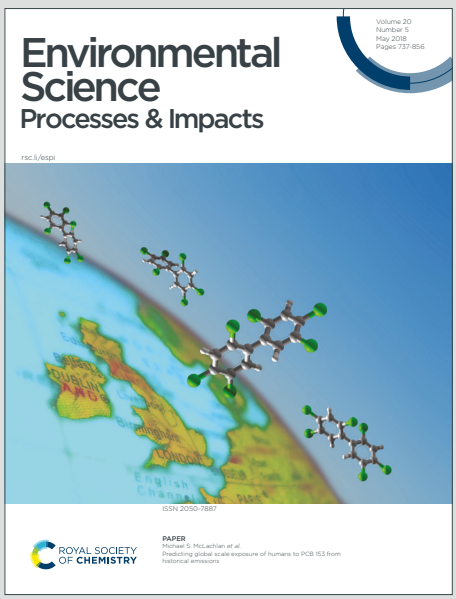
Environmental Science
Processes & Impacts

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: M. M. Joseph, J. B. Nair and A. M. Joseph, *Environ. Sci.: Processes Impacts*, 2025, DOI: 10.1039/D5EM00232J.



ROYAL SOCIETY OF CHEMISTRY

rsc.li/espi

View Article Online
DOI: 10.1039/D5EM00232J

Environmental Significance Statement

Microplastic (MP) pollution has emerged as a significant environmental issue with far-reaching implications for human health and ecological balance. This review addresses the dual nature of MPs as environmental contaminants and potential nanoscale entities that influence human biology. This article examines MPs' environmental persistence, accumulation in the biota, and potential to participate in carcinogenesis. MP properties at the nanoscale make them amenable to accumulation within the environment and living cells as well as binding to biomolecules, sparking anxiety over participation in oxidative stress, inflammation, genotoxicity, and endocrine disruption, the very processes being essential to tumour growth and expansion. This review encapsulates current knowledge, points out key areas for further research, and recommends avenues for the future investigation of the long-term implications of MP exposure.

Microscopic Menace: Exploring the Link Between Microplastics and Cancer Pathogenesis

Manu M. Joseph [1], Jyothi B. Nair [2], Anu Mary Joseph [3]*

[1] Department of Life Sciences, CHRIST University, Bengaluru - 560029, Karnataka, India.
[2] Leibniz Institute of Photonic Technology, Albert-Einstein-Straße 9, Jena 07745, Germany
[3] Department of Chemistry, Newman College, Thodupuzha 685585, Kerala, India.

Corresponding Author

Dr. Manu M. Joseph
Assistant Professor
Department of Life Sciences
CHRIST University
Bengaluru – 560029
Karnataka, India.
Email: manu.joseph@christuniversity.in/ manumjoseph2000@gmail.com
Orcid ID: 0000-0003-3647-7620

Abstract

Microplastics represent a group of emerging environmental contaminants widely recognized for their potential impacts on human health, particularly concerning the pathogenesis of cancer. Generally defined as plastic particles between 1 µm and 5 mm, microplastics and nanoparticles are major environmental contaminants and potential health hazards. This review aims to engage with the intricate dimensions of microplastics, classification and persistence across different ecosystems. It underscores their bioaccumulation and pervasive presence. Although significant insights have been garnered, much remains to be elucidated regarding the full spectrum of impact microplastics have on human health. Evidence derived from both epidemiological and experimental studies underscores the urgent necessity for clinical research to elucidate the microplastic-cancer connection. It is a very important concern in biomedicine as cancer remains the leading cause of mortality irrespective of the advancement in diagnostic and therapeutic regimens. Furthermore, improvements in the detection and analysis of microplastics within biological samples are also scrutinized. The article concludes with future directions which advocate for standardized research protocols, regulatory measures and interdisciplinary collaboration to confront the microscopic threat posed by microplastics in cancer pathogenesis. However, this endeavour necessitates concerted efforts across various scientific domains, because only through such collaboration can we hope to achieve meaningful progress in understanding this critical issue.

Keywords:

Nanoplastics, Oncology, Bioremediation, Pollution, Polymer, Genotoxicity, Epigenetics View Article Online DOI: 10.1039/D5EM00232J

1. Introduction

Microplastics refer to minute pieces of plastic, normally less than 5 mm in size, and have recently become a key emerging environmental concern over the past few decades. Microplastics can be generated through physical degradation of plastics, industrial processes, and consumer products like cosmetics and synthetic textiles, and are widely dispersed in marine, freshwater, and terrestrial habitats, raising concerns about ecosystem impacts and human health [1, 2]. Unlike organic pollutants, plastics do not biodegrade easily; instead, they break into smaller particles that are further reduced in size at the nanoscale (<1 μm), thus becoming difficult to detect and control. These microplastics remain in the environment for hundreds of years and hence accumulate in water bodies, sediments, and soils. Of specific concern is the persistence of microplastics in the ecosystems. Arbind et al. referred to microplastics as "the hidden poison" by considering the long-lasting effects [3]. Microplastics have been found in oceans, rivers, lakes, and even in the atmosphere; they may be transported over long distances. They are especially distributed in marine environments: microplastics enter water and sediments, accumulate, and are ingested by organisms, from plankton to larger fish and marine mammals [4, 5]. This bioaccumulation in the food chain indicates how microplastic pollution goes far beyond national borders and represents an environmental risk factor for aquatic organisms and possibly even for humans [6].

Microplastics can physically block digestive tracts or change growth patterns, and they can transport toxic compounds such as persistent organic pollutants (POPs) and heavy metals into the organism's body upon ingestion. A major concern is that microplastics are also effective vehicles for environmentally persistent organic chemicals, such as POPs, besides heavy metals and pesticides [7, 8]. When eaten, these polluted microplastics allow toxic substances to get into an organism's system, triggering cancer, reproductive issues, and endocrine disruption. Microplastics cause oxidative stress, inflammation, and damage in organisms, disrupt ecosystem functions, and pose concerns for agriculture's soil and human food chain [9]. Human exposure routes for microplastics have been identified as ingestion, inhalation, and contact through the skin; they have been detected in human organs, blood, and placentas. While the overall health effects from microplastic exposure are not fully quantified, early indications show correlations to inflammation, immune disruption, and possibly cancer [10, 11].

Microplastics are classified into primary and secondary classes based on their origin. Primary microplastics, such as polyethene abrasives in toothpaste, plastic pellets, and textile fibers, are small and can enter the environment through improper disposal or industrial spills. Secondary microplastics, produced through the breakdown of larger plastic products, are shredded and end up in marine habitats due to environmental conditions. (**Figure 1**). The process is continuously operational, making the environmental issue significant and critical. Both primary and secondary microplastics have considerable environmental and health impacts [12, 13, 14]. Understanding the distinction between the two is decisive for developing strategies to decrease plastic pollution.

View Article Online
DOI: 10.1039/D5EM00232J

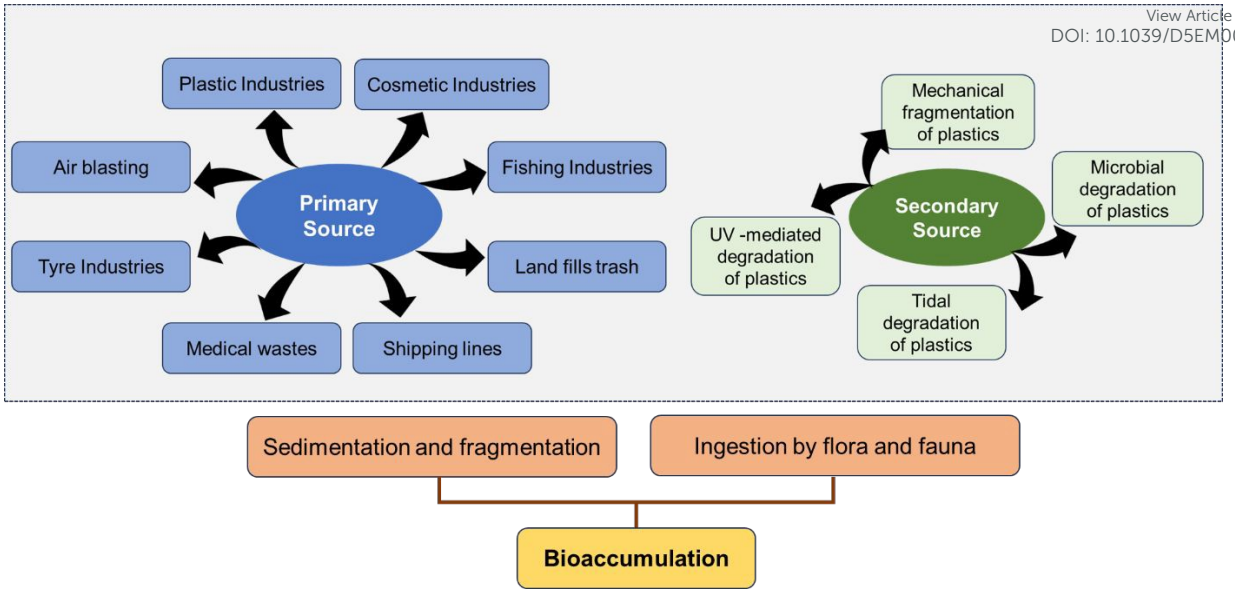


Figure 1: A comprehensive overview of the sources of microplastics and their bioaccumulation in the living world. This figure illustrates the various sources of microplastics, categorised into primary and secondary sources.

The general awareness of plastic contamination in the environment and potential human health-associated risks has recently highlighted the necessity to study microplastics about human health, especially cancer. This raises concerns about the exposure of humans in general, because of their ubiquity in contaminated food and drinking water, through breathing in of airborne particles and through dermal contact. Once inside the human body, these microplastics accumulate within different tissues and organs, which is an obvious sign that their adverse health effects are likely to occur (**Figure 2a**). Research on microplastics' impact on health, particularly cancer, is crucial for public health action and regulatory decisions, focusing on carcinogenesis support and long-term exposure risk assessment [15, 16]. The importance of studies regarding microplastics in the context of cancer goes beyond mere individual health concerns to their broader public health and policy influence [17]. Microplastics carry hazardous chemicals, which can enter the human body through ingestion or inhalation, causing endocrine disruption, immune system alteration, and other health issues. (**Figure 2b**). Moreover, microplastics can cause inflammation and oxidative stress, causing cancer. These effects are particularly concerning as they damage cell development and progression. Recently, microplastics were found in human stool, lung, and placental tissue, which may increase the risk of cancer [18]. The small size of microplastics permits them to penetrate biological barriers and, thus, probably accumulate in organs with the potential to cause harmful effects later on. This damage may further support carcinogenic development through mutations and alterations in cell processes. Furthermore, phthalates and bisphenol A (BPA), both substances used in the production of plastic, may be endocrine disruptors that are associated with several malignancies, particularly prostate and breast cancer. Concerns concerning microplastics' adverse health consequences and their involvement in carcinogenesis are further heightened by their ability to survive and accumulate in the body over time [19].

Microplastics, once internalized through means such as ingestion or inhalation or dermal contact, can reside within tissue for an indefinite period given their resistance to biological degradation. The small size of microplastics gives them the ability to translocate across epithelial barriers and thus able to accumulate in organs such as the liver, kidneys, intestines, and possibly the brain. Furthermore, this accumulation of microplastics poses an enormous

View Article Online
DOI: 10.1039/D5EM00232J

concern when considered against long-term exposure scenarios involving chronic low doses that are more representative of what occurs in real-world scenarios. In contrast to acutely toxic agents, very few clinical signs may be produced after long-term low-dose exposure; however, it may still induce chronic oxidative stress, inflammation, immune dysregulation, and genotoxicity, all considered hallmarks of carcinogenesis. Ultimately, chronic cellular stress may initiate DNA damage, obstruct DNA repair mechanisms and ultimately interfere with signalling pathways, which affects initiation and progression of carcinogenesis. The cumulative nature of long-term low-dose microplastic exposure thus necessitates mechanistic studies and regulatory interest, for even the smallest amount of microplastic exposure can greatly affect human health when considered over decades.

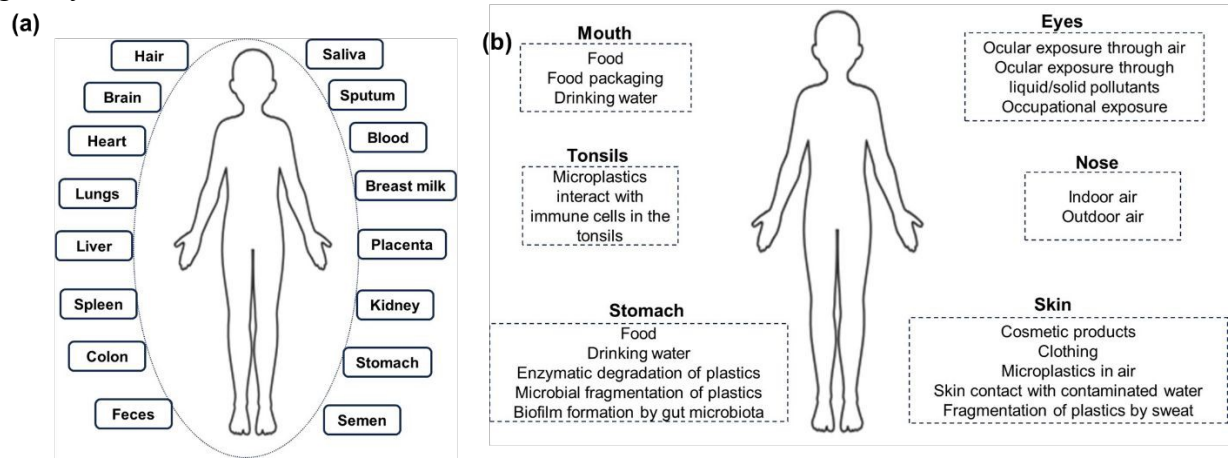


Figure 2: Illustration of microplastic (a) accumulation routes and (b) potential deposition sites in the human body. The diagram highlights primary exposure pathways: ingestion, and dermal contact. Deposition sites include the gastrointestinal tract, lungs, and systemic circulation, with potential bioaccumulation in organs such as the liver, kidneys, and lymphatic system.

This review examines the link between microplastic exposure, cancer development, and cellular dysfunction. It discusses current research on interactions between biological systems and microplastics, focusing on carcinogenesis effects. It also discusses current methodologies, knowledge gaps, and future research directions. The goal is to guide public health policy, suggest risk assessment strategies, and stimulate further research in this crucial area of environmental health science.

2. Microplastics: Sources, Characteristics, and Environmental Persistence

Microplastics originate from a wide variety of sources and have an array of surface qualities, sizes, forms, and types of polymers. One of the more significant variables in relation to the pollutants of concern that microplastics are going to display is environmental persistence. The global pollution issue will require a multidisciplinary approach that integrates insights from materials science, environmental chemistry, ecology, toxicology, and policy studies. At the same time, its heterogeneous sources, diverse characteristics, and high persistence make microplastic pollution of the environment complex and, at the challenging platform, scientific investigation and environmental management. This will help researchers to build the knowledge base on the fundamental properties and behaviours of microplastics in the environment, therefore providing a base support for the development of innovative solutions toward impact mitigation and ensuring evidence-based policy to reduce plastic pollution at its source.

2.1 Sources of microplastics

View Article Online
DOI: 10.1039/D5EM00232J

Microplastics originate from a variety of sources, which can be broadly categorised as primary and secondary sources. Regardless of the source, microplastics contribute significantly to global pollution in terrestrial, freshwater, and marine ecosystems. An estimated volume of approximately 360 million tons of plastic is produced globally every year [20]. Microplastics in the marine environment are creating problems for marine biodiversity and food webs. These microplastics are ingested by marine organisms and accumulate in their tissues, eventually passing into humans through the intake of seafood. Terrestrial ecosystems are also severly suffering from microplastic pollution, with 63,000-430,000 tons of microplastics reaching agricultural soils in Europe each year. Globally, it is estimated that 0.8~2.5 million tons of microplastics enter ecosystems every year from sources such as synthetic textile fibers, tire abrasion, and urban runoff. The contamination of our food and drinks is terrifying: sea salt contains 1,200 particles per kilogram, while bottled water contains an average of 94 particles per liter [21, 22].

Primary microplastics are intentionally manufactured to be small in size for specific applications, whereas secondary microplastics result from the degradation of larger plastic items. It is important to understand both primary and secondary sources of microplastics from an environmental viewpoint. Primary microplastics are plastics that are purposely manufactured to be microscopic. These are intentionally made for a wide range of commercial and industrial practices. Applications of such kind of particles include microbeads found in personal care products, pre-production plastic pellets utilised in manufacturing plastics, and microfibers coming from synthetic textiles. Microplastics traverse both living and non-living systems; thus, they form complex contamination networks that pose significant risks to ecological balance and human health [23, 24, 25]. Developing effective strategies for reducing their effects requires an in-depth knowledge of their various sources and interactions **(Figure 3a, b)**. Primary microplastics are generated to cause direct environmental discharges through industrial effluents, wastewater systems, and airborne deposition. Rinse-off cosmetics, personal care, and cosmetic products, such as facial scrubs, toothpaste, and shower gel, are the traditional sources of primary microplastic pollution. The problem with this source is that even though most countries have banned the use of microbeads in rinse-off cosmetics, it creates legacy pollution, and some regions continue their use. The textile industry is another important source of primary microplastics since synthetic fabrics during the process of their production and washing also release microfibers. A single wash can release tens of thousands of microfibers into wastewater systems, with many bypassing conventional treatment plants and entering aquatic environments.

When bigger plastic items eventually break into smaller plastic pieces, this results in secondary microplastics, which account for the majority of microplastic pollution. These processes are driven by environmental factors such as UV radiation, mechanical forces like wave action and wind abrasion, and biological processes. Secondary microplastics are frequently generated by the breakdown of larger plastic trash, such as abandoned fishing equipment and industrial plastics, as well as by the degradation of single-use plastic products, such as bags, bottles, and packaging materials. The automobile sector is a significant contributor to secondary contamination from microplastics [26]. Tire wear particles are generated in normal vehicle operation and may be transported from roads and other surfaces into aquatic environments by runoff [27]. The same sources release microplastic particles into the environment through weathering and fragmentation of paints applied in buildings, ships, and road markings. The weathering of plastic construction materials and the breakdown of insulation and sealants also contribute to the overall environmental load from plastic construction weathering in general. Urban stormwater runoff is a significant channel for anthropogenic microplastics. Research

quantifies how various types of microplastics, such as black rubbery fragments, are transported into aquatic ecosystems [28]. This analysis highlights stormwater's considerable role in introducing microplastic pollution into urban water systems. This underscores the urgent need for targeted mitigation strategies to reduce environmental contamination because the implications of this pollution are far-reaching (**Figure 3c**).

