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# A review on the combined toxicological effects of microplastics and their attached pollutants

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ABSTRACT

As an emerging environmental pollutant, microplastics (MPs) can adsorb various contaminants, including heavy metals and persistent organic pollutants (POPs). This ability stems from their small size and high specific surface area. Once adsorbed, the adherents can act in combination with MPs to produce synergistic toxic effects when they enter organisms through MPs, exacerbating their toxicity when introduced into organisms. This review examines the toxicological effects of the combination of different MPs and environmental pollutants on terrestrial and marine invertebrates, vertebrates, and microorganisms. In conclusion, the combined toxicological effects of MPs and their attachment to organisms are complex and multilayered. Existing studies have identified certain underlying mechanisms, underscoring the need for societies and governments to account for the combined toxic effects of MPs and their associated pollutants.


## 1. Introduction

Plastics are important organic synthetic polymer materials with a range of advantages, such as high corrosion resistance, low cost, low thermal conductivity, and water resistance; these properties contribute to their widespread use in daily life [1]. Globally, over 8.3 billion tons of virgin plastic have been produced, with annual production peaking at 400 million tons; this figure is projected to triple by 2060 [2]. However, only 21 % of global plastic waste is either recycled or incinerated, while the remaining 79 % is discarded into the environment [3]. Owing to their stable physical and chemical structures, plastic products are highly resistant to degradation in natural environments and persist for extended periods [4]. During this period, plastic fragments further disintegrate into plastic particles of varying sizes through physical abrasion, chemical interactions, and biological erosion. Depending on their size, plastic fragments in the environment can be classified into four categories: microplastics (MPs) (<0.5 cm), medium plastics (0.5–5 cm), large plastics (5–50 cm), and macroplastics (>50 cm) [5]; the concept of MPs was first proposed by British scientists in 2004 [6], with plastic particles smaller than 5 mm collectively referred to as MPs [7]. Moreover, MPs can be transformed into nanoplastics (1–100 nm) through physical, chemical, and biological

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degradation upon exposure to the environment. At this scale, their high cellular affinity enables them to penetrate biological barriers in the blood, cells, tissues, and organs, potentially causing more severe harm to organisms [8]. Moreover, the combined toxic effects of MPs and their attachment to organisms profoundly affect the ecological balance and human health. Studies have demonstrated that MPs can adsorb heavy metals, persistent organic pollutants, and other harmful substances into the environment to form complex pollutants whose combined effects on organisms are significantly greater than those of a single pollutant [9].

The MP sources can be divided into two categories: primary and secondary. Primary MPs in the environment primarily originate from the direct release of products containing MPs, such as plastic beads used as additives in personal cleaning products (such as toothpaste, and cosmetics) [10], studies have shown that certain cosmetics, such as facial cleansers, use a large number of PE plastic microbeads as additives, and these plastic microbeads produce an average of 15.2 mg MP per person per day after use, which is eventually discharged into the sewage system [11]. Secondary MPs are plastic particles formed from large plastic waste (such as ropes, packaging, and clothing) that are fragmented and reduced in size through processes such as mechanical abrasion, chemical corrosion, and biodegradation. The majority of MPs formed in aquatic environments are secondary MPs resulting from the breakdown of larger plastics; studies have demonstrated that due to constant friction, a garment made of acrylic can emit 120,000 plastic fibers per kilogram per wash, while a PET wool blanket can release 0.0012 wt% of microfibers [12]. Moreover, the study found that the plastic bottles of refrigerated carbonated beverages would also become the source of MPs and nanoscale MPs (NPs), and after several freezings, the release of MPs and NPs in the bottles significantly increased, reaching 450 ± 38.65 MPs/L and $2.91 \pm 0.10 \times 10^8$NPs/L, respectively [13].

MPs can be categorized based on various criteria. Depending on the initial chemical material, MPs are classified as PE, polypropylene (PP), polystyrene (PS), or polyvinyl chloride (PVC) [14]. In a previous study, MPs with an abundance of 0.23 ± 0.45 MP/ml were discovered in human semen, with PE- and PVC-MPs predominant [15]. In addition, using laser direct infrared spectroscopy, researchers also found MPs with an average windage of 2.70 ± 2.65 MP/g in human placentas, with PVC- and PP-MPs accounting for 43.27 and 14.55 %, respectively [16]. Regarding PS-MPs, it was shown that the average density of PS-MPs in the Florida Keys lagoon water, USA, ranged from 8000 to 24,000 MP/L, and at their peak, the average particle density of PS-MPs reached a level approximately the same as that of the average microplanktonic algal density [17]. In addition to their chemical composition, MPs can be classified as suspended or sedimentary, according to their state in the atmosphere or water [18]. In terms of shape, MPs can be classified into the most common granular types: fibers, primarily originating from textiles; films, originating from film products such as cling films; and foams, originating from foam products [19]. In addition, MPs of different shapes commonly accumulate at different locations in the body. Plastic fibers often accumulate in the lungs and cause adverse consequences, such as cancer, whereas granular MPs are often found in the human liver, spleen, and abdominal lymph nodes [20].

## 2. Distribution of MPs

The distribution of MPs is a complex issue involving multiple environmental domains including marine, freshwater, and terrestrial environments. They exist in various forms worldwide and are potentially harmful to ecosystems and organisms [21]. For example, the soil is the hardest hit by MP contamination, with statistical results showing that the abundance of MPs in the soil is significantly higher than that in marine and freshwater environments [22]. In a study conducted along the middle and lower reaches of the Yangtze River in China, the average MP content in soil along the river reached 37.32 MP/kg [23]. Moreover, the amount of MPs in the soil has been gradually increasing, and the abundance of MPs collected from urban soil in Nanjing increased from 326.7 to 480.9 MP/kg between 2010 and 2020 [24]. MP contamination has been identified in soil not only in China but also worldwide. For example, in Brazil, the MP concentration in the soil can reach an average of 10,732 kg [25]. In Iran, this concentration was reported to be 92.85 ± 119.24 MP/kg on average [26]. In Mauritius, MPs in the soil ranged from 73.3 to 293.3 kg in shallow surface soils and from 80 to 393.3 kg in deep soils [27]. Although the removal rate of MPs in the equalization tank of a sewage treatment plant can reach 46.67−87.91 %, the remaining MPs are still discharged into the environment [28]. Some of these MPs are deposited in contaminated soils, whereas others are eventually discharged into the sea [29]. One report studied the abundance of MPs in the Bohai Sea, China, throughout the year and measured the average density of total plastics in all seasons as 0.49 ± 0.18 plastic/$m^3$ [30]. In addition, the surface MP abundance was reported to fluctuate between 50 and 66 MPs/100 ml in the Egyptian Red Sea, whereas it ranged from 46 to 69 MPs/100 ml [31]. Oceans are considered important hubs of MP pollution [32], and nanoscale MPs (NPs) form aerosols in marine environments and enter the atmosphere [33]. The average distribution of MP abundance in the Pacific Ocean atmosphere was reported to be 0.027 ± 0.018 MP/$m^3$, whereas as many as 845 MP species were identified in the urban atmosphere of Mexico, in which MP concentrations in human respirable sizes of PM2.5 and PM10 reached 0.110 ± 0.055 and 0.205 ± 0.061 MP/$m^3$, respectively [34]. In addition to seawater systems, MPs have also been found in freshwater systems, such as lakes and rivers; for example, MP concentrations in South Indian lakes reached 0.423 and 0.117 MP/L during the monsoon and post-monsoon periods, respectively [35]. A team of researchers also analyzed the abundance of MPs in the Yangtze River and coastal reservoirs and found that the average abundances of MPs in the reservoirs and river water were 3696 and 2826 MP/$m^3$, respectively [36]. MPs have even been found in some extreme regions, such as the North and South Poles [37,38], and even on plateaus and deserts [39,40].

