

Review

A Critical Review of Advanced Removal and Degradation of Antibiotics from Pharmaceutical Wastewater

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Abstract

The discharge of antibiotic residues into aquatic environments promotes antimicrobial resistance (AMR). Conventional wastewater treatment is ineffective at removing these persistent micropollutants, necessitating the use of advanced strategies. This review critically assesses the efficacy of advanced oxidation processes (AOPs), adsorption, membrane separation, and advanced biological treatments for antibiotic removal from pharmaceutical wastewater. While techniques like photocatalysis and ozonation achieve high degradation rates (>90%) in controlled settings, significant challenges, including energy consumption, catalyst management, toxic byproduct formation, and economic feasibility, hinder their scalability. Findings indicate that successful demonstrations remain confined mainly to synthetic wastewater in laboratory studies. This review identifies a gap between lab research and real-world use. We conclude that overcoming this barrier requires a dedicated focus on developing hybrid treatment systems. This review therefore recommends prioritizing the development of scalable, cost-effective solutions validated with complex, real-world wastewater to mitigate the environmental and public health risks posed by antibiotic pollution.

Keywords: pharmaceutical wastewater, antimicrobial resistance, advanced oxidation processes, hybrid treatment systems, water purification, environmental remediation

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Introduction

Antimicrobial resistance (AMR) is growing worldwide. The WHO has declared it one of the top ten global public health threats. This crisis is fueled by antibiotic residues spreading in the environment. The proliferation of antibiotic residues in the global aquatic environment represents a significant environmental challenge, directly fueling the spread of AMR [1]. While essential in medicine, a significant portion of administered antibiotics is excreted unmetabolized, entering wastewater streams from municipal, hospital, and industrial sources [2, 3]. Conventional wastewater treatment plants (WWTPs) are poorly equipped to remove these persistent, bioactive compounds, often achieving highly variable and incomplete elimination (20-90%) [4, 5]. Consequently, WWTPs become significant point sources for the discharge of antibiotic residues, along with antibiotic-resistant bacteria (ARBs) and antibiotic resistance genes (ARGs), into receiving water bodies [6, 7]. Hospital wastewater has been identified as a major reservoir for ARGs, with recent meta-analyses confirming their high abundance and transfer dynamics of intracellular and extracellular resistomes [8, 9].

This pollution creates two main problems. First, even low levels of antibiotics in the environment create pressure that drives bacteria to evolve resistance. This promotes the spread of antibiotic resistance genes (ARGs) among microorganisms, expanding the pool of resistance traits in nature [10]. Second, certain antibiotics and their transformation products can induce ecotoxicological effects on aquatic flora and fauna, disrupting microbial community structures and ecosystem functions [11, 12].

These persistent threats represent a continuous environmental burden, but their magnitude can be sharply amplified during global health emergencies that trigger mass antibiotic consumption and altered waste streams. The COVID-19 pandemic exemplifies this amplification, where escalated consumption of antibiotics like azithromycin and doxycycline led to their increased environmental detection, underscoring the fragility of our current wastewater management infrastructure in the face of emerging public health emergencies [13]. The challenge of remediation is compounded by the structural complexity and stability of antibiotic molecules from β -lactams and fluoroquinolones to tetracyclines and sulfonamides, which are designed to resist degradation and target specific biological functions [11, 12]. Their persistent and polar nature, coupled with the complex matrix of real wastewater (high COD, BOD, and competing organic matter), renders traditional biological treatment processes largely ineffective [13, 14]. Comprehensive overviews of the environmental occurrence, toxicity, degradation pathways, and removal methods for antibiotics in wastewater are available [18, 19].

Therefore, advancing beyond conventional treatment paradigms is not merely an engineering challenge but an urgent need for public and environmental health. This review critically examines the frontier of advanced remediation technologies for antibiotic removal from pharmaceutical wastewater, providing a critical evaluation of advanced oxidation processes, adsorption, membrane separation, and advanced biological treatments. While previous reviews have cataloged individual technologies for antibiotic removal, this analysis provides a critical synthesis that explicitly maps a gap between lab research and real-world use. We argue that the paradigm must shift from optimizing standalone units to the intelligent design of synergistic, smart, and circular systems, and we provide a concrete roadmap to bridge this gap. By bridging the gap between laboratory innovation and full-scale implementation, this analysis aims to guide the development of sustainable, efficient, and scalable solutions that safeguard water resources.

Experimental

This review employed a systematic literature review to identify and evaluate advanced technologies for removing antibiotics from pharmaceutical wastewater. A comprehensive search was conducted in the Web of Science Core Collection for peer-reviewed articles published from 2010-01-01 to 2025-12-09, using the key terms (“pharmaceutical wastewater” OR “antibiotic wastewater”) AND (“antibiotic remov*” OR “antibiotic degrad*”) within titles, abstracts, and keywords. The search was focused on English-language publications. Duplicate records were identified and removed using Zotero. The screening and selection process followed the PRISMA framework, as illustrated in Fig. 1. A total of 135 records were identified from the Web of Science.

After the removal of duplicate and ineligible records, 114 records were screened by title and abstract, resulting in 92 reports sought for retrieval, 83 of which were assessed for full-text eligibility. Ultimately, 60 studies met the inclusion criteria, which required quantitative performance data on advanced treatment technologies (e.g., AOPs, adsorption, membrane processes, hybrid systems) applied to real or synthetic wastewater containing antibiotics. Articles limited to conventional activated sludge without modification, purely theoretical studies, and non-English publications were excluded. Relevant studies were also identified in reference lists.

