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Review

Microplastics as vectors for antibiotic resistance genes and their implications for gut health

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Abstract
Microplastic pollution contributes to the rise of antibiotic-resistance. Everyday items like food containers, water bottles, clothing, and cosmetics can increase people's resistance to antibiotics. Microplastics in the environment serve as a suitable substrate for the production of "antibiotic-resistant genes" (ARGs). These genes are protected by bacterial chromosomes, phages, and plasmids, which are biological vectors capable of spreading and transferring antibiotic-resistance to humans, thereby reducing their ability to fight infections. In this study, we reviewed several articles that evaluated the abundance of ARGs and the changes in their expression in different environments. These changes were observed upon exposure to antibiotics such as tetracycline, sulfamethoxazole, macrolides, and others, as well as microplastics, nanoplastics, or a combination of both. To assess the impact of these stressors on ARG abundance, we compiled data from various studies using heatmaps and tables of ARG abundances in tissues or various environments. By synthesizing this information, we aimed to identify which ARGs were upregulated or downregulated in response to each stressor. Our findings provide insights into the potential risks posed by environmental pollutants and underscore the importance of understanding the dynamics of ARGs in response to different stressors.

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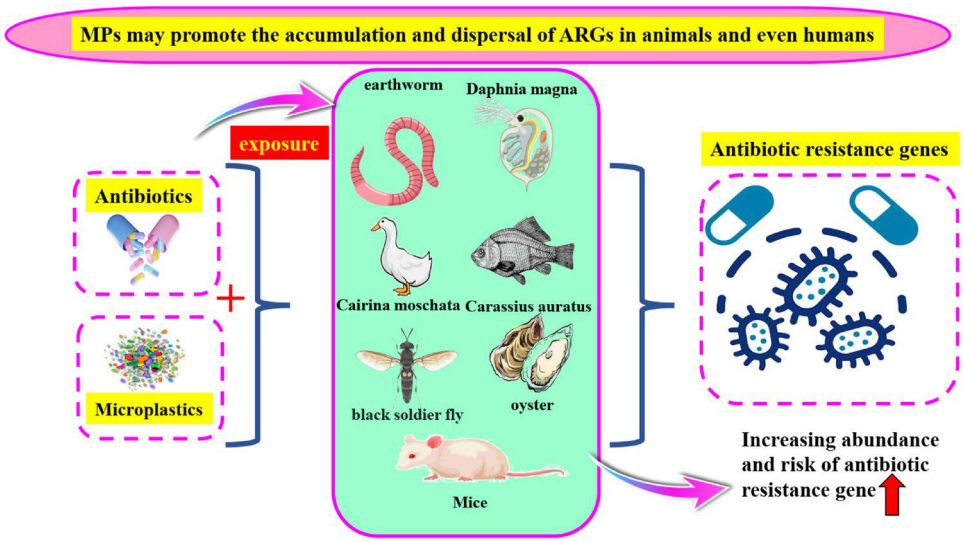
Graphical Abstract



Keywords Microplastics · Nanoplastics · Antibiotic-resistant genes (ARG) · Microbiota

