ROMAN, Jakub, GONDKO, Daniel, DĘBIEC, Patrycja and PIETRZAK, Nikodem. The Hidden Health Crisis: Microplastics and Their Medical Consequences. Journal of Education, Health and Sport. 2024;72:51690. eISSN 2391-8306.
https://dx.doi.org/10.12775/JEHS.2024.72.51690
https://apcz.umk.pl/JEHS/article/view/51690

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).© The Authors 2024;
This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 25.04.2024. Revised: 10.05.2024. Accepted: 22.05.2024. Published: 03.06.2024.

The Hidden Health Crisis: Microplastics and Their Medical Consequences

Jakub Roman
kuba_roman1998@o2.pl
https://orcid.org/0009-0005-6032-7579
Medical University of Silesia, Faculty of Medical Sciences in Katowice, 18 Medyków St., 40-752 Katowice, Poland

Daniel Gondko
danielwieslaw1998@gmail.com
https://orcid.org/0009-0000-9590-2987
Medical University of Silesia, Faculty of Medical Sciences in Katowice, 18 Medyków St., 40-752 Katowice, Poland

Patrycja Dębiec
patrycjad345@gmail.com
https://orcid.org/0009-0003-0853-2247
Medical University of Silesia, Faculty of Medical Sciences in Katowice, 18 Medyków St., 40-752 Katowice, Poland

Nikodem Pietrzak
nikopi1212@gmail.com
https://orcid.org/0000-0002-6669-9876

Medical University of Silesia, Faculty of Medical Sciences in Katowice, 18 Medyków St., 40-752 Katowice, Poland

Abstract

Introduction and Purpose: Microplastics, ubiquitous environmental contaminants, are increasingly recognized for their potential to impact human health. This review aims to consolidate existing knowledge on the pathways through which microplastics interact with biological systems and to elucidate their health implications.

State of Knowledge: Microplastics are pervasive in various environments, from aquatic to terrestrial ecosystems, and they eventually enter the human body via ingestion, inhalation, or dermal absorption. Studies have suggested that microplastics carry toxic substances, such as heavy metals and organic pollutants, which are known endocrine disruptors and carcinogens. Additionally, the physical presence of microplastics has been linked to inflammation and other negative health outcomes. Research in this field is complex and interdisciplinary, involving toxicology, environmental science, and public health disciplines.

Summary: The presence of microplastics in the human body is concerning, and there is a clear need for further research to understand the extent of health risks associated with chronic exposure. Public health strategies should include both reducing microplastic pollution and strengthening regulations on plastic waste. Meanwhile, medical professionals should consider the potential for microplastic exposure when diagnosing and treating chronic conditions. Future research should aim to clarify the mechanisms of toxicity and establish safe levels of exposure, with a multidisciplinary approach being essential for comprehensive understanding and effective intervention.

Keywords: Microplastics; Enviromental Exposure; Toxicity Tests

Introduction and purpose

Plastic production has seen an immense increase over the past seven decades, rising sharply from a mere two million tonnes in 1950 to an astounding over 450 million tonnes today. This significant growth in plastic manufacturing has had substantial environmental consequences. Inadequately managed plastic waste – not recycled, incinerated, or securely stored in landfills – turns into a serious environmental threat. Each year, between one and two

million tonnes of plastic waste end up in our oceans, adversely affecting wildlife and ecosystem health. To combat this growing issue, better waste management practices are crucial globally, especially in lower-income countries where the majority of oceanic plastic originates. The surge in plastic production has been particularly notable in recent years, with the rate nearly doubling in the last two decades, indicating a nearly 230-fold increase since the 1950s[1].

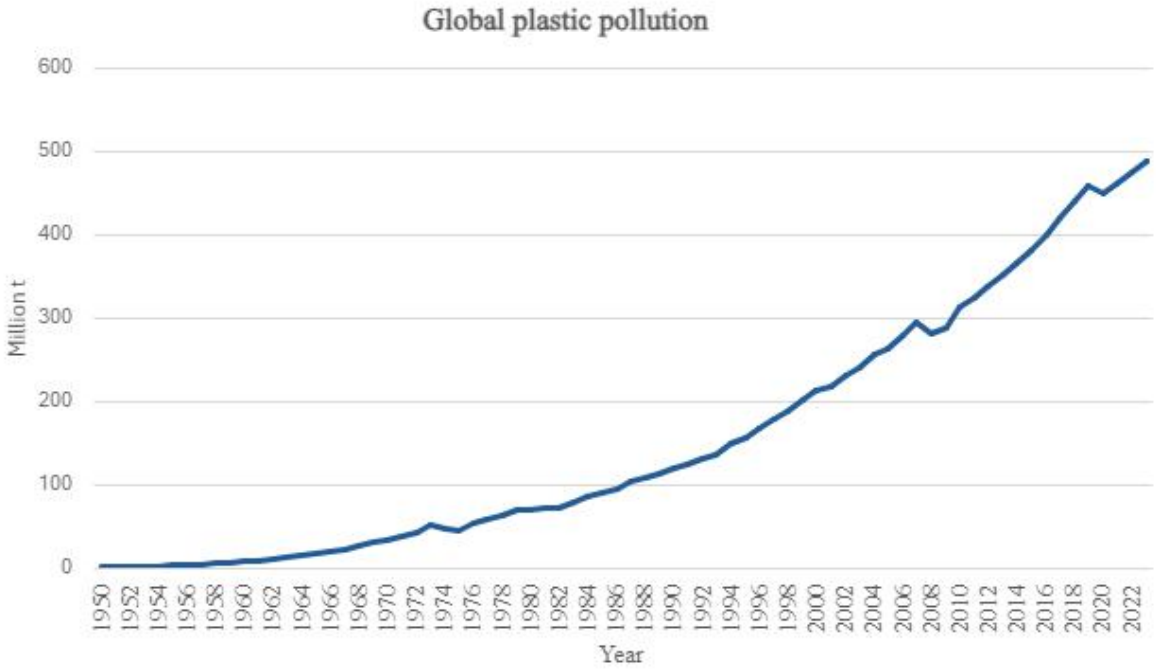

Figure 1. Global plastic pollution over the years

Microplastics are defined as fragments of any type of plastic less than 5 mm length. This definition is according to the U.S. National Oceanic and Atmospheric Administration (NOAA) and the European Chemicals Agency [2] .They are known to cause pollution by entering natural ecosystems from various sources, including cosmetics, clothing, food packaging, and industrial processes. There are two main classifications of microplastics[3]:

Primary Microplastics: These are plastic fragments or particles that are already 5.0 mm in size or less before entering the environment. Examples include microfibers from clothing, microbeads, and plastic pellets (also known as nurdles)[4,5].

Secondary Microplastics: These are formed from the degradation of larger plastic products through natural weathering processes after entering the environment. Sources of secondary microplastics include plastic bottles, fishing nets, plastic bags, and tire wear[3,6].

Microplastics persist in the environment at high levels, especially in aquatic and marine ecosystems, causing significant water pollution. They also accumulate in terrestrial

ecosystems and even in the air. Due to their slow degradation rate (often over hundreds to thousands of years), microplastics have a high probability of being ingested by organisms, accumulating in bodies and tissues, and affecting ecosystems adversely. Regarding the amount of microplastic in the environment, it was estimated in 2014 that there are between 15 and 51 trillion individual pieces of microplastic in the world's oceans, estimated to weigh between 93,000 and 236,000 metric tons[7]. Following the Microbead-Free Waters Act of 2015, there has been a notable shift in the US away from the use of microbeads in toothpaste and other rinse-off cosmetics. However, since the enactment of this legislation, many industries have pivoted towards incorporating FDA-approved "rinse-off" metalized-plastic glitter as their primary abrasive agent. This change, while adhering to the legal framework, raises questions about the environmental and health impacts of these alternatives, considering their composition and potential for contributing to microplastic pollution.

Source of microplastic	**Explanation**
Car tires	Per person, the estimated emission ranges from 0.23 to 4.7 kg annually, with an average of 0.81 kg globally. Emissions from car tires, which can wear down completely, are much higher compared to other microplastic sources such as airplane tires (2% wear), synthetic sports fields (12-50% wear), brakes (8% wear), and road markings (5% wear). A recent study revealed that road markings are less impactful, contributing only 0.1 to 4.3 g per person each year, due to a protective layer of glass beads[8].
Bottled water	A global study on eleven brands of bottled water revealed 93% contained microplastics, with an average of 325 particles per liter, predominantly polypropylene from bottle caps. This widespread contamination, likely originating from packaging and bottling processes, underscores the need for research into the health impacts of micro- and nano-plastics[9].
Single-use plastic products	It's estimated that regular use of plastic cups could lead to the inadvertent consumption of 37,613 to 89,294 microplastic particles annually, emphasizing the need for serious consideration of this contamination source[10].
Cosmetic industry	Many firms have substituted natural scrubbing elements with microplastics, commonly known as "microbeads" or "micro-exfoliates," mainly made from plastics like polyethylene, polypropylene, PET, and nylon. These microplastics are prevalent in

	products like face washes and hand soaps, and typically end up in sewage systems after use[11].
Clothing	The increasing number of scientific studies in the last decade highlights growing concerns about the environmental release of fiber fragments from textiles, with an average European using 25 kg of textiles per person per year and washing their clothes regularly. This frequent washing, estimated at 6 kg twice a month, results in approximately 14,400 mg of fiber fragments released per person annually[12].
Shipping	Commercial shipping has been a major contributor to ocean pollution, with reports showing over 23,000 tons of plastic waste dumped by fleets in 1970 [13] . Shipping continued to be a significant pollutant, adding approximately 6.5 million tons of plastic to the oceans in the early 1990s. Plastic containers have the potential to release tiny plastic particles and nanoparticles into the food and drinks they hold[14].

Table 1. The main sources of microplastic in the enviroment.

Influence of microplastics on human health

The influence of microplastics on human health is an area of growing concern and active research. Research findings indicate that microplastics can be present in human organs such as the liver, blood, heart, placenta, breast milk, sputum, semen, testis, and urine. This widespread presence raises concerns about their potential impacts on human health, particularly regarding their possible toxicological effects on various physiological processes within these organs. Microplastics can enter and accumulate in human organs and bodily fluids through various pathways, including invasive medical procedures which may allow direct access of microplastics to the bloodstream and tissues. Understanding these pathways is crucial for developing effective mitigation strategies and preserving human health and the environment. Additionally, the persistence of microplastics in the environment and their diverse composition challenge traditional risk-based regulatory frameworks. This complexity necessitates a collaborative approach between different sectors to address environmental and health impacts. There's a pressing need for integrated research efforts to understand the pervasive effects of microplastics, not only on marine life but also on terrestrial ecosystems, particularly soil function [15,16] . All this has prompted us to gather the latest scientific information on microplastics and their impact on health, as well as a closer look at the mechanisms through which microplastics enter the human body.

Materials and Methods

A literature review was conducted following the PRISMA guidelines[17] on February 1, 2024, utilizing the online database PUBMED. The research query was formulated as: "Plastic Particles AND Human Health (i) OR Microplastic AND Human Health (ii) OR Nanoplastic AND Human Health (iii)". One thousand three hundred ninety (n =1390) results from PUBMED were obtained. After the removal of five hundred sixty three (n= 563) duplicates, eight hundred twenty seven (n = 827) records were selected for further analysis. Two independent authors conducted the initial screening of these records. Inclusion criteria were studies published in either Polish or English (a), focusing on the influence of microplastics on human health (b). Studies excluded were those older than 2 years (c), conducted in the form of conference reports, or letters to the editor (d). Following the selection process, sixteen (n = 16) reports that met these criteria were included for review (Figure 2).