Results and Discussion

The Complexity and Environmental Significance of Pharmaceutical Wastewater with Antibiotics

Effectively reducing antibiotic pollution is challenging because pharmaceutical wastewater, the primary source, is inherently complex. Unlike

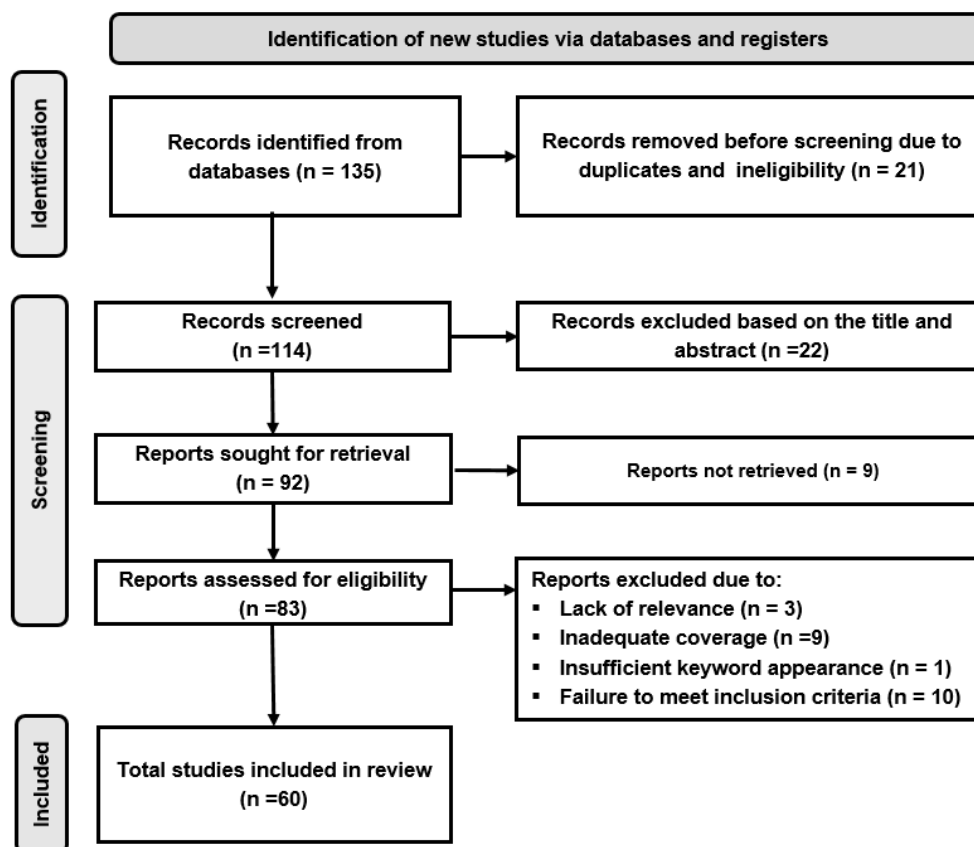


Fig. 1. PRISMA flow diagram illustrating the record identification, screening, and inclusion process.

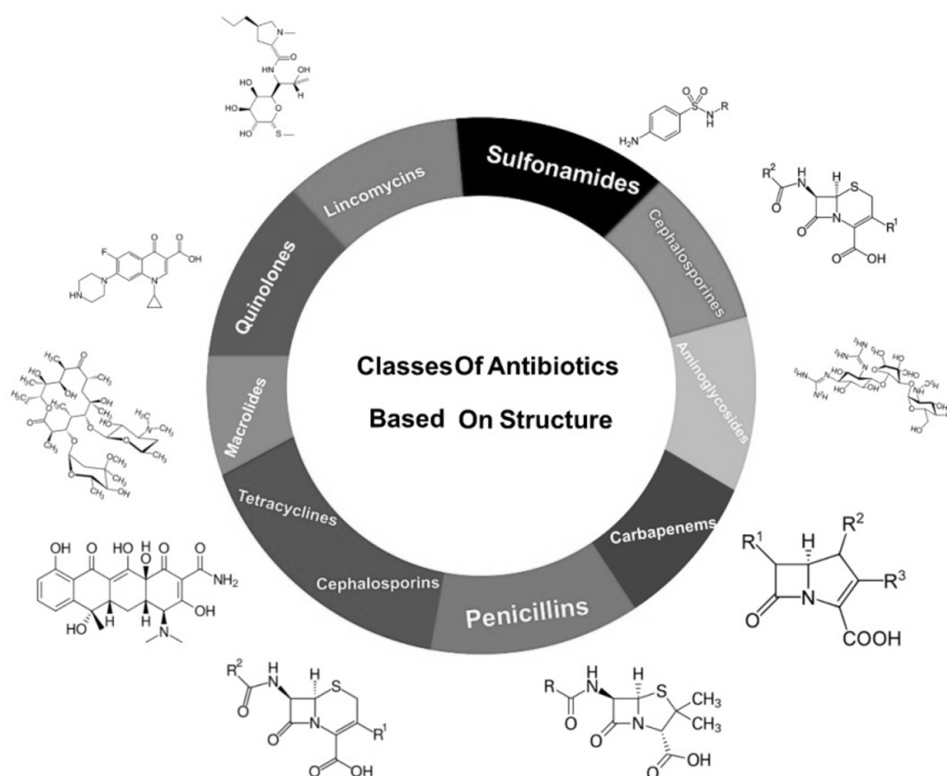


Fig. 2. Classification of antibiotics according to their structures, with the main structural types provided for each category. This structural diversity (e.g., β -lactam rings, tetracyclic systems) directly influences antibiotic persistence, reactivity, and the selection of appropriate removal technologies, underscoring the need for tailored treatment approaches.

Table 1. Sources and classification of pharmaceutical wastewater.

