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Mitigating Antimicrobial Resistance through Pharmaceutical Effluent Control: Adopted Chemical and Biological Methods and Their Global Environmental Chemistry Implications

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Abstract
Mitigating the global challenge of antimicrobial resistance (AMR) requires a multifaceted approach, with increasing attention directed toward environmental contributors such as pharmaceutical effluents. The unchecked discharge of active pharmaceutical ingredients (APIs) from manufacturing plants, healthcare facilities, and post-consumer waste into aquatic environments creates persistent antibiotic residues that exert selective pressure on microbial communities. This process facilitates the evolution and spread of resistant genes, posing a significant threat to public health and ecological integrity. This paper critically reviews adopted chemical and biological methods for controlling pharmaceutical effluents to mitigate AMR and examines their broader implications in environmental chemistry. Chemical treatment methods such as advanced oxidation processes (AOPs), ozonation, and chlorination have demonstrated high efficiency in degrading complex pharmaceutical compounds. However, these methods often generate toxic by-products and require high operational costs and energy input, raising concerns about sustainability and secondary pollution. On the other hand, biological methods—particularly activated sludge systems, constructed wetlands, and enzymatic treatments—offer eco-friendly alternatives capable of biodegrading pharmaceutical residues under controlled conditions. These systems leverage microbial metabolism and plant-microbe interactions to reduce pollutant load, although their effectiveness can be influenced by environmental factors and the chemical structure of target compounds. The global environmental chemistry implications of these approaches are profound. While chemical treatments may alter the speciation and mobility of pharmaceutical residues, biological methods influence nutrient cycling, microbial diversity, and ecological resilience. Understanding the environmental fate and transformation pathways of pharmaceuticals and their metabolites is crucial for evaluating treatment efficacy and minimizing unintended consequences. Furthermore, integrating these treatment strategies with regulatory frameworks and real-time monitoring tools can significantly enhance risk mitigation, especially in low- and middle-income countries where effluent management is often inadequate. In conclusion, effective pharmaceutical effluent control through tailored chemical and biological methods is pivotal to addressing AMR. A comprehensive approach that combines scientific innovation, environmental monitoring, and global policy alignment is essential to safeguard ecosystems and human health from the escalating threat of antibiotic resistance.

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1. Introduction

Antimicrobial resistance (AMR) has emerged as one of the most pressing global health challenges of the 21st century, threatening to undermine decades of medical progress. The ability of microorganisms to resist the effects of antibiotics not only complicates the treatment of infectious diseases but also leads to prolonged illnesses, increased mortality, and substantial economic burden

on healthcare systems worldwide (Abimbola, Otieno & Cole, 2021). While the misuse and overuse of antibiotics in human and veterinary medicine are widely recognized contributors to AMR, environmental pathways are increasingly acknowledged as critical but often overlooked drivers of resistance proliferation (Singh & Yeh, 2017).

One of the most significant environmental contributors to AMR is the discharge of pharmaceutical effluents into natural ecosystems. Pharmaceutical manufacturing plants, hospitals, and domestic sources release wastewater containing active pharmaceutical ingredients (APIs), including antibiotics, into water bodies. These residues, often present at sub-lethal concentrations, exert selective pressure on environmental microbial communities, promoting the emergence and horizontal transfer of resistant genes (Acero, *et al*., 2010; Singer, *et al*., 2016). This phenomenon transforms natural environments into reservoirs and conduits for AMR, ultimately affecting human and animal health through the water-food-human continuum.

This paper explores the mitigation of antimicrobial resistance through the control of pharmaceutical effluents, focusing on both chemical and biological treatment methods. It critically examines the mechanisms, effectiveness, and limitations of approaches such as advanced oxidation processes, ozonation, activated sludge systems, and constructed wetlands. Additionally, the paper investigates the global environmental chemistry implications of these methods, including their influence on the fate, transformation, and ecological impact of pharmaceutical compounds. The review aims to provide a comprehensive understanding of how effluent management intersects with environmental protection and public health (Adegoke, *et al*., 2016; Šimatović & Udiković-Kolić, 2019). By synthesizing current practices, challenges, and innovations in effluent treatment, the paper offers strategic insights for policymakers, researchers, and environmental managers working to curb the environmental spread of AMR.

2. Methodology

This study adopted a systematic review methodology, employing a conceptual synthesis of current research and empirical findings on chemical and biological interventions in pharmaceutical effluent management and their implications for mitigating antimicrobial resistance (AMR). A structured literature retrieval and evaluation process was conducted using peer-reviewed journal articles, reports, and authoritative reviews, with a focus on global studies that emphasize the intersection between effluent treatment technologies and the control of AMR in aquatic ecosystems and human health domains.

Articles were selected based on relevance, recency, methodological rigor, and geographical representativeness. Databases such as Scopus, Web of Science, PubMed, and Google Scholar were searched using keywords like "pharmaceutical effluent," "antimicrobial resistance," "advanced oxidation processes," "bioremediation," "hospital wastewater," and "AMR mitigation strategies." The review included studies exploring the physicochemical characteristics and microbial implications of pharmaceutical effluents, the degradation kinetics of antibiotic compounds, and the efficacy of chemical and biological treatment systems.

The reviewed studies encompass assessments of chlorination (Acero *et al*., 2010), advanced oxidation processes (Bartolomeu *et al*., 2018; Giwa *et al*., 2021), and microbial consortia (Bhatt *et al*., 2021) for degrading antibiotic residues and resistance genes. The inclusion of planetary health perspectives (Abimbola *et al*., 2021) contextualized these interventions within global ethical and ecological frameworks. Studies by Adegoke *et al*. (2016), Aslam *et al*. (2018), and Arshad & Zafar (2020) provided foundational evidence of the environmental dissemination of resistant pathogens and resistance genes, highlighting the urgent need for integrated control mechanisms.

Articles evaluating global occurrence patterns (Aus der Beek *et al*., 2016), persistence in aquatic systems (Bu *et al*., 2016), and environmental risk from hospital and municipal wastewater (Al Aukidy *et al*., 2014; Aydin *et al*., 2019) helped frame the scope of contamination and pathways of AMR propagation. Methodological emphasis was placed on comparative analysis of removal efficiencies, transformation products, and environmental risk indicators from processes like ozonation, photocatalysis, peracetic acid oxidation, and bioelectrochemical systems (Ahmed *et al*., 2017; Akhil *et al*., 2021; Hassan *et al*., 2021).

This conceptual synthesis integrated chemical treatment frameworks—e.g., chlorination, peracetic acid, UV-based oxidation—with microbial approaches such as bioaugmentation and enzymatic degradation, exploring their synergistic use to degrade persistent pharmaceuticals and disrupt AMR pathways. Studies exploring the co-occurrence of antimicrobial agents and resistance genes across clinical, agricultural, and urban effluent sources were incorporated to underscore the necessity of cross-sectoral interventions.

Qualitative insights were also drawn from governance-related literature (Baekkeskov *et al*., 2020; Khor, 2019; Khan *et al*., 2021), regulatory strategies, and low- and middle-income country-specific challenges (Sartelli *et al*., 2020; Ferri *et al*., 2017), which allowed for the framing of practical implementation considerations in diverse socioeconomic contexts. These studies informed the multi-dimensional implications of effluent-based AMR evolution, such as bioaccumulation, resistome expansion, and trophic-level transfers in aquatic food chains.

Findings were synthesized using thematic content analysis and comparative cross-study evaluations to identify prevailing trends, promising innovations, and critical gaps. Particular attention was paid to chemical-biological hybrid models (Guieysse & Norvill, 2014) and real-time monitoring potentials (Nguyen *et al*., 2021), culminating in the formulation of a conceptual process flow for integrated AMR mitigation through effluent control.

This flowchart provides a comprehensive visualization of the sequential and integrative approach required for mitigating AMR through pharmaceutical effluent control, emphasizing synergy between chemical oxidation and biological treatment, and incorporating monitoring and governance elements to ensure environmental and public health safety.

