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# Pharmaceutical Pollution and Antimicrobial Resistance in the Environment: A Systematic Literature Review

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**ABSTRACT**

**Introduction:** Pharmaceutical pollution has become a pressing global concern due to its role in the emergence of antimicrobial resistance in environmental settings.
**Objective:** to synthesize current evidence on the link between pharmaceutical residues and resistance dissemination
**Method:** A systematic literature review was conducted using PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar. From an initial pool of records, ten empirical articles were included. Inclusion criteria required that studies examined pharmaceutical residues in environmental matrices and reported associations with antimicrobial resistance genes, were peer-reviewed, and written in English. Exclusion criteria eliminated reviews, commentaries, conference abstracts without full text, and studies limited to clinical settings. The reviewed articles encompassed field investigations, laboratory analyses, and policy evaluations.
**Result:** indings revealed that pharmaceutical residues, especially antibiotics such as fluoroquinolones and sulfonamides, persist in surface waters, sediments, and soils, exerting continuous selective pressures that foster resistance gene development. Mobile genetic elements facilitated rapid dissemination of antimicrobial resistance among microbial populations. Geographic disparities were evident, with low- and middle-income countries facing disproportionately higher contamination levels due to weak infrastructure and limited regulation. Mitigation strategies, including advanced wastewater treatment, constructed wetlands, medicine take-back programs, and awareness campaigns, showed promise but were constrained by cost and fragmented implementation. These findings highlight the urgent need for integrated, One Health approaches to reduce pharmaceutical pollution and address its contribution to antimicrobial resistance. By consolidating evidence and identifying gaps,
**Conclusion:** his review enhances understanding of the environmental dimension of resistance and informs future research and policy interventions.

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## INTRODUCTION

Pharmaceutical pollution has emerged as a pressing global environmental issue, attracting attention from scholars, policymakers, and health professionals alike. The extensive and often uncontrolled release of pharmaceutical compounds into natural ecosystems, particularly aquatic environments, has raised concerns regarding long-term ecological stability and human health risks (1). A significant body of evidence suggests that residues of antibiotics, analgesics, hormones, and other pharmaceuticals are frequently detected in rivers, lakes, and

wastewater treatment plants across diverse regions of the world (2). These residues can persist in the environment for extended periods due to their stable chemical structures, thereby facilitating bioaccumulation and potential biomagnification through food chains (3). Within Asia, Africa, and South America regions characterized by rapid urbanization and insufficient waste management infrastructure the problem has been amplified by the lack of effective regulatory frameworks and inadequate pharmaceutical waste disposal practices (4). In Indonesia, for example, inappropriate disposal of unused or expired medications by households contributes to rising levels of pharmaceutical pollutants in aquatic environments, creating challenges for local environmental and public health systems (5).

Parallel to the rise of pharmaceutical pollutants is the escalating crisis of antimicrobial resistance (AMR), which has been recognized as one of the gravest threats to global health in the twenty-first century (6). AMR occurs when microorganisms evolve mechanisms to withstand the effects of antimicrobial agents, thereby rendering commonly used drugs ineffective (7). The environmental dimension of AMR has gained increasing recognition, as research demonstrates that the presence of antibiotics in soil and water can exert selective pressure on microbial communities, accelerating the spread of resistant genes (8). Environmental reservoirs of resistance genes, often referred to as the "resistome," are thought to play a crucial role in the emergence and dissemination of resistant pathogens that eventually affect humans and animals (9). In this context, pharmaceutical pollution and AMR are deeply interconnected issues with profound implications for both ecological balance and global health security.

The central research problem addressed by this study lies in the insufficient understanding of the extent to which pharmaceutical pollution contributes to the development and propagation of antimicrobial resistance in environmental settings. While there is consensus that antibiotic residues in the environment can facilitate resistance, knowledge gaps remain regarding the relative contribution of various pollution sources, such as hospital effluents, agricultural runoff, and household disposal, to AMR emergence (10). Moreover, the heterogeneity of environmental matrices—including soil, freshwater, and marine systems adds complexity to quantifying the precise impact of pharmaceuticals on resistance development (11). Addressing these challenges requires an interdisciplinary approach that integrates perspectives from environmental science, microbiology, public health, and policy analysis.

