

Review



Environmental Emerging Contaminants Drive Bacterial Antimicrobial Resistance Evolution: Evidence, Mechanisms, and Challenges

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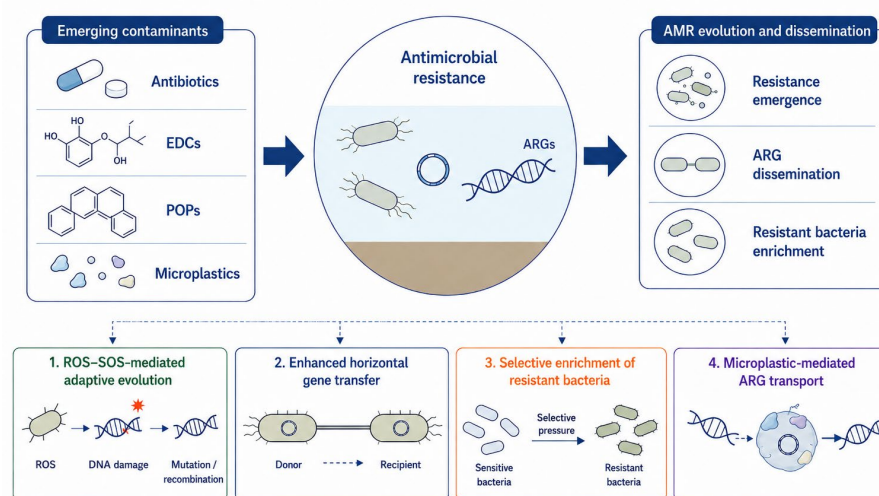
Keywords

antibiotics; endocrine-disrupting chemicals (EDCs); persistent organic pollutants (POPs); microplastics; antimicrobial resistance

Highlights

- Emerging contaminants can drive antimicrobial resistance evolution in environmental systems
- Antibiotics, EDCs, POPs, and microplastics exhibit distinct AMR-driving potentials
- Four mechanisms link emerging contaminants to AMR evolution and dissemination
- Multi-omics, modeling, and AI will advance contaminant-driven AMR risk assessment and management

Abstract: Antimicrobial resistance in the environment has become a major challenge to global public health. In addition to antibiotics themselves, emerging contaminants such as endocrine-disrupting chemicals (EDCs), persistent organic pollutants (POPs), and microplastics also significantly influence the emergence, evolution, and dissemination of bacterial antimicrobial resistance. This systematic review, based on a structured literature search, first summarizes current evidence linking emerging contaminants to bacterial antimicrobial resistance across diverse environmental matrices. It also provides a mechanistic analysis of four major pathways by which emerging contaminants promote antimicrobial resistance evolution: ROS–SOS-mediated adaptive evolution, enhanced horizontal gene transfer (HGT), selective enrichment of resistant bacteria, and microplastic-mediated migration and dissemination of antimicrobial resistance genes (ARGs). Finally, we highlight current knowledge gaps and propose future research directions, including long-term field investigations, multi-omics approaches, experiment–model integration, and artificial intelligence-assisted analyses, to establish a cross-scale framework for understanding emerging contaminant-driven antimicrobial resistance evolution. This review provides new mechanistic insights into the environmental evolution of bacterial antimicrobial resistance and offers a theoretical foundation for environmental risk assessment and pollution control of emerging contaminants.



1. Introduction

WHO has ranked bacterial antimicrobial resistance (AMR) among the top ten global public health threats. In 2021, an estimated 4.71 million deaths worldwide were associated with bacterial AMR. Without effective interventions, this number could reach 8.22 million by 2050 [1]. AMR in environmental matrices, including water, soil, and air, has also attracted growing concern because of the One Health connectivity between environmental and clinical compartments. For example, antibiotic-resistant bacteria (ARB) and AMR genes (ARGs) are widely present in hospital wastewater, municipal wastewater, and domestic sewage as a result of human discharge [2–4], and can subsequently enter receiving rivers through wastewater treatment plant effluents [5]. In parallel, agricultural practices such as wastewater irrigation and sewage sludge application drive ARG accumulation in topsoil. Bioaerosols may also act as airborne vectors, facilitating the atmospheric dissemination of ARGs [6,7]. These ARB and ARGs can reach humans through various exposure pathways such as drinking water, food, and inhalable aerosols, thereby posing substantial but often underestimated risks to public health. This One Health transmission is supported by accumulating genetic evidence. For example, soil-derived ARGs have nearly identical sequences to those in human pathogens [8]. Similarly, multidrug-resistant strains isolated from hospital environmental surfaces share high genetic homology with clinical isolates recovered from infected patients [9]. Therefore, understanding how environmental AMR forms, develops, and evolves is urgently needed.

Bacterial AMR in the environment may be influenced by various coexisting pollutants. Previous studies have shown that heavy metals [10,11] particulate matter [12], and toxic organic compounds can promote resistance dissemination by acting as carriers for resistance transmission and by inducing co-selection effects. Recently, emerging contaminants, particularly antibiotics, EDCs, microplastics, and POPs have attracted considerable attention because of their persistence, bioactivity, and ecological risks. Antibiotics are a category of pharmaceuticals applied to treat and prevent bacterial infections. As direct selective agents, antibiotics are widely recognized as key drivers of resistance development. EDCs are exogenous substances or mixtures that disrupt endocrine function and may cause reproductive, neurological, and immune disorders [13–15]. Microplastics mainly originate from the fragmentation of larger plastic products and the degradation of agricultural plastic mulch [16–18]. POPs are persistent organic compounds that bioaccumulate and may cause neurological, reproductive, and immune damage, as well as increased cancer risk [19].

While most research on emerging contaminants has focused on their intrinsic toxicity and health risks,

mounting evidence indicates that they also directly and indirectly drive resistance evolution through selective pressure, co-selection, and facilitation of HGT. In this systematic review, we systematically analyze and critically assess the impacts and mechanisms of four typical emerging contaminants (antibiotics, EDCs, microplastics, and POPs) on bacterial AMR evolution, based on a structured literature search and study-selection process reported with reference to the PRISMA 2020 guidelines. Furthermore, from a One Health perspective, we discuss potential strategies for mitigating the spread of AMR through improved management of emerging contaminants, aiming to provide theoretical support for the risk assessment, prevention, and integrated management of environmental AMR.

2. Literature-Search Methodology

The literature search and study-selection process was conducted and reported with reference to the PRISMA 2020 guidelines. The Web of Science Core Collection was searched for original research articles published between 2012 and 2026, with the final search date of 13 August 2026. Document types were limited to original research articles. Review articles were additionally consulted for background information and contextual synthesis but were not included in the quantitative fold-change dataset. Four search strategies, one for each contaminant category, combined contaminant-related keywords with antimicrobial resistance-related terms. The specific search strings were as follows:

Antibiotics: TS = (antibiotics) AND TS = (“antibiotic resistance” OR “antimicrobial resistance”)

EDCs: TS = (“EDCs” OR “triclosan” OR “bisphenol A” OR “triclocarban” OR “DMP”) AND TS = (“antibiotic resistance” OR “antimicrobial resistance”)

POPs: TS = (“POPs” OR “PFASs” OR “OCPs” OR “PAHs” OR “PCBs”) AND TS = (“antibiotic resistance” OR “antimicrobial resistance”)

Microplastics: TS = (“microplastics” OR “nanoplastic” OR “plasticsphere”) AND TS = (“antibiotic resistance” OR “antimicrobial resistance”)

Four researchers, working in two independent teams, screened the retrieved records. Eligible studies addressed the relationships between the target contaminants and bacterial AMR, including occurrence and correlation studies, controlled exposure experiments, and mechanistic investigations, without restriction on the direction of the reported effects. Representative studies from the eligible literature were subsequently synthesized in this review. The literature identification and selection process is summarized in the PRISMA 2020 flow diagram (Figure 1), and the corresponding PRISMA 2020 checklist is provided in Table S1 of the Supporting Information.

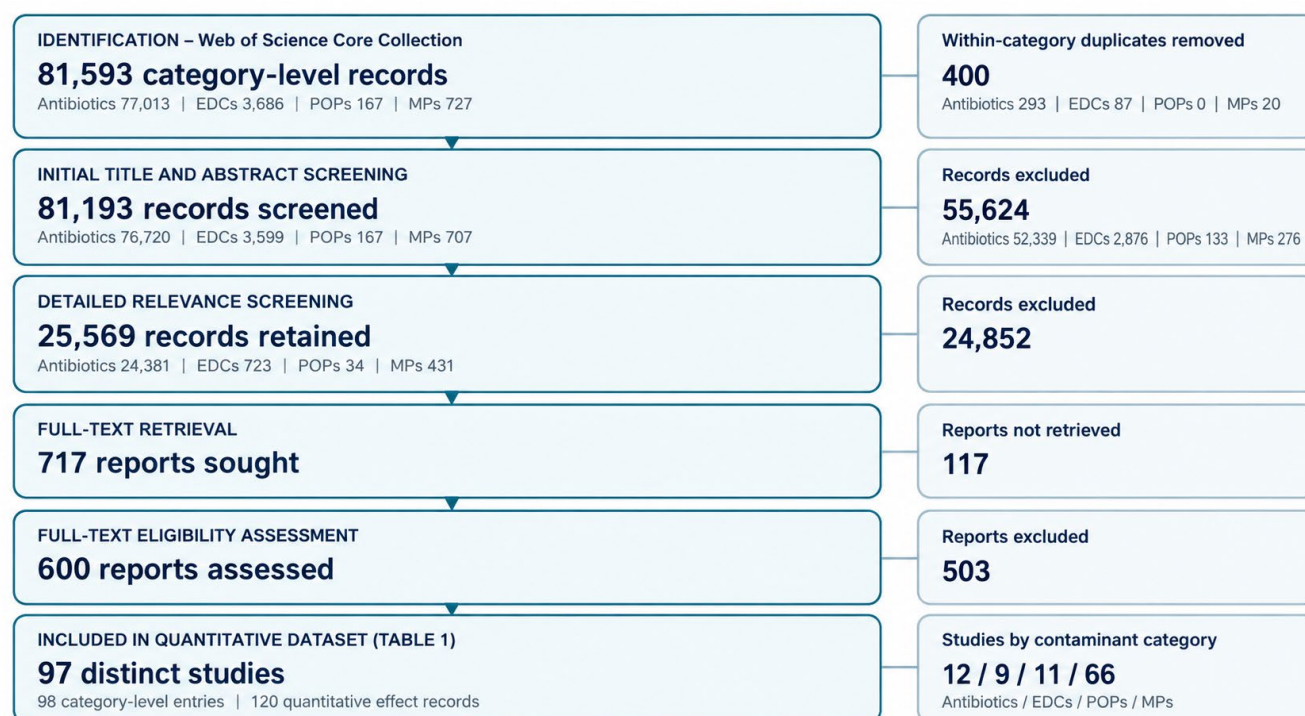


Figure 1. PRISMA 2020-informed flow diagram of literature identification and selection.

3. Evidence of Emerging Contaminant-Associated Bacterial Antimicrobial Resistance

Four types of emerging contaminants are widely present in the environment, generally at relatively low concentrations (ng/L–μg/L in water and ng/kg–μg/kg in soil), while substantially higher levels can be detected in highly contaminated areas. Among them, microplastics are typically quantified by particle abundance rather than mass concentration, with reported levels reaching 10⁰–10³ items/m³ in aquatic systems and even higher concentrations in soils (10²–10⁵ items/kg).

