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Microplastics and Antibiotics in Aquatic Environments: A Review of Their Interactions and Ecotoxicological Implications

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ABSTRACT: Microplastics and antibiotics are two significant emerging pollutants found together in water bodies, raising concerns about their mutual effects. This review delves into how microplastics and antibiotics interact in aqueous environments and the ecotoxicological implications of such interactions, particularly the bioavailability of antibiotics and the prevalence of antibiotic-resistance genes. It outlines that antibiotics attach to microplastics primarily through hydrophobic, hydrogen-bonding, and electrostatic interactions. Other bonds, comprising halogen bonding, cation–π interaction, and negative charge-assisted hydrogen bonds, may also be involved to better explain antibiotic adsorption patterns. The adsorption of antibiotics to microplastics often follows the pseudo-second-order kinetic model and in some instances, the pseudo-first-order kinetic model. The common adsorption isotherms governing this interaction are the linear and Freundlich models. Microplastics may increase the biodegradation of adsorbed antibiotics due to the presence of antibiotic-degrading bacteria in the biofilms. They could also hamper direct photodegradation but facilitate indirect photodegradation of adsorbed antibiotics. However, their photodegradative effect remains inconclusive. Microplastics and antibiotics exhibit significant toxicity to algae, while their effects on fish and daphnia are less noticeable, suggesting that their combination does not pose an immediate threat to the well-being and proliferation of larger aquatic organisms. In some instances, microplastics reduce the deleterious effects of antibiotics on aquatic life. Microplastics serve as catalysts for gene transfer, enhancing the propagation of antibiotic-resistance genes in these ecosystems. This review underscores the importance of understanding the regulatory mechanisms of microplastics on antibiotic-resistance gene diversity, particularly at the gene expression level.

KEYWORDS: Antibiotics; antibiotic resistance genes; adsorption; biodegradation; photodegradation; microplastics

1. Introduction

Plastics are widely used in many sectors and everyday life because they are durable, lightweight, and affordable. This widespread use results in a significant release of plastic waste into the environment [1, 2]. Currently, the majority of the world's plastic materials derive from

eight primary polymers, with polyethylene (PE) and polypropylene (PP) making up 45% of these polymer outputs [3]. When exposed to physical, chemical, and biological processes in the environment, plastics break down into smaller pieces, with those under 5 mm in size referred to as microplastics (MPs). MPs are characterized by their extensive surface area and high porosity, which allows them to adsorb pollutants from water bodies and facilitate the transport of these contaminants [4]. Moreover, MPs negatively impact non-target species and can become integrated into food chains, leading to bioaccumulation at higher food chain levels. Consequently, MPs are garnering attention due to their prevalence, complexity, and the potential risks they pose to the environment [4].

MPs in the environment are categorized as either primary or secondary, depending on their origin. Primary MPs are deliberately produced tiny plastic beads commonly found in personal care items such as exfoliants, makeup, and medication carriers. In contrast, secondary MPs are the tiny pieces that form when larger pieces of plastic break down, whether in marine or terrestrial environments [5]. As a result of various degradation processes, including those caused by sunlight, these plastic pieces gradually disintegrate until they become so small that they are no longer visible without magnification [6]. MPs have been found in water bodies across the globe, with significant differences in their spatial distribution and concentrations. High concentrations of MP pollution are mainly found in East Asia, Europe, and the eastern United States because these regions have some of the highest population densities in the world and are hubs for industrial activities. In freshwater, the highest recorded MP levels reached 3,900,000 particles per cubic meter, while the ocean's peak concentration was 102,000 particles per cubic meter [7, 8]. The amount of MPs in aquatic settings is influenced by various factors, including the number of people in an area, the level of economic and city growth, the effectiveness of waste management practices, and the characteristics of the water cycle [9].

Upon entering the environment, MPs can interact with a multitude of chemicals. Antibiotics have received much attention due to their increasing presence in terrestrial and aquatic environments. Antibiotics are employed in medical treatments and to enhance agricultural and aquacultural yields [10]. However, many antibiotics are not fully broken down after consumption and consequently make their way into the environment. These substances are regarded as emerging contaminants due to their ongoing release and persistent nature [11]. Indeed, even at minimal concentrations, antibiotics can amplify the development of antibiotic-resistant bacteria and the proliferation of antibiotic-resistance genes [12]. For instance, exposure of microbial communities in the plastisphere to sub-lethal antibiotic pollution resulted in increased tolerance to antibiotics and selected different antibiotic-resistant bacteria and antibiotic-resistance genes [13]. The immediate harmful effects of antibiotics on simpler organisms, including bacteria, protists, and most invertebrates, are severe and enduring. They are linked to the tendency of the substances to accumulate biologically [14]. In contrast, the long-term toxicity of antibiotics more subtly impacts advanced organisms, affecting aspects such as growth, reproduction, and immune response [4]. A meta-analysis reveals that MPs intensify the build-up of antibiotics within water-dwelling organisms, markedly exacerbating the negative impacts on their growth, maturation, and immune system capabilities [15]. Fu et al. revealed that mice exposed to a combination of sulfamethoxazole and polystyrene (PS) MPs had sulfamethoxazole accumulated in their livers, causing evident histopathological changes, characterized by amyloidosis and necrocytosis [16]. The harmfulness and associated environmental risks of antibiotics are, therefore, critical concerns.