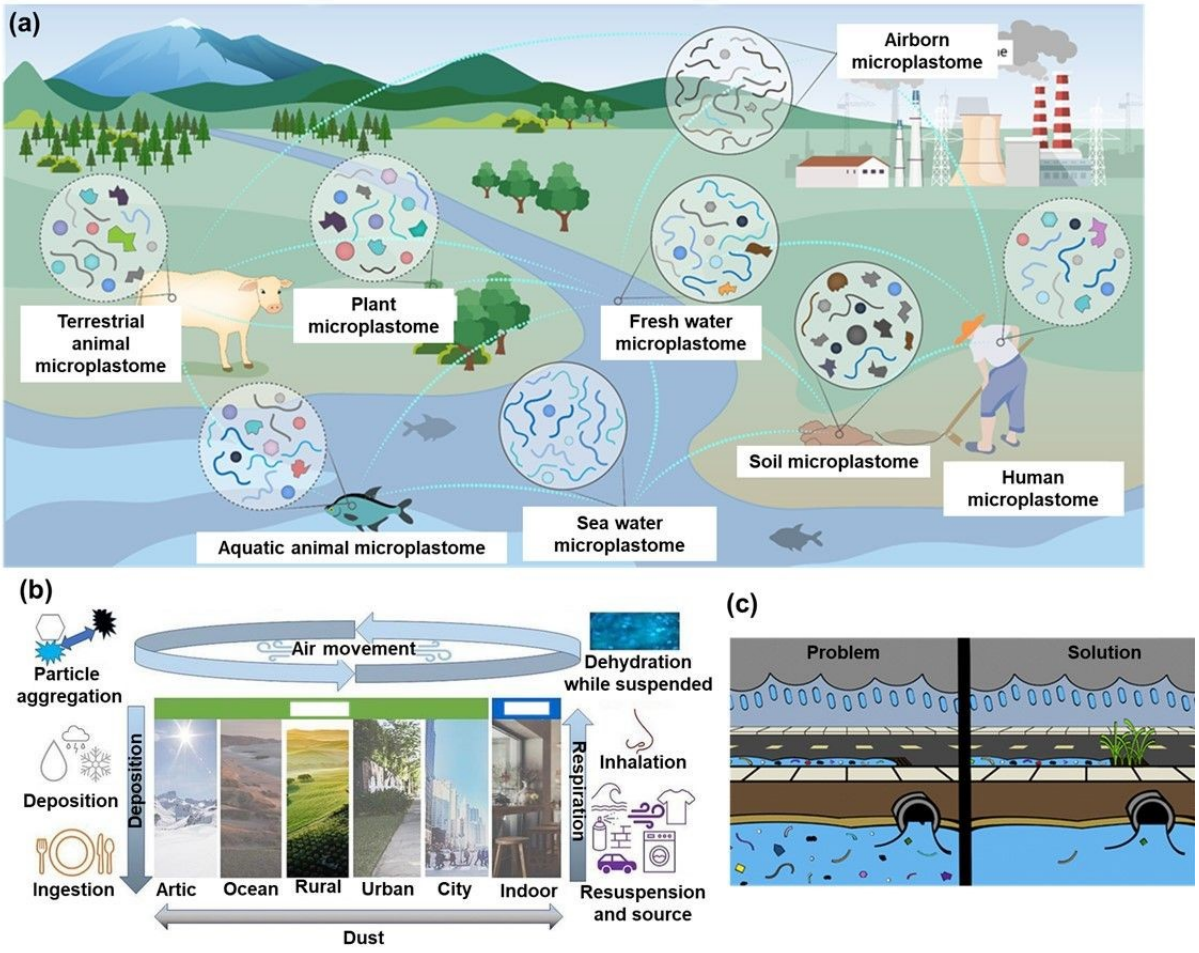


Figure 3: (a) Microplastics spread through our environment from factories, cities, synthetic clothing, and personal products. These tiny plastic fragments move across living and non-living systems, creating complex contamination patterns that threaten ecological balance and human health. Understanding their diverse sources and interactions is crucial for developing effective management strategies, adapted with permission [24]. Copyright 2024, American Chemical Society. (b) Schematic representation depicts microplastics' sources, distribution, and dynamic behaviour within atmospheric systems. The illustration integrates multiple pathways of microplastic entry, transport mechanisms, spatial prevalence, and potential interaction points across urban, industrial, and natural environments, adapted with permission [25]. Copyright 2023, Elsevier. (c) Urban stormwater runoff is a critical conduit for anthropogenic particles, particularly microplastics. Research quantifies the transport of diverse microplastic types, including black rubbery fragments, to aquatic environments. This analysis reveals stormwater's substantial role in introducing microplastic pollution to urban water systems, highlighting the urgent need for targeted mitigation strategies to reduce environmental contamination, adapted with permission [28]. Copyright 2021, American Chemical Society.

Agricultural practices have been seen as one of the direct and indirect sources of microplastics. Plastic mulch films used in agriculture, though good for crop production, may contaminate soils upon degradation. In addition, microplastics can also be introduced into agricultural soils through the application of sewage sludge and compost as fertilisers, because their particles are not completely removed by wastewater treatment processes [29, 30]. There is further exacerbation due to improper disposal and littering of plastic waste in urban settings because these items eventually turn into microplastic particles. Marine activities, in the form of fishing, aquaculture, and shipping, also result in high levels of microplastic pollution in the aquatic environments. This fishing gear is often lost or intentionally abandoned and is referred to as ghost gear. These items continue to fragment in the marine environment, leading to a high production of secondary microplastics. Further sources of direct release of microplastics into marine ecosystems include the use of expanded polystyrene buoys in aquaculture and the wear of anti-fouling marine paints. Meanwhile, transport through the atmosphere has been recognised as a key mechanism for microplastic distribution, and recent studies suggest that microplastics can be detected even in extremely isolated and nearly pristine regions [31, 32, 33]. Airborne transport is one of how microplastic is conveyed. The procedures include wind actions on large plastic objects, emissions of synthetic fibres from textiles, and friction wear particles from tyre wear. Upon becoming airborne, these particles are driven far away by the wind and add to the pollution [34, 35]. The global diversity and wide sources of microplastics make controlling and mitigating microplastics even harder. Thus, this complication can be solved by first gaining comprehensive information regarding the relative contribution from the diverse sources and pathways through which microplastics enter and move within the environment. An understanding of the diverse sources of microplastics is fundamental for developing targeted prevention and mitigation strategies (**Table S1, S2**).

2.2 *Physical and chemical properties of microplastics*

Physical and chemical properties highly influence the behaviour, fate, and potential environmental impacts of microplastics. The importance lies in the key role these properties have in the interaction of microplastics with biota, transportation between the different environmental compartments, and ecosystem persistence. The key physical properties include size, shape, colour, and density, while crucial chemical properties entail polymer type, additives, and surface characteristics. Particle size, shape, density, and surface area are the physical characteristics of microplastics that largely control their distribution into different environmental compartments, which include air, soil, and water. Their chemical properties, polymer composition, surface chemistry, and the presence of additives regulate their interaction with organisms and pollutants. These properties are critical given environmental risks from microplastic pollution and the assessment of proper strategies for its detection, monitoring, and remediation [36, 37]. The particle size of microplastics determines the distribution, bioavailability, and potential for uptake by organisms. Continuous fragmentation processes turn the size distribution of microplastics, normally skewed to smaller particles in the environment. The smaller microplastics have a superior surface area-to-volume ratio and hence higher adsorption capacity for environmental pollutants, which may end up enhancing their toxicological effect [38, 39].

The shape is another key and varied physical property of microplastics, variously found as spheres, fibres, fragments, films, and foams. This parameter directly affects the hydrodynamic behaviour, the transport in air and water, and the potential for uptake by organisms. Fibres, for example, can have a much greater tendency to entangle within the digestive system than spherical particles [40, 41]. Indeed, the effect of colour on the uptake of particles by an

View Article Online
DOI: 10.1039/D5EM00232J

organism has been studied for decades and should not be underestimated in the case of microplastics. Brightly coloured particles can be misinterpreted as food items by several organisms and may therefore be taken up and transferred throughout the food web. Additionally, the heating of a particle through the absorption of solar radiation may alter the photo-degradation rate and buoyancy [42]. One important physical property of microplastics that will determine their distribution in the vertical profile of aquatic environments is density. Those with densities less than water, for instance, polyethene and polypropylene, will float and preferably be found on surface waters and shorelines. Denser particles, on the other hand, sink mostly, like those made up of polyvinyl chloride and polyethene terephthalate, and get deposited at great depths in sediments [43]. However, the real effective density of microplastics may be dynamic, given biofouling with organic matter over time or adsorption of other materials and, hence, alter their distribution in the water column (**Table S3**).

The chemical composition of microplastics is largely determined by the type of polymer. Most of the common polymers associated with microplastic pollution are polyethylene (PE), polypropylene (PP), polystyrene (PS), polyvinyl chloride (PVC), and polyethylene terephthalate (PET). The chemical structures of these common polymer types are all different, and as a result, they exhibit various levels of crystallinity, glass transition temperatures, and mechanical properties. Compounds used in the manufacture of plastics, which are also present as additives and colorants, contribute greatly to chemically controlling microplastic properties. These can make up to 50% of the weight of single-use plastic and consist mainly of additives, like plasticisers, stabilisers, flame retardants, pigments or antimicrobial agents. Most of these additives are not covalently linked to the polymer matrix and may diffuse over time into surrounding media, possibly exerting toxicological effects on organisms [44]. Environmental factors, including pH, temperature and salinity; the age of a polymer; and its level of weathering can affect how much additive leaches out. Changes in the surface properties of microplastics are a key factor influencing their environmental fate and risks associated with exposure to contaminants by biota [45]. The outer surface of microplastics with different hydrophobic and hydrophilic groups can likely lead to discrepancies in aggregation properties, leading to the removal rates influencing anchoring organic pollutants (**Table S4**). In the environment, weathering processes can modify the surface properties of microplastics. Moreover, biofilm development can change the surface properties of microplastics and directly or indirectly influence buoyancy, aggregation capacities and thus bioavailability [46].

According to the persistence in the environment, plastics are divided into two main categories: biodegradable and non-biodegradable. Biodegradable plastics are specifically designed to decompose under particular circumstances, whereas non-biodegradable plastics persist in ecosystems for extended periods, causing significant pollution and ecological deterioration [47]. This provides a more sustainable option **(Figure 4a).** The physical and chemical characteristics of microplastics indicate a complex mechanism of deterioration and fragmentation in the environment [48]. Biodegradation, thermal degradation, pyrolization, and nanoparticle-mediated methods are examples of currently emerging microplastic degradation techniques [49]. Through utilising their unique functional and structural characteristics to solve environmental pollution issues, metal-organic frameworks show great promise for effective microplastic degradation **(Figure 4b).** One of the primary pathways for the fragmentation of microplastics is photodegradation, which is triggered by UV radiation exposure. Different polymer types possess distinct susceptibilities to photodegradation; for example, polyethylene and polypropylene are more vulnerable to UV degradation than other polymers, like PET, which is generally far less susceptible [50]. A significant process of mechanical degradation, driven by abrasion and fragmentation forces in high-energy environments like beaches and the

ocean surface, is also present [51]. The degradation rate may be sensitive to polymer type and the presence of additives or environmental factors, such as temperature and microbial community composition. Physical and chemical properties of microplastics critically influence their environmental fate, potential ecological impacts as well and the efficiency of detecting or removing them from the natural environment; it is thus imperative to gain a thorough grasp in this regard (**Figure 4c**). The interplay of these properties with the environment highlights how our understanding should evolve as research continues to explore and uncover ecologically relevant behaviour and effects over time in different ecosystems.

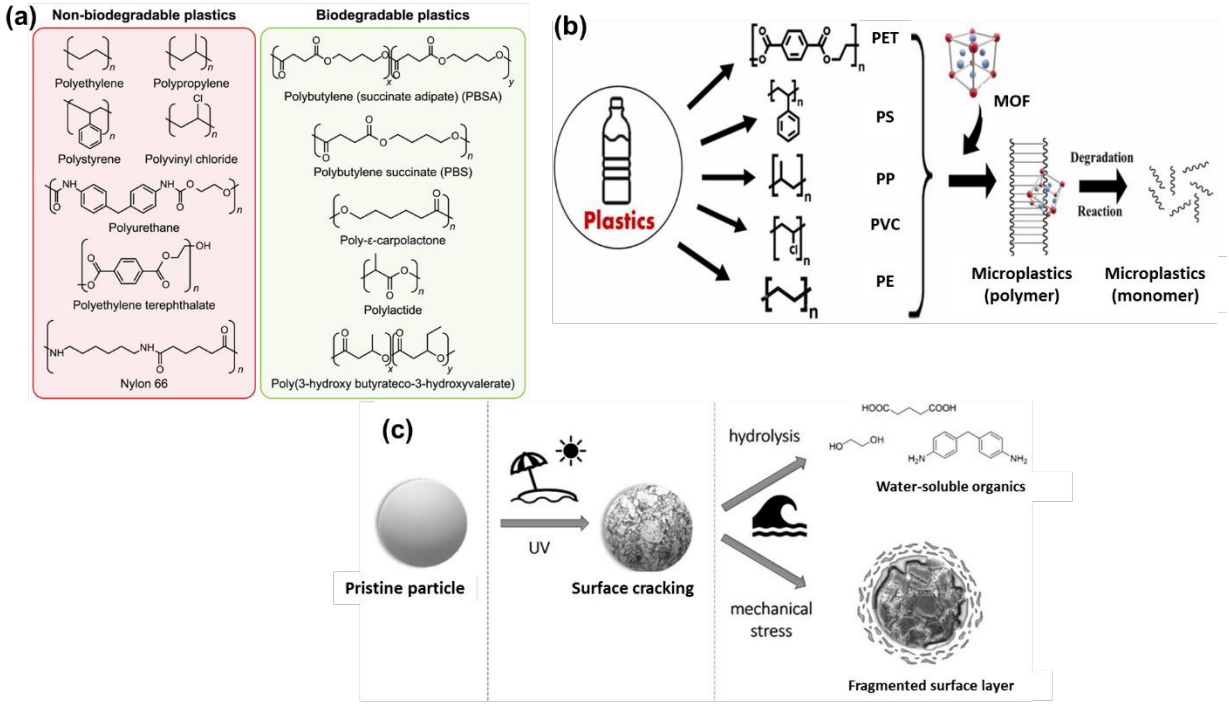


Figure 4: (a) Overview of different types of plastics, categorised into non-biodegradable and biodegradable types. Non-biodegradable plastics persist in the environment for extended periods, contributing to pollution. In contrast, biodegradable plastics are designed to degrade under specific conditions, offering more sustainable alternatives, adapted with permission [47]. Copyright 2024, Elsevier. (b) Emerging microplastic degradation strategies encompass biodegradation, thermal degradation, pyrolization, and nanoparticle-mediated approaches. Metal-organic frameworks offer exceptional potential for efficient microplastic degradation due to their unique structural and functional properties, adapted with permission [49]. Copyright 2024, Elsevier. (c) Environmental ageing of spherical microplastic particles at the beach due to UV photolysis, mechanical stress, and hydrolysis, leading to surface cracking, ablation, and the release of secondary micro- and nanoplastic fragments, adapted with permission [51]. Copyright 2022, American Chemical Society.

2.3 *Environmental retention and bioaccumulation of microplastics*

Because they are resilient and hard to break down, microplastics remain for a long time in many locations. The breakdown of conventional plastics in nature is very limited. Most synthetic materials resist being broken down by microbes because of their heavy molecular structure and the absence of functional groups that microbes can easily recognise. Because microplastics can carry additional contaminants with them, the problem is significantly more complex. Furthermore, viruses and heavy metals can adhere to the surfaces of microplastics, which might boost their availability and mobility in the environment. This effect not only makes these

View Article Online
DOI: 10.1039/D5EM00232J

pollutants more prevalent, but it also raises concerns regarding whether microplastics could be a pathway for hazardous substances that accumulate in living things. The way contaminants stick to and detach from microplastics is influenced by factors such as the type of polymer used the size and shape of the particles how weathered they are and environmental conditions like pH temperature and salinity [52]. As microplastics break down and get smaller in the environment their surface characteristics like a larger surface area and increased polarity, can change how they interact with pollutants and living organisms. Bioaccumulation and biomagnification explain the process by which toxic substances increasingly concentrate within organisms as well as food systems. This mechanism, however, significantly affects predatory species (**Figure 5a**). Several organisms, from huge marine mammals to microscopic plankton, have been found to ingest microplastics, highlighting the extent of microplastic exposure in aquatic environments [53].

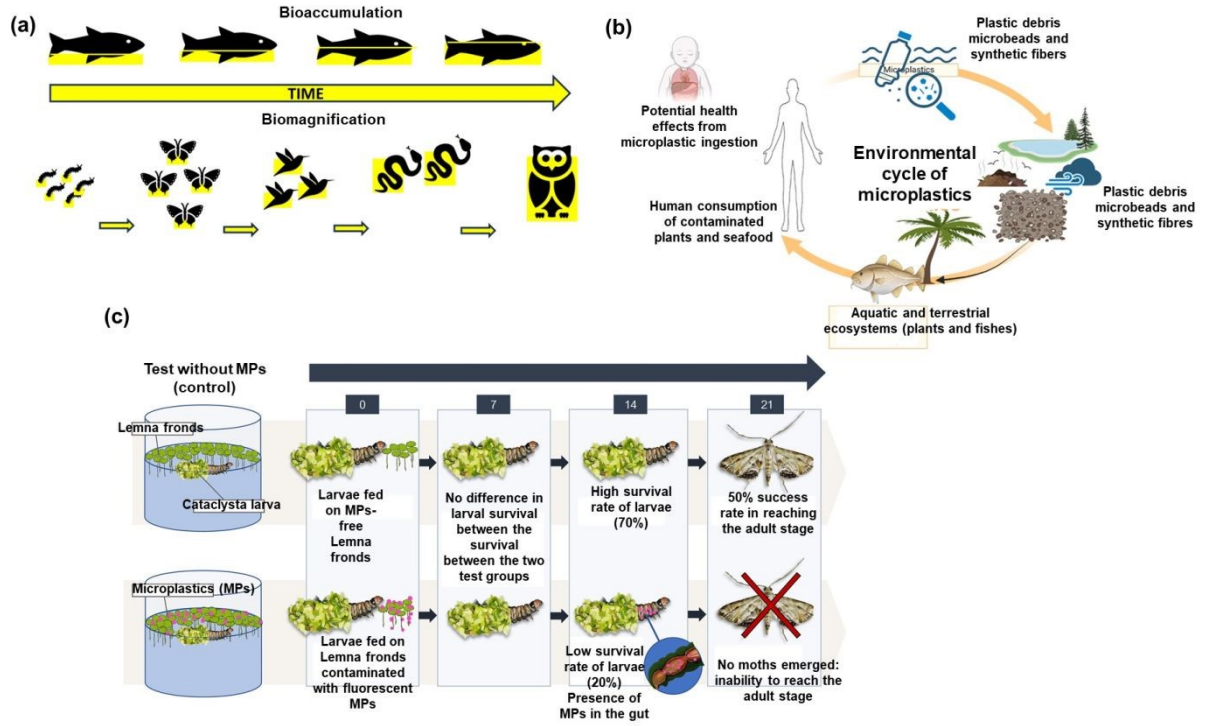


Figure 5: (a) Schematic representation of bioaccumulation and biomagnification, illustrating the progressive accumulation of contaminants in organisms and their increasing concentration across trophic levels in a food chain. (b) Schematic representation of the cycle of microplastics in the environment, depicting their sources, distribution through air, water, and soil, accumulation in ecosystems, ingestion by organisms, and potential re-entry into the food chain, highlighting their pervasive and persistent nature, adapted with permission [54]. Copyright 2024, Elsevier. (c) Schematic representation of trophic transfer of microplastics from Lemna minuta fronds to Cataclysta lemnata larvae in a freshwater food chain, showing ingestion, accumulation in the intestinal lumen and excrement, and its impact on larval survival and life cycle progression, adapted with permission [56]. Copyright 2023, Elsevier.

