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REVIEW

Micro(nano)plastics, an emerging health problem

Micro(nano)plásticos, un problema de salud emergente

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ABSTRACT

Introduction: environmental pollutants have become ubiquitous in the last two centuries; of these, plastics, and in particular microplastics (<5 mm), became the most prevalent pollutants. Microplastics are present in the air, water and food chain, and are produced as such or come from the decomposition of larger plastic materials. Despite the social advances that have enabled plastics, the mismanagement of their waste has become an urgent global problem. Pioneering studies on their toxicity have shown that exposure induces oxidative stress, inflammation and decreased cell viability in living organisms. Current research suggests that these microplastics are transported throughout the environment and can accumulate in human tissues; however, research on health effects, especially in mammals, remains very limited.
Method: an exploratory literature review was carried out, taking into account as inclusion criteria: years of publication 2018-2024, English and Spanish language, subject matter related to microplastics and their effects on the health of living beings, and in particular human health, from any geographical area, with open access and full text. The study variables were bibliometric, content and scientific quality.
Results: the presence of micro- and nanoplastics in the environment and their impact on human health is of increasing concern, as they act as vectors of hazardous substances and endocrine disruptors, can affect various body systems and trigger toxicological responses. Despite progress in understanding these effects, more research is needed to establish reference values and testing techniques. The importance of addressing this problem in a collaborative manner with governments, industry and civil society through public policies and continuous monitoring is highlighted. Comprehensive intervention is essential to address this urgent problem.

Keywords: Microplastics; Human Health; Exposure; Toxic Effects.

RESUMEN

Introducción: los contaminantes ambientales se han vuelto omnipresentes en los últimos dos siglos; de ellos, los plásticos, y en particular los microplásticos (<5 mm), se convirtieron en los contaminantes más prevalentes. Los microplásticos se encuentran presentes en el aire, el agua y la cadena alimentaria, y se producen como tales o provienen de la descomposición de materiales plásticos de mayor tamaño. A pesar de los avances sociales que han permitido los plásticos, la mala gestión de sus desechos se ha convertido en un problema mundial urgente. Estudios pioneros sobre la toxicidad de los mismos han demostrado que la exposición induce estrés oxidativo, inflamación y disminución de la viabilidad celular en organismos vivos. Las investigaciones actuales sugieren que estos microplasticos se transportan por todo el medio ambiente y pueden acumularse en los tejidos humanos; sin embargo, la investigación sobre los efectos en la salud, especialmente en los mamíferos, sigue siendo muy limitada.
Método: se llevó a cabo una revisión bibliográfica de tipo exploratoria, teniendo en cuenta como criterios de inclusión: años de publicación 2018-2024, lengua inglesa y española, temática relativa a los microplásticos y

sus efectos sobre la salud de los seres vivos, y en particular la humana, de cualquier ámbito geográfico, con acceso abierto y texto completo. Las variables de estudio fueron tanto bibliométricas, como de contenido y de calidad científica.
Resultados: la presencia de micro y nanoplásticos en el ambiente y su impacto en la salud humana es cada vez más preocupante, al actuar como vectores de sustancias peligrosas y disruptores endocrinos, pueden afectar diversos sistemas del cuerpo y desencadenar respuestas toxicológicas. A pesar del avance en la comprensión estos efectos, se necesita más investigación para establecer valores de referencia y técnicas de ensayo. Se resalta la importancia de abordar este problema de manera colaborativa con gobiernos, industria y sociedad civil mediante políticas públicas y monitoreo continuo. La intervención integral es fundamental para enfrentar esta problemática urgente.

Palabras clave: Microplasticos; Salud Humana; Exposición; Efectos Tóxicos.

INTRODUCTION

Plastics are a material of enormous importance in today's society, with applications in all areas of daily life due to their high durability and ease of production.[1,2,3] In recent years, they have become a source of great concern for the scientific community and the general public due to their harmful effects on the environment, living beings, and human health.[4,5,6]

According to a 2020 publication by Plastics Europe, 368 million tons of plastic were produced in 2019, which is expected to continue to rise.[7,8] Unfortunately, plastic waste management is inadequate in most countries, compounded by the fact that recycling rates remain very low.[9,10,11,12] This has led to the accumulation of plastics in the natural environment.[13,14,15,16,17] Much of this waste comes from land-based sources such as fishing nets, ropes, plastic bottles, and bags, which end up in marine and coastal environments.[18,19,20] It is estimated that between 4,8 and 12,7 million tons of plastic annually enter the oceans.[21,22]

These plastics that accumulate in the environment undergo slow degradation that culminates in losing the material's integrity, leading to its fragmentation into smaller pieces called microplastics (MP). This degradation is usually caused by a combination of chemical and physical processes, including photodegradation, oxidation, hydrolytic degradation, and mechanical disintegration. Depending on the type of polymer and its morphology, they can differ significantly.[9]

Microplastics can be classified as "primary" or "secondary." They are called primary when they are originally manufactured in small sizes to be used directly or as precursors for other products such as synthetic fibers, industrial pellets, and microbeads added to cosmetic products. Their origin and function then determine their shape, and primary microplastics can be found in different shapes (spherical, cylindrical, disc-shaped, or cubic). For example, microbeads are widely used in the cosmetics industry as replacements for certain natural exfoliants in single-use cosmetic products, such as makeup removers and toothpaste. These microbeads are supposed to be retained in the filters of wastewater treatment plants. However, many plants are not designed or capable of effectively separating these microplastics, which are ultimately released into aquatic systems. Secondary microplastics originate from the physical or chemical abrasion (as mentioned in the previous paragraph) of larger plastic elements or fibers that enter the environment due to poor waste management. These are the most abundant.[19]

In Argentina, secondary microplastics are mainly represented by synthetic microfiber threads or irregularly shaped fragments. They consist of small plastic threads from various products made of polyester, nylon, acrylic, and other synthetic textiles, found in clothing, tires, fishing nets, cigarette butts, and carpets, among others.[19]

In addition to being able to accumulate and deposit in the environment, microplastics are responsible for generating a local inflammatory response, currently posing a danger to human health. On the other hand, it should be noted that the toxicity associated with them depends mainly on the dose and polymer factors: type, particle size, surface chemistry, and hydrophobicity, and that the rate of accumulation on various human tissues and their distribution therein is directly related to the size of the microplastics.[7]

Although data on microplastic exposure levels in environments and organisms have increased rapidly in recent decades, little information is available on the chemicals associated with microplastics.

