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Review

Environmental occurrence, ecotoxicity, and management perspectives of β-lactam antibiotics

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ABSTRACT

β-Lactams are the most widely prescribed antibiotic class globally, comprising penicillins, cephalosporins, carbapenems, and monobactams. Their continual release to the environment raises concerns about both direct ecotoxicity and potential indirect effects on ecosystem function. This review highlights three key findings; 1) environmental concentrations can exceed predicted no-effect concentrations for resistance selection; for example ceftriaxone had been reported 6160 μg/L in wastewater influent and 4150 μg/L in effluent in India, indicating that many β-lactams have removal efficiency below 33%, 2) ecotoxicity data show that cyanobacteria (e.g. *Microcystis aeruginosa*, EC50 0.0037 mg/L for amoxicillin) are ≥ 1,000-fold more sensitive than macrofauna, and that chronic exposure at ng-μg/L levels may promote selection of antimicrobial resistance and facilitate horizontal gene transfer of these genes and 3). β-lactam resistance genes ($bla_{\text{CTX-M}}$, bla_{NDM}, bla_{OXA}) are ubiquitous in wastewater and manure-amended soils and can persist even after the degradation of the parent compounds. Collectively, these finding indicates that β-lactam antibiotics pose significant risks to aquatic and soil ecosystems by contributing to the proliferation and maintenance of antimicrobial resistance in environmental reservoirs. The widespread environmental occurrence and persistence of β-lactams, along with associated resistance determinants, represent emerging One Health concerns. This narrative review synthesizes current literature on the ecotoxicological effects of β-lactam antibiotics, focusing on their major environmental sources, distribution across environmental matrices, impacts on non-target organisms, and emerging strategies to mitigate their

List of abbreviations: AMR, Antimicrobial resistance; AOPs, Advanced oxidation processes; API, Active pharmaceutical ingredient; ARBs, Antibiotic-resistant bacteria; ARGs, Antibiotic resistance genes; BlaCTX-M, CTX-M-type extended-spectrum β-lactamase gene cefotaximase, Munich; BlaGES, GES-type β-lactamase genes; BlaKPC, Klebsiella pneumoniae carbapenemase gene; BlaNDM, New Delhi metallo-β-lactamase gene; BlaOXA, Oxacillinase β-lactamase gene; BlaSHV, SHV-type β-lactamase gene sulfhydryl variable; BlaTEM, TEM-type β-lactamase gene Temoneira; CZE, Capillary zone electrophoresis; DAD, Diode array detector; DID, Defined daily dose per 1000 inhabitants per day; EC50, Half maximal effective concentration; ESBL, Extended-spectrum beta-lactamase; FAO, Food and Agriculture Organization; GAC, Granular activated carbon; GO@SiO_2, Graphene oxide–functionalized silica; HGT, Horizontal gene transfer; HPLC, High-performance liquid chromatography; LC50, Median lethal concentration; LC–MS/MS, Liquid chromatography–tandem mass spectrometry; LOD, Limit of detection; LOQ, Limit of quantification; MGEs, Mobile genetic elements; MIC, Minimum inhibitory concentration; NOEC, No-observed-effect concentration; PHCs, Primary health centers; SPE, Solid-phase extraction; UHPLC, Ultra-high-performance liquid chromatography; UNEP, United Nations Environment Programme; WASH, Water, sanitation and hygiene; WHO, World Health Organization; WWTP, Wastewater treatment plant.

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environmental burdens. We further emphasize cross-disciplinary solutions spanning engineering, microbial ecology, policy, identify critical research gaps, and propose pragmatic pathways to reduce environmental selection pressure from β-lactams.

1. Introduction

β-Lactams are among the most widely used antibiotics in human and veterinary medicine (Klein et al., 2024). Their broad spectrum, low toxicity, and affordability have made them central to treating infections from minor skin diseases to severe conditions such as pneumonia, meningitis, and septicemia (Thakuria, 2013). β-Lactams exert their bactericidal effect by binding to penicillin-binding proteins and inhibiting peptidoglycan cross-linking in the bacterial cell wall, leading to cell lysis and death (Fernandes et al., 2013). This class comprises several major subclasses, including penicillins, cephalosporins, carbapenems, and monobactams. According to the 2024 report from the European Centre for Disease Prevention and Control, average antibiotic consumption in the EU reached 20.3 defined daily doses (DDD) per 1000 inhabitants, with β-lactams accounting for more than half of total use, predominantly penicillins and cephalosporins (ECDC, 2025). Usage patterns, however, vary substantially between community and hospital settings and across countries. Similarly, a U.S. hospital survey conducted in 2015 reported that 12.2% of inpatients received third- or fourth-generation cephalosporins, 9.8% first-generation cephalosporins, 8.7% penicillin-based combinations, and 3.7% carbapenems (Magill et al., 2021).

Widespread use has driven the rise of β-lactam-resistant bacteria, a major component of antimicrobial resistance (AMR) (Tiwari et al., 2022a; Al-Mustapha et al., 2025). Carbapenem-resistant Enterobacterales, carbapenem-resistant *Acinetobacter*, and ESBL-producing Enterobacterales are WHO priority pathogens (WHO, 2024). Inappropriate prescribing, incorrect dosing, and limited diagnostics accelerate resistance (Ahmed et al., 2024). Accurate diagnosis and appropriate dosing are essential to curb AMR (Puri et al., 2025). In 2019, AMR was associated with an estimated 4.95 million deaths, with β-lactam resistance a major contributor (Murray et al., 2022).

Beyond clinical misuse, growing evidence demonstrates that environmental contamination with β-lactams is an underappreciated driver of resistance evolution and ecological disruption. Their ecotoxicity to non-target microbial communities is often overlooked, despite the persistence of parent compounds and metabolites in aquatic and terrestrial systems, where they can affect ecosystem function even at low concentrations. β-lactams enter the environment via wastewater effluents (Jendrzejewska and Karwowska, 2022), pharmaceutical manufacturing (Rayan, 2023), hospital waste (Ugoeze et al., 2024), agricultural runoff (Tuts et al., 2025), and improper disposal of medicines (Barathe et al., 2024; Fakhri et al., 2024).

Although environmental levels are typically sub-therapeutic, chronic exposure can impose selective pressure, promote horizontal gene transfer, and sustain resistance genes within microbial communities (Ding et al., 2022; Gray-Hammerton et al., 2025; Tiwari et al., 2024). Environmental compartments therefore act as reservoirs and evolutionary hotspots for β-lactam resistance, with potential re-entry into clinical settings through food chains (Irrgang et al., 2017), drinking water (Ahammad et al., 2014) and direct human–environment interactions (Rega et al., 2023; Martak et al., 2024).

Previous studies have reviewed and synthesized the environmental occurrence, ecotoxicity, and management of various antibiotics (Barathe et al., 2024; Fakhri et al., 2024; Sharma et al., 2022a, 2022b; Yang et al., 2021). Yang et al. reported that wastewater contains the highest antibiotic concentrations compared to surface and groundwater, identifying it as a key environmental hotspot (Yang et al., 2021). Frequently detected classes included macrolides, fluoroquinolones, tetracyclines, and sulfonamides, with compounds such as erythromycin, ciprofloxacin, norfloxacin, tetracycline, sulfamethoxazole, and trimethoprim. These antibiotics pose ecological risks to non-target organisms, including algae and fish. The authors summarized removal processes such as adsorption, photodegradation, oxidation, and biodegradation, noting variable efficiency and emphasizing the need to address chronic low-dose exposure, with biodegradation highlighted as a promising sustainable approach. Reported removal pathways show that β-lactams mainly undergo hydrolysis, fluoroquinolones and sulfonamides can be biodegraded by specific microbes, and photolysis/oxidation are particularly effective for fluoroquinolones, tetracyclines, and sulfonamides.

Similarly, Albarano et al. reviewed veterinary antibiotics in European aquatic environments, highlighting their widespread occurrence and persistence due to continuous inputs from excretion, wastewater treatment plants, improper disposal, aquaculture, and pharmaceutical production (Albarano et al., 2024). They identified tetracyclines, fluoroquinolones, sulfonamides, and macrolides as priority contaminants based on prevalence and ecological risk, with macrolides and fluoroquinolones showing the highest risk scores. The authors emphasized the need for integrated risk assessment incorporating chronic toxicity, transformation products, mixture effects, and co-contaminants, alongside improved monitoring and mitigation strategies.