Source category	Description	Key characteristics & challenges
Industrial Effluents from Pharmaceutical Manufacturing (PIM)	Point-source pollution from antibiotic and drug production facilities.	<ul style="list-style-type: none"> Extremely high concentrations of Active Pharmaceutical Ingredients (APIs): hundreds to thousands of mg/L [3]. High organic solvent content, COD, and TDS [16]. Composition is specific to the manufacturing process (single compound or complex cocktail) [1, 2]. One of the most challenging streams to treat [16].
Hospital Effluents	Wastewater from healthcare facilities containing excreta from patients.	<ul style="list-style-type: none"> Lower concentration of individual antibiotics ($\mu\text{g/L}$ to mg/L) but a much greater diversity of compounds (antibiotics, analgesics, disinfectants) [2]. Complex matrix containing pathogens, hazardous chemicals, and Antibiotic-Resistant Bacteria (ARBs) [3, 4]. A significant hotspot for the horizontal transfer of Antibiotic Resistance Genes (ARGs) [5, 6].
Municipal WWTP Effluents	The ultimate receptor for pharmaceuticals from the general population, hospitals, and some industries.	<ul style="list-style-type: none"> A dilute but pervasive source of antibiotic pollution [6]. Conventional WWTPs are ineffective at removing many persistent, polar antibiotics [4]. WWTPs act as a significant point source for the release of antibiotic residues, ARBs, and ARGs into the environment [7]. Load can spike during events like pandemics [13].

municipal sewage, which has a relatively consistent pollutant profile, pharmaceutical wastewater is a highly heterogeneous and dynamic matrix whose composition reflects its diverse origins. This variability presents a formidable challenge for the development of universal treatment solutions and dictates that effective remediation strategies must be tailored to specific waste streams. A critical understanding of its sources and characteristics is therefore not merely a taxonomic exercise, but a prerequisite for designing intelligent, scalable treatment systems. This section delineates the significant sources of antibiotic-laden wastewater. It analyzes the key physicochemical and biological characteristics that govern its treatability, placing this in the broader context of its important environmental and public health impacts. Fig. 2 displays the classification of antibiotics by structure, with the main structural types for each category.

Sources and Pathways: A Multi-Sectoral Challenge

Pharmaceutical wastewater enters the aquatic environment through several distinct yet interconnected pathways, each contributing to a unique signature of contamination. These sources can be broadly classified into three categories, as summarized in Table 1. Advanced predictive models, such as neural networks, have been successfully applied to forecast removal of suspended solids and chemical oxygen demand in pharmaceutical wastewater treatment plants [20].

Key Characteristics Governing Treatability and Environmental Risk

The efficacy of any treatment technology depends on the physicochemical and biological properties of

the wastewater matrix and the pollutants it contains. For pharmaceutical wastewater, several intertwined characteristics critically influence treatability and ultimately determine environmental fate and risk, as detailed in Table 2.

Technological Responses: A Critical Analysis of Treatment Paradigms

The heterogeneous nature of pharmaceutical wastewater necessitates the use of advanced technologies. A critical evaluation of these approaches is essential to understand the current technological landscape. Table 3 includes Technology Readiness Level (TRL, 1-9) and Relative Cost & Energy Intensity (Low, Medium, High) for each technology to illustrate the gap between innovation and application. For example, photocatalysis has a TRL of 4-5 (experimental stage) with medium-to-high cost/energy, while adsorption using activated carbon is highly mature (TRL 9) with low-to-medium operational cost.

Advanced Treatment Technologies for Antibiotic Removal and Degradation

The inefficacy of conventional wastewater treatment plants (WWTPs) against antibiotic residues has catalyzed the development of advanced remediation strategies. These technologies primarily operate through two fundamental mechanisms: (i) destructive processes that mineralize antibiotics into innocuous end products (e.g., CO_2 , H_2O , inorganic ions) and (ii) separative processes that extract antibiotics from the aqueous phase for subsequent concentration and disposal or treatment. This section provides a critical evaluation of these advanced technologies, assessing their mechanistic

Table 2. Key characteristics influencing treatability.

Key characteristic	Impact on treatability
Complex and Variable Matrix	Real wastewater contains a high background of organic matter (COD/BOD), nutrients, salts, and other competing micropollutants. This matrix can scavenge reactive species (e.g., $\bullet\text{OH}$ in AOPs), foul membranes and catalysts, and shield microorganisms in biological processes, significantly reducing treatment efficiency for target antibiotics [10, 11].
Structural Complexity and Persistence of Antibiotics	Antibiotics are engineered to be stable, bioactive molecules that resist degradation. Structural features like β -lactam rings or complex aromatic systems are designed to withstand enzymatic breakdown, making them difficult to remove via conventional biological treatment [15].
Polarity and Water Solubility	The polar or ionizable nature of many antibiotics results in high water solubility. This prevents their effective removal via traditional separation processes such as sedimentation, thereby keeping them in the aqueous phase and facilitating their transport through aquatic environments [17].
Toxicity and Inhibition	The antimicrobial properties of these compounds can inhibit microbial consortia essential to biological wastewater treatment processes. High concentrations can disrupt activated sludge and impede advanced biological systems, necessitating robust pre-treatment or dilution [11].
Propagation of Antibiotic Resistance	Sub-inhibitory concentrations of antibiotics provide selective pressure that promotes the survival of ARBs and facilitates the horizontal gene transfer of ARGs among bacterial populations, thereby amplifying and dispersing resistance traits into the environment [10].

principles, efficacy, scalability, and limitations within the complex context of real pharmaceutical wastewater matrices. Methods for the removal and degradation of antibiotic pollutants are detailed in Fig. 3.

Destructive Technologies: Advanced Oxidation Processes

Advanced oxidation processes (AOPs) are a suite of chemical treatments designed to mineralize recalcitrant organic pollutants by generating highly reactive species in situ, most notably the hydroxyl radical (OH , $E^\circ = 2.8 \text{ V}$). Other essential oxidants include sulfate radicals ($\text{SO}_4\bullet^-$, $E^\circ = 2.5\text{-}3.1 \text{ V}$), which can be generated by the thermal or UV activation of persulfate (PS) or peroxymonosulfate (PMS), or by the action of transition metals or carbon-based catalysts. Sulfate radicals often exhibit higher selectivity for electron-rich organic compounds and greater persistence in complex water matrices compared to $\bullet\text{OH}$ [21]. The non-selective and potent nature of $\bullet\text{OH}$ enables the degradation of a broad spectrum of antibiotic classes. However, this non-selectivity can also lead to inefficient consumption of oxidants by background organic matter in real wastewater [22].