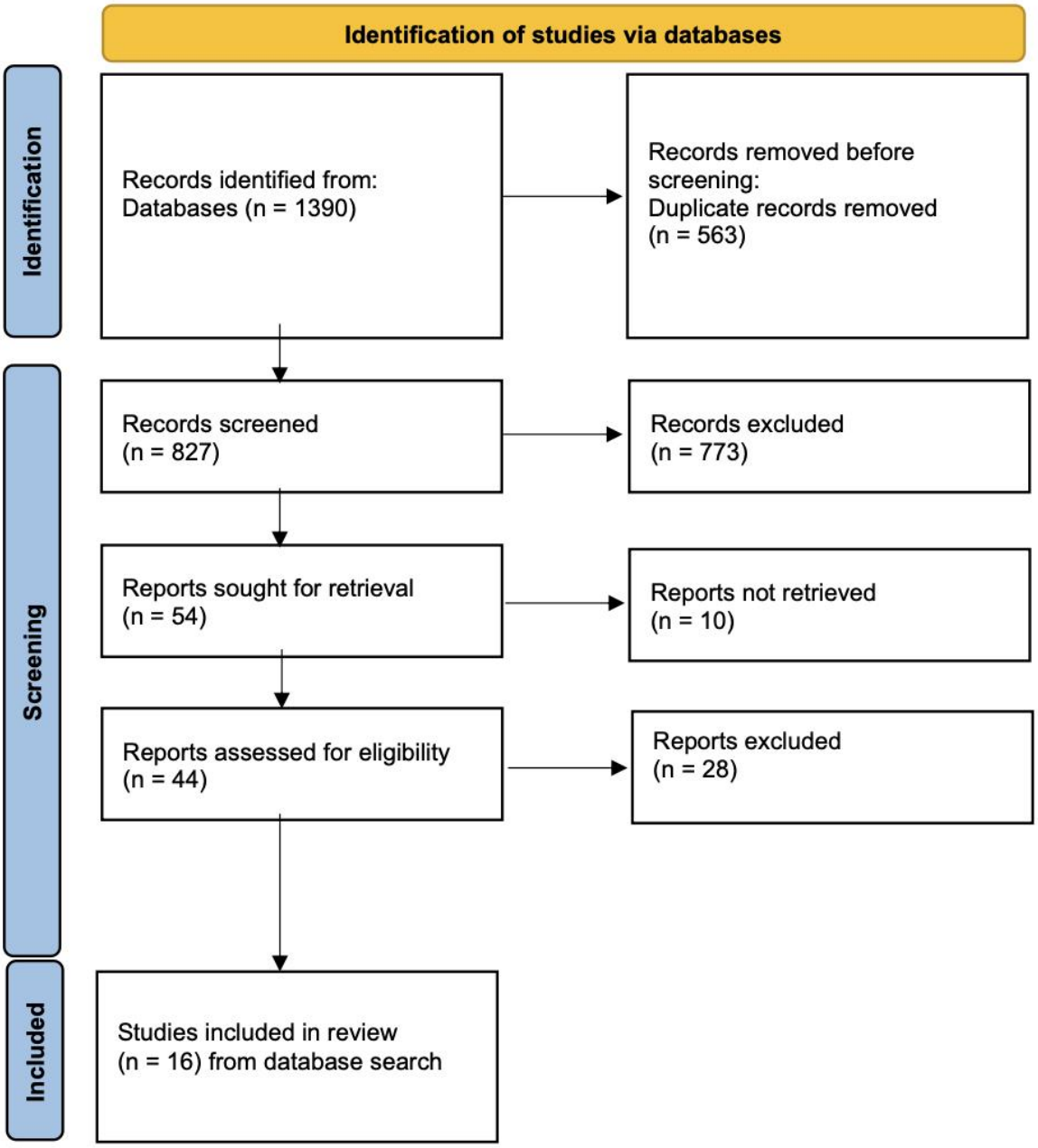

Figure 2. “PRISMA flow-chart” - Identifcation of studies via databases.

State of Knowledge

Jianli Yin et al. investigated the impact of microplastics (MPs) and nanoplastics (NPs) on liver health. Their research highlighted that microplastic can accumulate in the liver, causing morphological changes and potential harm to human health. The mechanism of toxicity includes oxidative stress and inflammation in liver cells, but what’s important, researchers took notice that MPs and NPs not only induce liver damage via oxidative stress and inflammatory processes but also disrupt liver function by altering lipid metabolism. Furthermore, the impact of MPs on hepatic lipid metabolism exceeded that of NPs. Metabolic

analysis of zebrafish exposed to polystyrene micro- and nanoplastics revealed that MPs and NPs prompted alterations in 21 and 11 metabolites, respectively[18].