Aspects that influence the bioaccumulation of microplastics comprise the size, shape and colour of the particles, as these characteristics can impact how strictly they look like natural food sources and how selectively organisms select to consume them. The capacity of smaller microplastics and nanoplastics to enter cells and travel throughout living things renders them especially dangerous. The ability of microplastics to go up the food chain, as demonstrated by

studies in both controlled and natural environments, raises the possibility that they could accumulate at trophic levels [54]. The extent and implications of microplastic transfer are still being actively studied by researchers. Diverse species and environmental circumstances display differences in the maintenance and accumulation of microplastics [55]. The knowledge regarding adverse side effects of microplastic bioaccumulation on the health of organisms and ecosystems is still infancy. Ingested microplastics can lead to effects such as gut blockage, reduced feeding capacity and changes in growth patterns. On a level, internalised microplastics may trigger stress, inflammation and changes in gene expression. Although studies have shown the transfer of pollutants from microplastics to organisms the significance of this pathway compared to other exposure routes in nature is still debated (**Figure 5b**).

The trophic transfer of microplastics in a freshwater food chain has been demonstrated through the ingestion and accumulation of these particles by *Cataclysta lemnata* larvae feeding on *Lemna minuta* fronds [56]. Microplastics were observed within the intestinal lumen and in the excrement of the larvae, indicating effective transfer along the food chain. This transfer has significant implications, including impacts on larval survival and disruptions to their life cycle progression, highlighting the ecological risks associated with microplastic contamination in aquatic systems (**Figure 5c**). Exploring the potential of enzymes and microorganisms that break down plastics shows promise for improving the breakdown of plastic waste, although scaling these methods up to combat environmental plastic pollution remains a challenge [57, 58]. It is essential to comprehend the factors influencing the environmental behaviour and accumulation of microplastics, to evaluate their impacts and establish reliable risk assessment frameworks. This understanding can support decision-making processes and shape interventions aimed at mitigating the consequences of microplastic pollution on ecosystems and human health.

3. Pathways of Human Exposure to Microplastics

Considering how common microplastics are in the environment and in many different items, human exposure to them varies. Finding the exposure route is very important to evaluate the potential health risk. The exposure of individual persons varies depending on their lifestyle. Tackling these exposure pathways necessitates an approach that involves monitoring and controlling sources of microplastics, enhancing waste management practices and creating alternatives to plastic products [59].

3.1 *Ingestion via food and water*

Because microplastics are so common in goods like seafood and bottled water, they represent a serious health risk [60, 61]. Ingestion is the principal pathway through which with microplastics enter from diverse food and beverage products, including seafood, drinking water, and table salt. Due to the high concentration of microplastics in the ocean, which reaches up to 102,000 particles per cubic meter, seafood has been identified as a major source of human microplastic exposure through ingestion [62]. The content of microplastics was found to be 550, 43, and 7 items/kg, respectively in sea salt, lake salt, and rock/well, showing a much higher contamination level by microplastics among ocean-related products [63]. Aquatic life is severely affected by microplastics to a larger extent [64]. Fish, a vital part of many diets also plays a role in exposing humans to microplastics. The transfer of microplastics through marine food chains adds complexity to this exposure route potentially leading to biomagnification, in higher-level species that are sought after for human consumption, like tuna and swordfish [65]. Microplastics in food sources have been recognised as contributors to their presence in our

diets. Fruits and vegetables can absorb microplastics through methods such as contaminated soil absorption, settling of airborne particles and the application of plastic mulching films in farming. Research has found microplastics in various fruits and vegetables, including apples, carrots, lettuce and broccoli, but the amount varies based on crop type and growing conditions. The use of treated wastewater and sewage sludge as fertilisers in agriculture poses another potential route for microplastic contamination of crops since standard wastewater treatment methods do not eliminate these particles. Additionally, foods and drinks offer pathways for microplastic consumption. Microplastics have been detected in items like beer, honey and sugar, probably entering through manufacturing, packaging or transportation stages [66, 67]. Table salt has been identified as a widespread source of microplastic exposure, with research showing these particles in different salt varieties from various regions. The levels of microplastics in salt can differ significantly depending on factors like the origin and the production techniques used. The contamination of microplastics is also influenced by food packaging. Plastics commonly used in packaging, like containers, wraps and utensils can deteriorate over time and release microplastic particles into food [68]. The food industry heavily relies on packaging, and as these materials age and break down, they can release microplastics that might be consumed with food. This mode of exposure raises concerns, due to the prevalence and extensive use of plastic packaging in the food sector. Research estimates that humans may consume between 39,000 and 52,000 microplastic particles per year from these diverse sources through ingestion [69].

It is difficult to assess human exposure to microplastics through consumption for several reasons. First, the nature of microplastics, including variations in size, shape and polymer composition. Second, the absence of standardised protocols for the collection of samples for analysis. Moreover, personal exposure rates are significantly influenced by factors such as individual dietary preferences and regional variations in food consumption habits [70]. Attempts to assess daily microplastic intake through food and water have yielded inconsistent outcomes. Some research suggests an average annual ingestion of thousands of particles, while other studies project significantly higher figures by considering smaller size categories and exposure through inhalation. Contamination of water is another way that people ingest microplastics. Both bottled and tap water serve as a significant and consistent source of microplastic exposure for humans. Bottled water has been found to have surprisingly high levels of microplastics [71, 72]. The microplastics in bottled water come from various sources, including the water source itself, the bottling process and the breakdown of the plastic bottle over time [73]. The potential health effects of ingesting microplastics over the long term are not yet fully understood and continue to be studied. While it is thought that most microplastics consumed will pass through the digestive system without being absorbed, smaller particles, especially nanoplastics, can cross biological barriers and accumulate in body tissues. The presence of microplastics in the intestines could cause inflammation and disrupt gut microbiota to delay nutrient absorption. Moreover, the likelihood of microplastics serving as carriers for other environmental pollutants and heavy metals increases the risk evaluation process. Additionally, the leaching of additives from ingested microplastics raises toxicological concerns since many of these substances are known disruptors or carcinogens. Consuming food and water contaminated with microplastics is now recognised as a serious public health concern [74].

3.2 *Inhalation of airborne microplastics*

Inhalation of microplastics in the form of aerosol via industrial processing could have effects on respiratory health and overall well-being [75, 76]. This exposure mode raises apprehensions

for microplastics are found in indoor and outdoor settings and can potentially infiltrate deep into the respiratory system. Inhalation is a critical exposure route for any material which can be carried out by the air, particularly in enclosed settings. Research indicates that adults may inhale around 12,891 microplastic fibers annually, predominantly from domestic dust and indoor air [77]. Airborne microplastics originate from various sources and can travel long distances. Their presence in the air is ascribed to sources such as the direct release of microfibers from textiles and secondary sources such as the degradation of larger plastic items. Sectors that employ or manufacture fibers, such as the textile industry can also pay for airborne microplastics as fibers are released into the air during dispensation and usage [78]. People who are saying more in rooms are also getting airborne microplastic via various sources such as synthetic clothing, carpets furnitures or even from cosmetics [79]. Household dust often containing a proportion of microplastic particles can be resuspended in the air through activities leading to inhalation exposure [80]. Particles over 10 μm incline to get trapped in the part of the respiratory system, while those ranging from 2. 5 to 10 μm can go deeper into the airways. Particles under 2. 5 μm are particularly worrisome as they can reach the alveoli and potentially enter the bloodstream. Recent research has found microplastics as small as 11 μm in human lung tissue, offering proof of exposure and retention of these particles through respiration [81]. Fibrous microplastics with their elongated shape present distinct challenges when it comes to being deposited in the respiratory system and cleared from it [82, 83]. The contamination of microplastics varied between different geographical locations. For instance, the median concentration of microplastic fibers is 5.4 fibers/m3 in the outdoor air and 0.9 fibers/m3 in the indoor air in Paris [84]. Microplastic particles smaller than 5.5 μm and fibers with the size of 8.12–16.8 μm was detected in human lungs [85]. Research efforts should focus on establishing approaches for measuring airborne microplastic exposure carrying out extensive studies to uncover the health effects of prolonged inhalation and exploring the potential interactions between microplastics and other air pollutants.

3.3 *Dermal exposure*

Dermal exposure to microplastics is an important but less commonly talked about way for humans to come into contact with these widespread pollutants. While the likelihood of microplastics being absorbed through the skin is lower than through ingestion or inhalation long or repeated exposure to them can still pose potential health risks. The main sources of exposure to microplastics on the skin include care products, synthetic fabrics and work environments. Care products are a significant source of microplastics that can directly touch the skin [86, 87]. Microbeads, which are small plastic spheres found in scrubs, facial cleansers and body washes, are meant to have properties for scrubbing and cleaning purposes. Microbeads as small as 40 nm have shown penetration into the epidermal Langerhans cells, specifically around hair follicles, whereas larger particles of sizes 750 nm and 1500 nm are not considered to be taken up through skin. While these microbeads can be rinsed away during use, they may still leave traces on the skin. The concern about exposure is especially important for people who regularly use these products or apply them in large amounts. Although the main focus tends to be on the risk of microplastics entering the body through consumption, there is also a chance of direct skin contact occurring if these products are not properly washed off [88, 89]. Another significant way people come into contact with microplastics is through textiles. Fabrics and textiles made from fibres like polyester, nylon and acrylic release microplastic strands when worn or washed. These tiny fibres can touch the skin and end up in an environment where they can stick around for a long time. Rubbing against fabrics and skin while wearing them can cause microplastic particles to be released, directly exposing the skin. Moreover, microplastic fibres can also be released into the air by textiles settling on the skin

and adding to exposure [90]. Workers in industries such as plastic production, recycling and textile manufacturing may be exposed to microplastic particles through contact with materials, dust, and residue. For example, employees who work with the fabrication and management of plastic pellets or polyester fibers might come across microplastic particles adhering to their skin.

3.4. *Accumulation in human tissues and organs*

Studies specify that microplastics can cross barriers like the blood-brain barrier and placental barrier, possibly affecting fetal development and brain function [91, 92]. The infiltration of microplastics into tissues is influenced by their physical characteristics such as size, shape and chemical composition [93]. While the long-term impact of microplastic buildup in human tissues is still being studied, preliminary research indicates that exposure could result in inflammation, tissue damage and possible associations with diseases like cancer. Moreover, ongoing studies are exploring the relations among microplastics, the human microbiome and the immune system, raising alarms about the probable disturbance of normal bodily functions [94]. In addition, the occurrence of microplastics in human tissues raises fears about their potential to disrupt functions and interfere with normal bodily processes. While the extent of the health effects of microplastic accumulation in human tissues and organs is still being calculated early research suggests possible links to various health issues, such as hormonal imbalances, reproductive problems, and an increased risk of certain cancers. With the increase in plastic production and clearance worldwide, it is essential to further investigate the long-term effects of microplastic accumulation in the body and find ways to reduce exposure and potential health risks. Given the durability of plastics in nature and the growing evidence of their accumulation, understanding the full scope of their impact on human health is a crucial field for future scientific research.

Recent clinical research has demonstrated that most internal organs in the human body have been confirmed to host microplastic deposition, which will unduly raise concerns for possible health effects. Indeed, microplastics, such as PET, PVC and poly(methyl methacrylate), were identified in cardiac tissues and blood samples of patients who had undergone heart surgery. This means those patients have been directly or indirectly exposed to such chemicals through medical procedures [95]. Meanwhile, microplastics were also traced from cartilage and intervertebral discs of humans. Polypropylene is the most prevalent polymer at 35%, while ethylene vinyl acetate copolymer is at 30%, and polystyrene at 20%. These microplastics can enter the skeletal tissues through the bloodstream, so that inflammatory reactions and bone health could be affected. The abundance of microplastics in the human intervertebral disc was higher than that in the bone and cartilage tissue [96]. Microplastics were also discovered in the ovarian follicular fluid of women undergoing fertility treatment, raising alarm concerning possible reproductive health effects. The finding sparked concern regarding the possible implications of microplastics on reproductive health. Microplastics smaller than 10 μm were identified in 14 out of 18 follicular fluid samples collected from women undergoing assisted reproductive treatment at Southern Italy. The average concentration of 2,191 particles/mL and a mean particle diameter of 4.48 μm was reported [97].

Eight organ systems, including the cardiovascular, digestive, endocrine, respiratory, and reproductive systems, as well as various biological media, have been found to contain microplastics. Special mention is made of the biological fluids comprising breast milk, semen, and urine. The presence of microplastics in meconium and infant faeces adds another layer of concern, suggesting that exposure to these particles may continue beyond breastfeeding [98].

Such findings prove the omnipresence of microplastic contamination within human tissues, thus demanding more research efforts to fully comprehend the health risks that are most likely to arise. These alarming findings demand an urgent investigation into the long-term effects of microplastics on human health as well as potential risks associated with their exposure [99]. According to a proof-of-concept case series that was performed in Germany, tissue samples for microplastic detection came from six patients having liver cirrhosis as well as five individuals who were not suffering from any liver disease. Researchers developed a reliable detection method for microplastics within a range of 4 to 30 μm. No tissue was found to have microplastics from individuals without liver disease, but all the cirrhotic liver specimens tested positive, with markedly higher microplastic concentrations [100]. Another study assessed the presence of microplastics in synovial tissue from 45 patients undergoing hip or knee arthroplasty. A total of 343 microplastics representing nine common polymer types were detected, with an average abundance of 5.24 ± 2.07 particles/g [101]. The presence of microplastics in several organ systems of the human body raises concerns over pollution levels and the public health implications. More in-depth work must go into understanding the issue clearly and developing effective mechanisms to combat microplastic contamination effects. These findings bring microplastic contamination into the limelight in human tissues across the globe and call for further research in understanding their health impacts. Microplastics increase human exposure, which will shortly cause alarming health effects.

4. Mechanisms of Microplastic-Induced Cellular Dysfunction

Cellular functions in living organisms, including humans, can be hampered by microplastics through physical and chemical interactions. By releasing ROS and causing damage to proteins, lipids, RNA, and DNA, microplastics can induce stress in cells. Understanding how microplastics impact human health and the environment is crucial for developing effective strategies to mitigate their negative effects.

4.1 *Oxidative stress*

Microplastics are recognized for their two distinct functions in biological systems, behaving as messenger molecules at low concentrations while inducing oxidative stress and damage when produced in excess. One key mechanism involves the interaction of surfaces with membranes or cellular components. Due to their small size, wide surface area and capacity to engross environmental pollutants microplastics can penetrate tissues and cells triggering stress to membranes. When microplastics come into contact with cell surfaces they can exercise mechanical stress and disrupt the integrity of cell membranes. This triggers the production of ROS by enzymes such as NADPH oxidases [102]. This leads to oxidative stress causing damage to lipids, proteins and DNA and contributing to various diseases such as inflammation, cardiovascular conditions and cancer [103]. The dose and time-dependent cellular responses to stress exposures have been demonstrated in experiments performed with cytotoxic analogues, such as cytidine analogue 4'-azido-2'-deoxy-2'-fluoro(arbino)cytidine (FNC), as inhibition of proliferation, mitochondrial malfunctions, and cell death. FNC-induced injury was mediated by ROS overproduction, depolarisation of the mitochondrial membrane potential, and an apoptotic gene pattern disruption, with noted upregulation of pro-apoptotic Bax and downregulation of anti-apoptotic Bcl-2 and Bcl-xl, which finally led to mitochondrial-mediated oxidative stress-induced apoptosis with subsequent arrest at G2/M phase via p21 pathway activation, thereby reflecting cellular responses usual in microplastic-induced toxicity [104]. FNC has also demonstrated a time and dose-dependent increase in the levels of ROS

View Article Online
DOI: 10.1039/D5EM00232J

within Dalton's lymphoma cells, in particular, a significant amount of mitochondrial ROS production being noticed within minutes of the exposure [105].

Polystyrene plastics have been demonstrated to provoke developmental toxicity in zebrafish embryos by notable impacts on hatching rates, survival, heart rate, body length and behavior [106]. Exposure to polystyrene plastics also instigates oxidative stress; however, it disrupts the regulation of genes linked to the base excision repair pathway (**Figure 6a**). The lipophilic nature of microplastics can increase the affinity towards lipid membranes and can cause lipid peroxidation. When microplastics are taken up by cells through endocytic pathways they can accumulate in lysosomes and other cell compartments. This buildup may lead to the permeabilisation of membranes, releasing enzymes and promoting ROS production, through the Fenton reaction. [107] Research conducted on marine and terrestrial organisms has shown that microplastics induce stress, evidenced by increased ROS levels, damage markers and protein carbonylation. Aquatic life and the health of the ecosystem are also hampered to a greater extent by microplastics through a variety of mechanisms [108] (**Table S5**).