According to the reported fold-change statistics (Table 1), antibiotics are the most extensively studied class of emerging contaminants in relation to AMR. A substantial body of evidence from both field investigations and laboratory studies has consistently demonstrated their role as selective agents driving

bacterial resistance evolution. Increasing attention has been directed toward microplastics as potential facilitators of ARG dissemination, supported by growing evidence of their roles as microbial carriers and hotspots for horizontal gene transfer. However, several studies have also reported limited or even negative effects (fold change < 1), indicating that their impacts may vary depending on environmental conditions and experimental systems. By comparison, studies investigating the effects of EDCs and POPs on bacterial AMR remain relatively limited, and inconsistent responses, including negative effects reported for some POPs, have been observed. Considering the number of available studies, the consistency of reported observations, and the mechanistic evidence, the overall evidence levels for antibiotics, microplastics, EDCs, and POPs are considered strong, moderate to strong, emerging, and emerging, respectively.

Table 1. Comparison of research characteristics of different emerging contaminants in promoting antimicrobial resistance.

Indicator	Antibiotics	Endocrine-Disrupting Chemicals (EDCs)	Persistent Organic Pollutants (POPs)	Microplastics (MPs)
Environmental occurrence levels	Surface water: ng/L–μg/L Groundwater: μg/L Soil: μg/kg	Surface water: ng/L–μg/L Sewage sludge: mg/kg	Surface water: ng/L Soil: μg/kg–mg/kg	Water bodies: 10 ⁰ –10 ³ items/m ³ Soil: 10 ² –10 ⁵ items/kg
Reported fold change ^a	ARGs: 1.2–3845 (median = 5.35, n = 17) HGT/MGE: 1.4–10.7 (median = 6.05, n = 2)	ARGs: 10–99.99 (median = 55, n = 2) HGT/MGE: 1.3–4.39 (median = 2.87, n = 8)	ARGs: 0.1–105 (median = 2, n = 7); HGT/MGE: 0.6–50 (median = 2.9, n = 8)	ARGs: 0.24–12.45 (median = 1.36, n = 51) HGT/MGE: enhanced fold range 0.24–200 (median = 3.0, n = 25)
Overall evidence strength ^b	Strong	Emerging	Emerging	Moderate to strong

Table 1. Cont.

Indicator	Antibiotics	Endocrine-Disrupting Chemicals (EDCs)	Persistent Organic Pollutants (POPs)	Microplastics (MPs)
Major mechanisms driving antimicrobial resistance	(1) ROS–SOS response			
	(2) Promotion of horizontal gene transfer (HGT)	(1) ROS–SOS response (2) Promotion of horizontal gene transfer (HGT)	(1) ROS–SOS response (2) Promotion of horizontal gene transfer (HGT)	(1) physical vector
	(3) Selective enrichment of resistant bacteria			

Note: ^a The values in the “Reported fold change” row are descriptive summaries of the extracted effect estimates for the four contaminant classes. Source studies and record-level values are listed in Tables S2–S5. Eligible records reported a quantitative ARG, HGT, or MGE endpoint and an interpretable exposure contrast involving the target contaminant. Comparators included contaminant-free controls and, where clearly defined, lower-dose, pre-exposure, or site-based comparisons. Studies involving additional treatments, weathered materials, or host-associated settings were retained only when the relevant exposure contrast could be clearly identified and are labelled accordingly in Tables S2–S5. Quantitative values reported in the main text or Supporting Information, as well as values reliably extractable from figures, were eligible. Six records in Table S2 were manually estimated from clearly readable plots using the displayed axes; these values should therefore be regarded as approximate. For studies reporting a range, the midpoint was used as the representative fold change, whereas one-sided upper or lower bounds were retained as reported. Records lacking an interpretable comparison or a sufficiently readable figure scale were excluded. Fold changes < 1 indicate decreases. For each contaminant class and endpoint category (ARGs; pooled HGT/MGE), *n* represents the number of extracted records. Because the included studies differ substantially in organisms, environmental matrices, exposure designs, comparators, and analytical endpoints, the reported ranges and medians are descriptive summaries and should not be interpreted as pooled causal effect estimates or used for direct quantitative comparisons across contaminant classes. ^b Overall evidence strength was qualitatively assessed based on (i) the number of published studies identified through the structured literature search, (ii) the consistency of reported observations across independent studies, and (iii) the availability of experimental evidence supporting the underlying mechanisms. These ratings are intended to provide a qualitative overview rather than a quantitative assessment.

3.1. Antibiotics

Antibiotics are direct drivers of bacterial AMR. They are widely detected in surface water and sediments [20], particularly in densely populated and economically active regions [21]. Antibiotics can also enter groundwater through livestock wastewater and agricultural irrigation, with maximum concentrations in groundwater samples from different regions reaching the µg/L level [22,23]. Coastal waters are likewise affected by antibiotic inputs from both terrestrial sources and mariculture activities. For example, the average concentration of quinolones in Bohai Bay reached 388 ng/L [24]. Soil is another major reservoir. Antibiotics can also enter and persist in soils through pathways such as manure application, with residual concentrations reaching µg/kg to mg/kg levels; commonly detected classes include quinolones, sulfonamides, and tetracyclines [25,26]. Livestock farms, wastewater treatment plants, and hospitals are major point sources releasing antibiotics into the environment. Multiple antibiotics and ARGs are routinely detected in WWTP effluents and receiving waters, and hydrological transport facilitates their widespread dispersion in downstream aquatic environments [27–29]. The widespread occurrence of antibiotics across environmental matrices underpins their role in shaping environmental AMR.

Existing studies have primarily used statistical approaches, including meta-analysis and correlation analysis, to examine associations between environmental

antibiotic residues and ARB, ARGs, or MGEs. These investigations have mainly been conducted in China, the United States, and several European countries, covering diverse environmental compartments such as soil, surface water, groundwater, and coastal waters, as well as extreme environments, including polar regions. The most commonly investigated antibiotics are sulfonamides, tetracyclines, quinolones, and macrolides, which are among the most heavily used classes in both clinical and livestock farming settings. Overall, current evidence shows that antibiotic residues in various media are significantly and positively correlated with the formation, development, and spread of bacterial AMR (Table 2).

For instance, the meta-analysis by Voigt et al. [30] quantified the relationship between environmental antibiotic residues and ARB concentrations. They found that odds ratios (ORs) generally ranged from 3.0 to 5.0, suggesting that residues can reshape microbial community structure and promote ARB dominance. Numerous correlation analyses also report positive associations between antibiotic concentrations and ARG abundances, with correlation coefficients often ranging from 0.6 to 0.9. This further supports antibiotics as drivers of resistance evolution. In typical environments (soil, surface water, WWTPs), antibiotic exposure directly enriches ARB via selective pressure and accelerates horizontal gene transfer, as supported by increased co-occurrence or positive correlations between ARGs and MGEs.

Beyond statistical analyses, controlled experiments have provided further evidence for the causal role of

antibiotics in bacterial resistance evolution. For example, studies in mouse models have demonstrated that long-term antibiotic use enhances gut colonization by plasmid-

carrying resistant bacteria and promotes plasmid transfer to commensals, accelerating AMR spread [31].

Table 2. Reported cases of antibiotic effects on bacterial antibiotic resistance in environmental matrices.

Environmental Matrix	Scenario	Findings	References
Soil	Manure, composted manure, and manure-amended soils from three large commercial swine farms in China (Beijing, Jiaying, and Putian)	• The abundance of ARGs was positively correlated with antibiotic concentrations. In soils with high residual concentrations of tetracyclines, the top 63 ARGs were enriched by 192-fold (median) to 28,000-fold (maximum) compared with their respective antibiotic-free manure or soil controls. • ARG abundance was highly correlated with transposase abundance ($r^2 = 0.97$); transposase was enriched approximately 90,000-fold in manure and 1000-fold in soil.	[32]
Soil	Agricultural soils in Northern Italy, amended with dairy manure	• ARG abundance was positively correlated with antibiotic concentrations. Flumequine residues showed significant positive correlations with the abundance of <i>oqx4</i> ($r = 0.2836$) and <i>qnrS</i> ($r = 0.2715$).	[33]
Soil	Agricultural soils from a dairy farm in Idaho, USA, that received manure applications for four consecutive years	• ARG abundance was significantly correlated with florfenicol exposure; the manure application rate (reflecting high antibiotic concentration) showed a positive dose-effect relationship with soil ARG abundance. Under the high-manure treatment (52.0 Mg ha⁻¹), the abundances of <i>sul1</i>, <i>tet(W)</i>, and other genes were significantly higher than those under low-manure and control treatments ($p < 0.05$), with the highest absolute ARG abundance observed in the surface soil layer (0–15 cm).	[34]
Surface water	A carp farm in Guangdong, China, where florfenicol was used for disease control	• ARG abundance was significantly correlated with florfenicol exposure: on day 3 after administration, ARG abundance in carp intestines reached four times that of the control group; on day 10, it peaked at >9-fold that of the control. After the withdrawal period, ARGs remained significantly elevated above background levels. • Florfenicol treatment significantly increased the co-occurrence frequency of ARGs and MGEs; MGEs such as composite transposons carrying the <i>flor</i> gene were detected in water from long-term treated ponds.	[35]
Wastewater	Two municipal wastewater treatment plants in northern China (mainly treating domestic and industrial wastewater)	• Antibiotic residues in effluent were significantly positively correlated with the relative abundance of corresponding ARGs; for example, chlortetracycline with <i>tetX</i>, oxytetracycline with <i>tetB</i>, and etimicin with <i>ermC</i> all showed significant correlations ($r = 0.992–0.998$, $p < 0.05$).	[36]
Wastewater	Hospital wastewater, municipal wastewater treatment plants, and the receiving Ter River in the Girona region, Spain	• Antibiotic concentrations were significantly positively correlated with corresponding ARGs; for instance, ciprofloxacin with <i>qnrS</i>, ofloxacin with <i>qnrS</i>, cefazolin with <i>blaTEM</i>, clarithromycin with <i>ermB</i>, and sulfamethoxazole with <i>sul1</i> all showed significant correlations ($r = 0.81–0.89$, $p = 0.001$).	[29]
Wastewater	Various types of wastewater and influent/effluent of wastewater treatment plants from urban and rural catchments in Germany	• Antibiotic residues showed significant positive correlations with specific resistant bacteria; for example, ciprofloxacin with third-generation cephalosporin-resistant (3GCR) <i>Pseudomonas aeruginosa</i> (OR = 2.75, $p = 0.034$) and with ESBL-producing KEC (<i>Klebsiella-Enterobacter-Citrobacter</i>) group (OR = 4.29, $p = 0.003$); meropenem with 3GCR <i>P. aeruginosa</i> (OR = 5.00, $p = 0.000$); and ceftazidime with 3GCR <i>P. aeruginosa</i> (OR = 3.20, $p = 0.002$).	[30]
Seawater	Coastal waters and sediments of Bohai Bay, China	• ARGs were significantly positively correlated with concentrations of multiple antibiotics (e.g., sulfonamides and tetracyclines). Estuaries and aquaculture areas were identified as hotspots for both ARGs and antibiotics. In water samples, <i>sul2</i> showed a strong correlation with SMZ ($r = 0.94$); in sediments, <i>sul1</i> correlated with LOM ($r = 0.89$).	[37]

Table 2. Cont.