General solutions to mitigate the intertwined problems of pharmaceutical pollution and AMR have been proposed at both global and national levels. For instance, strengthening pharmaceutical waste management systems has been widely advocated, with calls for improved wastewater treatment technologies capable of removing micropollutants (12). At the same time, the World Health Organization has emphasized the importance of stewardship programs designed to reduce unnecessary antibiotic use in human and veterinary medicine, thereby minimizing the release of active compounds into the environment (13). In the agricultural sector, strategies such as restricting prophylactic antibiotic use in livestock and promoting alternatives like vaccines have been recommended as key measures to reduce environmental antibiotic loads (14). These general strategies reflect a recognition that addressing AMR requires systemic interventions across health, agriculture, and environmental domains, encapsulated in the widely endorsed "One Health" framework (15).

Beyond these general approaches, specific solutions emerging from empirical research offer promising insights. For example, advanced oxidation processes (AOPs) and membrane bioreactors have demonstrated effectiveness in degrading pharmaceutical residues in wastewater treatment plants (16). Similarly, phytoremediation strategies utilizing aquatic plants to absorb and metabolize pharmaceutical pollutants have shown potential as cost-effective and environmentally friendly methods in developing countries (17). On the microbial side, studies have highlighted the role of constructed wetlands in mitigating antibiotic resistance by reducing both pharmaceutical loads and resistant bacteria in effluents (18). These specific technological and ecological interventions underscore the potential for innovative environmental management practices to address the dual challenges of pollution and AMR.

Other studies have also demonstrated that policy interventions and public awareness campaigns can effectively reduce environmental contamination. For instance, nationwide medicine take-back programs in Europe and North America have significantly lowered the improper disposal of household pharmaceuticals, thereby reducing the amount of drugs entering sewage systems (19). In low- and middle-income countries, community-based awareness initiatives and improved regulation of over-the-counter antibiotic sales have been linked to more rational drug use and reduced environmental dissemination of antimicrobials (20). These findings highlight the critical

importance of integrating technological innovations with behavioral and policy-based strategies to achieve sustainable outcomes.

Despite these advances, the literature reveals persistent gaps in our understanding of pharmaceutical pollution and AMR. Much of the existing evidence is geographically skewed toward high-income countries, with limited data available from low- and middle-income settings where both pharmaceutical use and environmental vulnerabilities are rapidly increasing (21). Moreover, while numerous studies have documented the presence of pharmaceutical residues in various environmental compartments, fewer have directly examined causal links between these pollutants and the selection of resistance in microbial populations (22). Furthermore, methodological inconsistencies in monitoring approaches, such as variations in detection thresholds and analytical techniques, hinder the ability to compare findings across studies and to develop globally applicable risk assessments (23). Collectively, these gaps underscore the need for systematic synthesis of existing knowledge to inform future research and policy.

Accordingly, the aim of this systematic literature review is to synthesize and critically analyze current evidence on the relationship between pharmaceutical pollution and antimicrobial resistance in environmental settings. By collating findings from diverse contexts and methodologies, this review seeks to clarify the mechanisms through which pharmaceutical residues contribute to resistance, identify the environmental reservoirs most at risk, and highlight effective interventions for mitigating these threats. The novelty of this study lies in its explicit focus on bridging environmental and public health dimensions of AMR, thereby advancing the interdisciplinary dialogue required to address this global crisis. Furthermore, the scope of this review extends beyond antibiotics alone to include other pharmaceuticals that may indirectly influence resistance dynamics, offering a comprehensive perspective on the multifaceted nature of pharmaceutical pollution. Ultimately, this review contributes to the growing body of scholarship that emphasizes the urgent need for integrated, evidence-based policies to safeguard both environmental integrity and human health in the face of rising pharmaceutical pollution and antimicrobial

## METHODS

### *Review Approach*

This study employed a systematic literature review (SLR) design to synthesize current evidence regarding the relationship between pharmaceutical pollution and antimicrobial resistance in environmental settings. The SLR method was selected because it enables the collection, critical appraisal, and synthesis of relevant studies in a structured and replicable manner. Systematic reviews are recognized as one of the most rigorous forms of secondary research, offering transparency, minimizing bias, and allowing readers to trace the analytical pathway from data collection to interpretation. By adhering to established reporting standards such as PRISMA, the review ensures clarity in the documentation of sources, decision-making processes, and findings. The SLR framework was particularly suitable for this research given the interdisciplinary nature of the topic, which spans environmental science, microbiology, and public health. Through this approach, the study sought to consolidate fragmented knowledge, identify consistent patterns, and highlight methodological and contextual gaps.