Nanoplastics (NP): particles between 1 nm and 100 nm in size. Their presence in the environment is challenging to determine accurately due to technical difficulties in isolating and quantifying them. Still, they are released into the atmosphere due to the weathering of larger plastic fragments, and therefore also pose a significant threat to the environment and human health. They have different chemical properties depending on their size and surface area, and their small size makes them susceptible to being ingested by organisms at the bottom of the food chain. In addition, they have a fundamental characteristic that increases their harmful effects: their high surface-to-volume ratio, given that other pollutants, such as persistent organic pollutants

(POPs), could adsorb to them and undergo bioaccumulation and biomagnification. It should also be noted that prolonged contact with this type of plastic at high concentrations generates a potential teratogenic effect and impacts the central nervous system.[13]

Exposure to these micro- and nanoplastics can occur through ingestion, inhalation, and skin contact due to their presence in products, food, and air. Exposure to micro- and nanoplastics can cause particle toxicity, oxidative stress, inflammatory lesions, and increased uptake or translocation in all biological systems. The inability of the immune system to eliminate synthetic particles can lead to chronic inflammation and increase the risk of neoplasia. They can also release their components, adsorbed contaminants, and pathogens. However, knowledge about the toxicity of microplastics is still limited.[12]

This article aims to provide an overview of this emerging topic, emphasizing the impact of micro- and nanoplastics on human health and the challenges of detecting plastics in a biological environment. First, the possible sources of micro- and nanoplastics, their fate, and their effects on human health will be examined. Next, the likely routes of entry of these particles into the human body and their mechanisms of absorption at the cellular level will be described. Given that the potential risks of environmental micro- and nanoplastics to humans have not been studied, the focus will be on studies demonstrating cellular responses induced by micro- and nanoparticles. In particular, the influence of particle size and surface chemistry, as well as their toxicological effects, on bacterial resistance and their accumulation in different organs of the human body, with the pathological consequences that this entails, will be analyzed to understand the potential risks of micro- and nanoplastics to humans.

It is essential to be aware that micro- and nanoplastics are ubiquitous environmental pollutants. Due to the growing consumption of plastic, combined with their persistent nature, they are causing humans to be exposed to them in an increasing and inevitable way.

METHOD

The method used to conduct the literature review is deductive, starting from general concepts to establish specific hypotheses. The literature review begins with scientific articles with a general focus on keywords such as microplastics, toxicity, and pollution, before narrowing down to their various toxicity pathways and routes of human exposure. To this end, the literature search was conducted using PubMed, Scielo, and Lilacs databases, including English keywords such as microplastic, toxicity, and human health. Once the general information was obtained, it was refined using Google Scholar to get more up-to-date information. Based on the bibliography of the first articles collected, more articles focused on more precise concepts. The search was complemented by various queries on specific medical websites such as MedLinePlus medical encyclopedia (https://medlineplus.gov/), which were used to verify the information obtained in other scientific articles and to gain a more general understanding of the possible adverse effects of plastics on human health. The help of Argentine public health repositories (https://www.conicet.gov.ar/tag/repositoriodigital/) and international journals on environmental pollution (https://www.revistascca.unam.mx/rica/index.php/ric a) helped to understand the potential risk along with the possible adverse effects and impacts of microplastics on human health and the terrestrial ecosystem, including in our country.

For this purpose, the following inclusion criteria were established: Year of publication (between 2017 and 2024), language (English and Spanish), access (open access), type of publication (article, review article, and book chapters), and publication status (final).

RESULTS

Today, microplastics are widespread pollutants in the environment. They contain hazardous chemicals as part of their material but can also adsorb, magnify, and disseminate environmental contaminants.

Although the fate and effects of micro- and nanoplastics in the human body remain controversial, the impact on human health is concerning, as recent studies suggest that these plastic particles may act as vectors for endocrine disruptors, interfering with the nervous, respiratory, circulatory, gastrointestinal, hormonal, and reproductive systems, strongly affecting people's quality of life. Because these plastics can infiltrate human tissues and trigger a series of toxicological responses, such as inflammation, oxidative stress, and alterations in lipid metabolism, these effects may be due to their physical properties (size, shape, and length), chemical properties (presence of additives and type of polymer), concentration, or the growth of microbial biofilms.

In general, microplastic research has gained attention in the last five years. Studies have documented the amount of microplastics in surface waters, sediments, and ecosystems and the consequences of their ingestion, accumulation, and toxic potential in animal models and human populations. In addition, there is evidence of microplastics in drinking water and other consumer products.

Although significant progress has been made in understanding the cellular and molecular mechanisms involved in the health hazards of micro- and nanoplastics, extensive research is still needed. Reference values for each type of plastic and standardized testing techniques for universal use that can be verified through intercomparison exercises still need to be developed.

This helps us understand that micro- and nanoplastics are a problem growing over time and remain invisible in some fields, but require immediate and thorough intervention. It should be noted that addressing this problem requires a comprehensive and collaborative approach involving various actors, including governments (through public policies and state legislation to promote the continuous monitoring of these environmental microparticles), industry, civil society, and consumers.

DISCUSSION

Plastics are a material of enormous importance in today's society, with applications in all areas of daily life due to their excellent durability and ease of production. In recent years, they have generated enormous concern among the scientific community and the general public due to their harmful effects on the environment, living beings, and human health.

