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A Review on Emerging Contaminants: Effects on Human Health and Cancer Risks

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Abstract: Emerging contaminants are growing health concerns that pose potential threats to the environment and human health globally. They originate from multiple sources, including rapid industrial processes, agriculture, households, and wastewater treatment plants. Despite efforts to reduce the levels of such pollutants, these harmful elements remain a serious problem for public health and the overall quality of life. Exposure to emerging contaminants can lead to various health problems, including cardiovascular diseases, brain and developmental disorders, and cancer. These contaminants can harm aquatic life, disrupt ecosystems, and contaminate drinking water sources. Cancer, a complex heterogeneous disease, can be triggered by multiple causes, including genetic and environmental factors. The rapid increase in emerging contaminants has contributed significantly to the development and proliferation of cancer. This review highlights the dangerous effects of exposure to these contaminants and explores future directions in research. Additionally, it summarizes the emerging roles of inorganic contaminants, such as engineered nanoparticles, and biological contaminants, including pathogenic bacteria, antibiotic-resistant bacteria and resistance genes, viruses, protein contaminants, microplastics, and nanoplastics, in cancer progression and treatment.

Keywords: Cancer; Emerging contaminants; Pollutants; Nanomaterials

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1. Introduction

Cancer is a well-recognized condition characterized by the abnormal growth of cells, which causes harm to an individual's healthy body. In 2020, the World Health Organization (WHO) reported approximately 19.3 million new cancer cases and 10 million cancer-related fatalities. Of all cancer cases, 11.7% are attributed to breast cancer in women. Lung cancer accounts for 11.4%, colon cancer for 10.0%, prostate cancer for 7.3%, and stomach cancer for 5.6%. Lung cancer accounts for 18% of all cancer-related deaths. The prevalence of

colorectal cancer is 9.4%, liver cancer is 8.3%, stomach cancer is 7.7%, and breast cancer in women accounts for 6.9%. By 2040, it is projected that the number of individuals diagnosed with cancer will reach 28.4 million, representing a 47% increase from 2020. Cancer can be caused by various factors, including biological, chemical, physical, psychological, genetic, and environmental influences [1].

Emerging contaminants refer to newly discovered chemicals or pathogenic organisms in the environment. These hazards can be either artificial or naturally occurring, with a high potential to pose risks to both humans and ecosystems. Currently, there is a lack of comprehensive understanding regarding the hazards presented by these contaminants. Examples of compounds that have not been fully researched include per- and polyfluoroalkyl substances (PFAS), emerging pathogens, herbicides, industrial chemicals, micro/nanoplastics, antibiotic-resistant genes (ARGs), and other exogenous substances. These hazardous substances enter the environment through inappropriate waste disposal and industrial emissions, contaminating the atmosphere, water bodies, and soil. When combined, they can create hazardous chemical and biological mixtures [2]. These extracellular contaminants can undergo modifications and be transported over significant distances, resulting in the creation of unfamiliar and uncharacterized chemicals and pollutants in areas far from their origin.

Pollutants from various sources exhibit concentrations ranging from nanograms per liter (ng/L) to micrograms per liter (μg/L). These substances are commonly known as "emerging contaminants." **Table 1** lists several identified environmental contaminants, such as endocrine-disrupting chemicals (EDCs), pharmaceuticals and personal care products (PPCPs), microplastics, disinfection byproducts (DBPs), perfluorinated compounds (PFCs), organophosphate flame retardants (OPFRs), brominated flame retardants (BFRs), and other substances. Electromagnetic fields not only have detrimental effects on the environment but also pose potential health risks. Extracellular vesicles have been identified as contributing to several human diseases, including cancer. Specific environmental contaminants possess mutagenic and carcinogenic properties, which may contribute to the development of cancers, such as breast and prostate cancers. EDCs have also been associated with various cancers, including papillary thyroid, testicular, and kidney cancers. Several environmental contaminants have been identified as carcinogenic, including OPFRs, bisphenol A, and glyphosate. Currently, researchers are investigating the effects of newly discovered pollutants on tumors. However, no scientific investigation has yet explored the specific role of emerging contaminants in cancer research [3].

Environmental factors are responsible for the overwhelming majority of human cancers. These influences include tobacco smoking, alcohol consumption, dietary choices, pathogenic agents, radiation exposure, sunlight, contact with environmental contaminants, and other non-genetic variables. Although the attributable share of environmental factors may be less than infectious diseases and tobacco, exposure to certain chemicals in the environment, household, and workplace can significantly increase cancer risk. Environmental chemicals include molecules or components found in various ecological substances, such as air, water, food, soil, dust, and consumer items. The International Agency for Research on Cancer has classified several well-known environmental contaminants as carcinogenic to humans. These pollutants include indoor and outdoor air pollutants, toxins like arsenic in drinking water, and dioxin and polychlorinated biphenyls (PCBs) in soil and food [4].

