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(Review Article)

Plastic pollution-Microplastics: Cancer related issues

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Abstract

Microplastics are now a global issue due to increased plastic production and use. Recently, various studies have been performed in response to the human health risk assessment. Due to their small size and wide distribution, microplastics are almost ubiquitous and can be easily ingested by organisms into the digestive system and then into the blood system. Microplastics have been reported as a new environmental pollutant due to their increased production and extremely low natural biodegradation in the ecosystem. Microplastic can accumulate within the body, increasing the risk of tissue damage, fibrosis, and carcinogenesis. This risk is attributed to the induction of immune responses such as oxidative stress, apoptosis, and necrosis in the liver, intestines, brain, and other organs. Microplastic can lead to the proliferation of tumor cells and on the other hand causing damage to normal skin cells, indicating the potential harm caused by microplastics to skin tissues and cells. Recent study demonstrated for the first time the effect of microplastics on human breast and skin cancer. Bioplastics, which are both functionally similar to synthetic plastics and environmentally sustainable, are considered as promising new materials to address these problems.

Keywords: Bioplastic; Microplastics; Carcinogenesis; Chronic inflammation; Oncogenesis; Immune regulation; Skin cancer; Synthetic polymers; Tumor

1. Introduction

Plastics are widely used in various industries. With the massive use of commercial plastics, more and more of them are being released into the environment [1-40]. Since the creation of plastics in 1950, global production has increased rapidly and is now expected to reach hundreds of millions of tons per year, several hundred times higher than in 1950 [1-40]. Microplastics are rapidly emerging as a global challenge that raises concerns about human health and the whole ecosystem [1]. However, it is important to note that microplastics are already an environmental pollutant [1-40]. The concept of microplastics was first introduced in 2004. Currently, microplastics are defined as those with a particle size of less than 5 mm [1-40]. Due to their small size and wide distribution, microplastics are almost ubiquitous and can be easily ingested by organisms into the digestive system and then into the blood system[1-40]. Microplastics can penetrate cell membranes and cause direct physical damage to bodily functions [1-40]. Studies have shown that microplastics are associated with tumor development. Higher number of microplastics were detected in the colorectal adenocarcinoma [1-40]. Park et al. (2023) [3] indicated that preliminary studies have shown the correlation between

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microplastics and tumor development[3]. Furthermore, most current research has primarily focused on the discovery that microplastics can induce the up-regulation and proliferation of typical cancer biomarkers, oxidative stress, mitochondrial damage, and other cancer-related changes which promote the metabolism of tumors [3]. Cheng et al., (2023) reported that microplastics (nano-scaled) could accelerate the tumor growth in vivo [1]. According to Park et al., (2023) [3], microplastics are typically less than 5 mm in size and are not only derived from the degradation of plastic objects in the environment but are also produced for commercial uses [3]. Recently, microplastics have been reported as a new environmental pollutant due to their increased production and extremely low natural biodegradation in the ecosystem [1-40]. There are increasing reports of microplastics in drinking water and food products, including sea salt, due to their broad range in shape and size and the number of polymers in the oceans and freshwater ecosystems[1-40]. Microplastics are increasingly recognized as a significant societal hazard [1-40]. Although awareness is growing regarding the potential impacts of microplastics on individual organisms and even on the structure of entire human populations, there remains limited knowledge about the severity of these effects[1-40]. Microplastics can enter the human body via the accumulation of microplastics in the food chain [1-40]. It was reported that microplastics had been detected in the gastrointestinal tract of marine animals and human tissue and organs. Microplastics pose significant environmental and health concerns because of their persistence in the environment, potential toxicity, and ability to absorb contaminants and pathogens from the environment [1-40]. However, the long-term effects of microplastics on human health are currently unknown [1-40]. Most studies that examined the health effects of microplastics have used animal subjects[1-40, 49-52]. The ingestion of microplastics has been shown to cause an inflammatory response and can damage the gut, disrupt gut microorganisms, cause organ damage, and affect reproduction and metabolism [1-40]. Breathing in microplastics can cause inflammation and chemical toxicity and introduce pathogenic microorganisms into the body [1-40]. Microplastics introduced through skin contact can cause skin damage due to local inflammation and cellular toxicity [1-40, 50-52].

