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FROM WASTE TO RESISTANCE: PHARMACEUTICAL POLLUTANTS IN DRIVING ANTIBIOTIC RESISTANCE

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Abstract– Antibiotic resistance (AR) has become a major threat to public health across the globe, which has been linked to clinical misuse of antibiotics. Recent data indicate that the generation of antibiotic resistance genes (ARGs) and bacteria (ARBs) in the environment is largely caused by pollution from leftover medications, particularly antibiotics discharged by hospitals, manufacturing facilities, farms, and through household waste disposal. Several case studies from terrestrial and aquatic systems, environmental monitoring reports, and molecular data are all included in this review. Data from developed and developing countries were compared to understand the sources, transmission pathways, and potential control measures of antibiotic-resistant bacteria (ARB) and antibiotic-resistance genes (ARG). Pharmaceutical manufacturing plants and hospital wastewater were identified as the main environmental sources of antibiotics. These sources have drug levels significantly higher than calculated no-effect levels, which increases the selective pressures for resistance. Antibiotic resistance genes and multidrug-resistant bacteria have been regularly found in effluents, topsoil, and agricultural ecosystems, with effects exacerbated by co-selection with heavy metals and biocides. The case studies have shown high contamination levels near the pharmaceutical production facilities in developing countries. Resistance genes like blaNDM and blaCTX-M are commonly detected near the drug production sites. Comparisons across regions also revealed that even advanced wastewater treatments cannot fully remove resistance genes, which highlights the scale of the challenge. The findings suggest that pharmaceutical pollutants play a significant role in the development of antibiotic resistance, although it remains largely underrecognized. To protect ecosystems and human health, new strategies like phytoremediation processes, green chemistry, and biological remediation remain to be created developed and tested. This includes strict laws, open monitoring, eco–friendly treatment methods, and public awareness campaigns.

INTRODUCTION

Global health is seriously threatened by antibiotic resistance. It happens when parasites, fungi, bacteria, and viruses learn to withstand the effects of medications that are used to kill them or stop their growth (Lonare, 2024). Even though antimicrobial resistance, or AMR, has historically been associated with clinical antibiotic misuse, there is growing proof that indicates pharmaceutical wastes have polluted the environment and that increased use has exposed bacterial ecosystems and communities to significant levels of antibiotic residues (Polianciuc *et al*., 2022). Antibiotics are crucial for human health because they either eradicate or stop the growth of

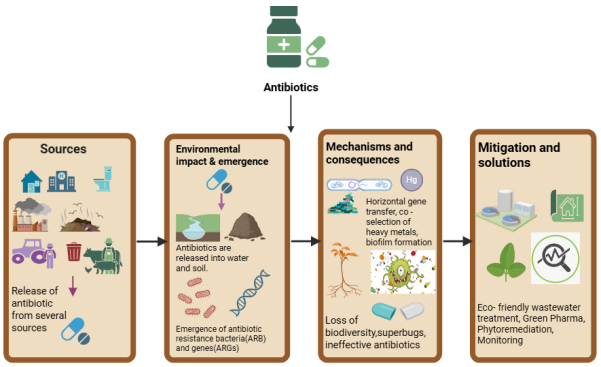

Fig. 1. Schematic diagram illustrating the pathways of antibiotic release, resistance emergence, and potential remediation strategies

bacteria. Their improper disposal or irrational use is harmful to health and can make people more susceptible to antibiotic resistance (Manaia *et al*., 2024). Due to the extremely concentrated active antibiotics released into the surrounding ecosystems by its effluents, the pharmaceutical sector is one of the most significant and underappreciated contaminants.

In the past ten years, it has been acknowledged that antibiotic manufacturing facilities' discharges can also contribute to the development of antibiotic resistance in human pathogens, although misuse and overuse of antibiotics are still likely the main causes. It has been demonstrated time and again that these discharges create the ideal environment for antibiotic concentrations that are particular for the enrichment of resistance. Determining the extent of antibiotic resistance and identifying the crucial control points that reduce its emergence and spread, thus, depends heavily on manufacturing facilities and the environments that receive their effluents (Šimatoviæ and Udikoviæ-Koliæ, 2019). Environmental reservoirs not only create resistant bacteria but also upset the ecological balance, which affects aquatic and terrestrial organisms over time in toxicological ways.

Essentially, one of the main reasons for concern is the widespread development of antibiotic resistance in bacteria, especially concerning antibiotics released into the environment (Ngqwala and Muchesa, 2020).

As of 2019, antibiotic resistance killed 4.92 million people worldwide, making it a serious public health concern that demands immediate attention (Ajekiigbe *et al.,* 2025). Longer hospital stays, higher medical expenses, and higher death rates result from this decrease in the efficacy of the available treatment options. Furthermore, it is becoming more challenging to treat infections caused by resistant pathogens, making it more difficult to combat common illnesses like urinary tract infections, pneumonia, and tuberculosis. Antibiotic resistance is a global issue that cuts across national borders and calls for international cooperation in addition to a multifaceted strategy that incorporates regulation, public awareness campaigns, and surveillance. The greatest risks are in low- and middle-income nations, where utilization of antibiotics is frequently uncontrolled (Gomes *et al*., 2017).

The World Health Organization (WHO) states that infections caused by *Streptococcus pneumoniae*, *P. aeruginosa*, among others, *Mycobacterium tuberculosis, N. gonorrhoeae*, and *K. pneumoniae* are some of the most common multidrug-resistant (MDR) bacteria. Because of this, many organizations, such as the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), the Infectious Diseases Society of America, and the World Economic Forum, is making a concerted effort to combat antimicrobial resistance (AMR). This study aims to assess the health effects of antibiotic pollution, with a focus on its contribution to antimicrobial resistance. It also aims to determine whether integrated partnerships and policies are necessary to reduce the risks that antibiotic waste and misuse pose to the environment, human health, and animal welfare (Solanki *et al*., 2022).