## 3. Contaminants attached to MPs

The small size of MPs implies a higher specific surface area (the specific surface area refers to the surface area per unit mass of a porous solid substance). The composition of MPs and their large specific surface area make them excellent carriers [41] and highly susceptible to absorbing toxic and hazardous pollutants from the environment [42]. These are exogenous pollutants attached to MPs.

For example, metal ions in the environment interact with MPs when they encounter them, a process that includes direct adsorption of cations, complexation of metal ions at charged sites or in neutral regions, and precipitation and co-precipitation processes [43]. Previously, Ashton et al. placed PE plastic pellets in a harbor body of water for eight weeks and found that the surface of the PE pellets appeared to be covered with attached organic and inorganic precipitates, which were analyzed and found to contain various metals such as Al, Fe, Mn, Cu, Pb, and Zn [44]. In addition, the researchers found the presence of Hg in the Cartagena Beach MPs, and overall, the highest Hg content was found in the secondary MPs, with a concentration of nearly 100 μg/g [45]. In addition to Hg, another study found significant differences in metal concentrations between natural and unused plastic particles; these particles, after degradation and wear and tear in nature, had significantly higher

concentrations of several metals such as Ti, V, N, Zn, As, Sr, Ba, and Cd compared to those found in unused plastics. This report suggests that elevated levels of these metals are adsorbed by MPs into the environment [46].

In addition, MPs and NPs potentially interact with environmental pollutants, such as persistent organic pollutants (POPs) and pharmaceuticals. The concentration of chemical contaminants on the MP surfaces is six times higher than that in the surrounding ambient water [47]. Although the production of many POPs has been banned or restricted under the Stockholm Convention, the global production of various types of pollutants has reached levels sufficient to be ecologically hazardous, including nearly three million tons of DDT and 1.51 million tons of PCBs [48]. It has been shown that MPs do adsorb DDT in the environment [49]. PCBs have also been shown to interact with MPs in water, increasing the risk of cancer in zebrafish, and adversely affecting the development of zebrafish larvae [50]. In addition to these POPs, the increasing amount of pharmaceutical residues in the environment, owing to the misuse of over-the-counter medicines in agriculture and aquaculture, also bind to MPs, and the combined pollutant system consisting of MPs and residual pharmaceuticals is likely to be more detrimental to aquatic ecosystems than individual pollutants [51]. For example, hygromycin, which is commonly used in aquaculture, has been detected in freshwater aquaculture systems at concentrations as high as 7028 ng/L [52]. In domestic wastewater, sulfamethoxazole, mephedrone, and ciprofloxacin are the most abundant antibiotics [53] for which MPs are good carriers, thereby enhancing antibiotic accumulation in aquatic organisms and causing combined toxicological effects [51]. In addition, PE and PS particles have the strongest adsorption capacity for antibiotics. Tetracycline and ciprofloxacin are more likely to be adsorbed onto MPs compared to other antibiotics [54]. When MPs are digested by organisms, harmful drugs are synchronously transferred and toxic substances bioaccumulate throughout the food chain and are eventually ingested by humans. In addition, the MP surfaces can act as carriers of bacteria and viruses [55]. Mercedes Masó et al. first discovered at the beginning of this century that MPs can contaminate the environment by adsorbing pathogenic microorganisms [56]. Many bacteria, diatoms, fungi, and viruses can attach to MP surfaces [57]. Several recent studies have found that certain marine bacteria produce organic bromines such as hydroxy polybrominated diphenyl ethers (PBDEs), methoxy PBDEs, and polybrominated pyrroles [58]. Pollution increases when microorganisms attach to the pollution they produce increases.

Endogenous pollutants can also attach to MPs. Plastics are prepared with appropriate additives, including plasticizers, flame retardants, and colorants, which are typically physically rather than chemically bonded to the primary polymer matrix [59]; these toxic additives are slowly removed from plastics when MPs circulate in the natural environment. Therefore, when MPs circulate in the natural environment, these toxic additives slowly migrate from the interior of the plastic to the external medium [60], and due to the increase in the surface area to volume ratio of MPs, they are more readily released from MPs, which can significantly increase their toxicity [18]. For example, bisphenol A (BPA) and its analogs (such as BPB, BPE, BPS, and BPF), which are endocrine disruptors, are often used as plasticizers and added to plastics. BPA is a monomer used in the production of PC plastics, with an annual production of millions of tons [61]. Significant amounts of BPA and its analogs have been detected in MPs deposited on beaches in Hong Kong [62], and BPA has been detected in plastic debris in the open sea and on beaches in European and American cities at levels ranging from 1 to 729.9 ng/g [63]. Other common additives, such as PBDEs and brominated flame retardants, such as hexabromocyclododecane (HBCD), tetrabromobisphenol A (TBBPA), phthalate esters, BPA, and nonylphenol, are also biotoxic.

In addition, some heavy metals are also added to MPs as additives; a study found large concentrations of Zn in the plastic film of five disposable paper cups tested; the study also detected heavy metals such as Pb, Ni, Cr, and Cu [64]. Antimony oxide, aluminum oxide, and zinc borate are well-known flame retardants used in the manufacture of plastics; however, Sb and Al have been found to be metalloestrogens in addition to the risk of breast cancer [63]. Cd is often used as a heat and UV stabilizer and inorganic pigment in PVC plastics [65] but has been found to promote apoptosis and DNA methylation, increase lipid peroxidation levels [66], and lead to renal insufficiency in sensitive populations (such as diabetic patients) [67], and $TiO_2$ is used as both a white pigment and UV stabilizer in plastics [68]. However, titanium is cytotoxic to human lung and colon epithelial cells [69], with ultimately potentially toxic effects on living organisms.

### 3.1. Factors affecting pollutant adsorption by MPs

Pollutant adsorption by MPs is a complex environmental process that relies on electrostatic interactions, surface complexation, and van der Waals forces [70], which are influenced by several factors (Fig. 1). First, the nature of the MPs, such as their size, shape, surface chemistry, and surface characteristics, as well as other attributes, affect their adsorption capacity for pollutants. Although the properties of plastics change significantly during the aging process, in the environment, the primary cause of plastic aging is sunlight or UV radiation [71]. This process can be divided into three steps: UV-induced chain breakage, polymer chain reaction, autooxidation, and formation of inert end products [72]. Additionally, UV radiation leads to plastic fragmentation, forming smaller particles [73,74]. It has been found that the smaller the size of MPs, the larger their specific surface area and ability to adsorb pollutants will be enhanced. It was found by Zhang et al. that when the particle size of PE- and PP-MPs was reduced from 1.7 to 0.15 mm, the adsorption capacity of both MPs for 9-nitroanthracene, a pollutant, was substantially increased, with PE-MPs increasing from 0.28 to 1.66 %, and PE-MPs from 0.30 to 1.63 % [75]. Moreover, when comparing the adsorption of MPs and NPs, the adsorption rate of NPs was one to two orders of magnitude higher [76]. In addition, during the aging process, microcracks and pores are formed on the surface of the MPs [77], which increase their adsorption capacity. The adsorption capacity of aged MPs for pollutants was much higher than that of ordinary MPs, and the adsorption capacities of aged PP-, PE-, and PS-MPs for pollutants increased 1.45-, 1.46, and 1.25 times, respectively [70]. The adsorption capacity of aged MPs for heavy metals was much higher than that of the original MPs, and the adsorption capacity of MPs for both Cu and Zn increased with increasing MP aging, which may be related to the increase in the oxygen function on the surface of the aged MPs after UV radiation [72]. Research has revealed that masks release a large number of MPs during the aging process, and the adsorption capacity of aging masks as adsorption carriers for Zn(II), Cr(VI), Tl(I), tetracycline (TC), and acenaphthene (Ace) is significantly increased compared with new masks, such as the adsorption capacity of Zn(II), which is enhanced by 23.46 μg/g [78]. Moreover, MPs that have undergone photoaging also release chemical additives from their bodies, which further increase the types of adherents on MP surfaces, as well as their toxicity [73]. It has been shown that nonpolar compounds (e.g., naphthalene and methylnaphthalene) adsorb to MPs mainly through dispersion forces, whereas polar compounds (e.g., naphthol) adsorb to MPs mainly through dipole-induced forces and hydrogen bonding [79]. In addition, the interaction between MPs and microorganisms is a major factor affecting adsorption. As hydrophobic artificial materials, MPs are easily