Photocatalysis

Photocatalysis harnesses light energy to activate a semiconductor catalyst (e.g., TiO_2 , ZnO , $\text{g-C}_3\text{N}_4$), generating electron-hole pairs (e^-/h^+) that drive redox reactions at the catalyst surface. The h^+ can directly oxidize pollutants or react with H_2O to form $\bullet\text{OH}$, while e^- can reduce O_2 to form superoxide radical anions ($\bullet\text{O}_2^-$), perpetuating the oxidative cycle (Fig. 4).

A critical aspect determining the practical and economic feasibility of photocatalysis is the operational light source. Laboratory studies predominantly employ artificial UV light sources (e.g., low- or medium-pressure

mercury lamps emitting at 254 nm or broadband UV) due to their high photon flux and reproducibility, which facilitate the activation of wide-bandgap semiconductors like TiO_2 [17, 18]. However, for real-world scalability, the shift toward solar-driven photocatalysis is essential to reduce energy costs and enhance sustainability. Solar irradiation, comprising both UV and visible spectra, necessitates the development of visible-light-responsive catalysts (e.g., doped TiO_2 , $\text{g-C}_3\text{N}_4$, or heterojunctions) [18, 19]. While solar photocatalysis offers significant operational cost savings, its efficiency is inherently variable due to diurnal and meteorological factors, and it often requires larger reactor footprints to capture sufficient irradiance, posing design and land-use challenges [24].

Strategies to enhance performance include doping with metals or non-metals (e.g., N-doped TiO_2), constructing heterojunctions (e.g., $\text{ZnO}/\text{g-C}_3\text{N}_4$), and coupling with materials that exhibit surface plasmon resonance (e.g., $\text{Ag}/\text{Ag}_3\text{PO}_4$). These approaches have significantly improved visible-light activity and quantum efficiency [19, 20]. For instance, one study reported that ZnO-doped $\text{g-C}_3\text{N}_4$ achieved 93.8% removal of ciprofloxacin, with a degradation rate 4.9 times faster than that of pure $\text{g-C}_3\text{N}_4$ [21, 22]. Similarly, innovative bio-based matrix photocatalysts and metal-organic framework (MOF) composites (e.g., MIL-100(Fe)/ TiO_2) have improved semiconductor efficiency, recovery, and dispersibility [23, 24].

Significant advancements have emerged in non-metal and metal-free catalysts, offering the advantages of low cost, high stability, and reduced metal leaching. Carbon-based materials, particularly carbon nanotubes (CNTs) and graphene oxide (GO) composites, have shown remarkable potential [31]. They can act as superior photocatalysts themselves or as conductive supports to enhance charge separation in semiconductor composites. For example, reduced graphene oxide

Table 3. Principles, pros, and cons of current pharmaceutical wastewater antibiotic removal and degradation technologies.

Treatment approach	Principle	Pros	Cons	References
Photocatalysis	Destruction of organic contaminant chemical structures using semiconductors and light.	Good stability of photocatalysts in aqueous solutions. High activity and non-toxicity. Efficient recovery and reasonable recyclability of the photocatalyst. It is inexpensive, easy to operate, and destroys the chemical structure of organic pollutants. Abundant resources such as sunlight, oxygen, and a photocatalyst are required.	Fast photogenerated electron-hole recombination. Limited visible light response. Poor treatment for highly concentrated organic pollutants. The degraded by-product has not been studied with respect to its chemical structure and toxicity.	[24]
Fenton	Destructive techniques with the aid of the Fe ion and H ₂ O ₂	In-situ production of reactive radicals such as OH·. No production of sludge and mineralization of the organic contaminants. Rapid degradation and efficiency for recalcitrant compounds.	Formation of unknown by-products that need further analysis and study. Laboratory scale. Technical constraints. A large amount of ferrous sludge was produced. Formation of a high concentration of anions in the treated wastewater.	[22]
Ozonation	Antibiotics are oxidized directly or through reactive oxygen species (ROS), breaking them into less harmful byproducts.	This technology can break down antibiotics within a very short period (4-5 min).	It generates degraded by-products that tend to accumulate in water and require treatment. Oxidation usually only breaks down microorganisms.	[44]
Electrochemical Oxidation	Electrochemical oxidation removes antibiotics by generating reactive species (e.g., hydroxyl radicals) at the electrode surface. These species oxidize and degrade antibiotic molecules into less harmful byproducts.	It is a zero-sludge process. It is not like Fenton technology; electrochemical oxidation can be both unselective and selective, depending on the oxidant produced by the electrochemical cell.	Capital-intensive process compared to the Fenton technology. Because different electrodes have varying capacities for oxidant production, electrode selection is critical for an efficient electro-oxidation process.	[48]
Adsorption	Non-destructive method using a solid material to remove antibiotics from an aqueous medium.	A highly effective process with fast kinetics. Good ability to separate various contaminants (heavy metals & organic pollutants). Adaptable to many treatment formats with simple equipment. Good quality of the treated effluent	Non-destructive and non-selective methods. The cost of regeneration is high and results in material loss. The treatment process can be varied with different pH values. After wastewater treatment, further processing of the adsorbent, such as incineration or regeneration, is required.	[50]
Membrane separation technology	It removes antibiotics by using selective membranes to separate and retain antibiotic molecules based on size, charge, or hydrophobicity. This allows clean water to pass through while filtering out contaminants.	High Energy Requirements Membrane Fouling and Scaling Environmentally Friendly	High Energy Requirements Energy-intensiveness hinders scalability in resource-constrained settings. Membrane Fouling and Scaling Economic Challenges Limited adaptability to diverse pollutants Membrane specificity may limit effectiveness against a wide range of pollutants.	[22]
Advanced biological processes	Microorganisms break down antibiotic compounds into simpler, non-toxic substances using enzymatic processes and metabolic pathways.	Require less energy and chemical inputs.	It remains a significant challenge in WWTP design to achieve effective, efficient, and simultaneous removal of conventional and emerging pollutants to reduce environmental impact and ARG proliferation.	[19]