Sources of Pharmaceutical Pollutants

Pharmaceutical waste encompasses a broad range of products, including prescription and over-the-counter drugs. These wastes can be solid pills or capsules, creams, liquids, or aerosols. Pet medications should be handled exactly the same way as human medications because many of them are identical or very similar (Ranjbar and Alam, 2023). Pharmaceutical waste came from a variety of sources, such as medical facilities, farms, and people flushing drugs down the toilet. Both the environment and people have an impact on these entities (Kadam *et al*., 2015). Antibiotic pollution of aquatic ecosystems is largely caused by wastewater released by the pharmaceutical industry. Hospital and manufacturing wastewater have the highest quantities of antibiotic residues, which are higher than the anticipated no-effect concentrations for antibiotic resistance (Booth *et al*., 2020). With concentrations ranging from nanograms to grammes per liter, these pharmacological agents are present in a variety of environmental niches, including soils, groundwater, surface water, and wastewater treatment facilities (Eapen *et al*., 2024). Key sources include the following:

Pharmaceutical production

In the pharmaceutical industry, managing pharmaceutical waste is crucial. Unwanted materials that are no longer useful in manufacturing processes are called wastes, and they may eventually become hazardous or nonhazardous to people or the environment. An essential component of the pharmaceutical industry is the management of hazardous waste. Pharmaceutical waste comes in

a variety of forms, primarily as manufacturing waste, expired products, and strips. It originates from hospitals, individual doctors, pharmaceutical manufacturers and developers, and everyone else involved in the healthcare system (Ahmed *et al.,* 2017).

No matter where it comes from - a healthcare medical facility, pharmacy, or private home - pharmaceutical waste can't be thrown away like regular trash. It needs to be handled specially. Through an invention that increases an unused product's value above zero, it can become a resource, joint product, or by-product. Pharmaceutical waste is a type of waste from medicine that includes over-the-counter personal care items, unused medications, and occasionally accessories like used test strips, sharps, and other supplies (Bhosale *et al*., 2022). Pharmaceutical pollution is prevented by a variety of regulatory bodies, including government agencies, waste management organizations, law enforcement agencies, and environmental protection organizations (Nyaga *et al*., 2020). Managing biomedical waste (BMW) was cited as a worldwide issue during the pandemic. In addition, the World Health Organization has emphasized that COVID-19 caused tens of thousands of tons of BMW to be produced. Pharmaceutical waste has a significant impact on the environment, and it involves waste from medical facilities, research labs, the pharmaceutical industry, etc. Among the waste products produced during diagnosis, research, vaccination, and treatment are vials, bottles, masks, gloves, needles, contaminated, spilled, or expired medications, radioactive materials, pharmacological waste, etc. (Agarwal *et al*., 2024). Both direct discharges, like wastewater from industries, and indirect discharges, like leaks, can contaminate the water cycle with residues of industrial chemicals used to make pharmaceuticals and active pharmaceutical ingredients (APIs). Localized hotspots may still happen even though this origin is generally thought to be insignificant worldwide in comparison to the amounts that patients expel. 2007 saw the publication of the first studies revealing extremely high pharmaceutical emissions from Indian drug manufacturing facilities. The antibiotic Ciprofloxacin is the most involved drug, with a predicted total daily discharge of 44 kg, which is enough to treat over 44,000 residents and equals Sweden's entire usage over five days. Excessive levels of APIs linked to manufacturing discharges were reported by similar studies conducted in the United States, Europe, and other Asian countries, such as South Korea, China, Taiwan, and Pakistan. The information on manufacturing-related pharmaceutical pollution is still largely inconsistent in spite of these reports (Murugan and Moovendhan, 2026).

Veterinary, Agriculture, and Animal Husbandry

One of the main ways that veterinary drugs make antibiotics less effective is by being used too much or in the wrong way on pets and livestock. In intensive farming systems, antibiotics are commonly used both prophylactically for preventing diseases and to promote growth, in addition to their therapeutic uses. The selection and spread of bacteria with resistance genes are facilitated by this unsupervised or improperly dosed use (Kosek *et al*., 2020). Humans can contract these resistant bacteria through direct animal contact, ingestion of products derived from animals, and environmental pathways like contaminated runoff or manure applied to fields (Mkala, 2022). Studies of beef cattle operations and poultry farms, for instance, show that regular use of veterinary medications contaminates soils and water with resistant bacteria and antibiotic residues (Economou and Gousia, 2015), turning agricultural environments into major reservoirs of resistance.A significant amount of resistance to widely used antibiotics is consistently found in studies on *Salmonella* spp. and *Escherichia coli* from a variety of animal sources, suggesting that agriculture serves as both a reservoir and an incubator for resistance genes (Wychodnik *et al*., 2020). Veterinarian medications have been found in sediments, surface water, and groundwater, making aquatic systems especially vulnerable. These drugs can have negative effects on the aquatic biota, including endocrine disruption and an increase in antibiotic resistance (Mruescu *et al.,* 2022). Through horizontal gene transfer (HGT), resistance to antibiotics from organic fertilizers is transferred to the plant microbiome. Humans can contract ARGS and ARB through plant microbiomes. ARB consumption poses health risks to people (e.g., increased morbidity and mortality, medication ineffectiveness) (Ben Ayed *et al.,* 2022). AMR in soils can be impacted by abiotic stressors such as water pollution and soil salinity, which lower agricultural product yield and quality. Livestock rearing is one of the significant causes of antibiotic resistance due to the extensive usage of antibiotics and the dissemination of animal droppings into the

environment. Resistant germs and genes resistant to antibiotics are deposited into the environment through animal dung, and thereby, the dissemination of antibiotic resistance is accelerated. Where birds and animals are reared on farms, these resistant germs and genes are transferred to humans through food, drinking water, or airborne dust and become a grave threat to the health of humans (Obimakinde *et al*., 2017).