Sta. Ana et al. reviewed β-lactam antibiotics and antibiotic resistance in Asian lakes and rivers, reporting widespread contamination linked to antibiotic-resistant bacteria (ARB) and antibiotic resistance genes (ARGs) (Sta Ana et al., 2021). Key sources include wastewater, hospital effluents, agriculture, aquaculture, and treatment plant discharges. Although β-lactams are typically detected at ng/L levels, their occurrence correlates with ARB and ARG prevalence, particularly in rivers, with most studies conducted in China. The review highlights increasing pressure on aquatic ecosystems that provide drinking water and food resources, while noting substantial monitoring gaps across Asia. The authors recommend expanded surveillance, especially in low- and middle-income countries, and further investigation of environmental fate, novel resistance genes, horizontal gene transfer, and ecological impacts. They also call for comparative studies in pristine environments and stricter regulation of effluent discharges. Analytical approaches include solid-phase extraction and LC–MS/MS for antibiotics, PCR for ARGs, and culture-based methods for ARB, although these remain resource-intensive.

Despite growing research on AMR, the environmental fate, ecotoxicity, and resistance-selective effects of β-lactam antibiotics remain poorly understood. This review synthesizes current knowledge on the occurrence, environmental fate, ecological impacts, and resistance-related effects of β-lactams, while identifying key knowledge gaps and research priorities. By integrating evidence across environmental, microbial, and public health domains, the review provides a One Health framework for understanding and mitigating the impacts of β-lactam pollution. We anticipate that this work will support future monitoring, risk assessment, environmental management, and policy efforts aimed at reducing antibiotic pollution and limiting the spread of antimicrobial resistance.

2. Research methodology

This study is a narrative literature review. A structured search was conducted in September–October 2025 using PubMed and Google Scholar. The search combined Boolean operators (“AND”, “OR”) and keywords such as β-lactam antibiotics, environmental contamination, pharmaceutical pollution, wastewater sources (municipal, hospital, industrial), agricultural runoff, environmental fate, ecotoxicity, resistance genes, selective pressure, monitoring methods, and treatment technologies. Only peer-reviewed, English-language studies were considered. To supplement the database search, reference lists of key papers were screened for additional relevant publications. Given the narrative scope, the review is based on a curated selection of relevant literature rather than a systematic, exhaustive search.

3. Environmental release of β-lactam residues

Environmental release of β-lactam residues refers to the introduction and dissemination of unmetabolized antibiotics and their transformation products into environmental compartments such as wastewater, surface waters, soils, and sediments. While antibiotic use is strictly regulated in many high-income countries (HICs), with sales largely prescription-based, many low- and middle-income countries (LMICs), face a limited diagnostic capacity and weak antimicrobial stewardship. In these settings, antibiotics are often readily accessible, and self-medication or non-qualified prescribing is common (Do et al., 2021; Knowles et al., 2020; Kotwani et al., 2021; Zequinao et al., 2020). As a consequence, β-lactams are frequently detected and quantified in high quantities across diverse environmental matrices (Zhu et al., 2013; Aydin and Talinli, 2013; Mirzaei et al., 2017; Schuster et al., 2022). The following sections outline the main pathways and environmental impacts of β-lactam contamination. Environmental dissemination of β-lactams is driven by multiple interconnected pathways, including human and veterinary excretion, insufficient wastewater treatment, and improper disposal of pharmaceutical waste. Together, these pathways govern their environmental occurrence, persistence, and distribution.

3.1. Municipal wastewater

Municipal wastewater is a major source of β-lactam antibiotics and antibiotics resistance genes, collecting inputs from households, healthcare facilities, veterinary clinics, and industry. Although wastewater treatment plants (WWTPs) reduce ARGs abundance, conventional technologies do not ensure complete removal. Studies have identified WWTPs effluents as key hotspots for β-lactam resistance genes, including $bla_{\text{CTX-M}}$, bla_{TEM}, bla_{OXA}, bla_{GES}, and bla_{VEB} (Gregova et al., 2021; Al-Mustapha et al., 2023; Tiwari et al., 2023, 2022b). In many regions, however, WWTPs coverage is limited and municipal wastewater is discharged untreated or partially treated into surface waters (Cacace et al., 2019; Tandukar et al., 2024), facilitating the entry of antibiotic-resistant bacteria and genes into drinking water systems and food chains (Al-Mustapha et al., 2023; Tiwari et al., 2022c).

Treatment inefficiencies are well documented. For example, ceftriaxone concentrations of 6160 μg/L were reported at the inlet of an Indian WWTP, only decreasing to 4150 μg/L at the outlet (Shipingana et al., 2022). Similarly, removal efficiencies of only 34.0% for cefixime and 55.6% for amoxicillin have been reported in Iranian WWTP (Shipingana et al., 2022; Shokoohi et al., 2017). These findings indicate substantial residual pharmaceutical loads in receiving waters. Overall, β-lactams, particularly penicillins and cephalosporins (Table 1) are widely detected in aquatic environments, reflecting high consumption and incomplete removal during treatment (Tiwari et al., 2024, 2022b; Zhang et al., 2024; Wada and Olawade, 2025).

Antibiotic occurrence in wastewater is driven by usage patterns and compound persistence, with more stable or frequently used drugs being more commonly detected (Tiwari et al., 2025). Among β-lactams, penicillins such as amoxicillin, ampicillin, ccephalosporins and penicillin G are frequently reported (Table−1), reaching surface waters, often indicating insufficient treatment. For example, compounds such as cefazolin, cefmetazole, and cefotaxime have been detected in the Songhua River (China), associated with mixed inputs from municipal, hospital, industrial, and agricultural sources (Wang et al., 2017). Similar contamination has been observed in drinking water reservoirs in China (Li et al., 2019), as well as in Pakistan (Khan et al., 2013) and Iran, where cephalexin and cefixime have been reported in groundwater (Mirzaei et al., 2018). These findings highlight the need for advanced treatment technologies, and integrated monitoring systems to reduce environmental β-lactam contamination and mitigate the growing threat of AMR.

Municipal wastewater thus acts as an integrator of antibiotic inputs from multiple sources. Conventional WWTPs remain inefficient at removing β-lactams, with removal rates often below 60% for compounds such as amoxicillin and cefixime. Consequently, WWTP effluents serve as major pathways for the dissemination of antibiotic-resistant bacteria and genes (e.g., $bla_{CTX\text{-}M}$, bla_{TEM}) into surface waters. Global evidence indicates that commonly used or environmentally stable β-lactams are ubiquitous in aquatic systems, reflecting systemic limitations in current wastewater infrastructure (Table 1).

3.2. Hospital wastewater

Clinical settings such as hospitals and primary care centers are major consumers of β-lactam antibiotics, largely due to empirical therapy and prophylactic use (Zhang et al., 2024; Bush and Bradford, 2016). After administration, β-lactams are only partially metabolized (Hiller et al., 2019), resulting in the excretion of active residues in urine and feces. For example, ~70% of meropenem (Zhanel et al., 2007) and 56–73% of piperacillin is excreted unchanged (Tjandramaga et al., 1978). These compounds are discharged via hospital wastewater (Yao et al., 2021), enter municipal sewer systems (treated or untreated) (Rodriguez-Mozaz et al., 2020; Astudillo et al., 2023), and ultimately reach aquatic (Sta Ana et al., 2021; Cha et al., 2006), and terrestrial environments (Graham et al., 2016; Kemper, 2008). Hospital effluents represent a major global source of environmental β-lactam contamination (Table 2).

Commonly reported β-lactams include cephalosporins (e.g., cefradine, cefepime, ceftriaxone), penicillins (e.g., amoxicillin, ampicillin, penicillin G), and carbapenems (e.g., meropenem). Concentrations vary widely, with exceptionally high levels reported in India (e.g., up to 11720 μg/L amoxicillin and up to 29150 μg/L ceftriaxone) (Shipingana et al., 2022), identifying it as a hotspot of pharmaceutical pollution (Sharma et al., 2022a). Significant residues have also been reported in hospital wastewater from high-income countries with advanced on-site WWTPs, indicating that even advanced treatment alone does not fully prevent environmental release (Table 2). In Germany, meropenem (up to 1900 μg/L) and piperacillin (up to 3500 μg/L) have been detected in hospital sewers (Schuster et al., 2022), while in China cefepime concentrations have reached 540 μg/L (Yao et al., 2021).

Even with removal efficiencies of 60–95%, depending on the compound and treatment process, residual concentrations may remain sufficient to exert selective pressure, promoting the persistence and spread of β-lactam resistance genes in receiving environments (Michael et al., 2013; Rodriguez-Mozaz et al., 2015). Elevated β-lactam levels can select for AMR, disrupt microbial communities, and enhance the spread concentrations range from trace levels to tens of thousands of μg/L, reflecting differences in antibiotic usage patterns, treatment efficiency, and regulatory frameworks across regions.