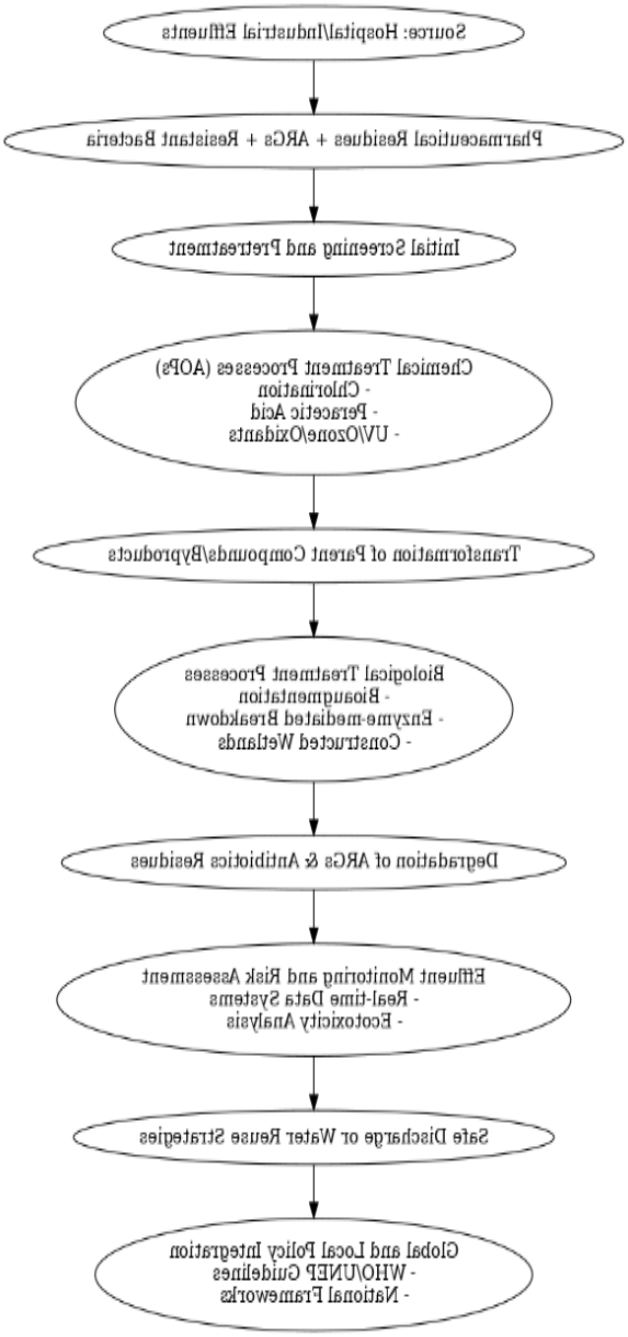

Fig 1: Flowchart of the study methodology

2.1 Sources and Composition of Pharmaceutical Effluents

Pharmaceutical effluents are a significant environmental concern due to their direct and indirect contributions to the growing challenge of antimicrobial resistance (AMR). These effluents are generated from a variety of sources, and their composition includes a wide range of bioactive substances that persist in natural ecosystems. Understanding the origins and chemical makeup of pharmaceutical effluents is critical to devising effective mitigation strategies aimed at curbing their ecological and public health impacts, particularly in the context of AMR (Singh, *et al*., 2016).

Pharmaceutical manufacturing plants are among the primary sources of effluents that contain high concentrations of active pharmaceutical ingredients (APIs). These facilities often use large volumes of water during the production, formulation, and packaging of pharmaceutical products. In many cases, waste management practices are inadequate or outdated, resulting in the discharge of partially treated or untreated wastewater directly into nearby rivers, lakes, and groundwater systems. Studies conducted in countries such as India and China—major hubs of global pharmaceutical production—have revealed alarmingly high levels of antibiotics like ciprofloxacin, norfloxacin, and sulfamethoxazole in industrial wastewater (Aga, *et al*., 2016; Serwecińska, 2020). The concentration of these compounds can be several orders of magnitude higher than therapeutic doses, providing ideal conditions for the selection and propagation of resistant microbial strains. Moreover, lax environmental regulations, insufficient enforcement, and the high cost of advanced treatment technologies often compound the problem in developing economies. Figure 2 shows Venn diagram of antibiotic-resistance genes detected in the hospital wastewater presented by Khan, Söderquist & Jass, 2019.

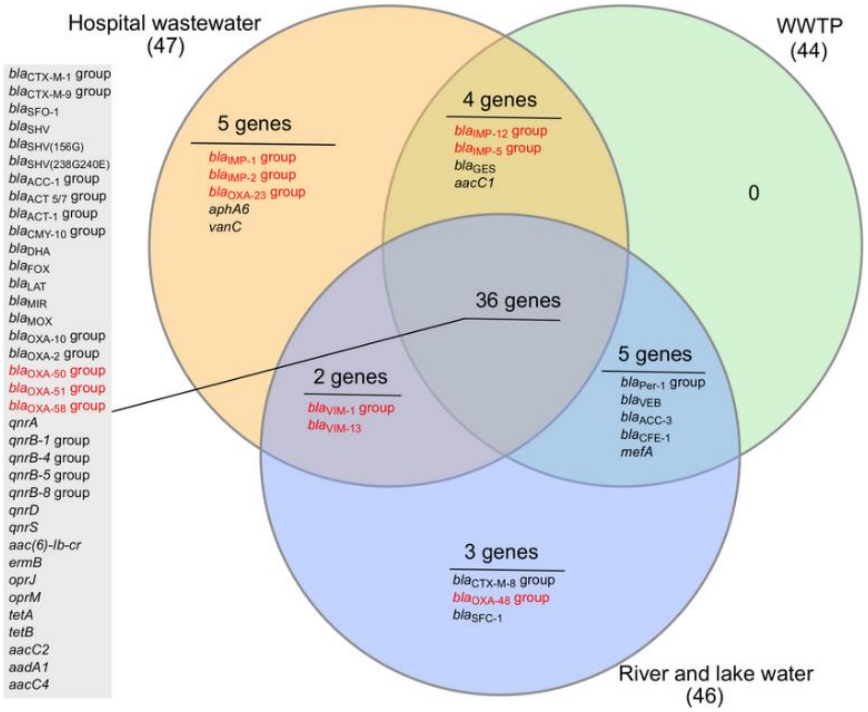

Fig 2: Venn diagram of antibiotic-resistance genes detected in the hospital wastewater (Khan, Söderquist & Jass, 2019).

Hospitals and healthcare facilities represent another major source of pharmaceutical effluents. These institutions administer a wide variety of drugs daily, ranging from antibiotics and analgesics to chemotherapy agents and contrast media used in imaging. A significant proportion of administered drugs are excreted unmetabolized through urine and feces, which then enter the sewage system. Hospital wastewater thus carries a complex mixture of pharmaceutical residues, pathogens, disinfectants, and radionuclides (Ahmed, *et al*., 2017; Sartelli, *et al*., 2020). These effluents are not typically subject to specialized treatment and are often co-processed with municipal wastewater, which lacks the capability to fully degrade or remove pharmaceutical compounds. The continuous inflow of hospital wastewater into the environment leads to chronic exposure of aquatic ecosystems to low concentrations of antibiotics and other drugs, creating an evolutionary pressure that fosters AMR.

Households also contribute significantly to the pharmaceutical load in the environment, primarily through the improper disposal of unused or expired medications. Many individuals dispose of leftover medicines by flushing them down toilets or discarding them with regular garbage. Additionally, like in hospital settings, a large portion of consumed medications is excreted unchanged or as active metabolites. These substances eventually reach sewage treatment plants (STPs) or enter the environment through septic systems (Santos, *et al*., 2013). Conventional STPs are not designed to target pharmaceutical compounds, allowing many of these substances to pass through untreated and accumulate in aquatic environments. As over-the-counter and prescription drug use increases globally, particularly in aging populations and in regions with rising chronic disease burdens, the household contribution to pharmaceutical pollution is expected to grow correspondingly (Akhil, *et al*., 2021; Slaughter, *et al*., 2019). Representation Illustrations of the different treatment processes of antibiotics presented by Hassan, *et al*., 2021 is shown in figure 3.

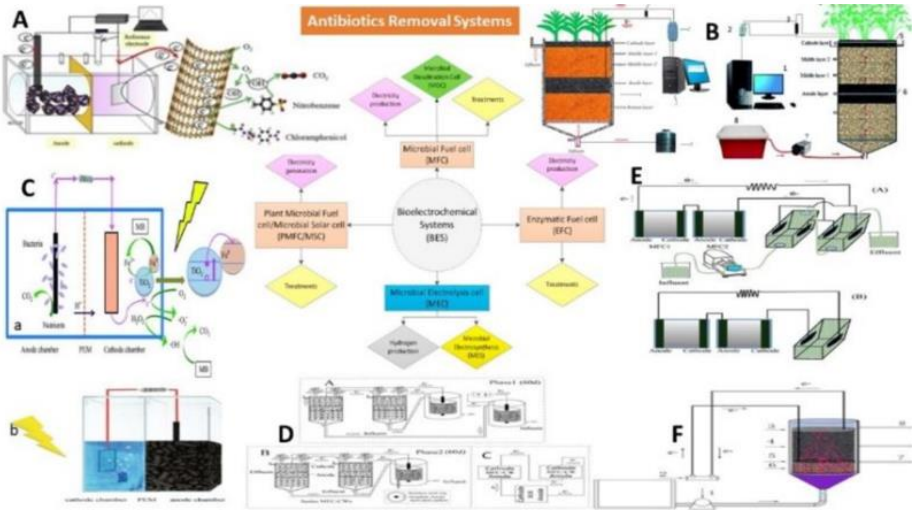

Fig 3: Representation Illustrations of the different treatment processes of antibiotics (Hassan, *et al*., 2021).

The composition of pharmaceutical effluents is highly complex, often reflecting the drug usage patterns and waste disposal practices of a particular region or facility. Commonly detected pharmaceutical compounds include antibiotics (e.g., tetracycline, amoxicillin, erythromycin), nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and diclofenac, anticonvulsants, beta-blockers, lipid regulators, and hormones. Antibiotics, due to their direct role in microbial inhibition, are of particular concern. These compounds are frequently detected in surface water, groundwater, and even drinking water sources, often at concentrations capable of exerting selective pressure on microorganisms. The presence of multiple antibiotics in combination can further exacerbate the development of multidrug-resistant bacteria (Al Aukidy, Verlicchi & Voulvoulis, 2014; Thongsamer, *et al*., 2021).

