

Antibiotic Residues in the Environment: Chemical Persistence and Antimicrobial Resistance

Prof. (Dr.) Udai Arvind

P.G. Department of Chemistry, Jai Prakash University, Chapra, Bihar. India

Mail- uarvind64@gmail.com

Abstract

Antibiotics released into soil and water through human and veterinary use persist in the environment for periods ranging from days to months, depending on their chemical structure, environmental matrix, and prevailing abiotic and biotic degradation processes (Kümmerer, 2009; Sarmah et al., 2006). Even at sub-inhibitory concentrations, these residues can exert selective pressure on environmental bacterial communities, promoting the emergence, maintenance, and horizontal transfer of antibiotic resistance genes (ARGs), with consequences that extend well beyond the immediate site of contamination (Martinez, 2009; Berendonk et al., 2015). This paper reviews the chemical persistence of major antibiotic classes in environmental matrices, presents illustrative degradation kinetic data, and examines the mechanistic link between residual antibiotic concentrations and the selection and spread of antimicrobial resistance. A comparative survey of reported environmental half-lives shows fluoroquinolones and tetracyclines to be markedly more persistent than β -lactams, largely reflecting differences in susceptibility to hydrolysis and photodegradation. First-order kinetic analysis of a model antibiotic in river water yields a degradation rate constant of 0.070 day^{-1} and a half-life of approximately 9.9 days, illustrating the timescales over which sub-lethal selective pressure can be sustained in aquatic systems. A schematic mutant selection window analysis further illustrates how declining environmental concentrations remain within the range that selectively favours resistant mutants for an extended period following a single contamination event. The paper concludes that chemical persistence and resistance selection are mechanistically linked through the duration and intensity of sub-inhibitory exposure, and that environmental risk assessment and mitigation strategies must account explicitly for antibiotic-class-specific degradation behaviour rather than treating antibiotic residues as a uniform contaminant category.

Keywords: Antibiotic residues, Environmental persistence, Antimicrobial resistance (AMR), Antibiotic resistance genes (ARGs), Degradation kinetics, Sub-inhibitory selection, Fluoroquinolones, Tetracyclines, Horizontal gene transfer; Environmental risk assessment.

1. Introduction

The widespread use of antibiotics in human medicine, livestock production, and aquaculture has resulted in the continuous release of antibiotic residues into soil, surface water, groundwater, and sediment through excretion, improper disposal, manure application, and wastewater effluent (Kümmerer, 2009; Sarmah et al., 2006). Unlike acute chemical pollutants whose primary hazard is direct toxicity, the environmental significance of antibiotic residues lies substantially in their capacity to act at sub-inhibitory concentrations as a chronic selective pressure on bacterial populations, favouring organisms that carry

or acquire resistance determinants (Martinez, 2009; Andersson & Hughes, 2014).

The environmental fate of an antibiotic — how long it persists, in what form, and at what concentration — is therefore not merely a question of chemical fate and transport but a direct determinant of the intensity and duration of resistance selection pressure in a given environmental compartment (Berendonk et al., 2015). Antibiotics vary enormously in their environmental persistence depending on their chemical structure: β -lactams are inherently unstable owing to a strained, hydrolytically labile ring system, whereas fluoroquinolones and tetracyclines are comparatively resistant to microbial and hydrolytic breakdown and

can persist for months in soil, particularly when strongly sorbed to organic matter or clay minerals (Sarmah et al., 2006; Boxall et al., 2004).

This paper reviews the principal chemical processes governing antibiotic persistence in the environment, compares the reported environmental half-lives of major antibiotic classes, presents an illustrative first-order degradation kinetic analysis, and examines the mechanistic pathway connecting residual antibiotic exposure to the selection and environmental spread of antimicrobial resistance genes.

The public-health stakes of this environmental pathway are substantial. The most comprehensive global assessment to date estimated that bacterial antimicrobial resistance was directly responsible for approximately 1.27 million deaths in 2019 and was associated with a further 4.95 million deaths, making AMR a leading cause of death worldwide and comparable in scale to HIV/AIDS or malaria (Murray et al., 2022). While clinical antibiotic use and stewardship receive the greatest policy attention, the environmental compartment reviewed in this paper constitutes a parallel and continuously replenished selective pressure that operates largely outside the reach of clinical antibiotic stewardship programmes, underscoring the importance of understanding the chemistry of environmental persistence as a component of the broader AMR mitigation agenda.