Effective mitigation requires targeted control at hospital discharge points. On-site pretreatment using advanced oxidation processes and membrane-based technologies can achieve 90–99% removal, significantly outperforming conventional treatment (Rizzo et al., 2019; Vijaya Kumar, 2024). Focusing on hospital effluent hotspots can substantially reduce environmental loading before dilution in municipal sewer systems (Brown et al., 2024; Vikesland et al., 2017). Integrating hospital wastewater monitoring into national AMR action plans is therefore essential to limit environmental dissemination and protect ecosystem and human health.

Table 1
Summary of global studies on the occurrence and analysis of β-lactam antibiotics in non-clinical wastewater.

Study Area	Groups within β-lactams	Names of β-lactam antibiotics	Source of contamination	Number of water samples	Linearity	Limit of detection (μg/L)	Limit of quantification (μg/L)	Range of recovery (%)	Standard deviation (%)	References
Surface water from the Minxin River and wastewater, Shijiazhuang (Hebei Province, China)	Penicillins Cephalosporins	Penicillin G Piperacillin Cloxacillin Oxacillin Nafcillin Mezlocillin Cefmenoxime Cefamandole Cefoperazone Ceftiofur Cefetamet	Municipal wastewater	35	1.0–200.0	0.01–0.92	0.05–2.78	75.57–114.20	< 8.99	Hao et al., (2024)
Qingshan Lake Basin, Eastern China	Penicillins	Penicillin V penicillin G	Municipal sewage plant (WWTP effluents), South Tiaoxi River and Jinxi River inflows, and general sources such as hospitals, livestock farms, pharmaceutical manufacturers, slaughterhouses, and households	51	0.5–200	0.001	NR	95.8–136.6	4.3–4.8	(Zhu et al., 2013)
River and a wastewater treatment plant in northern Colorado, USA	Penicillins Cephalosporins	Amoxicillin Ampicillin Oxacillin Cloxacillin Cephapirin	Municipal wastewater	200	±15	0.008–0.010 in surface water, 0.013–0.018 in the influent wastewater, 0.008–0.015 in the effluent wastewater	NR	Above 75 (except amoxicillin)	Lower than 10	(Cha et al., 2006)
Rivers, groundwater resources, drinking water treatment plants & wastewater treatment plants (WWTP B) in Tehran, Iran	Cephalosporins Penicillins	Cephalexin Cefixime Amoxicillin Penicillin G	Municipal wastewater	99	0.95–0.99	0.5233–0.9777 0.27865–0.4221 0.00830.0102	0.0200–0.1284 0.0250–0.0307	50–117	< 10	(Mirzaei et al., 2018)
Treated, ground and River water in Tehran, Iran	Penicillins Cephalosporins	Amoxicillin Penicillin G Cephalexin Cefixime Ceftriaxone	Municipal wastewater	12	0.95–0.99	Treated water: 0.001–0.010 Groundwater: 0.0008–0.010 River water: 0.0008–0.025	0.002–0.050	50–117	< 10	(Mirzaei et al., 2017)
Rivers, canal, dam & drug Formulation facility zones, Northern Pakistan	Cephalosporins	Cefotaxime	Municipal sewage, hospital effluent, drug formulation facility discharge, agricultural runoff	45	> 0.99	NR	0.016	NR	40–140	(Khan et al., 2013)
Sabarmati River, Gujarat (India)	Penicillins	Ampicillin	Municipal wastewater	60	0.9958	0.0005	0.003	105	6.7	(Kalugendo et al., 2025)
Buyukcekmece Lake, Istanbul, Turkey	Penicillins	Amoxicillin	Excretion through urine/ feces, unused medicines flushed down toilets, discharge of treated/ untreated wastewater.	29	≥ 0.99	0.001	0.0015	61–98	≈ 12.5–13.5	(Aydin and Talinli, 2013)

(continued on next page)

Table 1 (*continued*)

Study Area	Groups within β-lactams	Names of β-lactam antibiotics	Source of contamination	Number of water samples	Linearity	Limit of detection (μg/L)	Limit of quantification (μg/L)	Range of recovery (%)	Standard deviation (%)	References
Municipal WWTPs influent/effluent, New Mexico, USA	Penicillins	Penicillin G Penicillin V	Municipal wastewater	16	> 0.9911	0.01	NR	NR	NR	(Brown et al., 2006)
Okhla, Delhi, India WWTPs and Yamuna River (22 km stretch through Delhi)	Penicillins Cephalosporins	Ampicillin Cefuroxime	Human consumption/ excretion discharged as sewage and industrial effluent into the Yamuna River	28	0.999 0.998	0.30 0.50	0.90 1.50	25.5–108.8	< 10	(Mutiyar and Mittal, 2014)
Johor Bahru district, Malaysia (decentralized & conventional sewage treatment plants)	Penicillins	Ampicillin	Domestic sewage (human excretion after medical use)	18	0.991–0.999	0.0042	0.4911 ± 0.2543	06.7	< 6.5	(Chen et al., 2022)
WWTPs across European countries (Portugal, Spain, Ireland, Cyprus, Germany, Finland, Norway)	Penicillins Cephalosporins	Ampicillin Cefalexin	Municipal wastewater effluent	52	0.990–0.999	0.0066–0.0095 0.0051–0.0096	0.0220–0.0315 0.0170–0.0319	70 –120	< 15	(Rodriguez-Mozaz et al., 2020)
WWTPs in Harbin, north-east China.	Cephalosporins	Cefazolin Cefmetazole Cefotaxime	Municipal wastewater influenced by hospitals, pharmaceutical industry, and livestock wastewater discharge	18	-	0.00001–0.00095	NR	73.7 – 103.5	NR	(Wang et al., 2019)
Huangshui River, Xining (northeastern Tibetan Plateau), China	Penicillin Cephalosporins	Penicillin G Penicillin V Cefazolin Cefotaxime Cefalexin Ceftriaxone	River water (mainstream + tributaries), and effluents of WWTPs	37	0.991–0.999	0.000001–0.00035	NR	73.6 – 118.5	< 10	(Kuang et al., 2020)
Songhua River, Northeast China	Cephalosporins	Cefazolin Cefmetazole Cefotaxime	Pharmaceutical use, hospitals, animal husbandry, domestic wastewater	152	0.995	0.00001–0.00095	NR	73.7–104.6	NR	(Wang et al., 2017)
Xiong'an new area (XANA), Hebei, China	Penicillins Cephalosporins	Amoxicillin Cefazolin Cefmetazole Cefradine Cefalexin	Hospital & clinical wastewater, livestock & poultry farm runoff, domestic sewage discharge	38	> 0.995	0.00001–0.00132	0.00003–0.004	77 – 134	< 10	(Fu et al., 2022)
Zhuhai city, Pearl River estuary, South China	Penicillins Cephalosporins	Amoxicillin Ampicillin Penicillin G Cefalexin Cefotaxime	Intensive aquaculture (fish & mariculture), livestock wastewater, Municipal sewage discharge and urban/ industrial effluents	112	> 0.99	0.000004–0.0006	LOQ not explicitly stated; determined at S/N = 10 (typically ≈ 3 × LOD)	70–120	< 10	(Li et al., 2018)
Selangor, Malaysia	Penicillins	Amoxicillin	Pharmaceutical production, wastewater treatment, and treated sewage effluent.	18	> 0.94	ND – 0.00781	-	44.98–161.96	NR	(Praveena et al., 2018)
Danjiangkou reservoir, China	Cephalosporins	Cefalexin	Tributary River basins (non-point agricultural/	48	0.99	0.003	0.01	66.4–93.6	6.4	(Li et al., 2019)

(*continued on next page*)

Table 1 (*continued*)