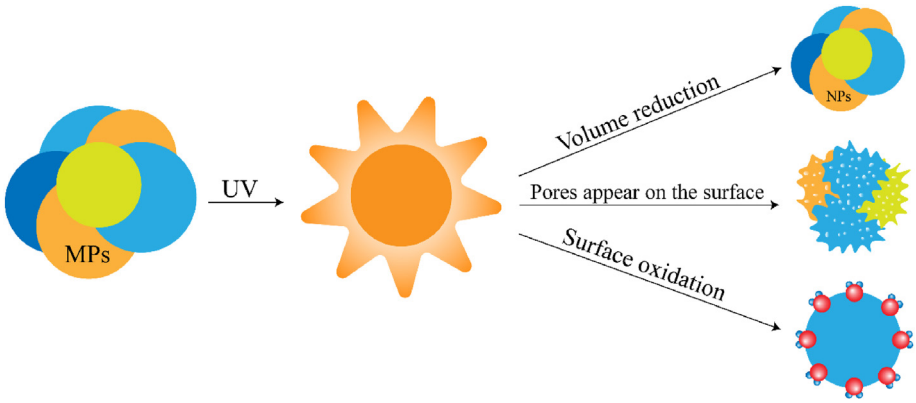


**Fig. 1. Factors affecting the attachment efficiency of pollutants on microplastics.** Microplastics undergo aging by UV radiation in sunlight, which results in volume reduction, surface porosity, surface oxidation, and other phenomena.

colonized by microorganisms, resulting in the formation of biofilms that may alter the chemical properties of the MP surfaces, thereby affecting pollutant adsorption behavior [80]. Biofilms on MP surfaces have been shown to facilitate metal–plastic interactions in several ways. As heavy metals adsorbed within biofilms are not as tightly bound as those adsorbed directly onto polymers, biofilms can accelerate the cycling of heavy metals in the environment by releasing hazardous metals from plastics containing heavy metal additives [81]. In addition, changes in the external environment can also have an impact on the adsorption properties of MPs. For example, other components in the solution, such as organics, inorganic salts, and colloids, can affect the adsorption behavior of MPs with pollutants as they can competitively interact with MP surfaces. For example, a higher concentration of $Na^+$ competes for the cation exchange sites on MP surfaces, thereby decreasing the adsorption capacity of the MPs for organic pollutants [82]. The degree of protonation of MPs and organic pollutants changes with the pH of the environment, thereby altering the adsorption capacity of MPs for pollutants. It has been found that the adsorption rate of PS-MPs on pollutants is higher when the environmental pH is in the range of 3.0–6.0, whereas when the pH is > 6.0 the adsorption rate of PS-MPs showed a significant decrease in the pollutant adsorption rate [83]. Finally, ambient temperature also affects the adsorption behavior. The adsorption of 3,3′,4,4′-tetrachlorobiphenyl (PCB77) by PP-MPs decreased by one-third when the ambient temperature was increased by 10 °C, which indicates that high temperature decreases the surface tension of the solution thus decreasing the adsorption ability of PP-MPs for PCB77 [84]. In addition, stirring or flow conditions affect the frequency of contact between the MPs and contaminants in the solution, which, in turn, affects the rate and extent of adsorption.

The age of MPs is also a critical factor affecting the absorption of pollutants. Primitive MPs usually have a relatively regular and smooth surface morphology. For example, plastic particles may have rounded surfaces with no visible cracks or breakage. In contrast, the appearance of aged MPs differs significantly. Under the combined effects of physical, chemical, and biological factors, the surfaces of aged MPs become rough and uneven, developing numerous cracks, holes, and scratches [72,73]. For example, in marine environments, the impact of waves, ultraviolet radiation, and microbial erosion causes the surfaces of aging MPs to be riddled with holes, and the original intact structure is destroyed [85]. These morphological changes increase the specific surface area of aged MPs, enhancing their interaction with substances in the surrounding environment [75].

The chemical compositions of original MPs are relatively homogeneous, consisting mainly of plastic polymers. However, aging significantly alters the chemical composition of MPs. Ultraviolet radiation and oxidation cause the plastic molecular chains to break and recombine, producing new functional groups [86]. After aging, oxygen-containing functional groups such as carbonyl and carboxyl groups may appear on the surface of the original MPs [87]. The appearance of these functional groups changes the surface chemistry of aged MPs, enhancing their hydrophilicity while lowering chlorine content and crystallinity [88]. In addition, aging MPs may adsorb other substances from the environment, such as heavy metal ions and organic pollutants, further enriching the chemical composition of their surfaces [89].

The sharp edges and rough structure of the surfaces of aging MPs facilitate mechanical damage to organisms [90]. When organisms ingest aged MPs, these sharp particles may scratch tissues such as the digestive and respiratory tracts, causing inflammation [91]. For example, in marine organisms, aging MPs may cause intestinal perforations in fish and gill damage in shellfish, seriously affecting their health and survival. The additives and polymers in the original MPs are relatively stable and release harmful substances at slower rates. Aging accelerates the release of these substances. Plasticizers, antioxidants, and other additives added to plastics during the production process dissolve more easily in aged MPs [92]. These additives may have toxic effects such as endocrine disruption and carcinogenesis. In addition, the aging process degrades plastic polymers, producing small molecular degradation products that may also be toxic. For example, some plastics release harmful substances such as phthalates and bisphenol A during aging, causing damage to the cells and tissues of organisms [73].

Although original MPs can also adsorb a certain amount of pollutants, their adsorption capacity is relatively weak owing to their small specific surface area and limited surface properties. Aging MPs have higher adsorption capacities owing to their larger specific surface areas and abundant surface functional groups. These aged particles can absorb heavy metal ions, polycyclic aromatic hydrocarbons, pesticides, and other pollutants in the environment, acting as effective carriers for microorganisms [93,94]. Studies have shown that for PLA-MPs and PE-MPs, the adsorption capacity of ciprofloxacin is greatly improved after aging, with the former increasing by 18.06 % and the latter even reaching 75 % [95]. Tao et al. demonstrated that the adsorption capacity of aged PE-MPs for carbendazim, difluorophenylurea, malathion, and phenacetoconazole was improved compared with the original PE-MPs [96]. Moreover, Wang et al. showed that when faced with the antibiotics tetracycline and Cd, a common heavy metal, the adsorption capacity of aging MPs for these two pollutants was also greatly

improved compared with the original MPs [89].

In conclusion, contaminant adsorption by MPs is influenced by several factors.

### 3.2. Combined toxicity effects on organisms

It has been found that MPs act synergistically with pollutants when co-existing and that MPs can act as organic pollutant carriers in the tissues and organs of organisms, thereby increasing the concentration of harmful substances. In most cases, MPs exacerbate the toxic effects of pollutants in organisms.