Numerous studies have been conducted on the interactions between MPs and antibiotics in aqueous environments. For instance, Atugoda et al. examined the adsorption of ciprofloxacin onto PE MPs [17], while Yu et al. investigated the sorption of levofloxacin onto polyvinyl chloride (PVC) in the presence of metal ions [18]. Guo and Wang were interested in unveiling the sorption behaviors of three common antibiotics, namely sulfamethoxazole, sulfamethazine, and cephalosporin onto aged PE and PS MPs retrieved from freshwater and marine environments [19]. However, few reviews in this genre have been conducted. Zhuang and Wang reviewed the recent updates in microplastic interactions with antibiotics, focusing on the sorption behaviors and mechanisms in aqueous environments without covering the ecotoxicological implications of such interactions [20]. The review by Zheng et al. was constrained to the sorption of antibiotics on MPs through biofilm and the effects of biofilm on the emergence of antibiotic-resistance genes facilitated by its sorption of antibiotics and the abundance of genetic materials in it [10]. Similarly, Syranidou and Kalogerakis conducted a review primarily on the interactions between MPs, antibiotics, and antibiotic-resistance genes in aqueous environments, particularly in wastewater treatment plants [21]. Even fewer reviews include the ecotoxicological effects of these interactions. Wang et al. included a small section on the toxicity resulting from microplastic-antibiotic interactions in their review, but it is primarily related to the alteration of antibiotic bioavailability [22].

In view of this, it is necessary to perform a balanced review of how MPs interact with antibiotics widely present in the aqueous environment and the ecotoxicological effects arising from such interactions. This review, therefore, aims to comprehensively present the latest progress in the microplastic-antibiotic interaction research, focusing on the aquatic environments, and the ecotoxicological implications of these interactions. It has the novelty of highlighting the various ecotoxicological risks caused by these interactions. It contributes to a better understanding of the potential risks posed by the interactions between MPs and antibiotics to ecosystems and human health. It also informs strategies for managing MPs and antibiotic resistance.

2. Interactions between MPs and antibiotics

Within aquatic settings, the dynamics of antibiotics encompass processes like adsorption, decomposition by organisms, and photodegradation, affecting their movement through the environment, and availability to organisms.

2.1. Adsorption.

MPs can attract and hold antibiotics, resulting in concentrations on MPs that are significantly elevated—up to 100,000 to 1,000,000 times greater—than in the water itself [23]. The binding of antibiotics to MPs is controlled by various factors, including hydrophobic and electrostatic forces, molecular interactions, and the filling of pores within the MPs (Table 1; also see Section 2.1.3 for the details of the bonds). Generally, the tendency of substances to bind to MPs is directly related to their octanol-water partition coefficients, showing a clear linear pattern. However, antibiotics often deviate from this pattern due to their unique molecular structures and functional groups, setting them apart from other organic compounds studied [24]. The main way that MPs and nonpolar antibiotics come together is through hydrophobic interactions. Antibiotics with higher log K_{ow} values tend to have a stronger attraction to MPs [25]. Electrostatic interactions are another way antibiotics can attach to MPs, and they are influenced

by the antibiotics' pKa and the pH level of the solution [26]. Additionally, van der Waals forces and π-π interactions play a role in how antibiotics interact with MPs [27, 28]. The concept of pore-filling describes how antibiotics can occupy the spaces within MPs, which can increase the amount of antibiotics that stick to the MPs [24].

Table 1. Bonds involved in the interactions between MPs and antibiotics.

Type of MPs	Antibiotics	Bonding	Reference
PET, PE	Macrolides	Hydrophobic interaction, hydrogen bonding	[29]
PE, PVC, PS	Enrofloxacin	Hydrophobic interactions, van der Waals forces, acid-base forces	[30]
PA and PVC	Ciprofloxaxin, tetracycline	Electrostatic interaction, hydrophobic interactions, cationic bridging (in the presence of Cd), complexation (in the presence of Cu)	[26]
Polylactic acid (PLA) and PE	Ciprofloxaxin	Electrostatic interactions, hydrogen bonding, π-π interaction, ion exchange	[31]
PP, PE, PS, PVC, synthetic resins	Sulfamethoxazole	Hydrogen bonding, π-π interaction	[28]
Highly aged PA	Ciprofloxacin, trimethoprim	Hydrogen bonding, hydrophobic interaction	[32]
PA, PS, PET and polyoxymethylene	Azithromycin, clarithromycin	Hydrogen bonding, hydrophobic interaction,	[33]
PE	Chlortetracycline, oxytetracycline, tetracycline	Electrostatic interaction, van der Waals force, hydrogen bonding	[27]
PS	Tylosin	Hydrophobic interaction, electrostatic interaction	[34]
PS	Ciprofloxacin	Electrostatic interaction, hydrophobic interaction, hydrogen bonding, π-π interaction	[35]