In article "Is There Evidence of Health Risks From Exposure to Micro- and Nanoplastics in Foods?" Elena Molina and Sara Benedé examine the health implications of MPs and NPs in human diets, with a particular focus on food allergies. The authors have shown than Nanoplastics may inflict physical damage on the intestinal mucosa simply through their presence. Their ability to obstruct the intestine or cause tissue abrasion highlights their potential toxicity. The intestinal epithelium serves as the primary defense against food allergens, with its barrier function largely dependent on tight junctions, which include zonula occludens 1–3, occludin, and claudins 1–5, 20. Disruption of these junctions could enhance trans-epithelial allergen transport. Additionally, in response to stress or injury, intestinal epithelial cells release pro-inflammatory cytokines such as IL-33, IL-25, and TSLP. These cytokines activate group 2 innate lymphoid cells, leading to the production of IL-4, IL-5, and IL-13, which not only prompt dendritic cells to encourage a Th2 phenotype in T cells but also directly stimulate adaptive Th2 immune responses and potential allergic reactions[19]. The topic of the presence of microplastic in food and its impact on the digestive system was also explored by Marlene Schwarzfischer and Gerhard Rogler, in "The Intestinal Barrier-Shielding the Body from Nano- and Microparticles in Our Diet," The paper discusses the specific risks associated with titanium dioxide (TiO2) and plastic microparticles in the diet and the importance of the intestinal barrier in protecting against these particles. Research has demonstrated that titanium dioxide (TiO2) nanoparticles are able to traverse the ileum epithelium and Peyer's patches, leading to epithelial deterioration and sustained damage [20].

The article "The potential toxicity of microplastics on human health" by Zhao B and colleagues focuses on the health risks associated with microplastics (MPs). After absorption, MPs can distribute throughout the body, affecting various organs and tissues. The interesting finding is that MPs accumulate primarily in the lungs, heart, liver, and intestines. The digestive tract is a key site for MP accumulation and toxicity[21].

In "The potential impacts of micro-and-nano plastics on various organ systems in humans," authors discusses the routes through which humans are exposed to MPs and their potential health effects, including oxidative stress, inflammation, and immune dysfunction. It highlights widespread plastic production, fragmentation into various sizes, and human exposure through diet, inhalation, and skin contact. Special attention is given to the presence of MPs in seafood and their potential to enter the food chain. The article also examines the

process by which MPs interact with and enter cells, with a focus on endocytosis and the effect of particle properties on cellular interactions. The translocation and distribution of MPs within organisms are discussed, particularly their accumulation in human tissues and organs[22]. In the article "Microplastics in dermatology: Potential effects on skin homeostasis, Miguel Aristizabal et al. discuss the concerns regarding MPs and NPs in dermatology. Evidence suggests that these particles can lead to skin alterations and disrupt physiological functions, partly due to their ability to penetrate the skin barrier. The authors conclude that while the exact effects of MPs and NPs on skin health are still under investigation, their presence is a significant concern[23].

In "Impact of plastic-related compounds on the gene expression signature of HepG2 cells transfected with CYP3A4," the authors focus on the interactions of these materials with key enzymes in the metabolism of xenobiotics, particularly cytochrome P450 monooxygenases (CYPs), with a spotlight on CYP3A4, a critical enzyme expressed in liver cells. The research process involved virtual compound screening and molecular docking of over 1000 plastic-related compounds to identify those that interact with CYP3A4. Following this, RNA-sequencing was used to analyze the transcriptome-wide gene expression levels affected by these compounds in HepG2 cells overexpressing CYP3A4. The study zeroes in on three candidate molecules, examining their binding affinity, cytotoxic effects, and interactions with metabolic pathways. Results reveal that these plastic-related compounds can disrupt crucial biological processes. They suppress pathways related to mitosis and DNA replication, confirmed by cell cycle analysis and single-cell gel electrophoresis. Additionally, mis-regulated metabolic and inflammation-related pathways were identified, suggesting potential hepatotoxicity[24]. In the article "The potential effects of microplastics on human health: What is known and what is unknown," authors Kirsty Blackburn and Dannielle Green discuss the widespread contamination of microplastics in various environments and their potential impact on human health. Microplastics are found in water, sediments, organisms, and the atmosphere, and while their effects on animal and plant life have been extensively studied, the impact on human health remains largely unknown. The study explores human exposure to microplastics through the ingestion of food and drink, and inhalation, and uses existing literature on wildlife to infer potential human health impacts. The review categorizes the effects of microplastics on human health into chemical, physical, and biological effects. This includes toxic additives from plastics like phthalates and Bisphenol-A, secondary toxins from microplastics adsorbing pollutants like Persistent Organic Pollutants (POPs), and physical effects through inhalation

of airborne microplastics and ingestion. Chemically, additives from plastics can cause toxicity and endocrine disruption. For physical effects, inhalation of fibrous microplastics from synthetic textiles is a concern, as they could cause inflammation or respiratory issues. In terms of ingestion, the presence of microplastics in food items like salt, water, and seafood raises concerns about internal exposure and its health effects. Overall, while the review acknowledges that concrete evidence linking microplastic consumption to adverse human health effects is currently lacking, preliminary studies and extrapolations from wildlife research suggest potential immune and stress responses, reproductive toxicity, and developmental issues. The authors emphasize the need for more research to understand the implications of this contaminant in our environment and its effects on human health[25].

In the article "Polystyrene microplastics induce hepatotoxicity and disrupt lipid metabolism in the liver organoids," by Cheng W. and team, focused on the health effects of MPs, especially in relation to human liver health. The study emphasizes that while some MPs exit the body via the gastrointestinal system, others accumulate in organs like the liver, causing oxidative stress and inflammation. The researchers point out the variability in MPs' effects depending on their physical and chemical properties. Specifically, they focus on how MPs can induce oxidative stress and inflammation across multiple species, with effects observed at both cytotoxic and non-cytotoxic concentrations. One of the key contributions of this study is its focus on the liver as a potential target organ for MPs. The researchers utilized liver organoids (LOs) derived from human pluripotent stem cells (hPSC) to mimic human liver response to MPs. These LOs serve as an advanced model for the human liver, providing a more accurate response to xenobiotics in terms of hepatic functions. By employing LOs, the study aimed to overcome interspecies differences that often limit the direct applicability of animal study results to humans. The findings revealed that polystyrene MPs disrupt metabolic enzymes and lipid metabolism markers in LOs, even at low dosages. This disturbance led to alterations in ATP production, increased reactive oxygen species (ROS) generation, oxidative stress, and inflammation response, emphasizing the lipotoxic effects of MPs [26] .In "Microplastics are detected in human gallstones and have the ability to form large cholesterol-microplastic heteroaggregates," Zhang D. and colleagues address the increasing concern over microplastic pollution and its potential impact on human health. The study specifically investigates the presence of microplastics in human gallstones and their role in gallstone formation. Study take place at Changhai Hospital between July and October 2020. The study sample include 16 people (8 man, 8 women). The average age was 55 years old. The study