In addition to antibiotics, effluents may also contain other pharmaceuticals that indirectly influence microbial communities or pose ecotoxicological risks. For instance, NSAIDs have been linked to the disruption of fish reproductive systems, while psychiatric medications like fluoxetine can alter fish behavior, thereby affecting ecosystem dynamics. Hormonal drugs, particularly synthetic estrogens, can lead to endocrine disruption in aquatic organisms, resulting in skewed sex ratios and impaired reproductive capacity (Arshad & Zafar, 2020; Sahota & Sharma, 2021). The presence of such diverse and persistent contaminants contributes to the complex challenge of addressing pharmaceutical pollution from an environmental chemistry standpoint. Mo, *et al*., 2017 presented the flow of antibiotics and antibiotic resistance genes in fish ponds as shown in figure 4.

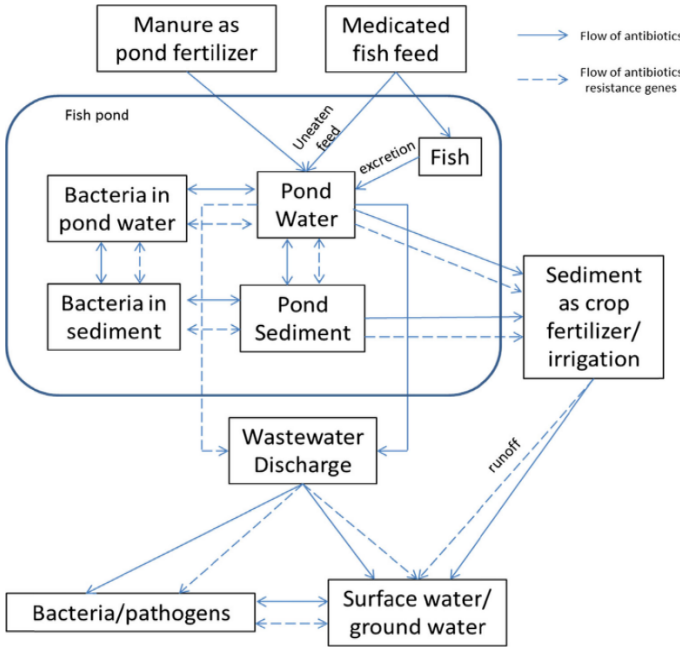

Fig 4: Flow of antibiotics and antibiotic resistance genes in fish ponds (Mo, *et al*., 2017).

A defining characteristic of pharmaceutical contaminants is their persistence in the environment. Many of these compounds are designed to be stable and bioactive for prolonged periods within the human body, and these same properties contribute to their environmental longevity. Some compounds exhibit half-lives ranging from days to several months in aquatic systems. Their resistance to biodegradation means that they can accumulate in sediments, bioaccumulate in aquatic organisms, and enter the food chain (Reid, 2020, Truong, *et al*., 2021). Furthermore, some pharmaceuticals can undergo transformation into metabolites or degradation products that may be equally or more toxic than the parent compound. For example, the degradation of certain sulfonamides can lead to the formation of more persistent and toxic derivatives.

The bioactivity of pharmaceutical contaminants poses another serious concern. Even at trace levels, these substances can exert pharmacological effects on non-target organisms. In microbial communities, sub-inhibitory concentrations of antibiotics do not kill bacteria outright but instead induce stress responses, enhance mutation rates, and promote horizontal gene transfer. These processes increase the likelihood of antibiotic resistance gene (ARG) propagation. Additionally, environmental compartments that receive pharmaceutical effluents, such as river sediments and sewage sludge, often act as reservoirs of ARGs and antibiotic-resistant bacteria (ARB), facilitating their dissemination across ecological and geographical boundaries (Reggiane de Carvalho Costa, Guerra Pacheco Nunes & Amaral Féris, 2021).

The environmental implications of pharmaceutical effluent contamination extend beyond the aquatic environment. Irrigation with wastewater containing pharmaceutical residues can result in the accumulation of drugs in agricultural soils and crops. Studies have detected antibiotics in vegetables irrigated with treated effluents, posing direct risks to human health and creating additional pathways for AMR transmission. Moreover, livestock exposed to contaminated water or feed may harbor resistant bacteria, further bridging the gap between environmental and clinical AMR (Verlicchi, *et al*., 2012).

The persistence and bioactivity of pharmaceutical compounds also complicate their removal during wastewater treatment. Conventional treatment methods—such as sedimentation, filtration, and biological degradation in activated sludge—are not specifically designed to eliminate pharmaceuticals. As a result, advanced treatment technologies such as ozonation, membrane filtration, and

activated carbon adsorption are being explored (Quintana, *et al*., 2010). However, these methods are often expensive, energy-intensive, and not widely implemented in low-resource settings.

In summary, pharmaceutical effluents originate from diverse sources including industrial manufacturing, healthcare facilities, and households, and contain a wide range of biologically active and persistent compounds. These substances accumulate in the environment, exerting selective pressure on microbial populations and significantly contributing to the development and spread of antimicrobial resistance. Their presence in water, soil, and biota raises serious ecological and public health concerns, especially given their stability, potential for bioaccumulation, and capacity to alter microbial genetic structures. Effective control of these effluents through tailored chemical and biological treatment methods is essential not only for environmental protection but also for mitigating the long-term global threat of AMR. Understanding the sources and composition of pharmaceutical effluents is a foundational step toward developing comprehensive and sustainable mitigation strategies.

2.2 Impact of Pharmaceutical Effluents on Antimicrobial Resistance

Pharmaceutical effluents have emerged as a significant contributor to the global challenge of antimicrobial resistance (AMR), primarily through their ability to exert selective pressure on microbial communities, promote genetic mutation, and facilitate the spread of resistance traits via horizontal gene transfer. The persistence of pharmaceutical compounds, especially antibiotics, in the environment creates an artificial evolutionary landscape that enables bacteria to adapt and survive in hostile conditions, often leading to the emergence and dissemination of resistant strains. These impacts are particularly pronounced in aquatic ecosystems, which receive a continuous influx of pharmaceutical waste from industrial, healthcare, and domestic sources.

Selective pressure is a fundamental mechanism by which pharmaceutical effluents drive antimicrobial resistance. When antibiotics are released into the environment, even at sub-therapeutic or trace concentrations, they exert a constant selective force on microbial populations. Unlike in clinical settings where antibiotics are administered in controlled doses to treat infections, environmental exposure to these compounds is indiscriminate, chronic, and often involves multiple antibiotics simultaneously (Pruden, *et al*., 2013, Wang & Zhuan, 2020). This prolonged exposure does not necessarily kill the microorganisms but creates a stressful environment that favors those with mutations or inherent traits that confer resistance. Over time, these resistant strains proliferate while susceptible ones are eliminated, leading to a shift in the microbial population toward resistant phenotypes.

In addition to selecting for resistant bacteria, sub-lethal antibiotic concentrations can induce microbial stress responses that increase the rate of mutation. Certain antibiotics are known to trigger the bacterial SOS response, a global regulatory system that promotes DNA repair and mutagenesis under stress. This process increases the likelihood of acquiring beneficial mutations, including those conferring resistance to antibiotics. Moreover, some antibiotics have been found to directly promote mutagenic activity, enhancing the evolution of resistance even in non-target microbial species (Aslam, *et al*., 2018; Wang, *et al*., 2016). These mutations may alter drug target sites, increase efflux pump activity, or modify membrane permeability, all of which contribute to bacterial survival in the presence of antimicrobial agents.

Perhaps more concerning than individual mutation events is the role of pharmaceutical effluents in facilitating horizontal gene transfer (HGT) among bacteria in aquatic environments. HGT enables the transfer of genetic material—including antibiotic resistance genes (ARGs)—between different bacterial species, accelerating the spread of resistance far beyond what would occur through vertical transmission alone. There are three primary mechanisms of HGT: transformation (uptake of free DNA), transduction (bacteriophage-mediated transfer), and conjugation (direct transfer via plasmids) (Aus der Beek, *et al*., 2016; Postigo & Richardson, 2014). Conjugation, in particular, is the most relevant in the context of pharmaceutical-contaminated water bodies, as it allows for the rapid exchange of plasmids carrying multiple resistance genes among both pathogenic and non-pathogenic bacteria.

Pharmaceutical effluents contribute to HGT in several ways. First, antibiotics in the environment act as selective agents that enrich for bacteria carrying resistance genes. These bacteria often harbor plasmids and integrons—mobile genetic elements that serve as vehicles for gene exchange. Second, the stress induced by antibiotic exposure can increase membrane permeability, making bacteria more receptive to DNA uptake and plasmid conjugation (Pikkemaat, *et al*., 2016). Third, pharmaceutical effluents often co-occur with heavy metals and other pollutants that also select for resistance and co-select for multi-resistance traits due to shared genetic loci. This synergistic interaction compounds the threat of AMR proliferation in environmental settings.