2.1.1. Adsorption kinetics.

MPs typically adhere to antibiotics following the pseudo-second-order kinetic model, but sometimes the pseudo-first-order model is a better match. For example, the adsorption rate of sulfamethazine on materials like polyamide (PA), PE, PVP, and PP aligns more closely with the pseudo-first-order model, while for PS and polyethylene terephthalate (PET), the pseudo-second-order model is more suitable [36]. Each model has its own theoretical significance and conditions for use, fitting certain adsorption situations. Specifically, the pseudo-first-order kinetic model is a simplification used in chemical kinetics where a reaction that is second-order, or bimolecular, is approximated as a first-order reaction. This approximation is valid when one of the reactants is present in a much greater concentration than the other, effectively remaining constant during the reaction. As a result, the rate of the reaction depends primarily on the concentration of the other reactant [37]. The pseudo-second-order kinetic model assumes that the rate of occupation of adsorption sites is proportional to the square of the number of

unoccupied sites. This model is often applied when the adsorption process is controlled by chemisorption, which involves valence forces through the sharing or exchange of electrons between the adsorbent and the adsorbate [38]. It was found that the pseudo-first-order and pseudo-second-order models correspond to the initial and majority filling of the adsorbent's active sites, respectively [39]. Additionally, a hybrid version combining elements of both models, known as the mixed-order model, has been introduced [40].

2.1.2. Adsorption isotherm.

The linear model is the predominant mathematical approach for analyzing the equilibrium of antibiotic adsorption onto MPs [41]. Research indicates that the binding of various antibiotics to different types of MPs often follows a linear pattern. For example, the linear model aptly describes the adsorption behavior of sulfamethazine and sulfamethoxazole on five types of microplastic polymers (PET, PVC, PS, PP, PE, and PA), with the partition coefficient (K_d) between MPs and water ranging from 22.2 to 284 l/kg for sulfamethoxazole and 11.5 to 38.7 l/kg for sulfamethazine. Consistent findings were observed for the adsorption of tetracycline on nylon MPs [42], sulfonamides on aged thermoplastic polyurethane/PAs [43], and tylosin on PS MPs [34], all exhibiting a highly linear relationship. The linear model effectively captures the distribution of adsorbed substances between the solid and liquid phases, which is influenced by electrostatic, van der Waals, and hydrophobic forces [41].

Extensive research has been conducted on the nonlinear Langmuir, Freundlich, and Temkin isotherms. The Langmuir isotherm models the adsorption of a single layer of molecules; the Freundlich isotherm, an empirical model, is used for adsorption that is either multi-layered physical or chemical with half the sites occupied; and the Temkin isotherm accounts for multi-layered adsorption where the heat of interaction diminishes in a linear fashion as more sites are covered [44]. Among these, the Freundlich isotherm often aligns better with the adsorption behavior of antibiotics on MPs, suggesting that non-covalent interactions like van der Waals and electrostatic forces are significant in the adsorption process. The most suitable model can vary between seawater and freshwater due to the distinct properties of these environments, affecting how a particular antibiotic adheres to MPs [41].

2.1.3. Bonds involved in adsorption.

Partitioning of hydrophobic antibiotics onto MPs is primarily controlled by hydrophobic interactions [45]. These antibiotics naturally seek affinity with hydrophobic MPs to reduce their exposure to water, leading to their adsorption and removal. Conversely, hydrophilic antibiotics exhibit a lack of attraction when encountering hydrophobic MPs due to these same hydrophobic forces [17]. These hydrophobic interactions are generally stronger than other types of weak intermolecular forces, such as van der Waals forces or hydrogen bonding, especially when measured by octanol-water partitioning. The degree of hydrophobicity for both antibiotics and MPs is quantified by log K_{ow} values and water contact angles (θ), respectively. Antibiotics with a log K_{ow} greater than 4 are deemed highly hydrophobic, while MPs with a θ exceeding 90° are categorized as hydrophobic. Specifically, the water contact angles for PS, PP, and PA are reported to be 145°, 138°, and 52°, respectively [35, 46]. Aging processes typically reduce the hydrophobic nature of materials; for example, the water contact angle of PS MPs dropped from 127.75° to 99.81° after a 9-day treatment with Fenton solution [37]. This

type of interaction is characteristic of non-polar molecules, which tend to avoid polar molecules like water [17, 41].