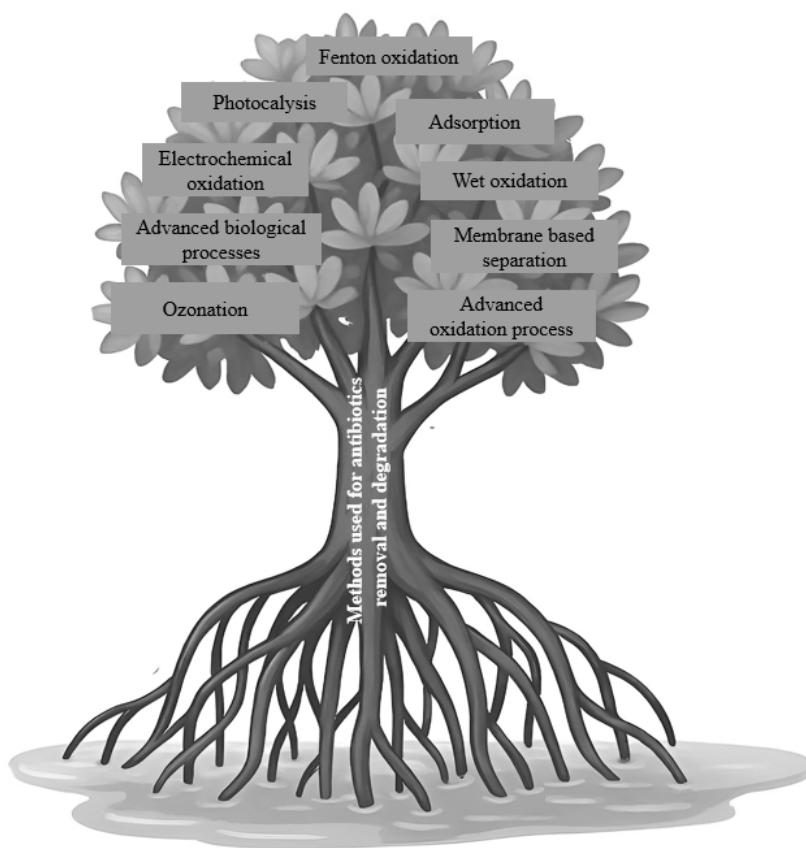


Fig. 3. Conceptual overview of the primary methods for the removal and degradation of antibiotic pollutants from wastewater, categorized into destructive, separative, and biological processes.

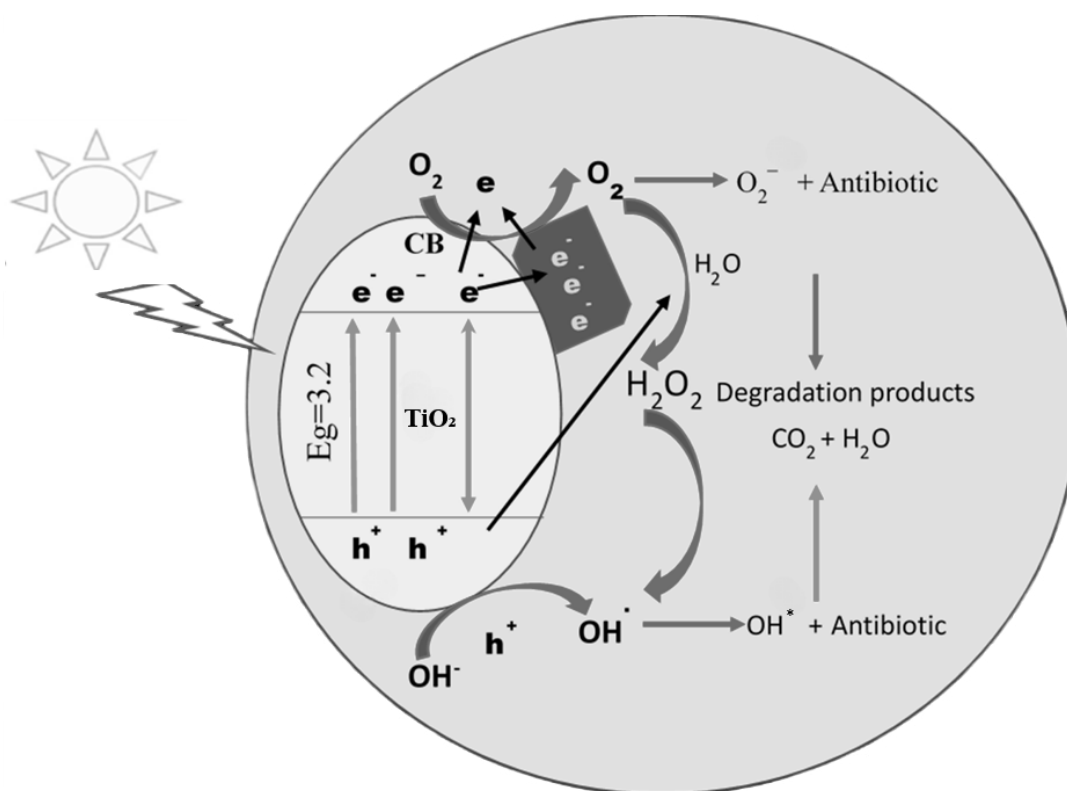


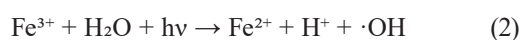
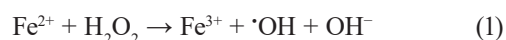
Fig. 4. Generalized mechanism of photocatalytic degradation for a typical antibiotic molecule. The process involves photogeneration of electron-hole pairs on a semiconductor catalyst, leading to the production of reactive oxygen species (ROS) that non-selectively oxidize organic contaminants. Key challenges illustrated include charge recombination and the need for catalyst recovery from treated water.

(rGO) hybrids with TiO₂ or g-C₃N₄ significantly inhibit electron-hole recombination, extending the lifespan of photo-induced charge carriers and boosting degradation rates for antibiotics like tetracycline and ofloxacin [31]. Furthermore, Z-scheme heterojunction systems represent a cutting-edge design to spatially separate redox reactions and achieve a more substantial redox potential [32]. In a direct Z-scheme system, such as g-C₃N₄/Bi₂WO₆ [33] or α -Fe₂O₃/g-C₃N₄, photogenerated electrons from one semiconductor combine with holes from another, preserving the most energetic electrons and holes for reduction and oxidation reactions, respectively. This leads to more efficient ROS generation and superior photocatalytic performance compared to conventional type-II heterojunctions.