Moreover, a diverse range of environmental contaminants is thought to have the potential to cause cancer in humans, although further evidence is needed. Additionally, chemicals present in the atmosphere, water, food, and soil are relatively lower in concentration compared to occupational environments. As a result, the potential risk of cancer caused by exposure to environmental chemicals in the general population is considered limited, especially when compared to the dangers found in industrial settings. However, despite this assumption of

limited exposure, a significant percentage of people are affected based on their location, lifestyle, and dietary habits. Therefore, it is crucial to ascertain exposure levels specific to different communities and examine how they are linked to cancer risk [5].

Since the mid-twentieth century, there has been a substantial surge in the production of artificial chemicals, often referred to as the second chemical revolution. This revolution corresponds to the rapid development and use of novel synthetic compounds. The growth of the Chemical Abstract Service Registry, from 20 million in 2002 to over 204 million by 2023, illustrates a significant increase, adding over 15,000 new compounds daily. Furthermore, there has been a notable rise in genetic modification efforts. While synthetic chemicals have had a beneficial impact on human well-being—enabling the development of novel medicines, improved materials, and enhanced agricultural output—concerns about their potential hazards to human health and the environment remain [6].

Table 1. Effects, actions, and prevention of contaminants on human health and cancer

Contaminant	Effects on cancer	Actions/roles	Prevention	References
EDCs	Disrupt hormone balance, leading to cell proliferation, altered gene expression, and increased cancer risk	Mimic or block natural hormones, interfere with hormone synthesis, metabolism, or action	Reduce the use of hormone-disrupting chemicals, improve wastewater treatment, develop sensitive detection methods	[7]
PPCPs	Hormone disruption, antibiotic resistance, genotoxicity, and carcinogenicity	Enter the environment through wastewater, contaminate water bodies, and bioaccumulate in organisms	Proper disposal of medications, advanced wastewater treatment, and development of safer alternatives	[8]
Microplastics	Inflammation, oxidative stress, genotoxicity, and potential cancer risk	Absorb pollutants, transport harmful chemicals, and induce cellular stress	Reduce plastic consumption, improve waste management, develop effective microplastic removal technologies	[9]
DBPs	Genotoxicity, carcinogenicity, and reproductive toxicity	Formed during water disinfection, can be inhaled or ingested	Optimize disinfection processes, explore alternative disinfection methods, develop advanced treatment technologies	[10]
PFCs	Immune suppression, oxidative stress, hormone disruption, and potential carcinogenicity	Persistent in the environment, bioaccumulate in the food chain	Reduce PFC use, develop alternative products, implement stricter regulations on PFC emissions	[11]
OPFRs	Endocrine disruption, neurotoxicity, and potential carcinogenicity	Widely used in consumer products, can leach into the environment	Phase out OPFRs, develop safer alternatives, improve recycling and waste management	[12]
BFRs	Endocrine disruption, thyroid disruption, neurotoxicity, and potential carcinogenicity	Persistent in the environment, bioaccumulate in the food chain	Phase out BFRs, develop safer alternatives, improve recycling and waste management	[13]

2. Role of pollutants and contaminants in human health

The toxicity of metalloids such as lead, mercury, cadmium, arsenic, cobalt, and chromium, along with dichloro-diphenyl-trichloroethane (DDT) and PCBs, is well documented and acknowledged (**Table 2**). The harmful environmental and health impacts of these pollutants have led to efforts to control their quantities in water, sediments, and other environmental media. Consequently, their usage has been prohibited or restricted. While there is already a substantial body of knowledge regarding legacy pollutants, advancements in toxicology and analytical technologies continue to reveal new hazards to human health and the environment. This has led to a

deeper understanding of the origins, persistence, mobility, and toxicity of these pollutants [14].

PFAS are synthetic chemical compounds containing organofluorine, used in various industrial and commercial applications such as firefighting foams, non-stick cookware, waterproof clothing, cosmetics, and food packaging coatings. Classified as persistent organic pollutants (POPs), they resist natural degradation and remain in the environment for extended periods. Their widespread use has resulted in their detection in the bloodstream of most populations, where they can accumulate, with serum elimination half-lives ranging from 3 to 8 years. Perfluorooctanesulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) are the most extensively studied among the many PFAS due to their higher prevalence in the environment. The International Agency for Research on Cancer has assessed PFOA's cancer-causing potential, classifying it as a possible human carcinogen based on limited evidence from human and animal studies, linking it to testicular and kidney cancers [15].

Additionally, there is modest evidence suggesting the existence of carcinogenic pathways. Epidemiological studies show a positive correlation between increased incidences of testicular and kidney cancer and exposure among people living or working near PFAS-manufacturing plants. Research indicates that PFOA may induce oxidative stress, which can lead to DNA damage, though it is unlikely to cause direct genotoxicity. Animal studies have shown that the activation of peroxisome proliferator-activated receptor alpha, a key regulator of lipid metabolism and inflammation, is a probable mechanism. Other studies suggest that PFAS possess oestrogenic and anti-androgenic properties and may act as endocrine disruptors [16].