Study Area	Groups within β-lactams	Names of β-lactam antibiotics	Source of contamination	Number of water samples	Linearity	Limit of detection (µg/L)	Limit of quantification (µg/L)	Range of recovery (%)	Standard deviation (%)	References
			livestock sources, and municipal discharge)							
Taipu River - Jinze reservoir system, Shanghai, China	Penicillins	Amoxicillin Penicillin G Penicillin V	Anthropogenic activities, including human healthcare, livestock use, and wastewater discharges	80	0.99	NR	0.000039–0.000850	63.9–112.4	NR	(Li et al., 2020)
	Cephalosporins	Cefalexin								
Hanoi (urban canals & lakes), Vietnam	Penicillins	Ampicillin Amoxicillin	Municipal & hospital wastewater, stormwater runoff, sewer leakage, illicit discharge	53 (28 canal + 25 lake)	0.991–0.999	Lake: 0.0005 Canal: 0.0010	Lake:0.0020 Canal: 0.0035	94.2–111.5	0.8–13.4	(Tran et al., 2019)
	Cephalosporins	Cefixime				Lake: 0.015 Canal: 0.025	Lake: 0.050 /Canal: 0.080			
						Lake:0.00050 Canal:0.00030	Lake:0.00015Canal:0.00100			
		Ceftazidime				Lake: 0.020 Canal: 0.030	Lake: 0.060 Canal: 0.100			
		Meropenem				Lake: 0.007 Canal: 0.005	Lake: 0.002 Canal: 0.015			
Receiving River (of a penicillin G production WWTP in China)	Penicillins	Penicillin G	Wastewater discharge from a penicillin-G production facility (WWTP effluent)	270	–	0.03	0.093	80.6 – 98.7	4.2– 6.8	(Li et al., 2008)
Reservoirs in North China (Luan River to Tianjin diversion)	Penicillins	Penicillin G	Aquaculture (cage culture), municipal wastewater discharge, and agricultural runoff.	160	> 0.99	0.00003–0.0003	0.0001–0.0010	67.58–133.30	0.60–12.29	(Li et al., 2014)
Rivers in Western Romania	Penicillins	Ampicillin Penicillin G Amoxicillin Cloxacillin	Municipal wastewater & drinking water	42	NR	0.00004	0.00008	> 80%	< 8%	(Gaspar et al., 2023)
	Cephalosporin	Ceftiofur								

Note: NR = Not reported; ND= Not detected

Table 2
Global distribution, source, and concentration range of β-lactam antibiotics detected in hospital wastewater.

Study Area	Groups within β-lactams	Names of β-lactam antibiotics	Source of discharge	Point of receipt	Number of hospitals	No of sample studies	No of hospitals represents detection of β lactams	Concentration (μg/L), maximum concentration or range	References
China	Cephalosporins	Cefradine Cefepime	Hospital wastewater effluent	Municipal WWTPs	3	36	H1 H3	2.38 540.39	(Yao et al., 2021)
Romania	Penicillins	Ampicillin			3	12	3	3.67–53.05	(Szekeres et al., 2017)
India	Penicillins	Amoxicillin		Hospital wastewater	11	66	9	150–11720	(Sharma et al., 2022a)
India	Penicillins	Amoxicillin			15 10 PHCs	15 10	2 3	270–1000 230	(Sharma et al., 2022b)
	Cephalosporins	Ceftriaxone			15 10 PHCs	15 10	2 3	50–590 120	
Germany	Carbapenems Penicillins	Meropenem Piperacillin		Wastewater sewer	1	264 (hourly composite samples	264	Up to 1900 Up to 3500	(Schuster et al., 2022)
Ethiopia	Cephalosporins	Ceftriaxone		Wastewater from public sewer	1	regular interval	NR	83	(Tesfa et al., 2024)
India	Cephalosporin	Ceftriaxone		Drainage	2	8	2	58.3–59.5	(Diwan et al., 2010)
India	Cephalosporin	Ceftriaxone		Hospital effluent	7	7	4	1250–29150	(Shipingana et al., 2022)
				Municipal WWTPs (Inlet)	1	1	1	6160	
				Municipal WWTPs (outlet)	1	1	1	4150	
Kenya	Penicillins	Ampicillin Oxacillin	Raw hospital wastewater	Wastewater treatment plant	2	9	l	1	(Ngigi et al., 2020)
Iran	Cephalosporins	Cefazolin	Hospital wastewater	NR	1	NR	1	4.1–42.3	(Esfandyari et al., 2019)
Taiwan	Penicillins	Oxacillin	Hospital effluent	Toucian River	1	15	1	0.0001–0.01	(Esfandyari et al., 2019)
USA	Penicillins	Penicillin G Penicillin V		Surface water	5	5	4	0.85–5.2 0.01	(Brown et al., 2006)
Spain	Penicillins	Ampicillin	Veterinary hospital effluent	Municipal wastewater treatment system	1	NR	1	0.007–10.253	(Lucas et al., 2016)

NR = Not reported

3.3. Pharmaceutical industrial wastewater

Pharmaceutical industries are another important environmental source of antibiotic residues. Industrial production of β-lactams by the pharmaceutical industry can serve as significant environmental source. Despite good manufacturing practices, residues of β-lactams, organic solvents, and intermediates can still be released into the environment (González-Plaza et al., 2019). Reported concentrations in pharmaceutical effluents vary widely. For example, a penicillin G plant in China reported ~153 μg/L in raw wastewater, reduced to 1.7 μg/L after treatment (Li et al., 2008). Cephalosporin production facilities can discharge extremely high concentrations, with cefdinir reported at 125000–175000 μg/L in untreated effluent, while ceftazidime has been detected at lower levels (~5 μg/L) in hospital-associated wastewaters (Das et al., 2019). Mixed cephalosporin streams have been reported at 12–142 μg/L before treatment and 0.05–24 μg/L after treatment (Yu et al., 2016). In contrast, some regulated facilities have reported much lower levels, with piperacillin and ceftazidime often below 0.00001–0.01 μg/L in both influent and effluent (Kamatham et al., 2024). Overall, these data indicate strong global variability, with poorly regulated sites (often in parts of Asia) exhibiting discharge concentration levels of μg/L–mg/L, while well-regulated systems in Europe typically achieve ng/L–μg/L levels.

Additional risks arise from improper waste handling, including direct discharge, co-treatment with municipal sewage, and poorly managed solid wastes such as fermentation sludge. To address these challenges, recent studies have recommended sustainable production and mitigation strategies, including green chemistry approaches, solvent recovery, water reuse, and advanced treatment technologies such as advanced oxidation processes, nanofiltration, and enzyme-based biodegradation (Kafle et al., 2024). Global initiatives, including WHO guidelines on antibacterial manufacturing, emphasize zero-liquid discharge, stricter effluent monitoring, and cross-sector coordination under a One Health framework (WHO, 2024).

Overall, pharmaceutical manufacturing sites can act as extreme point sources of β-lactam release. Poorly regulated facilities particularly in parts of Asia may discharge effluents containing mg/L to g/L concentrations of parent compounds and intermediates, whereas well-regulated plants maintain ng/L–μg/L levels. These industrial emissions can strongly contribute to localized selection of antimicrobial resistance genes and mobile genetic elements in aquatic environments. Strengthening global standards through zero-liquid discharge, green chemistry, and stringent monitoring is essential to prevent large-scale environmental loading.

3.4. Animal husbandry

Animal husbandry widely utilizes β-Lactams in poultry, swine, and cattle farming, as well as aquaculture for therapeutic and prophylactic purposes (Landers et al., 2012). β-Lactams are frequently detected in animal wastes such as manure, litter, slurry, and manure-amended soils (Al-Mustapha et al., 2023; Oliver et al., 2020; Bhowmick et al., 2023). However, their environmental persistence is generally low due to rapid hydrolysis of the β-lactam ring under neutral to alkaline pH, elevated temperatures, and high microbial activity typical of manure systems (Mitchell et al., 2014).

Reported concentrations of amoxicillin and ampicillin in poultry and pig manure are generally < 1 mg kg^{-1} (dry weight), with degradation occurring within days to weeks during storage (Berendsen et al., 2018). Penicillins in swine manure are often at concentrations of < 0.5 mg/kg or below detection limits, despite veterinary use (Van Epps and Blaney, 2016). Large-scale studies in Chinese livestock systems have reported amoxicillin, ampicillin, and penicillin G as undetectable or only present at trace levels (<0.1–0.3 mg/kg), whereas more stable antibiotics such as tetracyclines and sulfonamides, are more frequently detected (Tian et al., 2021). Similar patterns have been observed on European cattle and pig farms, where β-lactams been rarely been quantified in manure or soil (Marutescu et al., 2022).

Fresh manure may contain transient concentrations sufficient to exert selective pressure during storage, transport, and land application. Experimental and field studies have demonstrated that short-term exposure to sub-mg/kg levels can enrich β-lactam resistance genes such as bla_{TEM}, bla_{SHV}, and bla_{CTX-M} in manure, amended soils, and runoff waters (Zalewska et al., 2021; Zeng et al., 2025). These resistance determinants can persist after antibiotic degradation through horizontal gene transfer and co-selection with other antimicrobials, metals, and biocides in agricultural systems.