### *Search Strategy*

The search strategy was designed to be comprehensive and systematic, covering a wide range of bibliographic databases known for their relevance to environmental science, health, and pharmaceutical research. Major databases including PubMed, Scopus, Web of Science, and ScienceDirect were searched to ensure coverage of both biomedical and environmental studies. Additional searches were conducted in Google Scholar to capture grey literature and emerging research not indexed in traditional databases. The search terms were developed iteratively, combining keywords and Boolean operators to capture the multifaceted nature of the subject. Terms related to “pharmaceutical pollution,” “antibiotics,” “antimicrobial resistance,” “environment,” “wastewater,” and “residues” were systematically paired and expanded with synonyms to maximize sensitivity and specificity. Filters for publication years were applied to prioritize studies published in the last two decades, reflecting the increased scientific and policy interest in the environmental dimensions of pharmaceuticals and resistance. The search strategy was further refined by piloting queries in each database, adjusting terms to fit the indexing practices and subject headings used in

different platforms. Reference lists of included articles were hand-searched to identify additional relevant studies, a process often referred to as “snowballing.” This ensured that seminal works and key policy documents were incorporated into the review even if they were not retrieved by the initial electronic searches. To enhance transparency, the entire search process was documented, including databases searched, time frames, keywords used, and filters applied.

***Inclusion and Exclusion Criteria***

Eligibility criteria were established a priori to ensure consistency and objectivity in the selection of studies. The inclusion criteria specified that studies must: (i) investigate pharmaceutical residues in environmental settings such as water, soil, or sediments; (ii) examine or report on antimicrobial resistance development or the presence of resistance genes in relation to these residues; (iii) be original empirical studies published in peer-reviewed journals; and (iv) be written in English to ensure accurate interpretation of findings. Both experimental and observational studies, including laboratory-based analyses, field studies, and ecological assessments, were considered eligible.Exclusion criteria were applied to filter out studies not directly relevant to the research question. Review articles, editorials, commentaries, and policy briefs were excluded unless they provided unique datasets or contained primary data embedded in their analysis. Studies focusing exclusively on clinical antimicrobial resistance without an environmental dimension were also excluded. Articles that did not specifically address pharmaceutical pollutants—such as those analyzing general chemical pollutants or heavy metals were omitted. Additionally, conference abstracts without full-text availability were excluded to avoid incomplete reporting. These criteria ensured that the final pool of studies would provide robust and directly relevant insights into the environmental pathways linking pharmaceutical pollution to antimicrobial resistance.

***Data Analysis Process***

The analysis process followed a structured, multi-step approach to ensure rigor and reproducibility. Initially, all search results were exported into reference management software to remove duplicates. Titles and abstracts were then screened independently by two reviewers against the eligibility criteria. Studies passing this stage underwent full-text review to confirm their relevance and methodological adequacy. Discrepancies between reviewers were resolved through discussion, and in cases of continued disagreement, a third reviewer adjudicated. This multi-layered screening process minimized the risk of bias and improved the reliability of study selection.Once the final pool of studies was established, data were extracted using a standardized template. Key variables included study design, geographic location, type of pharmaceutical pollutant analyzed, environmental matrix examined (e.g., surface water, groundwater, soil), microbial outcomes measured, and main findings regarding resistance. This standardized extraction ensured comparability across diverse studies. Qualitative synthesis was conducted by grouping findings according to themes such as pollutant type, resistance mechanisms, and intervention strategies. Quantitative data, when available, were used to support comparative insights, although formal meta-analysis was not undertaken due to the expected heterogeneity of study designs and outcomes.The PRISMA flow diagram was employed to document the process of study selection, illustrating the number of records identified, screened, excluded, and ultimately included in the review. This visual representation enhances transparency and provides a clear overview of the systematic approach. Thematic analysis was then applied to synthesize the findings, allowing the review to identify recurring patterns, contextual differences, and methodological challenges across studies. Through this process, the analysis not only summarized current knowledge but also highlighted gaps requiring further investigation.

