerous for living organisms than microplastics (MPs) because of their large quantity within the ecosystem and reactiveness and they potentially could reach more remote locations within the human body, damaging organ-system level completely (Sharma et al., 2022). Some of the studies show that in combination with solar light radiations, weathering processes, and natural enzymes can transform bulk amounts of plastics into microplastics and nanoplastics, contributing to a large amount of production of MNPs in the global ecosystem (Sorasan et al., 2022; Othman et al., 2021). Recent studies have revealed that MNPs can induce both particulate toxicity and chemical toxicity to the organisms (Koelmansetal., 2022; Ebrahimi et al., 2022). According to some reports, many other very small particulate matters, such as PM_{10} (aerodynamic equivalent < 10 μm), $PM_{2.5}$ (aerodynamic equivalent < 2.5 μm), and some genetically engineered nanoparticles have been found to show almost similar effects on humans like MNPs and a significant correlation has been found particularly between the exposure to $PM_{2.5}$ with lung damage and high mortality rate (Xing et al., 2016). Epidemiological studies revealed that lung damage and some forms of cardiovascular diseases are predominantly found due to prolonged exposure to genetically engineered nano-particles (Tang et al., 2015). However, there is a

paucity regarding epidemiological studies on the potentially hazardous effects of MNPs on human health to date and there is an urgent need to fill the vacuum at an enormous pace not only to identify the potential hazards for the future but also to eliminate it at the earliest.

Different pathways of exposure of MNPs to humans:

Inhalation:

Inhalation of MNPs through air:

People can be exposed to MNPs whether they are inside or outside of their rooms. In both conditions, they are being exposed to MNPs unknowingly. It has been found that individuals spend almost 89% of their daily time in their rooms and the amount of MNPs present in their surrounding air affects their health conditions significantly (Zhang et al., 2020). The rate of deposition of MPs varies significantly in different indoor conditions with the highest surprising at home (up to 1.96×10^4 particles/m^2/day) and lowest in classrooms (up to 6.20×10^3 particles/m^2/day) (Yao et al., 2022). On the other hand, it has been found that the air in the dormitory (9.9×10^3 particles/m^2/day) contains 5.5 times more MPs than in the office (1.8×10^3 particles/m^2/day) (Zhang et al., 2020). Thus the amount of MPs present in the air varies from room to room significantly and this variation has been attributed to various factors affecting the quality of air within rooms, such as utility of the room, abundance of people, amount of MPs present just outside of the room etc (Zhang et al., 2020). Normally infants spend more time at home than adults (Cox et al., 2019). Thus there is a very high probability that they may inhale the indoor dusts that too contain MPs and affect their health badly (Feng et al., 2023).

However, the outdoor air is more extensive and mobile than indoors. Therefore the concentration of MNPs is generally much lower than indoors (Feng et al., 2023). Thus the potential impacts of MPs present in the outdoor air generally have a much lesser effect on human health than in the indoor air (Feng et al., 2023). However, more extensive outdoor studies are required especially on roadsides, building construction sites, or landfills not only to assess the air quality parameters in these sites properly but also to assess the potential health risks of MNP exposure for those people living or working at that place.

Ingestion:

MNPs exposure to humans can also occur through ingestion of foods which is considered to be a major route of exposure other than inhalation. Some commonly used foods are contaminated by MNPs and people are consuming these foods unknowingly, affecting their health conditions badly.

Human exposure through consumption of sea foods:

It has been reported that there are almost 690 marine animals including some species of fish, mollusks, and crustaceans consumed by humans regularly (James et al., 2020; Curren et al.,

2020; Leung et al., 2021). It has also been reported that most of the MP contamination is found within the intestine of fish rather than its meat (Wootton et al., 2021). Fortunately, the intestines of fish generally are not consumed by people and are discarded during cleaning. On the other hand, the whole body of marine mollusks such as clams, mussels, and oysters are also consumed by humans quite regularly. Thus there is a high chance of MP exposure in humans who are consuming these mollusks regularly. Some crustaceans such as crabs and shrimps are also consumed by humans. Some researchers have reported that the amount of MPs present within the inedible part (such as gills, stomach, etc) (4.4 particles/animal) is much higher than the edible part (1.2 particles/animal) (Yin et al., 2022). Thus to reduce the MPs exposure, it is suggested that do not consume the inedible parts such as gills, stomach, intestine, etc of crustaceans and other fish species.