Electrostatic interactions are another common mode of interaction between MPs and antibiotics. Electrostatic interactions comprise attraction between molecules of the same charges, and repulsion between molecules of different charges. They are usually pH-dependent, thus, subjecting adsorption contributed primarily by electrostatic interactions to the influence of solution pH [47]. Electrostatic interactions are typically deduced from the charged conditions of MPs and the ionization characteristics of antibiotics. The electrostatic interactions are influenced by several factors: the pKa values of antibiotics, the point of zero charge of MPs, the pH of the solution, and the presence of coexisting ions or dissolved organic matter [48]. For example, tetracycline primarily exists in cationic and neutral states when the pH is below 7.7, given its pKa values of 3.3, 7.7, and 9.7. PE MPs exhibit a consistently negative zeta potential within a pH range of 2 to 11, leading to an electrostatic attraction with tetracycline. However, as the pH rises, tetracycline transforms into an anionic form, switching the attraction to repulsion [27]. Additionally, the presence of ions or dissolved organic matter can modify the electrostatic characteristics of both antibiotics and MPs. For instance, the presence of humic acid on PE MPs can shift the interaction with ciprofloxacin from repulsion to attraction [17]. Electrostatic interactions also come under the influence of ionic strength, with the increase in ionic strength of a solution potentially affecting or compressing the charge double layer on the surface of a microplastic particle. This reduces electrostatic interactions between MPs and antibiotics [44].

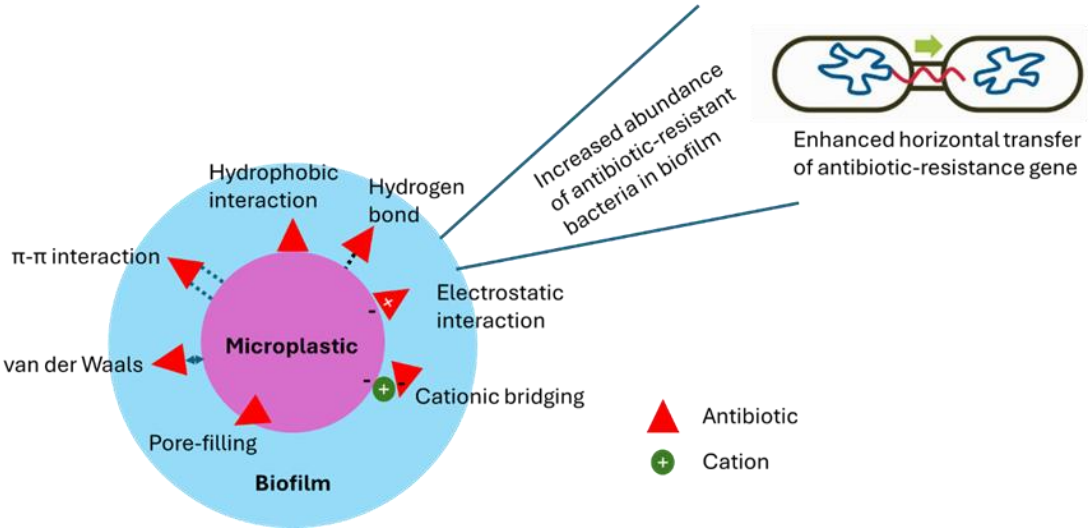

Figure 1. Interactions between microplastics and antibiotics cause the concentrations of antibiotics on microplastics to increase, leading to the increased abundance of antibiotic-resistant bacteria and the transfer of antibiotic-resistance genes in the biofilm.

Additional interactions may contribute to the adsorption of antibiotics on MPs, and this is influenced by the distinct structures and properties of both antibiotics and MPs. Liu et al. highlighted that ciprofloxacin adsorbs onto PS and PVC MPs mainly through partitioning, as indicated by the linear nature of their adsorption isotherms [46]. PS engages generally in van der Waals forces and specific π–π interactions, whereas PE relies solely on van der Waals forces, resulting in greater adsorption capacities for ciprofloxacin, trimethoprim, and sulfadiazine on PS [27, 30, 35]. Chen et al. proposed that the adsorption of tetracyclines on PE is predominantly governed by van der Waals forces and microporous filling mechanisms. The