#### 3.2.1. Combined toxicity effects on aquatic organisms

*3.2.1.1. Effects on aquatic invertebrates.* We investigated the combined toxicity of PS-MPs and ammonium perfluorooctanoate in Daphnia magna at different concentrations (Fig. 2 and Table 1). By analyzing intestinal fullness, histology, and lipid peroxidation in Daphnia, we found that the combined toxicity of these two pollutants was primarily concentrated in the intestine. The damage to the intestinal tract of Daphnia varies with pollutant concentration [97]. Another study found that after exposing freshwater Daphnia to MPs and triclosan (TCS) for two days, although exposure to MPs alone did not show significant physiological toxicity, Daphnia exposed to both TCS and MPs showed significantly greater deleterious effects, including increased mortality and altered antioxidant enzyme activity, compared to that of Daphnia exposed to TCS alone. In addition, MXR inhibition led to TCS accumulation, resulting in synergistic toxic effects [98]. By studying oysters, researchers found significant combined toxicity of the synthetic hormone 17α-ethinylestradiol (EE2) and MPs. Oysters exposed to EE2 and MPs show changes in phase 2 enzymes and antioxidant systems, and reduced lysosomal membrane stability in the gills [99]. In addition, by assessing antioxidant enzymes, oxidative stress parameters, and digestive system enzyme activity in mussels exposed to PS-, PP-, and PET-MPs in combination with the toxic metal Cd for seven days, the development of oxidative stress, tissue damage, and neurotoxicity was induced. Moreover, the combination of two MPs (PS and PP) with Cd resulted in higher Cd accumulation in mussels than in the other groups, suggesting that exposure to different types of MPs may have different effects on Cd retention in biological tissues [100]. For the shellfish study, Wang et al. exposed oysters to 50 μg/L perfluorooctanoic acid (PFOA) and its replacement 50 μg/L hexafluoroepoxypropane dimeric acid (PG) and 1 mg/L fluorescent PS-MPs for seven days, and found that the PS-MP + PG group caused more pronounced histopathological damage to the gills and intestines. The levels of antioxidant enzymes were higher in the PG-induced groups than those in the PFOA groups. These enzymes include superoxide dismutase (SOD), catalase (CAT), glutathione reductase, and glutathione peroxidase (GPx). In addition, the expression levels of several immune-related genes such as tnfα, cat, stat, tlr-4, sod and β-gbp were significantly up-regulated in both the PG and PF groups. Co-exposure also induced significant changes in the gut flora of oysters, resulting in a decrease in beneficial bacteria and an increase in pathogenic microorganisms [101]. Kong et al. investigated the relationship between PS-NPs and PCB77 on the combined toxicity of hard white clams and found that exposure to either PS-NPs or PCB77 alone caused damage to the gills, digestive glands, and intestines. In contrast, co-exposure to these two contaminants induces greater toxicity, including histopathological changes, altered antioxidant capacity, and disruption of the gut microbiota [102].

*3.2.1.2. Effects on aquatic vertebrates.* Avermectin benzoate (EMB) is widely used as an insecticide. Studies have shown that carp exhibit shortened intestinal cilia, lysosomal damage, and excessive production of reactive oxygen species (ROS) when exposed to a combination of EMB and MPs, leading to impaired intestinal barrier function. Expression of immune-related genes (such as

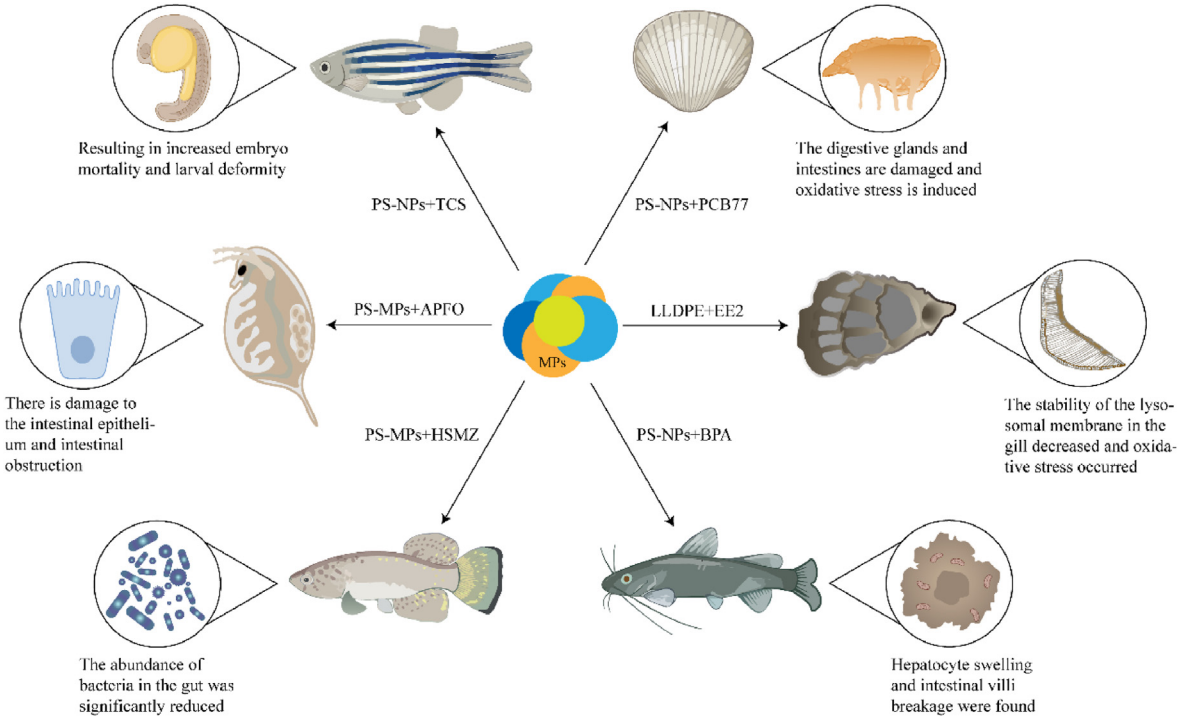


**Fig. 2. Combined toxic effects of microplastics and the attached pollutants on terrestrial organisms.** Microplastics in combination with different types of pollutants can affect the liver, kidneys, reproductive system, respiratory system of mice, and damage the wall structure and digestive system of earthworms and nematodes.

**Table 1**
The combined toxicity of microplastics and the attached pollutants on aquatic invertebrates and vertebrates.

| Types of microplastics | Attached pollutants | Affected organisms | Adverse effects | Reference |
|---|---|---|---|---|
| **PS-MPs** | APFO | Water flea | Damage to the intestinal epithelium and intestinal obstruction. | [97] |
| **Modified polystyrene** | TCS | Water flea | Increased mortality and altered antioxidant enzyme activity, resulted in inhibition of MXR activity. | [98] |
| **Linear low-density polyethylene** | EE2 | Oyster | GPx activity increased, increased ROS production and decreased lysosomal membrane stability in the gill | [99] |
| **PS-MPs, PP-MPs, PET-MPs** | Cd | Mussel | Induced oxidative stress, tissue damage, and neurotoxicity. | [100] |
| **PS-MPs** | PFOA, PG | Oyster | Increased expression of antioxidant enzymes, the expression levels of immune-related genes, and the change of intestinal flora. | [101] |
| **PS-NPs** | PCB77 | Hard clam | Induced oxidative stress and the damage of gills, digestive glands, and intestines. | [102] |
| **PS-MPs** | EMB | Carp | Intestinal cilium shortening, lysosome injury and excess reactive oxygen species production, leading to impaired intestinal barrier function. | [103] |
| **PS-MPs, PVC-MPs** | METH | Zebrafish | Stimulation of steroid hormone synthesis pathway and C-type lectin signaling pathway, leading to apoptosis and immune response | [106] |
| **PS-MPs** | MT | Zebrafish | Reduced ratio of mature oocytes to mature sperm in the gonads, delayed offspring incubation time and development. | [107] |
| **HDPE-MPs** | Cu, Cd, Pb | Seahorse | Hippocampal lipid peroxidation and oxidative damage resulted in increased mortality. | [108] |
| **PS-MPs** | Cd | Carp | Upregulated immune-related genes and altered amino acid metabolic pathway. | [109] |
| **PS-NPs** | TCS | Zebrafish | It slowed the inhibitory effect of TCS on ovarian development while exacerbating the inhibitory effect on sperm, resulting in increased embryo mortality and larval deformity, and PS-NPs disrupted the HPGL axis, thereby altering the TCS-induced reproductive toxicity | [111] |
| **PE-MPs** | PTH | Zebrafish | PE-MPs can enhance the toxicity of pentapyran in the short term, and lead to increased intestinal oxidative stress damage in the long term (7d) | [112] |
| **PS-NPs** | MC-LR | Silver carp | The intestinal short villi length of silver carp was significantly shortened, pathological changes of liver, intestinal tract and gill tissue, intestinal flora disorder and glycerophospholipid metabolism imbalance were observed | [113] |
| **PS-MPs** | 3,6-DBCZ | Zebrafish | It has antagonistic effect on oxidative stress and apoptosis of embryo | [114] |
| **PS-MPs** | HSMZ | Bluefish | The bacterial richness in the gut of the killifish decreased significantly, and several functional pathways were dysfunctional after environmental recovery, and the incidence of pathogenic bacteria was higher | [115] |
| **PS-NPs** | BPA | Catfish | Pathological damage such as intestinal villi rupture and hepatocyte swelling occurred | [116] |