Numerous case studies from around the world have demonstrated the real-world consequences of pharmaceutical effluent discharge on AMR development. One of the most cited examples is from Patancheru, near Hyderabad, India—an industrial hub for generic drug manufacturing. Wastewater from pharmaceutical factories in the region was found to contain extraordinarily high levels of antibiotics, particularly ciprofloxacin, with concentrations exceeding therapeutic doses by several thousand times. Environmental monitoring revealed that nearby water bodies were heavily contaminated, and microbial testing confirmed the presence of multidrug-resistant bacteria in sediments, effluent channels, and surface water (Aydin, *et al*., 2019; Ort, *et al*., 2010). Importantly, resistance genes identified in these environmental samples matched those found in clinical pathogens, highlighting the potential for environmental reservoirs to act as sources of infection.

Another critical case was documented in China, where pharmaceutical manufacturing facilities were linked to the contamination of rivers and wetlands with fluoroquinolones and macrolides. Similar to the situation in India, these environments showed elevated levels of ARGs, particularly those associated with plasmid-borne resistance. Studies indicated that resistance genes in aquatic bacteria could be transferred to Escherichia coli and other clinically significant pathogens under laboratory conditions, confirming the viability of environmental-to-clinical gene flow. Moreover, resistance to last-resort antibiotics such as colistin has also been traced back to agricultural and pharmaceutical pollution in parts of China, raising alarms over the erosion of remaining

treatment options (Baekkeskov, *et al*., 2020).

In Europe, several studies have demonstrated the impact of hospital and urban wastewater on local AMR patterns. For example, in Germany, researchers found that wastewater from healthcare institutions contained a higher abundance and diversity of resistance genes than municipal wastewater, particularly those conferring resistance to beta-lactams and aminoglycosides. In downstream environments where treated and untreated effluents mixed, resistant strains and resistance genes were detected in aquatic organisms and biofilms, providing further evidence of environmental dissemination (Bairán, *et al*., 2020; Oluwole, Omotola & Olatunji, 2020). While pharmaceutical concentrations in European waters are typically lower than those found in Asia due to stricter regulation, the presence of resistance genes even at these levels suggests that there may be no truly safe threshold for antibiotic discharge.

The implications of these findings are far-reaching. Once established, environmental reservoirs of resistance genes can persist for extended periods, even after the removal or dilution of the initial selective pressure. These reservoirs can seed resistant bacteria into drinking water sources, irrigation systems, and recreational waters, increasing the risk of human and animal exposure. Moreover, aquatic environments often serve as melting pots where diverse microbial species coexist and interact, creating ideal conditions for gene exchange (Bakkeren, Diard & Hardt, 2020; Oliveira, *et al*., 2015). Aquatic sediments, in particular, provide anoxic and nutrient-rich environments that support the survival of both resistant bacteria and mobile genetic elements. Sludge from wastewater treatment plants, frequently used as agricultural fertilizer, can also act as a vector for ARG dissemination into soils and crops.

The global movement of water, people, and goods further exacerbates the spread of resistance. For example, ARGs detected in remote environments, such as Arctic lakes and Antarctic soils, have been linked to anthropogenic activities and long-distance environmental transport. This underlines the fact that pharmaceutical pollution and AMR are not localized problems but global issues requiring coordinated action. Without comprehensive control measures, resistance developed in one region due to pharmaceutical effluents can rapidly become a worldwide threat (Oliveira, Al Aukidy & Verlicchi, 2018).

In conclusion, pharmaceutical effluents play a critical role in driving the development and spread of antimicrobial resistance through mechanisms such as selective pressure, microbial mutation, and horizontal gene transfer. The impact of these effluents has been clearly demonstrated in numerous global case studies, where high levels of antibiotic contamination have created AMR hotspots in both urban and rural settings. The environmental consequences of unchecked pharmaceutical discharge are severe and enduring, with potential feedback loops into clinical settings and public health systems. Addressing this issue requires urgent investment in wastewater treatment technologies, stricter regulatory frameworks, and global cooperation to minimize the ecological footprint of pharmaceutical production and consumption. Only by tackling environmental drivers such as pharmaceutical effluents can the escalating crisis of antimicrobial resistance be effectively mitigated.

2.3 Chemical Methods of Effluent Treatment

Chemical methods of effluent treatment play a critical role in mitigating pharmaceutical pollution, which is a major driver of antimicrobial resistance (AMR) in environmental settings. As pharmaceutical compounds, particularly antibiotics, are released into aquatic environments from manufacturing sites, healthcare facilities, and households, their persistence and bioactivity create ideal conditions for the emergence and spread of resistant microorganisms. Chemical treatment methods are employed to remove or degrade these compounds before they reach the environment, thereby reducing their selective pressure on microbial communities. Among these methods, advanced oxidation processes (AOPs), ozonation, chlorination, and adsorption techniques are the most widely studied and implemented.

Advanced oxidation processes (AOPs) are a group of chemical treatment technologies that rely on the generation of highly reactive species, particularly hydroxyl radicals (•OH), to oxidize and break down organic pollutants, including pharmaceuticals. Hydroxyl radicals are non-selective oxidants capable of reacting with a broad range of chemical compounds, leading to their transformation into less harmful or more biodegradable substances. Common AOPs include the Fenton reaction, photocatalysis, ozonation combined with hydrogen peroxide (O_3/H_2O_2), and UV-based treatments such as UV/H_2O_2 and UV/TiO_2 systems (Bansal, 2019; Ojemaye & Petrik, 2019).

In the Fenton reaction, hydrogen peroxide (H_2O_2) reacts with ferrous iron (Fe^{2+}) under acidic conditions to produce hydroxyl radicals. This method is particularly effective for degrading antibiotics and other persistent pharmaceutical compounds. Photocatalysis, on the other hand, uses light-activated catalysts such as titanium dioxide (TiO_2) to generate reactive species that degrade pollutants in water. These methods can achieve high degradation efficiencies, making them suitable for treating pharmaceutical effluents with complex chemical profiles.

Despite their effectiveness, AOPs present several limitations. The operational costs associated with chemical reagents, energy consumption (particularly for UV-based systems), and the need for pH adjustment can make large-scale implementation economically challenging. Moreover, incomplete oxidation may result in the formation of intermediate by-products that could be more toxic or persistent than the parent compounds. For example, the breakdown of some antibiotics during AOPs has been found to generate transformation products with unknown or potentially adverse ecological effects (Baquero, *et al*., 2021; Nguyen, *et al*., 2021). Additionally, the presence of competing substances such as natural organic matter can reduce the availability of hydroxyl radicals, lowering treatment efficiency.

Ozonation and chlorination are traditional disinfection methods commonly used in water and wastewater treatment. Ozonation involves the application of ozone (O_3), a strong oxidizing agent, to degrade organic contaminants, including pharmaceutical compounds. It is particularly effective for removing antibiotics, endocrine-disrupting chemicals, and other micropollutants. Ozone reacts rapidly with electron-rich functional groups, leading to the breakdown of complex molecules into smaller fragments. The process can be enhanced by combining ozone with hydrogen peroxide or UV light to generate additional reactive species, increasing the overall degradation capacity.

Chlorination, using chlorine gas or sodium hypochlorite, is also used to oxidize pharmaceutical residues. It is effective

for treating pathogens and certain organic pollutants, and is widely available and cost-effective. However, both ozonation and chlorination have important environmental trade-offs. One of the major concerns is the formation of toxic by-products. Ozonation can lead to the generation of bromate, a potential human carcinogen, especially in waters containing high levels of bromide (Bartolomeu, *et al*., 2018; Nagarnaik, Batt & Boulanger, 2012). Similarly, chlorination is associated with the formation of chlorinated disinfection by-products (DBPs) such as trihalomethanes (THMs) and haloacetic acids (HAAs), which have been linked to cancer and reproductive toxicity in humans.

In addition to their toxicity, these by-products can contribute to the selection of resistant microorganisms. For instance, the sub-lethal exposure of bacteria to residual disinfectants and their by-products has been shown to induce stress responses, enhancing the potential for mutation and horizontal gene transfer. Furthermore, resistance to disinfectants like chlorine has been observed in environmental microbial communities, suggesting that disinfection processes may inadvertently contribute to the proliferation of AMR under certain conditions.

Adsorption techniques represent another class of chemical treatment methods, widely employed for the removal of pharmaceutical compounds from wastewater. These techniques rely on the physical or chemical binding of contaminants onto the surface of solid materials. Activated carbon—both powdered (PAC) and granular (GAC)—is the most commonly used adsorbent due to its high surface area, porosity, and adsorption capacity for a wide range of organic compounds, including antibiotics, NSAIDs, and hormones (Bhatt, *et al*., 2021; Monapathi, *et al*., 2021).

The mechanism of adsorption depends on various factors such as the chemical structure of the pharmaceutical, the surface characteristics of the adsorbent, pH, and the presence of co-contaminants. Activated carbon is effective in removing compounds that are hydrophobic or have a strong affinity for carbon surfaces. In practice, PAC is typically added directly to wastewater as a slurry, while GAC is used in fixed-bed filters. Both forms can significantly reduce the concentration of pharmaceutical residues in treated effluents.

While adsorption is a straightforward and efficient method, it is not without challenges. The adsorption capacity of activated carbon decreases over time as binding sites become saturated, necessitating periodic regeneration or replacement of the material. Regeneration processes, such as thermal reactivation, are energy-intensive and may not fully restore the original adsorption capacity. Additionally, the disposal of spent adsorbents containing concentrated pharmaceutical residues poses a secondary environmental risk if not managed properly (Bilal, *et al*., 2021).