4.2. *Inflammation*

Microplastics can provoke reactions upon entering the body through inhalation, ingestion or contact. Once inside, they interact with immune cells such as macrophages, neutrophils and dendritic cells that identify these particles as intruders. Microplastics can induce inflammation through interactions with tissues and cells. When microplastics come into contact with surfaces in the respiratory system, digestive tract or skin they can cause irritation or damage [109]. This disruption triggers the recognition of receptors on cells like Toll-like receptors and NOD-like receptors. These receptors are involved in the response. They initiate signalling pathways that result in the release of cytokines and chemokines such as tumor necrosis factor alpha, interleukin 1 beta, and interleukin 6. These substances attract cells to the area, intensifying and prolonging the inflammatory reaction [110]. Additionally, internalisation of the microplastic can be done via endocytosis, leading to activation of NLRP3 and Couse inflammation [111]. Microplastic exposure causes inflammation in various macrophages and epithelial cells, inducing lysosomal damage, inflammasome activation and the secretion of pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α. Chronic exposure maintains oxidative stress, mitochondrial dysfunction, and immune imbalance, promoting fibrosis, tissue remodelling, and potentially tumorigenesis. Microplastics could serve as carriers of endotoxins and/or microbes, further enhancing inflammation through TLR-mediated signalling. Organ-specific inflammatory responses have been studied in the gut, liver, lungs, and brain, which indicate barrier disruption, altered microbiota, and immune infiltration. These systemic effects illuminate the need to start working on long-term risks and risk mitigation strategies urgently [112].

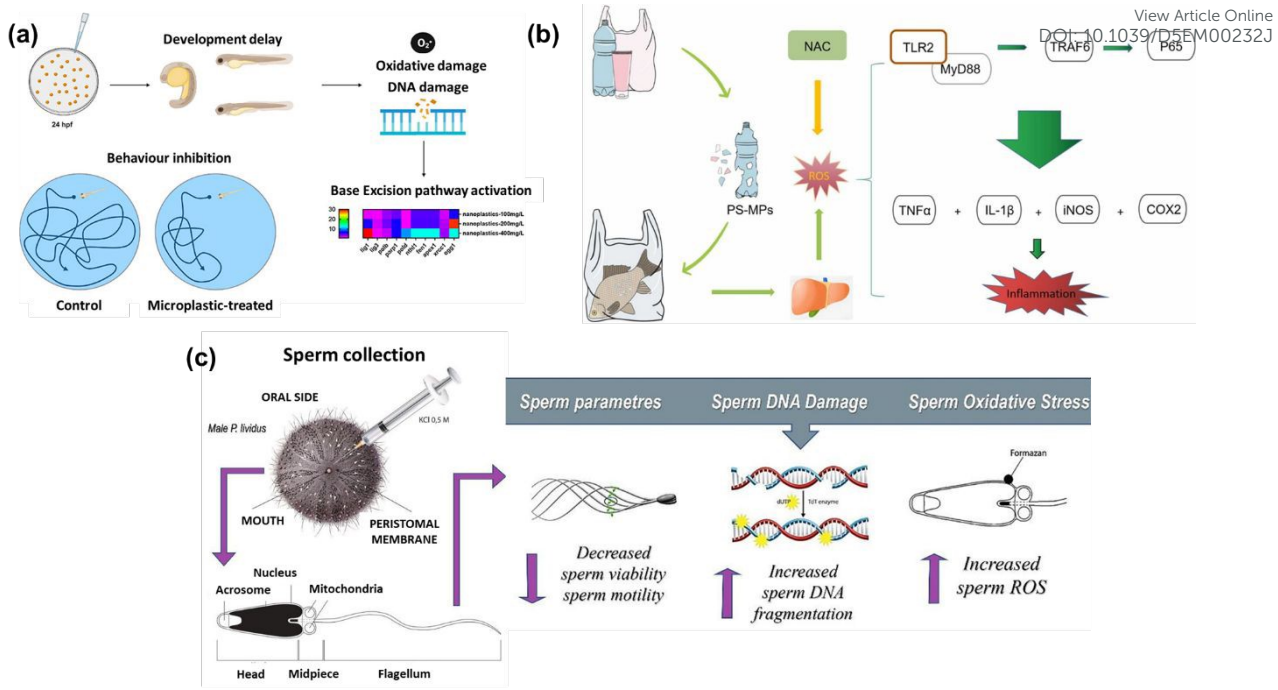


Figure 6: (a) Schematic representation of developmental toxicity induced by polystyrene plastics in zebrafish embryos, showing effects on hatching, survival, heart rate, body length, and behaviour. The exposure triggered oxidative stress and altered base excision repair pathway-related gene expression, adapted with permission **[**106]. Copyright 2022, American Chemical Society. (b) Schematic representation of immune disruption in carp (Cyprinus carpio) caused by polystyrene microplastics, showing hepatopancreas damage, oxidative stress, TLR2 pathway activation, and increased inflammatory markers and enzyme activities, adapted with permission [114**]**. Copyright 2023, Elsevier. (c) Schematic representation of the reproductive geno-toxicological effects of polystyrene microplastics on Paracentrotus lividus spermatozoa. Microplastic exposure reduced sperm viability and motility, induced DNA fragmentation via reactive oxygen species, and caused sperm agglutination, impairing movement and reproductive potential, adapted with permission [119]. Copyright 2024, Elsevier.

Microplastics contribute to inflammation by carrying pollutants and harmful microbes. When these contaminated particles enter cells or organisms the pollutants they carry can seep out causing damage to cells and oxidative stress. This stress can activate factors like nuclear factor kappa B (NF B) that control the expression of inflammatory genes. Moreover, microplastics can transport microorganisms potentially introducing them into body tissues and triggering inflammatory responses as part, of the immune defence system [113]. Chronic low-level inflammation sometimes referred to as inflammaging has been linked to the onset of various diseases such as heart problems metabolic syndrome and certain cancers. The impact of polystyrene microplastics on the immune system of carp is significant [114]. It highlights damage to the hepatopancreas, oxidative stress, activation of the TLR2 pathway and elevated levels of inflammatory markers like TNF-α, IL-1β, iNOS and COX2. Moreover, it portrays increased enzymatic activities, such as AKP, ALT, AST and LDH (**Figure 6b**). Microplastics in body tissues may trigger inflammatory responses, which affect the overall health [115]. According to recent research, microplastics may alter the gut microbiome, which could impact inflammation and immunological responses. Increased intestinal barrier depletion, inflammation, and bacterial transmission may all arise from increased gut permeability (**Table S6**).

View Article Online
DOI: 10.1039/D5EM00232J

4.3. *Genotoxicity*

The genotoxicity of microplastics arises from their capacity to interact with components, particularly DNA resulting in genetic damage and subsequent disruption [116]. Several mechanisms have been suggested to elucidate the genotoxic effects of microplastics such as the generation of ROS direct physical interaction with material and the release of toxic additives or adsorbed contaminants [117]. The strain caused by microplastics can lead to changes in chromosomes and disruptions in the spindle during cell division resulting in an abnormal number of chromosomes and other types of genetic instability. These disruptions, in cellular integrity can hinder cell function and contribute to the development of conditions [118]. Moreover, numerous plastic products contain additives like plasticizers, stabilizers and flame retardants that can seep, from the particles and demonstrate their harmful effects on genes. Exposure to polystyrene microplastics has significantly compromised spermatozoa of *Paracentrotus lividus* [119]. It reduces the viability and motility of the sperm. Furthermore, it induces DNA fragmentation, mediated by ROS and causes sperm agglutination. These effects collectively impair sperm movement, thus reducing reproductive potential (**Figure 6c**). The interaction between cells and microplastics can trigger genomic damage [120]. Researchers are exploring long-term effects and potential cancer involvement. Microplastics can also disrupt gut microbiota, leading to inflammation and increased risk of genetic harm.

4.4 *Disruption of cell signalling pathways*

The effect of plastics on cell signalling pathways raises worries in the areas of environmental toxicity and public health. Microplastics disrupt signalling primarily by interfering with receptor-mediated cell entry. They can carry pollutants that can interact with receptors on the cell membrane. For example, chemicals that disturb the endocrine system (EDCs) associated with microplastics can bind to hormone receptors and either replicate or hinder natural hormones. This can interfere with signalling pathways resulting in alterations, in cellular responses and disruptions and can be linked to various health issues including developmental problems and cancer [121]. Similar to mechanisms observed with therapeutic nanoparticles, microplastics can interfere with cell cycle regulation and apoptosis. Green-synthesised gold nanoparticles, derived from Moringa oleifera leaf extract, demonstrate notable anticancer activity by disrupting key cell signaling pathways in Dalton's lymphoma cells [122, 123]. Microplastics can trigger an imbalance in the mitogen-activated protein kinase (MAPK) pathway and the phosphoinositide 3 kinase (PI3K)/Akt pathway [124]. Microplastics interact with various cell signalling pathways that, in turn, disrupt communication and balance among cells. Microplastics can interfere with receptors on cell membranes and hence can modify pathways involved in metabolism, such as the insulin signalling pathway, potentially contributing to metabolic disorders. Blockage of calcium signalling within cells creates an imbalance in neurotransmission, muscle contraction and gene expression [125]. Microplastics also affect the immune system by disturbing both innate and adaptive immune responses, which can trigger many infections and autoimmune diseases [126]. Understanding these interactions is vital for evaluating the environmental and health risks associated with microplastic contamination and for formulating strategies to effectively address these challenges.

5. Microplastics and Cancer Development

Microplastics may contribute to cancer mainly by inducing stress that can damage DNA and cause mutations. Moreover, microplastics often carry substances, including carcinogens like polycyclic aromatic hydrocarbons (PAHs), heavy metals and compounds that disrupt the

View Article Online
DOI: 10.1039/D5EM00232J

endocrine system potentially advancing cancer progression. Research indicates that humans commonly consume microplastics via food, water and air. Once inside the body, microplastics can inflict harm through various mechanisms. Research suggests that long-term inflammation caused by exposure to microplastics may contribute to the development of tumours by creating an environment. While studies on the connection between microplastics and cancer in humans are still ongoing, there is evidence from studies and cellular models that points to potential mechanisms through which these particles could play a role in cancer formation. Some laboratory and animal experiments have shown that types of microplastics can harm DNA, change gene expression and promote cell growth. Additionally, microplastics have been found to accumulate in organs such as the liver, potentially leading to inflammation and an increased cancer risk over time [127]. Emerging evidence indicates that microplastics may play a silent yet significant role in the induction of cancer by acting as persistent stressors to the body. When not performing their physical roles, microplastics act as carriers of many other carcinogenic compounds and endocrine modifiers. Tissue alienation of ingestion or inhaling through almost all pathways allows particles to find their way to vital organs and result in chronic inflammation, oxidative stress, and even genotoxic effects. Toxicity studies using cytotoxicity and animal models show that microplastics can destroy DNA, vary the expression levels of genes involved in the cell cycle, and induce uncontrolled cell proliferation. Human data are being investigated, but those molecular disruptions associated with microplastic exposure in human tissues, such as the liver, raise the possibility of the initiation and progression of cancer.

5.1 *Carcinogenic properties*

The study of the cancer-causing properties of plastics and their associated chemicals is gaining momentum. The potential of microplastics to be carcinogenic arises from factors such as their physical attributes, chemical makeup and capacity to carry other environmental toxins. These plastics can absorb pollutants from their surroundings increasing their concentration on particle surfaces which poses a significant health risk when ingested, inhaled or absorbed through the skin. A major concern surrounding the carcinogenic nature of plastics is their potential to induce stress within biological systems. When microplastics enter cells, they can cause the production of ROS that can damage components, like lipids, proteins and most critically DNA. Impairment to DNA can lead to changes in the genetic code, which play a role in the onset of cancer. Besides, microplastics have been found to activate inflammation, a state that has been associated with the development of cancer for a long time. Inflammation can create an environment by modifying cellular signalling pathways promoting cell growth and suppressing programmed cell death apoptosis. This in turn supports the beginning and advancement of tumours. The physical assets of microplastics, including size, shape, and surface charge, also play a part in their carcinogenic potential [128, 129]. Smaller microplastics can pierce cellular membranes and gather in tissues, leading to extended exposure and amplified risk of carcinogenesis [130].

The chemical composition of microplastics is an additional grave feature in their carcinogenic potential. Furthermore, some microplastics encompass additives like plasticizers and flame retardants, many of which are recognized carcinogens. Phthalates, used as plasticizers, are also connected to reproductive cancers. PAHs, which are absorbed onto the surface of microplastics in the environment, are deep-rooted carcinogens associated with lung, skin, and bladder cancers. Long-term exposure to these chemicals, mainly through ingestion or inhalation of contaminated air and water, raises fears about the cumulative risk of cancer [131]. Recent research has started to uncover the mechanisms through which microplastics and their linked chemicals may contribute to cancer development. Studies have indicated that exposure to

View Article Online
DOI: 10.1039/D5EM00232J

microplastics can modify gene expression patterns, especially in genes related to cell cycle control, programmed cell death and DNA repair [132]. In two-dimensional monolayer preparations, microplastic exposure considerably accelerates the proliferation of cancer cells. Microplastic exposure boosts spheroid growth in three-dimensional spheroid models as well [133] (**Figure 7a**). While there is a lack of human epidemiological data directly linking microplastics to cancer, studies conducted on animals and cellular models have shown that exposure to microplastics can promote cancer development through various mechanisms, including oxidative stress, inflammation and direct damage to genetic material (**Table S7**). The link between microplastics, their associated chemicals, and biological systems calls for further studies to uncover the mechanisms involved in cancer-triggering pathways and evaluate the possible risks associated with human health [134, 135].

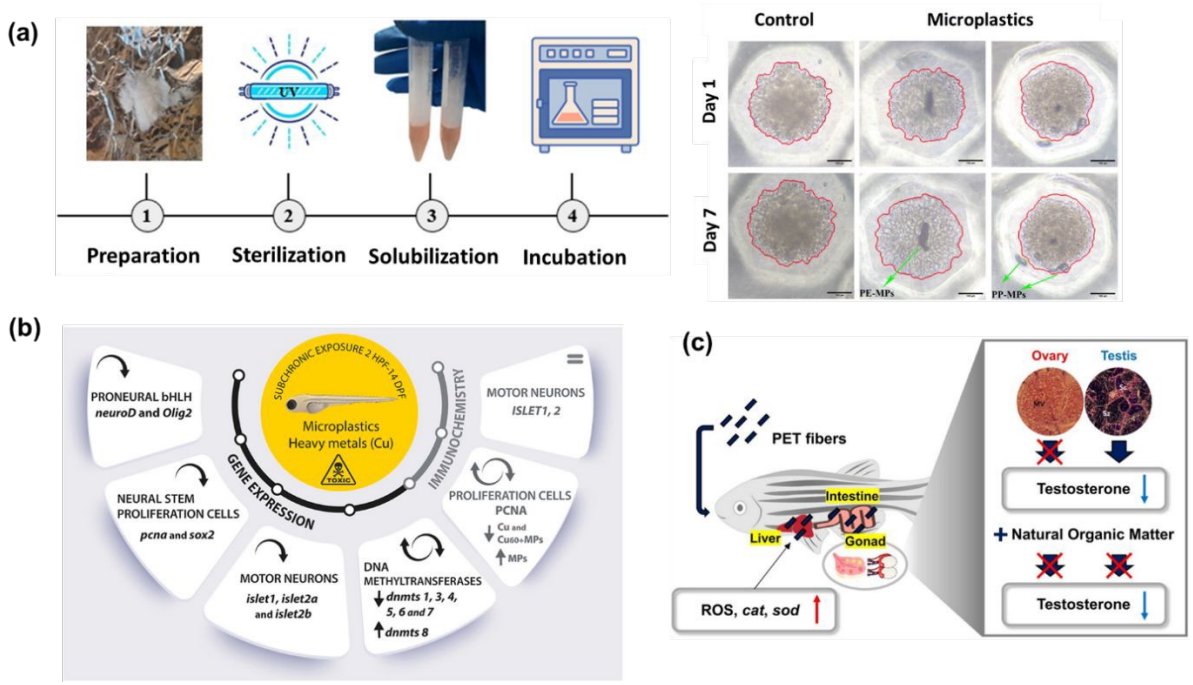


Figure 7: (a) Schematic representation of exposure of microplastics on cancer cells. Increased cancer cell proliferation in 2D models and enhanced growth of spheroids in 3D models exposed to microplastics, suggesting their potential role in tumor progression, adapted with permission [133]. Copyright 2024, Elsevier. (b) Schematic of neurotoxic effects in zebrafish embryos exposed to microplastics and copper for 14 days, showing altered neurogenesis-related genes, disrupted DNA methylation, increased retinal cell division and reduced brain and retinal proliferation, potentially impairing cognitive functions, adapted with permission [143]. Copyright 2022, Elsevier. (c) Schematic representation of microplastic accumulation in zebrafish intestines and livers, inducing oxidative stress and sex hormone disruption. Alleviated oxidative stress and hormonal dysregulation were observed, highlighting PET microplastics' ecotoxicity and endocrine disruption, adapted with permission [147]. Copyright 2024, Elsevier.

5.2 *Epigenetic changes*

Epigenetics includes differences in the expression of genes without modifying the DNA sequence [136]. These particles often carry toxic substances that can interact with the body mechanisms such, as DNA methylation histone modifications and the regulation of non-coding RNAs all of which can modify gene expression and cell function. These variations are significant for controlling processes within cells and can be affected by features like contact

View Article Online
DOI: 10.1039/D5EM00232J

with microplastics. Microplastics make changes in the way DNA is methylated, which is the process of the addition of a group to cytosine residues in precise regions of the DNA. Normally this process helps regulate gene expression by suppressing certain genes. However, exposure to microplastics disrupts these methylation patterns causing either an increase or decrease in the methylation of specific genes [137]. Hypomethylation can stimulate genes related to cancer risk while hypermethylation can silence genes that suppress tumors, endorsing the development of cancer. Moreover, microplastics and the chemicals they contain like BPA can interfere with DNA methylation patterns across the genome affecting genes involved in essential biological functions, such as cell growth, programmed cell death and immune responses [138]. Microplastic exposure also influences histone modifications. It is believed that the particles may directly interact with enzymes that modify histones or indirectly affect them by generating ROS. Microplastics can lead to changes in histone acetylation and methylation patterns resulting in altered chromatin states that either promote or hinder gene expression [139]. Microplastics are known to interact with non-coding RNAs (ncRNAs) which play a role in regulating gene expression. The impact of microplastics on miRNA expression levels has been linked to changes in gene regulation related to inflammation, cancer progression and metabolic functions. Certain miRNAs that are disrupted by microplastics can play roles as either promoting factors for tumours (oncomiRs) or inhibiting factors for tumours, depending on the situation. Through modifying levels, microplastics can encourage the growth of cells boost the potential for spreading and contribute to the onset of chronic diseases like cancer and heart conditions. Research conducted in aquatic species and mammalian cell cultures has shown that exposure to microplastics can result in varying expressions of miRNAs involved in processes such as development, immune response and stress adaptation [140, 141].