PFAS have been linked to elevated oxidative stress, which can cause DNA damage and mutations, potentially serving as the initial stage of cancer formation. Endocrine disruption may occur when certain PFAS mimic or interfere with the function of hormones, leading to hormonal imbalances that affect cell growth and contribute to cancer development [17]. Additionally, PFAS exposure has been associated with immune system dysfunction, potentially impairing the body's ability to eliminate damaged or precancerous cells. Changes in gene expression, including DNA methylation and histone modifications caused by PFAS, can lead to inflammation by activating inflammatory pathways. PFAS can also promote cellular growth, division, and angiogenesis (the formation of new blood vessels), creating a favorable environment for tumor growth, progression, and metastasis [18].

Furthermore, positive associations have been identified between PFAS exposure and prostate and renal cancers. Cadmium-induced carcinogenesis may occur through several mechanisms: cadmium disrupts epigenetic regulation and signal transduction pathways, leading to abnormal cell proliferation. It also affects DNA repair processes and tumor suppressor proteins, resulting in chromosomal damage and genomic instability [19]. In addition, cadmium exhibits oestrogenic properties, as shown in both *in vitro* and *in vivo* studies. One study found that women exposed to proteinuria, glucosuria, and glucoproteinuria had an increased mortality risk from total cancer, particularly renal and uterine cancers. The relationship between cadmium exposure and cancer rates among the Japanese population in non-polluted areas has also garnered attention, as the average daily cadmium intake in Japan (26 μg/day) exceeds that of China (10 μg/day) and Sweden (15 μg/day) [20].

2.1. Cardiopulmonary diseases

Airborne particulates have the potential to carry various ecologically harmful chemicals, such as metallic substances (metalloids), POPs, nanoparticles (NPs), and viruses. The respiratory and cardiovascular systems are the primary areas of concern, with potential consequences ranging from minor irritations like wheezing to more serious long-term cardiopulmonary conditions, such as hypertension and chronic obstructive pulmonary

disease. A recent meta-analysis, which consolidated multiple studies, revealed a significant correlation between increased levels of PFAS exposure, including PFOS and PFOA, and hypertension. It is essential to recognize that smaller particulates are considerably more harmful than larger ones due to their longer atmospheric lifespan and greater ability to penetrate deep into the respiratory system. Therefore, the health risks associated with emerging contaminants may be exacerbated by fine particulate matter in the air. For instance, research has shown that the interaction between airborne fine particles and viruses can worsen respiratory tract infections and facilitate viral spread [21].

2.2. Neurotoxicity

Compelling evidence suggests that certain environmental pollutants, including heavy metals such as arsenic and mercury, cyanotoxins, and perfluoroalkyl compounds, can cause neurotoxic effects. Prolonged exposure to these substances is linked to an increased risk of neurological issues, including neurodegenerative disorders. Even small amounts of these pollutants can cause significant and lasting damage to the nervous system. Early-life exposure to such contaminants has been recognized as a critical factor contributing to the later development of Alzheimer's and Parkinson's diseases. Notably, regions with PFAS contamination showed a 33% higher mortality risk from Alzheimer's disease compared to non-contaminated areas [22].

2.3. Immune system impacts and allergic reactions

Emerging contaminants may impair immune function or trigger hypersensitive responses by disrupting immune system processes. Studies indicate that these compounds may contribute to the development of allergies and other hypersensitivities by affecting the activation and lifespan of specific immune cells. For example, PFAS exposure has been linked to negative impacts on immune responses in both children and adults, including an increased risk of asthma and lower antibody levels following vaccinations. A recent study found that exposure to PFOS and PFOA doubled the incidence of non-atopic asthma in six-year-old children [23].

3. Engineered nanoparticles

Engineered nanoparticles (ENPs) undergo chemical transformation, aggregation, and dissolution as they accumulate in the environment through physical, chemical, and biological processes. The interactions between these mechanisms and the movement of ENPs ultimately determine their fate. The dissolution and transformation of ENPs are key elements of the chemical conversion process. The disintegration of NPs is influenced by both inherent properties of the particles and environmental conditions, as shown in several studies. For instance, the common process of nanoparticle sulfidation makes their surface nearly unreactive, which affects their overall reactivity [24].

The fate and ecological impact of ENPs are largely controlled by their colloidal stability. The homo-aggregation of nanoparticles—interactions between identical NPs—correlates positively with NP concentration. However, homo-aggregation is less likely due to the low expected ambient concentrations of ENPs, which typically range from picograms per liter (pg/L) to low micrograms per liter (μg/L) in surface waters. Multivalent cations are more effective than other cations, and the rate of NP aggregation increases based on the properties of the surrounding medium. Despite this, hetero-aggregation—NPs binding with mineral particles—is more common in natural environments. This process has significant implications for the potential ecological harm

ENPs may cause. The behavior of NPs in saturated and unsaturated porous media, as well as aquatic systems, is influenced by factors such as ionic composition, natural organic matter, and solution pH, which in turn affect their environmental fate. An increasing body of research suggests a link between these parameters and the absorption of ENPs by plants [25].