Medical and domestic use

Hospital wastewaters are a significant source of pharmaceutical pollutants and known hotspots of AMR and consistently harbor high levels of several antibiotic classes, as well as antibiotic resistance genes. Multi-drug resistant (MDR) pathogens, including *Acinetobacter, Klebsiella*, and *Pseudomonas*, are also found to be routine in hospital effluent. For a few cases, the number of ARGs can actually rise following wastewater treatment, indicating an environment where resistance can be selected and enhanced (Khmaissa *et al.,* 2024). Wastewater treatment plants (WWTPs) are "hotspots" of antibiotics, heavy metals, and other pollutants, exerting a high selective pressure on microbial populations. This leads to the selection of resistant bacteria and the enrichment of the pool of resistance mechanisms - mainly efflux pumps and antibiotic inactivation enzymes, such as OXA-beta-lactamases and Major Facilitator Superfamily pumps (Ullah *et al*., 2024). Hospital pollutants, such as antibiotics and ARGs, will eventually find their way into natural aquatic environments through the spread of effluent release. The release of untreated or poorly treated hospital wastewater results in the spread of bacteria carrying the genes to rivers, lakes, and soil, with enhanced risk of environmental and human exposure with extended-spectrum beta-lactamase (ESBL) producing bacteria in animals in or around hospital areas, further demonstrating the inter-ecological spread of resistance (Rad *et al.,* 2022; Abdurahman *et al*., 2021). Even outside of hospital settings, hospital pollutants make infections more difficult or even impossible to treat, contributing to the growing global threat of antibiotic resistance. Antibiotic-resistant strains have been found by surveillance in environmental isolates (marine organisms, terrestrial animals, and plant surfaces), illustrating the extensive effects of pollutants originating from hospitals (Shi and Wang, 2018).

One vital but usually neglected source of pharmaceutical pollutants is the home. Domestic usage of antibiotics leads to the sustained emission of drug residues to wastewater systems, causing antibiotic resistance. While it is well-documented that the occurrence of antibiotic resistance genes (ARGs) in drinking supplies and their probable horizontal transfer of genes to pathogenic microbes is hazardous to human health, their levels of pollution and probable anthropogenic emission sources are unknown. New micropollutants, antibiotic-resistant bacteria, and genes inducing antibiotic resistance are present in household greywaters (Ahmed *et al.,* 2023). Pharmaceuticals excreted upon ingestion are the highest emitter at the household level. Usually, 30–90% of orally dosed drugs are eliminated either in their unchanged or metabolized forms. Skin-rinsed creams and ointments may also find their way into wastewater systems. Combined medical and household discharge antibiotics are a significant contributing factor to the emission of antibiotic resistance in the environment, and increase risk in both the ecosystem and human health (Fatimazahra *et al.,* 2023).

Illegal and irregular dumping

When antibiotics and other drug residues are dumped illicitly or inadequately (e.g., dumped in dumpsites with little or no cover or sanitation, dropped in watercourses, or flushed down latrines), these chemicals may remain in the environment at concentrations strong enough to exert selection pressure on environmental bacteria. This selection pressure facilitates the growth, persistence, and dissemination of antibiotic-resistant bacteria (ARB) and antibiotic resistance genes (ARGs), both within environmental microbial populations and to human pathogens (Pot *et al.,* 2020). Municipal solid waste (MSW) dumps and open dumps with poor pharmaceutical waste disposal are prime sites of dissemination of ARB and ARG. Leachate from these sites contaminates soil and aquifers and causes damage to vegetation and animals nearby, in addition to an impact on human health through agriculture and drinking water (Mehboob, 2022). Illegal dumping around water bodies - with lakes and rivers around pharmaceutical facilities - involves sites with exceptionally high concentrations of antibiotics and ARG. The contaminated sites result in horizontal gene transfer and sustain populations of multidrug-resistant bacteria (Wang *et al*., 2023). Research on hospital and pharmaceutical waste dump sites has identified

organisms such as multidrug-resistant bacteria and strains of Pseudomonas aeruginosa with 100% resistance to applied antibiotics (Itzhari and Ronen, 2023). Pharmaceutical effluents and hospital wastes are key sources of contamination by antibiotics in Indian water bodies. Flies and other vectors in urban dump yards have even been discovered to carry multidrug-resistant pathogens from dump yards to further spread them into animal and human habitats (Gorgich *et al.*, 2020; Baroka, 2025).

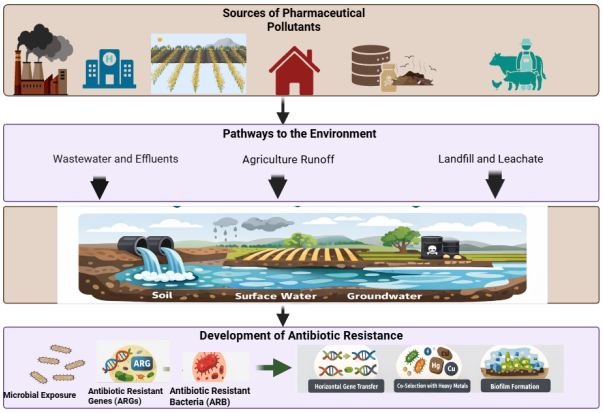

Fig. 2. Flowchart illustrating the environmental fate of pharmaceutical contaminants and the subsequent emergence of antibiotic-resistant bacteria and genes

Environmental pathways & Fate of pharmaceutical pollutants

Pharmaceutical pollutants are new types of contaminants that get into the environment in several ways. These include activities from industries, human waste, throwing away unused medicines, and using them in farming, especially when they are directly released into water and leak through landfills. These methods facilitate the spread of pharmaceutical compounds and antibiotic resistance genes (ARGs) into soil and water ecosystems. Their lasting presence, changes, buildup in living things, and harmful effects are serious problems for the environment and public health.