latter typically occurs when the micropore size is 1.7 to 3 times larger than the adsorbate molecule [27]. Furthermore, the adsorption of sulfamethazine on PA, PS, PVC, and PP MPs in neutral conditions could be attributed to both electrostatic and van der Waals interactions [36]. Chlorine atoms present on PVC may serve as electron acceptors, while the benzene rings and hydroxyl groups on bisphenols could be electron donors, leading to the formation of halogen bonds between PVC and bisphenols [49]. Consequently, it is theorized that PVC could form halogen bonds with antibiotics that have hydroxyl groups and benzene rings. The amino groups on antibiotics, which are prone to protonation like those on ring R3 of ciprofloxacin and ring C4 of tetracycline, might create cation−π bonds with the π electrons of MPs, particularly PS [50]. Interactions between CH/π, involving alkyl groups and aromatic rings, have been identified as a driving force for adsorption between polyolefin materials and substances that contain benzene rings [51]. Additionally, it has been established that charge-assisted hydrogen bonds form between various functional groups like hydroxyl, carboxyl, and amine of ionic organic compounds and the oxygen-containing functional groups on the surfaces of carbonaceous materials [52]. Charge-assisted hydrogen bonds typically arise in aqueous solutions when the hydrogen donor and acceptor have similar acid dissociation constants, with the strength of the bond increasing as the difference in pKa values decreases [53]. For instance, at a pH of 8.5, over 99.5% of sulfamethoxazole molecules are anionic, and the difference in pKa between the hydrogen donor ($-SO_2NH-$) and acceptor ($-NH_2$) is about 0.6, suggesting the involvement of charge-assisted hydrogen bonds in the adsorption of sulfamethoxazole on amine-modified polystyrene-divinylbenzene resins, along with proton exchange with water [53]. In natural settings with a pH range of 5 to 10, anionic antibiotics may act as hydrogen donors to form charge-assisted hydrogen bonds with MPs like polyhydroxybutyrate, PLA, and PA which have oxygen-containing functional groups such as carbonyl and carboxyl, especially when the difference in pKa between the antibiotics and MPs is less than 4.0 [22].

2.2. Biodegradation.

Biodegradation plays a vital role in altering antibiotics within the environment. This transformation is largely driven by enzymes within microbes that break down antibiotics into smaller chemical entities. This process is especially significant for the degradation of certain antibiotics, like tetracyclines, in water-based environments [54]. A typical example of enzymes involved in biodegradation is the cytochrome P450 monooxygenases, which play a crucial role in the microbial oxidation of xenobiotic chemicals. These enzymes are present across all life domains, including unicellular green algae. They can transform organic pollutants, including some persistent ones, into hydrophilic compounds by adding electrophilic groups (such as -COOH). Additionally, they can further convert hydrophilic compounds into less toxic forms through processes like epoxidation and electrophilic addition [55]. However, MPs can affect this natural breakdown. Studies have shown that when exposed to PS MPs, the effectiveness and quantity of CYP450 enzymes, which are crucial for breaking down antibiotics in the algae *Chlorella vulgaris*, are reduced [55]. This reduction hinders the biodegradation of the antibiotic levofloxacin. Additionally, the ability of organisms to adsorb and accumulate levofloxacin is weakened in the presence of MPs, which further diminishes the biodegradation process [54]. In a microcosm study, researchers introduced PE MPs and ciprofloxacin to investigate their combined effects on sediment microbial communities and CIP degradation behavior. When compared to the individual addition of ciprofloxacin, the simultaneous presence of

ciprofloxacin and MPs led to a reduction in ciprofloxacin degradation efficiency and decreased microbial diversity in the sediment [56]. MPs act as solid platforms and habitats for microorganisms in water settings, offering a perfect spot for them to settle. The variety and balance of bacteria found on the surfaces of MPs tend to surpass those in the nearby milieu [57]. Research indicates that these surface-dwelling microbes can break down foreign contaminants [58]. For example, bacteria that can decompose microcystins and live on MPs have been shown to boost the breakdown of these toxins [57]. On the same note, bacteria on MPs are expected to positively influence the breakdown of the antibiotic [59]. However, the results have not been conclusive. In fact, a study showed that the biofilms associated with PLA and PVC (also called the plastisphere) had a lower ability to degrade tetracycline compared to that formed on quartzite. Additionally, more antibiotic-resistance genes were detected in the plastisphere [60]. While bacteria that attach to MPs and create biofilms enhance the capture of pollutants, more studies are needed to ascertain if they facilitate the breakdown of the pollutants [61].

Table 2. The effects of microplastics on the biodegradation of antibiotics.

Microplastic Type	Antibiotic	Experimental Setting	Observation	Reference
PS	Levofloxacin	Simulated wastewater from tortoise and turtle breeding pond	The removal of levofloxacin by *Chlorella vulgaris* was affected (23.24% in the MPs-added group versus 46.71% in the control) due to additional stress exerted by MPs on the growth of *C. vulgaris.*	[62]
PE	Ciprofloxacin	Microcosm over 35 days	Degradation of ciprofloxacin was reduced; microbial diversity decreased with the co-contamination.	[56]
PLA, PVC	Tetracycline	Incubation of PLA MPs, PVC MPs, and quartzite in an urban waterbody for 28 days	24% of tetracycline was degraded in the quartzite treatment, in comparison to 17.3% and 16.7% in the PLA and PVC treatments respectively.	[60]