Environmental Matrix	Scenario	Findings	References
Seawater	13 major mariculture farms along the southeastern coast of China	Significant positive correlations were found between antibiotics and corresponding ARGs. In the water phase, <i>sul3</i> abundance was significantly correlated with the total concentration of sulfonamides. In sediments, <i>sul2</i> abundance was significantly correlated with sulfadiazine concentration ($r = 0.815$), and <i>tetM</i> abundance with oxytetracycline concentration ($r = 0.923$).	[38]
Seawater	Seawater around multiple research stations on King George Island, Antarctica	Bacterial resistance was correlated with the classes of antibiotics detected in samples. For example, 21.7% of isolates were resistant to trimethoprim, which was frequently detected; 4.3% of isolates were resistant to nalidixic acid, corresponding to the frequent detection of ciprofloxacin and norfloxacin.	[39]
Groundwater	Groundwater from multiple regions globally (affected by point-source pollution from pig farming, landfills, aquaculture, etc.)	Tetracycline concentrations in groundwater were significantly positively correlated with corresponding ARGs. In a US site, tetracycline and related <i>tet</i> genes were co-detected in groundwater contaminated by pig farm facilities. In China, Romania, and other locations, tetracycline and related <i>tetG</i>, <i>tetQ</i>, and <i>tetX</i> were co-detected in groundwater influenced by pig farms. Sulfonamide antibiotics and related <i>sul1</i> and <i>sul2</i> were co-detected in groundwater near landfills and wastewater treatment plants.	[23]
Groundwater	Groundwater under wastewater-irrigated farmland in Braunschweig, Germany	<i>sul1</i> abundance was significantly positively correlated with the total concentration of sulfonamides in groundwater ($R = 0.56$, $p = 0.045$). Sulfamethoxazole concentration increased with irrigation time and remained high after irrigation ceased. Relative abundances of <i>sul1</i> and <i>int1</i> continued to rise during the irrigation period.	[40]
In Vivo	Mouse gut model (<i>in vitro</i> evolution experiment + <i>in vivo</i> colonization experiment)	Under long-term antibiotic exposure, evolved <i>E. coli</i> strains carrying the multidrug-resistant plasmid <i>RP4</i> showed enhanced colonization ability in the mouse gut. The plasmid was more readily transferred to the endogenous gut microbiota.	[31]

3.2. EDCs

EDCs are discharged into the environment through multiple pathways, including domestic sewage, industrial wastewater, hospital wastewater, aquaculture wastewater, livestock breeding waste, and landfill leachate [41,42]. Because of their environmental recalcitrance [43], EDCs can persist in environmental matrices for extended periods and eventually enter aquatic systems. In WWTP effluents, EDC concentrations typically range from sub-ng/L to µg/L levels, with nonylphenol (NP) and BPA frequently detected as major EDCs [44]. Six typical EDCs (E1, E2, E3, EE2, BPA, and NP) have been quantified in surface water across China, Japan, France, the United States, and other nations, with concentrations falling in the ng/L range [41]. Compared with surface water, groundwater generally contains lower EDC concentrations, particularly for steroid hormones. Spatially, elevated EDC pollution often overlaps with regions of high population density and intensive economic activity [42].

Table 3 summarizes current evidence on the effects of EDCs on AMR in real environments. Available studies

show significant associations between EDCs and ARG/MGE enrichment and dissemination in aquatic environments. Most relevant studies have been conducted in Asian countries such as China and India, as well as in Spain, the United States, and other regions, with particular attention to TCS, triclocarban (TCC), BPA, bisphenol AF (BPAF), and dimethyl phthalate (DMP). Overall, EDCs show consistent positive correlations with the abundances of ARGs and MGEs. For instance, exposure to high levels of TCC can increase the abundances of multidrug efflux pump genes, such as *mexB* and *mexF1*, by 1–2 orders of magnitude, while integron genes, including *int1* and *int13*, can increase by 3.5–5.1-fold. Co-exposure to DMP and antibiotics has also been shown to increase the abundance of *sul1* by more than threefold. Furthermore, evidence from pure cultures, wastewater consortia, and animal models shows that EDCs at environmentally relevant concentrations enhance plasmid conjugative transfer frequencies by 2.1–6.2-fold. This effect has been observed for HGT both within and between genera, suggesting that EDCs may be important but often overlooked drivers of AMR spread in aquatic environments.

Table 3. Evidence for EDC-associated bacterial antimicrobial resistance in various environmental settings.

Environmental Matrix	Scenario	Findings	References
Water	Urban wastewater treatment plants, water sources, and drinking water treatment plant systems in Bhopal, India	• EDC concentrations were significantly positively correlated with the abundances of various MGEs and ARGs ($p \leq 0.05$), e.g., DMP with <i>tmaA-02</i>, <i>tmaA-07</i>, <i>sul1</i>, <i>intI1</i>, and <i>clin-intI1</i>; DiNOP with <i>tmaA-05</i>; DEP with <i>tmaA-02</i> and <i>sul1</i>; DBP with <i>blaTEM</i>. ARGs such as <i>blaTEM</i>, <i>blaCTX-M-32</i>, and <i>mecA</i>, as well as MGEs including transposase genes (<i>tnpA-04</i>, <i>tnpA-05</i>) and integron genes (<i>intI1</i>, <i>clin-intI1</i>), were detected in all water samples.	[45]
In Vivo	Mouse <i>in vitro</i> and <i>in vivo</i> experimental models (using <i>RP4-7</i> plasmid, BPAF)	• BPAF significantly increased conjugation frequency: <i>in vivo</i>, administration of 50 mg/kg BPAF to mice increased <i>RP4-7</i> plasmid conjugative transfer frequency in the gut by 2.1-fold at 24 h, with further enhancement over time. BPAF upregulated the expression of conjugation-related genes (e.g., <i>traI</i>, <i>traD</i>, <i>trbC</i>, etc.).	[46]
Laboratory microbial community	Laboratory model system (<i>E. coli</i> and <i>Pseudomonas</i> , TCS)	• TCS significantly increased conjugation frequency: <i>RP4</i> at environmentally relevant concentrations (0.02–20 µg/L), it significantly promoted plasmid (carrying multidrug resistance genes) conjugative transfer. At 2 µg/L TCS, intragenetic transfer frequency increased 6.2-fold, and intergeneric transfer increased 2.3-fold.	[47]
Wastewater	Activated sludge microbial community (wastewater treatment system, TCS)	• TCS significantly increased conjugation frequency: at environmentally relevant concentrations (0.01–1 µg/L), TCS significantly promoted <i>RP4</i> plasmid conjugative transfer, with the maximum increase of 2.5-fold at 0.1 µg/L.	[48]
Wastewater	Various wastewater treatment systems	• Low environmental concentrations of TCS significantly enriched ARGs and MGEs: in anaerobic digesters, 100–2500 mg/kg TCS increased <i>Bacteroides</i> abundance and enriched <i>traG</i>, <i>traK</i>, and other genes; in aerobic granular sludge systems, 6.0 mg/L TCS enriched <i>intI1</i>, <i>sul1</i>, <i>mexB</i>, and other ARGs.	[49]
Wastewater	Laboratory-scale anaerobic digesters (TCC concentration gradient: 30–850 mg/kg)	• High concentrations of TCC enriched ARGs: at 680 mg/kg TCC, <i>tet(L)</i> abundance increased by three orders of magnitude compared with the control; at 30 mg/kg TCC, <i>mexB</i> abundance was significantly higher than the control ($p < 0.05$).	[50]
Wastewater	Nitrifying granular sludge system (TCC concentration gradient: 0.20–19.70 mg/L)	• TCC enriched ARGs and MGEs: the <i>mexF1</i> gene increased by up to 99.99-fold under TCC treatment; integron genes <i>intI1</i> and <i>intI3</i> increased by 3.49-fold and 5.08-fold, respectively. • TCC-degrading bacteria such as <i>Pseudomonas</i> spp. were enriched in the system and showed significant positive correlations with ARGs (e.g., <i>sul1</i>, <i>tetB</i>) and MGEs (e.g., <i>intI1</i>, <i>Tn916/1545</i>).	[51]
Wastewater	Sludge anaerobic digestion system (simulated wastewater treatment environment, DMP)	• Co-exposure of DMP (10.0 mg/L) with antibiotics significantly promoted the proliferation of typical ARGs. Compared with sulfamethazine alone, co-exposure with DMP increased <i>sul1</i> abundance by >3-fold (from 3.07×10^{-2} to 1.13×10^{-1} copies/16S rDNA). • DMP (10.0 mg/L) elevated the abundance of mobile genetic elements (MGEs); it significantly increased the abundances of dominant integrons (e.g., <i>orf442</i>, <i>orf403</i>), insertion sequences (e.g., IS5 family), and plasmids (e.g., NZ_CP019912.1).	[52]
Wastewater	Laboratory wastewater microbial conjugation model (using <i>RP4</i> plasmid, DMP)	• DMP significantly increased conjugation frequency: at environmentally relevant concentrations (2–50 µg/L), it significantly promoted <i>RP4</i> plasmid conjugative transfer; intergeneric conjugation frequency increased by up to 4.96-fold (at 10 µg/L DMP), and intragenetic conjugation increased by up to 3.82-fold (at 20 µg/L DMP). • DMP exposure led to a significant increase in cell membrane permeability (NPN fluorescence intensity increased by up to 59%) and upregulated the expression of outer membrane protein genes (<i>ompC</i>, <i>ompF</i>) and efflux pump genes (<i>acrA</i>, <i>acrB</i>) (up to 4.2-fold).	[53]

3.3. POPs

POPs are characterized by environmental persistence, bioaccumulation potential, and long-range transport capacity, leading to their widespread occurrence across diverse environmental matrices. They comprise a broad group of contaminants, including polycyclic aromatic hydrocarbons (PAHs), organochlorine pesticides (OCPs), polychlorinated biphenyls (PCBs), dioxins, and related compounds. Although only some PFASs are formally classified as persistent organic pollutants (POPs), many others exhibit similar environmental persistence and behavior. For organizational purposes in this review, PFASs are discussed together with conventional POPs. POPs enter aquatic environments mainly through industrial and domestic wastewater discharge, agricultural runoff, and atmospheric deposition [54]. They are particularly prevalent in surface waters. For example, POPs have been routinely detected in 19 rivers across China, the United States, Germany, and other countries [55,56]. The concentrations of 6:2 Cl-PFESA in Chinese lakes and rivers range from 1.1 to 7.8 ng/L, while the concentration of HFPO-DA at one sampling site in the Rhine River reached 86.1 ng/L. In soils, historical pesticide use, industrial contamination, and combustion emissions have resulted in widespread POP residues, including PAHs, OCPs, and PCBs. For instance, PAH concentrations in urban soils across China range from 0.092 to 4.733 µg/g [57], while legacy DDT residues in agricultural soils in Azerbaijan range from 0.01 µg/kg to 21,885.9 mg/kg [58].

Table 4 summarizes current evidence regarding the effects of POPs on AMR in environmental and

experimental settings. Overall, residual POPs are widely associated with the enrichment and dissemination of ARGs and MGEs. Most relevant studies have been conducted in Asia, Europe, and the Americas, focusing mainly on PAHs, PFASs, OCPs, organophosphorus pesticides, PCBs, and TCDD. Field studies show that in POP-contaminated soils and waters, POP concentrations positively correlate with ARG abundances, especially for multidrug efflux pump genes. For example, in PAH-contaminated soils, total ARG abundance can increase ~15-fold, and efflux pump genes can be ~14-fold higher in heavily polluted versus less polluted sites. In PFAS-impacted rivers, PFOS and PFBS have been significantly correlated with high-risk ARGs, such as *bacA*, *dfrA1*, and *aadA* ($p < 0.05$).