Epigenetic changes can occur through the stress caused by microplastics. This stress, resulting from the disproportionate production of ROS, has the potential to harm DNA, lipids and proteins involved in regulating epigenetics. Precisely, ROS can disrupt the activity of DNA methyltransferases accountable for maintaining DNA methylation patterns, as well as enzymes that change histones, leading to epigenetic changes that influence gene expression [142] Neurotoxic effects were observed in zebrafish embryos that were exposed to microplastics and copper over 14 days [143]. This exposure resulted in altered expression of neurogenesis-related genes and also disrupted DNA methylation patterns. Additionally, there was increased retinal cell division, but a reduction in proliferation in both brain and retinal tissues (**Figure 7b**). Notably, nanoplastics, have shown more noticeable epigenetic effects due to their capacity to penetrate cell membranes and interact with nuclear material more readily.

5.3 *Hormonal disruptions*

Endocrine-disrupting chemicals (EDCs) present in microplastics could pose risks to health because of their potential connections to tumor development. These chemicals can disrupt the systems by imitating, blocking or modifying natural hormonal functions. The tiny plastic particles may carry a range of these substances, each with varying degrees of toxicity. Notable instances include various industrial compounds and contaminants linked to tumors in hormone-sensitive organs such as the breast, prostate, ovaries, testes and thyroid. Their capacity to interfere with hormone activity might play a role in abnormal cell proliferation. Substances like BPA and phthalates can duplicate the effects of hormones like estrogen and testosterone by attaching to exact receptors. Breast and prostate cancers may be triggerd from the stimulation of estrogenic and androgen receptor signalling pathways by EDCs such as BPA and phthalates. Microplastics and associated EDCs also raise the risk of thyroid cancer by interacting with thyroid hormone signalling [144]. Microplastics can carry EDCs that disrupt hormone

signaling, potentially promoting cancers in hormone-sensitive organs like the breast, prostate, and thyroid, underscoring the urgent need for deeper investigation into their carcinogenic risks.

Another factor linking EDCs in microplastics to cancer is oxidative stress [145]. Many EDCs can produce ROS to damage DNA, proteins and lipids. BPA and phthalates have been shown to boost ROS production in various cell types resulting in DNA damage and the initiation of tumor formation. Besides causing DNA damage directly, oxidative stress can activate factors such as NF-κB and AP-1 that control the expression of genes associated with inflammation and cell growth. Persistent inflammation triggered by oxidative stress from EDCs is known to contribute to cancer advancement by creating an environment that fosters tumor growth, blood vessel formation and spread. Furthermore, the interplay between stress and epigenetic changes induced by EDCs can establish a feedback mechanism that speeds up cancer progression [146]. The accumulation of microplastics in the intestines and livers of zebrafish has induced oxidative stress and disrupted sex hormones [147]. This finding emphasizes the ecotoxicity and endocrine-disrupting potential of PET microplastics. This raises concerns because they highlight the pervasive nature of microplastics in aquatic environments (**Figure 7c**). Many studies heightened the presence of specific EDCs, in biological samples and an increased cancer risk [148, 149].

6. Evidence of Microplastics-Triggered Carcinogenesis

As microplastics accumulate in every corner of nature, they may pose health risks, including the potential to cause cancer. Microplastics can trigger carcinogenesis through various known mechanisms like inflammation, oxidative stress and many more. They can infiltrate tissues, leading to the generation of ROS, which in turn leads to stress [150]. Moreover, microplastics can serve as carriers for other harmful substances, which are known as carcinogens [151].

6.1 *Animal models studying the carcinogenic effects of microplastics*

Animal models are used to investigate the cancer-causing effects of microplastics. This is mainly significant given the complications of conducting long-term studies on humans and the challenges of simulating real-world exposure situations. Rodent models, especially mice and rats, are commonly used due to their physiological similarities to humans, well-established genetic backgrounds, and ability to control exposure [152]. Animal models, whether studying microplastic foreign-body distribution, bioaccumulation, and expulsion, or assessing primary toxicological endpoints like inflammation, oxidative stress, DNA damage, and histopathological changes of major organs, still bolster human relevance. Such exposures have led to long-term studies in rodents, which have revealed the first potential for neoplastic changes in the organs such as the liver, colon, and reproductive organs and the first hints of carcinogenic risk. In addition, very crucial for the animal models in dose-response screening to ascertain accumulation in specific organs and tissues, and reveal molecular mechanisms such as genotoxicity, endocrine disruption, and signaling pathways for tumorigenesis. They are also translational models aimed at the validation of risk assessment biomarkers for human health. The initiation and progression of cancer is a multifactorial event. Sex-related differences may further influence the outcome of an inflammatory reaction, leading to additional pathophysiological changes dependent on sex, and thus affecting the type and onset of cancer that might develop. Studies have demonstrated that long-term repeated oral or airborne microplastic exposure in rodent models leads to pre-cancerous lesions, gut dysbiosis related to carcinogenesis, and immune dysregulation. Therefore, these models are significant for regulatory toxicology and cancer research [153, 154].

In animal studies, microplastics are given through methods such as oral gavage, drinking water or inhalation to mimic the most common pathways of human exposure. Oral ingestion studies are especially prevalent since food and water serve as primary routes for human exposure. Once consumed, microplastics can transfer from circulation and accumulate in various tissues and organs. Animal studies have shown that microplastics promote stress, inflammation and cytotoxicity to cells, which are aspects that can contribute to the development of cancer [155]. For example, constant consumption of microplastics in mice has caused lesions, liver scarring and increased levels of ROS [156]. Experimental studies on mice have shown that long-term exposure to PE microplastics can lead to inflammation in the colon and changes in gut microbiome structure leads to risk factors for colorectal cancer [157]. This accumulation was linked, to changes in metabolism and oxidative stress markers both of which play roles, in cancer progression [158]. Regarding cancer studies involving female rats have indicated that exposure to bisphenol A (BPA), a common plastic additive found in microplastics, can promote the formation of tumors in the mammary glands. Specifically, exposure to BPA at levels found in the environment during pregnancy affected the growth of mammary glands and heightened the risk of cancer-causing substances in adult rats. Inhalation studies on rats suggested the potential cancer-causing effects of microplastics in the air. Research indicated that breathing in polyethene and polyvinyl chloride microplastics resulted in inflammation of the lungs and oxidative stress, which are factors that could potentially play a role in the onset of lung cancer over extended periods [159].

In toxicology studies, zebrafish serve as a model for examining the impact of microplastic exposure on various stages of development [160]. Studies have revealed that microplastics can harm tissues and elevate the expression of the p53 gene in zebrafish embryos. Extended exposure to plastics in zebrafish leads to bioaccumulation, oxidative stress and impaired cell function, potentially playing a role in tumor formation. Additionally, the transparent nature of zebrafish embryos enables real-time monitoring of these detrimental effects [161]. Invertebrate models like Drosophila melanogaster can also offer an additional outlook on the impact of microplastics on cancer development [162]. Although animal models shed light on possible carcinogenic effects of microplastics, it is debatable whether these models can be applied to actual circumstances. The spread of microplastics in animal tissues can be studied with the use of advances in imaging techniques [163].

6.2 *Studies on cell lines for the carcinogenic effects of microplastics*

Recent studies evaluating the potential toxicity, genetic toxicity, and carcinogenic factors of plastics in controlled laboratory environments have sparked considerable attention on the effects of plastics on cell lines [164]. Findings indicate that microplastics can lead to stress, inflammation and DNA damage, which are all crucial factors, in the process of cancer formation. Research has shown that microplastics can trigger immune system responses by stimulating cytokine production in cells like macrophages. This process may lead to promoting an environment that promotes tumour growth. Future research should focus on combining studies, with 3D cell culture models and organoid systems to gain a better understanding of the effects of microplastic exposure on human health [165].

6.3 *Epidemiology linking microplastic exposure to cancer incidence*

Microplastics can serve as carriers for harmful chemicals and plastic additives, many of which are also documented as carcinogens or disruptors of the endocrine system [166]. Prolonged exposure to these substances has been associated with various types of cancer, such as breast,

View Article Online
DOI: 10.1039/D5EM00232J

prostate and liver cancer. Certain studies have explored the risks of encountering plastic dust in workplaces such as manufacturing and recycling, where employees are more likely to breathe in microplastic particles. These investigations have shown occurrences of lung diseases, including cancer, suggesting that long-term exposure to airborne microplastics could have cancer-causing effects [167, 168]. With the increasing prevalence of microplastics in our surroundings, examining their potential involvement in cancer development remains an important field of study. Linking microplastic exposure with cancer incidence is still emerging and remains very limited due to some of the major challenges. For example, microplastics have already been discovered to carry non-exclusively carcinogenic additives and endocrine-disrupting chemicals, and some occupational studies report inhaled plastic dust with increased risk for lung diseases, including cancer; however, these studies were based on small sample sizes and did not involve a thorough assessment of exposure. Most of the available studies rely on indirect indicators of exposure, such as occupational setting or environmental contamination, rather than precise quantification of microplastics, leading to uncertainties in dose-response relationships. These limitations mean that clear causal inferences on humans will not be available between exposure and cancer development. Future epidemiological studies should focus on the standardized implementation of methodologies for microplastic detection in biological samples, better control of confounding factors, and longitudinal designs to capture the cumulative effects of chronic low-dose exposure. While waiting for this data to be generated, epidemiological results available today are to be interpreted with caution, further emphasizing the urgent need for more human studies.

7. Different Types of Cancers Caused by Microplastic Exposure

Recent studies have raised concerns over microplastic materials as potential carcinogens, because they have become widely distributed in the environment and bioaccumulate. As physical irritants of the body, microplastics also act as chemical vectors for toxic additives and adsorbed pollutants, thereby presenting complex risks to human health. Although evidence regarding direct effects on humans is yet scant, consistent in vivo and in vitro evidence suggests that microplastic exposure may be associated with the development of different types of cancers, including colorectal, liver, lung, reproductive, renal, and possibly haematological malignancies. Oral exposure in some cases has been linked with impaired gut barrier function, dysbiosis, and inflammation, which are known to result in DNA damage, susceptible to the development of colorectal cancer [166]. The effects of microplastic exposure precondition the body for the development of different cancers through gut, liver, and lung exposure. Oral ingestion causes gut barrier dysfunction, dysbiosis, inflammation, and DNA damage, which are factors known to contribute to colorectal cancer. In the liver, microplastics are also known to cause oxidative stress, thus promoting fibrosis and accumulation of toxicants, resulting in the possible development of hepatocellular carcinoma [169]. Inhaled microplastics can get stuck in the alveolar tissues, leading to a chronic inflammatory response along with fibrotic changes, which can lead to lung cancer [170]. Moreover, microplastics containing endocrine-disrupting chemicals include BPA and phthalates, and these endocrine disruptors are related to hormone-driven cancers, mainly those found in the breast, ovary, and prostate [171, 172]. In addition, they have been shown to have reproductive toxicity in rodent models. Exposure to kidneys and bladder due to contaminated water has induced nephrotoxic and genotoxic effects in animal studies, probably to urinary cancers [173]. In addition, microplastics might be involved with hematopoietic cells and affect immune function, thus raising concerns about blood cancers.

Microplastics can trigger cancer, probably through oxidative stress, inflammation, genotoxicity, endocrine disruption, and immune modulation. With rising exposure levels to microplastics, it is critical to conduct further mechanistic and longitudinal studies that trace clear causal relationships and aid in risk mitigation strategies. Polyethene-derived microplastics (5–60 μm), assumed to be taken into the body through food and water contamination, were shown in vitro to reduce viability and induce mitochondrial oxidative stress on human colorectal adenocarcinoma cells (Caco-2 and HT-29). Such findings suggest that polyethylene may promote gastrointestinal carcinogenesis through cytotoxicity and mitochondrial dysfunction, two key player mechanisms in cancer initiation [174]. Due to their small size, microplastics can penetrate tissue barriers and cellular membranes, engendering inflammatory responses and oxidative stress that may further enhance carcinogenesis. The present knowledge indicates that while microplastics may not be primary carcinogens, they are likely to function in conjunction with other carcinogenic agents, thus acting as co-carcinogenic agents or tumor promoters in several processes, which may add to the complex multifactorial development of several types of cancer.

8. Detection and Analysis of Microplastics in Biological Samples

Detecting and studying microplastics in biological samples is crucial for assessing their effects on both human and environmental health. The process of analysing microplastics in tissues, fluids or cells involves several steps, like collecting samples isolating the plastic particles and characterizing them (**Figure 8a**). Common approaches include using digestion protocols to eliminate matter followed by filtration to separate microplastics from the sample. Density-mediated separation procedures, enzymatic digestion and filtration are widely used to separate microplastics from biological sources. Microscopic methods including light and electron microscopy deliver insights into morphological features [175]. Techniques like Fourier Transform Infrared Spectroscopy (FTIR) and Raman spectroscopy are frequently employed to confirm the chemical composition of microplastics. By examining their distinct vibrational patterns, these techniques can distinguish between different kinds of polymers. Pyrolysis Gas Chromatography Mass Spectrometry (Pyr GC MS) is a further successful method that not only measures the number of microplastics in biological specimens but also ascertains the polymer content by breaking the particles down into their components. Fluorescent tagging can also be used to track the absorption as well as distribution of microplastics in tissues and cells. More detailed and effective analyses of microplastics in biological samples may be possible with the use of more recent technologies such as hyperspectral imaging and Thermal Extraction Desorption Gas Chromatography Mass Spectrometry (TED GC MS) [176].

View Article Online
DOI: 10.1039/D5EM00232J

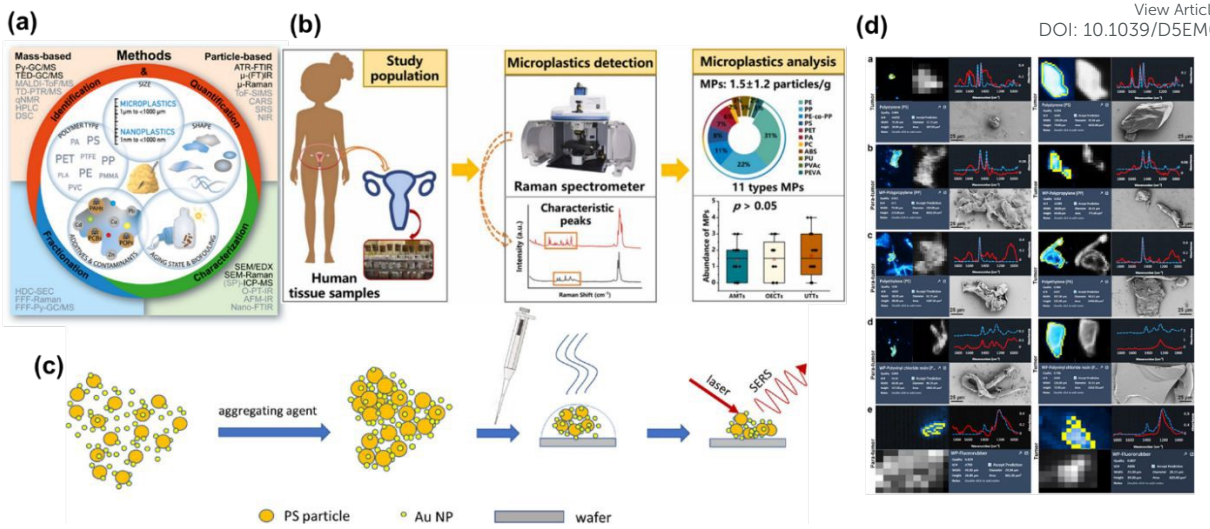


Figure 8: (a) Schematic representation of the chemical analysis of microplastics, outlining current challenges, advanced analytical methods, and future perspectives, adapted with permission [177]. Copyright 2021, American Chemical Society. (b) Schematic of microplastic detection in adenomyosis, ovarian ectopic cysts, and uterine tube tissues using micro-Raman spectroscopy. Most microplastics were fibres or fragments and under 20 µm, highlighting their presence in reproductive tissues and potential links to disease, adapted with permission [179]. Copyright 2024, Elsevier. (c) Schematic representation of microplastic detection using SERS adapted with permission [186]. Copyright 2023, Elsevier. (d) Representative laser direct infrared spectroscopy and SEM images of microplastics in paired para-tumour and tumor prostate tissues from patients undergoing radical prostatectomy. The study provided qualitative and quantitative evidence of the microplastics presence as well as their properties, types, and abundance in paired para-tumour and tumor samples of human prostate, adapted with permission [192]. Copyright 2024, Elsevier.

8.1 *Techniques for detecting microplastics in human tissues*

Detecting microplastics in human tissues involves using sophisticated techniques and methods to identify, measure and analyze these tiny particles, which usually vary in size from a few microns to millimetres [177]. Advanced techniques like Raman and FTIR spectroscopy are used to find microplastics in human tissues. While Raman spectroscopy offers spatial resolution for recognizing tiny particles embedded in tissues, FTIR uses vibrational patterns to identify plastic particles [178]. Additionally, Raman microscopy can penetrate deeper into samples and even detect nanoplastics. Microplastics have been detected in adenomyosis, ovarian ectopic cysts and uterine tube tissues via micro-Raman spectroscopy [179]. The primary forms identified were fibers and fragments, with most measuring less than 20 µm in size. These findings highlight the existence of microplastics in reproductive tissues; however, they also suggest potential associations with disease pathogenesis (**Figure 8b**). FTIR proves effective in examining particles exceeding 10 micrometers in size, whereas Raman spectroscopy can identify particles down to 1 micrometer [180]. Scanning electron microscopy (SEM) combined with energy-dispersive X-ray spectroscopy (EDS) is employed to offer insights into the structure and elemental composition of microplastics. SEM unveils the form and surface characteristics of particles, potentially revealing their origin and level of deterioration.

Another technique that is gaining traction is pyrolysis gas chromatography-mass spectrometry (Py GC MS). It is highly sensitive and can detect microplastics in low concentrations within

complex biological samples. Additionally, Nile Red staining a fluorescent dye that adheres to particles like plastics, is used for quickly screening microplastics in tissues. Under a microscope, this dye reveals the presence of plastic particles although it sometimes lacks specificity as it can also bind to other hydrophobic substances. Another approach called thermogravimetric analysis (TGA) assesses the degradation pattern of tissue samples to differentiate between matter and synthetic polymers, offering a means to estimate the amount of microplastics based on their distinct thermal breakdown properties [181]. Laser direct infrared (LDIR) imaging, chromatography combined with mass spectrometry (LCMS) and field flow fractionation (FFF) are currently used in in laboratory but their application in biological tissues is still in its infancy. Additionally, sample preparation methods like digestion with strong chemicals can lead to a decrease in accuracy [182]. The integration of these methods, along with a redefined sample preparation strategy, can enhance the positive results. (**Table S8**).