In recent decades, nanotechnology has seen growing use in medicine, particularly in areas like tumor targeting, diagnostics, and therapy, with applications becoming increasingly safe and efficient. Nanotechnology-based drug delivery systems offer several advantages in cancer treatment, such as targeted delivery to tumor cells, improved pharmacokinetics, fewer side effects, and the ability to circumvent drug resistance. The selection or design of nanoparticles for drug delivery systems is based on size and properties that align with the pathophysiology of tumors. In cancer treatment, nano-carriers utilize the targeting capabilities of NPs and the affinity of targeted chemicals to selectively deliver drugs to tumor cells, leading to their destruction. These nano-carriers can be used for both gene therapy and cytotoxic therapy, as they can deliver traditional chemotherapeutic agents and nucleic acids [26].

Furthermore, NPs provide a platform for encapsulating and transporting poorly soluble drugs into the bloodstream. Nano-carriers enhance drug retention in the body and concentration in tumor tissues due to their improved permeability and retention effects, as well as their specific size and surface characteristics. At the same time, the targeting system protects healthy cells from the toxic effects of drugs, reducing the adverse consequences of cancer treatment. For example, PEGylated liposomes loaded with doxorubicin significantly reduced cardiotoxicity compared to free doxorubicin. Additionally, nanoparticle albumin-bound paclitaxel showed fewer side effects and allowed for higher tolerable doses compared to solvent-based taxanes. Research has also explored NP-based drugs in immunotherapy and ablation therapy for cancer, alongside chemotherapy and gene therapy. Nanoparticle-based drug delivery is expected to enhance immunotherapy and counteract the immunosuppressive environment of tumors [27].

Table 2. Summary of various contaminants, their nature and actions, as well as effects on cancer and overall human health

Contaminants	Nature	Actions	Effects on cancer	Effects on overall human health	References
PFAS	Synthetic chemicals used in various products	Persistent, bioaccumulative, and toxic; interfere with hormone regulation, immune system, and liver function	Linked to kidney, testicular, and other cancers; potential association with thyroid disease, immune dysfunction, and reproductive issues	Reduce PFAS use, improve wastewater treatment, develop safer alternatives, and implement stricter regulations.	[28]
DDT	Pesticides used to control insect populations	Persistent, bioaccumulative, and toxic; disrupts endocrine system	Linked to certain types of cancer, reproductive issues, and neurological disorders	Ban the use of DDT, implement effective pest control methods, and promote sustainable agriculture.	[29]
PCBs	Industrial chemicals used in various applications	Persistent, bioaccumulative, and toxic; disrupt the endocrine system, immune system, and reproductive system	Linked to various cancers, including liver, blood, and lymphatic cancers; reproductive issues, and neurological disorders	Phase out PCB use, implement proper disposal, and develop safer alternatives	[28]

Table 2 (Continued)

Contaminants	Nature	Actions	Effects on cancer	Effects on overall human health	References
Cadmium	Naturally occurring metal	Bioaccumulates in the food chain; toxic to multiple organs	Linked to kidney cancer and prostate cancer; bone disease, kidney damage, and respiratory problems	Reduce cadmium emissions from industrial processes, improve waste management, and promote healthy diets	[30]
ENPs	Tiny particles with unique properties	Can enter cells, interact with biomolecules, and induce oxidative stress	Potential to induce DNA damage, inflammation, and cancer; evidence is still emerging	Toxicity varies based on size, shape, and composition; potential for respiratory, cardiovascular, and neurological issues	[31]
Bacteria	Microscopic organisms	Can cause infections, produce toxins, and contribute to inflammation	Certain bacterial strains (e.g., *Helicobacter pylori*) link to specific cancers (e.g., stomach cancer); complex role in cancer development	Contribute to various infectious diseases, antibiotic resistance, and immune system dysregulation	[32]
Viruses	Infectious agents	Replicate within host cells, causing cell damage and immune response	Certain viruses (e.g., HPV, HBV, HCV) linked to specific cancers; complex role in cancer development	Cause various infectious diseases, including respiratory, gastrointestinal, and neurological illnesses	[33]
Protein contaminants	Proteins present in various products	Can trigger immune responses, induce allergic reactions, and potentially interact with cellular processes	Potential role in cancer development through inflammation and immune dysregulation; evidence is limited	Can cause allergic reactions, autoimmune diseases, and other adverse health effects	[34]
Nanoplastics	Tiny plastic particles	Can enter cells, induce oxidative stress, and interact with biological molecules	Potential to cause inflammation, DNA damage, and cancer; evidence is still emerging	Environmental pollution, ingestion by wildlife, and potential human health risks	[35]

4. Biological contaminants

4.1. Pathogenic bacteria

The complexity of this issue is emphasized by the delicate interplay between pathogenic microbes and various environmental conditions, particularly in agricultural contexts. Agricultural soils are often overlooked as reservoirs of contaminants that can lead to health problems, affecting the purity of the environment, food, and water. Certain bacterial species can cause serious illness and, in some cases, death through direct contact. For example, foodborne diseases like *Escherichia coli* O157 can infiltrate the food chain and trigger widespread outbreaks with significant health consequences [36].

