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Microplastics and Human Health: A Review of Possible Risk and Clinical Consequences

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Abstract

In 2023, annual worldwide plastic production rose to 400.3 million metric tons, resulting in widespread nano- and microplastic (NMP) pollution and significant risks to human health. NMPs are defined as plastics that measure 1 nm to 5 mm in size. NMP exposure can happen through ingestion, inhalation and dermal contact, and have been detected in brain, lung, blood and placental human tissues. This review will provide relevant scientific evidence about exposure pathways and biological impacts of NMPs, including cytotoxicity, genotoxicity and inflammation reported in in vitro studies, as well as neurological, reproductive, and skeletal impacts observed in retrospective in vivo evidence. The main route of human exposure to NMPs is through the ingestion of contaminated food and water. Thus, humans have been reported to ingest upwards of 5 g of microplastics each week. Humans can also be exposed through inhalation and dermal contact, followed by either inhalation or dermal absorption into the tissues or body. There are numerous issues and gaps within the literature that hinder risk assessment attempts including, but not limited to, methodological inconsistencies, underreported or unpublished long-term study outcomes, and ethical challenges in experimental research and studies. The path forward includes the need for standardized protocols, diverse in vitro human models, ethical and longitudinal in vivo methods, and interdisciplinary collaboration and research. The promotion of biodegradable plastics and public education campaigns can also help reduce NMP exposure. The review demonstrates the urgent need for integrated research approaches to better understand and reduce NMP risks to human health, along with safer materials and informed policy intervention.

Keywords: Nano and microplastics, human health, exposure pathways, toxicity, biodegradable plastics

1. Introduction

Plastics, or synthetic polymers, play an important role in today's society as a result of their versatile mechanical and chemical properties afforded by polymerization and numerous inclusions such as carbon fibers (Andrady & Neal, 2009; Kik et al., 2020). Since reaching tremendous production levels in the 1960s, capacity ballpark estimates for 2023 are approximately 400.3 million metric tons annually (Rhodes, 2018; Plasticseurope.org, 2024). Given the versatility in different plastics and their basic polymeric forms, plastics can be separated into polyethylenes (PE), polypropylenes (PP), polyurethanes, and halogenated plastics (Napper & Thompson, 2020). Their persistence in the environment, however, has resulted in significant environmental contamination in recent years as they continue to accumulate. Littoral environments continue to be severely impacted. In addition to polypropylene and polyethylene, researchers are finding microplastics also represent a risk in the environment (i.e., pools of plastics that range in size from 1 nm to 5 mm), known as nano- and microplastics (NMPs). Potential environmental or health impact of NMPs is a concern as these materials can behave in a similar manner to other toxicological threats (Collignon et al., 2014; Filella, 2015a).

Reducing uncertainties about NPs and MPs requires defining what microplastics are. MP refers to a water insoluble man-made particle or synthetic polymer matrix with a size of 1 μ m to 5 mm; MPs can be derived from a number of sources in their primary form (e.g., microbeads) or exhibit secondary fragmentation (Andrady, 2011a; Frias et al., 2019). However, NPs, smaller than 1 μ m, are not yet well defined, with proposed size variations of 1–1000 nm, or for engineered nanomaterials, a size of 1-100 nm (Gigault et al., 2018a; Cole & Galloway, 2015; Schwaferts et al., 2020). Environmental degradation through sunlight, water, wind, or biological activity enhances the distribution of non-microplastics (NMPs) (Filella, 2015b; Lehner et al., 2019a). NMPs have been identified in different environments from our oceans to our glaciers and have been found in human tissues, which brings into question their health implications (Andrady, 2011b; Cózar et al., 2014b).

This review combines the pathways of NMP exposure, millions of years of biological impact, and the difficulty in estimating risk potential to human health. It integrates findings of retrospective in vivo and in vitro research and calls for standardized methods and collaborative multidisciplinary research to combat this emerging public health issue.

2. Methodology

This review uses an exploratory approach to analyze the health consequences related to NMP, deliberately avoiding the strict protocols typical of Cochrane reviews, which can inadvertently ignore some relevant studies (Heddagaard & Møller, 2020). A thorough literature search was conducted using PubMed, with search terms like "nanoplastic," "microplastic," "human cell lines," "human digestive tract," "human lungs," and "human nervous system." The use of logical operators ("AND," "OR") allowed combining different sets of keywords. From the 1,230 citations and abstracts screened, retrospective research, case reports, and specific in vitro studies using human cell lines were chosen to be included. Further articles mentioned in the included studies to ensure adequate coverage are referenced (Kutralam-Muniasamy et al., 2023; Zhao et al., 2023).

3. Exposure pathways to Nano and Microplastics

Nanoplastics and microplastics, defined as particles between 1 nm and 5 μ m in size, enter the human body through three main pathways: ingestion, inhalation, and dermal contact. The level of exposure and consequences will be based on several variables, including the particle size, chemical composition, surface changes, and environmental conditions. Each pathway allows for nano- and microplastics to enter different systems within our body, leading to potential systemic distribution and bioaccumulation. The gastrointestinal (GI) tract is the primary route of exposure for nanomaterial particles (NMPs), which come from consuming contaminated food and drinks. There is evidence of contamination in a broad range of consumer products, including seafood, milk, beer, honey, sugar, salt, and tap water, which illustrates the

rarely invisible contamination reaching many parts of the food supply chain (Kwon et al., 2020; Liebezeit & Liebezeit, 2013, 2014, 2015; Yang et al., 2015; Mason et al., 2018). One international research study found microplastics in 81% of 159 tested tap water samples, with the majority of those indicated fibers less than 5mm (Kosuth et al., 2018). Also, bottled water (in glass or PET plastic) had more microplastics, with a count of up to 6,292 particles per liter with sizes ranging between 5 and 1,350 μ m, indicating greater contamination in bottled water than tap water (Schymanski et al., 2018; O β mann et al., 2018). The similar particle densities observed in the glass and PET packaging suggest contamination during processing or through environmental sources, and not as the product of the packaging material per se.