Human exposure through consumption of polluted drinking water and beverages:

Like other food sources drinking water has also been contaminated by MNPs and people are consuming these polluted waters regularly worsening their health conditions. Some research works have revealed that the abundance of MPs found in tap water varies significantly with bottled water (Feng et al., 2023). The particle size of MPs in bottled water normally ranges from 1 µm to 5 µm (Akhbarizadeh et al., 2020). Overall, the maximum amount of MPs found in the tap water (maximum up to 930 particles/lit) was much lower than the bottled water (up to 2649 ± 2857 particles/lit in single used PET bottles and 6292 ± 10,521 particles/lit in glass bottles) (Obmann et al., 2018; Kristein et al., 2021). Moreover, MNPs have also been detected in high amounts in some useful beverages like milk, tea, beer, and soft drinks (Li et al., 2022; Shruti et al., 2020; Da Costa Filho et al., 2021). Thus it can be stated that close monitoring regarding the presence of MNPs in drinking water and beverages is really necessary for establishing a proper food safety standard to improve the health conditions of people.

Human exposure through consumption of contaminated salt, sugar, and honey:

Edible salts can also be contaminated with MPs like that of other food products. It has been found that the amount of MPs present within the salt varies greatly from country to country across the globe. In the case of China, the total amount of micro-plastic material present in edible salts varies significantly, from 550-681 particles/kg in sea salts (Yang et al., 2015). The situation in India is also very similar to that of China. It has been reported from Gujarat which is one of the largest salt-producing states in India that total micro-plastic materials present in edible salt range from 46 to 115 particles/200 gms and in Tamilnadu, it is from 23 to 101 particles/200 gms (Vidyasakar et al., 2021). Almost similar reports have been found for edible sugar and honey. It has been reported from Germany, France, and Spain that the total amount of micro-plastic materials present in edible sugar and honey are 560 particles/kg and 540 particles/kg respectively (Liebezeit & Liebezeit, 2013). Therefore, other food items like cooking oils, soy sauce, tomato sauce, spices, etc should be properly examined before use to ensure food safety in humans. Moreover, present studies on micro-plastic contamination in

crops and livestock are very few and it is really necessary to examine the impacts of MNPs exposure to humans through the food chain and assess any kind of biomagnification effect of MNPs.

Dermal contact:

Human skin is exposed directly to various cleansing products such as toothpaste, soaps, sun cream lotions; hair gel, face wash gel, etc, and all of them are contaminated with MPs (Lei et al., 2017; Feng et al., 2023). Some airborne MNPs along with some particulate matter can also settle down over the skin surface (Feng et al., 2023). Unfortunately, due to a lack of research evidence, it is really difficult to estimate the number of MNPs absorbed by the skin. So a large amount of research work is needed not only to quantify the amount of MNP absorbance through the skin but also to understand the probable pathways triggering the process.

Accumulation of MNPs within different human tissues and their translocation:

In recent years, various types of micro- and nano-plastics have been detected in various tissues or organ systems within the human body. This type of tissue accumulation indicates that MNPs can enter the circulatory system and can translocate through the plasma membrane of cells. MNPs also possess the capability of escaping from the immune cells of the body's immune system and can accumulate within different tissues of the human body.