immunoglobulin and IFN-γ) was reduced, whereas expression of inflammation-related genes (such as TNF-α and IL-1β) was increased (Table 1). These symptoms were significantly higher after combined exposure to the two pollutants than after exposure to a single pollutant [103]. In contrast, MP intake is positively correlated with the bioaccumulation of PBDE congeners in fish [104]. A meta-analysis has shown that the co-existence of MPs with other pollutants exacerbates their toxic effects on the immune system, metabolism, and oxidative damage in fish [105]. In aquatic ecosystems, the coexistence of MPs and methamphetamine (METH) results in a significant increase in the turning angle of zebrafish during locomotion, which is not observed upon exposure to a single pollutant. RNA sequencing and quantitative gene analyses have shown that simultaneous exposure to MPs and METH stimulates steroid hormone synthesis and C-type lectin signaling pathways in zebrafish, leading to apoptosis and immune responses [106]. In addition, Rong found that combined exposure to 17α-methyltestosterone (MT) and PS-MPs resulted in a gradual decrease in the ratio of mature oocytes to mature spermatozoa in the gonads of zebrafish over time, with the ratios being controlled > PS-MPs > MT > MT + PS-MPs. This exacerbates MT toxicity, making the transgenerational effect more obvious in the offspring, resulting in delayed hatching time, slow development, or even death and malformation [107]. Another study on seahorses showed that when MP particles accumulated in their intestines, although the MPs themselves did not have major obvious effects on their growth and development, heavy metal ion attachment greatly increased lipid peroxidation and oxidative damage, leading to increased mortality. This confirmed that MPs carrying heavy metals caused greater harm to seahorses than single MPs [108], which was not confined to the hippocampus. Researchers have found that MPs have a cumulative effect on Cd accumulation and toxicity in rice carp, and can enhance Cd accumulation when rice carp are exposed to both Cd and MPs. In addition, the combined toxicity of MP and Cd upregulated immune-related GO terms and aspartate aminotransferase 1 related to amino acid metabolic pathways in C. inaequalis, thereby negatively affecting its health [109]. TCS is also a novel contaminant that can be detected in the human body [110]. Studies in zebrafish have shown that PS-NPs can adsorb TCS, altering its physical properties. Moreover, when zebrafish were exposed to both TCS and PS-NPs, the TCS levels in the different organs of female and male zebrafish showed different changes. Additionally, co-exposure slowed the inhibitory effect of TCS on ovarian development and exacerbated its inhibitory effect on spermatozoa, leading to increased embryonic mortality and larval malformation. These results differ significantly from those of TCS exposure alone. Transcriptomic analyses have shown that PS-NPs disrupt the HPGL axis, thereby altering TCS-induced reproductive toxicity through sex-specific effects [111]. As an organic pollutant, pentothiopyran (PTH) is a common fungicide, and a study by Zhao et al. found that short-term exposure of zebrafish to PTH and PE-MPs revealed that PE-MPs enhanced the acute toxicity of PTH. Long-term exposure to PE-MPs also enhances the accumulation of pyranopentapyrine in zebrafish, leading to increased intestinal oxidative stress damage, a condition that may be related to alterations in the intestinal flora [112]. Cyanobacteria often occur in aquaculture, and the microcystins (MC) released by cyanobacteria are adsorbed onto MPs during aquaculture. It was found that co-exposure to PS-NPs and MC-LR significantly shortened the length of intestinal short villi into significantly shrunken chubs and that the diversity and abundance of intestinal microorganisms in fish increased significantly after exposure to PS-NPs, which was amplified by MC-LR co-

action, ultimately affecting the enrichment pathways of glycerophospholipid metabolism and folate biosynthesis [113]. In addition, Zhang found that PS-MPs as carriers promoted the accumulation of 3,6-dibromocarbazole (3,6-DBCZ) and its dioxin-like toxicity in zebrafish larvae via ingestion. Furthermore, although the exposure of zebrafish embryos to 3,6-DBCZ or PS-MPs increases ROS levels and induces apoptosis, this environment is antagonistic to oxidative stress and apoptosis when zebrafish embryos are exposed to both pollutants [114]. Wang et al. found a significant decrease in bacterial abundance and a change in the flora structure in the medaka gut after exposure to sulfadimethoxine (HSMZ) and PS-MPs. In addition, after placing medaka fish in a decontaminated environment, although the bacterial flora recovered, medaka fish in the PS-MPs + HSMZ group showed less stable intestinal bacterial flora and several functional pathways were dysfunctional, with a higher prevalence of pathogenic bacteria [115]. Zheng et al. found a significant reduction in bacterial abundance in the gut of catfish when exposed to PS-NPs alone or to BPA, with intestinal villus breakage and hepatocytic swelling, whereas histopathological damage was exacerbated when co-exposure occurred. In addition, co-exposure significantly increased SOD and CAT activities and MDA levels in the gut and liver and altered the composition of the gut microbiota, leading to an increase in the Shannon index and a decrease in the Simpson index [116].

However, the concentrations of contaminants in most experiments were much higher than those detected in the real environment, which may not accurately reflect real-world exposure. In the real environment, pollutants usually exist in relatively low concentrations, such as MPs, the average concentration in the ocean is only 0.01 to 10/$m^3$, and in the soil is generally less than 1000/kg [24,26,30]. Even in living organisms, this concentration is limited to a few hundred micrograms per gram [117]. For other pollutants, such as various heavy metals, the concentration in soil is generally less than 100 mg/kg and even a few micrograms per liter in water [118,119]. Various organic pollutants are generally not present in high concentrations in nature [120]. In various studies, the concentration of pollutants used can often reach hundreds or even thousands of times the ambient concentration [97,112,121]. Experiments with high concentrations of pollutants may quickly induce obvious toxic reactions in organisms, helping researchers observe and analyze toxic effects. However, this acute reaction is not equivalent to the consequences of chronic exposure of organisms to the natural environment over months, years, or even decades. The response mechanism of organisms exposed to low doses for extended periods may differ significantly from that of organisms exposed to high concentrations for a short period. Certain organisms may rapidly activate emergency defense mechanisms such as the synthesis of specific stress proteins when exposed to high pollutant concentrations [122]. However, when living in low-concentration pollution environments for extended periods, organisms may gradually adapt by changing their own metabolic pathways, which is difficult to reflect in high-concentration short-term experiments [123].