Plastic food packaging makes a significant contribution to non-microplastic particle intake, especially when exposed to high temperatures. There is evidence to prove the large-scale release of microplastics in teabags, plastic kettles, and baby bottle feeding under increased temperatures, with their leaching mechanism amplified by heat (Hernandez et al., 2019; Li et al., 2020). For example, plastic teabags being heated to their optimal brewing temperatures can lead to the release of billions of nanoplastics and microplastics per liter, significantly increasing human exposure levels (Hernandez et al., 2019). Likewise, baby bottle feeding also releases microplastics when exposed to sterilization or contact with hot fluids, thereby increasing risk to susceptible human subjects (Li et al., 2020).

Quantitative studies suggest that human beings consume between 0.1 and 5 grams of microplastics weekly, an amount that is roughly the same as the weight of a credit card. Infants receive significantly higher levels of exposure because they rely on bottled milk and have relatively lower body weights (Senathirajah et al., 2021; Zhang et al., 2021a). Analysis of human fecal samples offers conclusive evidence of nanoplastic ingestion and excretion.In an exploratory study, nine plastic types, which were primarily polypropylene (PP) and PET, were identified in all eight fecal samples, showing a median of 20 microplastic particles (from 50 - 500 micrometers) in 10 grams of feces (Schwabl et al., 2019). In a much larger 26 subject study, microplastics were identified in feces of 23 of the students, where the particles ranged in size from 20 - 800 micrometers and 0.01 - 14.6 mg per person of total mass (Zhang et al., 2021b). These studies support the hypothesis that microplastics travel through the GI tract and point to a chance of accumulation and absorption, especially of the smallest nanoplastic particles.

Animal studies also support the potential bioaccumulation of NPMs in the food chain. For example, controlled studies show that nanoplastics are absorbed by aquatic organisms and transferred to higher trophic levels, increasing the potential for human exposure through consumption of seafood (Cedervall et al., 2012). Considering the GI tract serves as one of the first routes of exposure, this also highlights the importance of contamination in food and water supplies and risks to human health.

Inhalation is one of the major routes of exposure to airborne nanoplastics (NMPs) from various sources like synthetic fibers, debris from tire rubbers, agricultural residues, and desiccated sewage sludge (Lehner et al., 2019b). The alveolar surface area of the human lungs is about $150~\text{m}^2$, and the epithelial membrane is extremely thin at <1 μ m, which makes it subject to infiltration by nanoparticles (Amato-Lourenço et al., 2021). Once inhaled, nanoplastics can permeate through these membranes, enter the bloodstream via capillary walls, and disseminate throughout the body and most organs.

Investigating autopsy results leads to an important indication of microplastic deposition in human pulmonary tissue. 13 of the 20 lung tissue samples had definitive evidence of microplastics—both particles and fibers—which indicated exposure via respiration (Amato-Lourenço et al., 2021). Research on occupational exposure has demonstrated the risks of inhalation, particularly among workers in plastic manufacturing. Risk assessment for exposure to polystyrene involves the study of urinary levels of styrene (StyU) and its metabolites, mandelic acid (MA) and phenylglyoxylic acid (PGA), which are markers of exposure (Persoons et al., 2018). Workers who do not use respiratory protection show considerably high levels of these metabolites, indicating high inhalation of polystyrene particles or vapors (Persoons et al., 2018).

Environmental sources are often responsible for the presence of airborne nanoplastic particles. As examples, tyre degradation causes the formation of microplastics, which, in turn, reduce air quality in urban

areas (Lehner et al., 2019b). Likewise, synthetic clothing emits microfibers during their uses and washing cycles, which allow particles to reach the air and potentially be breathed in (Hernandez et al., 2017). Additionally, farming practices involving plastic mulching film also result in emissions of microplastics, so as to increase exposure levels (Lehner et al., 2019b). The susceptibility of the respiratory system due to systemic dissemination following nanoplastic uptake, as well as their detection in human lung tissue, heightens the worry and necessitates precautions in risky areas.

The integumentary system, as the largest organ of the human body and an important immune system barrier, can potentially serve as a route of exposure to nanoplastics (NMP), especially through contact with cosmetics, clothing, and contaminated water sources (Hernandez et al., 2017). The likelihood of transdermal uptake depends on the size of the particles, where smaller nanoplastics have a higher potential to penetrate the epidermis. Potential entry points are sweat glands, hair follicles, and zones of impaired skin integrity, e.g., lacerations and abrasions (Yee et al., 2021).

Studies using porcine skin, which is often used as the human skin model, show that polystyrene nanoparticles (PS-NPs) fail to break the stratum corneum, the outer skin layer, unless this is breached by means of exfoliation (Campbell et al., 2012; Alvarez-Román et al., 2004). Research specifically focusing on human skin is also increasing the body of understanding within this area.