Despite high efficiencies in synthetic lab-scale systems (>90% for many antibiotics), the scalability of photocatalysis is hampered by challenges in catalyst recovery, fouling in real wastewater matrices, and the economic feasibility of deploying and maintaining large-scale photoreactors [24]. Future research must pivot toward developing robust, immobilized catalyst systems and leveraging solar irradiation to achieve economic viability.

Fenton-Based Processes

The classical Fenton reaction uses Fe²⁺ as a catalyst to decompose H₂O₂ into •OH under acidic conditions (Eq. (1)) [34]. Its effectiveness is constrained by the narrow optimal pH range (2.5-3.5) and significant iron sludge production. To circumvent these limitations, advanced Fenton variants have emerged: the Photo-Fenton process, in which UV/Vis irradiation enhances the regeneration of Fe²⁺ from Fe³⁺ (Eq. (2)) [35], improving •OH yield and allowing operation at a slightly higher pH [34]; the Electro-Fenton process, in which H₂O₂ is produced in situ via the 2-electron reduction of O₂ at the cathode (Eq. (3)) [34], while the anode facilitates the regeneration of the Fe²⁺ catalyst, eliminating the need for continuous external chemical addition and reducing sludge volume; and the Heterogeneous Fenton process, in which solid iron catalysts (e.g., Fe₃O₄, Fe⁰ supported on carbon) are used to prevent sludge formation and enable operation at near-neutral pH, though often with slower kinetics due to mass transfer limitations [35]. These systems have demonstrated remarkable efficacy, achieving complete degradation of antibiotics like tetracycline and norfloxacin within minutes under optimized conditions [30, 31].



Emerging research is exploring metal-free Fenton-like catalysts to overcome limitations associated with

metal ions [38]. Carbonaceous materials like nitrogen-doped carbon nanotubes (N-CNTs) [39], reduced graphene oxide (rGO), and nanodiamonds have shown catalytic activity for activating peroxydisulfate (PMS) or persulfate (PS) to generate sulfate radicals (SO₄^{•-}). These materials contain defective sites and functional groups (e.g., carbonyl, ketonic C=O) that act as active centers for oxidant activation [40]. For instance, nitrogen-doped graphene can effectively activate PMS for the degradation of sulfamethoxazole, with the doped nitrogen modulating the electron density of adjacent carbon atoms to facilitate electron transfer [41]. These metal-free systems eliminate concerns about secondary metal pollution and sludge generation, offering a promising direction for greener AOPs.

Critical Perspective for Scaling: The economic burden of chemical inputs (H₂O₂, acid for pH adjustment) and energy for irradiation/electrolysis remains a primary barrier [22]. The heterogeneous Fenton process offers the most promising path for scale-up but requires further development of highly active, stable catalysts that resist leaching in complex water matrices.

Ozonation

Ozonation (O₃) degrades antibiotics via two pathways: direct oxidation by molecular ozone (selective for compounds with electron-rich moieties) and indirect oxidation by •OH generated from ozone decomposition at high pH. It is highly effective, often achieving >90% removal of antibiotics like amoxicillin, ciprofloxacin, and sulfamethoxazole in short contact times [36, 37]. For example, Iakovides et al. [43] reported that continuous ozonation of urban wastewater achieved 92-99% removal of various antibiotics, including ciprofloxacin and sulfamethoxazole, while also reducing antibiotic-resistant *E. coli* by 3-4 log units. Similarly, Feng et al. [44] demonstrated rapid (>95%) removal of flumequine via ozonation, with reaction pathways clearly elucidated. A key advantage is its dual function: oxidation of micropollutants and disinfection. However, a significant drawback is the potential formation of toxic transformation products (e.g., bromate in bromide-containing waters) and aldehydes [44]. Consequently, ozonation is frequently followed by a biological post-treatment step (e.g., sand filtration) to remove biodegradable oxidation by-products.

Electrochemical Oxidation

Electrochemical Oxidation (EO) destroys pollutants directly at the anode surface or via electrogenerated oxidants (e.g., •OH, active chlorine). The anode material is critical; non-active electrodes like Boron-Doped Diamond (BDD) generate physisorbed •OH that non-selectively mineralizes organics, while active electrodes (e.g., Pt, IrO₂) form chemisorbed 'active oxygen' that participates in more selective oxidation reactions [45]. BDD anodes are particularly effective for the

complete mineralization of fluoroquinolones and other persistent antibiotics [46]. For example, [47] achieved complete electrochemical oxidation of ciprofloxacin and norfloxacin using BDD electrodes, with complete loss of antibacterial activity of the treated solutions. Another study by [48] reviewed multiple applications where electrochemical oxidation removed 85-99% of various fluoroquinolone antibiotics from wastewater. The main challenge for EO is its high energy consumption and operational costs associated with electrode wear and the need for supporting electrolytes [48]. Research is focused on developing cost-effective, stable anode materials and optimizing reactor designs to maximize current efficiency.

Catalytic Wet Peroxide Oxidation

Catalytic Wet Peroxide Oxidation (CWPO) is a thermochemical AOP that operates at elevated temperatures (150-350°C) and pressures (20-200 bar) to oxidize organic matter using air or oxygen. It is highly effective for high-strength industrial wastewaters but is energy-intensive. The development of heterogeneous catalysts (e.g., Fe-supported activated carbon) has enabled milder reaction conditions, bringing CWPO closer to practical application for concentrated pharmaceutical waste streams [49].

Separative and Concentrative Technologies

These technologies remove antibiotics without immediate degradation, concentrating them into a smaller waste stream for subsequent treatment or disposal.