Other adsorbents, such as zeolites, biochar, and synthetic resins, have been explored as alternatives or supplements to activated carbon. Biochar, for example, is a carbon-rich material produced through the pyrolysis of biomass and has shown promise for pharmaceutical removal due to its tunable surface properties. However, its adsorption performance can be inconsistent and is often affected by the source material and production conditions. Synthetic resins offer greater specificity and can be engineered for targeted removal, but they are typically more expensive and less widely available than activated carbon (Bottoni, Caroli & Caracciolo, 2010; Mohapatra, *et al*., 2014).

Despite these limitations, adsorption techniques are valuable for polishing treated effluents, especially in combination with other treatment processes. They can be integrated into multi-barrier treatment systems to achieve higher removal efficiencies and minimize the release of pharmaceutical residues into the environment. Moreover, adsorption does not involve chemical transformation of pollutants, reducing the risk of generating toxic by-products.

In conclusion, chemical methods of effluent treatment—including advanced oxidation processes, ozonation, chlorination, and adsorption—play a pivotal role in mitigating the environmental release of pharmaceutical compounds and their associated risks of promoting antimicrobial resistance. Each method offers unique advantages and limitations depending on the specific treatment objectives, infrastructure capacity, and environmental conditions. AOPs are highly effective but costly and complex; ozonation and chlorination are accessible but produce harmful by-products; adsorption is versatile and efficient but challenged by regeneration and waste management issues. Integrating these chemical methods with biological treatment processes and regulatory frameworks can enhance their effectiveness and sustainability. As the environmental chemistry implications of pharmaceutical effluents become more widely recognized, it is essential to invest in research, innovation, and policy to advance the development and deployment of safer and more efficient effluent treatment technologies globally.

2.4 Biological Methods of Effluent Treatment

Biological methods of effluent treatment are increasingly recognized as sustainable and eco-friendly approaches for mitigating pharmaceutical pollution and its contribution to antimicrobial resistance (AMR). Unlike chemical treatments that often rely on high energy inputs and may produce toxic by-products, biological treatments harness the natural degradative abilities of microorganisms, plants, and enzymes to remove pharmaceutical compounds from wastewater. These methods aim to reduce the concentration of active pharmaceutical ingredients (APIs) before they enter aquatic environments, thereby lowering the selective pressure that drives microbial mutation and the spread of resistance genes. Among the most prominent biological treatment strategies are activated sludge systems, constructed wetlands, and enzymatic or bioaugmentation approaches.

Activated sludge systems represent one of the most widely used biological wastewater treatment processes globally, especially in municipal and industrial settings. These systems operate on the principle of aerobic microbial degradation, where a consortium of microorganisms—primarily bacteria, protozoa, and fungi—is maintained in a suspended growth environment (Bu, *et al*., 2016; Merker, *et al*., 2020). Wastewater containing pharmaceutical residues is aerated in large tanks, enabling microbial communities to metabolize organic pollutants. The resulting biomass, known as sludge, is then separated from the treated water in a clarifier. The microbial communities in these systems play a pivotal role in breaking down biodegradable organic compounds, including some pharmaceutical residues.

Despite their widespread application, activated sludge systems face several limitations when it comes to the degradation of pharmaceutical contaminants. Many APIs are designed to be biologically stable to withstand metabolic processes in the human body, and this same stability makes them resistant to biodegradation in treatment facilities.

Compounds such as carbamazepine, diclofenac, and certain fluoroquinolone antibiotics persist through activated sludge processes and are commonly detected in effluent discharges (Caracciolo, Topp & Grenni, 2015; McCarthy, *et al*., 2021). Furthermore, conventional systems are not optimized for removing trace-level micropollutants, as their operational focus is typically on reducing biochemical oxygen demand (BOD), nitrogen, and phosphorus. The microbial consortia in these systems may also lack the metabolic pathways required to degrade complex or synthetic pharmaceutical molecules. Additionally, the continuous influx of antibiotics into activated sludge systems can exert selective pressure on microbial communities, potentially promoting the emergence of antibiotic-resistant bacteria and resistance genes within the treatment infrastructure itself.

Constructed wetlands offer an alternative and nature-based solution for the treatment of pharmaceutical-laden wastewater. These systems mimic the filtration and degradation functions of natural wetlands by combining hydrological, biological, and chemical processes. Constructed wetlands consist of shallow basins filled with substrates such as gravel, sand, or soil, and are planted with vegetation like reeds, cattails, and bulrushes. As wastewater flows through the system, a combination of plant uptake, microbial activity, sediment adsorption, and photodegradation works to reduce contaminant levels (Chen, *et al*., 2017; Mazivila, *et al*., 2019).

The effectiveness of constructed wetlands in removing pharmaceutical compounds is largely attributed to synergistic plant-microbe interactions. Plant roots provide a habitat for microbial biofilms and secrete exudates that stimulate microbial metabolism. In turn, microorganisms break down organic contaminants, including antibiotics, into less harmful or inactive forms. Wetland plants also contribute to oxygen transfer and nutrient cycling, further enhancing microbial activity. The diversity and density of plant species, substrate composition, hydraulic retention time, and climatic conditions all influence the removal efficiency of pharmaceutical compounds.

Numerous case studies have demonstrated the success of constructed wetlands in reducing pharmaceutical loads in effluents. In Germany, a hybrid constructed wetland treating hospital wastewater achieved significant reductions in ibuprofen, ketoprofen, and sulfamethoxazole concentrations. In China, wetlands treating municipal wastewater showed high removal rates for erythromycin and ofloxacin, two antibiotics commonly used in both human and veterinary medicine (Cuerda-Correa, *et al*., 2019; Marican & Durán-Lara, 2018). While removal efficiencies can vary depending on the system design and influent characteristics, constructed wetlands offer a cost-effective and environmentally friendly option for secondary or tertiary treatment of pharmaceutical-contaminated water, especially in decentralized and rural contexts.

However, constructed wetlands are not without challenges. Their performance is generally lower for highly persistent or hydrophilic compounds, and treatment efficiency can be inconsistent under variable flow or loading conditions. Seasonal temperature fluctuations can affect microbial activity and plant growth, leading to reduced treatment performance during colder months. Furthermore, wetlands require relatively large land areas for effective operation, which may limit their applicability in densely populated or urban regions (De Oliveira, *et al*., 2020; Manyi-Loh, *et al*., 2018).

Enzymatic and bioaugmentation approaches represent more targeted biological strategies for the degradation of pharmaceutical compounds. Enzymatic treatments utilize specific enzymes—biological catalysts—to break down complex organic molecules into simpler, non-toxic products. These enzymes can be isolated from naturally occurring microorganisms or produced through recombinant DNA technology. Enzymatic degradation is highly selective, making it well-suited for targeting specific pharmaceutical compounds that are resistant to conventional biological or chemical treatment processes.

For example, laccases and peroxidases have been employed to degrade antibiotics, analgesics, and hormonal compounds in aqueous environments. These enzymes work under mild operating conditions and produce fewer secondary pollutants, offering a green alternative to oxidative chemical treatments. However, the practical application of enzymatic treatments in full-scale wastewater treatment systems remains limited due to challenges in enzyme stability, cost, and potential inhibition by wastewater constituents (Deblonde & Hartemann, 2013; Luongo, *et al*., 2020).

Bioaugmentation involves the introduction of specialized microbial strains into existing treatment systems to enhance the degradation of pharmaceutical pollutants. These microbes are either naturally occurring or genetically engineered to possess the metabolic pathways necessary for breaking down specific pharmaceutical compounds. Bioaugmentation can be used to supplement activated sludge systems or constructed wetlands, especially when indigenous microbial communities are insufficient for degrading particular contaminants.

Recent innovations in microbial engineering have led to the development of bacteria capable of degrading persistent pharmaceuticals such as diclofenac, carbamazepine, and sulfamethoxazole. In some cases, consortia of microbes are introduced to perform sequential degradation steps, increasing the overall efficiency and breadth of compound removal (Diaz-Sanchez, *et al*., 2015; Lofrano, *et al*., 2017). These engineered systems offer promising solutions for the targeted treatment of pharmaceutical effluents, especially when integrated with sensor technologies and process control systems that optimize environmental conditions for microbial activity.

Despite their potential, bioaugmentation approaches also face significant hurdles. The survival and activity of introduced microbes depend on environmental conditions, competition with native microorganisms, and the presence of toxic substances that may inhibit metabolic functions. Moreover, concerns about the environmental release of genetically modified organisms (GMOs) and horizontal gene transfer necessitate rigorous biosafety protocols and regulatory oversight. Scalability and cost-effectiveness remain critical barriers to the widespread adoption of enzymatic and bioaugmentation methods in wastewater treatment (EFSA BIOHAZ *et al*., 2021).