Beyond statistical associations, controlled experimental studies have provided further evidence for the causal effects of POP exposure on antibiotic resistance. For example, in mouse intestinal models, TCDD exposure significantly enriches 14 ARGs (≥ 2 -fold). In addition, environmentally relevant concentrations of several POPs, including PAHs, PFASs, and certain pesticides, have been shown to increase the conjugative transfer frequencies of different plasmids by approximately 3-fold. POP exposure can also reshape microbial community composition and selectively enrich bacterial taxa with both pollutant-degrading capacity and multidrug resistance. These findings suggest that POPs may promote AMR not only through co-selection and community restructuring but also by enhancing horizontal gene transfer and stabilizing resistance determinants in environmental microbial communities.

Table 4. Reported evidence of POP-associated bacterial antimicrobial resistance across environmental and experimental settings.

Environmental Matrix	Scenario	Findings	References
Soil	PAH-contaminated soil from a petrochemical plant in Guangzhou, China (sampled from three different polluted areas: front garden P1, tank area P2, and wastewater pool P3)	• PAH pollution levels were significantly positively correlated with ARG abundance: total PAH concentration at P3 reached 529 µg/g, >50-fold higher than at P1 and P2, and total ARG abundance at P3 was approximately 15-fold higher than at P1 and P2 ($p < 0.05$). In highly PAH-contaminated soils, efflux pump-encoding genes (e.g., <i>acrA</i> , <i>acrB</i> , <i>amrB</i> , <i>tolC</i>) were particularly enriched, showing ~14-fold higher abundance than in low-pollution soils.	[59]
Soil	Soils from five bayberry orchards in China (affected by antibiotic and pesticide residues)	• High residues of pesticides (e.g., imidacloprid, pyraclostrobin) in orchard soils significantly increased ARG and MGE abundances. ARG abundances in fruit fly guts and soils were significantly higher than in bayberry fruits; relative ARG abundance in fruit fly guts was 2.1-fold that in mature fruits. Structural equation modeling indicated that pesticide residues indirectly affected ARG distribution via MGEs ($\lambda = 0.63$, $p < 0.001$), and fungal communities were significantly correlated with ARGs in fruit fly guts.	[60]
Soil	PCB-contaminated soils (e.g., electronic waste recycling sites)	• PCB contamination significantly altered soil microbial community structure: PCBs led to the dominance of genera such as <i>Acinetobacter</i> , <i>Pseudomonas</i> , and <i>Alcanivorax</i> , which include multiple known antibiotic-resistant strains.	[61]

Table 4. Cont.

Environmental Matrix	Scenario	Findings	References
Surface water	Sediments of Lake Bizerte, Tunisia (co-contaminated with PAHs, heavy metals, and antibiotics)	PAH-contaminated environments enriched bacterial communities possessing both PAH-degrading capacity and multiple antibiotic/heavy metal resistance. Among PAH-degrading isolates from sediments, 90% of strains were resistant to at least 2 antibiotics and 2 heavy metals; 89% were resistant to ≥ 5 antibiotics, and 8% were resistant to all 8 tested antibiotics.	[62]
Surface water	Eight lakes and wetlands in Iran (contaminated with organophosphorus pesticides and heavy metals)	- Tetracycline resistance genes <i>tetA</i> and <i>tetB</i> were significantly positively correlated with parathion concentration ($p = 0.0289$). - Multiple bacterial taxa (e.g., Acidobacteria, Mb-NB09, etc.) showed significant correlations with organophosphorus pesticides such as diazinon, methyl parathion, and malathion ($r = 0.7133$–0.8671).	[63]
Surface water	Receiving rivers (Dongzhulong River and Xiaojing River) of the largest fluoropolymer production facility in China	PFOS and PFBS were significantly positively correlated with high-risk ARGs such as <i>bacA</i>, <i>dfrA1</i>, <i>aac(6')-I</i>, and <i>aadA</i> ($p < 0.05$). Short-chain PFAAs (e.g., PFHxA, PFPeA) exhibited effects on the ARG profile similar to those of long-chain PFOA/PFOS.	[64]
Seawater	Laboratory exposure experiments with microbial communities from coastal waters of Dalian, China	- PAHs (naphthalene and phenanthrene) significantly enriched ARGs: after 24-day exposure to 10 mg/L phenanthrene, the relative abundances of <i>int11</i>, <i>sul1</i>, and <i>aadA2</i> increased by 74-, 22-, and 200-fold, respectively, compared with the control. Exposure to 100 mg/L naphthalene also increased them by 26-, 10-, and 56-fold, respectively. - PAHs significantly increased conjugative transfer frequency: in conjugation experiments, 100 mg/L naphthalene and 10 mg/L phenanthrene increased the conjugative transfer frequency of ARGs by at least 3-fold.	[65]
Wastewater	Laboratory-simulated wastewater/aquatic systems	- PFOA and PFOS at 0.1–10 $\mu\text{g/L}$ significantly elevated the natural transfer frequency of the kanamycin resistance plasmid (<i>KanR</i>): 10 $\mu\text{g/L}$ PFOA increased it by 2.54-fold, and 1 $\mu\text{g/L}$ PFOS by 3.26-fold. - PFOA and PFOS induced upregulation of ARG expression: fluorescent reporter gene expression increased by 1.33-fold and 1.37-fold, respectively, and the transcriptional level of the <i>KanR</i> gene also increased correspondingly. - PFAS also significantly enhanced the <i>in vivo</i> stability of ARGs in transformants: under 100 $\mu\text{g/L}$ PFOA exposure, the plasmid loss rate decreased from 68.5% (control) to 6%; under PFOS exposure, it decreased to 38.7%.	[66]
Wastewater	A typical drinking water treatment plant in eastern China exposed to PFASs (from source water to finished tap water)	PFASs were significantly positively correlated with specific ARGs ($p < 0.05$). They were closely associated with host bacterial genera such as <i>Aquabacterium</i>, <i>Methylobacterium</i>, and <i>Curvibacter</i>. Addition of 40 ng/L PFOA or PFOS to tap water significantly promoted bacterial growth (total bacterial 16S rRNA increased by ~ 8- to 10-fold) and elevated the absolute abundances of ARGs (e.g., <i>mexA</i>, <i>int1</i>, <i>sul1</i>, <i>catA1</i>).	[67]
Laboratory	Laboratory conjugation transfer model and soil microbial community model	The two pesticides cyprodinil and Kre significantly increased conjugative transfer frequency: at environmentally relevant concentrations, cyprodinil (0.1 $\mu\text{g/mL}$) and Kre promoted <i>RP4-7</i> plasmid conjugative transfer, increasing frequencies by 2.97- and 2.68-fold, respectively, compared with the control. Both pesticides also facilitated cross-species transfer of multidrug-resistant plasmids carrying <i>tet(X4)</i>, <i>blaNDM-5</i>, and <i>mcr-1</i> in clinical isolates. In the soil microbial model, cyprodinil and Kre increased conjugative transfer frequency by 1.28- and 1.23-fold, respectively.	[68]

Table 4. Cont.

Environmental Matrix	Scenario	Findings	References
<i>In Vivo</i>	C57BL/6 mouse gut model (exposed to TCDD)	• TCDD significantly enriched ARGs: exposure led to significant enrichment (≥ 2-fold) of 14 ARGs in the mouse gut, of which 13 were common in the family Enterobacteriaceae. Enriched ARGs included β-lactamase genes (<i>bla</i>CMY2, <i>ampC</i>) and multidrug resistance efflux pump genes (<i>mdtE</i>, <i>mdtF</i>, <i>acrA</i>, etc.). TCDD at doses ≥ 0.3 $\mu\text{g/kg}$ caused significant ARG enrichment, and the degree of enrichment was correlated with immunosuppression (e.g., downregulation of TLR5 expression).	[69]

3.4. Microplastics

Microplastics are characterized by their small size and resistance to degradation, which enables their widespread dispersion across diverse environmental matrices via multiple transport pathways. In soils, major sources of microplastics include traffic-related wear, residual agricultural mulch films, sewage sludge application to farmland, and atmospheric deposition [70]. Their spatial distribution correlates strongly with the intensity of anthropogenic activity, with soils from transportation areas, croplands, and urban residential districts generally containing much higher microplastic abundances than forests and other relatively pristine ecosystems [71,72]. Freshwater systems (surface water, groundwater, sediments) are also widely contaminated. Global river surveys confirm the ubiquitous presence of microplastics, with high levels in East Asia [73]. In marine environments, microplastic pollution is largely driven by land-based inputs. Estuaries, coastal zones, and nearshore waters receiving substantial terrestrial plastic inputs often accumulate high levels of microplastics [74–77].

The studies summarized in Table 5 indicate that microplastics, as emerging physical carriers in the environment, play an important role in enriching pathogenic microorganisms and disseminating AMR. Existing studies are mainly concentrated in countries such as China, Germany, and the United States, and commonly focus on typical microplastic polymers, including polyethylene (PE), polypropylene (PP), polystyrene (PS), polyvinyl chloride (PVC), and polyamide (PA). First, microplastic surfaces can harbor microbial communities distinct from those in the surrounding environment, forming a specific ecological niche known as the “plastisphere”. This plastisphere can significantly enrich potentially pathogenic bacteria. For example, Zhu et al. [78] found that in soil, the proportion of potential pathogens on microplastics was ~ 12.4 -fold higher than in surrounding soils. This suggests that microplastics offer favorable surfaces for pathogen attachment and growth. Such enrichment provides a reservoir of hosts for AMR emergence and spread.

Microplastics can further promote the enrichment and spread of intracellular antibiotic resistance genes

(iARGs). On the one hand, the high cell density and strong microbial interactions within microplastic-associated biofilms enhance the selection and enrichment of ARB. On the other hand, the unique microenvironment on microplastic surfaces, including nutrient enrichment and biofilm formation, favors the persistent colonization and competitive maintenance of resistant bacteria. Previous studies have shown that, in marine environments, the abundance of iARGs on microplastics can be 6–55 times higher than that in surrounding waters [79]. In urban freshwater rivers, the relative abundance of *int12* on environmental microplastics was approximately 19-fold higher than in surrounding water [80]. These findings highlight the important role of microplastics in amplifying resistance genes and enriching their bacterial hosts.

Furthermore, intracellular ARGs can be released as extracellular antibiotic resistance genes (eARGs) through microbial death, cell lysis, or active secretion, and microplastics also show a strong capacity to enrich these extracellular genetic elements. In marine environments, the enrichment factors of eARGs on microplastics can reach 5–140 times those in surrounding waters [79]. This indicates that microplastics may serve not only as a sink for ARGs but also as an important environmental reservoir of eARGs, thereby increasing the likelihood of their uptake by other microorganisms and subsequent transformation.

Unlike chemical contaminants, the capacity of microplastics to enrich ARGs is strongly influenced by their intrinsic physicochemical properties and environmental conditions. For example, under specific environmental conditions (e.g., agricultural-soil microcosms and freshwater plastisphere biofilm systems), biodegradable microplastics can induce higher abundance of ARGs and form tighter ARG-MGE associations compared with non-biodegradable microplastics [81,82]. Across aquatic environments, microplastics generally exhibit higher ARG enrichment efficiency in freshwater systems than in seawater [80]. Urbanization also drives ARG accumulation on microplastics, with ARG abundance increasing by approximately two orders of magnitude along river gradients from rural to urban reaches [83].