Pharmaceutical Pollutant Entry Routes into Water and Soil Systems

Pharmaceutical waste is generated from various sources such as farms, factories, households, and hospitals. When it is not properly disposed of, such as by dumping it directly or burying it in landfills or flushing it in sewage or throwing it inappropriately, drugs may end up in the soils and waters.

Direct release into waterbodies

One of the main pathways for contamination involves the immediate release of untreated or inadequately treated wastewater originating from hospitals, pharmaceutical production facilities, and municipal sewage treatment plants into aquatic systems, including rivers, lakes, and surface waters. As an example, effluents from industrial sources in proximity to Hyderabad, India, have been detected to possess remarkably elevated levels of antibiotics, specifically ciprofloxacin, with concentrations attaining 14 mg/l - values that significantly surpass standard environmental thresholds and indicate a substantial degree of pollution (Anand *et al.*, 2021). These discharges add a mix of pharmaceutical compounds, creating environments suitable for expanding antibiotic-resistant bacteria (ARB) and ARGs. Pharmaceutical compounds, after being ingested, are excreted from the human organism

Table 1. Sources of pharmaceutical pollutants

Sources	Main Pollutants	Environment affected	Resistance outcome
Pharmaceutical sector	Active pharmaceutical Ingredients (APIs), antibiotics	River, soil	Significant Enrichment of antibiotic Resistance genes (**ARG**) and antibiotic-resistant bacteria (**ARB**)
Health care facilities	Antibiotics, multidrug-resistant (**MDR**) bacteria	Effluents from wastewater Treatment plants (**WWTP**)	Resistance hotspots
Farming and livestock	Veterinary medications	Soil, runoff	Hotspots for resistance Reservoirs of ARG
Domestic households	Drugs excreted from the body	Municipal wastewater	Continuous selection pressure
Illicit disposal	Expired pharmaceutical products	Soil, groundwater	Ongoing spread of ARG

Table 2. Major environmental pathways of pharmaceutical pollutants and their role in antibiotic resistance dissemination

Route	Fate	Resistance effect	Matrix
WWTP discharge	Partial elimination	ARB mobility selection	Surfacewater
Landfill leachate	Persistence	ARGmobility	Soil, groundwater
Runoff from agriculture	Adsorption	Transfer to Microbiota	Soil, sediments
Aquaculture effluents	Bio-accumulation	ARG enrichment	Marine systems

within their parent molecule or as metabolites and conjugation forms. Among some of these commonly prescribed drugs or active pharmaceutical ingredients (APIs), some were found to be present in various water systems and were discovered to impact the quality of aquatic life. Acute toxicity is unlikely to be induced by the emission of pharmaceutical compounds into an aquatic stream within a definite scope, but their presence also impacts human health, as well as marine culture and agriculture (Bengtsson-Palme *et al.*, 2014). Ineffective sewage treatment methods and inadequate sanitation systems in Africa make the issue worse by directly contaminating water supplies with human waste that contains pharmaceuticals. These new micropollutants are dangerous for aquatic ecosystems, flora, biota, and human health (Miao *et al.*, 2021).

Leaching Through Dump Sites and Landfills

Due to the buildup and leaching of unused, expired, or discarded medications, trash dumps and illegal dumping sites act as tanks for pharmaceutical pollutants. Municipal solid waste (MSW) dumps produce a complex mixture of leachate that includes emerging contaminants, metal resistance genes, antibiotics, and ARGs. The physicochemical characteristics of groundwater as well as soil are significantly impacted by these leachates, according to studies, and ARB and ARGs have been found in landfill leachates all over the world. Illegal dumpsites with inadequate containment make this issue worse by allowing more leachate to seep into the surrounding environment and encouraging the spread of ARG (Kelly and Gleeson, 2025).

Environmental Persistence and Change of Pharmaceutical Pollutants

Based on their chemical structures, the environment, and their interactions with biotic and abiotic factors, pharmaceutical compounds exhibit varying degrees of persistence within environmental compartments.

Persistence of chemicals in water and soil

Numerous antibiotics have high environmental persistence, meaning they don't break down and stay biologically active for long stretches of time. Their environmental half-lives are prolonged by sorption to sediment and soil particles, hydrolytic stability, and resistance to photodegradation. Antibiotics such as tetracyclines and fluoroquinolones have a wide range of adsorption behaviors, which greatly affect their mobility. For instance, tetracyclines and fluoroquinolones firmly adhere to the soil and sediments, reducing their bioavailability right away but possibly allowing for long-term persistence (Riaz *et al.*, 2020). This adherence to solid matrices encourages accumulation in sediments and makes removal through traditional wastewater treatment more difficult. Drugs' physicochemical characteristics, which affect environmental fate processes like bioaccumulation and toxic potential, determine their persistence and transformation (Singh *et al.*, 2024). Certain transformation products, especially those belonging to major pharmaceutical groups like SSRIs, opioids, antibiotics, anti-histamine NSAIDs, and anticancer medications, may be just as dangerous as their parent compounds (Gashaw *et al.*, 2024). However, because of their complex environmental matrices and low concentrations, finding these transformation products is still difficult (Wet *et al.*, 2025).