1 Introduction

Plastic has been intertwined with human life for years[1–6]. Due to their low cost, lightweight, and durability, plastics are used in a wide range of products [7–10]. In 2021 alone, more than 390 million tons of plastic were produced worldwide, and this amount is rapidly increasing [11–13]. However, due to improper policies for disposing of these materials, a high percentage of plastics are released into the environment. Owing to their high durability, plastics are non-biodegradable and only break down into smaller pieces through physical, chemical, and biological reactions [14]. These particles, known as microplastics (MPs), are categorized into primary and secondary MPs. Primary MPs are used in the cosmetics and beauty industry, while secondary MPs result from the breakdown of larger plastics [15, 16]. In recent years, numerous reports have indicated the presence of MPs in water, soil, and the atmosphere [17]. Additionally, humans may become contaminated with these substances through ingestion, inhalation, or skin contact18. Surprisingly, MPs have been identified in human feces [19], urine [20], and organs, including the lungs [21], liver [22], spleen [23], and even human placenta [24], posing a threat to human health [25–27]. Antibiotic-resistance genes (ARGs) are emerging pollutants that have raised concerns due to the excessive and improper use of antibiotics in recent years. ARGs are indeed recognized as emerging environmental pollutants due to their potential to spread through ecosystems and impact human health[28, 29]. They have emerged as a serious concern for the effectiveness of antibiotics in clinical applications [30]. MPs act as a hub for horizontal gene transfer, leading to increased genetic exchange of various substances, such as antibiotic-resistant genes [31]. Antibiotic-resistance has been recognized by the world's leading health organizations as a global challenge for countries worldwide and a hazardous factor for human health and the environment in the twenty-first century [32]. In 2019, it was estimated that this factor led to the loss of 1.27 million human lives worldwide, and it is projected to increase eightfold by 2050 [33, 34]. Due to their large surface and hydrophobicity, MPs act as a preferred carrier for the placement of different types of pathogenic microorganisms and the spread of ARG s[35]. On the other hand, this increase in the accumulation of ARGs serves as a basis for the emergence of new genes and gene exchange [36], in such a way that by attaching antibiotics to these plastic components, their physical, chemical, and biological nature changes [37, 38]. MPs primarily promote the spread of acquired antibiotic resistance rather than increasing intrinsic or natural resistance [39]. Intrinsic resistance refers to the natural ability of certain bacterial species to withstand antibiotics due to inherent structural or functional traits. This form of resistance is encoded within the bacteria's core genome and is generally not influenced by external environmental factors like MPs. For instance, Gram-negative bacteria are naturally resistant to

some antibiotics because of their outer membrane structure, and this type of resistance is not altered by mechanisms like gene transfer or the presence of MPs [39].

In contrast, acquired resistance occurs when bacteria that were previously sensitive to antibiotics develop resistance through mutations or by gaining resistance genes from other bacteria. This is where MPs have a significant impact. MPs can serve as carriers for bacteria and environmental pollutants, creating conditions that enhance the transfer of antibiotic resistance genes (ARGs) through horizontal gene transfer (HGT). HGT enables the exchange of genetic material, such as plasmids, transposons, or phages, between bacteria, allowing them to acquire resistance traits they didn't originally possess [36].

Pollution caused by MPs has emerged as a significant environmental concern, with growing evidence pointing towards its role in exacerbating antibiotic resistance [40]. Antibiotic resistance genes (ARGs), which can be found in bacterial chromosomes, phages, and plasmids, act as biological vectors that facilitate the transfer and dissemination of resistance traits across microbial populations. This not only poses a direct threat to human health but also undermines the efficacy of antibiotics, making infections more difficult to treat [41–43]. The primary aim of this study is to provide a comprehensive overview of the interaction between MPs and ARGs, with a particular focus on their combined impact on gut microbiota. Gut microbiota plays a critical role in maintaining human health, and the disruption caused by MPs may further contribute to the spread of antibiotic resistance. This study will explore how MPs affect ARGs in microbial communities and the potential risks posed to both environmental ecosystems and human health.

Following this overview, the paper presents the first systematic review that investigates the impact of MPs on ARGs within the bodies of living organisms. By examining existing literature and research data, this review aims to deepen our understanding of the mechanisms through which MPs contribute to the dissemination of antibiotic resistance and to assess the broader implications of this phenomenon on public health and disease management strategies.

2 Materials and methods

For the literature search, a language limit was set, and only articles published in English were reviewed. The authors searched three electronic databases—PubMed, Web of Science, and Scopus—on December 19, 2023, for studies investigating the effect of microplastics (MPs) on antibiotic-resistance genes (ARG). The search strategy was defined as follows:

Scopus: TITLE-ABS-KEY (microplastic* OR nanoplastic*) AND TITLE-ABS-KEY ("antibiotic-resistance genes*" OR "antimicrobial resistance*" OR "antibiotic-resistance bacteria*" OR "Drug Resistance, Bacterial").

Web of science: (TS = (microplstic* OR nanoplastic*)) AND (TS = ("antibiotic-resistance genes*" OR " antimicrobial resistance*" OR "antibiotic-resistance bacteria*" OR "Drug Resistance, Bacterial")).