A global analysis revealed that plastic waste accumulated in landfills or the natural environment amounted to approximately 4,9 billion metric tons between 1950 and 2015, and that this figure will rise to approximately 12 billion tons by 2050, which will inevitably lead to widespread plastic pollution.[2]

In addition, the COVID-19 pandemic has exacerbated the situation, as the widespread use of masks made from plastic polymers (polypropylene) has led to the generation of even more plastic waste worldwide, which, due to poor control strategies for their final disposal, has ended up accumulating in the environment.[11]

These plastics that accumulate in the environment undergo slow degradation, resulting in a loss of material integrity. This leads to their fragmentation into smaller pieces called microplastics, which can also be manufactured as such. Recently, in 2020, ISO defined microplastic as "any solid particle insoluble in water with any dimension between 1 and 1,000 µm" (ISO/TR 21960:2020 Plastics - Environmental aspects - State of knowledge and methodologies), while Directive 2019/904 recognizes land and soil pollution by introducing microplastics as emerging and priority substances in water analysis.[9]

The degradation of plastics is caused by a combination of chemical and physical processes that may include photodegradation, oxidation, hydrolytic degradation, and mechanical disintegration. Depending on the type of polymer and its morphology, these processes can differ significantly. Photodegradation caused by sunlight's ultraviolet (UV) radiation can break synthetic polymers' chemical bonds. The process affects the polymers and additives incorporated into the materials, causing changes in their chemical structure and physical properties. Oxygen can increase the absorption of UV radiation by forming a complex with conjugated unsaturated hydrocarbons, thereby accelerating the degradation process. In addition, polymers such as polyesters or polyamides can also be degraded by hydrolysis, i.e., the cleavage of ester or amide bonds by reaction with water. External mechanical forces also contribute to fragmentation into smaller pieces, whose dimensions gradually decrease. Degraded plastic pieces form a very heterogeneous mixture, varying in the specific material's size, shape, density, and chemical composition.[9]

Microplastic (MP) pollution began as a marine pollution problem, but has become a public health issue.[23,24,25] Today, various studies reveal that MPs are distributed across all continents and oceans. Because MPs are continuously fragmenting and spreading across the earth, MP particles have been reported in the air, soil, sediments, inland and coastal waters,[26] beach sand,[27] marine systems, water columns, deep-sea sediments,[28] deep sea, and even reaching remote areas such as polar regions[29,30] and glaciers.[31] One study claims that, regardless of the location and sampling date, microplastics and even plastic pellets will always be found if a sample is taken.

Depending on their origin, microplastics can be classified as primary and secondary. Primary microplastics are explicitly created for particular applications, such as microbeads or pellets. These are used in various products, including cleaning products, cosmetics, paints, exfoliants, and toothpaste. The manufacture and use of these MPs contribute significantly to the increase in plastic pollution in the environment. Primary MPs are often preferred for their versatility and low cost, as they can replace more expensive natural ingredients. Acrylic, melanin, and polyester MP particles are also used in cleaning tools for machinery and boats. In addition, primary MPs produce macroplastics, such as pellets, which are used in molding and extrusion processes to shape different plastic products. Some primary MPs and their additives, such as phthalates, are used in various medical applications, including some medications. For example, the drug Asacol, used in the treatment of mild to moderate ulcerative colitis, contains monobutyl phthalate and dimethyl phthalate in specific concentrations that give it beneficial properties, such as resistance to gastric digestion and control of the rate of absorption of the active ingredient. Other medications, such as Videx EC and Creon, also contain phthalate compounds for various functions, such as excipients or artificial flavorings.[23]

Secondary microplastics are generated through the fragmentation and selective degradation of macroplastics exposed to external factors, which can occur during their transport to different ecosystems. This group also includes synthetic fibers from textiles. The fragmentation of macroplastics can occur through various processes, such as photodegradation, where sunlight oxidizes the chemical structure of polymers, causing breaks in the bonds and reducing the molecular mass, which makes them fragile and prone to fragmentation into small pieces. Biological degradation can also contribute to the fragmentation of plastics, as some are susceptible to biodegradation by bacteria and fungi. In environments such as the marine environment, macroplastics can also undergo mechanical degradation due to the combined action of wind, waves, and abrasion of plastic particles in sediments and sand. On the other hand, animal, plant, and synthetic fibers in clothing can be shed during washing, transporting themselves from washing machines to wastewater. Even the simple handling of plastic containers can generate microplastics through abrasion, releasing them into the environment.

Other notable sources of secondary microplastics include tire wear, which is considered a hidden source of microplastic pollution. This wear is influenced by factors such as the type of pavement, temperature, speed, age, and composition of the tires. In addition, secondary microplastics can originate in wastewater treatment plants, landfills, and industrial areas due to the incineration of plastic waste.[23]

In the marine environment, primary microplastics usually enter through wastewater. In contrast, secondary microplastics are introduced through additional sources, one of the most important being the degradation of plastic waste on beaches, where high concentrations of hazardous elements are found, particularly the toxic metals Cd and Pb. Microplastics are mainly found in the marine and atmospheric compartments. They are common in all the world's oceans and can be found ubiquitously in the air, water, biota, and sediments.[3]

Microplastics can contain two types of chemicals: (i) additives and polymeric raw materials (e.g., monomers or oligomers) from plastics, and (ii) chemicals absorbed from the surrounding environment.[9]

Additives are chemicals intentionally added during the production of plastics to give them qualities such as color and transparency, increase the performance of plastic products, and improve their resistance to degradation by ozone, temperature, light radiation, mold, bacteria, and moisture, as well as their mechanical, thermal, and electrical resistance. They include inert or reinforcing fillers, plasticizers, antioxidants, UV stabilizers, lubricants, dyes, and flame retardants.

Inert fillers include wood and rock powder, clay, kaolin, graphite, glass fibers, cotton flakes, jute or linen, cellulose paste, etc. According to the definitions proposed by the American Society for Testing and Materials (ASTM-D-883), inert fillers are materials used to modify the strength, working, and flow properties, and shrinkage of plastics, while reinforcing fillers, also called fillers, are defined as those with significantly higher strength properties than the base resin.[5] These fillers (such as carbon black in rubber), which are mixed with the polymer, give rise to an interface volume generated at the contact surface between the filler and the resin. The superior properties of this interface layer increase the modulus and mechanical properties, such as impact resistance or tensile strength, in the composite polymer. As the effect is surface-related, smaller particle sizes of the filler particles tend to produce a better reinforcing effect. There are different types: clays, silica, glass, chalk, talc, asbestos, alumina, rutile, carbon black, and carbon nanotubes.[9]

Because plastics are susceptible to the degrading effects of light, UV radiation, and heat, stabilizers prevent thermal decomposition during processing, oxidation, and the resulting breakdown of polymer chains (using phenols and aromatic amines). They mainly consist of organic or inorganic salts of cadmium, barium, or lead. Soluble or insoluble colorants are organic or inorganic substances in the form of fine powders that give the polymer the desired color. Soluble colorants maintain the transparency of the plastic, while insoluble colorants (pigments) cover the plastic to make it opaque. Many inorganic pigments contain heavy metals, while organic pigments include several chromophore families such as azo pigments, phthalocyanine anthraquinones, and other chromophores.