Fluorescence-tagged PS-NPs (40 nm) have been identified as localized in the stratum corneum and shallow regions around hair follicle pores and more so past the follicular epithelium (Vogt et al., 2006; Döge et al., 2018). One study in particular showed 40 nm nanoparticles were taken up by epidermal Langerhans cells near hair follicles, while larger particles (750 nm and 1,500 nm) did not exhibit evidence of penetration (Vogt et al., 2006). Such findings suggest hair follicles and the associated immune cells participate in nanoparticle uptake, particularly of the smaller particles.

Cosmetics and clothing constitute key routes of dermal exposure to nanoscale materials (NMP). The use of microbeads in personal care products and nanofibers in synthetic clothing leads to the release of particles during skin contact, thus increasing exposure hazards (Hernandez et al., 2017). While contaminated water does not typically penetrate intact epidermis, nanoparticles are capable of penetrating through damaged skin or hair follicle routes (Yee et al., 2021). Although these data are available, the available data on dermal penetration remain limited, and the contribution of nanoparticles to systemic exposure via skin remains poorly defined. Further investigation is needed to quantify dermal absorption and evaluate potential health risks, in particular occupational and consumer exposure. Figure 1 summarizes the exposure pathways and systemic distribution of micro- and nano-plastics (nmps) into humans.

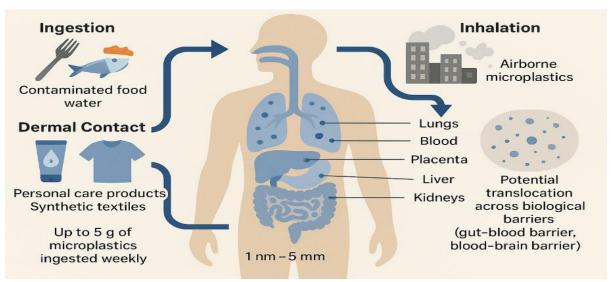


Figure 1. Exposure pathways and systemic distribution of micro- and nano-plastics (NMPs) into humans.

4. Biological Impacts of Nano and Microplastics

NMPs create various threats to human health based on their inherent physical nature, chemical composition, and ability to carry environmental pollutants along with them. These threats can be classified into three major forms: physical (like tissue injury), chemical (like leaching of additives), and biological (such as immune responses). Styrene, a popular chemical manufactured for use in plastic, has been associated with many different neurological symptoms, especially in the work environment. A large study in 2011 of 21,962 people who lived alongside the Gulf Coast of the United States (which contains half the production of styrene in the country) showed that one-third reported neurological symptoms of headache, fatigue, dizziness, paresthesia, visual disturbances, and feelings of nausea (Werder et al., 2018). In this study, environmental levels of styrene and the respective blood levels were measured in 874 participants, resulting in a strong association between higher exposure and symptom frequency, especially in non-whites, with nausea being a leading complaint (Werder et al., 2018). These findings suggest that the volatility of styrene, which is present in polystyrene, can make it neurotoxic via inhalation or systemic uptake.

Retrospective studies using Danish population registers have investigated the neurological consequences of exposure to styrene. Recurring encephalopathies and unspecified dementias numbered 228 and 565, respectively, in a cohort of 72,465 workers in the reinforced plastics industry between 1977 and 2011 (Kolstad et al., 1995b). The level of the participants' exposure was estimated in exposure assessment models by means of exposure levels at the workplace, occupational category, duration of employment, and so forth. No firm association between exposure to styrene and neurological illness as described was found, yet mortality due to degenerative neurological disease, including multiple sclerosis, Parkinsonism, and motor neuron disease, was observed to be increased (Kolstad et al., 1995b). The findings increase the plausibility of neurotoxicity by styrene use and highlight the need for future longitudinal studies to elucidate the mechanism and dose-response, all of which were examined in this thesis.

Periprosthetic osteolysis is known to be one of the greatest complications that occur from the repair procedure of a cementless total hip arthroplasty, which is the result of polyethylene (PE) particles that are the catabolites of prosthetic implants. The PE particles, \sim 530 nm in diameter, are phagocytized by macrophages and incite the production of pro-inflammatory cytokines such as TNF- α , which drives the differentiation of osteoclasts and causes the resorption of bone (Shanbhag et al., 1994). Evaluation of interphase membranes in 11 failing hip arthroplasties found significant evidence of PE particles, as well as titanium, bone debris, and stainless steel, providing further support for their role in causing osteolysis (Shanbhag et al., 1994). In another study, 11 patients with revisions of hip prostheses had higher levels of receptor activator of nuclear factor-kappa β (RANK) and RANK-ligand (RANKL), along with TNF- α , in PE debris-containing tissues, which was related to an increased degree of bone loss (Holding et al., 2006).

A critical threshold for osteolysis onset was identified at an implant wear rate of 0.2 mm/year, beyond which bone resorption accelerates (Orishimo et al., 2003). However, in vitro studies suggest that PE nanoparticles (<10 μ m) at concentrations of 10 μ g/mL do not exhibit cytotoxicity or genotoxicity, indicating that toxicity may depend on particle concentration and exposure context (Gajski et al., 2014). With global life expectancy increasing, the demand for arthroplasty is rising, elevating the risk of osteolysis due to PE wear (Bitar & Parvizi, 2015). These findings suggest that alternative materials, such as ceramics, could reduce osteolysis risks in long-term implant recipients, particularly younger patients with extended lifespans.