PubMed: ((("microplastic*"[Title/Abstract]) OR ("nanoplastic*"[Title/Abstract])) OR ("Microplastics"[Mesh])) AND (((("antibiotic-resistance genes*"[Title/Abstract]) OR ("antimicrobial resistance*"[Title/Abstract]) OR ("antibiotic-resistance bacteria*"[Title/Abstract)) OR ("Drug Resistance, Bacterial"[Mesh])) OR ("Drug Resistance, Microbial"[Mesh])).

EndNote was utilized during the screening process. Initially, the authors screened all abstracts and titles from the retrieved records based on the inclusion/exclusion criteria, excluding completely irrelevant studies. The total number of articles retrieved from the three databases was 469. After removing duplicates, 256 articles remained. Following further screening to remove errata, reviews, notes, conference proceedings, books, book chapters, replies, comments, viewpoints, discussions, and irrelevant articles, 9 articles remained that specifically focused on the effect of MPs on ARG in living organisms.

3 Result and discussion

3.1 The role of microplastics in the evolution of antibiotic-resistance in the environment

Tiny plastic fragments, known as microplastics, are quietly invading our water bodies. These omnipresent pollutants have a new and alarming threat: they are breeding grounds for antibiotic-resistant bacteria, more popularly known as 'superbugs.' MPs act like sponges, soaking up residual antibiotics from wastewater and other sources [44]. This produces a strong avenue for antibiotic-resistant bacteria to grow. But that is not all. More importantly, microplastics provide physical sites for pathogens to attach and colonize. This proximity supports horizontal gene transfer of ARGs between bacteria—in essence, an accelerated way of developing superbugs. The impacts spiral up the aquatic food web [45]. As

the microplastic-related ARG build-up continues to aggregate, the balance of microbial communities is altered. This will create a window of opportunity for the virus variants that are even more resistant, thus placing aquatic life in danger. However, the threat doesn't just linger in the water. MPs can be ingested by fish and other aquatic creatures, potentially transferring ARGs to their gut microbiome [46]. This raises a chilling possibility: the transfer of antibiotic resistance from the environment to the food chain, ultimately reaching human consumers. Human exposure to microplastics can occur through contaminated seafood or even through the ingestion of microplastics present in drinking water. If these microplastics harbor ARGs, they can contribute to the development of antibiotic resistance within the human gut microbiome [47]. This can make even common infections more challenging to treat, jeopardizing public health and potentially diminishing the effectiveness of life-saving antibiotics. One of the hotspots of ARGs and MPs is sewage treatment plants [48]. Antibiotic- resistant bacteria were identified abundantly on MPs in wastewater treatment plants, which indicates that MPs are carriers for ARGs [49]. According to Zhao et al.'s study 2021on wastewater, an essential carrier for bacteria with resistant genes is polyvinyl chloride (PVC). Studies also show that the presence of antibiotics or heavy metals in wastewater treatment plants has an increasing effect on the abundance of ARG in MPs [50]. Another hotspot of ARGs and MPs is aquatic environments. Studies on the North Pacific Ocean [51] and freshwater bioreactors[52] have shown a high abundance of ARGs in MPs. In the aquaculture system, the presence of antibiotic-resistant bacteria and ARGs has been proven [53, 54]. MPs show different behaviors in ARG absorption depending on the type of polymer. Polyethylene obtained from rivers has been reported to have a higher abundance of ARG compared with Polypropylene (PP) [55]. In fact, after releasing wastewater into the river, MPs and ARGs are ingested and used by aquatic plants [56, 57] and aquatic animals [58, 59] which can not only enter the human food chain but also exert negative effects on the living body.

Extensive studies have confirmed the presence of MPs in the soil of agricultural lands [35, 60–63]. In addition, ARGs in MPs act as a carrier in soil [64], and pollutants such as additives, soil heavy metals, or pesticides will influence their formation [65, 66]. Not many studies have been concerned with ARGs distribution and transport of MPs from soil [67, 68]. However, a previous study [67] reported that higher abundances of ARGs in MPs in plant soil generally result from larger, more heavily weathered MPs and longer years of cultivation. The following factors determine the selective enrichment of ARGs: MPs' size and weathering state, soil characteristics, and types of ARGs. Heterogeneous aggregates comprised of soil particles and MPs exhibit differential transport properties, influencing the horizontal and vertical migration of contaminants (e.g. ARGs, MPs, heavy metals) [69–71]. ARGs and MPs have the potential to be taken up by edible vegetables from the surrounding soil [72, 73].