Processes of Abiotic and Biotic Transformation

Incomplete breakdown frequently produces metabolites of unknown toxicity, even though some pharmaceutical pollutants change photolysis, hydrolysis, and degradation by microbes. In landfills and bodies of natural water, the efficiency of microbial breakdown is often limited and depends on environmental conditions and the existence of co-contaminants. In order to hasten the breakdown and mineralization of pharmaceutical residues, treatment technologies that target sophisticated oxidation or bioremediation techniques have been developed and put into practice at experimental scales (Fick *et al.*, 2009). By altering the substance bioavailability and activity, the processes of transformation may also have an

effect on the selective impact on microbial communities, which could influence the development and spread of resistance mechanisms.

Resistance Gene Dissemination and Horizontal Gene Transfer

Environmental compartments such as soils and contaminated aquatic sediments with pharmaceutical waste are hotspots for horizontal gene transfer (HGT) among microbes. Mobile genetic elements such as integrons and transposons facilitate ARG transfer to increase the spread of antibiotic resistance among environmental microbiota. Findings near where veterinary antibiotics were manufactured reveal highly abundant sulfonamide and β-lactam resistance genes highly correlated with mobile genetic elements among soils and downstream water samples near effluent pipes, which is an indication of a threat of gene propagation through environmental media (Raja and Kathiravan, 2021).

Pharmaceutical Bioaccumulation and Genes Associated with Antibiotic Resistance

Pharmaceutical contaminants can bioaccumulate, particularly in aquatic organisms, which can result in internal concentrations that are higher than environmental levels. This can have an impact on both human health and the environment. Antibiotic residues in particular are important environmental pollutants with a worrying capacity for bioaccumulation. The prevalence of antibiotic-resistant bacteria (ARB) as well as antibiotic-resistant genes (ARGs) is rising in environments affected by humans, particularly those that receive complex chemical mixtures or faecal waste (Kayode-Afolayan *et al.,* 2022).

Bioaccumulation in Aquatics

Invertebrates, fish, and other aquatic creatures can bioaccumulate antibiotic residues found in surface waters, which raises questions about trophic exchange and exposure to larger organisms, such as humans who eat contaminated seafood. Even at sub-lethal concentrations, the persistence of these medications and their metabolites creates chronic exposure scenarios. Furthermore, the persistence of antibiotic resistance genes in microbial communities linked to aquatic organisms may promote horizontal transmission of genes and the spread of resistance within food webs (Madikizela *et al.,* 2017).

Bioaccumulation in Terrestrial

Drug residues affect the diversity of bacteria and ecological interactions by bioaccumulating in soil biomass from bacteria and possibly transferring into soil fauna. Upon entering soil ecosystems, antibiotics affect the diversity of microbes and ecological interactions by bioaccumulating in soil microbial biomass and possibly transferring into soil fauna.In addition, human exposure occurs when contaminated animal products are consumed, allowing residues to enter the food chain. For example, residues in dairy products, eggs, and meat highlight the potential of passive AR dissemination to humans as well as the implications for food safety. Similar substances build up in aquatic organisms either directly or through trophic transfer from contaminated water; significant accumulation has been observed in invertebrates, fish, and microbial communities (Vumazonke *et al.,* 2020).

Effects of Ecotoxicology

Pharmaceutical contaminants have a variety of ecotoxic effects, such as altering aquatic fauna's behavior and physiology, interfering with different species' ability to reproduce and grow, and upsetting microbial communities that are essential to soil fertility and nutrient cycling. Concerns regarding long-term evolutionary ramifications have also been raised by the discovery that biological pharmaceutical waste in environmental waters has been linked to behavioral changes in aquatic wildlife, including modified feeding and reproductive patterns (Chavoshani *et al.,* 2020). Prolonged exposure to subtherapeutic antibiotic concentrations changes the composition of the microbial community and encourages the selection of resistant strains, which has a domino effect on the resilience of ecosystems (He *et al.,* 2021).

MECHANISM OF ANTIBIOTIC RESISTANCE

Antibiotic-resistant bacteria that cannot be effectively treated are increasingly frequent, leading to a worldwide health emergency. Even at low concentrations, these contaminants significantly impact the development and dissemination of antibiotic resistance among microbial communities. Widescale usage of antibiotics leads to the development of antibiotic resistance. Fresh mechanisms of resistance are being documented continuously, with new genes and modes of

transmission being discovered regularly. Resistance is developed by bacteria via intrinsic as well as acquired routes, such as genetic mutations and horizontal gene transfer. Molecular mechanisms refer to the means through which bacteria are either intrinsically resistant or gain antibiotic resistance through mutation as well as horizontal gene transfer. The principal classes of molecular mechanisms of bacterial antibiotic resistance include enzymatic drug inactivation being a consequence of metabolic breakdown of the drug, drug target alteration which causes an inability of the drug to bind to its site, permeability reduction mechanisms of drug that hinder cellular influx of a drug, active efflux of drugs from the bacterium leading to intracellular dilution of a drug, inhibition of antimicrobial access to their goal sites and biofilm production (Hrenoviæ *et al.*, 2018).

There are multiple pathways through which pharmaceuticals affect microbial populations, leading to heightened resistance and potential public health risks.