### 3.2.2. Combined toxicity effects on terrestrial organisms

*3.2.2.1. Effects on terrestrial invertebrates.* It has been found that when MPs were added to soil, the bioaccumulation of metals and polycyclic aromatic hydrocarbons (PAHs) in earthworms significantly increased in 17.4 % of the experiments owing to the adsorption of pollutants by MPs [124] (Fig. 3). The synergistic toxicity of MPs and the pollutants that they carry, compared with exposure to MPs or other pollutants alone, can cause greater oxidative damage to earthworms than exposure to MPs or other contaminants alone, thus causing increasingly severe negative effects on earthworm growth, behavior and their immune systems, as well as inducing an increase in intestinal permeability, thereby leading to changes in their intestinal bacterial communities [125] (Table 2). In addition to PAHs, naproxen, a common drug, also exerts toxicological effects on earthworms in combination with MPs, and the study results showed that while increased lipid metabolism was observed in the naproxen-exposed group, a decrease in lipid metabolism was observed in earthworms when co-exposed to naproxen and MPs. Moreover, MPs increase naproxen concentrations in earthworms at the suborgan and subcellular levels, further increasing the risk of exposure to contaminants [121]. In addition, when Xin et al. exposed earthworms to pyrimethanil (a commonly used insecticide) and four different PE-MP aging levels, pyrimethanil accumulation increased. Moreover, exposure to pyrimethanil and aged PE-MPs, either alone or in combination, may lead to oxidative damage in earthworms. In addition, the combination of PE-MPs and pyrimethanil at different levels of aging was more toxic to earthworms than exposure to pollutants alone, further confirming the enhancing effect of aged PE-MPs on the toxicity of pesticides to earthworms [126]. In addition, Wang et al. further evaluated the ecotoxicity of combined contamination with NPs and Ni in earthworms, and the experimental results revealed a synergistic effect, wherein CAT and SOD activities in earthworms decreased within 28 days of exposure. The combined contamination resulted in ROS accumulation, which caused severe oxidative damage due to the disruption of earthworm antioxidant systems, inducing increasingly severe lipid peroxidation and even disrupting the body wall structure [127]. Fu et al. combined PE-MPs of different sizes with a range of imidacloprid (IMI) concentrations and exposed earthworms to the simultaneous presence of PE-MPs and IMI. They found that combined exposure did not significantly increase acute toxicity in earthworms compared to exposure to either IMI or PE-MPs alone but significantly inhibited the increase in body weight and induced increasingly severe epidermal damage, with a magnitude effect (10 μm PE-MPs was the most toxic to earthworms in combination with IMI), and transcriptomics results showed that this was mediated by the superimposed effect of iron death and oxidative damage [128]. Researchers have assessed the combined toxicity of UV-aged polystyrene (UV-PS) and TBBPA in Hidradenitis elegans nematodes and found that UV-PS efficiently adsorbs TBBPA, rendering it more bioavailable in the environment. The combined exposure resulted in significant reductions in the nematode body length, locomotor behavior, and brood size, suggesting that UV-PS enhanced the toxic effects of TBBPA. In addition, co-exposure to UV-PS and TBBPA induced a stronger oxidative stress response, as evidenced by increased ROS production and lipofuscin content, further damaging the nematode gut structure and increasing gut permeability. These results reveal the active mechanism by which UV-PS enhances TBBPA toxicity [129].

*3.2.2.2. Effects on terrestrial vertebrates.* As a plasticizer, di-(2-ethylhexyl) phthalate (DEHP) is often used in conjunction with MPs. Li et al. found that exposure to either PS-MPs or DEHP alone led to inflammatory cell infiltration, rupture of cellular membranes, and spillage of renal tissue in mice (Table 2). Antioxidant enzyme levels were down-regulated, ROS levels were increased, and the NF-κB pathway was activated, however, when mice were co-exposed to both pollutants, the pollutants exhibited greater toxicity to renal tissues, inducing an oxidative stress process involving heat shock proteins, activating the NF-κB/NLRP3 pathway and exacerbating renal focal death and inflammation [130]. In addition, other researchers have exposed mice to PS-MPs and DEHP in a mouse model of allergic asthma and found that exposure to PS-MPs alone had a slight effect on airway inflammation and hyperresponsiveness, whereas concomitant exposure to both PS-MPs

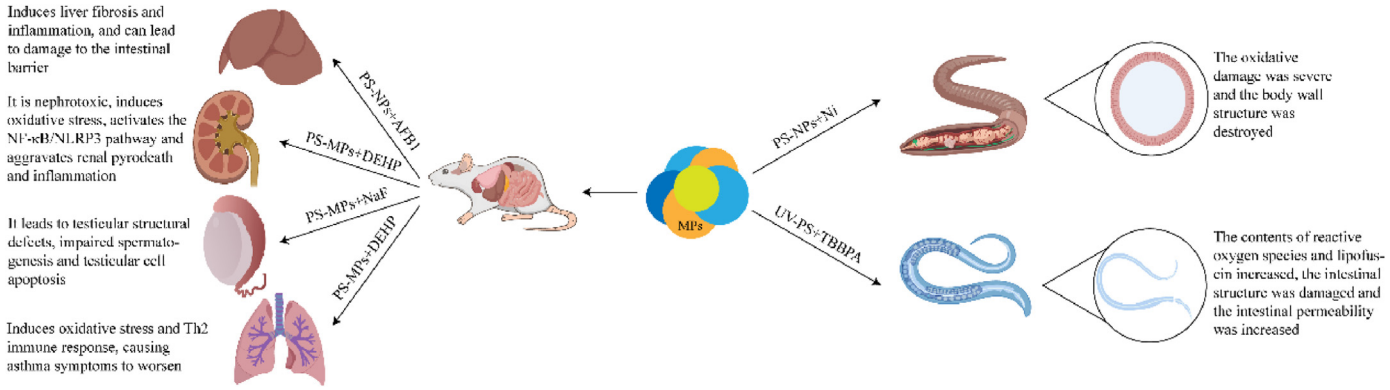


**Fig. 3. Combined toxic effects of microplastics and the attached pollutants on aquatic organisms.** Microplastics in combination with different types of pollutants can cause abnormal embryonic development in zebrafish, damage to the digestive system of white hard clams, oxidative stress in the gills of oysters, a range of adverse effects on the hepatocytes of catfish, alteration of intestinal flora of killifish, and alteration of digestive system of daphnia.

**Table 2**
The combined toxicity of microplastics and the attached pollutants on terrestrial invertebrates and vertebrates.

| Types of microplastics | Attached pollutants | Affected organisms | Adverse effects | Reference |
|---|---|---|---|---|
| **PS-MPs** | Naproxen | Earthworm | Reduced lipid metabolism. | [121] |
| **PS-NPs** | Ni | Earthworm | Accumulation of reactive oxygen species, induced lipid peroxidation and destruction of the body wall structure. | [127] |
| **PE-MPs** | IMI | Earthworm | Induced severe epidermal damage by the superimposed effect of iron death and oxidative damage. | [128] |
| **UV-PS** | TBBPA | Caenorhabditis elegans | Reduced body length, movement behavior and brood size. Induced reactive oxygen species and lipofuscins. Damaged the intestinal structure and increased intestinal permeability | [129] |
| **PS-MPs** | DEHP | Mice | Induced oxidative stress and aggravated renal pyrodeath and inflammation | [130] |
| **PS-MPs** | DEHP | Mice | Induces oxidative stress, Th2 immune responses, and asthma symptoms | [122] |
| **PS-MPs** | DEHP | Mice | Destroyed ovarian granulosa cell layer. Induced follicle fragmentation and atresia. | [131] |
| **PS-MPs** | DEHP | Mice | Induced oxidative stress, released inflammatory factors.Increased inflammation and inhibited fibrosis, leading to delayed wound healing | [132] |
| **PS-MPs** | NaF | Mice | Damaged testicular structure and impaired spermatogenesis. | [133] |
| **PS-NPs** | AFB1 | Mice | Colon inflammation and induced intestinal barrier damage and intestinal microbiota. Induced liver fibrosis and inflammation. | [134] |