mentions that adults may consume more than 5 grams of plastic each week, and various types of plastics have been detected in human stool. Focusing on gallstone disease, a significant gastrointestinal issue, the paper explores the formation of gallstones, particularly cholesterol gallstones, and the increasing prevalence of this disease. Despite knowing the symptoms and risks associated with gallstones, the exact pathogenesis, especially in young patients, remains unclear. The core of the study involves analyzing gallstones from patients to detect microplastics. The researchers identified several types of microplastics in the gallstones, with polystyrene being the most prevalent. This finding raises questions about the potential role of microplastics in the formation of gallstones. This study presents the novel idea that microplastics in gallstones might be contributing to gallstone lithiasis by forming cholesterol-microplastic heteroaggregates. The study sheds light on a new aspect of microplastic pollution, suggesting that microplastics may play a role in the formation of human gallstones[27].

In the article "Interactions between inhalable aged microplastics and lung surfactant: Potential pulmonary health risks," authored by Cao Y. et al. the focus is on the relationship between MPs and respiratory health, particularly examining how inhalation of aged MPs affects lung surfactant and the potential risks to pulmonary health. The research team conducted a thorough analysis of the MPs to determine their size and relevance to human inhalation. Understanding that MPs smaller than 5 μm can bypass immune clearance mechanisms and reach deep into the respiratory tract, the study closely examines the size of the MPs used in the experiments. The conclusions drawn from the study are significant. The researchers found that the presence of MPs, particularly aged ones, altered the interfacial properties of lung surfactant, including surface tension and foaming ability. This alteration is attributed to the adsorption of active components of lung surfactant (phospholipids and proteins) onto the MPs' surfaces. These interactions suggest a potential risk for pulmonary exposure to aged MPs, emphasizing the need for further investigation into the health implications of microplastic inhalation[28].

In "Molecular effects of polystyrene nanoplastics on human neural stem cells," Raquel Martin-Folgar and colleagues investigate the impact of nanoplastics on human health, focusing on their effects on neural stem cells. The research employs human neural stem cell line (hNS1) as a model to study the effects of exposure to 30 nm polystyrene nanoplastics. Over four days of exposure, the study identifies several molecular changes in the cells, including oxidative stress, cellular stress, DNA damage, alterations in inflammatory response, and apoptosis, which could potentially lead to tissue damage and neurodevelopmental

diseases. This approach allows for an accurate assessment of the effects of nanoplastics on human neural stem cells. The researchers found that nanoplastics affected gene expression in a concentration-dependent manner, with some genes being upregulated and others downregulated. They particularly observed significant changes in the expression of stress response genes, including hsp27/hspB1, hsp70/hspA5, and hsp90α, after exposure to nanoplastics[29].

In "Dietary exposure to polystyrene microplastics exacerbates liver damage in fulminant hepatic failure via ROS production and neutrophil extracellular trap formation," researchers investigate the interaction of microplastics with the human liver, specifically in the context of fulminant hepatic failure. The study explores how continuous exposure to risk factors like microplastics can contribute to acute liver injury or failure, which is already a significant health concern. One of the key findings is that polystyrene microplastics can bypass biological barriers, causing metabolic disorders and injury in multiple organs. The study conducted on Caco-2 cells showed that increased concentration and light irradiation of polystyrene microplastics reduced cell survival rates and destroyed cell membrane integrity. Microplastics can penetrate the intestinal barrier and accumulate in the liver, leading to oxidative stress and inflammation. In this study, an acute liver injury mouse model was developed to simulate fulminant hepatic failure. The model revealed that pre-exposure to polystyrene microplastics aggravates liver failure by increasing lipid peroxidation and reducing antioxidant capacity. Furthermore, the study examined the damage to the mouse immune system by conducting histological analysis, immunofluorescence, and in vitro cultures of mouse immune cells[30].

In "Hepatotoxic of polystyrene microplastics in aged mice: Focus on the role of gastrointestinal transformation and AMPK/FoxO pathway," authored by Xie P. et al., the study examines the hepatotoxic effects of MPs, particularly in aged organisms. The research investigated the FoxO signaling pathway in the liver by measuring the expression levels of FoxO1, FoxO3a, pFoxO1, and pFoxO3a. While there were no significant changes in the expression of FoxO1 and FoxO3a in aged mice exposed to microplastics (MPs), notable increases in phosphorylated FoxO1 and FoxO3a were observed in the M9 group compared to the control (M0). Immunohistochemical analysis indicated localization of the cell cycle regulator p21 in the nucleus, with significant upregulation in the M9 group. Additionally, with increasing doses of polystyrene microplastics, there was a marked increase in superoxide dismutase and catalase activities, particularly in the M6, M9, and M12 groups. The levels of

thiobarbituric acid reactive substance remained similar to the control in the M3 and M6 groups but rose significantly in the M9 and M12 groups, suggesting escalated lipid peroxidation. Moreover, the expression of 8-OHdG, a marker for DNA oxidative damage, showed