2. Chemical Persistence of Antibiotics in the Environment

2.1 Structural Determinants of Degradation Susceptibility

The environmental persistence of an antibiotic is governed primarily by its chemical structure and the specific functional groups that render it susceptible, or resistant, to hydrolysis, photolysis, and microbial biodegradation (Kümmerer, 2009). β -Lactam antibiotics (penicillins, cephalosporins) contain a four-membered β -lactam ring under considerable ring strain, which is readily hydrolysed by water, hydroxide ion, or bacterial β -lactamase enzymes; this structural vulnerability accounts for their generally short environmental half-lives, often on the order of hours to a few days (Sarmah et al., 2006). Tetracyclines, by contrast, possess a stable four-fused-ring system and

can persist for weeks to months, particularly when complexed with divalent cations (Ca^{2+} , Mg^{2+}) that reduce their bioavailability for microbial degradation while simultaneously enhancing their sorption to soil particles (Boxall et al., 2004).

Fluoroquinolones exhibit some of the longest reported environmental half-lives among common antibiotic classes, owing to the combination of a stable fused bicyclic core and strong sorption to organic matter and clay minerals via their carboxylic acid and ketone functional groups, which limits both leaching and microbial accessibility (Boxall et al., 2004; Sarmah et al., 2006). Sulfonamides and macrolides occupy an intermediate position, showing moderate susceptibility to both photodegradation and microbial breakdown, with reported half-lives typically in the range of one to several weeks depending on matrix and environmental conditions (Kümmerer, 2009). It is also important to note that the disappearance of the parent compound does not necessarily equate to loss of biological activity: hydrolysis and photolysis frequently generate transformation products that retain partial antimicrobial activity or, in some documented cases, exceed the parent compound in toxicity or persistence, so half-life values based solely on parent-compound quantification can understate the true duration of selective pressure exerted by a given contamination event (Kümmerer, 2009).

2.2 Environmental Matrix and Abiotic/Biotic Degradation Pathways

Beyond intrinsic chemical structure, the persistence of a given antibiotic is strongly modulated by the environmental matrix in which it resides. In surface water exposed to sunlight, direct and indirect photolysis is often the dominant degradation pathway for fluoroquinolones and sulfonamides, both of which absorb strongly in the near-UV region (Kümmerer, 2009). In soil and sediment, sorption to organic matter and mineral surfaces can substantially retard both photodegradation (by removing the antibiotic from the illuminated water column) and microbial biodegradation (by reducing bioavailability), effectively extending the apparent environmental half-life relative to the same compound in unsorbed, dissolved-phase conditions (Sarmah et al., 2006; Boxall et al., 2004). Biotic degradation by soil and

aquatic microbial communities is generally slower for antibiotics than for many other classes of organic contaminants, in part because antibiotics are, by their biological function, inhibitory to a substantial fraction of the microbial community that might otherwise metabolise them.

2.3 Environmental Concentrations and Analytical Detection

Measured environmental antibiotic concentrations are generally low in absolute terms, typically ranging from low nanograms-per-litre to a few micrograms-per-litre in surface water and wastewater effluent, with higher concentrations ($\mu\text{g kg}^{-1}$ to mg kg^{-1}) commonly reported in soils receiving manure or biosolid amendments and in sediments downstream of aquaculture or pharmaceutical-manufacturing discharge (Sarmah et al., 2006; Boxall et al., 2004). These concentrations are almost invariably far below the minimum inhibitory concentrations relevant to clinical dosing, which is precisely what places most environmental exposure scenarios within the sub-inhibitory selective range discussed in Section 5.1 rather than in a directly bactericidal range. Reliable quantification at these trace levels generally requires solid-phase extraction coupled with liquid chromatography–tandem mass spectrometry (LC-MS/MS), which offers the sensitivity and specificity needed to distinguish individual antibiotic compounds, and increasingly their transformation products, from the complex chemical background of environmental water, soil, and sediment matrices (Kümmerer, 2009). Because detection limits, extraction efficiency, and matrix effects vary considerably between analytical laboratories and published studies, reported environmental concentrations and half-lives, including those summarised in Figure 1, should be interpreted as order-of-magnitude indicators rather than precise, directly comparable values.