The last environmental matrix that can be the hotspot of ARGs is air. Inhalation of ARGs and MPs present in the atmosphere may lead to detrimental health effects in humans and animals. In addition, they can be transported by wind to long distances [74–77]. Extensive studies have reported the inhalation of MPs through air in open and closed environments [78, 79]. ARGs and MPs were detected in heavily polluted air [80]. However, Research on the interaction between ARGs and MPs in both outdoor and indoor environments is currently lacking.

3.2 Disturbance of the intestinal tract

MPs cause serious damage to the organism's gut [81], which weakens the gut barrier against pollutants. A study investigated the effect of MPs and sulfamethoxazole together on mice. The results showed that MPs cause intestinal disorders, and the destruction of the intestinal barrier, and they can reduce the effect of the drug sulfamethoxazole and cause an increase in antibiotic- resistance genes[18]. Microorganisms that live in the intestines of animals are called intestinal microbiota[82] which is effective in host nutrition, growth, and immune response [83]. In a similar study, it was stated that MPs cause disturbances in the intestinal microbiota and intestinal microbial and fungal populations[84]. In addition to affecting intestinal bacteria and fungi, MPs can affect intestinal metabolic pathways and microbial genes encoding antibiotic-resistance[84]. In addition, MPs cause damage to epithelial cells along with peristalsis and intestinal friction, as a result of which reactive oxygen species are released and activate the antioxidant enzyme system [85]. These results are consistent with the results of studies conducted on soil organisms [86]. Damage to the intestinal barrier causes the entry of pollutants and pathogens. As a result, it leads to an increase in ROS and inflammation and an increase in interleukin 10 and interleukin 6, inflammatory cytokines [85]. The pathways are shown in Fig. 1.

3.3 Intensification of antibiotic-resistance by MPs

In the studies reviewed, various living organisms are exposed to different drugs and MPs of various sizes through different methods and under specific conditions (Table 1). This leads to changes in genes and the functioning of various