a progressively higher activity in the experimental groups, with the most substantial damage in the M12 group. The complement component C3 showed decreased formation across all exposed groups, while C4 levels remained unchanged compared to the control. The pro-inflammatory cytokine IL-6 was significantly elevated only in the M12 group, and IL-8 levels were notably higher in the M3, M9, and M12 groups, indicating an increasing trend in inflammatory response [31] . The study entitled "Polystyrene micro- and nanoplastics induce gastric toxicity through ROS mediated oxidative stress and P62/Keap1/Nrf2 pathway," scientists focused particularly on the gastrointestinal tract, a primary route for human exposure to MPs through food and water. Exposure to 50 nm and 250 nm microplastics at concentrations of 0.1 mg and 2.5 mg significantly altered the gastric environment, evidenced by an increase in the pH of gastric juice compared to the control group ($p < 0.05$). Additionally, both the concentration of free acids and total acidity in the gastric juice were significantly reduced following exposure to polystyrene microplastics ($p < 0.05$). An ELISA assay revealed changes in gastric mucosa-related factors; gastrin levels were decreased in the groups exposed to 0.5 mg and 2.5 mg of 50 nm MPs compared to the control ($p < 0.05$), although pepsin levels remained unchanged across most MPs groups. However, in the groups exposed to 0.5 mg and 2.5 mg of 250 nm MPs, pepsin levels were significantly lower compared to the 0.1 mg 250 nm MPs group ($p < 0.05$).

Further investigation into mucosal integrity using PAS staining indicated a dose-dependent reduction in the area of purplish-red labeled gastric tissue in both 50 nm and 250 nm MPs groups when compared to the normal control ($P < 0.001$), suggesting a decrease in mucin content. This comprehensive analysis highlights significant disruptions in gastric chemistry and mucosal integrity due to microplastic exposure, with potential implications for gastrointestinal function and health. Moreover, researchers also investigated the expression levels of tight junction (TJ) proteins occludin, ZO-1, and claudin-4 and adherent junction proteins E-cadherin and β-catenin using immunohistochemical staining. The results revealed significant reductions in the levels of these junctional proteins in groups exposed to 50 nm and 250 nm polystyrene microplastics compared to controls, with the changes being statistically significant ($p < 0.001$). This decrease was noted in both TJ and AJ proteins and

occurred in
a dose-dependent manner for occludin, claudin-4, and β-catenin. The findings suggest that MPs may compromise the structural integrity of the gastric barrier, potentially impacting its functionality[32].

In the study "Polystyrene micro and nano-particles induce metabolic rewiring in normal human colon cells: A risk factor for human health," authored by Marcella Bonanomi et al. the impact of MPs and NPs on human health is rigorously examined. To assess the metabolic effects of polystyrene NPs and MPs on human colon CCD-18Co cells, researchers conducted a comprehensive metabolomic analysis using mass spectrometry. They utilized azoxymethane (AOM), a known carcinogen for inducing colon cancer in rodent models, to explore the carcinogenic potential of these particles. Hierarchical clustering revealed that the metabolic profile of cells exposed to NPs was similar to those treated with 10 μg/ml AOM after 48 hours, distinct from controls and other test groups. The analysis suggested significant involvement of metabolic pathways such as the Warburg effect, amino acid metabolism, and redox processes, with 47 key metabolites shared between NPs exposure and AOM treatment. Further pathway analysis indicated early metabolic shifts involving the Warburg effect, glutamate metabolism, and glutathione metabolism under NPs and AOM conditions. Enhanced levels of glycolysis-related metabolites, the tricarboxylic acid (TCA) cycle, and the pentose phosphate pathway were observed, alongside a notable decrease in the GSH/GSSG ratio, indicating oxidative stress. Additionally, patterns of increased glutamine metabolism were consistent across NP, MP, and AOM treatments. In-depth metabolic tracing using isotopically labeled [U-13C6] glucose and [U-13C5] glutamine demonstrated elevated oxidation of glucose to lactate across all treatments. Increased production of metabolites involved in antioxidant pathways, such as 6-phosphogluconolactone and glutathione from glucose and glutamine respectively, were detected particularly in NP-treated cells. This indicates a physiological response to oxidative stress. Elevated labeling of TCA cycle intermediates and increased levels of TCA metabolites derived from glutamine under short-term exposure were also noted. These findings underscore a metabolic adaptation to stress akin to changes observed during tumorigenesis, suggesting that brief exposure to NPs could induce significant metabolic rewiring in human colon cells[33].

In the study "Chronic exposure to polystyrene microplastics increased the chemosensitivity of normal human liver cells via ABC transporter inhibition," authored by Chen Z. et al, the researchers explore the health implications of microplastic pollution,

focusing specifically on the effects of polystyrene microplastics on the human liver. The functionality of ABC transporters, which are crucial for hepatic detoxification, was examined to understand how disruptions in their activity might lead to increased intracellular xenobiotics and heightened chemosensitivity. Using the fluorescent probe CAM, researchers assessed the efflux activity of ABC transporters in THLE-2 cells treated with polystyrene microplastics. CAM, metabolized into calcein within cells, highlights transporter activity as calcein is not expelled by ABC transporters and remains trapped in the cytoplasm. Increased fluorescence, observed using MK571 as a positive control for inhibiting ABC transporter activity, indicated that chronic exposure to PS MPs, particularly the 0.1 μm particles, significantly decreased the efflux of xenobiotics. Further investigations using arsenic (As), a known substrate of ABC transporters, as a xenobiotic pollutant, revealed that MPs exposure significantly elevated ROS generation in response to arsenic, suggesting an increase in the cytotoxic potential of arsenic due to the inhibited transporter activity. This finding is consistent with previous research where various nanomaterials at low concentrations acted as chemosensitizers by blocking ABC transporter activity in different cell types. Interestingly, the concentration of MPs causing chemosensitivity in human colon adenocarcinoma Caco-2 cells was 100 times higher than that used in this study, highlighting the potential cell line and exposure duration dependencies in response to MPs. This disparity suggests that using normal cell lines may provide a more sensitive and predictive model for assessing the chronic toxicity of microplastics and other particulate substances. Moreover, the observed cytotoxicity changes were more pronounced with the 0.1 μm MPs compared to the 1 μm MPs at environmentally relevant concentrations, indicating that smaller microplastics may pose greater health risks, potentially leading to more severe biological effects such as oxidative stress, DNA damage, reproductive toxicity, and metabolic disorders. These findings underscore the importance of understanding particle size impacts on health, particularly for nanosized microplastics[34].