Selection Pressure

Environmental microbial communities are continuously under selective pressure from pharmaceutical antibiotics that are discharged into the environment through inappropriate disposal, discharge of wastewater, and agricultural runoff. Antibiotics can outcompete susceptible strains of bacteria by selecting for those that carry resistance genes, even when administered at low, sub-therapeutic concentrations. This selection pressure eventually makes it easier for antibiotic-resistant bacteria (ARB) to appear and spread in soil and water environments (Harrower *et al.*, 2021). It has been shown that areas close to pharmaceutical manufacturing, like rivers and lakes that receive unprocessed industrial effluent, have incredibly high concentrations of antibiotics, far above the minimum selective concentrations needed for resistance to develop (Palacios-Rosas and Castro-Pastrana, 2017). Antibiotic resistance is caused by a variety of mechanisms in environmental bacteria due to complex selection pressures. Co-selective pressure between toxic metals and antibiotics promotes the spread and persistence of resistance genes in environmental reservoirs by means of genetic linkage via integrons, transposons, and plasmids, as well as shared resistance mechanisms (Maculewicz *et al.*, 2022). A comparison of 128 antibiotics shows that their selective pressure potential varies by four orders of magnitude. Tetracycline, ciprofloxacin, norfloxacin, and enrofloxacin were found to be especially problematic for resistance selection in lakes, rivers, and hospital effluents (Babic *et al.*, 2017).

Human-induced pollution has been shown to improve the selection of environmental bacterial pathogens. Concentrations of environmentally significant metals (≥365 mg kg^{-1} copper and ≥264 mg kg^{-1} of Zn) rise dramatically in resistance in agricultural soils, indicating that hazardous metals like zinc and copper can exert stronger selection pressure for tetracycline resistance than tetracycline itself. The microbial population is subject to selective pressure from antibiotics found in both aquatic and soil environments. While resistant strains of bacteria continue to exist and grow, sensitive strains are observed to be eliminated or inhibited. This causes resistant bacteria to eventually take over the contaminated area. The development of resistance is supported by these selective methods in contaminated environmental compartments, which also create the conditions for horizontal transfer of genes between bacterial communities subjected to these ongoing selective pressures. Ex. Tetracycline remains in wastewater treatment facilities, favoring strains of *E. coli* and *Pseudomonas* that have resistance genes (Geetha, 2025).

Horizontal Gene Transfer

The primary mechanism driving the proliferation of antibiotic-resistant genes (ARGs) in bacterial populations is horizontal gene transfer (HGT). HGT is a mechanism by which conjugation, transformation, and transduction cause bacteria to become resistant to antibiotics, posing a significant risk to global public health. Historically, bacteria acquire exogenous genetic information via three basic routes: i) transformation (uptake of free DNA), ii) transduction (bacteriophages), and iii) conjugation (usually described as bacterial "sex"). Transformation is perhaps the simplest mode of horizontal gene transfer (HGT), but only a few clinically important bacterial species can "naturally" take up naked DNA to confer resistance. Development of resistance in hospital environments often involves conjugation, a very efficient mode of gene transfer that relies upon direct cell-to-cell contact and is probably occurring at high frequencies within the gastrointestinal tract of antibiotic-treated humans. As a general rule, conjugation uses mobile genetic elements (MGEs) as

its carriers for the exchange of critical genetic information where necessary, but one-to-one transfer from one chromosome to an adjacent one has also been comprehensively proven (Wachino, 2025). Most important MGEs comprise plasmids and transposons, which play central roles in Horizontal gene transfer (HGT), in which bacteria exchange genetic material—specifically, antibiotic-resistant genes (ARGs)—through mobile genetic elements such as plasmids, integrons, and transposons (Berisha *et al.,* 2024). It is a crucial mechanism for the evolution and spread of resistance. Water bodies located downstream of industrial discharge, wastewater treatment facilities, and landfill leachate zones are examples of environmental hotspots that have a variety of pollutants and dense microbial communities. The frequency and effectiveness of HGT are increased by these circumstances, which also improve biofilm formation and microbial stress responses. Leachates from landfills and disposal sites serve as ARG reservoirs, containing resistant bacteria and mobile elements that promote gene exchange. Illegal dumping hotspots contain multidrug-resistant strains and high ARG burdens, illustrating anthropogenic enhancement of these hotspots. The physicochemical and biological properties of these environments facilitate the aggregation and gene exchange among bacteria, thereby enhancing the horizontal dissemination of resistance appearance as well as dissemination of antimicrobial resistance among clinically important pathogens (Kamajian, 2023).

The mechanism of co-selection by multiple pollutants

Co-selection is a method by which being exposed to one selective agent, like biocides or heavy metals, also sustains or increases antibiotic resistance because of shared resistance mechanisms or genetic linkage. Co-localization of genes for resistance on mobile elements such as integrons or plasmids frequently causes this phenomenon. In many contaminated environments, antibiotics coexist with biocides and heavy metals (like copper, arsenic, and mercury). Antibiotic and heavy metal resistance genes are frequently physically connected on the same genetic elements. Thus, even in the absence of antibiotics, the existence of toxic metals can preserve or even favor antibiotic resistance - a process known as "co-selection." Remediation efforts are made more difficult by this synergistic effect, since eliminating one pollutant might not lessen resistance if others are still present (Irfan and Alatawi, 2019). As persistent co-selecting agents, heavy metals preserve and enhance the presence of ARG even in settings with low or no antibiotic residues. The environmental persistence of these heavy metals guarantees that resistance genes continue to be beneficial, promoting their retention in microbial communities. Numerous co-selective agents are also found in leachates from landfills and industrial waste, confirming these locations as sources where ARGs endure because of the combined effects of the pollutants. These findings highlight the potential shortcomings of single pollutant control strategies and the need for comprehensive management strategies that address chemical mixtures. Even when antibiotic use is limited, ARGs co-occur with heavy metal and biocide resistance genes in pig gut microbiomes, suggesting that non-antibiotic selective stresses can sustain antimicrobial resistance within particular bacterial clades (Abebe *et al.,* 2016).