In summary, biological methods of effluent treatment provide valuable and sustainable approaches to mitigating the environmental impact of pharmaceutical residues and their role in promoting antimicrobial resistance. Activated sludge systems form the backbone of municipal wastewater treatment but have limited efficacy for pharmaceutical degradation and may serve as hotspots for resistance development (Ferri, *et al*., 2017; Lima, Domingues & Da Silva, 2020). Constructed wetlands offer a nature-based

alternative that leverages plant-microbe interactions to remove contaminants, though they require careful design and management to maintain performance. Enzymatic and bioaugmentation approaches offer high specificity and adaptability, with growing potential through advancements in biotechnology and microbial engineering.

Together, these biological treatment methods contribute to a more holistic and ecologically sound strategy for managing pharmaceutical effluents. When integrated with chemical treatment technologies, real-time monitoring systems, and supportive policy frameworks, they can enhance the resilience and effectiveness of wastewater treatment infrastructure. Addressing the environmental pathways of AMR requires not only innovation in treatment technologies but also a systemic shift toward recognizing wastewater treatment as a frontline defense in global public health. As the environmental chemistry of pharmaceutical contaminants becomes more complex, continued research and interdisciplinary collaboration are essential for developing next-generation solutions that safeguard both ecological integrity and human health.

2.5 Comparative Assessment of Chemical vs Biological Methods

A comparative assessment of chemical and biological methods for pharmaceutical effluent treatment is essential in the global effort to mitigate antimicrobial resistance (AMR). Both approaches aim to reduce the concentration of active pharmaceutical ingredients (APIs) in wastewater and prevent them from reaching natural ecosystems where they can exert selective pressure on microbial communities and foster resistance development. However, the effectiveness, environmental sustainability, cost, scalability, and by-product management of these methods vary significantly, making it necessary to evaluate their respective advantages and limitations within real-world treatment scenarios.

In terms of effectiveness, chemical methods, especially advanced oxidation processes (AOPs), offer rapid and robust degradation of a broad spectrum of pharmaceutical compounds. These processes, including photocatalysis, ozonation, and Fenton reactions, generate highly reactive radicals that can oxidize even the most persistent and complex pharmaceutical molecules. For example, AOPs are particularly effective in breaking down antibiotics such as ciprofloxacin, sulfamethoxazole, and carbamazepine, which are known to resist conventional wastewater treatments (Frédéric & Yves, 2014; Li, 2014). Similarly, chlorination and ozonation are capable of achieving high pathogen kill rates and reducing pharmaceutical concentrations quickly. However, their effectiveness may be influenced by the physicochemical properties of the wastewater, such as pH, organic matter content, and the presence of scavengers that can neutralize reactive species.

Biological methods, such as activated sludge systems, constructed wetlands, and enzymatic treatments, operate more slowly but offer considerable effectiveness for biodegradable pharmaceutical compounds. Microorganisms in these systems can metabolize or transform APIs into less toxic and more stable products. While biological methods are generally less effective for highly persistent compounds, ongoing innovations in microbial engineering and enzymatic treatment are improving their efficacy (Fuchs, Boll & Heider, 2011; Li, *et al*., 2021). The specificity of enzymes and the adaptability of bioaugmentation approaches are promising for the targeted removal of certain pharmaceuticals. Nevertheless, biological methods often fail to fully eliminate all pharmaceutical residues, especially those with stable chemical structures, and may require integration with chemical processes for enhanced removal.

Environmental sustainability is a crucial parameter in evaluating treatment methods, particularly in the context of long-term ecological and public health implications. Biological methods are generally more sustainable because they mimic natural processes and rely on renewable biological agents rather than synthetic chemicals. Constructed wetlands, for example, leverage plant-microbe interactions in a passive system that requires minimal energy input and generates few harmful emissions. Similarly, activated sludge processes, while energy-intensive in aeration stages, are largely based on natural microbial degradation. These systems avoid the introduction of additional pollutants and minimize the risk of secondary contamination.

Chemical methods, in contrast, often carry significant environmental burdens. The use of powerful oxidants and disinfectants in AOPs and chlorination can lead to the formation of harmful by-products, such as bromate, trihalomethanes (THMs), and haloacetic acids (HAAs), which are carcinogenic and pose additional risks to aquatic ecosystems and human health. While these methods are efficient in removing APIs, they can disrupt natural biogeochemical cycles and may generate transformation products with unknown toxicity (Fuentes, *et al*., 2014; Li, *et al*., 2011). Furthermore, energy consumption in UV-based AOPs and the need for chemical reagents increase the carbon footprint of chemical treatments. Thus, while chemical processes can achieve high removal rates, they must be carefully managed to avoid exacerbating environmental harm.

Cost and scalability are major considerations, especially in low- and middle-income countries where resource constraints limit the implementation of advanced treatment technologies. Chemical methods, particularly AOPs, involve high capital and operational costs due to the need for specialized equipment, chemical reagents, and energy input. Maintenance and monitoring requirements further increase the financial burden (Gallandat, *et al*., 2019; Lees, 2021). These costs often make chemical treatments less feasible for decentralized or rural settings, where funding and technical expertise may be limited. Chlorination, while more affordable, still requires careful handling and monitoring to prevent disinfection by-products and ensure worker safety.

Biological methods are generally more cost-effective and scalable, particularly when designed as low-tech or decentralized solutions. Constructed wetlands, for instance, have low operational costs and can be built using locally available materials, making them suitable for small communities, peri-urban areas, and healthcare facilities in developing regions. Although they require larger land areas and longer treatment times, their simplicity and low maintenance make them an attractive option for sustainable wastewater management. Activated sludge systems, while more complex and requiring energy for aeration, benefit from established infrastructure and widespread technical knowledge (Giwa, *et al*., 2021; Le Roux, *et al*., 2011). Bioaugmentation and enzymatic treatments, though potentially costly at the research and pilot stages, offer opportunities for modular deployment and integration with

existing systems, improving scalability over time.

Another key issue in comparing chemical and biological methods is the management of by-products resulting from the treatment process. Chemical methods often lead to the formation of intermediate transformation products that may be more persistent or toxic than the parent compounds. For instance, incomplete oxidation during AOPs can yield chlorinated or nitrosylated derivatives with unknown environmental and toxicological profiles. These by-products may not only pose direct risks to aquatic organisms but can also influence microbial community structures, potentially driving new forms of resistance. Furthermore, residual chemicals from the treatment process, such as excess oxidants or catalysts, may accumulate in the environment if not properly neutralized.

Biological methods, on the other hand, generally produce fewer harmful by-products. Microbial degradation pathways typically convert pharmaceutical compounds into carbon dioxide, water, and biomass, although some intermediate metabolites may persist, depending on the compound and conditions. In enzymatic treatments, the products are often simpler, non-toxic molecules, especially when the enzymatic pathways are well-characterized. Bioaugmentation strategies also strive to avoid the accumulation of undesirable by-products by tailoring microbial consortia to specific degradation pathways (Grenni, 2011; Le Quesne, *et al*., 2018). However, there is still a need for more comprehensive studies on the fate of transformation products in biological systems to ensure that they do not pose unforeseen risks.

While both chemical and biological methods have their merits and limitations, the growing consensus among environmental scientists and public health experts is that hybrid treatment systems may offer the most effective and sustainable solution for pharmaceutical effluent control. By combining the strengths of chemical and biological approaches—such as the rapid degradation capacity of AOPs with the environmentally friendly and cost-effective benefits of biological treatments—integrated systems can achieve high removal efficiency while minimizing adverse effects. For instance, using AOPs as a pre-treatment step to break down persistent compounds can enhance the subsequent biological degradation in wetlands or activated sludge systems. Similarly, adsorption processes can polish effluents following biological treatment, capturing any residual APIs or by-products (Guieysse & Norvill, 2014; Landecker, 2019).

Ultimately, the choice between chemical and biological treatment methods should be guided by context-specific factors, including the nature and volume of pharmaceutical effluents, local environmental conditions, available infrastructure, regulatory frameworks, and community needs. For industrial pharmaceutical plants with high concentrations of persistent compounds, chemical treatment may be necessary to ensure adequate pollutant reduction. In contrast, for municipal and hospital wastewater with moderate pharmaceutical loads, biological systems or hybrid solutions may be more appropriate and sustainable (Harris, Cormican & Cummins, 2012).

In conclusion, the comparative assessment of chemical and biological methods for pharmaceutical effluent treatment reveals a trade-off between treatment efficiency and environmental compatibility. Chemical methods offer high effectiveness but are constrained by cost, scalability, and the risk of harmful by-products. Biological methods are more environmentally sustainable and cost-effective, though they may be limited by slower degradation rates and compound specificity. As antimicrobial resistance continues to pose a global health threat, optimizing and integrating these treatment approaches will be critical to reducing pharmaceutical pollution and protecting both ecosystems and public health. Interdisciplinary collaboration, continuous research, and supportive policy development are essential to advancing the implementation of safe, effective, and sustainable wastewater treatment systems worldwide.

2.6 Environmental Chemistry Implications

The environmental chemistry implications of pharmaceutical effluent control are central to addressing the global threat of antimicrobial resistance (AMR). Pharmaceutical compounds released into the environment through industrial discharge, hospital wastewater, and household sewage are chemically active and can persist in various environmental compartments. Their fate and transformation, interaction with aquatic systems and biota, and long-term ecological effects are complex and multifaceted, demanding a thorough understanding to inform effective treatment and mitigation strategies. The success of both chemical and biological methods in curbing pharmaceutical pollution must therefore be evaluated not only in terms of removal efficiency but also in relation to the broader environmental chemistry dynamics they influence.