Accumulation of MNPs within human lungs and its translocation:

It has been reported that inhalation is one of the most important biological processes through which MNPs can enter the human body (Zhang et al., 2020). The average size of these MNPs is known to be 1730 ± 150 µm (Baeza-Martinez et al., 2022). Although some amount of comparatively larger particles are being cleared out by the action of nasal hairs, mucus secretion within nasal passage, ciliary movements within the respiratory tract, the action of macrophage within respiratory pathways, or coughing and sneezing, unfortunately, smaller particles can translocate through the respiratory pathways and can enter into the circulatory system (Geiser, 2002). Particle size ranging from 0.5-5 µm can easily cross the mucus villi and tissue macrophage system of the lungs in comparison to larger particles ranging from 15-20 µm (Wright et al., 2017; Ruge et al., 2013). As a result, comparatively smaller plastic particles adhere to the wall of the lungs or with alveoli and are translocated easily to the blood circulation of humans. Then these smaller fragments go to other organs carried by the bloodstream, causing damage to these organs.

Accumulation of MNPs within the human intestine and its translocation:

Like the respiratory pathway, MNPs also can enter the human body through the gastrointestinal pathway. MNPs enter through the gastrointestinal pathway mainly with contaminated foods and water. After entering into the intestine, MNPs are translocated to the circulatory system mainly using 3 pathways: (i) endocytosis of epithelial cells, which is capable

of transporting mainly nano-plastics (NPs), (ii) transcytosis transport of microfold (M) cells of Peyer's patches of ileum which is believed to be the main transport process of MNPs and it can translocate particles (with a diameter of < 10 µm) to the mucosal lymphoid tissue of Peyer's patch and (iii) perception process, in which shedding of cells from intestinal tips occurs and this process can generate poresand comparatively larger particles [eg. Polyvinyl chloride (PVC) particles with a diameter ranging from 5 µm to 110 µm] can pass through these pores (Feng et al., 2023). However, more intensive research works are still needed not only to understand the complete mechanism of transportation of MNPs through the gastrointestinal tract but also to determine the distribution of MNPs within the gastrointestinal system.

Accumulation of MNPs within the skin and its translocation:

It has already been known that the skin is the most important organ of the human body and not only does it serve as a barrier to prevent the penetration of different particulate matters into the human body but also prevents the entry of different microbes, serving a very important function of the innate immune system. Although, research works regarding the process of accumulation and translocation of MNPs through the skin are rare, very few of them have suggested that nano-plastics (NPs) have the potential to penetrate the skin barrier and enter into the circulatory system and can reach anywhere within the body (Filon et al., 2016). Presently, there are 3 known pathways through which NPs can travel from the outer skin layer to the innermost parts of the body. These are: (i) through cellular bypass: in this process, molecules with a diameter <1 nm to 4 nm can pass through the skin; (ii) through sweat gland and hair follicles: in this process, molecules with a diameter 4 nm to 20 nm can pass through the skin and (iii) through damaged skin or skin lesions: in this process, molecules with a diameter 21 nm to 45 nm can pass through the skin (Filon et al., 2016).

Accumulation of MNPs within other organ systems and its translocation:

MNPs enter the stomach through foods that reach to the intestine and pass to the bloodstream through the intestinal villi. It has been found that the diameter of the largest blood vessel (aorta) of humans is around 25000 µm and the diameter of the smallest blood capillary of humans is around 8 µm (Muller et al., 2008). Thus, due to the very small size of MNPs, they can be translocated through the bloodstream quite easily. Moreover, recently traces of MNPs have also been detected in the human liver, spleen, kidney, and placenta (Horvatits et al., 2022; Ragusa et al., 2021). However, more research evidence is required to assess the potential impacts of MNPs on other organs of the human body.

Effects of MNPs on different organs of the human body:

MNPs exposure could lead to the toxicity of different organ systems of humans producing various significant effects particularly on the digestive system, respiratory system, circulatory system, immune system, reproductive system, endocrine system, nervous system, excretory

system, and even causing some forms of cancers. All these effects of MNPs are summarised by obtaining knowledge from both *in vivo* and *in vitro* studies (Figure 1).