Adsorption

Adsorption is a surface phenomenon where atoms, ions, or molecules (adsorbates) from a gas or liquid phase accumulate on the surface of a solid or liquid (adsorbent). This process is driven by intermolecular forces such as van der Waals interactions, electrostatic attraction, hydrogen bonding, and chemical bonding (chemisorption). In environmental remediation, adsorption is used as a physical separation process to concentrate and remove contaminants from aqueous matrices. In the specific application of antibiotic removal from wastewater, the method relies on physicochemical interactions (e.g., π - π stacking, electrostatic attraction, hydrogen bonding, hydrophobic interactions) between antibiotic molecules and a solid adsorbent [44, 45].

Activated carbon (AC) is the industrial benchmark due to its high surface area and porosity. Research explores novel materials like graphene oxide (GO), carbon nanotubes (CNTs), biochar, and metal-organic frameworks (MOFs), which can exhibit superior capacities, selectivities, and tailored surface chemistries for specific antibiotic classes. For instance, [52] demonstrated that graphene oxide had an adsorption

capacity of 398 mg/g for tetracycline, while Feizi [53] showed that magnetic tire pyrolysis char effectively removed multiple pharmaceuticals from aqueous solutions.

The core limitation of adsorption in pollutant remediation is phase transfer, not destruction. The process generates spent adsorbent saturated with concentrated antibiotics, which becomes hazardous solid waste requiring costly, energy-intensive regeneration (thermal or chemical) or secure disposal. This translates to additional operational costs and potential secondary environmental burdens. Therefore, adsorption is most sustainable when integrated with a regeneration loop that destroys the adsorbed contaminants, effectively turning the adsorbent into a reusable concentrator [51].

Membrane Separation

Pressure-driven Microfiltration (MF), Ultrafiltration (UF), Nanofiltration (NF), and Reverse Osmosis (RO) separate antibiotics based on size exclusion, charge repulsion, and adsorption. NF and RO are particularly effective, achieving >90% removal for many antibiotics [54]. For instance, [54] reviewed membrane bioreactor applications, showing that NF membranes consistently achieved >95% removal of antibiotics such as sulfamethoxazole and trimethoprim from wastewater streams. The paramount challenge is membrane fouling, which reduces flux, increases energy demand, and requires frequent chemical cleaning, shortening membrane life. Innovations focus on developing antifouling membranes (e.g., zwitterionic coatings, nanocomposite membranes) and integrating membranes with pre-treatment steps (e.g., coagulation) or post-treatment AOPs for the concentrated retentate.

Advanced Biological Processes

Advanced biological treatments leverage specialized microbial communities or hybrid systems to biodegrade or biosorb antibiotics.

Membrane Bioreactors (MBRs): MBRs combine biological degradation with membrane filtration, retaining slow-growing specialist bacteria within the reactor, thereby enhancing the removal of some biodegradable antibiotics compared to conventional activated sludge. For example, [55] reviewed microalgae-based systems that achieved 70-90% removal of amoxicillin and other β -lactam antibiotics through combined biosorption and biodegradation mechanisms.

Microalgae-Based Systems: Microalgae remove antibiotics through biosorption, bioaccumulation, and biodegradation, simultaneously fixing CO₂ and producing biomass for biofuel. They show promise for compounds such as amoxicillin, but are sensitive to antibiotic toxicity and require long hydraulic retention times [55]. A dedicated review of microalgae-based technology for antibiotic removal from wastewater further supports these mechanisms [56].

Table 4. Consolidated quantitative comparison of major advanced antibiotic removal technologies. TRL: Technology Readiness Level (1-9); EEO: Electrical Energy per Order (kWh/m³/order); Cost: Relative operational cost.

Technology	Typical antibiotic removal efficiency (%)	Key strengths	Major limitations for scalability	TRL	Relative energy intensity	Relative operational cost	Best suited for	Key references
Photocatalysis	>90 (Lab-scale, specific antibiotics)	Solar-driven potential, non-selective destruction	Catalyst recovery/fouling, limited real-wastewater testing	4-5	Medium-High	Medium-High	Polishing step, hybrid systems	[18, 55, 56]
Fenton-Based	>90 (Optimized conditions)	Rapid kinetics, effective for recalcitrant compounds	Sludge production (classical), chemical costs, pH sensitivity	6-7	Medium	Medium	Pre-treatment of high-strength industrial waste	[28, 30, 57]
Ozonation	>90 (Short contact times)	Dual disinfection & oxidation, fast	Toxic byproduct formation, high energy consumption	8-9	High	High	Municipal WWTP polishing, hybrid pre-treatment	[36, 37]
Electrochemical Oxidation	High (BDD anodes for mineralization)	Zero sludge, tunable selectivity	Very high energy consumption, electrode wear/cost	5-6	Very High	Very High	Concentrated streams, final destruction in hybrids	[39, 42]
Adsorption (AC)	Varies (60-99, compound-dependent)	Simple, fast, effective for broad contaminants	Phase transfer only, spent adsorbent disposal/regeneration	9	Low	Low-Medium	Emergency removal, polishing, and coupled regeneration	[44, 46, 47]
Nanofiltration/RO	>90 (For many compounds)	High removal efficiency, physical barrier	Membrane fouling, concentrate management, and high pressure	9	High	High	Final purification, concentrate for downstream destruction	[48, 55]
Advanced Biological (e.g., MBR)	Variable (20-90, compound-dependent)	Low energy/chemical input, removes organics/nutrients	Slow, sensitive to toxicity, potential ARG enrichment	7-8	Low	Low-Medium	Post-AOP polishing, low-toxicity streams	[4, 49, 54]

Table 5. Examples of Integrated methods for removing and degrading antibiotic pollutants.

Integrated methods	Antibiotic Removal Efficiency	References
Fenton-+microalga	Amoxicillin (96.86-99.86%) Cefradine (93.98-95.5%)	[56]
Ozone + Fenton	Ofloxacin, 96.7%	[58]
UV + Microalgae	Cefradine, 73% (UV treatment), 78% (UV-algae treatment) 84.96-99.84% for amoxicillin, 44.42-63.18% for cefradine	[58]
Photocatalytic + ozonation	Tetracycline, 85%	[57]
Light-Fenton + Ceramic Membrane Filtration	Sulfadiazine 100%	[59]
Ultrafiltration Membrane + Photocatalysis	Sulfadiazine, 91.4%	[59]
Fenton + nanofiltration processes (NF/FT)	Amoxicillin 92.3%	[60]

Bioaugmentation and Constructed Wetlands: Introducing specific degrading strains (bioaugmentation) or using engineered wetland systems can enhance removal, but predictability and stability in full-scale applications remain challenging.