Once introduced into the environment, pharmaceutical compounds do not remain static. They undergo a series of physical, chemical, and biological transformations that determine their persistence, mobility, and toxicity. The fate of these compounds depends on their molecular structure, solubility, partitioning behavior, and susceptibility to degradation processes such as hydrolysis, photolysis, and microbial metabolism. For instance, some antibiotics like sulfamethoxazole and ciprofloxacin exhibit low biodegradability and high environmental persistence, allowing them to accumulate in sediments and biofilms (Hasan & Upadhyay, 2020). Others may break down into intermediate products that retain or even enhance biological activity, thus continuing to exert selective pressure on microbial populations.

Chemical treatment methods, particularly advanced oxidation processes (AOPs), aim to transform pharmaceutical molecules into simpler, less toxic compounds. However, the oxidative degradation of complex pharmaceuticals can yield a cascade of intermediate by-products with varying environmental properties. For example, the ozonation of antibiotics may result in the formation of nitroaromatic compounds or chlorinated organics that are not only persistent but may also display greater toxicity than the parent compounds. These transformation products can interfere with natural biogeochemical cycles, disrupt microbial communities, and affect aquatic organisms at multiple trophic levels (Hernando-Amado, *et al*., 2019; Landecker, 2016). The challenge in chemical treatment, therefore, lies in ensuring that degradation leads to complete mineralization or results in metabolites that are environmentally benign.

Biological methods such as activated sludge systems and constructed wetlands introduce different transformation pathways, primarily through microbial enzymatic activity. These processes tend to produce a more diverse range of metabolites, as microbial consortia break down pharmaceutical compounds through oxidative and reductive

reactions. While biological transformations are generally slower and often incomplete, they may be more environmentally compatible, especially when the end products integrate naturally into existing nutrient cycles. However, the presence of antibiotics and other bioactive substances can inhibit key microbial functions such as nitrification, denitrification, and phosphorus removal, potentially compromising the operational efficiency of biological treatment systems.

In aquatic ecosystems, the chemistry of pharmaceutical residues and their transformation products affects both abiotic and biotic components. Pharmaceuticals can alter the pH, redox potential, and chemical speciation of water bodies, influencing the solubility and bioavailability of other contaminants such as heavy metals. For example, tetracyclines are known to chelate with metal ions like iron and calcium, modifying their mobility and potentially altering nutrient dynamics in aquatic sediments (Hey, *et al*., 2012; Kumar & Pal, 2018). Additionally, the accumulation of pharmaceutical residues in sediments can lead to chronic contamination that persists over long periods, acting as a continual source of exposure for benthic organisms.

The impact of pharmaceutical pollution on aquatic biota is particularly concerning. Antibiotics, hormones, and non-steroidal anti-inflammatory drugs (NSAIDs) are frequently detected in rivers, lakes, and estuaries at concentrations ranging from nanograms to micrograms per liter—levels sufficient to exert biological effects on non-target organisms. Exposure to antibiotics can lead to dysbiosis in microbial communities, reducing microbial diversity and impairing essential ecosystem functions such as organic matter decomposition and nutrient cycling. In fish and amphibians, pharmaceutical compounds have been associated with behavioral changes, reproductive dysfunction, and developmental abnormalities (Hickok & Shapiro, 2012). Synthetic estrogens, for instance, can cause feminization of male fish populations, leading to skewed sex ratios and reproductive failure.

Transformation products of pharmaceuticals may further complicate these impacts. Some metabolites, while not directly toxic, can act as endocrine disruptors or enzyme inhibitors, interfering with physiological processes in aquatic organisms. Moreover, the bioaccumulation of pharmaceutical residues in aquatic food webs can lead to trophic transfer and magnification, ultimately reaching terrestrial predators and even humans (Hotinger, Morris & May, 2021). The consumption of contaminated fish and shellfish represents a potential pathway for low-level, chronic exposure to pharmaceuticals and antibiotic-resistant bacteria, raising significant food safety and public health concerns.

Over time, the continuous release of pharmaceutical effluents into aquatic and terrestrial environments can have far-reaching ecological consequences. One of the most critical outcomes is the establishment of environmental reservoirs of antimicrobial resistance. Natural environments, once considered dilution zones, are now recognized as hotspots for the emergence, persistence, and dissemination of resistance genes. Sediments, biofilms, and sludge serve as repositories of antibiotic-resistant bacteria (ARB) and antibiotic resistance genes (ARGs), which can be mobilized and transferred to human pathogens via horizontal gene transfer mechanisms (Krzemiński & Popowska, 2020). These reservoirs are particularly resilient, as ARGs can persist in the environment long after the removal of selective pressure, and may spread across geographical boundaries through water movement, migratory species, and human activities.

The presence of pharmaceutical residues and ARGs in agricultural soils, resulting from the use of wastewater and sludge as fertilizers, represents another long-term ecological concern. Antibiotics can affect soil microbial diversity and function, altering nutrient cycling and plant-microbe interactions. Resistant bacteria introduced through irrigation or fertilization can colonize crops and enter the food chain, perpetuating the cycle of resistance. The widespread use of reclaimed wastewater in agriculture, while addressing water scarcity issues, must therefore be approached with caution and proper treatment to minimize the risk of AMR propagation.

Climate change may further exacerbate the environmental chemistry implications of pharmaceutical effluent pollution. Rising temperatures, altered precipitation patterns, and extreme weather events can influence the fate and behavior of pharmaceuticals in the environment. Increased temperatures may accelerate microbial activity and transformation processes, but may also enhance the mobility and persistence of some compounds (Kong, *et al*., 2017). Flooding and runoff events can transport contaminants from treatment plants and agricultural fields into previously unaffected ecosystems, expanding the geographic scope of AMR hotspots.

Mitigating these long-term consequences requires a holistic understanding of the environmental chemistry of pharmaceutical effluents and a commitment to sustainable treatment and management practices. Chemical and biological treatment methods must be optimized not only for removal efficiency but also for minimizing the formation of harmful by-products and preserving ecological balance. Advanced monitoring technologies, including high-resolution mass spectrometry and metagenomic sequencing, can provide deeper insights into the transformation pathways, bioavailability, and ecological impacts of pharmaceutical compounds and their metabolites.

In conclusion, the environmental chemistry implications of pharmaceutical effluent control are critical to the global effort to mitigate antimicrobial resistance. The fate and transformation of pharmaceutical compounds, their effects on aquatic chemistry and biota, and the long-term ecological consequences of their presence in the environment underscore the need for integrative and context-sensitive treatment solutions. Chemical and biological methods, while differing in their mechanisms and outputs, must be employed strategically to balance pollutant removal with environmental sustainability. Effective management of pharmaceutical pollution requires a multidisciplinary approach that combines environmental science, chemistry, microbiology, public health, and policy, ensuring that treatment efforts are not only technically sound but also ecologically responsible.

2.7 Policy and Global Management Perspectives

Mitigating antimicrobial resistance (AMR) through the control of pharmaceutical effluents requires not only technological innovation but also strong policy and global management frameworks. While chemical and biological methods are vital in reducing the environmental load of pharmaceutical residues, their efficacy and sustainability depend heavily on regulatory enforcement, international cooperation, and strategic planning. The growing recognition of AMR as a transboundary threat has led to the development

of international guidelines and policy tools; however, implementation and impact vary widely, particularly between high-income countries and low- and middle-income countries (LMICs).

The World Health Organization (WHO), the United Nations Environment Programme (UNEP), and other international bodies have been instrumental in framing global policy responses to the environmental dimensions of AMR. WHO's Global Action Plan on Antimicrobial Resistance, launched in 2015, outlines five strategic objectives, including improving awareness and understanding of AMR, strengthening surveillance and research, and reducing the incidence of infection through effective sanitation, hygiene, and infection prevention measures (Khor, 2019). A key component of this plan is the recognition of the environment as a reservoir and vector of resistance genes (Kotwani, Joshi & Kaloni, 2021). WHO has emphasized the importance of monitoring and managing antimicrobial pollutants in environmental matrices, including water, soil, and sediment, to reduce the risk of resistance emergence and spread.

UNEP has also contributed significantly by publishing reports that highlight the environmental dimensions of AMR. The UNEP report "Bracing for Superbugs" underscores that environmental pollution, particularly from pharmaceuticals, plays a critical role in the development and dissemination of AMR. The report calls for improved wastewater treatment infrastructure, stricter discharge regulations, and cross-sectoral coordination to reduce the environmental burden of antimicrobials. These global frameworks serve as guiding documents for national governments, urging them to incorporate environmental considerations into their AMR strategies and align with One Health principles that integrate human, animal, and environmental health.

Despite these international efforts, the integration of pharmaceutical effluent control into national regulatory frameworks remains inconsistent. In many high-income countries, environmental agencies have begun to regulate the discharge of pharmaceutical compounds through licensing conditions, effluent standards, and environmental risk assessments. For example, the European Union mandates environmental risk assessments for all new pharmaceutical products before they can be approved for market entry. These assessments evaluate the potential environmental concentrations of drugs, their persistence, bioaccumulation potential, and ecotoxicity. In some countries, such as Sweden and Germany, voluntary green pharmacy initiatives have also been introduced, encouraging manufacturers to design environmentally safer drugs and promote take-back programs (Khan, *et al*., 2021).