2.3. Photodegradation.

Most antibiotics are highly sensitive to light, which makes photodegradation a crucial process in altering antibiotics in aquatic environments, particularly at the surface level [63, 64]. There are two main categories of photodegradation for antibiotics: direct and indirect. Direct photodegradation occurs when antibiotics absorb light, resulting in their immediate instability and breakdown. Indirect photodegradation occurs when solar radiation produces reactive intermediates that break down antibiotics [64]. MPs possess a polymer composition that enables them to absorb light. As they age, they develop more chromophores and unsaturated groups, leading to heightened absorbance in the ultraviolet (UV) spectrum. This, however, also leads to reduced light absorption and a subsequent decline in antibiotic degradation, as noted by previous studies [65, 66]. Moreover, aged PS MPs can diminish the formation of the triplet excited state of sulfamethoxazole, which in turn curtails its direct photodegradation and lowers both the diversity and quantity of sulfamethoxazole by-products [66]. Extracellular polymeric

substances are crucial for the indirect breakdown of antibiotics through the creation of reactive oxygen species [67]. In a similar vein, chlorophyll acts as a photosensitizer, either by directly interacting with antibiotics post-light absorption or by producing reactive oxygen species, thus aiding in their indirect breakdown [64]. MPs add complexity to this process in the environment. They reduce the amount of chlorophyll by suppressing genes involved in its and porphyrin's metabolisms, which may impact the indirect breakdown of antibiotics [68, 69]. Conversely, MPs appear to boost the levels of extracellular polymeric substances, which algae use as a defense mechanism, thus aiding the breakdown of antibiotics [70, 71]. The rise in the levels of extracellular polymeric substances might also improve the algal ability to biodegrade antibiotics, changing the balance between different antibiotic degradation methods. Moreover, the UV-driven photo-oxidative degradation of MPs is associated with the production of free radicals [72].

Research has shown that when PS and PE are exposed to conditions that mimic sunlight aging, the early stages of treatment reveal the emergence of environmentally persistent free radicals, along with hydroxyl and superoxide radicals [73]. In water settings, the photo-oxidative breakdown of plastics results in the creation of photo-reactive amphiphilic polymers. These polymers act as sources of singlet oxygen or as locations for electron transfer, which aids in the breakdown of chemicals in the environment [72]. Supporting this, a study has verified that MPs can enhance the photodegradation of organic substances by generating free radicals under UV light exposure. In environments where PS and PP coexist, the PS polymer can interact with water to produce hydroxyl radicals. This reaction aids in the photodegradation and breaking apart of PP [46]. Even more crucial is the role of environmentally persistent free radicals in breaking down antibiotics, which are seen as key to the catalytic degradation process [74, 75]. Consequently, it seems that aged MPs have the ability to indirectly cause the degradation of antibiotics, despite previous suggestions that light absorption by MPs could reduce the direct photodegradation of these substances.

3. Ecotoxicological Implications

3.1.Toxic effects on organisms.

MPs and antibiotics exhibit significant toxicity to algae, while their effects on fish and daphnia are less noticeable, suggesting that their combination does not pose an immediate threat to the well-being and proliferation of larger aquatic organisms [76]. Extensive research has been done to understand how MPs and antibiotics affect algae. The presence of MPs and antibiotics, whether individually or together, can result in a decline in algal mass, a reduction in photosynthetic efficiency, an escalation in reactive oxygen species, and irregularities in gene activity [77, 78]. Furthermore, MPs are able to bind with algal cells, thereby facilitating the absorption of antibiotics by the algae, which in turn intensifies the toxic effects of the antibiotics [79]. The interaction mechanisms, such as antagonistic, synergistic, or additive effects, are more intricate in higher organisms that can consume MPs and process antibiotics. Research has shown that MPs can decrease the availability of antibiotics in freshwater red tilapia, triggering the activation of superoxide dismutase, which combats the oxidative stress caused by antibiotics. This indicates a possible antagonistic relationship between MPs and antibiotics [80]. Conversely, the combined presence of MPs and antibiotics can lead to

oxidative stress in young *Eriocheir sinensis* and reduce the number and health of hemocytes in bivalves [81, 82].

Previous study [83] found that when tetracycline binds to negatively charged PS MPs, it lessens the electrostatic repulsion with marine diatoms, which increases contact between cells and particles, leading to a rise in the short-term toxicity of the MPs. Additionally, antibiotics on MPs can heighten toxicity against some microbes. Another study [84] investigated how MPs and triclosan affect the growth and stress levels of the microalgae *Skeletonema costatum*. They discovered that both triclosan and various MPs hindered the algal growth, with the order of impact being PVC800, then PVC, PS, and PE. Interestingly, when triclosan was combined with PVC and PVC800, the toxic effect was less than with PE and PS, likely because triclosan binds more strongly to PVC and PVC800, with PVC800 showing the most substantial reduction in combined toxic effect. In a similar vein, the hydrophobicity of positively charged PS MPs increased with tetracycline sorption, which decreased the contact between cells and particles, thus reducing the toxicity [83].