Resistance Gene Reservoirs in the Environment and Public Health

Some environmental compartments are persistent repositories of ARGs, most significantly soils influenced by agricultural runoff and animal husbandry practices, aquatic systems surrounding wastewater effluent, and man-made locations such as landfills and illegal dump sites (Gillieatt and Coleman, 2024). These repositories constantly feed resistant genes to environmental microorganisms as well as potential pathogens to humans. River systems and lakes surrounding pharmaceutical production plants have ARG abundances orders of magnitude higher than unpolluted controls, emphasizing environmental modalities of antibiotic resistance dissemination. Environmental repositories pose a critical planetary threat as sources of antibiotic resistance genes that can infect humans. Carbapenem-resistant Enterobacteriaceae (CRE) are especially sinister because carbapenems represent the last-resort antibiotics to treat multidrug-resistant infections (Emara *et al.,* 2022). Large marine environments also host huge repositories with diverse antibiotic resistance genes, with 44% being present among rich marine taxa such as Pelagibacter, Prochlorococcus, and Vibrio (Buelow *et al.,* 2021). Environmental bacteria most probably constitute an ancestral origin point for resistance determinants that pathogenic bacteria

acquire via horizontal gene transfer (Song *et al.*, 2017).

Mobile Genetic Elements (MGEs) Promote ARG Mobility

The main means by which resistance genes spread quickly are mobile genetic elements like integrons, transposons, and plasmids. The extensive microbial networks present in biological films and aggregations close to pollutant sources, as well as stress responses brought on by pollutants, increase their frequency and activity (Swain and Sahoo, 2025). Multiple resistance genes are frequently carried by MGEs, increasing the likelihood that environmental bacteria will develop multidrug resistance. Environmental bacteria are more likely to develop multidrug resistance because MGEs often carry multiple resistance genes. MGE-mediated gene exchange is facilitated by structured environments like aggregated sediments and biofilms, which improve cell-to-cell contact. The dynamics of ARG mobility are impacted by seasonal variations and spatial heterogeneity, which also modify the quantity of MGEs in ecological compartments (Li *et al.*, 2018). The intricate control of MGE-driven resistance proliferation is influenced by these ecological factors. Multiple resistance genes are frequently co-localized by MGEs, which facilitates co-selection and encourages simultaneous transfer. Permanent inheritance and longevity of resistance characteristics across environmental gradients are made possible by this co-regulation. Strategic interventions that target the activity of mobile elements and integrated monitoring are necessary to address MGE-driven resistance (Matylonok *et al.*, 2021).

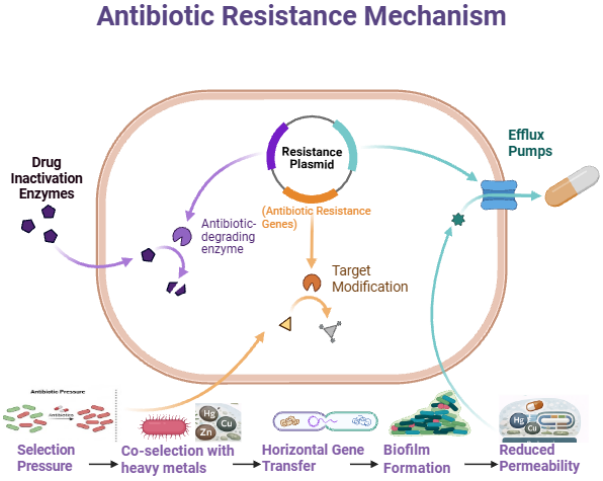

Fig. 3. Mechanisms of antibiotic resistance in bacteria. [Resistance genes, often carried on plasmids, enable bacteria to inactivate antibiotics, modify drug targets, reduce permeability, or expel drugs via efflux pumps. Biofilm formation and horizontal gene transfer further enhance the spread and persistence of resistance.]

Case Studies and Evidence

A global concern, the spread of antibiotic-resistant genes (ARGs) and bacteria (ARB) in freshwater and marine environments is largely caused by effluents from the pharmaceutical industry. To clarify these dynamics, we examine important case studies and supporting data here. We concentrate on patterns of resistance in freshwater systems, marine and coastal environments, pharmaceutical pollution differences between developed and developing nations, and particular ARGs found in environmental matrices.

Freshwater Ecosystems: Lakes, Rivers, and WWTP Effluents

In freshwater systems, wastewater treatment facilities are critical sites for the spread and possible containment of ARGs. Nevertheless, their effectiveness varies greatly based on local wastewater inputs and technology. ARG prevalence was found to be significantly different between WWTPs in Germany (a developed country) and Namibia (a developing country); the former had roughly three times as many ARG subtypes (277 vs. 93) as the latter, and there was a significant difference in the quantity of multidrug resistance genes. This disparity demonstrates how wastewater treatment technology type has a significant impact on ARG occurrence and reduction effectiveness (Gunarathne *et al.*, 2024).

Several ARG types, including sul1, and the group of 1 integron integrase genome intI1, have been identified. were universally detected in European studies examining 16 WWTP effluents from ten different countries. These findings are suggestive of anthropogenic contamination and genetic components that are mobile, which drive horizontal gene transfer (Amarasiri *et al.*, 2019).

River water studies of the discharge of WRP effluents from the United States into the Los Angeles River watershed indicated high fecal indicator bacterial levels and ARG numbers such as sul1, ermF, and blaSHV, indicating reclamation plant and urban operations have a high impact on ARG burden in freshwater environments. Of interest is that a co-location among ARGs, mobile genetic

elements, and pathogens has been noted to represent intricate relations whose cascades would ease the spread of resistance (Munita and Arias, 2016).