While there is currently very little quantitative evidence to suggest that nanomaterial particles (NMPs) have effects on human reproductive health, estimates derived from animal studies suggest the possibility of reproductive toxicity that warrants careful consideration. Studies of the nematode, Caenorhabditis elegans, for example, demonstrated that exposure to nanoplastics during reproduction resulted in decreased brood size in the next generation, and amine-modified nanoplastics (NPs-NH2) had greater toxicity on reproductive function and gonad development than their unmodified counter parts (Yu et al., 2021; Sun et al., 2021a). In a similar study, zebrafish exposed to polystyrene nanoplastics (PS-NPs) were reported to have gonadal impairment, while embryos were noted to have extensive pericardial edema, decreased

cardiac output, and reduced bloodstream velocity at exposure doses above the no-observed-adverse-effect level (NOAEL) (Qiang & Cheng, 2021; Sun et al., 2021b).

There are studies showing that nanoplastics can cross placental barriers in mammals. For example, pregnant Sprague Dawley rats were treated intratracheally with 20 nm polystyrene nanoparticles; their tissues (lungs, heart, spleen) and fetal tissues (liver, lungs, heart, kidneys, brains) were found to possess the deposited nanoparticles (Fournier et al., 2020). The exposure also led to decreased placental and fetal weight, which indicated developmental toxicity (Fournier et al., 2020). In females, microplastics triggered apoptosis and fibrosis within ovarian granulosa cells, while males showed reduced sperm viability due to these substances (An et al., 2021; González-Acedo et al., 2021b).

Studies with human subjects yield preliminary results on reproductive exposure. A total of six human placentas were analyzed following the recovery of 12 microplastic particle fragments ranging in size between 5 and 10 μ m from four of the samples, which included similarly sized microplastic particle fragments of polypropylene, polystyrene, and polyethylene identified on both the fetal and maternal side and across the chorioamniotic membranes (Ragusa et al., 2021). Through the use of an ex vivo human placental perfusion model, it has been shown that polystyrene nanoparticles measuring 240 nm in diameter were able to cross the placental transfer mechanism without major effects on cell viability, with the nanoparticles of size 50-80 nm having the greatest efficiency for translocation (Wick et al., 2010). Microplastics >50 μ m were also found in human placentas and meconium via cesarean delivery, which would also include polypropylene, polystyrene, polyethylene, and polyurethane had the potential for named contamination sampling (Braun et al., 2021). This evidence is concerning and presents the possibility that an increasing prevalence of nanoplastics may disrupt reproduction and developmental activity, which warrants further study.

Occupational exposure to styrene, which is commonly used as a precursor in making reinforced plastic materials, has been shown to have genotoxic properties. In a study of 52 workers at five plastic plants, styrene in the ambient air was sampled, urinary metabolites (mandelic acid and phenylglyoxylic acid) were monitored, and genetic aspects including sister chromatid exchange (SCE), micronucleus formation, and DNA damage were examined (Teixeira et al., 2010). The mean styrene concentration in the occupational environment was greater than the time-weighted average of 20 ppm, and the exposed workers had significantly more SCE and DNA damage than a control population (54 unexposed office staff) (Teixeira et al., 2010). Greater microsomal epoxide hydrolase activity was associated with high frequencies of SCE, suggesting that genetic polymorphisms of the metabolic enzymes CYP2E1 and EPHX1 may modify expression of genotoxic properties (Teixeira et al., 2010). These findings suggest a potential carcinogenic risk of styrene exposure in humans, which necessitates better measures for health and safety management in the workplace and reinforces the call for additional NMP-related studies to evaluate its genotoxicity.

In vitro studies provide critical insight into the cellular effects of nanoplastic materials (NMPs), revealing their cytotoxic, genotoxic, inflammatory, apoptotic and oxidative stress-generating effects on human cell lines (Brachner et al., 2020). Polystyrene (PS) is the most studied polymer, but it is not even one of the five most produced plastics globally, highlighting a critical research gap in other commonly used polymers such as polyethylene terephthalate (PET) and polyvinyl chloride (PVC) (Brachner et al., 2020). Toxicity outcomes are also significantly affected by particle size, surface chemistry (e.g., amine or carboxyl), and exposure time. For example, nanoparticles (that is < 100 nm in size) are taken up by and are cytotoxic to cells at a greater level than larger microplastics, presumably because they can enter cellular membranes (Brachner et al., 2020). The significant issues in in vitro work deal with the difficulty of isolating and quantifying NMPs in biological samples, and thus, it is hard to even determine dosages (Brachner et al., 2020). Most studies address only acute exposures, ignoring the chronic exposure implications, which are pertinent to bioaccumulation and long-term impacts. Additionally, the lack of standard operating procedures for characterizing NMPs in complicated matrices limits both the comparability and reproducibility of studies on NMPs (Brachner et al., 2020). Despite these limitations, in vitro data form the foundation of understanding the cellular actions of NMPs, which can in turn guide risk assessment and inform future in vivo studies. Figure 2 represents the summary of the biological impact of NMPs.