MPs could potentially reduce the harmful effects of antibiotics on aquatic life in three distinct ways. Firstly, MPs can act as a reservoir for antibiotics, preventing their consumption by aquatic organisms, thereby reducing the organisms' exposure to antibiotics [85]. Secondly, when antibiotics bind to MPs within organisms, the availability of antibiotics to affect vital organs is lessened. For example, when roxithromycin is absorbed by PS MPs, it diminishes its harmful impact on the enzyme acetylcholinesterase, which is crucial for the nervous system, thereby reducing its neurotoxicity in freshwater red tilapia [80]. Thirdly, antibiotics and MPs can have opposing effects on the same biological target or function. For instance, PS MPs can stimulate the activity of the enzyme superoxide dismutase, which helps combat oxidative stress caused by roxithromycin in freshwater red tilapia [80]. However, the combination of antibiotics and MPs can sometimes increase the toxicity of antibiotics. For example, MPs can enhance the toxicity of the antibiotic doxycycline in the marine microalgae *Tetraselmis chuii* by facilitating the uptake of doxycycline or its derivatives through interactions with the algal cell walls [86]. At concentrations of 4 and 40 mg/l, PS MPs can suppress superoxide dismutase activity and trigger oxidative stress in juvenile *Eriocheir sinensis* crabs [82]. Consequently, it is theorized that MPs and antibiotics together may cause oxidative stress or other types of damage to organisms. PS MPs have been shown to intensify various harmful effects of antibiotics, such as oxytetracycline and florfenicol, on bivalve species. These effects include an increase in intracellular reactive oxygen species, changes in the expression of genes related to the cytoskeleton and immune system, and a reduction in the total number and viability of hemocytes [81, 87]. This impairs the ability of the hemocytes to detect and engulf pathogens, posing a significant risk to bivalve species with innate immunity, like the thick-shell mussel and blood clam, compared to vertebrates like teleost fish [81, 87].

3.2.Antibiotic resistance.

The interaction between MPs and antibiotics has significant implications for antibiotic distribution in aquatic environments. The adsorption-desorption behavior of antibiotics on MPs is influenced by environmental factors and the aging process of the MPs. As a result, adsorbed antibiotics can be released, becoming new sources of pollution and extending their migration pathways [79]. Additionally, the presence of antibiotics on MPs increases their persistence in the environment, potentially exposing vulnerable organisms to antibiotics. When antibiotics

bind to MPs, the higher antibiotic concentration can contribute to the development of antibiotic-resistant bacteria [88]. The localized areas of high antibiotic levels created during adsorption expose bacteria to sub-lethal doses over extended periods. Continuous antibiotic exposure exerts selective pressure, favoring the survival and growth of resistant strains. Furthermore, elevated antibiotic levels hinder susceptible bacteria growth while providing an environment conducive to antibiotic-resistant bacteria. This selective pressure drives the acquisition of resistance mechanisms, leading to the emergence of superbugs capable of thriving in high antibiotic concentrations [88, 89].

The global public health community is increasingly concerned about the rampant spread of antibiotic-resistance genes and the growing issue of antibiotic resistance, which is exacerbated by the overuse of antibiotics [90]. MPs in water bodies offer a conducive environment for microbes to adhere to and develop biofilms. These MPs become hotbeds for antibiotic-resistance genes, leading to their build-up and sustained presence in aquatic systems [91]. Additionally, MPs serve as catalysts for gene transfer, enhancing the propagation of antibiotic-resistance genes in these ecosystems [92]. Within these biofilms, genetic materials, including antibiotic-resistance genes, are transferred among bacteria via horizontal gene transfer methods like conjugation or transformation (Figure 2). Studies have indicated that MPs in natural settings show a greater concentration of antibiotic-resistance genes than in the surrounding aquatic environment [93]. Various antibiotic-resistance genes were found on MPs collected from sewage treatment facilities in China [94]. This suggests that MPs may enhance the exchange of antibiotic-resistance genes among different microbial species, potentially accelerating the spread of antibiotic resistance in water ecosystems.