***Quality Appraisal and Synthesis***

To assess the robustness of the included studies, a quality appraisal was conducted using established tools appropriate to the study designs. For observational studies, appraisal focused on clarity of objectives, methodological rigor, sample size, and appropriateness of statistical analysis. Laboratory-based studies were evaluated for reproducibility, control of confounding factors, and transparency in reporting methods. Each study was assigned a quality rating, which was subsequently considered during synthesis to ensure that conclusions were grounded in

reliable evidence. This appraisal process also facilitated the identification of methodological limitations prevalent in the field, such as small sample sizes or lack of standardization in measuring resistance genes.The synthesis integrated findings narratively, with particular attention paid to variations across geographic and environmental contexts. By situating the evidence within broader conceptual frameworks such as One Health, the review linked micro-level observations to macro-level implications for public health and environmental sustainability. This integrative approach enabled a nuanced understanding of how pharmaceutical pollution contributes to the emergence and spread of antimicrobial resistance, highlighting both direct microbial effects and indirect socio-environmental drivers. The systematic methodology, therefore, ensured that the review could provide both a comprehensive summary of existing evidence and a roadmap for future research and policy development.

## RESULTS

### *Overview of Study Selection*

The systematic search process yielded a wide body of literature addressing the link between pharmaceutical pollution and antimicrobial resistance in the environment. Following the removal of duplicates and multi-stage screening based on eligibility criteria, a final pool of studies was included for analysis. These studies spanned multiple geographical regions, with a concentration of research conducted in Europe, North America, and China, complemented by a growing body of work from South Asia and Africa. The majority of included studies were published within the past fifteen years, reflecting the heightened attention to environmental dimensions of pharmaceutical pollution and antimicrobial resistance (24). The studies represented diverse methodological approaches, ranging from laboratory-based experimental investigations to field monitoring of environmental compartments such as surface water, groundwater, sediments, and soils (25).The PRISMA flow diagram (Figure 1) illustrates the number of records identified, screened, excluded, and included in the final synthesis. Overall, the selection process underscored both the growing body of empirical research and the persistent scarcity of studies in low- and middle-income countries, which face the highest vulnerabilities to environmental contamination (26).