Colon cancer, liver cell carcinoma, and pancreatic cancer are among the most common gastrointestinal (GI) malignancies. The GI tract contains the most diverse and prolific colonies of bacteria compared to other parts of the body. As a result, early studies identifying correlations between microbiota and cancer primarily focused on the gut microbiome and digestive cancers. Recent studies have demonstrated a strong association between liver disease progression and the composition of gut flora. The gut microbiota of individuals with nonalcoholic steatohepatitis (NASH) is characterized by elevated levels of *Parabacteroides* and *Allisonella*, while levels of *Faecalibacterium* and *Anaerosporobacter* are reduced. Individuals with cirrhosis exhibit a gut

microbiota marked by an increased presence of species from the *Veillonellaceae* and *Streptococcaceae* families, such as *Streptococcus salivarius*, *Veillonella parvula*, and *Ruminococcus gnavus*, alongside members of the *Lachnospiraceae* family. During hepatocellular carcinoma (HCC) development, significant microbial presence is often observed in the tumor area and within the tumor itself [37].

Conversely, healthy liver tissue contains relatively few bacteria. The tumor-associated microbiota in HCC typically consists of *Bacteroidetes*, *Firmicutes*, and *Proteobacteria*. Moreover, *Ruminococcus gnavus* was predominantly detected in the microbial profile of tumors in HCC patients who tested positive for hepatitis B and C viruses. Another study found that individuals with HCC and non-alcoholic fatty liver disease-related cirrhosis had a decreased abundance of *Bifidobacterium* and an increased prevalence of *Bacteroides* and *Ruminococcaceae* species in their fecal microbiota compared to the HCC group [38].

Gastric cancer is a highly aggressive disease and is the second leading cause of cancer-related deaths globally. Approximately 90% of gastric cancers are adenocarcinomas, which arise from the glands in the stomach's mucosal layer. Traditionally, the stomach was believed to be sterile due to its acidic environment. However, *Helicobacter pylori* infection is now recognized as a major risk factor for gastric cancer. *H. pylori* can contribute to cancer through indirect inflammatory mechanisms and direct epigenetic effects, often working in conjunction with other microbes. *H. pylori*-induced atrophic gastritis leads to chronic inflammation, with both innate and adaptive immune responses involved. The primary driver of this inflammation is the CD4 Th1-cell response [39].

The activation of neutrophils and macrophages during infection generates reactive oxygen and nitrogen species (ROS/RNS), increasing oxidative stress and DNA damage in mucosal cells. *H. pylori* also triggers programmed cell death in macrophages and elevates the expression of proinflammatory factors. The persistence of infection promotes bacterial colonization in specific areas, enabling the bacterium to spread, which increases pH levels, reduces stomach acid production, and leads to widespread stomach inflammation, ultimately contributing to adenocarcinoma development. *H. pylori* directly promotes cancer through virulence factors such as the Cag Pathogenicity Island (CagPAI), which encodes cytotoxin-associated gene A (CagA) and vacuolating cytotoxin A (VacA). Strains containing the cagA gene can elicit heightened inflammatory responses, accelerating gastric cancer progression. The *CagPAI* gene encodes a type IV secretion system in bacteria, responsible for secreting CagA and peptidoglycan into epithelial cells. Tumor formation is driven by the activation of various cellular signaling pathways, including the MAPK cascade and the phosphoinositide-3 kinase (PI3K-AKT) pathway, by CagA and peptidoglycan [40].

4.2. Antibiotic-resistant bacteria and resistance genes

Antibiotics and antibiotic-resistant bacteria (ARBs), along with ARGs, have existed for hundreds of thousands of years, long before humans discovered them. However, the extensive industrialization and widespread use of antibiotics in human and animal populations have exerted unprecedented selection pressure on bacteria in interconnected environments, including human, animal, and environmental microbiomes. As a result, the global rate at which antibiotic resistance traits are emerging has significantly increased. The current problem of antibiotic resistance is further exacerbated by the emergence of ARBs, the genetic factors that confer resistance, and their transmission among humans, animals, and the environment due to human activities [41]. For example, the widespread use of antibiotics and intensive agricultural practices have transformed soil ecosystems into potential reservoirs of ARGs and pathogenic microbes. The biopollutome, a complex network of pathogens and

ARGs, originates in soil environments and poses a substantial and widespread threat to ecosystems. Despite various obstacles, bacteria can acquire new genetic material from other species, leading to the persistence of infections and diminishing our capacity to prevent and treat bacterial diseases effectively. Therefore, urgent and effective measures must be implemented to regulate the emergence and dissemination of ARBs [42,43].