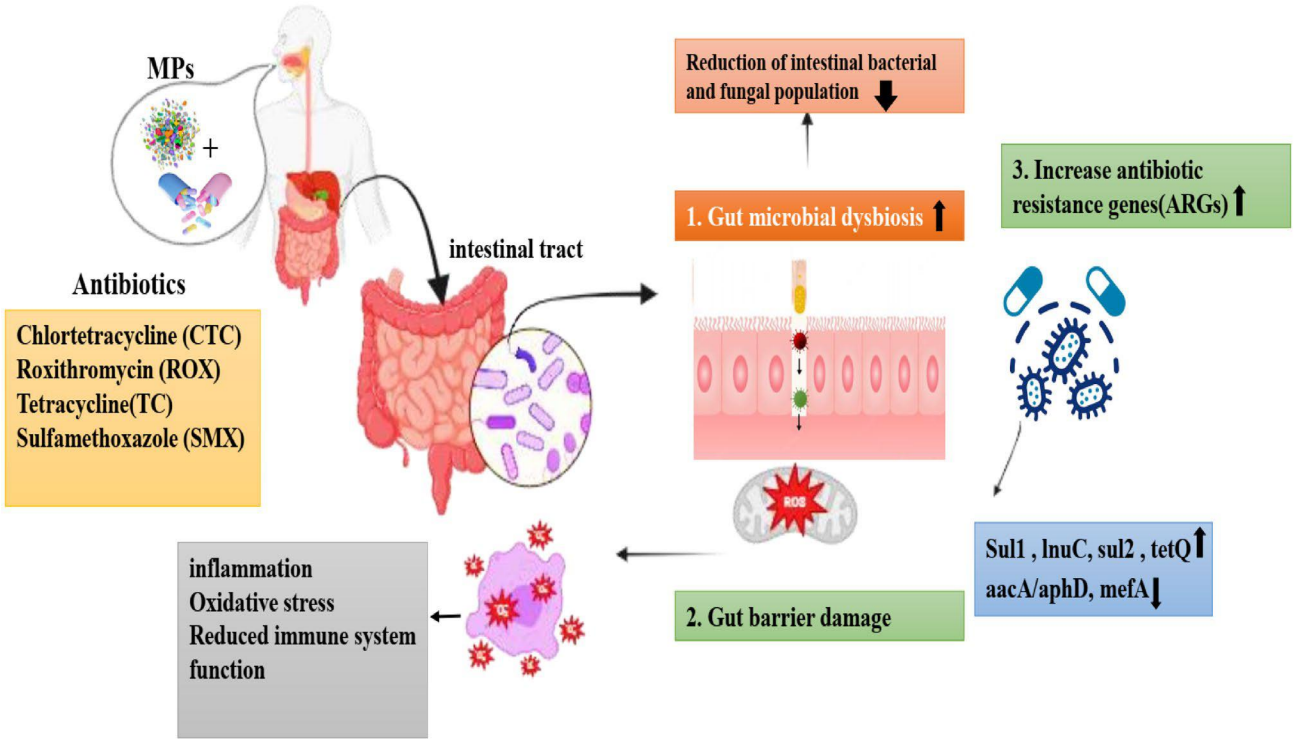


Fig. 1 The effects of MPs on gut microbiota and ARGs

organs in the relevant organisms, which can be precisely examined by extracting the DNA, and the exact effect of MPs on altered genes can be identified.

Liu et al. [18] found that the exposure of mice to polystyrene MPs leads to a decrease in the bioaccumulation of *sulfamethoxazole (SMX)* in the liver, lung, spleen, heart, and kidney tissues of mice. It also increased the antibiotic-resistance of mice. In this study, ARG was extracted by high-throughput quantitative PCR (HT-qPCR) using the Wafergen SmartChip Real-time PCR system. Their study reported an increase in *sul1-lnuC-acrA-03-mefA-ermB* but a reduction in *aacA/aphD*. The effects of microplastics on gut microbiota and antibiotic-resistance genes are shown in Fig. 1.

Gao et al.[84] showed that MPs can hurt the intestinal microbiota (microorganisms that live in the intestines of animals) [90]. Gut microbiota is involved in nutrition, growth, and immune response [83, 91]. The animal gut can act as a reservoir of ARGs for various reasons [92–95]. Previous studies have shown that changes in gut microbiota can affect the amount of ARGs in the gut of animals [96]. Research suggests that fungi in our gut are more vulnerable to PS than bacteria. These gut fungi can influence our immune system by triggering T helper cells, which can help to control inflammation [97]. Disruptions in the balance of gut fungi could have further negative effects on the health of the host organism. In this study, male mice were fed polystyrene of different sizes of MPs. It was shown that MPs affect antibiotic-resistance in the mouse model. For example, *Sul2* and *VanSD* were increased and *MepR-macrolide-efflux* protein-reverse transcriptase was decreased. Zhimin Xu also confirms that microplastics (PVC) can not only lead to the release of inflammatory cytokines to induce intestinal inflammation but also harden stools due to mucus released from black soldier flies (BSFs). As a result, they prevent organic mineralization and antibiotic degradation. Also, there was an increase in *tetX2- tetQ- tetG- tetM- tetA(G)- tetA(P)- sul1- sul2* genes, especially those ARGs that code for *tetracyclines and sulfonamides* [85].

Similar studies also confirm the accuracy of this article [87]. It is necessary to mention that MP pollution is creating new breeding grounds for bacteria in water [98] These bacteria can form layers on the MPs, which can make them more resistant to antibiotics [99, 100] and harbor genes that spread antibiotic-resistance [52]. As MPs become more widespread, this could lead to the increased transfer of ARGs among bacteria, harming both the environment and living things [54, 101]. For example, in D. magna as an important part of the aquatic food chain, similar effects on the intestine and the increase of the ARG *sul1* have been observed. This study deals with the effect of MPs particle size, types, and concentration, which are important factors in the emergence of effects. Since nanoplastics have a smaller size and a larger specific surface area than MPs, the possibility of combining them with antibiotics is higher[37]. Also, studies have shown that MPs can cause more damage when they are older [88]. In this study, exposure to 20–30 µm polystyrene MPs led to the