Table 5. Reported evidence of microplastic-associated bacterial antimicrobial resistance across environmental settings.

Environmental Matrix	Scenario	Findings	References
Soil	Agricultural soils from multiple regions in China (Yunnan red soil, Heilongjiang black soil, Jiangsu yellow-brown soil) with four types of microplastics (PE, PA, PS, PVC) embedded	• The ratio of potential pathogens to total bacteria in the plastisphere was 12.4-fold higher than in the surrounding soil ($p < 0.001$). • ARG and MGE abundances in the plastisphere of PE, PA, and PS were generally higher than in soil, but no significant enrichment was observed for PVC.	[78]
Soil	Long-term fertilized agricultural soils exposed to biodegradable microplastics (PLA, PBAT) and conventional microplastics (PE, PVC)	• Biodegradable microplastics significantly increased ARG abundances: PLA increased relative ARG abundance by 21.5–62.2%, and PBAT by 38.7–78.0%. Risk ARGs (e.g., <i>aadA5-02</i>, <i>sul1</i>, <i>tolC</i>, <i>tetL</i>) increased by 51–85% under PBAT treatment, higher than conventional microplastics (20–37%). • Correlations between ARGs and MGEs were significantly enhanced under biodegradable microplastic exposure: under PBAT treatment, the correlation between risk ARGs and MGEs reached $R^2 = 0.97$ ($p < 0.001$).	[82]
Soil	Laboratory study on the effects of plastic diversity (1, 3, and 6 types) on grassland soil microbiome and resistome	• Microplastic diversity was significantly positively correlated with ARGs: as plastic diversity increased, total ARG abundance in soil significantly increased (D6 vs. D1: $p = 0.00012$), by approximately 2.4-fold. High-risk ARGs (e.g., <i>APH(6)-Id</i>, <i>tet(M)</i>, <i>floR</i>) were also significantly enriched.	[84]
Surface water	Comparison of urban river water samples and microplastic surface microbiota in Jiaxing City, Zhejiang Province, China	• Microplastics harbored distinct bacterial communities: compared with water samples, microplastic-associated bacterial communities exhibited significantly lower richness (mean OTU: 1230 vs. 1860) and diversity (Shannon index: 1.51–4.78 vs. 4.37–5.15), with markedly different community structures ($R^2 = 0.748$, $p = 0.001$). • Microplastics selectively enriched specific ARGs and MGEs: tetracycline resistance genes (e.g., <i>tetM</i>, <i>tetS</i>, <i>tetW</i>) showed higher relative abundances on microplastics. Relative abundances of <i>int11</i> and <i>int12</i> were both higher on microplastics than in water; <i>int12</i> abundance (6.4×10^{-3} copies/16S rRNA) was significantly higher ($p < 0.01$) than in water.	[80]
Surface water	Study along the entire Beilun River basin in Guangxi, China, deployed across a coastal urbanization gradient, with five types of microplastics (PE, PP, PS, PF, and PFP)	• Microplastics enriched ARGs: absolute ARG abundances on microplastics ranged from 4.11×10^3 to 5.60×10^6 copies/g, which were significantly higher than those in water (ca. 10^5 copies/L). A total of 314 ARG subtypes were detected on microplastic samples, covering β-lactam, aminoglycoside, multidrug, tetracycline, and other resistance classes, with <i>tetA(P)</i>, <i>tetB(P)</i>, <i>sul1</i>, and <i>qacH</i> being the dominant genes.	[83]
Surface water, seawater	PE microplastics in three salinity gradients: river, estuary, and seawater	• PE microplastics selectively enriched antibiotics and ARGs from water; the enrichment capacity decreased with increasing salinity (e.g., sulfadiazine adsorption amounted to 37.55 $\mu\text{g/g}$ in river water, compared with 17.17 $\mu\text{g/g}$ in estuarine water and 12.13 $\mu\text{g/g}$ in seawater). In the river water environment, PE microplastics harbored the highest ARG abundances, including <i>sul1</i>, <i>tetA</i>, <i>tetC</i>, <i>tetX</i>, <i>ermE</i>, and <i>ermF</i>. • Abundances of ARGs (e.g., <i>sul1</i>, <i>tetX</i>, <i>ermE</i>) were significantly correlated with class 1 integron gene <i>int11</i>. • Bacterial community structure on PE microplastics differed markedly from that in the surrounding water; PE microplastics enriched <i>Acidobacteria</i>, <i>Saccharibacteria</i>, and other taxa.	[85]
Seawater	Coastal waters near the estuaries of major rivers in eastern China (Jiangsu Province)	• Microplastics significantly enriched ARGs: enrichment folds ranged from 6- to 55-fold for iARGs and 5- to 140-fold for eARGs, with the highest enrichment (up to 140-fold) observed for <i>sul1</i>. • Bacterial abundance on microplastic surfaces was 10-fold higher than that in the surrounding seawater.	[79]

4. Mechanisms of Emerging Contaminant-Driven Antimicrobial Resistance

Emerging contaminants promote AMR through diverse but interconnected mechanisms (Figure 2). Antibiotics primarily drive resistance evolution through ROS–SOS response activation, enhancement of HGT, and selective enrichment of resistant bacteria. Beyond antibiotics, non-antibiotic emerging contaminants,

including EDCs and POPs, can also stimulate AMR development by inducing ROS–SOS responses in cells and facilitating HGT. In contrast, microplastics mainly contribute to AMR dissemination by acting as physical vectors that enrich resistance determinants and provide favorable niches for resistant microorganisms. These distinct mechanisms ultimately converge to promote the enrichment and dissemination of ARGs, ARB, and MGEs across environmental systems.

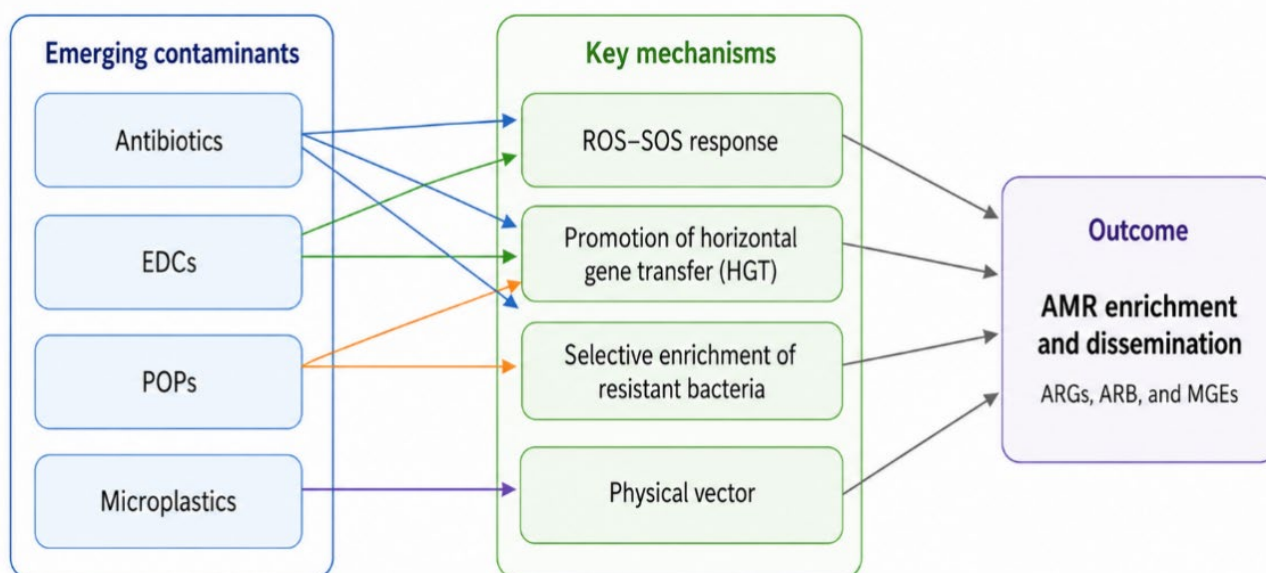


Figure 2. Coupling framework of four major mechanisms for bacterial antimicrobial resistance evolution driven by emerging contaminants.

4.1. ROS–SOS-Mediated Adaptive Evolution

Many emerging contaminants are intrinsically cytotoxic and can induce reactive oxygen species (ROS) overproduction, direct or indirect DNA damage, and subsequent activation of the bacterial SOS stress response. This process generally follows a canonical cascade: ROS generation/direct DNA injury → SOS response activation → elevated mutation frequency and enhanced genetic recombination (Figure 3).

On the one hand, emerging contaminants like TCS and POPs have been reported to trigger ROS-related stress responses [86,87]. Excessive ROS can oxidize DNA molecules and generate oxidative lesions, including 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxo-dG), which may lead to G:C → T:A transversion mutations during DNA replication. On the other hand, genotoxic pollutants such as PAHs can intercalate into the DNA double helix, form DNA adducts, or induce oxidative DNA damage [59,65]. In addition, antibiotics themselves (e.g., fluoroquinolones, trimethoprim, β -lactams) also cause direct or indirect damage to bacterial DNA [88]. Collectively, these multi-origin forms of DNA damage initiate the *RecA/LexA*-mediated SOS response system in bacteria. The strength of experimental evidence supporting the upstream

triggering pathways varies greatly among emerging contaminants. The ROS–SOS cascade induced by antibiotics is well supported by multiple experimental studies. In contrast, research on non-antibiotic emerging contaminants (EDCs and POPs) mostly relies on correlation analysis or indirect inference, which still requires direct experimental verification across additional compounds and bacterial systems.

Activation of the SOS response drives the evolution of bacterial AMR via two well-supported molecular pathways. First, SOS activation induces error-prone DNA polymerases involved in translesion synthesis. Although this process allows bacteria to bypass DNA lesions and maintain replication, it also substantially increases genome-wide random mutation rates, thereby raising the probability of resistance-conferring mutations, such as those affecting antibiotic target sites. Second, the SOS system enhances genetic recombination and HGT by regulating mobile genetic elements. For example, several antibiotics can induce the SOS response and relieve repression of the integrase gene *intI*, thereby accelerating integron-mediated gene cassette recombination [89,90]. Guerin et al. [88] further showed that, under antibiotic stress, class 1 integron integrase expression increased by approximately 4.5-fold, while chromosomal integrase

expression in *Vibrio cholerae* increased by approximately 37-fold. Correspondingly, gene cassette excision frequencies increased by 141-fold and 340-fold, respectively. These changes collectively facilitate the acquisition, rearrangement, and dissemination of AMR determinants.

In addition, ROS-mediated oxidative stress can activate oxidative stress-responsive transcriptional regulators, such as *SoxR*, leading to the upregulation of defensive resistance determinants, including multidrug efflux pumps. This

response not only enhances bacterial tolerance to antibiotics and environmental contaminants, but may also further promote genomic instability and genetic rearrangement events [91–93]. However, the direct correlation between *SoxR* activation and enhanced bacterial tolerance to environmental pollutants is supported by limited preliminary evidence and requires further causal validation under environmentally relevant conditions.