Land application of manure further promotes the spatial dissemination of β-lactam resistance. Although antibiotic residues rapidly degrade, ARGs and ARBs can spread via runoff, leaching, dust, and crop contamination, creating indirect exposure pathways for humans and animals. Soils consistently receiving manure display elevated abundances of β-lactam resistance genes even when antibiotics are no longer detectable (Heuer et al., 2011). Thus, agricultural systems act less as sinks and more as reservoirs and dissemination hubs of resistance within a One Health context.

Overall, intensive antibiotic use in agriculture promotes selective pressure that drives the spread of antibiotic-resistant bacteria and genes, which can reach humans through food, direct contact, and environmental pathways (Berendonk et al., 2015; Graham et al., 2019).

Table 3
Ecotoxicity of β-lactam antibiotics.

Study area	Groups within β-lactams	Names of β-lactam antibiotics	Test organism	Toxicity (mg/L)	NOEC (mg L^{-1})	Test method/ exposure duration	References
China	Penicillins	Amoxicillin	Cyanobacteria (*Microcystis aeruginosa*)	0.0037 and 0.0083 (EC_{50})	NR	Chlorophyll concentration assay, Algal growth inhibition test after 7d exposure	(Liu et al., 2012)
Japan	Penicillins	Ampicillin	Eight cyanobacteria	MIC; 0.0032 to > 200, EC_{50}; 0.00020 to > 200	0.000031–100	Algal growth inhibition test after 144 h	(Ando et al., 2007)
Korea	Penicillins	Ampicillin & Amoxicillin	Bacteria (*Vibrio fischeri*), Invertebrates (*M. macrocopa* and *D. magna*) and fish (*Oryzias latipes*)	For *V. fischeri* EC_{50}. Ampicillin: 1056 (5 mins), 262 (15 mins.). Amoxicillin: 1320 (5 mins.), 3597 (15 mins.). For invertebrates and vertebrates > 1000 for both ampicillin and amoxicillin (no 50% effect at highest tested conc.)	≥ 1000 for both invertebrates and vertebrate	Growth inhibition test of *Vibrio fischeri* after 5 and 15 mins, survival test of invertebrates after 24 h and 48 h, survival test of vertebrate after 48 h and 96 h.	(Park and Choi, 2008)
Spain	Penicillins	Amoxicillin	*P. subcapitata* and recombinant *Anabaena* CPB4337	EC_{50}> 1500 and 56.3, respectively	NR	Growth inhibition, after 72 h, bioluminescent assay after 10 mins	(González-Pleiter et al., 2013)
China	Penicillins	Amoxicillin	*V. fischeri*	LC_{50} 3990	NR	Bioluminescent assay after 15 mins	(Ji et al., 2013)
Korea	Penicillins	Amoxicillin	Microalga (*P. subcapitata*), invertebrates *(M. macrocopa* and *D. magna)*	EC_{50} 213.14 for alga, > 1000 for invertebrates	> 266 for invertebrates (survival), 27.2 and 2.05 for *D. magna* (21d chronic reproduction) and *M. macrocopa* (7 d chronic reproduction)	Growth inhibition 72 h for *P. subcapitata*, reproductive endpoints acute 48 h for invertebrates, chronic 21-d *D. magna* and 7-d *M. macrocopa* tests were also conducted	
Brazil	Penicillins	Amoxicillin	Fish (*Oreochromis niloticus*), aquatic plant (*Lemna minor*) and invertebrates (*Daphnia magna*)	> 2600 (no EC_{50} detected at highest tested conc	2600	Growth inhibition test. 48 h for *O. niloticus* and *D. magna*, and 7 days for L. minor	(De Moraes et al., 2022)
Argentina	Penicillins Cephalosporins	Ampicillin Amoxicillin Cephalothin	Green alga (*P. subcapitata*)	EC50 > 2000 for AMP and AMX, and > 600 for CEP	NR	Growth inhibition test after 72 h	(Magdaleno et al., 2015)
India	Cephalosporins	Cefixime Cefotaxime	*Daphnia magna*	EC_{50} 77.9 and 28.82, respectively	NR	Acute mobility tests after 48 h	(Dutta and Ahmad, 2019)
China	Cephalosporins	Cephalexin, Cefradine	*V. fischeri* and *D. magna*	EC_{50} to *V. fischeri* 1, LC_{50} 0.831 to *D. magna*	NR	Bioluminescent assay after 15 mins and survival test after 48 h	(Hu et al., 2022)
India	Cephalosporins	Cefaclor	Zebrafish embryos	LC_{50} estimated to be 7020, 3189, 1464, and 775 mg/L respectively, at 24, 48, 72, and 96 h	NR	Survival tests up to 96 h	(Kumari et al., 2023)

Note: NR = Not reported

Mitigation requires prudent antibiotic use, including diagnosis-based treatment, correct dosing, preference for narrow-spectrum agents, and the elimination of growth promotion use. Improved water, sanitation, hygiene, and farm management can further reduce the disease burden and dependence on prophylactic antibiotics.

Agriculture, including intensive poultry, swine, and aquaculture farming, uses β-lactams for therapy and prophylaxis. These antibiotics are frequently detected in manure, litter, and slurry, but their persistence is generally low due to rapid hydrolysis at neutral to alkaline pH and high microbial activity. Despite this rapid degradation, agricultural systems remain important reservoirs of resistance. Short-term exposure to sub-mg/kg levels in soil can enrich β-lactam resistance genes, which may persist and spread via runoff and leaching long after the parent compounds have degraded. Consequently, agricultural systems facilitate resistance dissemination through food chains and environmental pathways, underscoring the need for diagnosis-based veterinary prescribing and improved on-farm waste management.

4. Ecotoxicity of β-lactams

Ecotoxicity refers to the potential of a chemical to cause harmful effects on the environment and non-target organisms (Roy and Kar, 2016; He et al., 2024). Due to their widespread use, β-lactam antibiotics and their metabolites are now recognized as relevant environmental contaminants, with toxicity varying according to compound and organism. Experimental studies have demonstrated that even low concentrations can affect algae, invertebrates, and fish (Table 3) (Ando et al., 2007; Dutta and Ahmad, 2019; Hu et al., 2022; Magdaleno et al., 2015).

Cyanobacteria are particularly sensitive. *Microcystis aeruginosa* growth was inhibited at concentrations as low as 0.0037 mg/L after 7 days (Lützhøft et al., 1999). Amoxicillin and related β-lactams can also reduce algal growth, the chlorophyll content, and bioluminescence in cyanobacteria (González-Pleiter et al., 2013). Aquatic invertebrates such as *Daphnia magna* and *Moina macrocopa* display reduced reproduction or mortality under exposure, with chronic effects observed down to ~2 mg/L. Fish (e.g., *Oreochromis niloticus*) and aquatic plants (e.g., *Lemna minor*) are generally less sensitive, with effect concentrations reaching the mg/L to g/L range in some cases (De Moraes et al., 2022; Lee et al., 2021; Park and Choi, 2008).

Cephalosporins (e.g., cefixime, cefotaxime) also exhibit toxicity toward crustaceans and fish embryos. Reported EC50/LC50 values for *Daphnia magna* can be as low as 0.83 mg/L, while fish embryo toxicity varies over time, with LC50 values decreasing from ~7020–775 mg/L over 96 h (Dutta and Ahmad, 2019; Hu et al., 2022; Kumari et al., 2023). These differences highlight strong species and time-dependent variability in sensitivity.

Although β-lactams are often considered non-persistent due to rapid hydrolysis, even low environmental concentrations and short-lived exposure can cause ecological effects (Tiwari et al., 2025). Cephalosporin exposure has been linked to developmental toxicity in zebrafish embryos (Zhang et al., 2013), and chronic exposure at ng–µg/L levels can select for resistant microorganisms and promote ARG dissemination (Harbottle et al., 2006). Thus, even low-level discharges can exert measurable ecological and evolutionary pressure (Kumar and Pal, 2018; Löffler, 2025).

Importantly, β-lactam degradation can produce transformation products that may retain antimicrobial activity or exhibit different ecotoxic profiles. These processes occur in wastewater, surface water, and soil, and their formation and effects have been reported previously (Timm et al., 2019; Baquero et al., 2022; Löffler et al., 2023). This review does not comprehensively address transformation products, which will be covered in future work. Overall, while β-lactams are not typically acutely toxic at environmentally relevant concentrations, chronic low-dose exposure can disrupt aquatic communities and contribute to antimicrobial resistance selection (Xue et al., 2023). Therefore, ecotoxicological assessment should be an integral part of environmental risk evaluation for antibiotics.