8.2 *Advances in analytical methods for microplastic characterization*

Recent advancements in modifying current analytical techniques for characterizing microplastics have greatly improved our capability to identify and quantify the microplastics across various environmental and biological samples. Innovations like micro FTIR, optical photothermal infrared (O-PTIR) spectroscopy and confocal Raman imaging systems make this task a bit easier. Raman spectroscopy has been upgraded with setups that deliver sub-micron spatial accuracy, allowing for the discovery of even smaller microplastic particles, including nanoplastics. Innovative methods such as coherent anti-Stokes Raman scattering (CARS) microscopy hold the potential for fast imaging of microplastics in biological tissues without the need for labels. Surface-enhanced Raman spectroscopy (SERS) represents a sophisticated analytical approach that significantly amplifies Raman fingerprints of molecules that are interacting with the nanostructured metal surfaces. In the realm of microplastic detection. SERS improves both the sensitivity and specificity when it comes to identifying various polymer subtypes, even at nanomolar concentrations (**Figure 8c**). This quality renders SERS especially valuable for investigating microplastics within intricate matrices, such as biological tissues or environmental samples, although challenges remain in achieving consistent results [183, 184, 185, 186].

Atomic force microscopy (AFM) offers insights into surface features that can uncover how microplastics interact with their surroundings. Particularly, LDIR stands out by swiftly mapping the chemical composition of microplastics across extensive regions proving to be an asset, for monitoring purposes. The introduction of mass spectrometry techniques like Orbitrap and Fourier transform ion cyclotron resonance has made it possible to detect nanoplastics and better understand their degradation products [187]. Methods such as field flow fractionation FFF show potential in analyzing microplastics by separating particles based on size and mass although they are still being developed. Moreover, synchrotron-based methods like X-ray microtomography and X-ray fluorescence microscopy are being investigated for non-destructive three-dimensional analysis of microplastics in complex environments [188]. New approaches in microplastic characterisation involve using dyes and probes for quick screening and flow cytometry for efficient size and polymer type assessment. Additionally, advancements in learning and artificial intelligence AI are starting to assist in microplastic analysis through algorithms that automate particle identification and classification in spectroscopic data, reducing errors and expediting the process [189].

View Article Online
DOI: 10.1039/D5EM00232J

8.3 *Challenges in quantifying microplastic exposure in biological samples*

Measurement of microplastics in biological samples is challenging because both the microplastics and the biological materials involved are heterogeneous. One main complication is the absence of standardized procedures for collecting, preparing and analyzing samples. This inconsistency results in variations in findings across different studies [190]. Direct detection methods such as FTIR and Raman spectroscopy might face challenges in spotting nanoplastics due to lack of sample concentration. Py GC MS and TGA could miss out on details regarding the particle's origin shape, or surface features due to losing spatial or morphological information. Microplastics typically ranging in size from 1 μm to 5 mm require a mix of techniques for analysis since no single approach can effectively capture and describe particles throughout this entire spectrum [191]. Laser direct infrared spectroscopy and SEM imaging were employed to analyze microplastics in paired para-tumour and tumor prostate tissues from patients undergoing radical prostatectomy [192]. The study provided both qualitative and quantitative evidence of microplastic presence, detailing their properties, types, and abundance in the paired tissue samples (**Figure 8d**). Tissues, blood and other bodily fluids often necessitate sample preparation procedures such as digestion and purification, which may alter or damage the microplastics in the sample [193]. Stringent contamination control measures, like using blank samples and maintaining clean air cabinets, are essential, though not always practical in every laboratory setting. Likewise, distinguishing between microplastics and other particles in biological tissues is not an easy task. Particles like soot, minerals or decomposed natural materials can be wrongly identified as microplastics, especially when basic visual or optical microscopy techniques are used. While methods offer accuracy, they require equipment that can be costly and complex, making them less accessible for many researchers. Besides the challenges in detection, measuring the concentration of microplastics in samples is also difficult due to variations in sensitivity among current analytical methods [194].

9. Future Directions and Research Needs

Future studies assessing the impact of microplastics on tumor progression and cellular impairment can unravel how microplastics contribute to tumor formation. In this line, it is important to conduct long-term exposure studies in appropriate *in vitro* and *in vivo* models to assess the impact on various tissues and organs. In-depth investigations to understand the possible interactions between microplastics and associated carcinogens could yield valuable insights. The accumulation of microplastics in immune cells and tissues needs to be carefully calibrated as it can damage the homeostasis of the entire physiological system, leading towards a multitude of diseases [195].

9.1 *Standardized protocols for microplastic research in oncology*

Launching defined protocols for conducting studies on microplastics related to oncology is essential to ensure consistent and trustworthy results. At present the absence of standard approaches hinders the comparison of data across different studies making it challenging to reach definitive conclusions regarding the influence of microplastics on the onset of cancer. In terms of collection procedures protocols need to consider various sources of microplastics such as air, water, food and consumer products as well, as methods for obtaining samples from humans and animal subjects. Uniform procedures for extracting microplastics from matrices like tissue samples or blood are vital since existing techniques vary significantly and could

introduce bias or inaccuracies. Additionally, analytical protocols should encompass a range of methods, including techniques and advanced microscopy approaches, for identifying and characterizing microplastics. To ensure reporting of microplastic concentrations in different sample types it is crucial to standardize quantification methods. Additionally developing guidelines for experimental models, in vitro and in vivo is essential. Establishing toxicological assays to evaluate key endpoints like cytotoxicity, genotoxicity, oxidative stress and inflammation is crucial for assessing the cancer risk associated with microplastic exposure. Aligning these approaches will improve the consistency of research results and support meta-analyses and regulatory evaluations [196, 197].

9.2 *Emerging technologies for removing microplastics from the environment*

Magnetic nanocomposites are attracting interest due to their capacity to absorb microplastics and their easy removal through magnetic fields. In terms of methods, new coagulation and flocculation agents are being developed to specifically target microplastics causing them to clump together for removal through traditional water treatment processes. Another technology in progress is based on filtration systems that use natural materials such as cellulose, chitosan and alginate to capture microplastics in water. These biodegradable filters decompose after use to minimize the risk of pollution. Photocatalysts like titanium dioxide (TiO2) and zinc oxide (ZnO) can crack microplastics when exposed to UV light. In the meantime, bioremediation methods using certain bacteria and fungi to degrade plastics into smaller molecules are also explored. Many microorganisms have enzymes capable of managing the polymer. Moreover, the development of plastic-eating caterpillars and other organisms offers interesting possibilities for bioengineered approaches to combat plastic pollution. Autonomous cleanup technologies can be developed to collect microplastics from the surface in an easy manner. As these innovative solutions are developed further it will be important to expand their implementation and incorporate them into comprehensive environmental management plans to address the microplastic pollution challenge [198, 199].

9.3 *Regulatory measures to mitigate human exposure to microplastics*

As more evidence emerges regarding the presence of microplastics in air, water, food and consumer goods several nations have already enacted laws prohibiting microplastics in personal care products setting a precedent for additional regulations across other sectors [200]. In this context, the European Union has put forward a strategy to ban the use of microplastics in products like cosmetics, cleaning agents and fertilizers. Comparable measures have also been announced or suggested in countries such as the United States, Canada and South Korea [201]. In addition to tackling plastic waste, governments are introducing standards to curb microplastic emissions from activities like industries, wastewater treatment plants and stormwater runoff. These standards mandate the use of technologies to filter out microplastics before they seep into natural ecosystems. In the textile and automotive sectors, regulations are being crafted to reduce the release of microfibers from synthetic fabrics and particles from tyre wear, both major contributors to microplastic pollution. [172] Moreover, efforts are underway to establish frameworks for monitoring and controlling microplastics in drinking water and food products, especially seafood, where contamination levels can be significant goal is to gather a more consistent and comparable set of data on microplastic pollution levels that can guide future regulatory choices. It is indispensable for organizations like the World Health Organization (WHO) and the United Nations Environment Programme (UNEP) to work

View Article Online
DOI: 10.1039/D5EM00232J

together in launching global standards and coordinating efforts to minimize human exposure. As more information is gathered on the toxic effects of microplastics, the regulatory frameworks need to be regularly revised to integrate new findings and adopt policies for reducing the presence and impact of microplastics in the environment and food supply [203].

9.4 *Need for interdisciplinary research*

Researchers play a role in examining the properties of microplastics such as their size, shape and surface characteristics to gain insights into their biological interactions. To improve methods for detecting and studying microplastics in different settings and biological specimens, analytical chemists and materials scientists are crucial. They also explore how various types of plastics influence interactions, based on their physical and chemical attributes. Their expertise is vital for creating detection methods that can spot microplastics, within human tissues [204]. By working alongside oncologists these research initiatives aim to evaluate the potential effects of microplastics on tumor formation and cellular signaling pathways. Additionally, pharmacologists and biomedical scientists are required to study whether microplastics affect drug delivery systems, particularly in terms of transporting chemicals or impairing the effectiveness of cancer treatments. Immunologists play a critical role in examining the potential effects of microplastics on the immune system, which could end up in immunological suppression or chronic inflammation, both of which are associated with the growth of cancer. It is possible to simulate the interactions between microplastics and biological processes and anticipate their long-term health impacts by leveraging developments in bioinformatics and modelling. By planning and carrying out studies to investigate possible relationships between exposure to microplastics and cancer rates in populations, as well as by creating risk assessment frameworks, epidemiologists and public health researchers also contribute [205, 206]. Bridging knowledge gaps, integrating various approaches, and comprehending the risks associated with microplastics in the development of cancer are all made possible through collaborative research, which also helps to shape future studies, strategies, and regulatory policies.

10. Conclusions

Human health problems arising due to microplastics have become a growing concern especially in relation to cancer risk. While the initial data tend to show a potential correlation between microplastic exposure and cancer, many knowledge gaps remain. This includes a dearth of knowledge in such areas as mechanism-specific causation, long-term effects of chronic low-dose exposure, and the influence of particle size, type, and environmental interactions. The complex nature of microplastics puts a further complication into risk assessment. Clinical and epidemiological studies of comprehensive proportions are urgently needed to fill in these gaps and delineate these risks toward the development of evidence-based prevention programs. Closing these knowledge gaps is vital to support relevant public health decision-making and to protect human health in the long run.

11. **Acknowledgement**

Author (MMJ) thanks CHRIST University for the Seed Money Grant (CU-ORS-SM-24/04). The author JBN Thanks to European Union Horizon PF research and innovation program under the Marie Skłodowska-Curie grant agreement No 101151173.

12. Reference

1. Xu S, Ma J, Ji R, Pan K, Miao A J. Microplastics in aquatic environments: Occurrence, accumulation, and biological effects. Sci. Total Environ. 2020; 703:134699.
2. Schmid C, Cozzarini L, Zambello E. Microplastic's story. Mar. Pollut. Bull. 2021; 162: 111820.
3. Kumar N, Lamba M, Pachar AK, Yadav S, Acharya A. Microplastics - a growing concern as carcinogens in cancer etiology: emphasis on biochemical and molecular mechanisms. Cell Biochem Biophys. 2024;82(4):3109-3121.
4. Carvalho FH, Lôbo-HG. Microplastics in coastal and oceanic surface waters and their role as carriers of pollutants of emerging concern in marine organisms. Mar. Environ. Res. 2023; 188: 106021.
5. Issac MN, Kandasubramanian, B. Effect of microplastics in water and aquatic systems. Environ Sci Pollut Res Int. 2021; 28(16): 19544–19562.
6. Zhu X, Qiang L, Shi H, Cheng J. Bioaccumulation of microplastics and its in vivo interactions with trace metals in edible oysters. Mar. Pollut. Bull. 2020; 154: 111079.
7. Scott JW, Gunderson KG, Green LA, Rediske RR, Steinman AD. Perfluoroalkylated substances (pfas) associated with microplastics in a lake environment. Toxics. 2021; 9(5): 106.
8. Wang LC, Lin JC, Dong CD, Chen CW, Liu TK. The sorption of persistent organic pollutants in microplastics from the coastal environment. J. Hazard. Mater. 2021; 420: 126658.
9. He S, Wei Y, Yang C, He Z. Interactions of microplastics and soil pollutants in soil-plant systems. Environ. Pollut. 2022; 315: 120357.
10. Raza M, Lee JY, Cha J. Microplastics in soil and freshwater: Understanding sources, distribution, potential impacts, and regulations for management. Sci. Prog. 2022; 105(3): 368504221126676.
11. Caba-Flores MD, Martínez-Valenzuela C, Cárdenas-Tueme, M, Camacho-Morales A. Micro problems with macro consequences: accumulation of persistent organic pollutants and microplastics in human breast milk and in human milk substitutes. Environ Sci Pollut Res Int. 2023; 30(42): 95139–95154.
12. Zhu G, Yue K, Ni X, Yuan C, Wu F. The types of microplastics, heavy metals, and adsorption environments control the microplastic adsorption capacity of heavy metals. Environ Sci Pollut Res Int. 2023; 30(33): 80807–80816.
13. Rhodes C J. Plastic pollution and potential solutions. SCI Prog.2018; 101(3): 207–260.
14. Li W, Zu B, Yang Q, Guo J, Li J. Sources, distribution, and environmental effects of microplastics: a systematic review. RSC advances. 2023; 13(23): 15566–15574.
15. Shahsavaripour, M, Abbas, S, Mirzaee, M, Amiri H. Human occupational exposure to microplastics: A cross-sectional study in a plastic products manufacturing plant. Sci. Total Environ. 2023; 882: 163576.
16. Domenech, J, Annangi B, Marcos R, Hernández A, Catalán J. Insights into the potential carcinogenicity of micro- and nano-plastics. Mutation research. Mutat Res-Rev Mutat. 2023; 791: 108453.

17. Barguilla I, Domenech J, Ballesteros S, Rubio L, Marcos R, Hernández A. Long-term exposure to nanoplastics alters molecular and functional traits related to the carcinogenic process. J. Hazard. Mater. 2022; 438: 129470.
18. Ullah S, Ahmad S, Guo X, Ullah S, Ullah S, Nabi G, et al. A review of the endocrine disrupting effects of micro and nano plastic and their associated chemicals in mammals. Front. Endocrinol. 2023; 13: 1084236.
19. Li Y, Chen L, Zhou N, Chen Y, Ling Z, Xiang P. Microplastics in the human body: A comprehensive review of exposure, distribution, migration mechanisms, and toxicity. Sci. Total Environ. 2024; 946: 174215.
20. Thacharodi A, Meenatchi R, Hassan S, Hussain N, Bhat MA, Arockiaraj J, et al. Pugazhendhi A. Microplastics in the environment: A critical overview on its fate, toxicity, implications, management, and bioremediation strategies. J Environ Manage. 2023; ;349:119433.
21. Steiner T, Zhang Y, Möller JN, Agarwal S, Löder MGJ, Greiner A, et al. Municipal biowaste treatment plants contribute to the contamination of the environment with residues of biodegradable plastics with putative higher persistence potential. Sci Rep. 2022; 12(1): 9021.
22. Zhou C, Bi R, Su C, Liu W, Wang T. The emerging issue of microplastics in marine environment: A bibliometric analysis from 2004 to 2020. Mar Pollut Bull. 2022; 179:113712.
23. Sun M Y, Guo JY, Wang XY, Chang X. Sources and distributions of microplastics and the hazards to plants, animals and human health: A review. J. Appl. Ecol. 2024; 35(8): 2301–2312.
24. Li C, Li X, Bank MS, Dong T, Fang J K., Leusch FDL., Rillig MC, et al. The "microplastome" - a holistic perspective to capture the real-world ecology of microplastics. Environ. Sci. Technol. 2024; 58(9): 4060–4069.
25. O'Brien S, Rauert C, Ribeiro F, Okoffo ED, Burrows SD, O'Brien JW, et al. There's something in the air: A review of sources, prevalence and behaviour of microplastics in the atmosphere. Sci. Total Environ. 2023: 874, 162193.
26. Andrady A L. The plastic in microplastics: A review. Mar. Pollut. Bull. 2017; 119(1): 12–22.
27. Polukarova, M, Hjort M, Gustafsson M. Comprehensive approach to national tire wear emissions: Challenges and implications. Sci. Total Environ. 2024; 924: 171391.
28. Werbowski LM, Gilbreath AN, Munno K, Xia Z, Grbic J, Wu T, et al. Urban stormwater runoff: a major pathway for anthropogenic particles, black rubbery fragments, and other types of microplastics to urban receiving waters. ACS EST Water. 2021; 1(6): 1420–1428.
29. Rezaei M, Abbasi S, Pourmahmood H, Oleszczuk P, Ritsema C, Turner A. Microplastics in agricultural soils from a semi-arid region and their transport by wind erosion. Environ. Res. 2022; 212(Pt B): 113213.
30. Tang KHD. Microplastics in agricultural soils in China: Sources, impacts and solutions. Environ. Pollut. 2023; 322: 121235.
31. Shim WJ, Thomposon RC. Microplastics in the ocean. Arch. Environ. Contam. Toxicol. 2015; 69(3): 265–268.
32. Andrady AL. Microplastics in the marine environment. Mar. Pollut. Bull. 2011; 62(8): 1596–1605.

33. Janakiram R, Keerthivasan R, Janani R, Ramasundaram S, Martin MV, Venkatesan R, et al. Seasonal distribution of microplastics in surface waters of the Northern Indian Ocean. Mar. Pollut. Bull. 2023; 190: 114838.
34. Liss P S. Microplastics: All up in the air?. Mar. Pollut. Bull. 2020; 153: 110952.
35. Xie Y, Li Y, Feng Y, Cheng W, Wang Y. Inhalable microplastics prevails in air: Exploring the size detection limit. Environ. Int. 2022; 162: 107151.
36. Kelkar VP, Rolsky CB, Pant A, Green MD, Tongay S, Halden RU. Chemical and physical changes of microplastics during sterilization by chlorination. Water Res. 2019: 163: 114871.
37. Lin T, Su J. The fate of microplastics and organic matter leaching behavior during chlorination. Chemosphere. 2022; 302: 134892.
38. Glazier HA. Microplastics and Nanoplastics in Atheromas. N Engl J Med. 2024; 390(18): 1727–1728.
39. Ferreira I, Venâncio C, Lopes I, Oliveira M. Nanoplastics and marine organisms: What has been studied?. Environ. Toxicol. Pharmacol. 2019; 67: 1–7.
40. Tanoiri H, Nakano H, Arakawa H, Hattori RS, Yokota M. Inclusion of shape parameters increases the accuracy of 3D models for microplastics mass quantification. Mar. Pollut. Bull. 2021; 171: 112749.
41. Schenkel CA, Brown MRM, Lenczewski ME. Impact of type and shape of microplastics on the transport in column experiments. Ground Water. 2024; 62(4): 537–547.
42. Ríos JM, TesitoreG, de Mello FT. Does color play a predominant role in the intake of microplastics fragments by freshwater fish: an experimental approach with *Psalidodon eigenmanniorum*. Environ Sci Pollut Res Int. 2022; 29(32): 49457–49464.
43. Huang Y, Yang Z, Wang T, Sun N, Duan Z, Wigmosta M, et al. Quantifying the influence of size, shape, and density of microplastics on their transport modes: A modeling approach. Mar. Pollut. Bull. 2024; 203: 116461.
44. Kedzierski M, Palazot M, Soccalingame L, Falcou-Préfol M, Gorsky G, Galgani F, et al. Chemical composition of microplastics floating on the surface of the Mediterranean Sea. Mar. Pollut. Bull. 2022; 174: 113284.
45. Muthulakshmi L, Mohan S, Tatarchuk T. Microplastics in water: types, detection, and removal strategies. Environ Sci Pollut Res Int. 2023; 30(36): 84933–84948.
46. Ning Z, Zhou S, Li P, Li R, Liu F, Zhao Z, et al. Exaggerated interaction of biofilm-developed microplastics and contaminants in aquatic environments. Chemosphere. 2023; 345: 140509.
47. Ali SS, Elsamahy T, Al-Tohamy R, Sun J. A critical review of microplastics in aquatic ecosystems: Degradation mechanisms and removing strategies. Environ Sci Ecotech. 2024; 21: 100427.
48. Du H, Xie Y, Wang J. Microplastic degradation methods and corresponding degradation mechanism: Research status and future perspectives. J. Hazard. Mater. 2021; 418: 126377.
49. Nikhar S, Kumar P, Chakraborty M. A review on microplastics degradation with MOF: Mechanism and action. N. Nanotechnol. 2024; 5: 100060.
50. da Silva LF, Soroldoni S, Kessler F, Fernandes AN, Pinho GLL. Influence of UV exposure time and simulated marine environment on different microplastic degradation. Environ Sci Pollut Res Int. 2023; 30(58): 121450–121464.