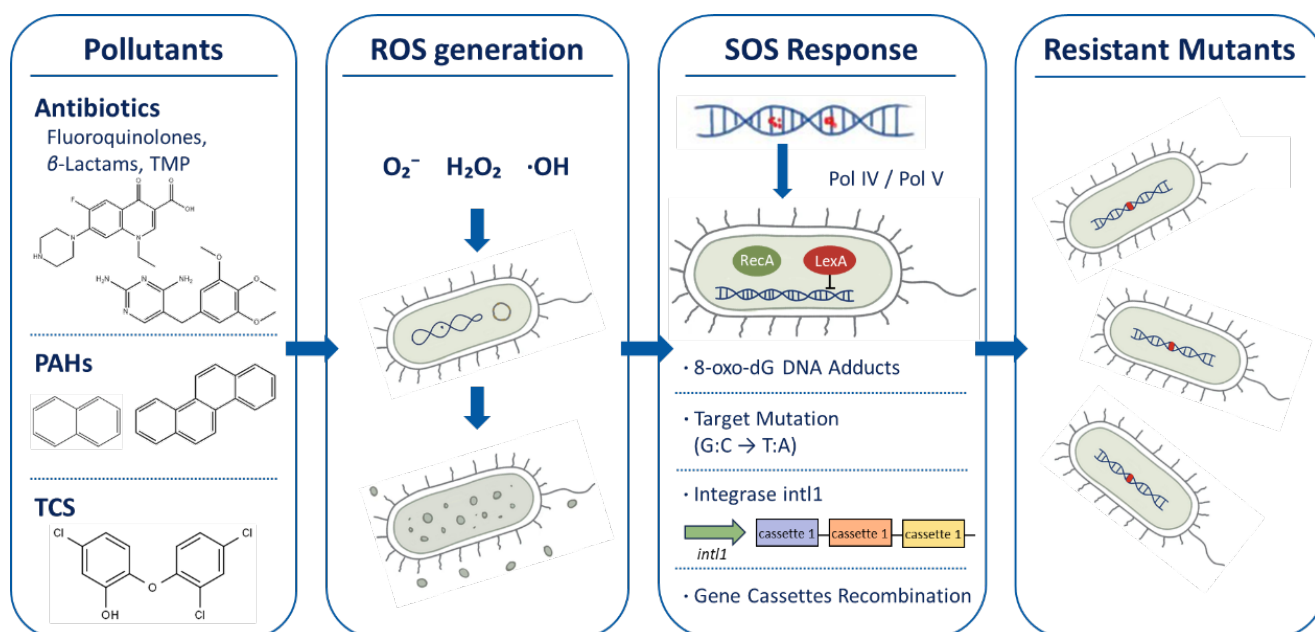


Figure 3. Schematic illustration of ROS-SOS-mediated adaptive evolution of bacterial antimicrobial resistance induced by emerging contaminants.

4.2. Enhanced Horizontal Transfer of ARGs

HGT describes the transfer of genetic determinants between organisms, most notably across distinct taxonomic groups, and represents another core mechanism of AMR dissemination. HGT proceeds via three canonical pathways: conjugation (transfer of plasmids and other mobile elements through sex pili or direct cell-to-cell contact), transformation (uptake of exogenous free DNA from the environment), and transduction (DNA delivery mediated by bacteriophages) [94,95]. All these transfer processes are largely facilitated by MGEs such as plasmids, integrons, and transposons. Current studies on the effects of emerging contaminants on HGT predominantly focus on conjugation and transformation. The driving mechanisms fall into three categories: enrichment of MGEs, transcriptional regulation of transfer-associated genes, and modulation of bacterial physiological status to boost DNA uptake efficiency (Figure 4).

4.2.1. Promoting the Enrichment and Dissemination of MGEs

Emerging contaminants can promote MGE enrichment through co-resistance and co-localization effects. For instance, PAHs have been demonstrated to

elevate the conjugative transfer frequency of class 1 integron-associated ARGs by >3-fold [65]. This effect is attributed to the co-localization of PAH degradation genes (e.g., fatty acid metabolism genes *fadD* and *fadK*) and ARGs within the same integron gene cassette. Under PAH-induced selective pressure, bacteria carrying such integrons are co-selected and enriched, driving widespread non-targeted MGE dissemination. Nevertheless, this “co-localization hypothesis” has not been directly verified by metagenomic analysis or cloning of integron gene cassettes, and it requires further molecular validation. Likewise, TCS exposure significantly boosts the abundance of MGE markers, including *int1*, further amplifying the potential for MGE-driven horizontal gene transfer.

4.2.2. Regulating Transfer-Related Gene Expression to Enhance HGT Activity

Several emerging contaminants can directly facilitate horizontal gene transfer by modulating the expression of transfer-associated genes. For example, exposure to environmentally relevant concentrations of DMP (2–50 $\mu\text{g/L}$) upregulates porin genes (*ompC*, *ompF*) and increases bacterial cell membrane permeability [53].

In mouse intestinal models, BPAF (50 mg/kg) significantly upregulates conjugation machinery genes (e.g., *traI*, *traD*, *trbC*), boosting the conjugative transfer frequency of plasmid *RP4-7* by 2.1-fold [46]. These studies quantified changes in target gene expression by RT-qPCR and simultaneously observed alterations in transfer frequency. Consistent results have been repeatedly

verified across multiple pollutants (DMP, BPAF, TCS, etc.) and various donor-recipient models, indicating a general pattern. Collectively, these findings show that emerging contaminants enhance bacterial gene transfer efficiency by activating conjugation machinery and membrane-channel genes.

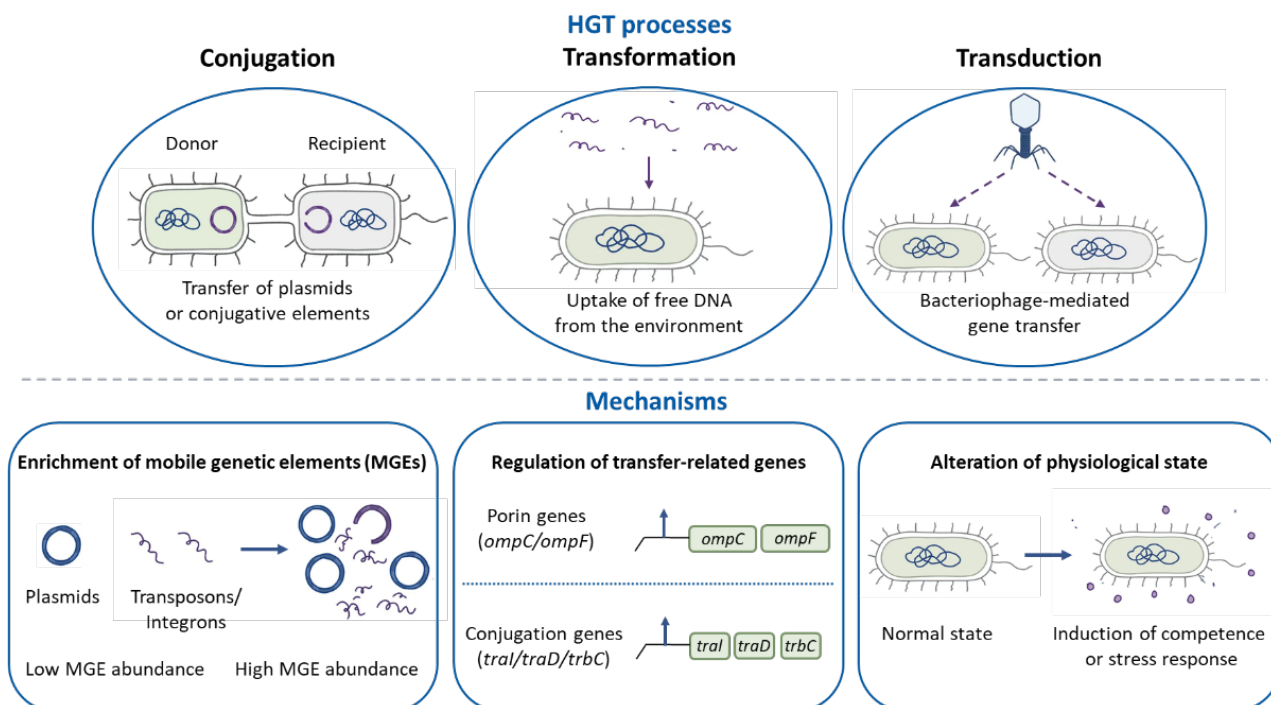


Figure 4. Mechanisms by which emerging contaminants promote HGT of antimicrobial resistance genes.

4.2.3. Altering Bacterial Physiological States to Promote Competence Development and DNA Uptake

Emerging contaminants can also modulate bacterial physiological status by inducing oxidative stress, ultimately enhancing cellular uptake of exogenous DNA. Exposure to pollutants such as microplastics and PAHs provokes intracellular ROS overproduction, which oxidizes unsaturated fatty acids in cell membranes and induces lipid peroxidation [96–98]. The resulting impairment of membrane integrity and fluidity facilitates the entry of exogenous DNA, including plasmids and free environmental ARGs, which would otherwise be less likely to penetrate intact bacterial membranes.

In parallel, oxidative stress can promote extracellular polymeric substance (EPS) secretion. PVC microplastic exposure has been shown to increase bacterial EPS production [99,100], and PAHs (naphthalene, fluorene, etc.) upregulate the synthesis and secretion of EPS protein fractions, which strengthens cell-cell adhesion and elevates conjugative transfer efficiency [101]. Together, these alterations shape a cellular microenvironment that favors horizontal gene transfer. Notably, although the logical chain “pollutant exposure → ROS generation → membrane damage → improved DNA uptake” is supported by multiple experimental studies with antibiotics, evidence

for microplastics and PAHs remains limited and requires further validation across more environmental systems.

4.3. Selective Enrichment of Resistant Bacteria

Emerging contaminants can reshape the competitive dynamics of microbial communities by exerting both direct and indirect selective pressures (Figure 5). These pressures disrupt native ecological equilibria and can ultimately confer a growth advantage on ARB.

4.3.1. Direct Selective Pressure

Some emerging contaminants are intrinsically antibacterial, disrupting bacterial physiology and exerting pressure on susceptible strains. Antibiotics are the classic example, killing or inhibiting bacteria by targeting cell wall synthesis, protein synthesis, or DNA synthesis [102]. This mechanism has been extensively investigated and is well supported by experimental evidence at the molecular, cellular, and community levels under a range of laboratory and controlled conditions, making it one of the most clearly defined selective pressure pathways. In addition to antibiotics, certain EDCs such as TCS also possess antibacterial activity; for example, TCS targets the fatty acid synthase *FabI* and exerts selective pressure against sensitive strains [49]. At

high environmental levels, these contaminants can induce growth arrest or death in susceptible bacteria, freeing ecological niches and nutrient resources for resistant strains that may otherwise be competitively disadvantaged. As a result, resistant bacteria can proliferate and become dominant within microbial communities. Even at subinhibitory concentrations,

antibiotics suppress the growth of susceptible bacteria without killing them, granting resistant strains a competitive edge and driving their enrichment. This selection threshold is known as the minimal selective concentration (MSC), which can be as low as 1/100 of the minimum inhibitory concentration (MIC) [103].