3. Comparative Persistence Across Antibiotic Classes

Figure 1 summarises representative ranges of reported environmental half-lives in soil for five major

antibiotic classes, compiled from the persistence literature discussed above.

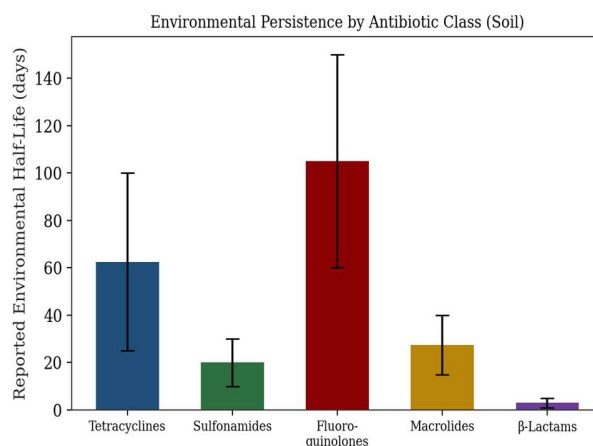


Fig. 1. Reported ranges of environmental half-life (days) in soil for five major antibiotic classes.

Fluoroquinolones show the longest and most variable reported half-lives (60–150 days), consistent with their strong sorption behaviour and resistance to microbial breakdown, followed by tetracyclines (25–100 days). Macrolides and sulfonamides show intermediate persistence (15–40 and 10–30 days, respectively), while β -lactams are the least persistent by a wide margin (1–5 days), consistent with their inherent hydrolytic instability (Sarmah et al., 2006; Boxall et al., 2004; Kümmerer, 2009). This more-than-order-of-magnitude variation across classes has direct implications for resistance selection: a compound that persists for months provides a sustained selective window during which resistant strains can be favoured and can proliferate, whereas a compound that degrades within days limits the duration of any selective pressure to a comparatively narrow interval following release.

The wide error bars shown for fluoroquinolones and tetracyclines in Figure 1 are themselves informative: they reflect genuine variability driven by soil organic-matter content, clay mineralogy, pH, and temperature across the underlying studies, rather than simple measurement imprecision, and indicate that site-specific conditions can shift a given compound's effective persistence by several-fold in either direction relative to the class average (Sarmah et al., 2006; Boxall et al., 2004). This variability means that class-level persistence rankings, while useful as a first-order screening tool for prioritising monitoring and mitigation effort, should not substitute for site-specific

characterisation when precise resistance-selection risk estimates are required for a particular location.

4. Degradation Kinetics: A Worked Example

Environmental degradation of most antibiotics under a given set of conditions can often be approximated by first-order kinetics, $C = C_0 \cdot e^{(-kt)}$, where C_0 is the initial concentration, k is the first-order degradation rate constant, and t is time; the corresponding half-life is $t_{1/2} = \ln(2)/k$ (Kümmerer, 2009). Figure 2 presents an illustrative first-order kinetic analysis for a model antibiotic in river water under natural sunlight and ambient microbial activity.

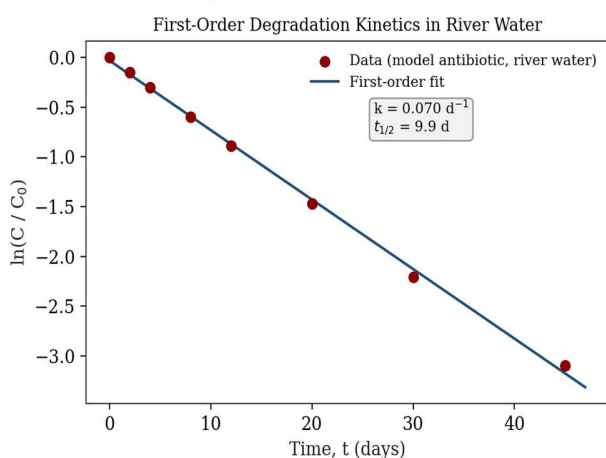


Fig. 2. First-order degradation kinetics ($\ln(C/C_0)$ vs. time) for a model antibiotic in river water, yielding $k = 0.070 \text{ day}^{-1}$ and $t_{1/2} \approx 9.9 \text{ days}$.