51. Pfohl P, Wagner M, Meyer L, Domercq P, Praetorius A, Hüffer T, et al. (2022). Environmental degradation of microplastics: how to measure fragmentation rates to secondary micro- and nanoplastic fragments and dissociation into dissolved organics. Environ. Sci. Technol. 2022; 56(16): 11323–11334.
52. Lv M, Jiang B, Xing Y, Ya H, Zhang T, Wang X. Recent advances in the breakdown of microplastics: strategies and future prospects. Environ Sci Pollut Res Int. 2022; 29(44): 65887–65903.
53. Roy S, Sarkar DJ, Chakraborty N, Mondal K, Das BK. Bioaccumulation of polystyrene microplastics and changes in antioxidant and AChE pattern in a freshwater snail (*Filopaludina bengalensis*) from river Ganga. Aquat. Toxicol. 2023; 263: 106697.
54. Awewomom J, Ashie WB, Dzeble F. Microplastics in Ghana: An in-depth review of research, environmental threats, sources, and impacts on ecosystems and human health. Heliyo. 2024; 10(11): e32554.
55. Au SY, Lee CM, Weinstein JE, van den Hurk P, Klaine SJ. Trophic transfer of microplastics in aquatic ecosystems: Identifying critical research needs. Integr Environ Asses. 2017; 13(3): 505–509.
56. Mariani F, Di Lernia, D, Venditti I, Pelella E, Muzzi M, Di GA, et al. Trophic transfer of microplastics from producer (*Lemna minuta*) to primary consumer (*Cataclysta lemnata*) in a freshwater food chain. *Sci. Total Environ*. 2023; 891: 164459.
57. Sahu S, Kaur A, Khatri M, Singh G, Arya SK. A review on cutinases enzyme in degradation of microplastics. J. Environ. Manage. 2023; 347: 119193.
58. Pan Y, Zhang H, Zhu L, Tan J, Wang B, Li M. The role of gut microbiota in MP/NP-induced toxicity. Environ. Pollut. 2024; 359: 124742.
59. Kannan K, Vimalkumar K. A review of human exposure to microplastics and insights into microplastics as obesogens. Front. Endocrinol. 2021; 12: 724989.
60. Sharma S, Sharma B, Dey SS. (2022). Microplastic profusion in food and drinking water: are microplastics becoming a macroproblem?. Environ Sci Process Impacts. 2022; 24(7): 992–1009.
61. Nirmala K, Rangasamy G, Ramya M, Shankar VU, Rajesh G. A critical review on recent research progress on microplastic pollutants in drinking water. Environ Res. 2023; 222:115312
62. Rahman A, Sarkar A, Yadav OP, Achari G, Slobodnik J. Potential human health risks due to environmental exposure to nano- and microplastics and knowledge gaps: A scoping review. Sci Total Environ. 2021; 757:143872
63. Yang D, Shi H, Li L, Li J, Jabeen K, Kolandhasamy P. Microplastic pollution in table salts from china. Environ Sci Technol. 2015; 49(22):13622-7.
64. Vivekanand AC, Mohapatra S, Tyagi VK. Microplastics in aquatic environment: Challenges and perspectives. Chemosphere. 2021; 282: 131151.
65. Alberghini L, Truant A, Santonicola S, Colavita G, Giaccone V. Microplastics in fish and fishery products and risks for human health: a review. Int J Environ Res Public Health. 2022; 20(1): 789.
66. Khalid N, Aqeel M, Noman A. Microplastics could be a threat to plants in terrestrial systems directly or indirectly. Environ. Pollut. 2020; 267: 115653.
67. Lazăr NN, Călmuc M, Milea ȘA, Georgescu PL, Iticescu C. Micro and nano plastics in fruits and vegetables: A review. Heliyon. 2024; 10(6): e28291.

68. Zhang Q, Xu EG, Li J, Chen Q, Ma L, Zeng EY, et al. A review of microplastics in table salt, drinking water, and air: direct human exposure. Environ. Sci. Technol. 2020; 54(7): 3740–3751.
69. Li Y, Tao L, Wang Q, Wang F, Li G, Song M. Potential health impact of microplastics: a review of environmental distribution, human exposure, and toxic effects. Environ Health (Wash). 2023; 1(4):249-257.
70. Wu P, Lin S, Cao G, Wu J, Jin H, Wang C, et al. Absorption, distribution, metabolism, excretion and toxicity of microplastics in the human body and health implications. J. Hazard. Mater. 2022; 437: 129361.
71. Gambino I, Bagordo F, Grassi T, Panico A, De DA. Occurrence of microplastics in tap and bottled water: current knowledge. Int J Environ Res Public Health. 2022; 19(9): 5283.
72. Li H, Zhu L, Ma M, Wu H, An L, Yang Z. Occurrence of microplastics in commercially sold bottled water. Sci. Total Environ. 2023; 867: 161553.
73. Acarer S. A review of microplastic removal from water and wastewater by membrane technologies. Water Sci. Technol. 2023; 88(1): 199–219.
74. Prata JC, da Costa JP, Lopes I, Duarte AC, Rocha-Santos T. Environmental exposure to microplastics: An overview on possible human health effects. Sci. Total Environ. 2020; 702: 134455.
75. Prata JC. Airborne microplastics: Consequences to human health?. Environ. Pollut. 2018; 234: 115–126.
76. Borgatta M, Breider F. Inhalation of microplastics-a toxicological complexity. Toxics. 2024; 12(5): 358.
77. Ageel HK, Harrad S, Abdallah MA. Occurrence, human exposure, and risk of microplastics in the indoor environment. Environ Sci Process Impacts. 2022; ; 24(1):17-31.
78. Batool I, Qadir A, Levermore JM, Kelly FJ. Dynamics of airborne microplastics, appraisal and distributional behaviour in atmosphere; a review. Sci. Total Environ. 2022; 806(Pt 4): 150745.
79. Zhai X, Zheng H, Xu Y, Zhao R, Wang W, Guo H. Characterization and quantification of microplastics in indoor environments. Heliyon. 2020; 9(5): e15901.
80. Zhao, X., Zhou, Y., Liang, C., Song, J., Yu, S., Liao, G., et al. Airborne microplastics: Occurrence, sources, fate, risks and mitigation. Sci. Total Environ. 2023; 858(Pt 2): 159943.
81. Amato-Lourenço LF, Carvalho-Oliveira R, Júnior GR, Dos SGL, Ando RA, Mauad, T. Presence of airborne microplastics in human lung tissue. J. Hazard. Mater. 2021; 416:, 126124.
82. Song Z, Liu K, Wang X, Wei N, Zong C, Li C, et al. To what extent are we really free from airborne microplastics?. Sci. Total Environ. 2021; 754: 142118.
83. Vattanasit U, Kongpran J, Ikeda A. Airborne microplastics: A narrative review of potential effects on the human respiratory system. Sci. Total Environ. 2023; 904: 166745.
84. Brahney J, Mahowald N, Prank M, Cornwell G, Klimont Z, Matsui H, et al. Constraining the atmospheric limb of the plastic cycle. Proc Natl Acad Sci U S A. 2021; 118(16): e2020719118.

85. Liu K, Wang X, Fang T, Xu P, Zhu L, Li D. Source and potential risk assessment of suspended atmospheric microplastics in Shanghai. Sci Total Environ. 2019; 675:462-471.
86. Banerjee A, Shelver WL. Micro- and nanoplastic induced cellular toxicity in mammals: A review. Sci. Total Environ. 2021; 755(Pt 2): 142518.
87. Saha G, Chandrasekaran N. (2023). Isolation and characterization of microplastics from skin care products; interactions with albumin proteins and in-vivo toxicity studies on Artemia salina. Environ. Toxicol. Pharmacol. 2023; 99: 104112.
88. Guerranti C, Martellini T, Perra G, Scopetani C, Cincinelli A. Microplastics in cosmetics: Environmental issues and needs for global bans. Environ. Toxicol. Pharmacol. 2019; 68: 75–79.
89. Sun Q, Ren SY, Ni HG. Incidence of microplastics in personal care products: An appreciable part of plastic pollution. Sci Total Environ. 2020; 742: 140218.
90. Šaravanja A, Pušić T, Dekanić T. Microplastics in wastewater by washing polyester fabrics. Materials. 2022; 15(7): 2683.
91. Zhu L, Kang Y, Ma M, Wu Z, Zhang L, Hu R. Tissue accumulation of microplastics and potential health risks in human. Sci. Total Environ. 2024; 915: 170004.
92. Shan S, Zhang Y, Zhao H, Zeng T, Zhao X. Polystyrene nanoplastics penetrate across the blood-brain barrier and induce activation of microglia in the brain of mice. Chemosphere. 2022; 298: 134261.
93. Deng Y, Yan Z, Shen R, Huang Y, Ren H, Zhang Y. Enhanced reproductive toxicities induced by phthalates contaminated microplastics in male mice (Mus musculus). J. Hazard. Mater. 2021; 406: 124644.
94. Hirt N, Body-Malapel M. Immunotoxicity and intestinal effects of nano- and microplastics: a review of the literature. Part. Fibre Toxicol. 2020; 17(1): 57.
95. Yang Y, Xie E, Du Z, Peng Z, Han Z, Li L, et al. Detection of various microplastics in patients undergoing cardiac surgery. Environ Sci Technol. 2023; 57(30):10911-10918.
96. Yang Q, Peng Y, Wu X, Cao X, Zhang P, Liang Z, et al. Microplastics in human skeletal tissues: Presence, distribution and health implications. Environ Int. 2025;196:109316.
97. Montano L, Raimondo S, Piscopo M, Ricciardi M, Guglielmino A, Chamayou S, et al. First evidence of microplastics in human ovarian follicular fluid: An emerging threat to female fertility. Ecotoxicol Environ Saf. 2025; 291:117868.
98. Zhu L, Zhu J, Zuo R, Xu Q, Qian Y, An L. Identification of microplastics in human placenta using laser direct infrared spectroscopy. Sci Total Environ. 2023;856(Pt 1):159060.
99. Roslan NS, Lee YY, Ibrahim YS, Tuan Anuar S, Yusof KMKK, Lai LA, et al. Detection of microplastics in human tissues and organs: A scoping review. J Glob Health. 2024;14:04179.
100. Horvatits T, Tamminga M, Liu B, Sebode M, Carambia A, Fischer L, et al. Microplastics detected in cirrhotic liver tissue. EBioMedicine. 2022; 82:104147.
101. Li Z, Zheng Y, Maimaiti Z, Fu J, Yang F, Li ZY, et al. Identification and analysis of microplastics in human lower limb joints. J Hazard Mater. 2024; 461:132640.

102. Das A. The emerging role of microplastics in systemic toxicity: Involvement of reactive oxygen species (ROS). Sci Total Environ. 2023; 895: 165076.
103. Ding R, Ma Y, Li T, Sun M, Sun Z, Duan J. The detrimental effects of micro- and nano-plastics on digestive system: An overview of oxidative stress-related adverse outcome pathway. Sci Total Environ. 2023; 878: 163144.
104. Kumar N, Shukla A, Kumar S, Ulasov I, Singh RK, Kumar S, et al. FNC (4'-azido-2'-deoxy-2'-fluoro(arbino)cytidine) as an effective therapeutic agent for nhl: ros generation, cell cycle arrest, and mitochondrial-mediated apoptosis. Cell Biochem Biophys. 2024; 82(2): 623-639.
105. Kumar N, Delu V, Ulasov I, Kumar S, Singh RK, Kumar S, et al. Pharmacological insights: mitochondrial ROS generation by FNC (azvudine) in Dalton's lymphoma cells revealed by super-resolution imaging. Cell Biochem Biophys. 2024; 82(2): 873-883.
106. Feng, M, Luo J, Wan Y, Zhang J, Lu C, Wang M, et al. Polystyrene nanoplastic exposure induces developmental toxicity by activating the oxidative stress response and base excision repair pathway in zebrafish (*Danio rerio*). ACS omega. 2022; 7(36): 32153–32163.
107. Liu L, Xu K, Zhang B, Ye Y, Zhang Q, Jiang W. Cellular internalization and release of polystyrene microplastics and nanoplastics. Sci Total Environ. 2021; 779: 146523.
108. Wang S, Chen L, Shi X, Wang Y, Xu S. Polystyrene microplastics-induced macrophage extracellular traps contributes to liver fibrotic injury by activating ROS/TGF-β/Smad2/3 signaling axis. Environ. Pollut. 2023; 324: 121388.
109. Gaspar L, Bartman S, Coppotelli G, Ross JM. Acute exposure to microplastics induced changes in behavior and inflammation in young and old mice. Int. J. Mol. Sci. 2023; 24(15): 12308.
110. Yin, K., Wang, D., Zhang, Y., Lu, H., Hou, L., Guo, T., et al. Polystyrene microplastics promote liver inflammation by inducing the formation of macrophages extracellular traps. J. Hazard. Mater. 2023; 452: 131236.
111. Płuciennik K, Sicińska P, Misztal W, Bukowska B. Important factors affecting induction of cell death, oxidative stress and DNA damage by nano- and microplastic particles in vitro. Cells. 2024; 13(9): 768.
112. Vlacil AK, Bänfer S, Jacob R, Trippel N, Kuzu I, Schieffer B, et al. Polystyrene microplastic particles induce endothelial activation. PLoS One. 2021; 16(11): e0260181.
113. Joo SH, Liang Y, Kim M, Byun J, Choi H. Microplastics with adsorbed contaminants: Mechanisms and Treatment. Environ. Challenges. 2021; 3: 100042.
114. Cui J, Zhang Y, Liu L, Zhang Q, Xu S, Guo MY. Polystyrene microplastics induced inflammation with activating the TLR2 signal by excessive accumulation of ROS in hepatopancreas of carp (*Cyprinus carpio*). Ecotoxicol. Environ. Saf. 2023; 251: 114539.
115. Vlacil AK, Bänfer S, Jacob R, Trippel N, Kuzu I, Schieffer B, et al. Polystyrene microplastic particles induce endothelial activation. PloS one. 2021; 16(11): e0260181.

116. Jiang X, Chen H, Liao Y, Ye Z, Li M, Klobučar G. Ecotoxicity and genotoxicity of polystyrene microplastics on higher plant Vicia faba. Environ Pollut. 2019; 250: 831–838.
117. Tagorti G, Kaya B. Genotoxic effect of microplastics and COVID-19: The hidden threat. Chemosphere. 2022; 286(Pt 3): 131898.
118. Çobanoğlu H, Belivermiş M, Sıkdokur E, Kılıç Ö, Çayır A. Genotoxic and cytotoxic effects of polyethylene microplastics on human peripheral blood lymphocytes. Chemosphere. 2021; 272: 129805.
119. Mottola F, Carannante M, Barretta A, Palmieri I, Rocco L. Reproductive cytotoxic and genotoxic impact of polystyrene microplastic on *Paracentrotus lividus* spermatozoa. Curr Res Toxicol. 2024; 6: 100173.
120. Wu H, Liu Q, Yang N, Xu S. Polystyrene-microplastics and DEHP co-exposure induced DNA damage, cell cycle arrest and necroptosis of ovarian granulosa cells in mice by promoting ROS production. Sci. Total Environ. 2023; 871: 161962.
121. Yang W, Jannatun N, Zeng Y, Liu T, Zhang G, Chen C, et al. Impacts of microplastics on immunity. Front. Toxicol. 2022; 4: 956885.
122. Kumar S, Shukla A, Singh SP, Singh RK, Patel AK, Verma PK, et al. Synthesized gold nanoparticles with moringa oleifera leaf extract induce mitotic arrest (G2/M phase) and apoptosis in Dalton's lymphoma cells. Cell Biochem Biophys. 2024 ;82(2):1043-1059.
123. Kumar S, Verma PK, Shukla A, Singh RK, Patel AK, Yadav L, et al. Moringa oleifera L. leaf extract induces cell cycle arrest and mitochondrial apoptosis in Dalton's Lymphoma: An in vitro and in vivo study. J Ethnopharmacol. 2023 ;302(Pt A):115849.
124. Xie X, Deng T, Duan J, Xie J, Yuan J, Chen M. (2020). Exposure to polystyrene microplastics causes reproductive toxicity through oxidative stress and activation of the p38 MAPK signaling pathway. Ecotoxicol. Environ. Saf. 2020; 190: 110133.
125. Donisi I, Colloca A, Anastasio C, Balestrieri ML, D'Onofrio N. Micro(nano)plastics: an emerging burden for human health. Int. J. Biol. Sci. 2024; 20(14): 5779–5792.
126. Wang J, Wang X, Zhang C, Zhou X. Microplastics induce immune suppression via S100A8 downregulation. Ecotoxicol. Environ. Saf. 2022; 242: 113905.
127. Goswami S, Adhikary S, Bhattacharya S, Agarwal R, Ganguly A, Nanda S, et al. The alarming link between environmental microplastics and health hazards with special emphasis on cancer. Life Sci. 2024; 355: 122937.
128. Dzierżyński E, Gawlik PJ, Puźniak D, Flieger W, Jóźwik K, Teresiński G, et al. Microplastics in the human body: exposure, detection, and risk of carcinogenesis: A state-of-the-art review. Cancers. 2024; 16(21): 3703.
129. Kumar N, Lamba M, Pachar AK, Yadav S, Acharya A. Microplastics - a growing concern as carcinogens in cancer etiology: emphasis on biochemical and molecular mechanisms. Cell Biochem. Biophys. 2024; 82(4): 3109–3121.
130. Gigault J, El HH, Nguyen B, Grassl B, Rowenczyk L, Tufenkji N, et al. Nanoplastics are neither microplastics nor engineered nanoparticles. Nat. Nanotechnol. 2021; 16(5): 501–507.