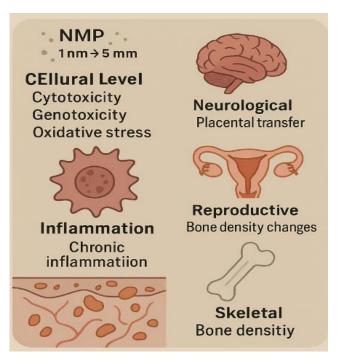


Figure 2. Summary of the biological effects of micro- and nanoplastics.

5. Research Limitations and Challenges

Scientific research into the role of nano- and microplastics (NMPs) and their effects on human wellbeing faces several major challenges in understanding the related risks. One of the main challenges lies in the lack of standardized methods of collecting and analyzing NMPs in environmental and human biofluid samples. The methodological differences lead to data of variable quality, thus hampering the quantification of NMP levels and comparison of results between studies (Kutralam-Muniasamy et al., 2023). The variability also makes it highly challenging to determine baseline exposure levels and unambiguously identify any adverse effects on human well-being.

Another major limiting factor is the limited availability of data related to long-term exposure. Most recent research focuses on acute exposure situations; yet, NMPs are likely to bioaccumulate in the human body throughout one's lifetime, causing long-term adverse health consequences (Brachner et al., 2020). Focusing on short-duration studies imposes significant uncertainties in understanding the combined effects of long-term exposure to NMPs, especially related to systemic and organ-based toxicity.

The literature so far has been sparse in plastic types. With polystyrene (PS) dominating experimental research despite it not being among the most common plastics produced in the world (unlike polyethylene teraphthalate (PET), or polyvinyl chloride (PVC) (Brachner et al., 2020)), the focus on this one plastic limits transferability to the wide variety of other plastics in our environments, and there is potential benefit for research to include a more varied selection of polymers to better represent environmental representations and human exposures.

Ethical constraints heavily impact research related to NMP. The potential for performing in vivo research involving human subjects poses huge ethical challenges, as controlled and intentional exposure to potentially harmful substances becomes unworkable. As such, researchers have relied heavily on retrospective studies and case studies, which often lack controlled conditions needed to ascertain causality or identify dose-response relationships (Heddagaard & Møller, 2020). The reliance on observational data limits the scope of understanding related to the healthcare impacts of NMP.

In the end, differences between people in their exposure to NMPs create a sizeable problem. Age, gender, genetic composition, and lifestyle significantly affect the body's ability to absorb, distribute, and metabolize NMPs, leading to differences in their effects on various population groups (Zhao et al., 2023). The diversity

comes with the need for research methods specifically customized to cover the different effects of NMPs on various sectors, particularly on vulnerable demographics like infants and workers who are exposed to the chemicals in their workplaces.

6. Future Directions and Recommendations

An inclusive and holistic approach involving the advancement of research and reductions in exposure levels can limit the health impacts of nano- and microplastics. The first step towards limiting health impacts in human beings and animal models is to develop methods for measuring nano- and microplastics in human biological tissues and environmental samples. The adoption of standard protocols would greatly enhance the comparability and accuracy of data, thus enabling researchers to establish viable exposure levels and assess related health risks more effectively (Kutralam-Muniasamy et al., 2023). Such standards should include guidelines on sample collection methods, analytical processes, and reporting formats to ensure uniformity across studies.

Improving in vitro testing is of prime importance towards a greater understanding of NMP toxicity. Current research tends to focus on a specific set of cell lines and plastic types, mostly polystyrene, and short exposure times. Widening research to include various cell lines, plastic polymers like PET and PVC, and long-term exposure times better reflects the overall impact of the chronic effects, which is of prime significance due to the bioaccumulation of NMPs throughout the lifetime of an organism (Brachner et al., 2020). It could also open the path towards investigations concerning the role of particle size and surface modifications in modulating toxicity. The progression of in vivo studies requires the use of ethical techniques to measure NMP levels in humans and relate the measurements to specific health effects. Noninvasive strategies, such as biomonitoring of urine, blood, or feces samples, can potentially provide important information on NMP buildup and systemic impacts while maintaining ethical standards (Zhao et al., 2023). The use of such methods would enable the creation of direct associations between exposure levels and disorders related to health and fill current gaps in available retrospective data. Interdisciplinary collaboration is necessary in order to tackle the complex issues associated with nanomaterials and microplastics (NMPs). Through the integration of toxicology, environmental science, medicine, and public health, the understanding of the impact of NMPs can be holistic, including dissemination in the environment and human health impacts (Lehner et al., 2019b).

Moreover, these collaborative efforts can advance the design of novel methods of detection and analysis of NMPs in complex environmental and biological media. The improvement of materials represents an optimistic means of preventing the threat posed by NMP. Improvement in the development and utilization of biodegradable plastics can potentially significantly reduce environmental persistence and human exposure to harmful polymers (Rai et al., 2021; Narancic & O'Connor, 2019). Effort must be made to research sustainable replacements, specifically bio-based polymers, to replace conventional plastics in high-risk applications, such as food packaging and medical equipment. Public awareness campaigns are fundamental in educating people about the dangers posed by NMP and encouraging sustainable practices. By encouraging people to minimize their use of single-use plastics, choose eco-friendly materials, and support green products, these campaigns can help people minimize their exposure (Zubair & Ullah, 2020). Media outlets and pedagogical initiatives must be charged with disseminating a correct scientific truth to inform decision-making and empower subsequent societal change.