Acute ecotoxicity metrics (LC50/EC50/NOEC) generally fall in the mg/L range, above typical environmental concentrations (ng–µg/L). However, sub-inhibitory levels can still drive key ecological effects by selecting resistant bacteria and promoting horizontal gene transfer. These resistance-selective processes, distinct from direct toxicity, are addressed in the next section as a critical component of the environmental AMR risk (Ding et al., 2022; Bengtsson-Palme and Larsson, 2016).

5. Ecological impact of β-lactam antibiotics

Studies have increasingly demonstrated that β-lactam residues disrupt environmental microbial communities and promote AMR within a One Health context. Resistance is influenced by factors such as antibiotic misuse, hospital and industrial discharges, population density, and environmental exposure (Brepoels et al., 2025). Two key ecological effects are recognized: microbial community disruption and selection for resistant pathogens.

Environmental microbes provide essential ecosystem services, including nutrient cycling, organic matter decomposition, and contaminant degradation (Grenni et al., 2018). β-Lactam exposure can alter community composition, reduce functional diversity, and favor resistant strains. Metagenomic studies on river sediments downstream of pharmaceutical plants have reported an elevated prevalence of β-lactamase-producing bacteria and long-term shifts in community structure (Kristiansson et al., 2011), providing direct field evidence that β-lactam pollution can reshape indigenous microbiota. These changes can affect ecosystem functions, such as denitrification, carbon mineralization, and methane production. For example, wetland sediments exposed to mixed antibiotics, including β-lactams, displayed reduced denitrification efficiency and altered greenhouse gas emissions (Thiele-Bruhn and Beck, 2005). Although β-lactams were a major component, the study was not compound-specific, and direct evidence for single-compound effects remains limited.

Chronic exposure to β-lactams creates selective pressure that promotes resistance (Tiwari et al., 2025; Tello et al., 2012). Even low concentrations favor bacteria carrying resistance genes through mutation and horizontal gene transfer (HGT) (Tello et al., 2012; Emara et al., 2023). The extent of selection depends on the concentration, exposure duration, co-selection by metals or biocides, and microbial health (Bustamante et al., 2025). Clinically important enzymes such as ESBLs and carbapenemases ($bla_{\text{CTX-M}}$, bla_{KPC}, bla_{NDM}, and bla_{OXA}) illustrate how environmental pressures translate into public health risks (Al-Mustapha et al., 2025, 2023; Tiwari et al., 2023, 2022b; Bycroft and Shute, 1985; Sorg et al., 2016).

Sub-inhibitory β-lactam concentrations, commonly found in wastewater and receiving waters, do not eliminate bacteria but enhance tolerance and gene exchange (Kadri, 2020; Prestinaci et al., 2015). Laboratory studies have demonstrated that cefotaxime, ampicillin, and meropenem increase plasmid conjugation and the transfer of multidrug-resistance genes in *Escherichia coli* and *Klebsiella pneumoniae* (Liu et al., 2019). Evidence that sub-inhibitory β-lactam concentrations promote resistance amplification comes from laboratory mating experiments, where specific β-lactams increased plasmid conjugation rates and the transfer of multidrug-resistance genes. Similar effects have also been observed in environmental samples from hospital and sewage effluents.

These findings indicate that aquatic environments receiving β-lactam residues act as active reactors for resistance amplification and gene exchange. Thus, the ecological impact of β-lactams extends beyond direct toxicity to long-term evolutionary consequences. Ecotoxicological assessments should therefore consider resistance selection alongside conventional toxicity endpoints.

Table 4
Overview of environmentally friendly analytical methods for β-lactam antibiotic detection across different countries, highlighting sample types, instruments applied, detection accuracy, concentration ranges, and method sensitivity (LOD/LOQ).

Name of Instrument	Sample Matrix/ *n* = number of samples	Groups within β-lactams	Name of β-lactam antibiotics	Detection accuracy (%)	Concentration range (μg/L	LOD (μg/L)	LOQ (μg/L)	References
GO@SiO₂ packed capillary LC-MS/MS	Water sample (tap water, streams, swimming pool, and domestic wastewater) *n* = 10 from each source	Cephalosporins and Penicillins	Cefalexin, Cefoperazone, Ceftiofur and Benzylpenicillin	82.3–107.1	NR	0.2–0.3	1–2	(Maciel et al., 2023)
Large-volume direct injection LC-MS/MS	Bottled drinking water *n* = 3 bottles from 25 brands	Penicillins and Cephalosporins	Amoxicillin, Ampicillin, Cefalexin, Cefotaxime, Ceftiofur and Cefotaxime	66.8–124 (varies by analyte)	0.0000987–0.00442	0.0000184–0.000977	0.0000615–0.00326	(Wang et al., 2025)
Microfluidic paper-based devices (μPADs)	Antibiotics in tablets and liquid *n* = variables	Penicillins	Ampicillin, Amoxicillin, Penicillin V,	Qualitative / semi-quantitative	NR	NR	NR	(Boehle et al., 2018)
Ultrasound-assisted D-μ-SPE–UHPLC-DAD	Water (tap, surface and waste) *n* = 4 for each sample	Cephalosporins	Cefadroxil and Cephalexin,	73.5–98.1	<LOQ to 7.3	0.02–0.16	0.067–0.53	(Bangani et al., 2024)
Micellar liquid chromatography	Hospital wastewater *n* = 25	Penicillins and Cephalosporins	Ceftriaxone and Amoxicillin	96.2–104.6	150–10000	20–180	40–320	(Sharma et al., 2022b)
Micellar liquid chromatography	Maternity hospital wastewater *n* = 66	Penicillins	Amoxicillin	NR	150–11,720	NR	0.02–0.04	(Sharma et al., 2022a)
Green multiplex HPLC–DAD method	Industrial air dust and wastewater *n* = 20 air dust samples, not provided for wastewater	Penicillins	Amoxicillin, Ampicillin, Flucloxacillin, Penicillin G, Benzathine and Piperacillin	98–102	500–50000	100–300	500–1000	(El-Kimary et al., 2023)
Capillary zone electrophoresis tandem mass-spectrometry	Plasma *n* = 6 healthy people, spiked with β- lactam	Penicillins, Cephalosporins and Carbapenem	Amoxicillin Ampicilli, Flucloxacillin, Oxacillin, Piperacillin, Cefotaxime, Ceftazidime and Meropenem	20–40 (Low due to plasma extraction process)	500–40000	9–500	455–1000	(Cizmarova et al., 2024)
Capillary zone electrophoresis with UV-diode array detection (CZE-DAD), coupled with SPE and LVSS for preconcentration	Water (waste, well and river) *n* = NR	Penicillins	Nafcillin, Dicloxacillin, Cloxacillin,Oxacillin, Ampicillin, Penicillin G and Amoxicillin	94–99	N.R.	0.08 and 0.80	N.R.	(Bailón-Pérez et al., 2008)

Note: NR = Not reported; LOD = Limit of Detection; LOQ = Limit of Quantification; LC = Liquid Chromatography; MS/MS = Tandem Mass Spectrometry; SPE = Solid-Phase Extraction; UHPLC = Ultra-High-Performance Liquid Chromatography; DAD = Diode Array Detector; HPLC = High-Performance Liquid Chromatography.

6. β-lactam measurement methods in the environment

Several analytical methods are used in the quantification of β-lactam antibiotics in environmental samples, with their own unique strengths and limitations. Chromatographic methods, most notably liquid chromatography–tandem mass spectrometry (LC-MS/MS) and high-performance liquid chromatography with ultraviolet or diode-array detection, are considered the gold standard due to their high sensitivity, high selectivity and ability to measure multiple β-lactams in a single run, but require expensive instrumentation, well-trained operators and often significant amounts of organic solvent, and some β-lactams require derivatization for good detection (Riezk et al., 2023; Hernández et al., 2026). Immunoassays (e.g., enzyme-linked immunosorbent assays) offer a quick, inexpensive screening option that requires little sample preparation and can be used for high-throughput and field-deployable monitoring; however, they are typically semi-quantitative and may demonstrate cross-reactivity and limited specificity for β-lactam subgroups (Ecke and Schneider, 2021). Microbiological inhibition assays are direct measures of antimicrobial activity, simple to perform, but are not specific, are time-consuming, and can be confounded by the presence of other antimicrobial or toxic substances (Pikkemaat, 2009).