Table 1 Impact of MPs on Antibiotic Resistance in Organisms

Species	Antibiotics/MPs Exposure	Genes (ARGs)	Enrichment	Method for ARG extraction	Refs.
Mice	MPs + *SMX*	*sul1- lnuC- acrA-03- mefA- ermB*	Up-regulated	High throughput quantitative PCR (HT-qPCR)	[18]
		aacA/aphD	Down-regulated		
	SMX	*sul1*	No change		
		lnuC- acrA-03- mefA- ermB- aacA/aphD	Up-regulated		
	MPs	*sul1- lnuC- mefA- ermB-*	Down-regulated		
		acrA-03- aacA/aphD	Up-regulated		
D. Magna	MPs	*EcR- sul1*	Down-regulated	Polymerase chain amplification (PCR)	[87]
		AK- TRxR- Vtg1- CAT- GSTs	Up-regulated		
	MPs + *S. flexneri*	*AK- Vtg1*	No change		
		EcR- sul1	Down-regulated		
		GSTs- CAT- TRxR	Up regulated		
	S. flexneri	*Vtg1- GSTs*	No change		
		TRxR- EcR	Down-regulated		
		AK- CAT- sul1	Up-regulated		
oyster farm-Biofilms	MPs	*blaTEM- intI1- qnrS- sul1*	Up-regulated	qPCR	[39]
oyster farm-Water		*blaTEM- intI1- qnrS*	Down-regulated		
		sul1	Up-regulated		
Muscovy ducks (Cairina moschata)	MPs	*macB- bcrA- tetA (58)- msbA- tetQ*	Up-regulated	PCR	[36]
		tetA(46)- tetB (60)- tet (43)	Down-regulated		
	CTC + MPs	*tet(35)- tet36- tet37- tet38- tetA (60)- tetB (46)- tetW- tetS- otr (B)*	Up-regulated		
	CTC	*tetQ- tet37*	Up-regulated		
Carassius auratus	polystyrene MPs alone or in combination with the 100 μg/L *roxithromycin (ROX)*	*Baca- tetpb- sul1- tetpa- cml e3- tetg- ant2ia- teta- tetm- mefa- tetz- cml e8- lnub- aph6id- aph33ib- bl2a_nps- ermg- sul2- tetc- cml el- catb3*	Up-regulated	To extract metagenomic DNA, the intestinal contents were gently squeezed out by a sterile instrument and collected into a sterile container	[88]
mice	PS0.1	*VanSD- Sul2-* tetracycline resistance protein- dihydropteroate synthase- sulfonamide resistance protein	Up-regulated	ShortBRED was used to profile antibiotic-resistance genes	[84]
		MepR- macrolide-efflux protein- reverse transcriptase	Down-regulated		
	PS10	*ANT(6)-Ib-APH(3')-IIIa-TetX-TnpA*-aminoglycoside phosphotransferase-integrase-(*sigE*)RNA polymerase sigma-70 factor-microcompartment protein	Up regulated		
		MepR	Down-regulated		
black soldier fly	antibiotics	*tetX2- tetQ- tetG- tetM- tetA(G)- tetA(P)- sul1- sul2*	Up-regulated	HT-qPCR	[85]

Table 1 (continued)

Species	Antibiotics/MPs Exposure	Genes (ARGs)	Enrichment	Method for ARG extraction	Refs.
earthworms	*M4**	*tetX-sul1-QnrS2-TriC-Klebsiella pneumoniae acrA*	Down-regulated	Polymerase chain reaction	[89]
		FosB3-TRU-1-OXA-12-cphA2	Up-regulated		
soil fauna (Enchytraeus crypticus)	*TC**	*blaSHV-nisB*	Down-regulated	High-throughput quantitative PCR(HT-qPCR)	[86]
		ermX-aadA1-cfxA-blaGES-ttgB- tetG-aadA2-qacEdelta1-qacH-tetB-02-vanXD	Up-regulated		
	TC and NP	*aac(6")-Il- aac(6")-Ib(akaaacA4)- fox5-fosX- cmlA1- blaZ*	Up-regulated		