However, a major challenge lies in the fact that most wastewater treatment plants, even in advanced economies, are not specifically designed to remove pharmaceuticals. Therefore, integrating chemical and biological treatment methods into existing regulatory frameworks requires a systemic shift in wastewater management standards. Regulations must go beyond conventional parameters such as biological oxygen demand (BOD) and nutrient levels to include pharmaceutical residues, antimicrobial activity, and resistance gene loads. Moreover, pharmaceutical manufacturers, hospitals, and other point sources must be held accountable through policies that mandate pre-treatment of effluents and promote best management practices.

Incorporating environmental surveillance into AMR monitoring systems is another critical component. Currently, most national AMR action plans focus predominantly on clinical and veterinary sectors, with little emphasis on environmental surveillance. Including environmental indicators—such as concentrations of specific antibiotics, resistance genes, or resistant bacteria in water bodies—can help track the effectiveness of mitigation strategies and inform policy adjustments. Furthermore, linking environmental data with public health outcomes can strengthen the evidence base for regulatory interventions and improve risk communication (Kettle, *et al*., 2014).

In low- and middle-income countries, where the burden of AMR is disproportionately high, implementing pharmaceutical effluent control faces significant structural and resource-based challenges. Many LMICs lack centralized wastewater treatment infrastructure, especially in rural areas and informal urban settlements. As a result, pharmaceutical effluents—whether from manufacturing facilities, hospitals, or households—are often discharged untreated into rivers, lakes, and open land. In countries such as India, Bangladesh, Nigeria, and parts of Southeast Asia, studies have documented extremely high concentrations of antibiotics in surface waters adjacent to pharmaceutical industrial zones, creating AMR hotspots that endanger both local and global public health.

In addition to infrastructural deficits, regulatory enforcement is often weak or fragmented in LMICs. Environmental protection agencies may lack the authority, technical expertise, or financial resources to monitor and regulate pharmaceutical discharges effectively. In some cases, corruption, limited inter-agency coordination, and lack of political will further hinder regulatory implementation (Jjemba, 2018). Even when environmental standards exist, compliance monitoring is irregular, and violators frequently go unpunished. This regulatory vacuum enables polluting practices to persist, undermining global efforts to mitigate AMR.

Addressing these challenges requires international cooperation and capacity building. Donor agencies, development banks, and global health organizations must prioritize investment in wastewater infrastructure and regulatory strengthening in LMICs as part of broader AMR mitigation strategies (Jassim & Limoges, 2014). Technology transfer programs can help make advanced effluent treatment technologies—such as advanced oxidation processes and bioaugmentation systems—more accessible and affordable. In addition, training programs can build local capacity for environmental monitoring, enforcement, and research, enabling countries to develop context-appropriate solutions that align with global standards.

Innovative financing mechanisms, such as green bonds or results-based funding, may offer pathways to scale up investment in effluent treatment systems. Public-private partnerships can also play a role, especially when pharmaceutical manufacturers are incentivized or mandated to co-invest in treatment infrastructure. Some international pharmaceutical companies have already adopted environmental stewardship policies that include effluent management in their global supply chains (Jasovský, *et al*., 2016). Expanding such initiatives through regulatory frameworks, voluntary agreements, and industry coalitions can contribute to global risk reduction.

Public awareness and stakeholder engagement are equally important for ensuring policy uptake and sustainability. Community-level education campaigns can reduce improper

drug disposal and promote safe practices, such as returning unused medications to designated take-back facilities. Engaging civil society organizations, academic institutions, and the private sector in policy development can foster a more inclusive and transparent governance model, increasing accountability and public trust.

Ultimately, a multi-level governance approach is needed to align local, national, and global efforts in pharmaceutical effluent control. National governments must adopt legislation that reflects international guidelines while tailoring them to their specific contexts. Regional bodies can harmonize standards and facilitate cross-border collaboration on transboundary water management and AMR surveillance. At the global level, intergovernmental platforms should continue to advocate for environmental dimensions of AMR, monitor country-level progress, and foster knowledge exchange through research consortia and policy networks (Hu, Logue & Robinson, 2020).

In conclusion, the policy and global management perspectives of pharmaceutical effluent control are integral to the fight against antimicrobial resistance. While chemical and biological treatment technologies offer practical tools to reduce pharmaceutical pollution, their success depends on coherent and enforceable policies, inclusive regulatory frameworks, and global solidarity. International guidelines from WHO, UNEP, and others provide a valuable foundation, but their translation into action remains uneven. Low- and middle-income countries face disproportionate challenges due to weak infrastructure and limited regulatory capacity, yet they are often at the frontline of AMR emergence. Closing this gap requires coordinated investment, capacity building, and inclusive governance strategies that place environmental protection at the heart of public health. By embedding effluent control into the broader AMR response and environmental management agenda, the global community can make meaningful progress toward safeguarding ecosystems and human health for generations to come.

3. Conclusion, Future Directions and Recommendations

Mitigating antimicrobial resistance (AMR) through effective pharmaceutical effluent control demands a holistic approach that bridges technological innovation, environmental stewardship, and global policy alignment. The growing presence of pharmaceutical residues in natural ecosystems—originating from industrial, hospital, and household discharges—poses a direct threat to microbial ecology, public health, and long-term environmental stability. Both chemical and biological treatment methods have demonstrated varying degrees of success in addressing this challenge. While chemical processes such as advanced oxidation, chlorination, and ozonation offer high-efficiency degradation of persistent compounds, they are often associated with high costs, complex operation, and the production of potentially toxic transformation products. Conversely, biological approaches, including activated sludge systems, constructed wetlands, and enzymatic or microbial treatments, emphasize environmental sustainability and cost-effectiveness, though they may be limited by slower degradation rates and specificity of action.

The future of pharmaceutical effluent treatment lies in the strategic integration of these technologies into hybrid systems that maximize the advantages of both approaches. Combined chemical-biological treatment systems, such as coupling advanced oxidation with biofiltration or enzymatic polishing, can significantly enhance contaminant removal while minimizing secondary pollution. These hybrid models offer synergistic benefits—chemical processes can break down complex pharmaceutical molecules into intermediates more amenable to microbial degradation, while biological systems can then mineralize or stabilize those products under environmentally benign conditions. This layered treatment approach ensures more comprehensive purification of wastewater and reduces the ecological risk posed by residual bioactive compounds.

To support such advanced systems, real-time monitoring technologies and artificial intelligence (AI) integration are critical. Sensors capable of detecting trace pharmaceuticals, antibiotic resistance genes, and environmental toxicity markers can provide actionable data for dynamic treatment adjustments. AI algorithms can analyze vast datasets from treatment plants, predict pollutant load patterns, optimize operational parameters, and reduce energy consumption. When deployed at scale, these technologies can transform effluent management from a reactive to a predictive and adaptive system, enhancing treatment efficiency and regulatory compliance while lowering long-term costs.

However, technological innovation alone is insufficient without meaningful investment in capacity building and international cooperation, particularly in low- and middle-income countries where pharmaceutical pollution burdens are often highest and infrastructure weakest. Strengthening institutional capacities, training technical personnel, and establishing regional centers of excellence can accelerate the diffusion of best practices and innovations. Furthermore, international partnerships must focus on equitable technology transfer, funding for decentralized treatment infrastructure, and harmonized standards that address the unique environmental and public health contexts of each region.

The findings from this review affirm that the control of pharmaceutical effluents is not only a critical environmental priority but also a frontline defense in the global fight against antimicrobial resistance. The persistence of antibiotics and other pharmaceuticals in the environment facilitates the selection of resistant organisms, promotes gene transfer across microbial species, and creates long-term ecological disturbances that are difficult to reverse. Both chemical and biological methods have their respective strengths and limitations, but their combined use within well-regulated and monitored systems offers the most promising path forward. Moreover, the environmental chemistry of pharmaceutical residues, including their transformation pathways and bioaccumulation potential, must be a core consideration in any treatment or policy framework.

It is essential to reaffirm that integrated pharmaceutical effluent control is not optional but necessary for sustainable public health and environmental integrity. Addressing AMR from an environmental angle complements clinical and veterinary interventions and aligns with the One Health approach that recognizes the interconnectedness of human, animal, and environmental health. Governments, industries, researchers, and civil society must collaborate to create actionable policies, invest in scalable technologies, and promote community awareness. With rising global awareness of AMR and its far-reaching consequences, the opportunity now exists to institutionalize environmentally conscious pharmaceutical waste management into national and international agendas.

In conclusion, the path to mitigating AMR through

pharmaceutical effluent control lies in integration—of technologies, policies, and disciplines. By embracing hybrid treatment systems, leveraging real-time monitoring and AI, and investing in global cooperation and capacity development, the global community can build resilient wastewater treatment systems capable of protecting ecosystems and human health. The future must be proactive, data-driven, and inclusive, ensuring that no region is left behind in the collective effort to curb the spread of resistance and safeguard the sustainability of antimicrobial efficacy for generations to come.

4. References

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