Biological processes are often incomplete in the presence of persistent antibiotics, potentially enriching ARGs within the microbial community. Their role is best suited as a polishing step after a primary destructive treatment, such as AOPs.

The Path Forward: Integrated and Hybrid Systems

Given the limitations of any single technology, the future of antibiotic wastewater treatment lies in intelligent integration. Hybrid systems leverage the strengths of one process to mitigate the weaknesses of another. A consolidated comparison of the major advanced antibiotic removal technologies is presented in Table 4, which summarizes their typical removal efficiencies, key strengths, scalability limitations, technology readiness levels (TRL), relative energy intensity, operational cost, and best-suited applications. As shown in the table, while processes such as ozonation and nanofiltration exhibit high technology readiness (TRL 8-9), they often entail high energy demand or operational costs. Conversely, technologies such as photocatalysis show strong mechanistic potential but remain at lower TRL levels (4-5), hindered by challenges in catalyst recovery and real-wastewater validation.

In addition, several integrated methods have been demonstrated to enhance antibiotic removal efficiency by synergistically combining different treatment processes. These hybrid approaches often achieve higher removal rates and greater operational stability than standalone systems. Representative examples of such integrated methods are summarized in Table 5, which illustrates specific combinations, their target antibiotics, removal efficiencies, and key supporting references. For instance, systems combining Fenton oxidation with microalgae achieved amoxicillin removal exceeding 96%, while ozonation coupled with Fenton processes

removed over 96% of ofloxacin. Complementary hybrid configurations, such as ozone integrated with Fenton-like processes using iron-containing waste minerals, have also demonstrated promoted degradation of ofloxacin [57]. An integrated UV irradiation and algal treatment approach has additionally shown good compatibility and efficiency [58].

These examples underscore the practical potential of combining processes such as AOPs, membrane separation, and biological treatment to address the complex and variable nature of pharmaceutical wastewater. Promising hybrid configurations include: (1) AOP + Biological Treatment, where a mild AOP such as ozonation pre-treats wastewater to break down antibiotics into biodegradable intermediates, followed by a biological polishing step; (2) Membrane + AOP, in which nanofiltration or reverse osmosis concentrates antibiotics into a smaller stream, which is then efficiently degraded by an AOP such as electro-Fenton; and (3) Adsorption + Regeneration, where adsorbents like activated carbon are coupled with in situ catalytic regeneration (e.g., photocatalysis) to enable repeated use while destroying adsorbed contaminants.

This integrated approach promises not only higher removal efficiencies but also improved economic and environmental sustainability by optimizing energy and chemical use across the treatment train. By leveraging complementary mechanisms, integrated systems enhance process resilience, reduce chemical consumption, and facilitate resource recovery, key considerations for scalable and sustainable wastewater treatment solutions.

Conclusions

The release of antibiotics into the environment is a major environmental challenge, directly undermining planetary health by propagating antimicrobial resistance. This review unequivocally demonstrates that a compartmentalized approach to technological development is insufficient. The findings of this review

necessitate a paradigm shift from technology-specific optimization to the holistic design of intelligent, adaptive, and circular treatment systems. While advanced individual technologies show mechanistic promise, their scalability is fundamentally hampered by economic and operational constraints when faced with the significant complexity of real pharmaceutical wastewater. The critical path forward lies not in seeking a single silver-bullet technology, but in deliberately and intelligently integrating complementary processes.

Practical Implications

The findings of this review are directly relevant to policymakers, regulators, and industry stakeholders. For regulators, the evidence supports establishing stricter discharge limits for ARGs in treated wastewater and mandating advanced treatment at key point sources, such as pharmaceutical manufacturing plants and major hospitals.

For the water treatment industry, the analysis underscores the operational and economic rationale for adopting hybrid systems, for example, combining membrane filtration with advanced oxidation to improve removal efficiency, reduce chemical consumption, and manage concentrated waste streams. Investment in pilot and demonstration projects using real wastewater is essential to de-risk scaling and provide validated performance data. Finally, integrating antibiotic removal objectives into broader water reuse and circular economy strategies can align environmental protection with resource recovery, creating incentives for innovation and implementation.

Knowledge Gaps and Roadmap for Future Research

This study reveals a significant disconnect between laboratory success and field-scale applicability. To bridge this “innovation valley of death”, future research must move beyond incremental catalyst or material development and embrace a systems-thinking approach. We identify four critical research priorities:

1. **Smart and Adaptive Process Control:** Research must leverage machine learning (ML) and artificial intelligence (AI) for real-time, adaptive control of hybrid systems. ML algorithms can optimize energy consumption (e.g., adjusting UV intensity or ozone dosage in real-time based on incoming pollutant load detected by online sensors), predict membrane fouling, and manage catalyst regeneration cycles.

2. **Circular Economy and Resource Recovery:** The narrative must shift from “removal and disposal” to “valorization and recovery”. Future technologies should be designed to recover resources, such as extracting nutrients from microalgae biomass, regenerating and reusing catalysts/adsorbents indefinitely, or even recovering valuable elements from concentrated waste streams.

3. **Holistic Environmental Impact Assessment:** Studies must include a comprehensive analysis of the total life-cycle environmental impact of hybrid systems, including carbon footprint and the formation and toxicity of transformation products. The fate of ARGs must be a primary performance metric, not an afterthought.

4. **Standardized Testing Protocols:** The field urgently needs standardized testing protocols using complex, real wastewater matrices and a representative cocktail of antibiotics to allow for genuine cross-technology comparison. Benchmarks should include not only removal efficiency but also energy-per-order (EEO) and cost-per-volume metrics.

Conflict of Interest

The authors declare no conflict of interest.

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