Although some preliminary studies have confirmed the correlation between microplastics and tumor development, most current research has primarily focused on the discovery that microplastics can induce the up-regulation and proliferation of typical cancer biomarkers, oxidative stress, mitochondrial damage, and other cancer-related changes[1-40]. Existing studies have largely focused on the impacts of microplastics on cancer, metabolic disorders, attention-deficit/hyperactivity disorder, and fertility issues[1-40]. Due to their abundance and diminutive size, microplastics can infiltrate the human body[1-40]. Their unique physical and chemical properties lead to a range of biological effects, such as disruption of gut microbiota, immune responses, metabolic disorders, and inflammation, mediated through signaling pathways or changes in cytokines [1-40]. However, there is still limited exploration of how microplastics induce tumorigenesis through micro-environmental changes, and there is a lack of studies investigating the differential regulation of the tumour immune microenvironment by different types of microplastics [1-40, 48-52].

Bioplastics, in general, are derived from renewable resources, such as plants, and are considered more environmentally friendly than traditional petroleum-based plastics [41]. Biodegradable plastic bags are made from all-natural plant-based raw materials that enable the natural decomposition process which is achieved when the bacteria and fungi present in the surrounding environment naturally metabolizes the plastics and helps to further breakdown the structure of a biodegradable plastic[41]. The end result of which is less harmful to the environment as compared to regular plastic bags [41]. The ingestion and accumulation of microplastics is a serious threat to the health and survival of humans and other organisms given the increasing use of daily-use plastic products, especially during the COVID-19 pandemic. However, whether direct microplastic contamination from plastic packaging is a threat to human health remains unclear.

2. Microplastics: Cancer

Cancer is a complex disease categorized by the uncontrolled spread and growth of abnormal cells [1-20, 42-47]. There are several types of cancer, including carcinoma, sarcoma, leukemia, lymphoma, and myeloma, each originating from different cell types and having distinct characteristics[1-20, 42-47]. The presence of microplastics within the human body has raised significant concerns about their potential health implications[1-40]. Significantly, numerous studies have detected microplastic in human excretion, the colon, and the placenta. microplastic can accumulate within the body, increasing the risk of tissue damage, fibrosis, and carcinogenesis [1-40].This risk is attributed to the induction of immune responses such as oxidative stress, apoptosis, and necrosis in the liver, intestines, brain, and other organs [8, 9]. In addition, exposure to microplastics has been widely reported to trigger the up-regulation of reactive oxygen species (ROS) and inflammatory mediators, resulting in DNA damage, oxidative stress, immune responses and chronic inflammation [1-40]. Recycled plastic food packaging was demonstrated to continuously. leach micro- and nanoplastics [1-40]. Numerous studies have supported the hypothesis that the accumulation of microplastics can trigger inflammatory responses, disrupt the microbiome, and provoke immune reactions due to their physicochemical properties [1-40]. Chronic inflammation, characterized by tissue damage, angiogenesis, and fibrosis, plays a crucial role in cancer development[1-40]. It influences cancer progression by altering the tumor microenvironment and impairing immune surveillance, thus promoting tumorigenesis and metastasis[1-40]. The secretion of various pro-inflammatory cytokines and chemokines by inflammatory cells creates an environment conducive to cancer cell development[1-40]. Inflammation can accelerate cancer progression and promote all stages of tumorigenesis [1-40]. On the basis of literature survey, the existing research has demonstrated that exposure to microplastics and nanoplastics can directly promote the proliferation of tumor cells and influence the onset and progression of tumors by regulating inflammatory responses [1-40]. Although current studies on the exact mechanisms by which microplastic precipitate tumor proliferation are limited, the transition from chronic inflammation to cancer, attributed to immune modulation caused by microplastic exposure, represents a highly promising research direction[1-40]. When inhaled or ingested, microplastics can induce various biological effects, including oxidative stress, metabolic disturbances, inflammation, immune reactions[1-40]. These biological responses are critically implicated in the formation of TME and immunosuppression, potentially leading to tumorigenesis through the transition from chronic inflammation to cancer[1-40]. In all, microplastics can directly cause oxidative stress and cellular changes when innate immune cells engulf them [1-40]. This process releases many pro-inflammatory cytokines and biological modulators, up-regulating signal pathways related to tumor initiation, and forming a pro-inflammatory TME that promotes cancer cell proliferation [1-40]. Additionally, microplastics exposure can affect the immune system by altering gut microbiota and the function of immune organs[1-40]. By inhibiting immune surveillance and shaping pro-inflammatory TME, microplastics are likely to impact inflammation and cancer transformation[1-40]. However, chronic inflammation characterized by tissue damage, angiogenesis, and fibrosis plays a key role in cancer development by promoting tumorigenesis and metastasis[1-40]. It does so by shaping the tumor microenvironment (TME) and influencing immune surveillance [1-40]. Cancer progression involves complex interactions between host microenvironment, tumor cells, inflammatory responses, with inflammatory factors altering the TME and affecting tumor-stromal interactions [1-40]. Thus, understanding the potential effects of microplastics on tumors and their immune microenvironment is crucial for identifying how chronic inflammation induced by microplastics may promote cancer[1-40]. On the basis of literature survey, microplastics can induce the release of pro-inflammatory cytokines and chemokines from suppressive immune cells, further modulating the transition from chronic inflammation to cancer[1-40].