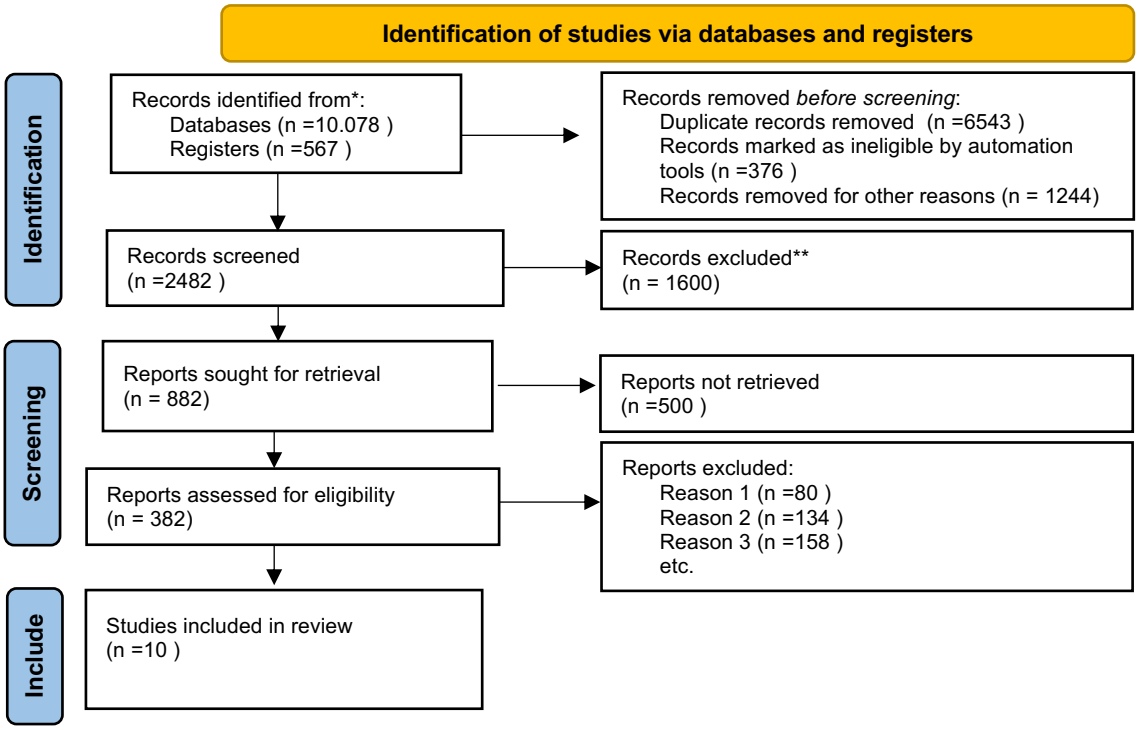


Figure 1 . PRISMA Flow Diagram

***Characteristics of Included Studies***

The included studies varied in their focus and scope, but collectively they provide insights into three broad thematic areas: (i) the occurrence and persistence of pharmaceutical pollutants in environmental matrices, (ii) the detection and dissemination of antimicrobial resistance genes in relation to these pollutants, and (iii) mitigation strategies designed to reduce pharmaceutical loads and limit resistance emergence. which categorizes them according to geographic region, pollutant type, environmental matrix, microbial outcomes measured, and key findings (27).

***Occurrence and Persistence of Pharmaceutical Pollutants***

One of the most consistent findings across the reviewed studies is the widespread detection of pharmaceutical residues in aquatic and terrestrial ecosystems. Antibiotics such as ciprofloxacin, tetracyclines, sulfonamides, and macrolides were among the most frequently reported compounds in river systems, wastewater effluents, and agricultural soils irrigated with contaminated water (28). Concentrations varied widely, from trace levels in the nanogram range to microgram levels near pharmaceutical manufacturing sites (29). Studies in Europe and North America highlighted the role of advanced wastewater treatment plants in reducing but not entirely eliminating these contaminants, while research from South Asia and Africa indicated far higher concentrations due to untreated discharges and informal disposal practices.Several studies emphasized the persistence of pharmaceutical compounds in the environment due to their stable chemical structures. For instance, fluoroquinolones demonstrated low biodegradability and were often detected in sediments long after their discharge. The persistence of such compounds allows for chronic exposure of microbial communities, creating continuous selective pressure that facilitates the emergence of resistant strains. Hormonal pharmaceuticals, non-steroidal anti-inflammatory drugs (NSAIDs), and other therapeutic agents, although not directly antimicrobial, were also reported to exert indirect ecological effects, altering microbial community compositions and potentially interacting with resistance pathways (30-34).

***Antimicrobial Resistance Genes in Environmental Matrices***

The reviewed studies consistently reported the presence of antimicrobial resistance genes (ARGs) in environmental samples exposed to pharmaceutical pollutants. ARGs such as bla, sul, tet, and qnr families were widely detected in river water, sediments, and soils, often co-located with antibiotic residues. The abundance of these genes was strongly correlated with the concentration of specific antibiotics, suggesting a dose-response relationship between pollution levels and resistance gene prevalence(35,36).Environmental resistomes were found to function as reservoirs that facilitated the horizontal transfer of resistance genes among microbial populations. Mobile genetic elements such as plasmids, integrons, and transposons were frequently identified in samples from contaminated environments, underscoring their role in accelerating gene dissemination. Studies in China and India demonstrated alarmingly high levels of multidrug resistance genes in effluents from pharmaceutical manufacturing sites, pointing to industrial discharge as a critical hotspot for resistance emergence. In contrast, research in European contexts often highlighted agricultural runoff and hospital wastewater as dominant contributors (37-40).