Microorganisms employ several mechanisms to acquire antibiotic resistance. These behaviors can be attributed to hereditary, mechanical, or combined factors. These strategies include acquiring resistance through horizontal gene transfer (HGT) or xenobiotic transfer, modifying target or receptor proteins, using drug efflux pumps, or blocking drug entry. Transposons, also known as "jumping genes," produce enzymes that facilitate the movement of genes to new positions within the same genome or to another organism. Additionally, the acquisition of alleles that confer antibiotic resistance, particularly through HGT, plays a crucial role in the development of drug resistance in conjunction with evolutionary processes. This drug-resistance mechanism is particularly powerful as it can result in significant changes to the bacterial genome without the need for mutations [44].

The rise of resistance to β-lactam antibiotics is one example that can be attributed to HGT. Drug resistance may occur due to genetic modifications in the genes encoding target proteins, impairing the drug's ability to bind to the protein effectively. R plasmids are primarily responsible for the majority of drug-resistance cases [45]. These genes are transferred to susceptible bacteria through a separate conjugation mechanism. Before the discovery of R plasmids, other genes had already developed resistance to commonly used antibiotics such as tetracycline, chloramphenicol, sulfonamides, and aminoglycosides. These discoveries were made recently through genome sequencing. Additionally, newly discovered integrons have revealed a gene coding for an integrase enzyme that inserts a resistance gene at a specific location downstream of a promoter [46,47].

Antibiotic resistance is often referred to as a hidden global epidemic and has become a significant issue in the context of biological environmental contaminants. The increasing prevalence of antibiotic-resistant microorganisms poses a serious threat to human health. Over the past decade, ARGs have been found in various habitats, including natural environments and human industrial ecosystems. Human actions play a crucial role in selecting genes from the environment and cells, allowing these genes to be later utilized to develop antibiotic resistance. The increased frequency of human activities has led to a higher rate of microorganism and substance transfer between humans, animals, and the environment. This, in turn, enhances the likelihood of spreading and developing ARBs and ARGs, which are emerging biological pollutants with the potential to disrupt natural ecosystems. Aside from antibiotics, a range of non-antibiotic contaminants, such as heavy metals and non-antibiotic medications, can influence bacterial behavior and contribute to the emergence of antibiotic resistance [48,49].

Furthermore, ARBs and ARGs can spread from human and animal microbiomes to the environment through various means, including food consumption, direct contact (e.g., swimming), and interaction with contaminated crops. This creates a cycle that connects the human, animal, and environmental microbiomes, perpetuating the spread of antibiotic resistance. Future studies should include quantitative data on how ARBs and ARGs spread from the environment to humans, including the likelihood of successful colonization and human exposure. It is essential to shift from descriptive, qualitative, or semi-quantitative research to investigations focusing on the mechanisms that contribute to the spread of antibiotic resistance in the environment and its transmission to the human microbiome [50].

5. Protein contaminants

Prions and Bt proteins are the primary types of newly discovered protein pollutants. These proteins can endure in the environment for extended periods, serving as significant sources for the spread of diseases by attaching to sediments and remaining suspended in water. Our understanding of how prion proteins move and spread in the environment is limited. Prior studies have shown that recPrP and pure PrPSc exhibit restricted mobility. The movement of recPrP in quartz sand columns was limited to less than 1 cm, with the majority of purified recPrP remaining at the contamination site in soil columns. This observation was made using sand or soil columns. It has been demonstrated that Bt proteins can be transported throughout the landscape by waste and debris during surface runoff. Furthermore, they have been found to persist in soils for durations of 2 months, 180 days, and up to 234 days, respectively. However, significant gaps remain in understanding the environmental risks, movement, and fate of protein pollutants such as prions and Bt proteins [51].

AKT plays a crucial role in several cellular functions, including glucose uptake, metabolism, cell viability, and proliferation. Its activation is mediated by phosphatidylinositol-3-kinase (PI3K). Many types of human cancers commonly exhibit increased AKT activity, and numerous mouse models with activated AKT develop cancer. A novel regulatory mechanism for AKT has been discovered through the process of palmitoylation at cysteine 344 (Cys344) in both HEK293T and preadipocyte HeLa Kyoto cells. The Cys344 mutation led to a decrease in AKT308 phosphorylation and the attraction of AKT to lysosomes. This mutation was induced by substances that promote oxidative stress and autophagy. These findings indicate that palmitoylation is essential for the activation of AKT and for preventing its degradation. Identifying the palmitoyl transferase responsible for catalyzing AKT palmitoylation and studying the role of AKT palmitoylation in the onset and progression of cancer would be of great interest [52].