Lubricants and anti-adhesives, which consist of calcium or magnesium stearates, facilitate the transformation of plastic materials and improve their fluidity characteristics.[10]

Flame retardants can cool or protect a material in the event of fire by preventing the oxidation of flammable gases or forming a layer of ash. These products contain, for example, chlorine and bromine, which are released by the action of the flame; phosphorus, which promotes transformation into carbon; and aluminum hydroxide, which generates water vapor and CO2 at 200°C. In almost all cases, the additives are not chemically bonded to the plastic polymer; only some flame retardants polymerize with the plastic molecules, becoming part of the polymer chain

. Although these additives improve polymer products' properties, many are toxic and have a high potential for contaminating soil, air, and water. Studies on their impact on aquatic organisms that come into contact with them through ingesting macro- and microplastics are ongoing.[6]

Nanoplastics: These are plastics that are between 1 nm and 100 nm in size. Their presence in the environment is challenging to determine accurately due to the technical difficulties in isolating and quantifying them. Still, they are released into the atmosphere due to the weathering of larger plastic fragments, and therefore also pose a significant threat to the environment and human health. They have different chemical properties depending on their size and surface area, and their small size makes them susceptible to being ingested by organisms at the bottom of the food chain. In addition, they have a fundamental characteristic that increases their harmful consequences, which is the high surface-to-volume ratio of nanoparticles, given that other pollutants, such as persistent organic pollutants (POPs), could adsorb to them and undergo bioaccumulation and biomagnification phenomena (Browne et al., 2011). It should also be noted that prolonged contact with this type of plastic at high concentrations generates a potential teratogenic effect and impacts the central nervous system.(13)

Due to their presence in products, food, and air, exposure to these micro- and nanoplastics can occur through ingestion, inhalation, and skin contact.

Detection strategies

Growing concern about environmental MP and NP pollution has led to a demand for accurate and sensitive analytical techniques for their identification. To address this challenge, various physicochemical analytical methods have been used to detect and quantify the presence of plastics in different environmental matrices. The analytical techniques that provide the best information on the presence of MP and NP in the environment are described below.

Fourier transform infrared spectroscopy (FTIR): FTIR is an analytical technique used to identify polymeric materials based on the absorption of infrared radiation by molecules. FTIR analysis is used to identify the unique spectral characteristics of plastic polymers, determine the chemical composition of unknown plastic fragments, and assess the degree of aging of samples collected from the environment. In addition, it allows the identification of different types of plastics and the determination of their abundance in environmental samples.

Inductively coupled plasma mass spectrometry (ICP-MS): ICP-MS is a technique used to quantitatively determine elements present in a sample at trace levels. It can be connected with separation techniques to identify and quantify the presence of additives and contaminants associated with MP and NP. This provides crucial information on the potential toxic effects of MP and NP on living organisms and ecosystems.

Scanning electron microscopy (SEM): This method is an analytical tool used to identify tiny plastic fragments and provides detailed information on their morphology, size, and elemental chemical composition, which can provide additional characteristics about their origin and degradation process.

Transmission electron microscopy (TEM) is another essential tool in identifying and characterizing MP and NP. It allows the sample to be observed at the molecular and atomic level, providing images with extremely high resolution, enabling the size and shape of MP and NP particles to be observed, which is essential for distinguishing between different types of materials, their size, and the nanometric shape of plastic particles to relate them to their origin.(15)

Effects of micro- and nanoplastics on different organs and systems of the human body

Gastrointestinal and urinary tract

Microplastics often enter the esophagus, stomach, and intestines through the mouth, so their toxic effects are evident throughout the digestive tract. These poisonous effects manifest as intestinal flora disorders, reduced mucus secretion, destruction of the ratio of probiotics and pathogenic bacteria; all of this leads to damage to the intestinal mucosal epithelium and ultimately to the destruction of the intestinal barrier, which leads to disorders of amino acid and fatty acid metabolism and nutrient absorption deficiency and even liver toxicity.(15)

A study conducted by the Key Laboratory of Public Health Safety, Ministry of Education, School of Public Health, Institute of Nutrition, Fudan University, Shanghai, China, on preschool children concluded that children who spent more time eating a meal in plastic containers had higher levels of PVC in their feces. In addition, dairy products, particularly formula milk, may influence children's exposure to microplastics. Growing evidence shows that using baby bottles may lead to increased release of microparticles during preparation. Participants who used silicone baby bottles had higher concentrations of total MP in their stools than those who used PPSU baby bottles. Therefore, it is believed that extensive use of baby bottles may be a particular source of contamination of formula milk, indirectly increasing the imperceptible ingestion of microparticles. In addition, microplastics in the air can be inhaled and can settle on utensils, food, and water, which are then ingested. Children also appeared to excrete more MP if their parents smoked. Smoking also produces fine MP particles. When parents smoke in the presence of children, they inhale these airborne particles, affecting the respiratory system, and fine particles can enter the circulatory system. These results suggest that high exposure to certain MPs may be associated with a higher incidence of gut-related diseases in children.(17)

In the urinary system, NPs that manage to cross epithelial barriers can leak through the kidneys and appear in urine, causing inflammation and kidney dysfunction.(15)

Endocrine System

Microplastics (MP) contain and leach many hazardous chemicals, including those that disrupt the body's hormonal systems, or Endocrine Disruptors (EDCs). Bisphenol A (BPA) is a well-known example used in polycarbonate plastics. In addition, a wide range of other plastic additives, including phthalates, flame retardants, and heavy metals, are known as EDCs.

EPs in plastics, bisphenols, and phthalates are the most studied for mimicking or interfering with processes regulated by estrogen and androgen, such as reproduction. These hormones are strictly regulated; if disrupted by EPs, reproductive dysfunctions such as reduced fertility, miscarriage, and infertility can occur.