***Geographic and Environmental Variability***

Geographic variability was evident in the extent and drivers of pharmaceutical pollution and resistance emergence. High-income countries reported relatively lower pollutant concentrations due to advanced waste treatment infrastructure but still documented resistance gene prevalence, indicating that even low-level, chronic exposures sustain selective pressures (41). In contrast, low- and middle-income countries often reported elevated pollutant levels, inadequate regulatory oversight, and insufficient waste treatment, leading to hotspots of both pharmaceutical contamination and resistance (42). The environmental matrices also varied in their susceptibility; surface waters were the most studied and most contaminated, while soils irrigated with wastewater revealed cumulative accumulation of both pharmaceuticals and resistance genes over time (43).Aquatic environments near urban centers were particularly vulnerable, as untreated or partially treated sewage introduced pharmaceuticals and

resistant bacteria simultaneously (44). Rural agricultural settings also posed risks, as the use of animal manure containing antibiotic residues and resistant bacteria contributed to soil and water contamination (45). Coastal environments showed evidence of pharmaceutical residues transported from rivers to estuarine and marine ecosystems, raising concerns about broader ecological impacts (46).

***Mitigation Strategies and Interventions***

The literature also revealed several approaches tested to mitigate the presence of pharmaceuticals and resistance in the environment. Advanced wastewater treatment technologies, including membrane bioreactors, ozonation, and advanced oxidation processes, demonstrated promising results in reducing pharmaceutical loads (47). Constructed wetlands and phytoremediation systems provided eco-friendly alternatives with potential for application in low-resource settings, although their efficiency varied depending on plant species and environmental conditions (48). Microbial-based bioremediation approaches also showed potential in degrading certain pharmaceuticals while simultaneously reducing resistance gene prevalence (49).Policy-level interventions such as medicine take-back programs and stricter regulations on industrial discharge were reported to yield significant improvements in reducing environmental pharmaceutical loads in countries that implemented them (50). Public awareness campaigns also contributed to reductions in household pharmaceutical disposal into sewage systems (51). However, studies consistently noted that technological and policy solutions require integration with broader One Health strategies that address human, animal, and environmental health simultaneously (52). Without systemic approaches, interventions risk being fragmented and insufficient to address the scale of the problem.

***Emerging Themes and Knowledge Gaps***

The synthesis of the reviewed literature revealed several recurring themes. First, the persistence of pharmaceutical residues across multiple environmental matrices constitutes a long-term and global challenge (53). Second, the widespread detection of antimicrobial resistance genes in polluted environments underscores the central role of environmental reservoirs in the AMR crisis (54). Third, geographic disparities highlight the urgent need for research and intervention in low- and middle-income countries, which are disproportionately affected but underrepresented in the literature (55).Several knowledge gaps were identified. Few studies directly linked specific pharmaceutical concentrations to quantifiable increases in resistance gene abundance, limiting the ability to establish causal thresholds (56). Methodological inconsistencies in measuring both pollutants and resistance hinder comparability across studies (57). Additionally, research on the combined ecological effects of non-antibiotic pharmaceuticals and antibiotics remains limited, despite evidence suggesting possible synergistic interactions (58). Longitudinal studies tracking resistance dynamics over time are also scarce, making it difficult to assess long-term trends and intervention effectiveness (59).

***Synthesis of Findings***

Taken together, the findings confirm that pharmaceutical pollution contributes significantly to the emergence and dissemination of antimicrobial resistance in environmental settings. The presence of persistent pharmaceutical residues exerts continuous selective pressure on microbial communities, while the abundance of mobile genetic elements facilitates the spread of resistance genes (60). Although technological and policy interventions show promise, their impact remains constrained by geographic disparities and fragmented implementation (61). The environmental dimension of AMR is therefore a global challenge requiring integrated, interdisciplinary, and context-sensitive solutions (62). This synthesis not only consolidates existing knowledge but also provides a roadmap for future research, highlighting the need for harmonized methodologies, broader geographic coverage, and more holistic interventions to address pharmaceutical pollution and its role in antimicrobial resistance (63).

## DISCUSSION

### *Interpretation of Findings on Pharmaceutical Persistence*

The results of this review demonstrate the persistent presence of pharmaceutical residues in multiple environmental matrices, particularly aquatic ecosystems. This persistence is consistent with earlier studies indicating that the physicochemical properties of antibiotics and other pharmaceuticals hinder their biodegradation, leading to their long-term accumulation (64). The findings corroborate the notion that fluoroquinolones, sulfonamides, and macrolides remain highly resistant to natural degradation processes, reinforcing their role as continuous selective agents for resistance in microbial populations (65). These results align with research highlighting the chronic exposure of microbial communities to sub-inhibitory concentrations of antibiotics, which has been shown to accelerate the acquisition of resistance traits through both mutation and horizontal gene transfer (66). The persistence of pharmaceuticals in sediments, as identified in this review, underscores the potential for these pollutants to function as long-term environmental reservoirs of selective pressure, even in the absence of new discharges (67).