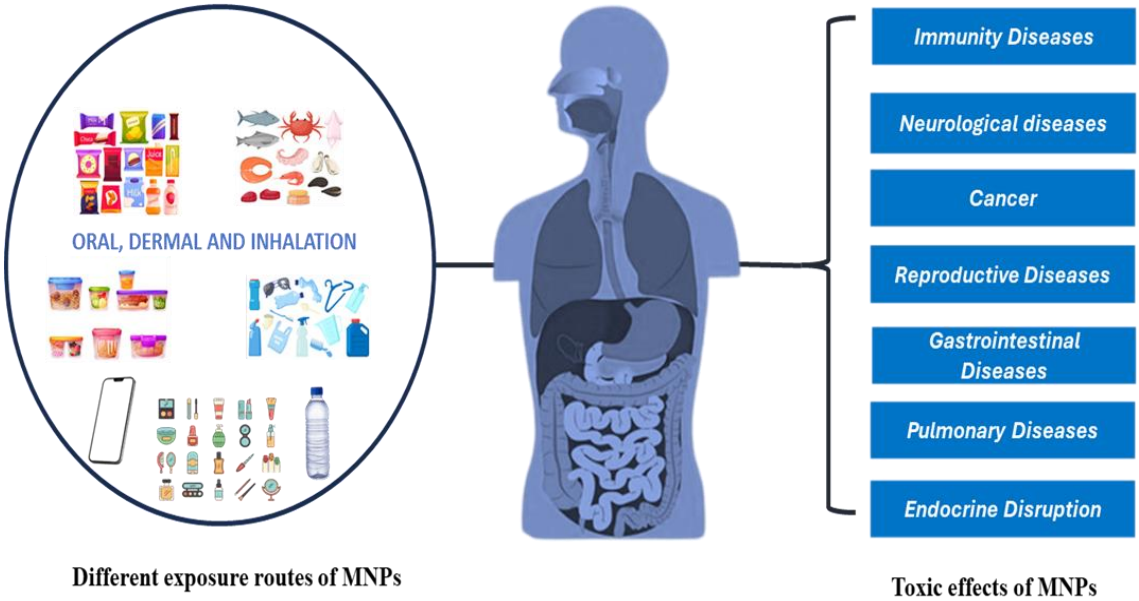

Figure 1. Different Modes of MNPs Induced Toxicity in Human.

Effects on digestive system:

The digestive system plays a very important role including the breakdown of solid food particles, their digestion and absorption particularly from the small intestine, and maintaining the internal homeostasis of humans. Exposure to MNPs showed an adverse effect, particularly on the intestinal wall, proteins, carbohydrates, and lipid digestion, and interfered with nutrient absorption, causing gastrointestinal disturbances (Tan et al., 2020). Moreover, MNPs exposure could lead to a reduction in the bio-accessibility of vitamin D3 for Ca^{+2}absorption through the gastrointestinal wall (Li et al., 2020). A stable gastrointestinal microbial status is essential for maintaining human health. Exposure to MNPs also hampers internal microbial status as reported in mice (Li et al., 2020). Thus, it can be stated that MNP exposure exerts a significant negative impact not only on the digestive system but also on the overall health status of humans.

Effects on respiratory system:

As stated above, apart from the digestive system, another major route of exposure is through the respiratory pathway by which numerous amounts of MNPs could reach to the internal body parts disrupting the internal homeostatic equilibrium of the body. It has been reported that MPs could reach not only the sputum through the nasal cavity (Jiang et al., 2022) but also the alveoli and lung tissue (Baeza-Martinez et al., 2022; Jenner et al., 2022). However, concrete evidence suggesting the direct link between MNP's exposure to lung diseases is still lacking and more extensive research works are needed to draw such a conclusion. However, few studies indicate

that exposure to MNPs could alter the endogenous surfactants of human lungs, decreasing the activity of lung cells which makes them more susceptible to various pulmonary disorders, such as pulmonary fibrosis, asthma, pulmonary frosted glass nodules, etc (Feng et al., 2023).