and DEHP caused more significant damage. Co-exposure also increases oxidative stress and Th2 immune responses, as well as activation of the TRPA1 and p38 MAPK pathways, which ultimately exacerbate asthma symptoms [122]. Furthermore, Wu et al. found that mice co-exposed to PS-MPs and DEHP showed disruption of the ovarian granulosa cell layer, follicular fragmentation, atresia, and induced oxidative stress, leading to oxidative DNA damage, cell cycle arrest, and increased necrotic apoptosis in ovarian granulosa cells [131]. In addition, co-exposure to DEHP and MPs also affected wound healing and net formation in mouse skin; both MP and DEHP exposure delayed skin healing, which was more pronounced in the co-exposed group, where oxidative stress was increasingly pronounced with an increase in the release of nets and inflammatory factors. The overactivation of ROS/nets can exacerbate inflammation and inhibit fibrosis, ultimately leading to delayed wound healing [132]. In addition to the study on DEHP, Tan et al. conducted a study on support cells (SCs) in male mice, revealing that co-exposure to sodium fluoride and MPs increased MP accumulation in SCs. This co-exposure resulted in testicular structural defects, impaired spermatogenesis, and testicular apoptosis. Co-toxicity induces apoptosis and iron-dependent death in SCs, leading to reduced cell numbers and dysfunction [133]. In addition, aflatoxin B1 (AFB1) is widely present in moldy foods, and the widespread use of plastic tableware exacerbates the co-exposure to PE-MPs and AFB1. Sun et al. found that exposing mice to PS-NPs (with a particle size of 100 nm) and AFB1 resulted in colonic inflammation and intestinal barrier damage and that co-exposure exacerbated AFB1-induced gut microbiota dysbiosis and fecal metabolome remodeling, further exacerbating AFB1-induced liver fibrosis and inflammation [134].

### 3.2.3. *Effects on microorganisms*

Considering the biofilms formed by Escherichia coli on the surface of MPs, when erythromycin is adsorbed onto their surfaces, the combined effect suppresses the expression of rpoS, a global regulator of biofilm bacteria, and the expression of two DNA mismatch repair genes, mutS, and uvrD, which may lead to an increase in the frequency of bacterial drug resistance mutations [135] (Table 3). Other researchers have found from studies on waste-activated sludge (WAS) that after hydrothermal pretreatment, the specific surface area and carbonyl index of MPs increase, leading to a higher adsorption capacity for heavy metals. The treatment process led to the release of toxic plastic additives (dibutyl phthalate, dimethyl phthalate, and bisphenol-A), which severely increased MPs and the combined toxicity of their attached contaminants led to a significant decrease in the abundance of important acid-producing anaerobic bacteria (Acetoanerrobium and Mesotoga), protein-hydrolysing bacteria (Proteiniborus), and methanogens (Methanosaeta) in the environment exposed to PE- and PVC-MPs [136]. It was also found that when Pseudomonas aeruginosa was treated simultaneously with PE-MPs and Cd, the combined treatment inhibited CAT activity more significantly than the single pollutant treatment, suggesting that the synergistic effect of MPs and Cd causes increasingly severe oxidative stress [137]. However, not all combined exposures inhibited microbial growth, and for Candida vulgaris, whereas aged PVC-MPs inhibited growth and

**Table 3**
The combined toxicity of microplastics and the attached pollutants on microorganisms.

| Types of microplastics | Attached pollutants | Affected organisms | Adverse effects | Reference |
|---|---|---|---|---|
| **PS-MPs** | erythromycin | Escherichia coli | Inhibited expression of global regulator rpoS and DNA mismatch repair genes mutS and uvrD. | [135] |
| **PE-MPs, PVC-MPs** | Dibutyl phthalate, dimethyl phthalate and bisphenol a | Anaerobe | Reduced abundance of important anaerobic bacteria such as acid-producing bacteria (Acetoanerrobium and Mesotoga), protein-hydrolysing bacteria (Proteiniborus) and methanogens (Methanosaeta) | [136] |
| **PE-MPs** | Cd | Pseudomonas aeruginosa | Inhibited content of chlorophyll *a* and the activity of CAT, resulting in severe oxidative stress | [137] |
| **Aged PVC-MPs** | Cu | Candida | Decreased concentration of SOD and MDA. Promoted the growth of Candida. | [138] |
| **PE-MPs** | hexabromocyclododecane | Soil bacteria | Change in the composition of soil bacteria. Enhanced the functions of amino acid metabolism, carbohydrate metabolism and membrane transport of bacteria. | [139] |
| **PS-NPs** | PCB-44 | Chlorella | Altered the cell cycle, inhibited growth, and reduced the hydrophobicity of the cell surface and the synthesis of chlorophyll *a* and chlorophyll *b*. | [140] |
| **PS-NH2** | B | Microcystis aeruginosa | Increased CAT activity and disturbed the integrity of the thylakoid membrane. | [142] |
| **PS-MPs** | CAP | Microcystis aeruginosa | Decreased expression of photosynthesis-related genes psaB and psbD, leading to induced membrane lipid peroxidation and oxidative stress damage | [143] |

caused severe cellular damage when exposed to both PVC-MPs (10 mg/L) and Cu (0.5 mg/L), Candida unusualis growth was promoted [138]. Wu et al. also found that soil bacterial communities were significantly affected by the combined exposure to HBCD and PE-MPs. It was shown that the combined exposure significantly affected the α-as well as β-diversity of soil bacteria, and analysis of the bacterial functions indicated that amino acid and carbohydrate metabolism and membrane translocation showed the three most important enrichments of bacterial functions after one and four months of pollutant exposure [139]. Similarly, Zheng et al. found that the simultaneous exposure of Chlorella to PS-NPs and PCB-44 produced significant toxic effects, including cell cycle effects, growth inhibition, reduced cell surface hydrophobicity, and chlorophyll *a and b* synthesis [140]. Yu et al. found that PET-MPs and $Pb^{2+}$ have a synergistic effect in producing strong physical and chemical stresses on Chlorella, with toxic effects being more significant than when exposed to the two pollutants alone [141]. In addition, the combined toxicity of MPs and boron (B) was found to adversely affect the algal growth. B was found to inhibit the growth of Microcystis aeruginosa, which was exacerbated by amino-modified polystyrene (PS-NH2), and the combination of PS-NH2 and B had a significant effect on oxidative damage to algal cells, cellular structure, and the production of MCs [142]. Chloramphenicol (CAP) and PS-MPs are also co-toxic to Microcystis aeruginosa, and the combined toxicity of the two pollutants is significantly higher than that of individual pollutants. CAP dominated the combined exposure and ultimately exacerbated the toxicity of MPs because of the common photosynthesis toxicity targets shared by CAP and PS-MPs [143].

### 3.2.4. *Effects on other organisms*

In addition, Chen et al. found that the co-accumulation of PS-NPs and decabromodiphenyl ether causes oxidative stress in ferns and hinders photosynthesis [144]. In addition, purple lettuce suffered from biomass inhibition when co-contaminated with PS-MPs and dibutyl phthalate [145]. After studying the combined toxicity of PS-NPs and polychlorinated biphenyl-52 (PCB-52) in aquatic duckweed, Pan et al. found that the combined toxicity of PS-NPs and PCB-52 exacerbated the destructive effects of PS-NPs on the antioxidant defense system, which was more evident in the root system [146]. Wang et al. found that NPs exacerbated the growth inhibition of submerged plants by Cd, downregulated cuticle synthesis, and upregulated pentose phosphate metabolism, resulting in starch accumulation [147].