The direct effects of EDCs on sperm count and quality, chromosomal abnormalities in eggs, and biological processes involved in sperm and egg production have been demonstrated.

BPA exposure is also associated with polycystic ovary syndrome (PCOS) in women, and in men, BPA decreases sperm quality and motility, causes oxidative stress, and alters steroidogenesis. In addition, BPA is associated with sexual dysfunction among men exposed to high occupational levels. Studies in humans have shown links between prenatal exposure to BPA and increased body fat or postnatal growth curves in children, findings that are relevant to obesity in early childhood.

BPA exposure has also been associated with impaired pancreatic ß-cell function and increased insulin resistance in adults, consistent with the health effects observed in type 2 diabetes, and with abnormal liver enzyme levels, consistent with impaired liver function and non-alcoholic fatty liver disease.

Perfluoroalkyl and polyfluoroalkyl substances (PFAS) were also associated with altered pubertal timing in children, as measured by age at menarche in females and serum testosterone concentrations in males. There is also some evidence that exposure to PFAS is associated with an increased risk of breast cancer. However, this association may be stronger in cancers that depend on estrogen receptors.

Brominated flame retardants (BFRs) disrupt thyroid hormone levels. This is especially concerning if exposure occurs during pregnancy and early life, as thyroid hormone is essential for neurodevelopment. Epidemiological studies have shown an association between developmental exposure to BFRs and subsequent deficits in children, including psychomotor development, attention-related behavior, and IQ performance. Evidence suggests that BFRs may interfere with hormones necessary for the body's response to stress.

Phthalates can be widely metabolized when absorbed by the body, creating potentially toxic metabolites. Phthalate metabolite levels are higher in humans exposed through occupational exposure or medical therapies requiring intravenous lines, blood bags, and oral medications containing phthalate coatings. Exposure to phthalates during fetal development has been associated with reduced sperm count and quality and an increased risk of gonadal dysgenesis. In addition, exposure to phthalates has also been associated with an increased risk of insulin resistance and other cardiometabolic risk factors.

Toxic metals such as cadmium and lead in microplastics are associated with abnormal hormone levels and reproductive development, subfertility/infertility in humans, and an increased risk of breast and prostate cancer, both of which are hormone-dependent. Both of which are hormone-dependent. Lead concentrations in the bloodstream are associated with delayed onset of puberty in girls and even in boys in some studies, as well as with earlier onset of menopause, suggesting that lead exposure may shorten women's reproductive lives. Lead and cadmium concentrations in the blood are associated with longer pregnancies in couples actively trying to conceive.[26]

Respiratory system

Most microplastics found in the atmosphere have been in the form of fibers. These tend to cause greater toxicity than fragments or spheres. Particles with a fiber morphology and greater length are the most capable of avoiding mucociliary clearance and are more durable in physiological fluids; their thin, elongated shape also hinders phagocytosis and elimination by alveolar macrophages, allowing them to accumulate and persist more easily when inhaled, compared to particles of other shapes and sizes.[27]

Inhalation of these microplastic fibers also risks human health because they reduce nutrient absorption, cause hormonal changes, oxidative stress, pulmonary fibrosis, immune dysfunction, biochemical and energy metabolism disorders, cell proliferation disorders, and abnormal organ development. Studies suggest that nanoplastics from fiberglass can penetrate deeper into the lungs and skin, causing more profound damage.[15]

Blood and the immune system

Microplastics can enter the bloodstream through the gastrointestinal or respiratory tract, as those smaller than 10 μm can pass through cell membranes and easily move into the circulatory system and alter immune system function. Scientific evidence has shown that exposure to these materials increases DNA damage in polymorphonuclear cells and monocytes in humans (causing genomic instability in lymphocytes), triggering chronic inflammatory responses and affecting the body's ability to fight infections. In addition, chronic exposure may ultimately lead to diseases such as cancer, given the damage caused to the genetic material of cells.[15,24]

Brain and nervous system

Preliminary studies suggest that micro- and nanoplastics may cross the blood-brain barrier, which could lead to neuroinflammation, oxidative stress, and neuronal damage, because they can produce highly oxidizing reactive oxygen species that can cause inflammation, cell death, and inhibition of acetylcholinesterase (AChE)

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activity, resulting in excessive accumulation of acetylcholine, which leads to overexcitation of cholinergic nerves and causes neurological disorders (abnormal behavior and depression). Although research is at an early stage, prolonged exposure could contribute to neurological and cognitive disorders.[4,15] According to a study conducted in an animal model at the George and Anne Ryan Institute of Neuroscience at the University of Rhode Island, USA (2023), it was concluded that short-term exposure to microplastics induces both behavioral changes and alterations in immune markers in liver and brain tissues. In addition, they observed that these changes differ with age, indicating a possible age-dependent effect. These findings suggest that further research is needed to understand better the mechanisms by which microplastics can induce physiological and cognitive changes.[4,15,18]

Embryos and the placental barrier

Microplastics have been shown to cross placental barriers, raising concerns about prenatal exposure. This exposure could affect embryonic development, causing alterations in gene expression and contributing to malformations or changes in the fetus's neurological and immune system development. Some studies have shown that the most common are polyvinyl chloride (PVC), polypropylene (PP), and polyethylene terephthalate (PET). These components within the placenta could affect maternal and fetal health, as they may contain chemical additives and contaminants that could be released into the placental environment and have toxic effects. Furthermore.[15,25]

When exposure occurs in a pregnant woman, her developing fetus is exposed, as are the germ cells within the fetus, which become the third generation affected. Thus, three generations are exposed simultaneously. EPs have been shown to cause various types of epigenetic modifications in germ cells, produced from sperm or eggs, which in offspring (children) lead to an increased propensity for endocrine and neurological disorders in the next generation (grandchildren). Therefore, exposure to EPs before conception or early life influences multiple generations.[26]

Cardiovascular system

Autophagy is a highly conserved cellular process that plays a key role in maintaining cellular homeostasis by recycling damaged organelles and proteins. This process is critical in the heart, where it helps keep the normal function of myocytes (heart muscle cells) and respond to various stressors, such as ischemia or pressure overload. Alteration of autophagy by micro- and nanoplastics (MNPs) could accumulate damaged organelles and proteins in myocytes, impairing their function and potentially contributing to the development or progression of cardiovascular disease (CVD). In addition, recent research has explored the impact of microplastics (MPs) on the vascular system.