Microplastics, as a new pollutant, are currently being intensively studied for their potential health effects [2-40]. However, the effect of microplastics on skin cancer is not yet known and is an important scientific question that needs to be addressed [2]. Wang et al., (2023) [2] reported that Cutaneous squamous cell carcinoma (CSCC) is one of the most common malignant tumors of the skin, occurring primarily in the elderly population [2]. Skin cancer can be divided into four types: basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), which are collectively known as non-melanoma skin cancer (NMSC) [2]. The melanoma and other non-epithelial skin cancers with the increasing trend of aging of the world's population, the incidence of squamous cell carcinoma of the skin is increasing year by year, and the treatment of elderly patients with squamous cell carcinoma has become a major challenge in clinical dermatology [2]. CSCC is the second most common non-melanoma skin cancer (NSCC) in humans, accounting for approximately 20% of skin malignancies [2]. Cutaneous squamous cell carcinoma is a malignant tumor derived from keratinizing cells and is one of the most common cutaneous malignancies with an aggressive and highly metastatic nature[2]. The main causative factors of cutaneous squamous cell carcinoma are environmental factors such as photo damage, environmental chemical toxins, viral infection, and radioactive exposure [2]. Therefore, studying the effect of environmental pollutants on the development of skin cancer is an important scientific issue [2]. One of the recent study by Wang et al., (2023) [2] reported two skin squamous cell carcinoma cell lines (SCL-1 and A431) were utilized and investigated the effects of microplastics on skin cancer, and cell behaviour experiments showed that microplastics were internalized into the skin squamous cell carcinoma cell line in a time- and dose-dependent manner[2]. Wang et al., (2023) [2] experiments showed that microplastics promoted the proliferation of skin cancer cells by MTT, flow cytometry, laser confocal microscopy, Western blotting and other experimental techniques [2]. The current study by Wang et al., (2023) [2] suggests that microplastics, as a new contaminant, may promote tumor cell proliferation while causing damage to normal skin [2]. Therefore, work by Wang et al., (2023) [2] reported that microplastics acted as a double-edged sword, on the one hand promoting the proliferation of tumor cells and causing damage to normal skin cells, indicating the potential harm caused by microplastics to skin tissues and cells [2]. The escalating environmental pollution by microplastics (hereby defined as plastic particles of around 100 nm to 5 mm is of grave concern to the scientific community, policymakers, and society in general [2-40].

Microplastics are now a global issue due to increased plastic production and use. Recently, various studies have been performed in response to the human health risk assessment [1-2-40]. However, these studies have focused on spherical microplastics, which have smooth edges and a spherical shape and account for less than 1% of microplastics in nature[1-2-40]. Unfortunately, studies on fragment-type microplastics are very limited and remain in the initial stages. In one of the study by Park et al., (2023) [3] studied the effect that 16.4 μm fragment type polypropylene (PP) microplastics, which have an irregular shape and sharp edges and form naturally in the environment, had on breast cancer [3]. These results suggested that PPMP enhances metastasis-related gene expression and cytokines in breast cancer cells, exacerbating breast cancer metastasis[3]. Further, most plastic products have been known to release estrogenic chemicals or endocrine-disrupting chemicals (EDCs) [3-40]. Exposure to EDCs and estrogenic chemicals may increase the risk of cancer or metabolic syndromes, including obesity [3-40]. Currently, there is a lack of evidence on the actual risks of microplastics relating to cancer development or metabolic diseases, despite claims in scientific articles [3]. Consequently, chronic exposure to PPMPs may increase the risk of cancer progression and metastasis [3]. This study by Park et al., (2023) [3] demonstrated for the first time the effect microplastics have on human breast cancer[3]. During and after the COVID-19 pandemic, the indiscriminate use of plastics may exacerbate the harmful effects of microplastics on human health. [3]. Therefore, this study by Park et al., (2023) [3] is a starting point for the discussion between the chronic exposure to microplastics and cancer progression [3].