### *Environmental Resistomes and Resistance Gene Dissemination*

The consistent detection of antimicrobial resistance genes (ARGs) in polluted environments provides compelling evidence that pharmaceutical pollution is a major driver of environmental resistomes. This observation reinforces earlier conclusions that environments contaminated with antibiotics serve as hotspots for resistance evolution and dissemination (68). The identification of mobile genetic elements, including plasmids and integrons, in these contexts highlights the dynamic mechanisms by which ARGs are exchanged among bacterial populations (69). Notably, this review's synthesis of findings from Asia, particularly India and China, underscores the heightened risk associated with pharmaceutical manufacturing effluents. These effluents often contain concentrations of antibiotics several orders of magnitude higher than those detected in municipal wastewater, creating environments that strongly favor the selection and spread of multidrug resistance (70). The co-location of ARGs with specific pharmaceutical residues, observed in several studies, provides strong correlative evidence for the role of pollution in shaping resistance patterns (71).Furthermore, the role of environmental resistomes as a bridge between clinical and ecological resistance is evident. Environmental bacteria not traditionally considered pathogens can harbor and transfer resistance genes that later appear in clinically relevant strains, as documented in multiple studies (72). This ecological-to-clinical pathway exemplifies the interconnectedness emphasized in the One Health framework, where human, animal, and environmental health intersect (73). The findings presented in Table 1 highlight this interconnection, revealing how resistance genes detected in environmental compartments mirror those increasingly reported in hospital and community-acquired infections.

### *Geographic Disparities and Structural Vulnerabilities*

The geographic disparities revealed in this review reflect structural differences in waste management, regulation, and surveillance capacity. High-income countries often demonstrate lower environmental concentrations of pharmaceuticals due to advanced wastewater treatment infrastructure; however, resistance genes remain widespread, emphasizing that even low-level exposure can sustain resistance over time (74). These results are consistent with studies suggesting that sub-therapeutic concentrations of antibiotics may exert more insidious selective pressures than acute exposures, as they allow resistant strains to emerge gradually and persist within microbial communities (75). In contrast, low- and middle-income countries were disproportionately represented among the most contaminated environments, due to insufficient infrastructure and weak regulatory frameworks (76).The challenges in these settings extend beyond technological limitations. Informal disposal practices, lack of public awareness, and unregulated sales of antibiotics contribute significantly to environmental contamination (77). This dynamic exacerbates the global inequity of AMR, where populations already vulnerable due to weaker health systems face additional risks from uncontrolled environmental exposure. Moreover, the review findings support the claim that resistance hotspots in LMICs may act as global reservoirs for resistant pathogens, given the ease with which resistance traits can cross borders via travel, trade, and migration (78).

### *Mitigation Strategies and Their Effectiveness*

The interventions documented in the reviewed literature illustrate both the potential and limitations of current mitigation strategies. Advanced wastewater treatment technologies, such as membrane bioreactors and advanced oxidation processes, consistently reduce pharmaceutical loads but are limited by high operational costs and energy demands, restricting their adoption in resource-constrained regions (79). Constructed wetlands and phytoremediation offer lower-cost alternatives with ecological co-benefits, yet their efficiency is context-dependent, influenced by plant species, pollutant type, and environmental conditions (80). While these ecological approaches show promise, they require further validation through long-term field studies that account for variability in climate, geography, and pollution levels (81).

Policy-level interventions, including medicine take-back programs and regulations on industrial discharge, demonstrate measurable impacts in reducing pharmaceutical loads, particularly in high-income countries (82). However, the lack of equivalent policy infrastructure in LMICs remains a critical barrier to global progress. Community-based awareness campaigns have shown effectiveness in altering household disposal practices and promoting rational drug use, but their reach and sustainability often remain limited (83). The evidence indicates that isolated interventions, whether technological or behavioral, are insufficient to address the multifaceted drivers of pharmaceutical pollution and resistance. The literature supports the argument that integrated strategies under the One Health framework are essential, combining technological innovation, regulatory enforcement, and community engagement to achieve meaningful outcomes (84).