The strong linearity of $\ln(C/C_0)$ against time confirms that first-order kinetics provide a good approximation of the degradation behaviour over the 45-day observation window, and the derived half-life of approximately 9.9 days falls within the intermediate persistence range typical of sulfonamide- or macrolide-class compounds in illuminated surface water (Kümmerer, 2009). This timescale is environmentally significant: a half-life of roughly ten days means that measurable residual concentrations, and thus measurable selective pressure on the local microbial community, can persist through several bacterial generation times following a single contamination event, and can be continuously replenished in systems receiving ongoing wastewater or agricultural runoff inputs (Andersson & Hughes, 2014).

The apparent first-order rate constant derived in Figure 2 is itself a composite quantity that folds

together several underlying processes and their respective environmental sensitivities. Direct photolysis depends on the compound's molar absorptivity at solar wavelengths and the incident irradiance, and therefore varies diurnally and seasonally as well as with water depth and turbidity, which attenuate light penetration; indirect photolysis mediated by photosensitisers such as dissolved organic matter, nitrate, and reactive oxygen species adds a further, matrix-dependent contribution (Kümmerer, 2009). Microbially mediated biodegradation, in turn, generally follows an approximately exponential dependence on temperature over the environmentally relevant range, such that the same river system can exhibit a measurably shorter half-life in summer than in winter. Because the worked example in Figure 2 reflects a single set of seasonal, matrix, and irradiance conditions, the derived $k = 0.070 \text{ day}^{-1}$ should be read as representative of comparable conditions rather than as a fixed, universal rate constant for the model compound.

5. From Persistence to Resistance Selection

5.1 Sub-Inhibitory Selection and the Mutant Selection Window

A central mechanistic concept linking antibiotic persistence to resistance is the 'mutant selection window' — the range of antibiotic concentrations, generally well below the minimum inhibitory concentration (MIC) required to kill susceptible bacteria, within which resistant mutants are selectively favoured over susceptible wild-type strains because they retain a growth advantage at concentrations still sufficient to partially inhibit susceptible competitors (Andersson & Hughes, 2014). Because environmental antibiotic concentrations following contamination events are typically several orders of magnitude below clinical or agricultural dosing concentrations, and decline further as the compound degrades, environmental exposure often falls squarely within this sub-inhibitory selective window for extended periods, particularly for the more persistent antibiotic classes identified in Section 3 (Martinez, 2009).

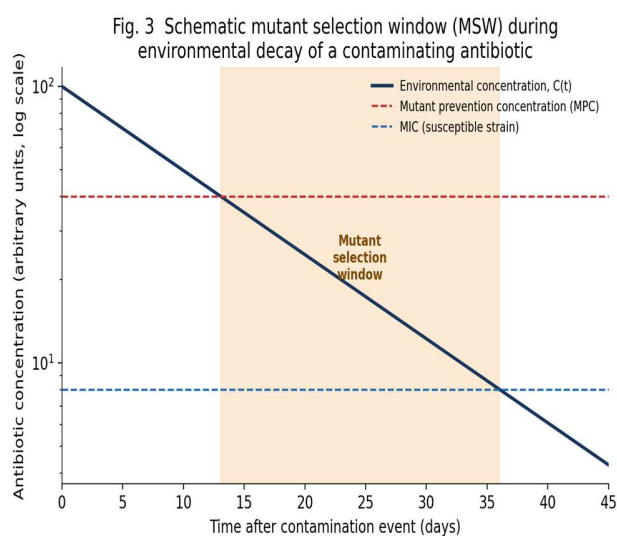


Fig. 3. Schematic mutant selection window (MSW) during environmental decay of a contaminating antibiotic, using the first-order decay constant from Figure 2 ($k = 0.070 \text{ day}^{-1}$) against illustrative MIC and mutant prevention concentration (MPC) thresholds.