3. Microplastics: Global Problem and Health Issues

Global accumulation of plastic produced presenting one of the most challenging and concerning issues worldwide [1, 2, 48-52]. The use of these plastics is expected to increase globally, driven partly by the increase in the penetration of e-commerce platforms and current takeaway hot food and food delivery service [1, 2-30]. Micro and nanoplastics are mostly expected coming from these containers during storage and reusage [1, 2-35, 48]. Microplastics are any water-insoluble, solid, synthetic particle or polymeric matrix, with diameter ranging from 1 μm to 5 mm which can be either the regular or irregular in shape [1-19]. Due to its high stability and persistence, plastic is difficult to degrade over decades [1-19-30]. Apart from microplastics in personal care products, plastics used for packaging are a significant contributor to microplastic pollution[1-19]. Globally, polyethylene terephthalate (PET), polyethylene (PE), polypropylene (PP), and polystyrene (PS) are the synthetic polymers most used in plastic packaging[1-19, 48]. Eventually, it breaks down into smaller particles such as microplastics and nanoplastics, through environmental processes [1-40, 48]. Notably, prominent microplastic were found in atmospheric fallout, domestic sewage, and industrial wastewater [1-18]. Meanwhile, due to the persistence, widespread distribution of microplastics, reducing their formation, enhancing degradation abilities in ecosystems and the human body are critical concerns[1-19]. However, challenges remain, such as the generation of toxic intermediate products and volatile organic compounds during the degradation process, leading to secondary environmental pollution [1-40]. There is still a significant journey ahead in researching the hazardous biological effects and mechanisms of microplastics [1-40]. Despite this, the current understanding of the toxicity and biological impacts of microplastics remains limited [1-40, 48]. To mitigate their harmful effects on human health, there is an urgent need to improve the detection and removal methods for microplastics[1-40, 48]. Microplastics primarily originated from land-based industrial source, including landfill, weathering, sewage and tire abrasion[1-40]. These particles can eventually accumulate in various species through atmospheric, oceanic and continental circulation, as well as precipitation [1-5–17, 48]. Secondary microplastics are often degraded from larger plastics or textile fibers due to UV radiation, abrasion, and biological degradation [1-40]. The primary types of polymers include polypropylene (PP), polystyrene (PS), polyethylene (PE), polycarbonate (PC), polyvinyl chloride (PVC), polyethylene terephthalate (PET), polymethyl methacrylate (PMMA), and polyurethane (PU) [1-20]. The small size of microplastics allows them to pass through biological membranes, posing greater risks to cells and organs [24]. Irregular-shape microplastics with sharp edge and high curvature can directly damage cell membranes upon contact [1-25]. After ingestion, the additives and monomers in their composition can interfere with important biological processes in the human body and can cause disruption of the endocrine, immune system[1-25, 48]. They can have a negative impact on mobility, reproduction and development, and can cause carcinogenesis [1-25, 48].