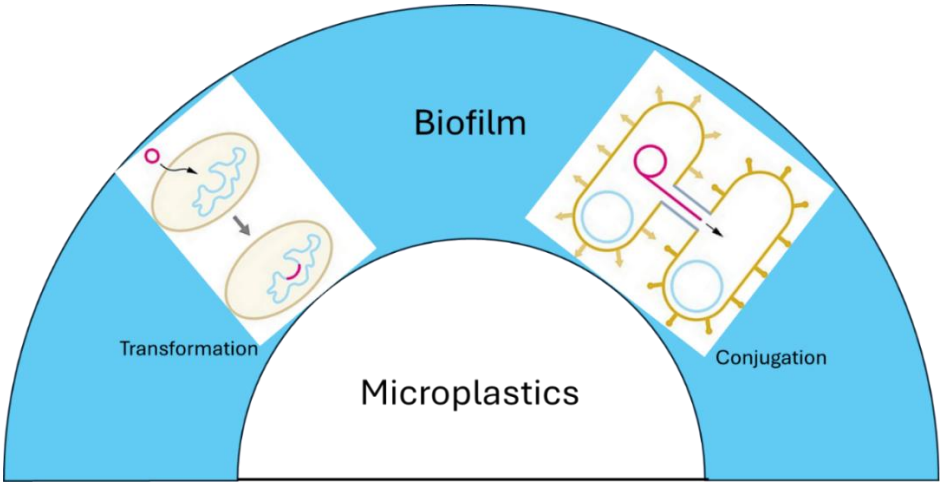

Figure 2. Horizontal gene transfer, particularly transformation and conjugation occurring in the biofilm of MPs. Transformation involves the uptake of genetic materials from the environment by a bacterium while conjugation is the direct transfer of genetic materials between two bacterial cells through a pilus.

Polyvinyl alcohol, when present in river water, has been observed to raise both the variety and number of antibiotic-resistance genes, which may contribute to the spread of antibiotic-resistant bacteria [95]. Bacterial membrane permeability can increase upon direct interactions with MPs, which aids in the uptake and transfer of antibiotic-resistance genes [96]. As MPs age, the reactive oxygen species they produce can disrupt bacterial cell membranes, leading to the release and uptake of DNA molecules and facilitating the horizontal transfer of antibiotic-resistance genes through conjugation [96, 97]. MPs can also serve as vehicles for antibiotics to

come into contact with bacteria, thereby increasing the levels of antibiotic-resistant bacteria and antibiotic-resistance genes. For instance, sulfamethoxazole attached to PS MPs can alter the gut microbiota of springtails and lead to the production of sul2 and intI1 genes [98]. However, there have been instances where the transfer of antibiotic resistance genes was inhibited. This could be due to a decrease in the of growth of antibiotic-resistant bacteria or the adsorption of antibiotics by larger MPs acting as a reservoir for these substances [99]. These processes may occur simultaneously during the transfer of antibiotic-resistance genes in the presence of MPs, and determining their specific contributions will require targeted future research. Interestingly, polyvinyl alcohol has been shown to decrease the diversity of antibiotic-resistance genes in estuary sediment, while polyvinyl chloride had minimal impact, yet both increased antibiotic-resistance gene diversity in river water [95]. Further investigation is needed to clarify these observations.

4. Conclusions

The adsorption of antibiotics on MPs is influenced by various mechanisms, primarily hydrophobic interactions, hydrogen bonding, and electrostatic forces. Other factors like partitioning, filling of micropores, van der Waals forces, and π–π interactions also play a role in partial absorption. Additionally, cation–π bonds, halogen bonds, and charge-assisted hydrogen bonds may also be involved. The toxicity of antibiotics to organisms can be either increased or decreased due to their adsorption on MPs, affecting the same biological targets or functions. Antibiotic-resistance genes tend to accumulate on the surface of MPs, with biofilms enhancing antibiotic-resistance gene abundance through horizontal gene transfer. MPs can promote the spread of antibiotic-resistance genes by supporting the growth of antibiotic-resistant bacteria, breaking down bacterial membranes, and facilitating contact between antibiotics and bacteria. Conversely, MPs might also reduce the proliferation of antibiotic-resistance genes by hindering the growth of antibiotic-resistant bacteria and absorbing antibiotics. In view of the constraints in studies pertaining to the interactions between MPs and antibiotics, research should be expanded to encompass interactions such as cation−π and charge-assisted hydrogen bonds, along with pertinent environmental variables. Future studies should aim to discern the specific impact of each mechanism within particular microplastic–antibiotic pairings. To comprehensively evaluate the ecological implications of MPs and antibiotics, it is crucial to investigate how MPs influence antibiotic bioavailability and the distribution and spread of antibiotic-resistance genes. However, limited research has focused on the molecular and cellular effects resulting from simultaneous exposure to MPs and antibiotics. Understanding the regulatory mechanisms of MPs on antibiotic-resistance gene diversity, particularly at the gene expression level, remains an important area for study. Additionally, exposure experiments involving diverse species are necessary to assess the combined toxicity of MPs and antibiotics, considering species-specific factors such as motility, feeding behaviors, and immunity. A holistic approach combining laboratory investigations and field tests is essential to bridge existing knowledge gaps. Furthermore, conducting exposure studies at environmentally relevant concentrations is recommended.

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Competing Interest

The authors declare that there is no competing interest.

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