Applying the degradation kinetics from Figure 2 to a schematic mutant selection window illustrates the point concretely: taking illustrative threshold values for the MIC of a susceptible strain and the mutant prevention concentration (MPC, the lowest concentration that blocks growth of the least-susceptible first-step mutant), the declining concentration curve remains within the mutant selection window for roughly three weeks following a single contamination event, a substantial fraction of the compound's overall persistence and easily sufficient time for many bacterial generations to pass under selective conditions (Andersson & Hughes, 2014). Because the width of the window in concentration terms, and thus its duration in time terms for a given decay rate, differs across antibiotic–pathogen combinations, compounds with both long environmental half-lives and wide mutant selection windows are expected to pose disproportionately elevated resistance-selection risk relative to their persistence ranking in Figure 1 alone.

5.2 Horizontal Gene Transfer and the Environmental Resistome

Sustained sub-inhibitory antibiotic exposure not only selects for pre-existing resistant strains but can

also promote horizontal transfer of antibiotic resistance genes between bacteria via plasmids, transposons, and integrons, a process that can be directly stimulated by sub-lethal antibiotic concentrations through induction of the bacterial SOS stress response and increased conjugation frequency (Martinez, 2009; Berendonk et al., 2015). Environments receiving persistent, recurrent antibiotic inputs — including wastewater treatment plant effluents, aquaculture facilities, and soils amended with animal manure — have been repeatedly identified as reservoirs of an expanded 'environmental resistome,' in which resistance genes accumulate, diversify, and are exchanged among both pathogenic and non-pathogenic bacteria (Berendonk et al., 2015).

Because more persistent antibiotic classes maintain sub-inhibitory concentrations for longer, the antibiotic-class-specific persistence data summarised in Figure 1 provide a first-order proxy for the relative resistance-selection risk associated with different antibiotic residues, with fluoroquinolone- and tetracycline-contaminated environments predicted, and in several field studies observed, to harbour a higher relative abundance of corresponding resistance genes than environments contaminated primarily with more rapidly degrading β -lactams (Berendonk et al., 2015; Martinez, 2009).

The resistome-expanding effect of persistent antibiotic residues is often compounded by co-occurring, non-antibiotic selective agents. Heavy metals such as copper, zinc, and silver, widely used as growth promoters and antimicrobials in livestock production and present as background contaminants in many soils, can co-select for antibiotic resistance genes when the corresponding resistance determinants are physically linked on the same plasmids, transposons, or integrons as metal-resistance genes, such that exposure to the metal alone is sufficient to maintain the antibiotic-resistance determinant in the population even in the complete absence of antibiotic residues (Berendonk et al., 2015). Biocides used in agricultural and clinical disinfection can act through an analogous linked-resistance or shared-efflux-pump mechanism. Because heavy metals in particular are essentially non-degradable and can therefore persist far longer than even the most recalcitrant antibiotic classes discussed in Section 3, environments with a history of combined antibiotic and metal contamination may sustain elevated antibiotic-resistance gene prevalence long

after the antibiotic residue itself has fallen below detectable concentrations.

6. Discussion and Implications for Mitigation

The persistence–resistance linkage developed in this paper has practical implications for both environmental monitoring and antibiotic stewardship. Because resistance selection risk depends jointly on antibiotic concentration and duration of exposure, mitigation strategies that reduce either variable — through improved wastewater treatment capable of removing persistent antibiotic classes, restrictions on the agricultural use of the most environmentally persistent compounds, or engineered degradation approaches such as advanced oxidation processes for fluoroquinolone-contaminated effluent — are expected to reduce resistance selection pressure more effectively than approaches that address antibiotic concentration alone without regard to persistence (Kümmerer, 2009; Sarmah et al., 2006).