TC tetracycline, *PS* polystyrene, *CTC* chlortetracycline, M4 = 100 mg/kg of 10 µm MPs

increase of *AK-TRxR-Vtg1-CAT-GSTs* genes, which shows that micro polystyrene may cause disturbance in the balance of vitellogenesis, and endocrine disorders. These MPs also led to the enrichment of ARGs (*sul1, qnrS and blaTEM*) in oysters [48] In addition to Daphnia, the effect of MPs with *roxithromycin (ROX)* on the intestine of Carassius auratus was investigated by Peng Zhang. The result showed that MPs caused the accumulation of *ROX* in the intestine of fish. *ROX* is an antibiotic that inhibits protein synthesis in cells [102]. In this study, *ROX* altered microbial diversity in the gut and reduced beneficial bacteria [103]. It also increased bacteria resistant genes *Baca, tetpb, sul1, tetpa, cml e3, tetg, ant2ia, teta, tetm, mefa, tetz, cml e8, Inub, aph6id, aph33ib, bl2a, nps, ermg, sul2, tetc, cml el, catb3*.

In addition to the studies conducted on aquatic animals, studies on terrestrial animals and earthworms [104] have also been conducted by Jun Ma [86] and Guanghui Xu [89] who exposed soil invertebrates Enchytraeus crypticus to MPs and tetracycline and investigated antibiotic-resistance genes using quantitative PCR method. Their results showed an increase in *aac(6")-II-aac(6")-Ib (akaaacA4)—fox5- fosX- cmlA1- blaZ*. Also, higher concentrations of MPs were found to have a direct effect on the increase of ARGs.

In the meantime, ARGs and MPs in the body of birds have received scholarly attention. Bing Liu, for instance, measured the effect of MPs and tetracycline on Muscovy ducks. In this study, *macB-bcrA-tetA -msbA-tetQ* were increased by exposure to MPs [36]. Bing Liu concluded that in addition to leading to an imbalance in ROS production and antioxidant capacity, MPs are capable of changing antibiotic-resistance and transferring ARGs to the ecosystem.

To explain the mechanisms should be mention that MPs can significantly affect the gut environment, which houses a diverse community of microorganisms, including bacteria that carry antibiotic resistance genes (ARGs) [105, 106]. Particularly smaller MPs can disrupt the natural balance of gut microbes (known as dysbiosis), creating conditions that favor the growth and survival of antibiotic-resistant bacteria. This disruption can be linked to the surface properties of MPs, which can act as carriers for ARGs or harmful bacteria. When bacteria carrying these genes come into contact with MPs, the plastics may encourage horizontal gene transfer (HGT), a process where genetic material, including ARGs like *Sul2* (*sulfonamide* resistance) and *VanSD* (*vancomycin* resistance), is shared between bacteria [36].

MPs can facilitate this transfer in a variety of ways. They may serve as platforms where bacteria can cluster together, increasing the chances of genetic exchange through mechanisms like transformation, transduction, or conjugation [106]. Research indicates that genes like Sul2 and *VanSD*, which are often found on mobile genetic elements such as plasmids or transposons, are more likely to spread when MPs are present. The physical interaction between bacteria on the surface of MPs increases the likelihood of HGT, thereby raising the prevalence of antibiotic resistance genes. In addition, MPs can influence the host's immune system [48]. The inflammation or immune suppression caused by MPs in the gut may reduce the body's ability to keep antibiotic-resistant bacteria in check, allowing these resistant strains to proliferate. The increase in bacteria carrying *Sul2* and *VanSD* may be a response to selective pressure from these changes in the gut environment, enabling them to survive and dominate [83, 84].

Moreover, MPs often interact with other environmental pollutants, such as heavy metals or chemical contaminants, that coexist in the gut. These pollutants can create extra pressure on bacteria to acquire and retain ARGs, contributing to the higher levels of *Sul2* and *VanSD*. Contaminants can also trigger stress responses or increase mutation rates in bacteria, making them more prone to absorbing or maintaining resistance genes [39].