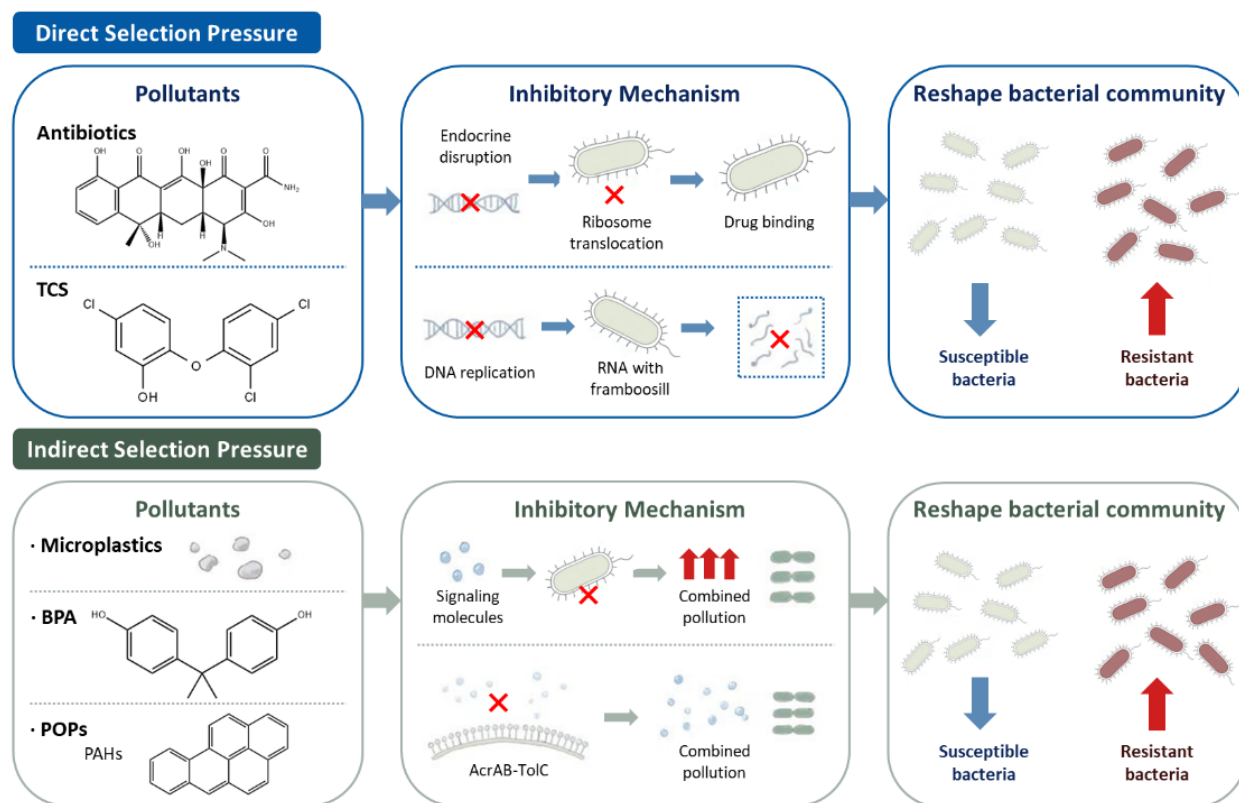


Figure 5. Schematic illustration of emerging pollutant-driven enrichment of resistant bacteria through selective pressure and bacterial community reshaping.

4.3.2. Indirect Selective Pressure

A substantial proportion of emerging contaminants do not directly kill bacteria. Instead, they indirectly alter microbial community structure by changing environmental physicochemical properties, modifying resource availability, or acting as stress signals. These changes can shift the competitive balance of microbial communities and favor populations that are better adapted to the altered conditions.

Some EDCs can act as stress signals to disrupt bacterial quorum sensing or activate stress responses, thereby disrupting cooperative interactions within microbial communities [104]. While such disturbances may not be directly lethal, they can destabilize native microbial homeostasis and favor taxa that tolerate physiological stress, some of which may overlap with antibiotic-resistant populations. The hypothesis that EDCs indirectly enrich resistant bacteria by interfering with quorum sensing is currently supported only by community-level observational data and lacks molecular

functional verification. Microplastics can also modify bacterial habitats by creating a novel ecological niche known as the *plastisphere*, which selectively enriches specific microbial taxa. In addition, microplastics can adsorb co-occurring antibiotics and heavy metals, forming localized combined-pollution hotspots that intensify resistance selection through multiple overlapping stressors. Although microplastic adsorption has been validated in many experiments, it remains difficult to quantitatively separate the independent contribution of adsorption from the overall influence of combined pollution on resistant bacterial enrichment.

Evidence shows that POPs such as PAHs enrich bacterial taxa with specialized detoxification and metabolic capacities, and these PAH-degrading/tolerant strains frequently harbor multiple AMR genes [59]. This co-selection effect may occur because PAHs and aromatic antibiotics (e.g., tetracycline, chloramphenicol) exert similar selective stress on bacteria, which can utilize shared broad-spectrum efflux pump systems such as AcrAB-TolC to detoxify both contaminant classes. As a

result, PAH-driven selective pressure can enrich not only PAH-degrading bacteria but also the AMR determinants they carry [65]. However, direct experimental evidence proving that AcrAB-TolC transporters can transport PAH molecules remains limited; relevant conclusions are mainly indirect deductions based on substrate spectra of homologous efflux proteins. In addition to co-selection, an emerging hypothesis—termed “molecular mimicry”—has been proposed. For instance, spinosad, an insecticide, shares structural features with macrolide antibiotics and has been suggested to induce resistance-associated stress responses in bacteria [105]. Unlike traditional co-selection, this hypothesis suggests that bacteria may actively defend against structurally similar pollutants rather than passively accumulating resistance genes alongside degradative genes. Building on this reasoning, other emerging contaminants beyond the four categories discussed here may exert similar effects through shared mechanisms, but further research is needed to assess the generality and environmental relevance of these pathways.

4.4. Microplastic-Mediated ARG Transport

With a large specific surface area, strong hydrophobicity, and unique surface charge properties, microplastics can efficiently adsorb and concentrate a wide range of environmental contaminants, including antibiotics, extracellular ARGs, and ARB [106–108], thereby generating the unique “plastisphere” habitat [81,109]. This

structure continuously sequesters ARGs and resistant bacteria from the ambient water column, leading to markedly higher ARG abundance and diversity than the surrounding environment and forming localized resistance pollution hotspots [108,110–112]. By providing a stable physical carrier for ARGs, the plastisphere acts as a key vehicle for ARG retention, transport, and dissemination (Figure 6). Systematic studies have used adsorption kinetics and isotherm models to explore the physical adsorption and enrichment of ARGs by microplastics. This enrichment has also been verified in multiple water body types under natural field conditions, with relatively strong supporting evidence.

At the microhabitat level, the high cell density and compact spatial organization of plastisphere biofilms create favorable conditions for bacterial interactions. Specifically, shortened intercellular distances and elevated cell contact frequency promote HGT events, especially conjugation. Mounting evidence indicates that plasmid-mediated gene transfer rates on microplastic-associated biofilms are several orders of magnitude higher than those in the surrounding water column [113]. This observation is supported by experimental data from specific laboratory and field studies, but its universality and quantitative contribution in complex natural environments remain to be confirmed. Thus, ARGs can spread rapidly across bacterial taxa (including pathogens) on microplastics, even without antibiotic pressure, heightening the ecological risk of AMR spread.

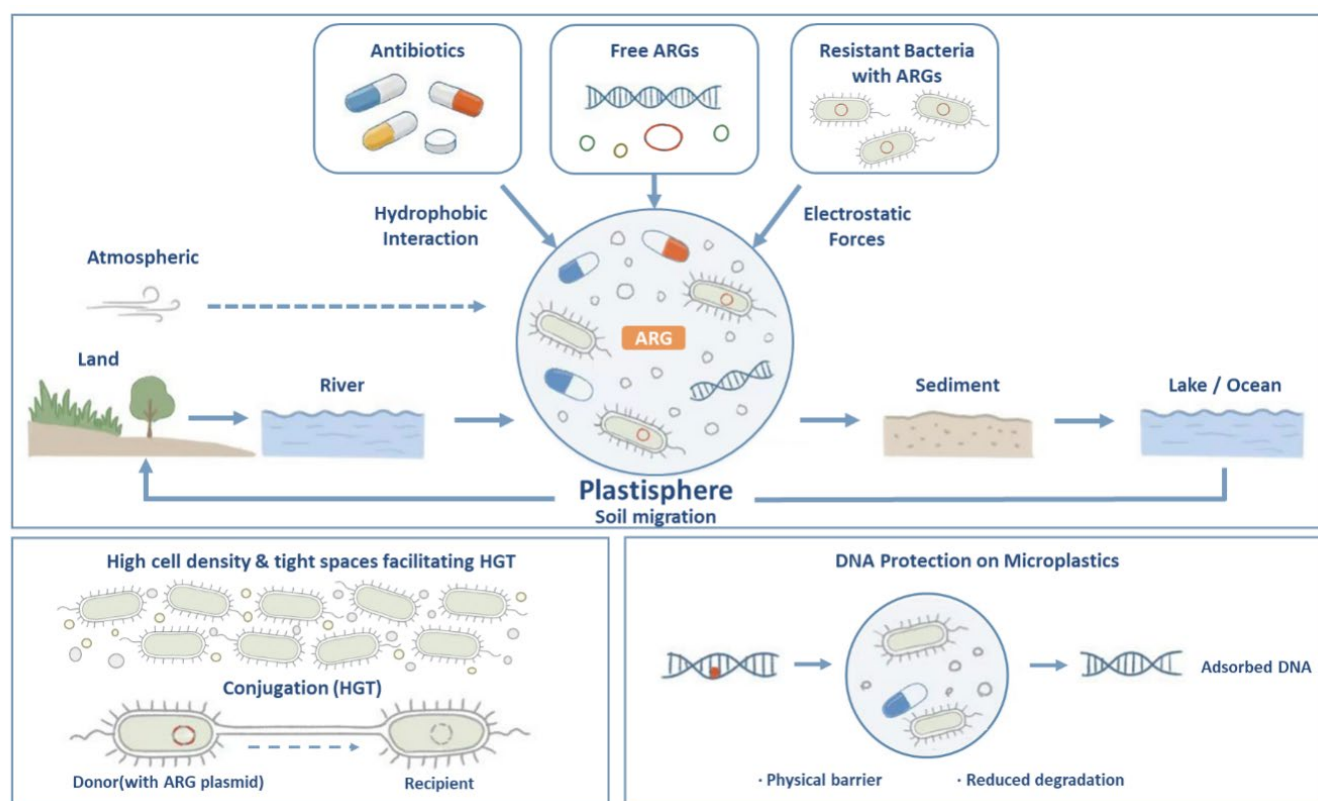


Figure 6. Mechanisms by which microplastics serve as carriers of antimicrobial resistance genes to promote their transport and dissemination.

At the environmental migration scale, the low density and high persistence of microplastics enable their long-distance horizontal and vertical transport through river and ocean currents, wind dispersal, and biological ingestion. This process breaks spatial barriers, spreading locally concentrated AMR to broader regions and even driving cross-compartment transfer between the water column and sediments [114]. During transport, microplastics act as physical shields for adsorbed DNA, slowing its degradation through encapsulation and isolation and thereby extending the environmental lifetime of ARGs and sustaining their associated ecological risks [73]. This conclusion is mostly inferred by analogy to the protective effect of solid interfaces on free DNA. Direct experimental data quantifying how much longer adsorbed ARGs persist on microplastics than in bulk water are still scarce. Collectively, microplastics function not only as passive carriers for ARGs but also as hotspots for gene transfer and vectors for cross-scale dissemination, synergistically exacerbating ARG propagation risks across multiple dimensions.