Set against the roughly 1.27 million deaths directly attributable to bacterial AMR each year (Murray et al., 2022), even a partial reduction in the duration of environmental sub-inhibitory exposure achieved by targeting the most persistent antibiotic classes could plausibly contribute a meaningful, if currently unquantified, reduction in the future trajectory of resistance-attributable morbidity and mortality. This argues for treating environmental persistence data of the kind summarised in Figure 1 as a practical prioritisation tool: regulatory and infrastructure investment aimed at reducing fluoroquinolone and tetracycline residues, which combine high persistence with substantial global usage volumes, is likely to yield a disproportionately large reduction in cumulative sub-inhibitory exposure per unit of investment relative to equivalent efforts directed at the comparatively short-lived β -lactam class.

A key limitation of the current evidence base, reflected also in the illustrative data presented here, is that most persistence and resistance-selection studies have been conducted under controlled laboratory conditions that may not fully capture the complexity of real-world environmental matrices, mixed-antibiotic exposures, and the co-occurrence of other selective pressures such as heavy metals and biocides, which

have been shown to co-select for antibiotic resistance through shared or linked resistance mechanisms (Berendonk et al., 2015). Field-scale, longitudinal monitoring that links antibiotic residue concentrations directly to resistance gene abundance over time would substantially strengthen the mechanistic case developed here.

7. Conclusion

Antibiotic residues persist in soil and water for durations that vary by more than an order of magnitude across major antibiotic classes, governed primarily by structural susceptibility to hydrolysis, photolysis, and microbial degradation, and secondarily by sorption behaviour within the environmental matrix. Illustrative comparative data show fluoroquinolones and tetracyclines to be substantially more persistent than β -lactams, and a first-order kinetic analysis of a model antibiotic in river water yields a half-life of approximately ten days, illustrating the timescales over which environmental selective pressure can be sustained. This persistence is mechanistically linked to antimicrobial resistance through sub-inhibitory selection within the mutant selection window and through stimulation of horizontal gene transfer, such that more persistent antibiotic classes are associated with a greater relative risk of environmental resistance gene accumulation. Addressing antibiotic residues as a driver of antimicrobial resistance therefore requires explicit attention to class-specific chemical persistence, not merely to initial release concentrations, in both environmental risk assessment and mitigation policy. Given that AMR is already among the leading causes of death worldwide, closing the gap between clinical antibiotic stewardship and environmental antibiotic management represents one of the more tractable, evidence-based opportunities available for reducing the future global burden of resistant infection.

References

- Andersson, D. I., & Hughes, D. (2014). Microbiological effects of sublethal levels of antibiotics. *Nature Reviews Microbiology*, 12(7), 465–478.
- Berendonk, T. U., Manaia, C. M., Merlin, C., Fatta-Kassinos, D., Cytryn, E., Walsh, F., Bürgmann,

- H., Sørum, H., Norström, M., Pons, M.-N., Kreuzinger, N., Huovinen, P., Stefani, S., Schwartz, T., Kisand, V., Baquero, F., & Martinez, J. L. (2015). Tackling antibiotic resistance: The environmental framework. *Nature Reviews Microbiology*, 13(5), 310–317.
- Boxall, A. B. A., Kolpin, D. W., Halling-Sørensen, B., & Tolls, J. (2004). Are veterinary medicines causing environmental risks? *Environmental Science & Technology*, 37(15), 286A–294A.
- Kümmerer, K. (2009). Antibiotics in the aquatic environment — A review — Part I. *Chemosphere*, 75(4), 417–434.
- Martinez, J. L. (2009). Environmental pollution by antibiotics and by antibiotic resistance determinants. *Environmental Pollution*, 157(11), 2893–2902.
- Murray, C. J. L., Ikuta, K. S., Sharara, F., Swetschinski, L., Robles Aguilar, G., Gray, A., et al. (2022). Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. *The Lancet*, 399(10325), 629–655.
- Sarmah, A. K., Meyer, M. T., & Boxall, A. B. A. (2006). A global perspective on the use, sales, exposure pathways, occurrence, fate and effects of veterinary antibiotics (VAs) in the environment. *Chemosphere*, 65(5), 725–759.