As demand for greener, more portable technologies has grown, a new generation of miniaturized and environmentally friendly technologies has emerged, with the aid of greenness assessment tools like the Analytical GREEness Metric (Vakh and Tobiszewski, 2023). These include graphene oxide–functionalized silica capillary (GO@SiO_2) LC-MS/MS, which has high recoveries (82–107%) and low detection limits (0.2–0.3 μg/L) with significantly reduced solvent consumption (Maciel et al., 2023); microfluidic paper-based devices that allow on-site testing with minimal reagents and high sensitivity (Boehle et al., 2018); capillary zone electrophoresis combined with MS or UV detection, which has reduced organic solvent use but still good sensitivity (Bailón-Pérez et al., 2008; Cizmarova et al., 2024); ultrasound-assisted dispersive micro solid-phase extraction with UHPLC-DAD for fast analysis with low solvent consumption (Bangani et al., 2024) and eco-optimized HPLC-DAD systems for industrial wastewater and air dust samples (El-Kimary et al., 2023) (Table 4).

These green platforms offer clear advantages in terms of reduced reagent waste, portability, and alignment with sustainable laboratory practice, but they are typically less sensitive than conventional LC-MS/MS, are still being validated for a broader range of β-lactams and complex matrices and often deliver semi-quantitative rather than fully quantitative results. The choice of method therefore depends on the monitoring goal whether high-sensitivity quantification, rapid screening, or sustainable field detection and future advances are expected to integrate these green technologies with automated sampling, renewable materials, and artificial-intelligence-assisted data processing for real-time, environmentally responsible antibiotic surveillance.

7. Management strategies to control environmental impacts of β-lactam antibiotics

Addressing antibiotic pollution requires integrated strategies, including green analytical technologies, pollution prevention, remediation, and data-driven monitoring (Fig. 1) (Kaya et al., 2022). Success depends not only on technical innovation but also on regulatory coordination, stakeholder engagement, and global commitment (Tutak and Brodny, 2025). Standardizing green analytical methods within national monitoring frameworks will be important for protecting ecological and public health (Durand et al., 2025).

Applying green chemistry principles to antibiotic production such as solvent reduction, waste valorization, and biodegradable intermediates can further limit pharmaceutical pollution (Alhmoud et al., 2025; Ncube et al., 2023; Zaidi, 2025). Likewise, greener analytical approaches that minimize solvent use, energy demand, and hazardous waste are essential (Kaya et al., 2022). Techniques such as miniaturized extraction, solvent-free preparation, and biosensor-based detection enable real-time, low-impact environmental surveillance while maintaining high monitoring standards (Płotka-Wasylka et al., 2015).

Beyond greener monitoring, advanced wastewater treatments such as the advanced oxidation process (AOP), membrane filtration and adsorption are mostly studied for mitigating β-lactam antibiotics, but

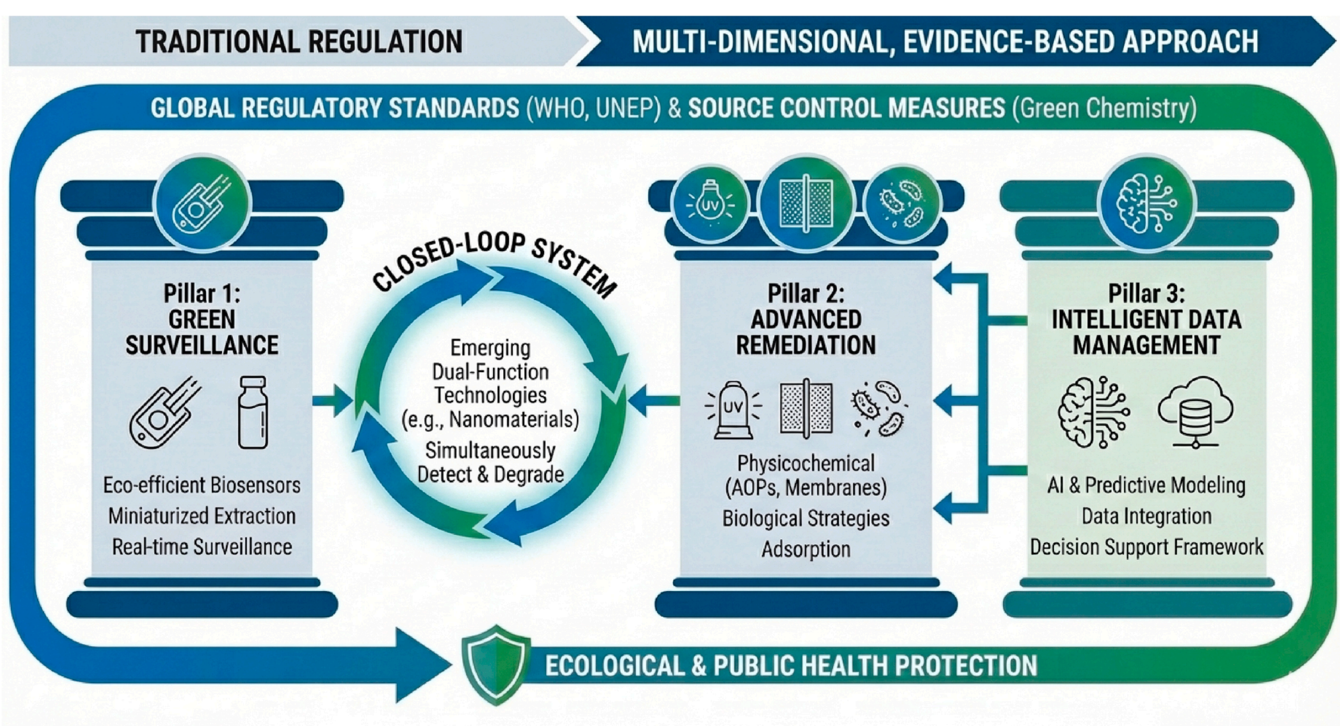

Fig. 1. Integrated sustainable management framework for β-lactam antibiotic residues in the environment.

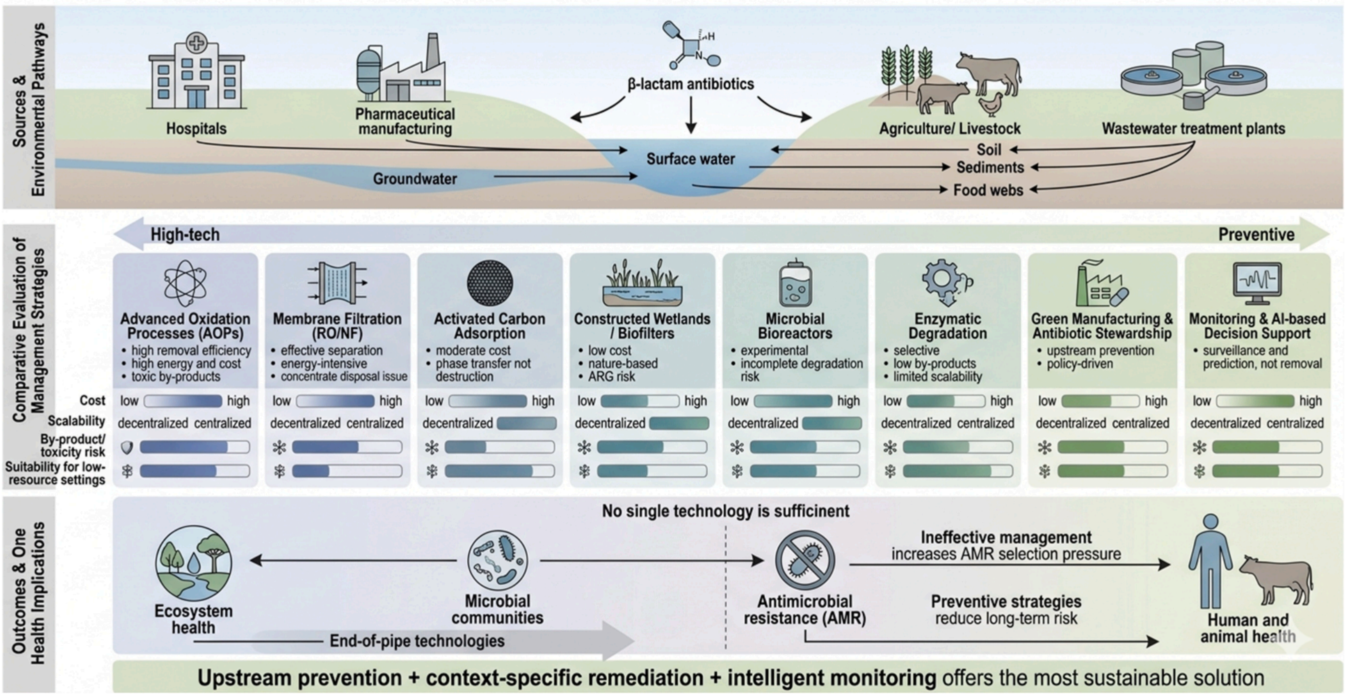

Fig. 2. Conceptual framework linking sources and pathways of β-lactam antibiotics to remediation and prevention technologies, key selection criteria (cost, scalability, by-product risk, low-resource applicability), and management outcomes. The integrated strategy of upstream prevention, context-specific remediation, and intelligent monitoring is emphasized as the most sustainable solution.