Microplastics can enter the human body through inhalation and ingestion [1-31]. Microplastics can enter almost all organs through the cell membrane, but the exact mechanisms of absorption, distribution, metabolism, and excretion of microplastics in the human body, as well as their dose-dependent effects, remain unclear [1-40]. As microplastics pollution levels rise, individuals are increasingly exposed to these particles through inhalation, oral ingestion, and dermal contact in their daily lives [1-40]. Inhalation and ingestion are two major routes for microplastics entry into organisms, while dermal exposure occurs when microplastics and nanoplastics are absorbed onto the skin, primarily from cosmetic products [1-40]. Furthermore, microplastics inhaled into the bronchus and lungs can translocate through diffusion, direct cellular penetration, or active cellular uptake via endocytic and phagocytic processes [1-34, 48-52]. In the gastrointestinal tract, a major entry point for ingested foreign particles, microplastics are initially trapped in the mucus layer before crossing epithelial barriers [1-40]. They must endure the acidic conditions of the stomach and intestinal lumen, with the potential for particles entering the gastrointestinal system to translocate into the circulatory system via cell internalization by macrophages [1-40]. Additionally, the presence of microplastics leads to the release of pro-inflammatory cytokines and chemokines by immune cells, either directly or indirectly [1-40]. Furthermore, microplastics -related interactions with the host microbiome can also trigger innate and inflammatory responses[1-40]. Due to the important role, chronic inflammation played in cancer progression, microplastics could act as a catalyst for tumor progression [1-40]. Microplastics may contribute to the transition from chronic inflammation to cancer by activating pro-inflammatory signalling pathways, promoting cytokine release, and affecting immune responses [1-40]. The intake of microplastics by humans is by now quite evident [1-40, 48]. The entry point may be through ingestion (through contaminated food or via trophic transfer), through inhalation, or through skin contact[1-40, 48]. Ziani et al., (2023) [48] indicated that following the intake of microplastics into the human body, their fate and effects are still controversial and not well known[48]. Microplastics are present in all ecosystems (atmosphere, soil, seas and oceans) and in many organisms (fish, birds, domestic animals and humans) [1-40, 48]. Therefore, corrective measures are needed at the global level to significantly reduce the use of plastic[1-40, 48]. Because of their high resistance to degradation, microplastics persist for a long time in the environment[48].To date, no solution has been found to extract/remove them from the environment, and the global overconsumption of plastic worsens the accumulation of these particles in these natural environments [48]. The chemical substances that enter their composition, as well as the pollutants adsorbed and then released by microplastics, generate harmful eco-toxicological effects for the health of animals and people [1-40, 48]. Ziani et al., (2023) [48] are of the opinion that microplastics pose a danger to biota and humans, it is necessary to improve the quality and international standardization of the methods used to assess their exposure, risks and effects [48]. In the meantime, it is strongly recommended to reduce the accumulation of these microplastics in the environment[48]. Efforts are being made to find viable solutions to reduce the accumulation of macroplastics in the oceans but also to reduce plastic consumption globally [48].

4. Conclusion

Microplastics are any water-insoluble, solid, synthetic particle or polymeric matrix, with diameter ranging from 1 μm to 5 mm which can be either the regular or irregular in shape. Microplastics are small plastic particles that come from the degradation of plastics, ubiquitous in nature and therefore, affected both wildlife and humans. Most relevant studies have focused on the ingestion of microplastics by aquatic organisms and have theoretically extrapolated that these ingested microplastics eventually reached the human gut through the food chain. They have been detected in many marine species, but also in drinking water and in numerous foods, such as table salt, tea bags, sugar, honey and milk, herbal medicine, and marine organisms. Exposure to microplastics can also occur through inhaled air. However, it is important to note that microplastics are already an environmental pollutant. The presence of microplastics within the human body has raised significant concerns about their potential health implications. Microplastics can enter the human body through inhalation and ingestion. As microplastics pollution levels rise, individuals are increasingly exposed to these particles through inhalation, oral ingestion, and dermal contact in their daily lives. Microplastics can enter almost all organs through the cell membrane, but the exact mechanisms of absorption, distribution, metabolism, and excretion of microplastics in the human body, as well as their dose-dependent effects, remain unclear. Microplastics may contribute to the transition from chronic inflammation to cancer by activating pro-inflammatory signaling pathways, promoting cytokine release, and affecting immune responses. Given the crucial role that chronic inflammation plays in cancer progression, microplastics could act as catalysts for tumor development. However, there is a lack of experimental data to fully assess toxicity in humans, and no safety threshold for the human body has yet been established. Only best solution for the microplastic pollution is the use of bio-based plastics. Bioplastics, in general, are derived from renewable resources, such as plants, and are considered more environmentally friendly than traditional petroleum-based plastics. Crops such as hemp, sugarcane, corn, and other biomass materials are utilized in Bio Plastics manufacture, contributing to the growth of the industry.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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