On the other hand, the reduction of certain genes, such as *MepR*, which is linked to macrolide-efflux proteins, could be a result of the gut's altered environment. In some cases, specific ARGs may be outcompeted or suppressed by other dominant ARGs or bacterial strains that are thriving in the presence of MPs. The new gut environment created by MPs may favor the survival of some resistant bacteria while causing a decline in others, leading to shifts in the abundance of different resistance genes [89].

Overall, the increase in ARGs like *Sul2* and *VanSD* in the presence of MPs can be attributed to a combination of disrupted gut microbial dynamics, enhanced gene transfer, immune system effects, and interactions with other pollutants. Together, these factors contribute to the spread and persistence of antibiotic resistance in living organisms exposed to MPs [44, 45, 87].

4 Limitations

- **Focus on Specific Classes of Antibiotics**: Even though the reviewed articles in this study ranged among different classes of antibiotics, further research needs to be undertaken to cover more classes of antibiotics to understand the general effect of microplastics on antibiotic resistance.

- **Non-Standardization of Designs**: Variability in study design, including sampling, methodologies of analysis, and exposure conditions, may make comparison and, importantly, synthesis of results between studies difficult.
- **Limited Data on Specific Microplastic Types**: The study would be further improved by focusing on specific types of microplastics, such as polyethylene, polypropylene, and polystyrene, to examine the specific effects of each type on antibiotic resistance.
- **Other Factors Might Intervene**: The study focused on microplastics and antibiotics; however, other environmental factors may be causing antibiotic resistance, such as heavy metals and organic pollutants. This should be considered in future studies.

5 Suggestions

- **Controlled Experiments**: There could be an increase in the observed causal relationship between microplastics and antibiotic resistance through experiments conducted in controlled environments, where test subjects are exposed to microplastics and subsequent changes in ARG abundance and expression are measured.
- **Long-term Studies**: Research the chronic effects of microplastic exposure on antibiotic resistance in diverse environments, considering factors like bioaccumulation and possible synergistic interactions with other pollutants.
- **Spatial and Temporal Analysis**: Investigate spatial and temporal analyses of ARG distribution related to microplastic pollution, identifying hotspots and time-course dynamics.
- **Risk Assessment**: Develop risk assessment models to determine the potential health and environmental risks associated with microplastic-mediated antibiotic resistance.
- **Interdisciplinary Collaboration**: Assemble a diverse team of experts across environmental science, microbiology, and public health disciplines to address multidisciplinary challenges related to microplastic pollution and antibiotic resistance.
- **Public Awareness and Policy Development**: Raise public awareness about the issue and build advocacy for policies on reducing microplastic pollution and promoting prudent antibiotic use

6 Conclusion

MPs are tiny plastic particles that pollute the environment through water and air. They have been found in drinking water, soil, air, seafood, and even the human body. MPs can accumulate in the respiratory and digestive systems, contributing to weight gain, insulin resistance, cancer, and reproductive health issues. Notably, they are linked to increased antibiotic resistance in humans, a major concern as antibiotic resistance caused around 1 million deaths in 2019.

While antibiotic resistance is often attributed to the overuse of antibiotics, recent studies indicate that MPs play a significant role. This study reviewed research on the frequency and expression of antibiotic-resistance genes (ARGs) in organisms exposed to MPs and antibiotics like tetracycline, sulfamethoxazole, and macrolides. The findings reveal that MPs enhance resistance to antibiotics such as macrolides, tetracyclines, and aminoglycosides, which are critical for treating respiratory infections.

The study highlights the alarming implications of continuous human exposure to MPs, which accelerates the emergence of antibiotic resistance. It underscores the need for further research on how MPs influence ARGs, particularly in humans. Future studies should investigate the size, type, and mechanisms of MPs affecting resistance genes, with a focus on their impact on human health. This research provides a foundation for understanding the synergistic effects of MPs on antibiotic resistance.

Author contributions N.J: Writing—review & editing, Investigation. B.A: Writing—review & editing. F.J: Writing—review & editing, Data curation, Preparation of article figure. P.A: Writing. M.M: Writing—review & editing.

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate This article does not contain any studies with human participants performed by any of the authors.

Consent for publication All authors approved the final approval of Manuscript.

Competing interests The authors declare no competing interests.

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