7. Preventive Initiatives

Individuals have many ways to reduce micro- and nano-plastics exposures through very simple practices to reduce contact with such pollutants. Basic behaviours to limit ingestion and environmental pollution activity are to decrease reliance on single-use plastics (e.g., plastic bags, straws, bottles, etc.) (Senathirajah et al., 2021). Minimizing greater exposure levels can also be achieved by choosing an alternative packaging material, such as choosing as much glass, metal, or biodegradable material packaging as possible. Representative clothing items made of natural fibres, such as animal or plant-based materials (e.g., cotton or wool), rather than synthetic clothing, could drastically limit dermal and inhalation exposures to microfibres, as well. Ultimately, policymakers must establish mandates that respect, limit, and develop plastic

waste strategies for waste management, thereby limiting pollution of our environment. Governments and industries need to invest in developing and using biodegradable alternatives to conventional plastics that offer a sustainable solution to reduce long-term environmental and health consequences (Rai et al., 2021). Providing incentives to manufacturers to switch to eco-friendly materials and putting stricter regulations on the disposal of plastic waste could also help further reduce the spread of non-microbial pollutants (NMP).

8. Conclusion

Nano- and microplastics are an ever-present and increasing risk to human health with the potential to cause detriment to the neurological, reproductive, and skeletal systems. In vitro studies indicate that nano- and microplastics can elicit cytotoxicity, genotoxicity, acute inflammation, and oxidative stress; while retrospective animal studies have suggested there may be systemic effects, including neurotoxicity and reproductive harm. However, the demonstration of clear causation of harm is complicated by variability in test methodologies, lack of long-term follow-up, and limitations to ethically experiment on human subjects. Addressing these obstacles will require standardisation of protocols; improvements to in vitro and in vivo assessment; and interdisciplinary collaboration to assess the risk associated with nano- and microplastics to its full extent. In the meantime, material innovations, such as bio-degradable plastics, and initiatives aimed at public education offer promising alternatives to limit exposure and reduce environmental persistence. By leveragint scientific advances, stakeholder engagement, and policy initiative, it is possible to reduce the potential risk to human health posed by nano- and microplastics, in a timely and efficient manner.

References

- 1. Alvarez-Román, R., et al. (2004). Skin penetration and distribution of polymeric nanoparticles. *Journal of Controlled Release*, 99(2), 223–234.
- 2. Amato-Lourenço, L. F., et al. (2021). Presence of airborne microplastics in human lung tissue. *Journal of Hazardous Materials*, 416, 126124.
- 3. An, R., et al. (2021). Microplastics induce apoptosis and fibrosis in ovarian granulosa cells. *Environmental Pollution, 286,* 117575.
- 4. Andrady, A. L. (2011a). Microplastics in the marine environment. *Marine Pollution Bulletin, 62*(8), 1596–1605.
- 5. Andrady, A. L. (2011b). Persistence of plastic litter in the oceans. *Marine Anthropogenic Litter*, 57–72.
- 6. Andrady, A. L., & Neal, M. A. (2009). Applications and societal benefits of plastics. *Philosophical Transactions of the Royal Society B, 364*(1526), 1977–1984.
- 7. Barnes, D. K. A., et al. (2009). Accumulation and fragmentation of plastic debris in global environments. *Philosophical Transactions of the Royal Society B, 364*(1526), 1985–1998.
- 8. Bitar, D., & Parvizi, J. (2015). Biological response to prosthetic debris. *World Journal of Orthopedics*, 6(2), 172–189.
- 9. Brachner, A., et al. (2020). Assessment of microplastics and nanoplastics toxicity in vitro. *International Journal of Molecular Sciences, 21*(6), 2108.
- 10. Braun, T., et al. (2021). Detection of microplastics in human placenta and meconium. *Environment International*, 146, 106274.
- 11. Campbell, C. S. J., et al. (2012). Skin penetration of polystyrene nanoparticles. *Journal of Controlled Release*, *158*(3), 430–437.
- 12. Cedervall, T., et al. (2012). Food chain transport of nanoparticles affects behaviour and fat metabolism in fish. *PLoS ONE*, 7(2), e32254.
- 13. Cole, M., & Galloway, T. S. (2015). Ingestion of nanoplastics and microplastics by marine fauna. *Environmental Science & Technology, 49*(24), 14625–14632.
- 14. Collignon, A., et al. (2014). Neustonic microplastic and zooplankton in the North Western Mediterranean Sea. *Marine Pollution Bulletin, 82*(1–2), 211–216.