The triggering or acceleration of autophagy may be due to a cardiotoxic response of MPs. Studies suggest that the cardiotoxicity of MNPs may cause cardiac dysfunction through mechanisms such as oxidative stress, mitochondrial dysfunction, and inflammation. Although plastic particles smaller than MPs, such as nanoplastics (NPs), are believed to play an essential role in human toxicity, studies focusing on their cardiovascular toxicity have not demonstrated that NPs are capable of causing cardiac dysfunction, as studies focusing on their cardiovascular toxic effects are scarce.

Recently, a study reported that exposure to polystyrene NPs with various functional groups significantly exacerbates type 2 diabetes mellitus (T2DM)- like conditions, mainly through the inhibition of the P-AKT/P-FoxO1 signaling pathway. This study highlights the potential of NP pollution to contribute to the development and progression of cardiometabolic disorders.

Inflammatory responses and lipid metabolism are essential in the onset and development of CVD. Recent studies have indicated the impact of MNPs on the systemic immune system, with a particular focus on effects on the cardiovascular system.[4,15]

In addition, NPs have been found to increase the release of proinflammatory cytokines in human monocytes and monocyte-derived dendritic cells. Furthermore, polystyrene NPs may also contribute to the development of atherosclerosis by affecting mitochondrial-mediated oxidative stress, promoting foam cell differentiation, and altering lipid metabolism.[28]

The mechanisms involved are surprisingly similar to those observed with NPs. Oxidized low-density lipoprotein (OxLDL), with a diameter of approximately 20-30 nm, plays a crucial role in the onset and progression of atherosclerosis. Not only does it promote the formation of foam cells, but it also triggers inflammation and affects endothelial cell function.[28]

In addition, another study suggested that 50 nm polystyrene NPs and long-chain acylcarnitine (LCAC) alone exacerbate lipid accumulation by upregulating macrophage receptors (MARCO) in Ox-LDL-activated foam cells, thereby promoting the development of atherosclerosis. These findings provide new insights into the mechanisms linking MNPs and atherosclerosis.[28] These results demonstrate that MNPs can cause inflammatory reactions, leading to vascular endothelial dysfunction through the activation of inflammatory cells, the

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induction of genomic instability, and the release of inflammatory mediators, such as cytokines and oxidative stress substances. They may also affect lipid metabolism and promote the development of atherosclerosis.[28]

Since studies have reported that MNPs, especially MPs, are found in human blood clots and can accumulate in arteries, scientists believe that the risk of exposure to MPs is seriously underestimated. Regarding the coagulation system, the study also revealed a significant positive correlation between the number of particles in the thrombus and platelet count after adjusting for possible confounding factors. Furthermore, a study reported that the interaction between MNPs, thrombosis, and the cardiovascular system depends mainly on their size and surface chemistry, suggesting that the effect of MPs is closely related to their size and surface chemistry. Surface-charged particles (such as amino-MNPs) may promote platelet aggregation and thrombosis by interacting with platelet surface receptors.[28]

Antibiotic Resistance

Antimicrobial compounds such as antibiotics, biocides, and heavy metals can drive the development of antibiotic resistance and stimulate the horizontal transfer of antibiotic resistance genes in microorganisms.

Microplastics provide a hydrophobic surface that favors the formation of microbial biofilms, in which environmental conditions are the main drivers of biofilm formation. Pathogenic bacteria such as Aeromonas spp. and Vibrio spp., as well as opportunistic human pathogens such as E. coli, may be invariably present in these biofilms. Microplastics can selectively adsorb antibiotics and antibiotic-resistant bacteria onto their surfaces in landfill leachates, freshwater, and seawater.[31]

Mitigation strategies

Plastic pollution can be prevented by applying waste hierarchies within the plastics economy to increase plastic waste reduction, reuse, and recycling dramatically.[19]

Given that the source of all secondary microplastics is always macroplastics that fragment in different ecosystems, most of the technologies applied for their mitigation are focused either on preventing their entry into the environment or on removing them in situ.[19]

It is essential to establish alternatives and strategies that contribute to solving this critical problem, some of which may revolve around:

- Reduction in the production and consumption of plastics: One of the most effective strategies is to reduce the production and consumption of plastics in general. This can be achieved by promoting the use of more sustainable and biodegradable alternative materials (for example, greenhouse plastics can be replaced by biodegradable materials such as wood or bamboo), encouraging the reuse of plastic products, and adopting responsible consumption practices, which are some of the measures that have been implemented in some countries.[4,13]
- Immobilization of microplastics: This can be a temporary solution to prevent them from dispersing into the environment. For example, coagulants or flocculants can precipitate microplastics from water, and these agents can be used to remove microplastics from irrigation water or wastewater before they are discharged into the environment.[13]
- Improved waste management: It is essential to improve waste management, especially when collecting and recycling plastics. This involves implementing efficient waste separation systems, promoting selective collection, and establishing adequate recycling infrastructure, such as efficient collection systems, door-to-door plastic waste collection, or installing plastic waste recycling containers in large population centers. Efforts should also be made to raise awareness and educate the public about the importance of disposing of plastics correctly and avoiding their disposal in the environment.[4,13]
- Promoting the circular economy: The transition to a circular economy, in which resources are used more efficiently and waste generation is minimized, is a key strategy for addressing the problem of microplastics. This involves promoting reuse, recycling, and designing more durable and easily recyclable products.[4,19]
- Research and development of alternative materials: It is necessary to promote research and development of alternative materials to plastic, such as bioplastics, biodegradable, and compostable materials. These materials can offer a more sustainable alternative and reduce the accumulation of microplastics in the environment.[4]
- Awareness and education: Public awareness and education are essential to promote changes in consumption habits and waste management. It is necessary to inform people about the environmental impacts of microplastics and encourage sustainable practices in their daily lives.[4,19]
- Government regulations and policies: Governments play a crucial role in reducing the harm caused by microplastics by implementing effective regulations and policies. This may include banning or restricting certain single-use plastic products, promoting stricter waste management standards, and establishing incentives for adopting sustainable alternatives. This topic will be explored in greater depth