## 4. Limitations and future research directions

When sorting past studies, the main problem we found was that most of the existing studies explored the combined toxicological effects of original MPs and environmental pollutants, and there were many limitations to the use of original MPs, which also led to toxicity conclusions based on this potential deviation. The limitations of using original MPs first manifest in the lack of environmental representation. MPs in the natural environment undergo aging processes such as photooxidation and biodegradation, and the surface structure, particle size distribution, and chemical composition of MPs are significantly different from those of the original MPs. Therefore, it is difficult to reflect the true state of MPS in the environment [71,72,77]. Second, the dynamic consideration of additive release was insufficient. The amount and rate of release of various additives added to the production of MPs change during aging, and the original MPs studies could not reflect this change or its impact [18,59]. Third, the simulation of biological interactions was distorted. The interaction between aged MPs and organisms is complex because of changes in surface characteristics, and it is difficult to simulate the original MPs study [148,149]. These limitations have led to skewed conclusions regarding toxicity. First, toxicity was underestimated. The original MPs study ignored the enhanced toxicity of aged MPs that adsorbed pollutants and released additives. For example, the acute toxicity test of the original MPs to organisms may reveal low toxicity levels; however, when considering carcinogens such as polycyclic aromatic hydrocarbons adsorbed by aged MPs and phthalate plasticizers released, the chronic toxicity to organisms will increase significantly, and the original MPs study cannot reflect these potential hazards [129,136,150]. The second reason is the misjudgment of the mechanism of action. The original and aged MPs have different biological mechanisms of action, and the mechanism derived based on the original MPs may cover the real situation; for example, the original MPs may affect biological tissue function through simple physical obstruction [151,152]. However, the physical blocking mechanism based on the original MPs study can mask the more complex and harmful chemical toxicity mechanisms of aged MPs. Third, the ecological risk assessment was inaccurate. Original MPs research cannot accurately reflect the transmission, accumulation, and amplification effects of MPs in the food chain, leading to a deviation of the ecological risk assessment from reality. For example, when aged MPs are ingested by organisms at the bottom of the food chain, they have more serious toxic effects on senior consumers during the food chain transmission process because of the pollutants adsorbed and the additives released by them. However, the original study underestimated the risk of MPs to the

entire ecosystem because these factors were not considered [153,154].

Another problem is that previous studies on MPs tended to focus on their size and type, ignoring the effects of their various shapes on toxicity and the pollutants they adsorb. As the most common fibrous MPs, they are easier to contact and ingest by organisms because of their elongated forms. Moreover, fibrous MPs are more toxic than granular MPs, which can lead to morphological changes in ingested organisms and even increase their mortality. In a water environment, owing to their larger specific surface area, fibrous MPs can interact more fully with heavy metal ions and organic pollutants, thus exhibiting stronger adsorption capacity [155–157]. Spherical granular MPs are generally less harmful to organisms than other irregularly shaped MPs. From the perspective of adsorbed pollutants, although the specific surface area of spherical granular MPs is relatively small, their more stable suspension in the water environment provides them with more opportunities to contact pollutants in the water. However, compared to fibrous MPs, the adsorption efficiency and adsorption capacity may be lower. However, when spherical granular MPs adsorb highly toxic pollutants, they can cause serious harm to organisms [158,159]. In contrast, owing to their planar shape, the main feature of thin-film MPs is that the activity of bacteria colonizing the surface of thin-film MPs increases with a decrease in their area [160]. However, current studies on the ecological effects of MPs of different shapes are still at a relatively preliminary stage. For example, long-term dynamic changes in MPs of different shapes in different ecosystems and their interaction mechanisms with other environmental factors have not been systematically studied.

Current research focuses on local areas, such as the middle and lower reaches of the Yangtze River and the Bohai Sea in China; the soils of Brazil, Iran, and Mauritius; and the Red Sea and Mediterranean Sea in Egypt, which reflect the local MP contamination situation, are not representative of the global situation [23,25,36]. In terms of research environments, most of the studies were conducted in common environments, such as soil, ocean, and freshwater, and few studies were conducted in special or extreme environments, which could not comprehensively show the whole picture of MPs and their attachments in all kinds of environments worldwide [45,51,124]. Moreover, most existing studies focus on short-term effects, and there is a lack of research on the long-term environmental and ecological impacts of MPs and their attachments, especially their intergenerational effects. Moreover, the combined toxicity of MPs and their attachments to the environment is affected by a combination of factors such as temperature changes and the presence of other pollutants. These complex interactions have not been fully studied, hindering the accurate assessment of their environmental effects. Future long-term monitoring and research should be conducted to assess the long-term environmental and ecological effects of MP attachment. In particular, the transgenerational effects and potential chronic toxicity need to be considered, as well as the combined toxicological effects of multiple environmental pollutants, to study the effects of synergies between plastic additives and other contaminants on toxicity assessment. Plastic additives can release and increase toxicity, which complicates the assessment of the combined effect and increases the difficulty in distinguishing whether the experimental toxicological effects are due to additives in MPs or other contaminants adsorbed from the outside. For example, bisphenol, a phthalate plasticizer used as a common plastic additive, is widely used in all types of plastic products. They may be released from MPs as they age in the environment, or come into contact with other organisms. Plasticizers often have endocrine-disrupting properties that mimic or interfere with the normal function of hormones in living organisms [60,161]. However, in the natural environment, MPs can easily adsorb external pollutants such as polycyclic aromatic hydrocarbons (PAHs), which can also affect metabolism and have potential carcinogenic, teratogenic, and mutagenic properties [162–164]. Therefore, when an organism is exposed to an environment containing MPs and toxicological effects occur, it is difficult to determine whether it is a plasticizer, an external pollutant such as adsorbed PAHs, or a combination of both. Moreover, there may be synergistic or antagonistic effects between plastic additives and externally adsorbed pollutants. Under synergistic action, the toxic effect of two or more substances combined may be far greater than the sum of their toxicities when they act alone. However, antagonism may reduce overall toxicity. This complex interaction further increases the difficulty in accurately assessing the source and mechanism of the toxicological effects of MPs [113,134,138]. In addition, the duration of the experiment played a key role. Short-term experiments can only observe the acute toxic effects of MPs and their substances, and it is difficult to detect the chronic effects caused by the slow release of additives or the long-term accumulation of pollutants. In long-term experiments, the continuous release of additives and continuous adsorption of external pollutants cause toxic effects to constantly change, and it is difficult to clearly distinguish which substances dominate the toxic changes at different stages [165,166]. To better understand the toxicological effects of MPs, future research will need to develop more advanced analytical techniques that can accurately identify and quantify the additives released in MPs, as well as adsorptive external contaminants. The interactions between plastic additives and external contaminants were explored to assess the potential risks of MPs to ecosystems and biological health accurately.

## 5. Conclusion

In this study, the types of MPs and their attachments, interaction mechanisms, environmental distribution, and synergistic effects on ecosystems were comprehensively analyzed by reviewing the existing literature. In conclusion, the synergistic impact of MPs and their attachment to environmental pollutants is a complex and multi-layered issue. The current study showed that MPs not only negatively affect ecosystems as stand-alone pollutants but are also exacerbated by a variety of pollutants attached to their surfaces. They cause significant harm to aquatic and terrestrial organisms and threaten human health throughout the food chain. In this context, there is a need to strengthen interdisciplinary cooperation, and multidisciplinary fields such as biology, chemistry, and environmental science should be involved in analyzing the environmental behavior and toxicological mechanisms of MPs and their attached pollutants from different perspectives. Develop novel preventive and control measures and increase public awareness. Through integrated research and concerted efforts, we can better understand and mitigate the hazards of these pollutants, and promote environmental protection and sustainable development.

## CRediT authorship contribution statement

**Mengzhen Li:** Writing – original draft, Visualization, Software, Resources, Methodology, Formal analysis, Data curation. **Wenhao Ma:** Visualization, Validation, Software, Resources, Formal analysis, Data curation. **James Kar Hei Fang:** Validation, Software, Methodology, Data curation. **Jiezhang Mo:** Visualization, Validation, Software, Methodology. **Lei Li:** Visualization, Software, Methodology. **Min Pan:** Writing – review & editing. **Rong Li:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Conceptualization. **Xiaoyun Zeng:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Investigation,

Conceptualization. **Keng Po Lai:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Conceptualization.

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## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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