- 15. Cózar, A., et al. (2014a). Plastic debris in the open ocean. *Proceedings of the National Academy of Sciences*, 111(28), 10239–10244.
- 16. Cózar, A., et al. (2014b). Plastic accumulation in the Mediterranean Sea. *PLoS ONE*, 9(4), e91215.
- 17. da Costa, J. P., et al. (2016). Nano-plastics in the aquatic environment. *Environmental Science: Processes & Impacts, 18*(1), 18–27.
- 18. Döge, N., et al. (2018). Penetration of polystyrene nanoparticles in human skin. *Toxicology in Vitro*, 48, 110–117.
- 19. Filella, M. (2015a). Questions of size and numbers in microplastic research. *Environmental Chemistry*, *12*(5), 527–538.
- 20. Filella, M. (2015b). Degradation of plastics in the environment. *Environmental Science & Technology*, 49(3), 1277–1284.
- 21. Fournier, S. B., et al. (2020). Nanopolystyrene translocation and fetal deposition after maternal lung exposure. *Nanotoxicology*, *14*(6), 773–789.
- 22. Frias, J. P. G. L., et al. (2019). Standardised protocol for monitoring microplastics in sediments. *Marine Pollution Bulletin*, 141, 20–26.
- 23. Gajski, G., et al. (2014). Genotoxicity and cytotoxicity of polyethylene nanoparticles. *Environmental and Molecular Mutagenesis*, 55(8), 637–646.
- 24. Gigault, J., et al. (2018a). Nanoplastics in the environment: Challenges and definitions. *Environmental Pollution*, *234*, 1031–1038.
- 25. Gigault, J., et al. (2018b). Sources and fate of nanoplastics in marine environments. *Environmental Pollution*, 242(Pt B), 1930–1937.
- 26. González-Acedo, A., et al. (2021b). Microplastics impair sperm viability in male rats. *Environmental Pollution, 287,* 117693.
- 27. Heddagaard, F. E., & Møller, P. (2020). Challenges in microplastic research. *Environmental Research*, 190, 109981.
- 28. Hernandez, L. M., et al. (2017). Plastic nanoparticles in cosmetics and textiles. *Environmental Science & Technology*, *51*(21), 12341–12349.
- 29. Hernandez, L. M., et al. (2019). Plastic teabags release microplastics into tea. *Environmental Science & Technology*, *53*(21), 12300–12310.
- 30. Holding, C. A., et al. (2006). Inflammatory response to polyethylene debris in hip arthroplasty. *Journal of Bone and Joint Surgery*, 88(6), 1174–1181.
- 31. Kik, K., et al. (2020). Polymer composites with enhanced properties. *Materials Science and Engineering: C, 108,* 110456.
- 32. Kolstad, H. A., et al. (1995b). Neurological effects of styrene exposure in plastics workers. *Scandinavian Journal of Work, Environment & Health, 21*(4), 279–287.
- 33. Kosuth, M., et al. (2018). Anthropogenic contamination of tap water with microplastics. *PLoS ONE,* 13(9), e0202806.
- 34. Kutralam-Muniasamy, G., et al. (2020). Microplastics in food and beverages. *Science of the Total Environment, 723,* 138104.
- 35. Kutralam-Muniasamy, G., et al. (2023). Microplastics in human tissues: A review. *Environmental Pollution, 327,* 121583.
- 36. Kwon, J. H., et al. (2020). Microplastics in food: A review. *Environmental Chemistry Letters, 18*(3), 645–659.
- 37. Lambert, S., & Wagner, M. (2016). Formation of secondary nanoplastics. *Environmental Science & Technology*, *50*(22), 12236–12244.
- 38. Lehner, R., et al. (2019a). Environmental degradation of plastics. *Environmental Science & Technology*, 53(13), 7277–7286.
- 39. Lehner, R., et al. (2019b). Inhalation of microplastics in urban environments. *Environmental Pollution*, 255(Pt 1), 113156.
- 40. Li, D., et al. (2020). Microplastics release from infant feeding bottles. *Nature Food*, 1(11), 746–754.
- 41. Liebezeit, G., & Liebezeit, E. (2013). Microplastics in seafood. Marine Pollution Bulletin, 74(1), 6–10.

- 42. Mason, S. A., et al. (2018). Microplastics in bottled water. Frontiers in Chemistry, 6, 407.
- 43. Napper, I. E., & Thompson, R. C. (2020). Plastic debris in the marine environment. *Annual Review of Environment and Resources*, 45, 165–189.
- 44. Narancic, T., & O'Connor, K. E. (2019). Biodegradable plastics: Opportunities and challenges. *Environmental Microbiology*, *21*(10), 3383–3396.
- 45. Orishimo, K. F., et al. (2003). Wear rate threshold for osteolysis in hip arthroplasty. *Clinical Orthopaedics and Related Research*, 416, 171–178.
- 46. Oβmann, B. E., et al. (2018). Microplastics in drinking water. Water Research, 139, 83–92.
- 47. Palm, E., et al. (2019). Biological degradation of plastics. *Science of the Total Environment, 676*, 392–400
- 48. Persoons, R., et al. (2018). Urinary biomarkers of styrene exposure. *Environmental Research*, 165, 396–402.
- 49. Plasticseurope.org. (2024). Global plastics production data. Retrieved from [website].
- 50. Qiang, L., & Cheng, J. (2021). Nanoplastics induce gonadal damage in zebrafish. *Environmental Pollution*, 284, 117374.
- 51. Ragusa, A., et al. (2021). Microplastics in human placenta. *Environment International*, 146, 106274.
- 52. Rai, P., et al. (2021). Biodegradable plastics: A sustainable solution. *Journal of Cleaner Production,* 312, 127816.
- 53. Rhodes, C. J. (2018). Plastic pollution and potential solutions. *Science Progress*, 101(3), 207–260.
- 54. Sarasamma, S., et al. (2020). Nanoplastics cause reproductive toxicity in zebrafish. *Science of the Total Environment, 742*, 140636.
- 55. Schneider, M., et al. (2009). Skin penetration of nanoparticles. *Journal of Controlled Release, 140*(2), 85–92.
- 56. Schwaferts, C., et al. (2020). Nanoplastics: Definitions and challenges. *NanoImpact*, 18, 100223.
- 57. Schwabl, P., et al. (2019). Detection of microplastics in human stool. *Annals of Internal Medicine*, 171(7), 453–457.
- 58. Senathirajah, K., et al. (2021). Estimation of microplastic ingestion in humans. *Nature Communications*, *12*(1), 3874.
- 59. Shanbhag, A. S., et al. (1994). Polyethylene particles in failed hip arthroplasties. *Journal of Bone and Joint Surgery*, *76*(12), 1850–1856.
- 60. Som, C., et al. (2011). Textile nanoparticles and skin penetration. *Environmental Science & Technology*, 45(19), 8344–8350.
- 61. Sun, H., et al. (2021a). Amine-modified nanoplastics toxicity in *C. elegans. Environmental Pollution,* 287, 117611.
- 62. Sun, M., et al. (2021b). Nanoplastics affect zebrafish embryonic development. *Science of the Total Environment*, 790, 148155.
- 63. Teixeira, J. P., et al. (2010). Genotoxicity of styrene exposure in plastics workers. *Mutation Research*, 697(1–2), 29–34.
- 64. Vogt, A., et al. (2006). Nanoparticle penetration in human skin. *Journal of Investigative Dermatology,* 126(6), 1316–1322.
- 65. Werder, E. J., et al. (2018). Neurological effects of styrene exposure. *Environmental Health Perspectives*, 126(2), 027002.
- 66. Wick, P., et al. (2010). Barrier capacity of human placenta for nanosized materials. *Environmental Health Perspectives*, 118(3), 432–436.
- 67. Yang, D., et al. (2015). Microplastic pollution in table salts. *Environmental Science & Technology*, 49(12), 13622–13627.
- 68. Yee, M. S. L., et al. (2021). Skin penetration of nanoplastics. NanoImpact, 22, 100317.
- 69. Yu, C. W., et al. (2021). Nanoplastics reduce brood size in *C. elegans. Environmental Pollution, 286,* 117576.
- 70. Zhang, Q., et al. (2021a). Microplastic exposure in infants. *Environmental Science & Technology,* 55(13), 8855–8865.