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later on.[4,19,24]

It is also important to implement methods for the recovery and disposal of microplastics, which are detailed below:

Physical removal methods

Different physical removal methods are used in wastewater treatment plants. The most widely used physical processes are described below:

- Mechanical filtration involves using physical filters to trap plastic particles of different sizes. Filters can be designed with specific pore sizes to capture MP and NP while allowing water to pass through. This method effectively removes a wide range of plastic particles, but pore clogging can affect efficiency, and there is a need for regular cleaning.[15]
- Centrifugation uses centrifugal force to separate plastic particles from water. It works well for larger particles but may be less efficient for NPs due to their comparatively lower mass and density.[15]
- Flotation is used because some MP and NP may be less dense than water and float to the surface. Air-assisted flotation or adding chemical agents can facilitate the separation of these plastics for subsequent removal.[15]

These physical MP and NP removal methods are essential for addressing plastic pollution. However, they face challenges such as effectiveness, which can vary depending on the size, shape, and density of the plastic particles; some methods can even be costly to implement on a large scale, limiting their viability for practical applications.

Chemical removal methods

The chemical methods used to remove these emerging contaminants are described below:

- Coagulation-flocculation is a chemical process commonly used in wastewater treatment to remove suspended particles. It involves the addition of coagulants, such as iron or aluminum salts, followed by flocculants to promote the formation of aggregates, which can be easily removed by sedimentation or filtration. This method has proven effective in removing MP and NP by forming flocs that trap plastic particles. However, its effectiveness varies depending on the characteristics of the plastics and the water conditions, generating unwanted by-products.
- Adsorption is a process by which particles or molecules adhere to the surface of a solid material, known as an adsorbent. Various adsorbents, such as activated carbon, zeolites, modified polymers, and nanomaterials, in the context of MP and NP removal, have been investigated. These materials can offer high adsorption capacity and selectivity towards plastics. Still, their effectiveness can be affected by factors such as the concentration of plastics in the water and competing organic compounds.
- Advanced oxidation processes (AOPs) involve the in situ generation of highly reactive oxidizing species, such as hydroxyl and superoxide radicals, to degrade recalcitrant organic compounds in water. This approach has been explored for removing MP and NP by breaking chemical bonds in the structure of plastics. However, applying advanced oxidation for this purpose still faces challenges related to degradation selectivity, efficiency, and the generation of toxic by-products. Photocatalysis, an AOP, uses oxides of semiconductor elements activated by ultraviolet or visible light to generate free radicals that can oxidize organic contaminants in water. Although photocatalysis shows potential for the degradation of plastics, its effectiveness may be limited by the availability of sunlight and the need to maintain specific pH and temperature conditions.

Chemical methods offer various strategies for removing MP and NP in water, each with advantages and limitations. However, further research is needed to improve these approaches' effectiveness, selectivity, and sustainability.[15]

Biological removal methods

Biological and biotechnological methods are emerging as promising approaches for removing MP and NP from the environment. One primary biological removal method is biodegradation by microorganisms such as microalgae, fungi, bacteria, and even some insects.

- In bioaccumulation and biodegradation, bacteria, fungi, and microalgae can degrade or accumulate plastic fragments, transforming them into less harmful products or eliminating them. In addition, microalgae can absorb plastic particles due to the generation of antioxidant enzymes, which excrete polymeric substances capable of interacting with MP and NP. However, some microalgae suffer toxic effects from MP, inhibiting the activity of the algae themselves.

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- Genetic engineering also plays a crucial role in the development of biotechnological solutions for eliminating MP and NP. By genetically modifying microorganisms, it is possible to enhance their ability to degrade plastics more efficiently. Recently, researchers have developed genetically modified bacterial strains that produce enzymes specialized in degrading plastic polymers into simpler components, facilitating their removal from the environment.
- Biotechnology has explored methods based on nanomaterials for capturing and removing plastic particles. Nanoparticles functionalized with specific chemical groups can attract and trap MP in water, allowing for their subsequent collection. The objective of using biological material for the degradation of MP and NP in biotechnology is to take advantage of generating extracellular enzymes when microorganisms form colonies on the surface of MP or NP, allowing long chains to be depolymerized and thus generating compounds that the environment can use. In addition, biotechnological processes are environmentally friendly technologies. However, it is critical to create the right conditions of pH, temperature, light intensity, and humidity to promote the growth of these microorganisms.(15,29,30)
- Models for evaluating mitigation strategies. Mathematical models or computer simulations can be used to evaluate the effectiveness of different mitigation strategies. These models can consider factors such as the amount of microplastics generated, the type of microplastics, the environment in which they are released, and climatic conditions. Assessment models are important tools for identifying the most effective mitigation strategies. The following factors should be considered: determining the amount of microplastics generated to recognize the magnitude of the problem; characterizing the type of microplastics, as different types can have different environmental impacts.

These mitigation strategies are just some of the possible solutions. More research is needed to evaluate their effectiveness and to develop new methods that are more efficient and sustainable.(21)

Current regulations

United Nations (UN): Within this organization, the United Nations Environment Programme (UNEP) promotes most studies, guidelines, and recommendations to address the problem and prevent its consequences, mainly in the marine environment. On the one hand, two notable guides from 2015 and 2016 focus on plastic waste, describing the problem and possible approaches for research and environmental policies. On the other hand, two reports published by GESAMP (Joint Group of Experts on the Scientific Aspects of Marine Environmental Protection) on the origin and effects of microplastics in the marine environment are also noteworthy. Such is the level of involvement that a series of workshops are planning to raise awareness of marine pollution caused by accumulated plastics and to share both good practices for plastic waste management and national policies and strategies for reducing the generation of microplastics.

In September 2017, the WHO Regional Office for Europe published a supporting document for the update of the European Directive on the quality of water intended for human consumption, which will replace Directive 98/83/EC. These recommendations do not mention microplastics, although they do mention nanomaterials, indicating that there are no adequate means for their measurement or standardization, and delegating their control to legislation on materials in contact with water.