Effects on circulatory system:

The circulatory system is very important in humans. It not only carries CO_2 and O_2 to and from the lungs respectively but also it carries various nutrients to different tissues for its survival. It also helps in the collection of different harmful metabolic waste products from tissues and transports these materials to kidneys for successful elimination. A recent hematological study conducted on 22 healthy individuals reveals the presence of MPs (>700 nm) in blood with an average concentration of 1.6 µg/ml MNPs (Leslie et al., 2022). Recent evidence suggests that exposure of MNPs to humans could show a harmful effect not only on RBCs but also on platelet formation and angiogenesis. Moreover, MNP exposure for a prolonged time could result in thrombosis in humans (Kim et al., 2022; Feng et al., 2023).

However, research on the effects of MNPs on the human circulatory system is limited to date and more extensive research evidence is required not only to understand the possible mechanism of action of MNPs on the circulatory system but also its impact on the overall health of human beings.

Effects on the immune system:

The immune system is one of the most important systems in humans which protect the body from foreign invaders, maintaining human health and wellness. The immune system is comprised of lymphoid tissues, immune-regulatory cells (both B cells and T cells and their subtypes), antibodies, tissue macrophages, NK cells, and different types of cytokines (such as IL1, IL2, IL 3, TNF α, TNF β, etc). These all help to eliminate foreign particles, bacteria, fungi, parasites, etc commonly known as antigens or more precisely, immunogens. Both *in vivo* and *in vitro* experiments, conducted on animals showed that exposure to MNPs could cause increased secretion of pro-inflammatory substances leading to the onset of different autoimmune diseases (Remmelts et al., 2021; Davidson et al., 2001). Autoimmune diseases are caused due to the formation of autoantibodies within the body due to some unknown reasons. Recent studies indicate that the onset of autoimmune disorders occurs due to genetic as well as environmental factors (Davidson et al., 2001).

The immune system is present in different organs of the human body including lymph nodes, bone marrow, spleen, tonsils, Peyer's patches, and many others. Although limited information is available regarding the impacts of MNPs on the immune system, so a detailed investigation is necessary to assess the potential impacts of MNPs exposure on these parts of the human body.

Effects on the reproductive system:

Nowadays, research is going on to observe the impacts of MNPs exposure on the reproductive system, especially after the discovery of MPs presence in the human

placenta(Ragusa et al., 2021). Jin et al., 2021 and some others have reported that *in vivo*polystryreneMPs exposure could cause reproductive toxicity in mice which could affect the overall reproductive health of individuals and hamper the production of healthy offspring. MNPs exposure affects the reproductive health of both male and female rats or mice. In male mice, decreased sperm count, damage in the blood-testes-barrier, and inflammation in seminiferous tubules are seen upon MNPs exposure. On the other hand, inflammation of both ovaries and decreased oocyte quality have been observed upon MNPs exposure as reported in the case of female mice (Jin et al., 2021; Feng et al., 2023). However, extensive investigations are required to observe the presence of the same effects in the human reproductive system and its transmission from one generation to the next.

Effects on endocrine system:

The endocrine system which produces different hormones plays a vital role in regulating various physiological activities in humans. Although limited reports are available to date claiming direct effects of MNPs on the endocrine system, few of them are claiming that certain MNPs carry some endocrine disrupting chemicals (EDCs), such as phthalates, bisphenol A (BPA) or steroid hormones along with them, disrupting the endocrine system and causing hormonal imbalances in humans (Campanale et al., 2020; Guedes-Alonso et al., 2021). Evidence coming out from laboratory animals suggests that EDCs can interfere with the production of different hormones leading to a variety of health problems such as the onset of type II diabetes mellitus, hypo or hyperthyroidism, obesity, reduced sperm count or sperm motility, etc(Guedes-Alonso et al., 2021). Additionally, other endocrine-disrupting elements such as dioxins and polychlorinated biphenyls (PCBs), etc are present along with EDCs and are also present in the environment showing combined toxicity in humans (Feng et al., 2023).