- 71. Zhang, N., et al. (2021b). Microplastics in human feces. Science of the Total Environment, 757, 143767.
- 72. Zhao, Q., et al. (2023). Microplastics in human tissues: A global overview. *Environment International*, 171, 107703.
- 73. Zubair, M., & Ullah, A. (2020). Biodegradable plastics: A sustainable future. *Journal of Environmental Management*, 275, 111240.

مخاطر المواد البلاستيكية الدقيقة على الصحة البشرية: مراجعة للمخاطر المحتملة والتداعيات السريرية

الملخص

في عام 2023، ارتفع الإنتاج العالمي السنوي للبلاستيك إلى 400.3 مليون طن متري، مما أدى إلى تلوث واسع النطاق بالمواد البلاستيكية النانوية والدقيقة بأنها جزيئات بلاستيكية يتراوح حجمها بين 1 والدقيقة (NMPs) ومخاطر كبيرة على الصحة البشرية. تُعرّف المواد البلاستيكية النانوية والدقيقة بأنها جزيئات بلاستيكية يتراوح حجمها بين 1 نانومتر و 5 ملم. يمكن أن يحدث التعرض لهذه المواد عبر الابتلاع، الاستشاق، والتلامس الجلدي، وقد تم اكتشافها في أنسجة بشرية مثل الدماغ، الرنتين، الدم، والمشيمة. تقدم هذه المراجعة أدلة علمية ذات صلة حول مسارات التعرض والتأثيرات البيولوجية للمواد البلاستيكية النانوية والدقيقة، بما في ذلك السمية الخلوية، السمية الجينية، والالتهابات التي تم الإبلاغ عنها في الدراسات المختبرية، بالإضافة إلى التأثيرات العصبية والتناسلية والهيكلية التي لوحظت في الأدلة الحية بأثر رجعي. المسار الرئيسي لتعرض الإنسان لهذه المواد هو ابتلاع الأطعمة والمياه الملوثة، حيث أفادت التقارير أن البشر يبتلعون ما يصل إلى 5 غرامات من المواد البلاستيكية الدقيقة أسبوعيًا. يمكن أن يحدث التعريب العامية التي تعيق جهود تقييم والتلامس الجلدي، يليه امتصاص هذه المواد في الأنسجة أو الجسم. هناك العديد من التحديات والفجوات في الأدبيات العلمية التي تعيق جهود تقييم المخاطر، بما في ذلك عدم الاتساق في الأساليب، نقص التقارير عن نتائج الدراسات طويلة الأمد، والتحديات الأخلاقية في الأبحاث التجريبية. تشمل الخطوات المستقبلية الحاجة إلى بروتوكولات موحدة، نماذج مختبرية بشرية متنوعة، أساليب حية أخلاقية وطويلة الأمد، والتعاون البحثي متعدد المراجعة الماحة إلى نهج بحثية مدمجة لفهم وتقليل مخاطر المواد البلاستيكية النانوية والدقيقة على الصحة البشرية، إلى جانب مواد أكثر أمائا المراجعة الحاجة الملحة إلى نهج بحثية مدمجة لفهم وتقليل مخاطر المواد البلاستيكية النانوية والدقيقة على الصحة البشرية، إلى جانب مواد أكثر أمائا وتخلات سياسية مدر وسة.

الكلمات المفتاحية :المواد البلاستيكية النانوية والدقيقة، الصحة البشرية، مسارات التعرض، السمية، البلاستيك القابل للتحلل الحيوى