Palmitoylation can indirectly regulate AKT signaling by enhancing AKT signaling through the palmitoylation of AKT itself. The palmitoylation of mTOR, facilitated by ZDHHC22, decreases the stability of mTOR, a kinase complex responsible for phosphorylating AKT. Consequently, this leads to a reduction in AKT signaling in breast cancer cells. The major palmitoylation sites of mTOR have been identified as Cys361 and Cys362 using site-directed mutagenesis. In liver cancer, the palmitoylation of proprotein convertase subtilisin/kexin type 9 (PCSK9) enhances its affinity for interacting with phosphatase and tensin homolog (PTEN), a crucial enzyme that regulates cholesterol metabolism. Consequently, the attachment of PCSK9 leads to the degradation of PTEN, which alleviates its ability to regulate AKT signaling. The regulation of AKT is contingent on specific circumstances and is facilitated by multiple levels of control [53].

6. Microplastics and nanoplastics

Over the past ten years, there has been a notable emphasis on micro- and nanoparticles as emerging contaminants. The widespread presence of micro- and nanoplastics (MNPLs) in the environment poses a health risk. This risk can arise from the intentional manufacturing of MNPLs of specified sizes for specific uses (primary MNPLs) or from the degradation and breakdown of larger plastic materials (secondary MNPLs). Humans are vulnerable to constant and inevitable exposure through various pathways, such as ingestion, inhalation, or skin contact, since MNPLs are widely distributed across different environmental habitats (in the air, water, and land) [54].

Microplastics are extensively distributed throughout the biosphere, atmosphere, and environment, making them one of the most significant emerging contaminants globally. Detecting micro- and nanoparticles in the

terrestrial environment and the human body is feasible. Microplastic fragmentation has been found to exacerbate global nanoplastic contamination. Plastic particles enter the environment from several sources, presenting a potential threat to human health, the atmosphere, and soil. Atmospheric microplastics are present in both indoor and outdoor air. Variations in the concentration of microplastics (MPs) in outdoor air have been identified across different regions. Urban areas exhibit a significantly higher abundance of MPs compared to rural areas, with cities in northern China showing higher levels of MPs than those in the southern region. Microplastics can enter plant stomata, which measure 20–40 μm in length and 5–10 μm in width, during the deposition process. Microplastics ranging from 20 to 200 nm in size accumulate in the stomatal lumen and then penetrate the leaf tissue. Research has confirmed that polystyrene (PS) nanoplastics can enter leaves and travel to plant roots, demonstrating their potential to penetrate plant leaves via exposure to foliage. Nanoplastics can be transported with water or fluids within a system, a phenomenon influenced by the composition of the exudate and the stem. Additionally, nanoplastics must navigate various physiological barriers, including intercellular spaces, vesicles, and conductive cells, as they migrate downward. Consequently, the ongoing accumulation of nanoplastics may hinder the movement of smaller nanoplastics by obstructing their path [55].

Metal nanoparticles accumulate in various species within the environment, contaminating the food chain and adversely affecting the health and well-being of all animals involved. Metal nanoparticles are particularly difficult for mammals to break down after ingestion, resulting in their prolonged presence in the body. According to research, ingestion of PS particles between 0.2 and 0.3 micrometers in size and at a concentration of 250 micrograms per microliter can allow these particles to enter the bloodstream, liver, spleen, and other organs via the digestive system. The absorption process could lead to poisoning that affects multiple systems. Magnetic nanoparticles found in human urine indicate extensive use of these particles. Unprocessed magnetic nanoparticles exit the body through the digestive system as feces after ingestion [56]. Nevertheless, smaller magnetic nanoparticles can penetrate deeper. Magnetic nanoparticles can be disseminated to different organs via the bloodstream, as evidenced by their detection in human blood in specific studies. However, the mechanism by which magnetic nanoparticles enter the body remains unclear and warrants further investigation. The structure of an organism's nutritional and digestive organs dictates the maximum size of particles, known as magnetic nanoparticles, that the organism can absorb. Magnetic nanoparticles primarily enter the body through the respiratory and gastrointestinal systems. Once inside, they can be transported to various organs depending on their size and shape [57].

The ongoing presence of MNPLs in the environment is causing growing alarm due to the potential adverse effects on human health. The accumulation of mutagenic and carcinogenic MNPLs in various organs and tissues may lead to the prolonged progression of cancer due to their persistent characteristics. The assessment of the potential for plastics to cause cancer in humans has broadened the understanding that ongoing exposure to microplastics is likely to harm health [58].