European Union (EU). Currently, the EU is taking an approach mainly focused on environmental risk and, to a lesser extent, health and consumer protection. In fact, in 2018, the European Commission published the communication: A European Strategy for Plastics in a Circular Economy, which, although it has no regulatory value, did set out the guidelines and priorities to be translated into the environmental policies of each member state. It includes a specific section on microplastics, describing their problems and proposing actions to reduce their impact on the environment, particularly the marine environment. Among other measures, it recommended improving wastewater treatment. It also highlighted the need to monitor microplastics in water for human consumption due to their potential health effects. Partly as a result of the adoption of this strategy, the European Parliament reached an agreement to, among other measures, ban certain single-use plastic products (cutlery, plates, straws, etc.), encourage industry to develop new materials, and raise public awareness of the environmental impact of plastic waste. The European Chemicals Agency (ECHA) also published a monograph in 2018 entitled Note on substance identification and the potential scope of a restriction on uses of microplastics, to assess their inclusion in the Regulation on the registration, evaluation, authorization, and restriction of chemicals (REACH). In addition, it called for scientific evidence to support its recommendations to the European Commission on restricting the use of microplastics. As a result of these actions, in January 2019, it presented a proposal to limit the use of microplastics intentionally added to mixtures of substances used in medicine, cosmetics, hygiene products, paints, coatings, construction materials, and agriculture. This measure aims to reduce microplastics by 400,000 tons over the next 20 years, especially in the terrestrial environment. In fact, some EU member states (France first in July 2016, followed by the UK and Sweden) have already taken the lead in legislating against manufacturing and marketing products containing plastic microbeads.

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Given the free movement of goods between member states, they urged the European Commission to support this proposal through EU legislation. The industry that uses these materials is looking for alternatives, such as minerals and natural salts, to replace them. In 2018, the European Environment Agency (EEA) published its report on the state of European waters and an assessment of status and pressures. Although the press release announcing its publication mentioned concerns about microplastics, these did not appear in the report. The report only mentioned microcontaminants, citing Switzerland's control over them in wastewater as an example. As mentioned above, the draft of the new Directive on the quality of water intended for human consumption, which will replace Directive 98/83/EC, is now available. It is striking that, despite the background, there is no mention of microplastics here either. However, new pollutants such as hormone disruptors, which may come from the degradation of plastics or their raw materials, are included.

Other countries: Countries with significant public health activity, such as the US, Canada, Australia, and Japan, also consider microplastics an emerging risk. Their respective agencies or ministries with environmental responsibilities have published reports and guidelines on the subject, highlighting the present and future impact. In the case of the US, the National Primary Drinking Water Regulations set out the parameters to be monitored in public water systems. Although these do not consider plastic a contaminant, they do take into account vinyl chloride, styrene, and cyanide, all of which are part of waste from the manufacture of plastics. Given that there are contaminants not covered by this Regulation on water for human consumption, the Unregulated Contaminant Monitoring Rule was created, establishing the collection of 30 different pollutants every five years in small supply areas of up to 10,000 inhabitants. The results serve as a source of information and consultation on contaminants for the Environmental Protection Agency (EPA) and other agencies. The EPA developed a line of research called Trashfree Waters, which confirmed the extensive presence of plastics in the marine environment. It stated that approximately 90% of the plastic found in this environment is in the form of microplastics and attributed toxic potential to it due to its persistence and ability to adsorb toxic, persistent, and bioaccumulative substances (TPBs), which are hydrophobic. Canada also legislated against microbeads in cosmetics and cleaning products, considering them an environmental threat. It has banned the sale or import of products containing them. It has set a target of zero plastic waste in microbeads in the medium term, applying the Microbeads Toiletries Regulations. Regarding water for human consumption, the legislation relating to plastics only refers to the manufacturing conditions and composition of packaging and the materials used in tanks or cisterns intended for drinking water. In Australia, the Australian Drinking Water Guidelines, as in the previous cases, only consider plastic as a source of contaminants, not as a contaminant or waste. The Department of Environment and Energy also promoted joint work with industry and central and regional administrations to ensure the voluntary elimination of microbeads in formulating cosmetics and personal hygiene products. In Japan, the Ministry of the Environment treats the problem of marine litter from microplastics as a global awareness issue. Measures were urged to reduce the amount of plastics in the aquatic environment through a harmonized approach to sampling methodology, mode and timing of net use, mapping and distribution of areas on the water surface, and types of polymers to be identified. The environmental impact and the potential impact on health were taken into account.[20]

Argentine legal framework

Growing concern about environmental pollution caused by plastic waste has impacted national legislation.

In 2018, bills reflecting concerns about issues such as marine pollution from plastic waste and post-consumer packaging management were submitted to the committees of the National Congress dealing with environmental and natural resource issues (Albareda 2019, cited in Environmental Report, 2019). Throughout 2019, significant legal progress was made in banning the intentional addition of microplastics in cosmetic and oral hygiene products for dental use.

Current levels of waste generation are caused by population growth, changing consumption patterns, and the availability of increasingly processed foods. The proportion of plastic materials is increasing, and packaging is one of the main waste components. For this reason, Argentina is seeking legislation for packaging management, among other things. The projects are based on the principle of extended producer responsibility: to make manufacturers responsible for their products throughout their life cycle, especially regarding recovery, recycling, or final disposal.[22]

CONCLUSIONS

Current scientific evidence demonstrates that micro- and nanoplastics constitute a growing environmental and health threat, whose complexity requires a multidisciplinary and global approach. Their ubiquitous presence in ecosystems and the human body, combined with their physical and chemical properties, makes them emerging pollutants with potentially profound effects on various organs and systems, including the endocrine, nervous, respiratory, cardiovascular, and reproductive systems. Despite advances in their study, significant knowledge gaps remain, especially regarding toxicity mechanisms, chronic exposure, and interaction with other chemicals.

Given this situation, it is essential to strengthen scientific research, develop more accurate detection technologies, and implement effective mitigation strategies at both the local and international levels. Likewise, robust public policies, updated regulatory frameworks, environmental education, and changes in consumption patterns that reduce plastic production and promote a circular economy are highlighted. Only through a joint commitment between governments, industry, the scientific community, and citizens will it be possible to address this challenge with the urgency and depth it demands, thus protecting human health and the integrity of the planet.

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