Effects on the nervous system:

The nervous system is made up of a complex network of neurons and also plays an important role in regulating various physiological activities in humans. Once entering the blood circulation, some forms of MNPs can cross the blood-brain barrier, causing damage or dysfunction in neuronal systems. It has been reported that MP exposure could lead to learning and memory dysfunction in mice when exposed to 2 µm PS particles (0.016 mg/gm) continuously for 8 weeks. This occurs due to the transport of PS particles through blood circulation, crossing the blood-brain barrier entering the hippocampus region of the brain, and producing neuroinflammation. This fatal neuroinflammation in turn alters the gene expression and finally alters the conformation of proteins responsible for synaptic plasticity (Lee et al., 2022). Moreover, it has also been reported in mice that PS particles with a diameter of around 5 µm could also induce oxidative stress and lower the levels of acetylcholine, thereby, altering the signal transduction process in neurons. These effects ultimately augment memory loss and neuronal dysfunction processes in mice (Wang et al., 2022).

However, more research works are needed not only to understand the exact mechanism of action of MNPs on the human nervous system but also to assess properly its activity, especially on neurotransmitter production, memory, learning process, cognitive function, and behavioral process of humans.

Effects on the excretory system:

MNPs show a marked negative impact on the excretory system, particularly on both kidneys. PS particles cause inflammation, malfunctioning mitochondria and endoplasmic reticulum, and autophagy in kidney cells (Wang et al., 2021). Thus the overall functions of both kidneys become jeopardized, retaining metabolic waste materials within the body and hampering the activity of other organs within the human body.

Effects on locomotor system:

It has been reported that MNPs could inhibit the locomotor ability of fish, soil animals, and birds (Feng et al., 2023). Fortunately, its effect on human locomotor activity remains minimal (Feng et al., 2023). However, more studies are required to assess the magnitude of the impact of MNPs on the human locomotor system.

Relationship between Microplastic toxicity with Cancer progression:

It has been known that MNPs show a marked negative impact on the overall human body and organ systems. Many recent research works have suggested a strong correlation between chronic microplastic toxicity and cancer progression in different cells of the body. It has been reported that the fragmented Polypropyoline Microplastics (PPMPs) promote the cell cycle, proliferation, and secretion of the inflammatory cytokine IL-6 in human breast cancer cells, thereby, promoting metastatic processes, while PPMPs neither induce cytotoxicity nor enhance cellular motility (Park et al., 2023). However, more studies are required not only to assess the magnitude of the impact of MNPs on the cancer progression process in different organs but also to understand the mechanism of action through which MNPs are producing such effects in humans.

Prospects for research works:

Based on the above discussion, it can be stated that the ongoing research processes on the potential impacts of MNPs on the environment and human health and wellness are at a very early stage. Thus there remains a big gap in the mechanism of actions of MNPs especially in different organ systems of humans. Therefore, systematic and in-depth studies are required to understand the whole process. A few research prospects are as follows:

(i) First of all, a standardized protocol for the detection of MNPs in the surroundings is needed to assess the quality of air, food, or drinking water. The process should be simple in form and applicable worldwide for all countries irrespective of race or financial status.

(ii) For the assessment, an *in vitro* model organism should be chosen to conduct all the necessary experiments, to mimic human exposure. For a better understanding of translocation, cellular uptake, and the mechanism of actions of MNPs within different organ systems, all of the modern tools and techniques should be applied.

(iii) Finally, a massive campaign is needed from the government as well as from social activists to educate people about probable upcoming environmental and health hazards due to the extensive use of plastics.

Conflicts of interest:

Declared none

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HOW TO CITE

Arindam Chakraborty, Rima Mondal, Saheli Ali, Koushik Sen*, Suasanta Roy Karmakar, Shubhadeep Roychoudhury (2023). The Invisible Threat: Understanding Effects of Micro- and Nano-Plastics on Human Health and Environment. © International Academic Publishing House (IAPH), Shubhadeep Roychoudhury, Tanmay Sanyal, Koushik Sen & Sudipa Mukherjee Sanyal (eds.), *A Basic Overview of Environment and Sustainable Development [Volume: 2]*, pp. 244-260. ISBN: 978-81-962683-8-1 DOI: https://doi.org/10.52756/boesd.2023.e02.016