Furthermore, MPs can serve as vehicles for transporting cancer-causing bacterial toxins to the cells lining the colon. The increased susceptibility to colorectal cancer is exemplified by the elevated risk associated with the presence of *Escherichia coli* in the colon, which produces a genotoxin. While *E. coli* is commonly found in the intestinal lumen, the observation of *E. coli* binding to MPs in an aquaculture model indicates that these bacteria can also adhere to MPs in the colon. If this occurs, MPs containing adhering pks^+ *E. coli* can transport these bacteria, which may cause genetic damage, to the surface of the colonic epithelium. Nevertheless, compelling evidence suggests that this process depends on the absence of a fully intact inner mucus layer [59].

In simple terms, the presence of pks^{+} *E. coli* near the colonic epithelium can be heightened by an imbalance in bacterial species that degrade colonic mucin, a change driven by dietary factors (dysbiosis). However, animals consistently exposed to PS MPs in their drinking water for six weeks exhibited colonic dysbiosis. As the number of colonic bacteria implicated in the development of CRC increases, the significance of this connection grows. The pro-carcinogenic mechanisms of different bacterial species vary, but it is convincing that the presence of these bacteria alongside MPs may facilitate the delivery of their bacterial toxins to the colonic epithelium. This finding supports the theory that the prolonged presence of toxin-producing bacteria may contribute to the development of cancer in an otherwise normal colon [60].

Moreover, a compromised mucus layer may facilitate the movement of MPs past the colonocytes and into the lamina propria. Once there, MPs are engulfed by intestinal macrophages located in this area. MPs can act as carriers for transporting particle-bound toxins to macrophages. Conversely, macrophages may also transport microorganisms attached to their surface through a process known as endocytosis of MPs. Macrophage polarization plays a crucial role in maintaining mucosal homeostasis and epithelial barrier integrity in the intestines. This process is governed by stimuli and the environment, influencing the functional phenotype of the macrophages. The predominance of M1 phenotype macrophages can sustain intestinal inflammation, which is associated with an increased risk of carcinogenesis, as activated macrophages can alter their characteristics. Chronic exposure to ingested MPs can affect macrophages' ability to change their physical characteristics, as evidenced by the shift to glycolysis in macrophages consuming MPs to generate energy. This further supports the notion that long-term exposure to MPs likely has a more significant impact than currently recognized in promoting inflammation-related colorectal cancer [61].

Reactive oxygen species (ROS) can be produced by MPs of various sizes, concentrations, physical and chemical properties, and durations of exposure. The oxidative stress resulting from prolonged macrophage activation and inflammation associated with MPs may enhance the risk of colorectal cancer. This process can be exacerbated by the delivery of harmful substances and microbes to macrophages via MPs. However, there is also evidence suggesting that MPs may not require surface-associated toxins to provoke an inflammatory response. Macrophages that ingest pristine MPs undergo a metabolic shift associated with changes in cell surface markers and the production of cytokine genes. Abnormal glycosylation of these proteins may lead to a dysfunctional mucus layer, even though the increased presence of pro-inflammatory cytokines has been shown to stimulate mucin production. This may enhance the generation of ROS that readily reacts with other molecules, such as DNA and proteins. Therefore, the consumption of MPs that results in ROS-induced oxidative damage to the DNA of the host can promote cancer-causing signaling and increase the likelihood of carcinogenesis [62].

7. Future perspective and conclusion

Numerous environmentally present contaminants of emerging concern (CECs) remain undetected due to limitations in detection techniques. Hence, it is imperative to develop robust, non-targeted monitoring methods that can identify unidentified substances with limited data. Establishing priority control lists for CECs is crucial to expedite regulatory measures. Furthermore, prioritizing the investigation and advancement of enhanced treatment techniques, such as Advanced Oxidation Processes or alternative technologies, is essential for addressing the presence of CECs in the environment. To mitigate the health hazards associated with

CECs, comprehensive studies into their origins and characteristics are necessary. In summary, implementing a comprehensive strategy that includes screening, assessment, control, prohibition, reduction, and treatment would ensure the efficient management of CECs and protect both human health and the environment.

Various substances disrupt natural, hormonally controlled biological processes and negatively affect development and reproductive functions by imitating or blocking the action of internal hormones, influencing hormone generation, or altering populations. These endocrine-disrupting substances exert their effects through multiple pathways, including receptor binding, signal transduction, and enzymatic processes involved in hormone production. Exposure to chemicals during vulnerable periods may modify the structure, development, and function of the mammary gland, thereby increasing the risk of cancer. These facts underscore the need for a deeper understanding of the intricate correlation between exposure to endocrine-disrupting substances and changes in the structure and genetic activity of the mammary gland, ultimately heightening the risk of disease. The functional relevance of various combinations of chemicals can be significant.

Additionally, the impact of time on the ability of low doses of these chemicals to induce estrogenic responses is a crucial aspect of environmental exposure. In dose-response studies, higher doses of chemicals may enhance tumor growth. However, the dose itself is not the only factor determining the development and progression of breast tumors, as their growth rates may vary.

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