131. Zarus GM, Muianga C, Brenner S, Stallings K, Casillas G, Pohl HR, et al. Worker studies suggest unique liver carcinogenicity potential of polyvinyl chloride microplastics. Am. J. Ind. Med. 2023; 66(12): 1033–1047.
132. Vincoff S, Schleupner B, Santos J, Morrison M, Zhang N, Dunphy-Daly MM, et al. The known and unknown: investigating the carcinogenic potential of plastic additives. Environ. Sci. Technol. 2024; 58(24): 10445–10457.
133. Rafazi P, Haghi-Aminjan H , Bagheri Z, Rahimifard M. Microplastics and cancer progression: A comparative study of 2D and 3D gastric cancer models using ISO-Compliant protocols. Results Eng. 2024; 24: 103329.
134. Ding R, Chen Y, Shi X, Li Y, Yu Y, Sun Z, et al. Size-dependent toxicity of polystyrene microplastics on the gastrointestinal tract: Oxidative stress related-DNA damage and potential carcinogenicity. Sci. Total Enviro. 2024; 912: 169514.
135. Wang Y, Xu X, Jiang G. Microplastics exposure promotes the proliferation of skin cancer cells but inhibits the growth of normal skin cells by regulating the inflammatory process. Ecotoxicol. Environ. Saf. 2023; 267; 115636.
136. Ortiz-Moriano MP, Masiá P, Acle S, Ardura A, Garcia-Vazquez E, Machado-Schiaffino G. Changes in global methylation patterns of Mytilus galloprovincialis exposed to microplastics. Aquat Toxicol. 2024;276:107115.
137. Im J, Eom HJ, Choi J. Effect of early-life exposure of polystyrene microplastics on behavior and DNA methylation in later life stage of zebrafish. Arch Environ Contam Toxicol. 2022; 82(4): 558–568.
138. Streifer M, Gore AC. Epigenetics, estrogenic endocrine-disrupting chemicals (EDCs), and the brain. Adv. Pharmacol. 2021; 92: 73–99.
139. Hamon MA, Batsché E, Régnault B, Tham TN, Seveau S, Muchardt C, et al. Histone modifications induced by a family of bacterial toxins. Proc Natl Acad Sci U S A. 2007; 104(33): 13467–13472.
140. Banikazemi Z, Farshadi M, Rajabi A, Homayoonfal M, Sharifi N, Sharafati CR. Nanoplastics: Focus on the role of microRNAs and long non-coding RNAs. Chemosphere. 2022; 308(Pt 1): 136299.
141. Fan Z, Xiao T, Luo H, Chen D, Lu K, Shi W, et al. A study on the roles of long non-coding RNA and circular RNA in the pulmonary injuries induced by polystyrene microplastics. Environ. Int. 2022; 163, 107223.
142. Li X, Huang Y, Zu D, Liu H, He H, Bao Q, et al. PMMA nanoplastics induce gastric epithelial cellular senescence and cGAS-STING-mediated inflammation via ROS overproduction and NHEJ suppression. Ecotoxicol. Environ. Saf. 2024; 287: 117284.
143. Santos D, Luzio A, Bellas J, Monteiro SM. Microplastics- and copper-induced changes in neurogenesis and DNA methyltransferases in the early life stages of zebrafish. Chem. Biol. Interact. 2022; 363: 110021.
144. Chen Q, Allgeier A, Yin D, Hollert H. Leaching of endocrine-disrupting chemicals from marine microplastics and mesoplastics under common life stress conditions. Environ. Int. 2019; 130: 104938.
145. Park J, Park C, Gye MC, Lee Y. Assessment of endocrine-disrupting activities of alternative chemicals for bis(2-ethylhexyl)phthalate. Environ. Res. 2019; 172: 10–17.

146. Haleem N, Kumar P, Zhang C, Jamal Y, Hua G, Yao B, et al. Microplastics and associated chemicals in drinking water: A review of their occurrence and human health implications. Sci. Total Enviro. 2024; 912: 169594.
147. Lee B, Min EK, Kim G, Hong G, Seo J, Choi JS, et al. Biodistribution of synthesised polyethene terephthalate fibers in adult zebrafish, their sex hormone disruption effect, and mitigation using natural organic matter. Ecotoxicol. Environ. Saf. 2024; 285: 117108.
148. Graca B, Rychter A, Staniszewska M, Pryputniewicz-Flis D. The seasonality of the concentration of endocrine phenolic compounds in the matter attached to the surface of microplastics. Sci. Total Enviro. 2024; 908: 168400.
149. Lauretta R, Sansone A, Sansone M, Romanelli F, Appetecchia M. Endocrine Disrupting Chemicals: Effects on Endocrine Glands. Front. Endocrinol. 2019; 10: 178.
150. Li S, Keenan JI, Shaw IC, Frizelle FA. Could microplastics be a driver for early onset colorectal cancer?. Cancers. 2023; 15(13): 3323.
151. Shen M, Li Y, Song B, Zhou C, Gong J, Zeng G. Smoked cigarette butts: Unignorable source for environmental microplastic fibers. Sci. Total Enviro. 2021; 791: 148384.
152. Cheon DJ, Orsulic S. Mouse models of cancer. Annu Rev Pathol. 2011; 6: 95–119.
153. Kumar N, Delu V, Shukla A, Singh RK, Ulasov I, Fayzullina D, et al. Safety Assessment of a Nucleoside Analogue FNC (2'-deoxy-2'- β-fluoro-4'-azidocytidine) in Balb/c Mice: Acute Toxicity Study. Asian Pac J Cancer Prev. 2023;24(6):2157-2170.
154. Singh RK, Verma PK, Kumar S, Shukla A, Kumar N, Kumar S, et al. Evidence that PKCα inhibition in Dalton's Lymphoma cells augments cell cycle arrest and mitochondrial-dependent apoptosis. Leuk Res. 2022;113:106772.
155. Zhai Z, Yang Y, Chen S, Wu Z. Long-term exposure to polystyrene microspheres and high-fat diet-induced obesity in mice: evaluating a role for microbiota dysbiosis. Environ Health Perspect. 2024; 132(9): 97002.
156. Xu M, Halimu G, Zhang Q, Song Y, Fu X, Li Y, et al. Internalization and toxicity: A preliminary study of effects of nanoplastic particles on human lung epithelial cell. Sci. Total Enviro. 2019; 694: 133794.
157. Bazan L, Bendas ER, El Gazayerly ON, Badawy SS. Comparative pharmaceutical study on colon targeted micro-particles of celecoxib: in-vitro-in-vivo evaluation. Drug Deliv. 2016; 23(9): 3339–3349.
158. Sun W, Yan S, Meng Z, Tian S, Jia M, Huang S, et al. Combined ingestion of polystyrene microplastics and epoxiconazole increases health risk to mice: Based on their synergistic bioaccumulation in vivo. Environ. Int. 2022; 166, 107391.
159. Betancourt AM, Eltoum IA, Desmond RA, Russo J, Lamartiniere CA. In utero exposure to bisphenol A shifts the window of susceptibility for mammary carcinogenesis in the rat. Environ Health Perspect. 2010; 118(11): 1614–1619.
160. Huang W, Wu T, Wu R, Peng J, Zhang Q, Shi X, et al. Fish to learn: insights into the effects of environmental chemicals on eye development and visual function in zebrafish. Environ Sci Pollut Res Int. 2023; 30(29): 73018–73030.

161. Cunningham B, Harper B, Brander S, Harper S. Toxicity of micro and nano tire particles and leachate for model freshwater organisms. J. Hazard. Mater. 2022; 429: 128319.
162. Wāng Y, Jiang Y. Drosophila melanogaster as a tractable eco-environmental model to unravel the toxicity of micro- and nanoplastics. Environ. Int. 2024; 192: 109012.
163. Zhang Q, He Y, Cheng R, Li Q, Qian Z, Lin X. Recent advances in toxicological research and potential health impact of microplastics and nanoplastics in vivo. Environ Sci Pollut Res Int. 2022; 29 (27): 40415–40448.
164. Bredeck G, Halamoda-Kenzaoui B, Bogni A, Lipsa D, Bremer-Hoffmann S. Tiered testing of micro- and nanoplastics using intestinal in vitro models to support hazard assessments. Environ. Int. 2022; 158: 106921.
165. Chen Y, Williams AM, Gordon EB, Rudolph SE, Longo BN, Li G, et al. Biological effects of polystyrene micro- and nano-plastics on human intestinal organoid-derived epithelial tissue models without and with M cells. Nanomed. 2023; 50: 102680.
166. Bruno A, Dovizio M, Milillo C, Aruffo E, Pesce M, Gatta M, et al. Orally Ingested Micro- and Nano-Plastics: A Hidden Driver of Inflammatory Bowel Disease and Colorectal Cancer. Cancers. 2024; 16(17): 3079.
167. Sharma MD, Elanjickal AI, Mankar JS, Krupadam RJ. Assessment of cancer risk of microplastics enriched with polycyclic aromatic hydrocarbons. J. Hazard. Mater. 2020; 398: 122994.
168. Rafazi P, Bagheri Z, Haghi-Aminjan H, Rahimifard M, Ahvaraki A. Long-term exposure of human U87 glioblastoma cells to polyethylene microplastics: Investigating the potential cancer progression. Toxicol. Rep. 2024; 13: 101757.
169. Deng X, Gui Y, Zhao L. The micro(nano)plastics perspective: exploring cancer development and therapy. Mol Cancer. 2025;24(1):30.
170. Busch M, Brouwer H, Aalderink G, Bredeck G, Kämpfer AAM, Schins RPF, et al. Investigating nanoplastics toxicity using advanced stem cell-based intestinal and lung in vitro models. Front Toxicol. 2023;5: 1112212.
171. Tian Z, Ding B, Guo Y, Zhou J, Jiang S, Lu J, et al. Microplastics accumulated in breast cancer patients lead to mitophagy via ANXA2-mediated endocytosis and IL-17 signaling pathway. Environ Pollut. 2025;364(Pt 2):125321.
172. Park JH, Hong S, Kim OH, Kim CH, Kim J, Kim JW, et al. Polypropylene microplastics promote metastatic features in human breast cancer. Sci Rep. 2023 ; 13(1):6252.
173. Hu X, Biswas A, Sharma A, Sarkodie H, Tran I, Pal I, et al. Mutational signatures associated with exposure to carcinogenic microplastic compounds bisphenol A and styrene oxide. NAR Cancer. 2021;3(1):zcab004.
174. Herrala M, Huovinen M, Järvelä E, Hellman J, Tolonen P, Lahtela-Kakkonen M, et al. Micro-sized polyethylene particles affect cell viability and oxidative stress responses in human colorectal adenocarcinoma Caco-2 and HT-29 cells. Sci Total Environ. 2023;867:161512
175. Nguyen B, Claveau-Mallet D, Hernandez LM, Xu EG, Farner JM, Tufenkji N. Separation and analysis of microplastics and nanoplastics in complex environmental samples. Acc. Chem. Res. 2019; 52(4): 858–866.

176. Shoopman CH, Pan X. Microplastics: a review of methodology for sampling and characterizing environmental and biological samples. Methods Mol. Biol. 2021; 2326: 339–359.
177. Ivleva NP. Chemical analysis of microplastics and nanoplastics: challenges, advanced methods, and perspectives. Chem. Rev. 2021; 121(19): 11886–11936.
178. Renner G, Sauerbier P, Schmidt TC, Schram J. Robust automatic identification of microplastics in environmental samples using FTIR microscopy. Anal. Chem. 2019; 91(15): 9656–9664.
179. Dong C, Xu H, Lin Y, Zhang B, Yu Z, Xie Y, et al. Microplastics detected in three types of female reproductive organs using micro-Raman spectroscopy. Ecotoxicol. Environ. Saf. 2024; 285: 117099.
180. Lenz R, Enders K, Stedmon CA, Mackenzie DMA, Nielsen TG. A critical assessment of visual identification of marine microplastic using Raman spectroscopy for analysis improvement. Mar. Pollut. Bull. 2015; 100(1): 82–91.
181. Yang T, Luo J, Nowack B. Characterization of nanoplastics, fibrils, and microplastics released during washing and abrasion of polyester textiles. Environ. Sci. Technol. 2021; 55(23): 15873–15881.
182. Williams WA, Aravamudhan S. Micro-nanoparticle characterization: establishing underpinnings for proper identification and nanotechnology-enabled remediation. Polymers. 2024; 16(19): 2837.
183. Joseph MM, Narayanan N, Nair JB, Karunakaran V, Ramya AN., Sujai PT, et al. Exploring the margins of SERS in practical domain: An emerging diagnostic modality for modern biomedical applications. Biomaterial. 2018; 181: 140–181.
184. Luo Y, Su W, Xu D, Wang Z, Wu H, Chen B, et al. Component identification for the SERS spectra of microplastics mixture with convolutional neural network. Sci. Total Environ. 2023; 895: 165138.
185. Lv L, He L, Jiang S, Chen J, Zhou C, Qu J, et al. In situ surface-enhanced Raman spectroscopy for detecting microplastics and nanoplastics in aquatic environments. Sci. Total Environ, 2020; 728: 138449.
186. Mikac L, Rigó I, Himics L, Tolić A, Ivanda M. Veres, M. Surface-enhanced Raman spectroscopy for the detection of microplastics. Appl. Surf. Sci. 2023; 608: 155239.
187. Wu P, Wu X, Huang Q, Yu Q, Jin H, Zhu M. Mass spectrometry-based multimodal approaches for the identification and quantification analysis of microplastics in food matrix. Front. Nutr. 2023; 10: 1163823.
188. He L, Rong H, Wu D, Li M, Wang C, Tong M. Influence of biofilm on the transport and deposition behaviors of nano- and micro-plastic particles in quartz sand. Water Res. 2020; 178: 115808.
189. Latwal M, Arora S, Murthy KSR. Data driven AI (artificial intelligence) detection furnish economic pathways for microplastics. J. Contam. Hydrol. 2024; 264: 104365.
190. Barbosa F, Adeyemi JA, Bocato MZ, Comas A, Campiglia A. A critical viewpoint on current issues, limitations, and future research needs on micro- and nanoplastic studies: From the detection to the toxicological assessment. Environ. Res. 2020; 182: 109089.

191. Wright S, Levermore J, Ishikawa Y. Application of infrared and near-infrared microspectroscopy to microplastic human exposure measurements. Appl. Spectrosc. 2023; 77(10): 1105–1128.
192. Deng C, Zhu J, Fang Z, Yang Y, Zhao Q, Zhang Z, et al. (2024). Identification and analysis of microplastics in para-tumor and tumor of human prostate. EBioMedicine. 2024; 108: 105360.
193. Wardani I, Hazimah MNN, Wright SL, Kooter IM, Koelmans AA. Nano- and microplastic PBK modeling in the context of human exposure and risk assessment. Environ. Int. 2024; 186: 108504.
194. Nguyen B, Tufenkji N. Single-particle resolution fluorescence microscopy of nanoplastics. Environ. Sci. Technol. 2022; 56(10): 6426–6435.
195. Xie X, Wang K, Shen X, Li X, Wang S, Yuan S, et al. Potential mechanisms of aortic medial degeneration promoted by co-exposure to microplastics and lead. J. Hazard. Mater. 2024; 475: 134854.
196. Cheng Y, Yang Y, Bai L, Cui J. Microplastics: an often-overlooked issue in the transition from chronic inflammation to cancer. J Transl Med. 2024; 22(1): 959.
197. Segovia-Mendoza M, Nava-Castro KE, Palacios-Arreola MI, Garay-Canales C, Morales-Montor J. How microplastic components influence the immune system and impact on children health: Focus on cancer. Birth Defects Res. 2020; 112(17): 1341–1361.
198. Noornama AMNZ, Abu BNK, Hashim NA. Innovative solutions for the removal of emerging microplastics from water by utilizing advanced techniques. Mar Pollut Bull. 2024 ;206:116752.
199. Lu Y, Li MC, Lee J, Liu C, Mei C. Microplastic remediation technologies in water and wastewater treatment processes: Current status and future perspectives. Sci. Total Environ. 2023; 868: 161618.
200. Cunningham BE, Sharpe EE, Brander SM, Landis WG, Harper SL. Critical gaps in nanoplastics research and their connection to risk assessment. Front. Toxicol. 2023; 5: 1154538.
201. Zuccaro P, Thompson DC, de Boer J, Llompart M, Watterson A, Bilott R, et al. The European Union Ban on Microplastics Includes Artificial Turf Crumb Rubber Infill: Other Nations Should Follow Suit. Environ. Sci. Technol. 2024; 58(6): 2591–2594.
202. Allan J, Belz S, Hoeveler A, Hugas M, Okuda H, Patri A, et al. Regulatory landscape of nanotechnology and nanoplastics from a global perspective. Regul. Toxicol. Pharmacol. 2021; 122: 104885.
203. Duncan TV, Khan SA, Patri AK, Wiggins S. Regulatory science perspective on the analysis of microplastics and nanoplastics in human food. Anal. Chem. 2024; 96(11): 4343–4358.
204. Alexy P, Anklam E, Emans T, Furfari A, Galgani F, Hanke G, et al. Managing the analytical challenges related to micro- and nanoplastics in the environment and food: filling the knowledge gaps. Food Addit. Contam. Part A Chem. Anal. Control Expo. Risk Assess. 2020; 37(1): 1–10.
205. Lamichhane G, Acharya A, Marahatha R, Modi B, Paudel R, Adhikari A, et al. Microplastics in environment: global concern, challenges, and controlling measures. Int. J. Environ. Sci. Technol. 2023; 20(4): 4673–4694.

206. Barguilla I, Domenech J, Ballesteros S, Rubio L, Marcos R, Hernández A. Long-term exposure to nanoplastics alters molecular and functional traits related to the carcinogenic process. J Hazard Mater. 2022;438:129470.

View Article Online
DOI: 10.1039/D5EM00232J

DATA AVAILABILITY STATEMENT

View Article Online
DOI: 10.1039/D5EM00232J

- The data supporting this article have been included as part of the Supplementary Information.
- Any additional data can be provided upon request