Table 5
Comparative evaluation of management strategies for mitigating environmental contamination by β-lactam antibiotic.

Technology	Feasibility	Capital/ operation cost	By-products/ Toxicity	Scalability	Complexity	Low-resource suitability	AMR/Env risk	References
Advance oxidation process (AOPs)	Centralized treatment only; poorly scalable to rural settings	High/High	Some toxic intermediates (e. g. bromate)	Centralized only	High (specialized)	Low	Low (if complete, but incomplete oxidation leaves residues)	(Fatima et al., 2025b)
Membranes filtration (RO/NF)	Proven but energy- and infrastructure -intensive	High/High	Concentrated waste brine, none in effluent	Centralized only	High (fouling control)	Low	Low (retained; concentrate disposal issue)	(Fatima et al., 2025a; Noor et al., 2021; Zhang et al., 2025)
Activated carbon adsorption	Simple, modular, suitable for low-resource settings[1]	Med/Med	No chemical by-products; generates spent carbon	Moderate (modular)	Low (operational)	Medium	Medium (antibiotics are not destroyed)	(Wang et al., 2023)
Constructed wetlands / biofilters	Decentralized and low-resource compatible	Low/Low	Generally benign; metabolites mostly mineralized	Decentralized possible	Low (natural)	High	High (risk of ARG if antibiotics present)	(Lv et al., 2022)
Microbial bioreactors (other)	Dependent on β-lactam biodegradability	Low/Med	Low (mostly biomass + CO_2)	Limited (requires maintenance)	Low to medium	High	High (ARG and incomplete removal)	(Oberoi et al., 2019)
Enzymatic degradation	Lab-scale; promising low AMR risk	Med/High	Minimal (water and innocuous by-products)	Limited (reactors needed)	Medium (bioengineering)	Low	Low (no living cells)	(Singh et al., 2024; Kumar et al., 2019)
Green manufacturing / stewardship	policy-driven, highly suitable for all settings	Low/Zero	None (prevention)	Global (systemic change)	Low (governance)	High	Low (reduces AMR load)	(Rayan, 2023; Haque et al., 2024)
Monitoring / AI systems (sensors, biosensors, data analytics and machine learning)	Scalable digital deployment; trace-level detection	Med/Med	None	Scalable (digital)	High (tech)	Low	NA	(Singh et al., 2023; Masud et al., 2023a)

NA = Not applicable; ENV = Environmental; AMR= Antimicrobial resistance; ARG = Antibiotic resistance gene
[1] Logistical challenges with continuous carbon media supply.

each has limitations that restrict large-scale application (Fig. 2, Table 5).

AOPs (e.g. UV/H_2O_2, ozonation, Fenton) can achieve high removal under controlled conditions yet require high energy and chemical inputs and may generate transformation products with residual antimicrobial or unknown ecotoxic effects, raising concerns about risk substitution rather than true mitigation (Fatima et al., 2025a). Membrane technologies such as nanofiltration and reverse osmosis provide effective physical removal but face challenges including membrane fouling, concentrate disposal, and high capital and operation costs, limiting their feasibility in decentralized or resource-limited system (Noor et al., 2021; Zhang et al., 2025). Adsorption using powdered or granular activated carbon is operationally simple and flexible but does not destroy contaminants, instead transferring them to a secondary waste stream that requires further handling. Its efficiency also declines in complex environmental matrices such as surface waters and agricultural runoff (Wang et al., 2023). Overall, these constraints suggest that physicochemical methods are better applied as targeted, complementary measures rather than standalone solutions for the sustainable management of β-lactam pollution.

Bioaugmentation and enzymatic degradation better align with sustainability goals because they require less energy and generate fewer harmful by-products. β-Lactamase-mediated breakdown and microbial consortia have demonstrated effective transformation of β-lactams in laboratory and pilot studies, but field performance is highly context-dependent, influenced by microbial variability, nutrients, and antibiotic levels. Incomplete degradation may also create selective pressure that supports AMR if poorly managed (Oberoi et al., 2019). Enzymatic degradation can rapidly convert β-lactams into less harmful compounds with minimal by-products, but limitations include enzyme stability, production cost, and the need for controlled conditions (Singh et al., 2024; Kumar et al., 2019). These approaches are best applied as complementary, targeted treatments rather than universal solutions.

Upstream prevention is often more sustainable than downstream remediation. Applying green chemistry principles in β-lactam productions such as avoiding toxic solvents, valorizing waste, and using biodegradable intermediates can reduce the environmental burden before antibiotics enter waste streams, with no remediation cost. Responsible antibiotic use is equally important; reducing misuse and overuse directly lowers environmental emissions and treatment burdens, reinforcing the value of preventive strategies (Rayan, 2023; Haque et al., 2024; Singh et al., 2023; Masud et al., 2023b). Thus, they should serve as decision-support systems rather than standalone solutions. Overall, no single management strategy can adequately address the environmental presence and ecotoxicity of antibiotics across diverse socio-economic contexts; integrated, multi-level approaches are essential.

8. Limitations of the study

This study has several limitations. First, substantial heterogeneity in the sample size, target compounds, environmental matrices, and analytical methods limited direct comparability across studies. Second, the broad scope of the topic, selected to provide a comprehensive overview of the state of the art, may have reduced analytical focus. Third, although most studies used sensitive LC–MS/MS, detection and quantification limits varied widely (LOD: 0.000001–0.01 μg/L; LOQ: 0.001–0.05 μg/L) due to differences in matrices, extraction protocols, and instrumental settings, potentially affecting detection frequencies and concentration. Fourth, reporting, selection, and publication biases may overestimate the occurrence of β-lactam residues. Finally, a clear geographical imbalance exists, with most data from high-income regions and limited data from LMICs, reducing the global representativeness of the findings.

9. Conclusion

β-Lactam antibiotics, an essential part of modern medicine, pose significant environmental challenges due to their poor management practices. Acute toxicity to macrofauna is often limited, but chronic, sublethal, and community-level effects combined with strong selection for ARGs create long-term ecological and public-health risks. Evidence demonstrates that β-lactams affect aquatic and terrestrial systems through direct toxicity to sensitive species (especially photosynthetic microorganisms), disruption of microbial community structure and function, and, most importantly, selection for AMR in environmental reservoirs. These effects occur at concentrations already detected in the environment, indicating real and ongoing ecological impacts.

Addressing β-lactam contamination requires integrated strategies. Advanced wastewater treatment technologies can reduce point-source emissions, while bioremediation offers more sustainable degradation pathways. Nevertheless, the most effective long-term solution is source control through green pharmaceutical design, antimicrobial stewardship, and improved prescribing practices. The environment is not a passive recipient of antibiotic pollution but an active arena for resistance evolution and spread. Protecting environmental integrity and preserving antibiotic efficacy are therefore inseparable goals, demanding a One Health approach that integrates human, animal, and environmental health.

CRediT authorship contribution statement

Nilesh Gupta: Writing – review & editing, Investigation, Formal analysis, Data curation. **Al-Mustapha Ahmad:** Writing – review & editing, Investigation, Formal analysis, Conceptualization. **Kunal Ranjan:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Devasish Bose:** Writing – review & editing, Supervision, Methodology, Investigation. **Girraj Sharma:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Ishi Keenum:** Writing – review & editing, Validation, Methodology, Investigation, Formal analysis. **Memon Shaheryar:** Writing – review & editing, Methodology, Investigation, Data curation. **Ananda Tiwari:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this manuscript, OpenAI ChatGPT was used to assist with language refinement, including spelling, grammar, and readability. Following its use, the authors carefully reviewed, edited, and verified all content. The authors take full responsibility for the accuracy and integrity of the final manuscript. The graphical abstract and figure were prepared with the Gemini tool.

Declaration of Competing Interest

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

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Data availability

No data was used for the research described in the article.

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Further reading

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