Summary

The comprehensive review of the literature on the influence of microplastics on human health reveals significant and varied impacts across multiple organ systems, underscoring the pervasive nature of microplastic contamination and its potential to interfere with fundamental biological processes, often in ways that could exacerbate existing health conditions or contribute to new ones. The key findings of the review are included in the Table 2.

Conclusion	Explanation
Accumulation and organ impact	Microplastics and nanoplastics are found to accumulate in critical organs such as the liver, lungs, heart, and intestines. This accumulation is associated with morphological changes and functional impairments, highlighting a direct toxicological threat to organ health
Metabolic and biochemical disruptions	Exposure to various sizes of MPs and NPs disrupts metabolic pathways and biochemical processes. Notably, alterations in the Warburg effect, glutamate metabolism, and the pentose phosphate pathway indicate profound metabolic rewiring reminiscent of tumorigenic processes. These disruptions are often dose-dependent and exacerbated by smaller particle sizes.
Gastrointestinal and Hepatic Effects	MPs compromise the integrity of the gastrointestinal barrier and induce hepatotoxicity. Studies illustrate how MPs interfere with tight and adherent junction proteins in the gut, facilitate the translocation of allergens, and disrupt liver lipid metabolism, leading to increased oxidative stress and inflammation.
Immunological and inflammatory responses	Chronic exposure to MPs triggers pro-inflammatory cytokine release and modifies immune responses, which could potentially lead to heightened susceptibility to allergies, immune disorders, and other inflammatory conditions.
Endocrine and reproductive implications	The presence of MPs in the human body disrupts hormonal pathways and reproductive functions, suggesting potential endocrine-disrupting properties that could impact human fertility and hormonal health.
Environmental and size-specific concerns	The review highlights that environmental exposure levels and particle sizes critically influence the health impacts of MPs and NPs. Smaller particles, such as nanoplastics, exhibit more severe effects due to their greater reactivity and ability to penetrate biological barriers more effectively.

Table 2. The key conclusions of the review

The existing body of research provides substantial evidence that microplastics pose a multifaceted threat to human health. However, significant gaps remain in our understanding of the long-term consequences and the full spectrum of health effects. The findings urge continued research to fully elucidate these impacts and guide public health interventions. It is also imperative to develop strategies to mitigate exposure and reduce the production of plastic pollutants to protect human health and the environment.

Disclosures

Author's contribution:

Conceptualization- Jakub Roman

Formal analysis- Jakub Roman, Nikodem Pietrzak, Daniel Gondko

Investigation- Patrycja Dębiec, Daniel Gondko

Writing-rough preparation- Patrycja Dębiec, Nikodem Pietrzak

Writing-review and editing- Jakub Roman, Patrycja Dębiec, Nikodem Pietrzak

Visualization- Jakub Roman, Daniel Gondko

All authors have read and agreed with the published version of the manuscript.

Conflict of interest: The author declare no conflict of interest.

Funding statement: No external funding was received to perform this review

Statement of institutional review committee: not applicable

Statement of informed consent: not applicable

Statement of data availability: not applicable

References

1. Global Plastics Outlook. OECD; 2022. doi:10.1787/de747aef-en
2. Arthur C, Baker J, Bamford H (eds.). *Proceedings of the International Research Workshop on the Occurrence, Effects and Fate of Microplastic Marine Debris*.; 2009.
3. Ghosh S, Sinha JK, Ghosh S, Vashisth K, Han S, Bhaskar R. Microplastics as an Emerging Threat to the Global Environment and Human Health. *Sustainability*. 2023;15(14):10821. doi:10.3390/su151410821
4. Karbalaei S, Hanachi P, Walker TR, Cole M. Occurrence, sources, human health impacts and mitigation of microplastic pollution. *Environmental Science and Pollution Research*. 2018;25(36):36046-36063. doi:10.1007/s11356-018-3508-7
5. Cole M, Lindeque P, Halsband C, Galloway TS. Microplastics as contaminants in the marine environment: A review. *Mar Pollut Bull*. 2011;62(12):2588-2597. doi:10.1016/j.marpolbul.2011.09.025
6. Conkle JL, Báez Del Valle CD, Turner JW. Are We Underestimating Microplastic Contamination in Aquatic Environments? *Environ Manage*. 2018;61(1):1-8. doi:10.1007/s00267-017-0947-8
7. Ioakeimidis C, Fotopoulou KN, Karapanagioti HK, et al. The degradation potential of PET bottles in the marine environment: An ATR-FTIR based approach. *Sci Rep*. 2016;6(1):23501. doi:10.1038/srep23501