5. Current Research Gaps and Future Perspectives

Research on the impacts of emerging contaminants on bacterial AMR has advanced considerably in recent years. Surveys across diverse environmental matrices have revealed statistical associations between emerging contaminants (antibiotics, EDCs, microplastics, and POPs) and the enrichment of ARGs and MGEs, while the driving mechanisms behind these associations have been preliminarily elucidated. Nevertheless, important knowledge gaps remain, particularly in terms of limited representativeness, causal inference, combined pollution effects, and mechanistic integration.

5.1. Limited Representativeness of Current Evidence

Current research is constrained by significant gaps in geographic coverage, contaminant scope, and temporal resolution. First, field investigations remain heavily concentrated in China, the United States, and Europe, with extremely limited data from rapidly industrializing and transitioning economies across Africa, South Asia, and Latin America. These regions often have intensive use and discharge of emerging contaminants, weak environmental governance, and high population density. These regions are therefore potential hotspots for AMR emergence and spread, but their resistance status remains unknown because of data scarcity. Moreover, remote and fragile environmental compartments, including groundwater, polar ecosystems, and the deep sea, remain understudied, introducing geographical bias into current understanding of global resistance dissemination patterns.

Second, existing studies focus overwhelmingly on a narrow set of representative contaminants, namely

sulfonamides, tetracyclines, and quinolone antibiotics, alongside TCS, BPA, PAHs, and PFASs. This narrow scope limits a holistic understanding of how diverse chemical stressors drive the evolution of AMR. Finally, most available monitoring data are based on static, single-time-point sampling, with few long-term time-series datasets. As a result, the temporal dynamics and evolutionary trajectories of AMR under sustained contaminant pressure remain largely unresolved.

5.2. Insufficient Causal Evidence

A core methodological limitation is the overreliance on correlation analysis and the lack of causal evidence. Most existing studies employ statistical tools, including correlation analysis and meta-analysis, to characterize associations between emerging contaminant residues and AMR, using both field-collected and laboratory-incubated samples. While these approaches can capture significant covariation, they cannot disentangle causal relationships from spurious correlations, nor can they exclude confounding by covariates such as heavy metals, temperature, and pH. Furthermore, systematic investigation into causal mechanisms remains limited. Notably, laboratory experiments have revealed direct effects of emerging contaminants on AMR evolution and molecular mechanisms, but they often use doses far above environmental levels. This discrepancy means that such experiments cannot accurately recapitulate the eco-evolutionary dynamics occurring under chronic low-dose environmental exposure.

5.3. Limited Understanding of Combined Pollution Effects

Another critical gap is the limited understanding of combined pollution effects. Existing studies have predominantly evaluated the impacts of individual emerging contaminants on AMR, while the joint effects of co-occurring contaminant mixtures remain largely understudied. In nature, contaminants occur as mixtures, and their interactions (synergistic, antagonistic, or additive) can substantially alter AMR evolution and spread.

Preliminary studies have begun to examine combined pollution scenarios. For example, microplastic-antibiotic co-contamination has been shown to synergistically enhance ARG enrichment and horizontal transfer [85,115]. Co-exposure to PFASs and antibiotics triggers a novel cross-resistance mechanism conferring resistance to both antibiotics and PFOS, thereby enhancing ARG transformation efficiency in recipient bacteria [116]. Additionally, microplastics adsorb heavy metals, forming localized high-contamination hotspots that upregulate bacterial efflux pump expression [117]. Nevertheless, systematic studies of interactions within and between contaminant classes are scarce, which limits accurate AMR risk assessment in complex environments.

5.4. Insufficient Mechanistic Depth and Cross-Mechanism Integration

Mechanistic understanding of emerging contaminant-driven AMR remains limited in both depth and integration. To date, four core pathways have been proposed: ROS–SOS response-mediated mutagenesis and recombination, enhanced horizontal transfer of ARGs, selective enrichment of resistant bacteria, and microplastic-facilitated ARG transport and dissemination. However, many studies remain at the level of phenomenological observation or single-pathway validation, with limited fine-scale mechanistic dissection across the molecular, cellular, community, and ecosystem levels.

Furthermore, these pathways are typically investigated independently, with a clear lack of integrative analysis across mechanisms. For example, ROS–SOS activation may not only increase mutation frequency but also promote MGE activity and HGT; selective pressure may enrich resistant hosts that subsequently facilitate ARG transfer; and microplastics may simultaneously serve as carriers, selective microhabitats, and hotspots for HGT. Therefore, future studies should adopt an integrated framework to examine how these mechanisms interact across scales. At the macro scale, the global distribution of emerging contaminants and AMR, their long-distance routes, and their links to human activity, climate, and land use also require systematic investigation.

To address the aforementioned research gaps, future studies should focus on the following directions:

(1) Establishing causal evidence under realistic exposure scenarios

To move beyond correlation-based analyses and establish robust causal links, future studies should adopt integrated research strategies under environmentally realistic exposure conditions. First, long-term *in situ* monitoring and natural experimental designs should be strengthened. For example, before–after comparisons from pollution source shutdowns, treatment upgrades, or stricter standards could identify causal effects of emerging contaminants on AMR dynamics. Second, long-term low-dose exposure experiments at environmentally relevant concentrations should be developed. Experimental systems should mimic natural environmental fluctuations and incorporate multigenerational evolution assays to track the accumulation of resistance mutations and the dynamics of ARG transfer over time. Third, advanced tools such as gene editing, isotope tracing, and functional validation should be applied to directly verify the contribution of key regulatory pathways, such as SOS response activation and efflux pump expression, under contaminant exposure. Together, these approaches could build a more complete evidence chain from statistical association to mechanistic causality.

On this basis, it is particularly important to establish an experimental research paradigm that can precisely distinguish different driving mechanisms through controlled exposure experiments, mechanistic validation, and multi-omics approaches.

(2) Coupling experiments and models to resolve combined pollution effects

Given the ubiquitous co-occurrence of diverse emerging contaminants in natural environments, future research should systematically evaluate combined pollution effects using well-controlled experimental systems and representative exposure scenarios. Priority should be given to typical combined pollution settings. These include microplastic–antibiotic co-contamination (e.g., in agricultural film, manure-amended soils, livestock/poultry farms, and WWTP discharges) and EDC–POP co-contamination (e.g., in aquaculture effluents, industrial hotspots, and e-waste sites). These studies should aim to clarify how contaminant mixtures synergistically, additively, or antagonistically affect ARG enrichment, HGT, and resistant bacterial selection.

In parallel, experimental data should be coupled with computational models to quantify interaction effects and predict resistance risks under complex pollution scenarios. Machine learning and mechanistic models can be used to identify key drivers, quantify nonlinear interactions among contaminants, and predict high-risk conditions for ARG enrichment and transfer. Such experiment–model integration will provide more realistic exposure scenarios and improve the robustness of environmental risk assessment for AMR.

(3) Integrating multi-omics and multi-mechanism analyses

To address limited mechanistic depth and fragmentation, future research should adopt integrated multi-omics strategies. These include metagenomics, metatranscriptomics, proteomics, and metabolomics. Metagenomics can reveal changes in ARGs, MGEs, and microbial community composition. Metatranscriptomics and proteomics can further identify active resistance pathways and functional responses under emerging contaminant exposure. Metabolomics can provide complementary data on cellular stress responses, energy metabolism, membrane alteration, and redox homeostasis, thereby linking contaminant exposure to physiological changes in bacteria. These multi-omics approaches may be further combined with single-cell sequencing, live-cell fluorescence imaging, and functional assays to resolve the interactions among ROS–SOS response activation, HGT, selective enrichment of resistant bacteria, and carrier-mediated ARG transport. Such integration would help move beyond single-pathway verification and identify key regulatory nodes connecting mutation, gene transfer, community selection, and environmental transport.

(4) Developing AI-driven cross-scale systems research.

Future studies should also develop AI-driven cross-scale systems research to address current gaps in spatial coverage, contaminant diversity, and temporal resolution. Monitoring efforts should be expanded to rapidly industrializing regions, including Africa, South Asia, and Latin America, as well as understudied vulnerable environments such as groundwater, polar regions, and the deep sea. The scope of emerging contaminants should also be broadened to include newly identified chemicals and transformation products, enabling early identification of potential high-risk drivers.

Long-term monitoring stations, time-series sampling, historical samples, and environmental archives should be integrated to reconstruct resistance trajectories and predict future trends. Artificial intelligence can further integrate multi-source datasets, including chemical monitoring, microbial community profiles, ARG abundance, hydrological data, climate variables, and human activity indicators, to map the global distribution of emerging contaminants and ARGs, identify cross-regional dissemination routes, and support cross-scale risk prediction for AMR evolution driven by emerging contaminants.

(5) From mechanistic understanding to risk assessment and management

Mechanistic insights into how emerging contaminants promote AMR provide an important foundation for improving environmental risk assessment and management. Future efforts should integrate AMR-related endpoints, such as ARG enrichment, horizontal gene transfer potential, and resistance selection thresholds, into existing chemical risk assessment frameworks. By considering contaminant-specific mechanisms, environmental persistence, and exposure scenarios, resistance-oriented risk indicators could complement traditional toxicity-based assessments. Such advances may support the development of improved monitoring strategies, priority contaminant identification, and more effective management approaches for emerging contaminants.

6. Conclusions

AMR evolution in the environment is not solely a consequence of antibiotic exposure. Based on the narrative synthesis of representative literature from a structured search, emerging contaminants, including antibiotics, EDCs, POPs, and microplastics, can function as selective agents, physiological stressors, genetic-transfer enhancers, and physical vectors that collectively influence the emergence, maintenance, and dissemination of bacterial AMR. Emerging contaminant-driven resistance evolution involves interactions across multiple biological and environmental scales, through mechanisms ranging from molecular mutation to community-level selection and environmental-scale transport. A cross-scale framework combining long-term monitoring, causal

experiments, multi-omics analysis, and AI-assisted prediction will provide a stronger scientific basis for understanding and managing AMR evolution in complex environmental systems.

Supplementary Materials

The additional data and information can be downloaded at: <https://media.sciltp.com/articles/others/2610230848116156/GES-26070117-SI.pdf>. Table S1: PRISMA 2020 reporting checklist. Table S2: Studies used for the quantitative summary of antibiotic effects on antimicrobial resistance in Table 1. Table S3: Studies used for the quantitative summary of endocrine-disrupting chemicals (EDCs) effects on antimicrobial resistance in Table 1. Table S4: Studies used for the quantitative summary of persistent organic pollutants (POPs) effects on antimicrobial resistance in Table 1. Table S5: Studies used for the quantitative summary of microplastics (MPs) effects on antimicrobial resistance in Table 1.

Author Contributions

X.Y.: Writing—original draft preparation; Q.Y.: Supervision, writing—original draft preparation; Y.D.: Writing—reviewing and editing; X.W.: Writing—reviewing and editing; Z.Y.: Writing—reviewing and editing; M.W.: Writing—reviewing and editing; Y.L.: Supervision, writing—reviewing and editing. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Record-level values used for the descriptive fold-change summaries are provided in Tables S2–S5 of the Supporting Information. No new experimental data were generated.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

During the preparation of this work, the authors used AI-assisted tools for literature screening, figure creation, and language polishing to improve writing efficiency. After using these tools, the authors reviewed

and edited the content as needed and take full responsibility for the content of the published article.

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