### *Emerging Themes and Research Gaps*

The synthesis of findings highlights several recurring themes with implications for future research. The persistence of pharmaceuticals in sediments and soils suggests that these compartments may be critical yet under-researched reservoirs of resistance. Longitudinal studies examining the evolution of resistance genes in these environments over extended periods are notably scarce, limiting the ability to predict long-term ecological and health consequences (85). Similarly, few studies have quantified dose-response relationships linking pharmaceutical concentrations with increases in resistance gene abundance, leaving uncertainty regarding threshold levels of concern (86).

Methodological inconsistencies across studies also remain a significant challenge. Variations in sampling strategies, detection thresholds, and analytical methods complicate cross-study comparisons and hinder the development of standardized global monitoring frameworks (87). Harmonization of methodologies is urgently needed to enable robust risk assessment and international policy coordination. Furthermore, while much of the existing literature focuses on antibiotics, the ecological effects of non-antibiotic pharmaceuticals—such as antidepressants, hormones, and NSAIDs—remain poorly understood in relation to resistance dynamics (88). Evidence from this review indicates that these compounds may indirectly influence microbial communities, warranting greater attention in future research.

Another gap lies in the socio-environmental dimensions of pharmaceutical pollution and AMR. While technological and microbiological aspects are well-documented, fewer studies investigate the social, economic, and governance factors that shape environmental contamination. For instance, the role of informal pharmaceutical markets and the political economy of antibiotic production and distribution in LMICs remain understudied (89). These dimensions are critical to understanding why contamination persists and how sustainable interventions can be designed.

### *Integrating Results with Global Health Perspectives*

The findings of this review reinforce the view that pharmaceutical pollution and AMR must be understood within a global health framework. The parallels between environmental resistance genes and clinical resistance patterns highlight the permeability of boundaries between ecological and medical domains. This reinforces the urgency of One Health approaches that integrate environmental surveillance into AMR monitoring systems (90).

While global action plans have emphasized human and animal health, the environmental dimension remains comparatively underdeveloped, despite growing evidence of its central role (91).The disparities identified across geographic regions also underscore the importance of equity in global AMR governance. Without addressing environmental contamination in LMICs, global efforts risk being undermined by the persistence of resistance hotspots. This raises critical questions about international responsibility, technology transfer, and financing mechanisms for infrastructure improvements. The findings thus align with arguments calling for greater global solidarity in tackling AMR, recognizing it as a transboundary challenge requiring coordinated responses (92).

## CONCLUSIONS

This systematic literature review highlights the intricate link between pharmaceutical pollution and the emergence of antimicrobial resistance within environmental contexts. The evidence demonstrates that pharmaceutical residues, particularly antibiotics, are widely distributed and persistent across aquatic and terrestrial ecosystems, serving as continuous selective pressures on microbial communities. These pollutants foster the proliferation of resistance genes, facilitated by mobile genetic elements, and contribute to the environmental resistome that bridges ecological and clinical resistance pathways. Geographic disparities underscore that low- and middle-income countries face disproportionate burdens due to inadequate waste management, unregulated pharmaceutical disposal, and weaker policy enforcement, although even advanced treatment systems in high-income countries cannot fully eliminate pharmaceutical residues or resistance genes. Mitigation strategies ranging from advanced wastewater treatment to ecological interventions and policy measures reveal promise but remain fragmented and unevenly implemented. The findings emphasize the necessity of adopting integrated, One Health approaches that address human, animal, and environmental dimensions simultaneously. This review contributes to the growing body of knowledge by consolidating fragmented evidence, identifying methodological and contextual gaps, and reinforcing the central role of environmental surveillance in global AMR strategies. Future research should prioritize standardized methodologies, longitudinal monitoring, and deeper exploration of socio-environmental drivers to design context-sensitive interventions capable of addressing the scale and complexity of this global challenge.

## CONFLICTS OF INTEREST

All Author Declare No. conflict of interest

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