8. Burghardt TE, Pashkevich A, Babić D, Mosböck H, Babić D, Żakowska L. Microplastics and road markings: the role of glass beads and loss estimation. *Transp Res D Transp Environ*. 2022;102:103123. doi:10.1016/j.trd.2021.103123
9. Mason SA, Welch VG, Neratko J. Synthetic Polymer Contamination in Bottled Water. *Front Chem*. 2018;6. doi:10.3389/fchem.2018.00407
10. Zhou G, Wu Q, Tang P, et al. How many microplastics do we ingest when using disposable drink cups? *J Hazard Mater*. 2023;441:129982. doi:10.1016/j.jhazmat.2022.129982
11. Anderson AG, Grose J, Pahl S, Thompson RC, Wyles KJ. Microplastics in personal care products: Exploring perceptions of environmentalists, beauticians and students. *Mar Pollut Bull*. 2016;113(1-2):454-460. doi:10.1016/j.marpolbul.2016.10.048
12. De Falco F, Di Pace E, Cocca M, Avella M. The contribution of washing processes of synthetic clothes to microplastic pollution. *Sci Rep*. 2019;9(1):6633. doi:10.1038/s41598-019-43023-x
13. Derraik JGB. The pollution of the marine environment by plastic debris: a review. *Mar Pollut Bull*. 2002;44(9):842-852. doi:10.1016/S0025-326X(02)00220-5
14. Hussain KA, Romanova S, Okur I, et al. Assessing the Release of Microplastics and Nanoplastics from Plastic Containers and Reusable Food Pouches: Implications for Human Health. *Environ Sci Technol*. 2023;57(26):9782-9792. doi:10.1021/acs.est.3c01942
15. Gross L, Enck J. Confronting plastic pollution to protect environmental and public health. *PLoS Biol*. 2021;19(3):e3001131. doi:10.1371/journal.pbio.3001131
16. Enyoh CE, Devi A, Kadono H, Wang Q, Rabin MH. The Plastic Within: Microplastics Invading Human Organs and Bodily Fluids Systems. *Environments*. 2023;10(11):194. doi:10.3390/environments10110194
17. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. Published online March 29, 2021:n71. doi:10.1136/bmj.n71
18. Yin J, Ju Y, Qian H, et al. Nanoplastics and Microplastics May Be Damaging Our Livers. *Toxics*. 2022;10(10):586. doi:10.3390/toxics10100586
19. Molina E, Benedé S. Is There Evidence of Health Risks From Exposure to Micro- and Nanoplastics in Foods? *Front Nutr*. 2022;9. doi:10.3389/fnut.2022.910094
20. Schwarzfischer M, Rogler G. The Intestinal Barrier—Shielding the Body from Nano- and Microparticles in Our Diet. *Metabolites*. 2022;12(3):223. doi:10.3390/metabo12030223

21. Zhao B, Rehati P, Yang Z, Cai Z, Guo C, Li Y. The potential toxicity of microplastics on human health. *Science of The Total Environment*. 2024;912:168946. doi:10.1016/j.scitotenv.2023.168946
22. Ali N, Katsouli J, Marczylo EL, Gant TW, Wright S, Bernardino de la Serna J. The potential impacts of micro-and-nano plastics on various organ systems in humans. *EBioMedicine*. 2024;99:104901. doi:10.1016/j.ebiom.2023.104901
23. Aristizabal M, Jiménez-Orrego K V., Caicedo-León MD, et al. Microplastics in dermatology: Potential effects on skin homeostasis. *J Cosmet Dermatol*. 2024;23(3):766-772. doi:10.1111/jocd.16167
24. Rosellini M, Omer EA, Schulze A, et al. Impact of plastic-related compounds on the gene expression signature of HepG2 cells transfected with CYP3A4. *Arch Toxicol*. 2024;98(2):525-536. doi:10.1007/s00204-023-03648-4
25. Blackburn K, Green D. The potential effects of microplastics on human health: What is known and what is unknown. *Ambio*. 2022;51(3):518-530. doi:10.1007/s13280-021-01589-9
26. Cheng W, Li X, Zhou Y, et al. Polystyrene microplastics induce hepatotoxicity and disrupt lipid metabolism in the liver organoids. *Science of The Total Environment*. 2022;806:150328. doi:10.1016/j.scitotenv.2021.150328
27. Zhang D, Wu C, Liu Y, et al. Microplastics are detected in human gallstones and have the ability to form large cholesterol-microplastic heteroaggregates. *J Hazard Mater*. 2024;467:133631. doi:10.1016/j.jhazmat.2024.133631
28. Cao Y, Zhao Q, Jiang F, et al. Interactions between inhalable aged microplastics and lung surfactant: Potential pulmonary health risks. *Environ Res*. 2024;245:117803. doi:10.1016/j.envres.2023.117803
29. Martin-Folgar R, González-Caballero MC, Torres-Ruiz M, et al. Molecular effects of polystyrene nanoplastics on human neural stem cells. *PLoS One*. 2024;19(1):e0295816. doi:10.1371/journal.pone.0295816
30. Ma S, Xiao Y, Zhang X, et al. Dietary exposure to polystyrene microplastics exacerbates liver damage in fulminant hepatic failure via ROS production and neutrophil extracellular trap formation. *Science of The Total Environment*. 2024;907:167403. doi:10.1016/j.scitotenv.2023.167403
31. Xie P, Li P, Zhu X, et al. Hepatotoxic of polystyrene microplastics in aged mice: Focus on the role of gastrointestinal transformation and AMPK/FoxO pathway. *Science of The Total Environment*. 2024;917:170471. doi:10.1016/j.scitotenv.2024.170471

32. Sun R, Liu M, Xiong F, et al. Polystyrene micro- and nanoplastics induce gastric toxicity through ROS mediated oxidative stress and P62/Keap1/Nrf2 pathway. *Science of The Total Environment*. 2024;912:169228. doi:10.1016/j.scitotenv.2023.169228
33. Bonanomi M, Salmistraro N, Porro D, Pinsino A, Colangelo AM, Gaglio D. Polystyrene micro and nano-particles induce metabolic rewiring in normal human colon cells: A risk factor for human health. *Chemosphere*. 2022;303:134947. doi:10.1016/j.chemosphere.2022.134947
34. Chen Z, Li Y, Xia H, et al. Chronic exposure to polystyrene microplastics increased the chemosensitivity of normal human liver cells via ABC transporter inhibition. *Science of The Total Environment*. 2024;912:169050. doi:10.1016/j.scitotenv.2023.169050