Water bodies like lakes are also reservoirs and mixing points of ARGs from various sources. An integrated study in Lake Maggiore, Italy, and its tributaries balanced the dynamics of ARGs like tetA and sul2 according to wastewater effluent and anthropogenic markers of pollution like ammonium concentration. Findings indicated tetA dynamics were influenced by wastewater inflows and riverine inflows, whereas sul2 abundance appeared independent of inflows, suggesting source-specific variation of ARG distribution and persistence (Demynyuk *et al.,* 2023).

Marine Ecosystems' Antibiotic Resistance (Estuaries and Coastal Aquaculture)

Marine environments, such as estuaries and coastal aquaculture areas, are being increasingly viewed as reservoirs and conduits for the development and transmission of antibiotic resistance caused by aquaculture's widespread use of antibiotics and pollution from urban and industrial effluents. Antibiotic resistance in marine ecosystems is a concern, particularly due to its connection with the food we obtain from aquaculture. High application of antibiotics in aquaculture results in enrichment of resistant bacteria and ARGs in marine coastlines. For instance, aquaculture-impacted water surveys have identified ARGs associated with tetracycline and beta-lactam resistance that indicate selection pressure from the application of antibiotics (Kotwani *et al.*, 2021).

A comparison between developing vs. developed countries

A worldwide health issue, antibiotic resistance exhibits distinct trends in developed and developing nations. In developing countries, the major contributors are the absence of surveillance systems, low-quality antibiotics, clinical abuse, and the ready availability of antibiotics. In the developed world, the main challenges lie in the lack of hospital-level control and the overuse of antibiotics in the animal sector (Chen *et al.,* 2017). Pharmaceutical waste pollution intensifies the issue of drug resistance globally. Large pharma firms of the world operate not only in high-income nations such as the USA, UK, Germany, but also in developing nations such as China, India, and Brazil (Yu *et al.,* 2020). It results in toxic material reaching our drinking water and food. Lack of proper treatment and irresponsible disposal of waste from drugs, particularly in middle- and low-income nations, poses severe environmental risks through the dissemination of antibiotic-resisting genes. It may drive 24 million into severe poverty by 2030 unless appropriate actions are taken (Brevik *et al.,* 2020).

Found ARGs (such as carbapenemases and ESBLs)

ESBL genes such as blaCTX-M, blaTEM, and blaSHV are widespread worldwide in clinical and environmental settings. Their occurrence in freshwater sediments, WWTP effluents, and environmental isolates emphatically denotes the environmental dimension of clinical resistance. Nigerian meta-analyses identified blaSHV at 24% pooled prevalence, with the various ESBL genes being prevalent among humans, animals, and the environment (Mills and Lee, 2019). ESBL-producing E. coli from European watersheds matched MLST profiles with clinical isolates, highlighting environments as reservoirs and dissemination routes of these important resistance determinants. Genes for carbapenem resistance, such as blaNDM, blaKPC, and blaOXA, are increasingly found in aquatic ecosystems, especially in developing nations with poor wastewater treatment. West African nations' hospital wastewaters harbored several carbapenemase genes, including extensive blaGES and mcr genes that give resistance to last-resort antibiotics, posing a chilling environmental reservoir. Mobile genetic elements, including Class 1 integrons, Tn402-like transposons, Tn3-like transposons, and IS26, allow ARG acquisition and transmission among environmental bacteria under exposure to pharmaceutical pollutants. These findings substantiate that human-specific pollutants, particularly pharmaceutical products, contribute to ARG thriving and HGT in aquatic ecosystems (Marathe *et al.,* 2018).

CONSEQUENCES FOR ENVIRONMENTAL AND HUMAN HEALTH

Given their potential impact on both the health of humans and the overall ecological balance, pharmaceutical pollutants in waterways are a rapidly expanding problem. For example, the exposure to some pharmaceuticals may interfere with the endocrine system of fish and other wildlife, causing reproductive malformations and population

Table 3. Global distribution and environmental drivers of antibiotic resistance genes (ARGs)

Environment / Region	Key ARGs Identified
Freshwater (WWTPs)	*sul1*, *intI1*, *ermF*, *blaSHV*
Rivers and Lakes	*tetA*, *sul2*
Marine & Coastal	Tetracycline & Beta-lactam genes
Developed Nations	Various clinical ARGs *blaSHV*, *blaNDM*, *blaGES*, *mcr*

loss. In addition, the long-term effects of pharmaceutical pollution on human health are not yet clear, and there are concerns regarding the possible risks of exposure through the consumption of drinking water and food. WWTPs are known to be major reservoirs of ARGs and sources of disseminating AMR, hence being a constant threat to human health. The ineffectiveness of traditional WWTPs in eliminating ARB contributes to their dissemination in natural water resources, thus worsening the issue of antibiotic resistance (Mosharaf *et al.,* 2024). Several factors and processes related to hydrology, ecology, and climate change have been known to strongly influence ARB in natural environments, thus impacting the fate and transport of antibiotic resistance.

The following factors provide a general understanding of these impacts:

Human exposure to antibiotic-resistant bacteria (ARB) through the food chain and water

Contamination of the Food Chain: ARB and ARGs can be passed to humans through the food chain. It entails eating aquatic and terrestrial organisms, therefore becoming the main pathway through which humans are exposed to antibiotic resistance. Contamination is possible at various levels of preparing food, such as farming, processing, and distribution. Animals in farms that use antibiotics may harbor ARB in their guts, which may pollute meat and poultry during slaughter and processing. Similarly, water animals, for example, fish and shellfish, may acquire ARB and ARGs through polluted water, posing a danger to individuals consuming these products. Much needs to be done to prevent contamination at various points of the food supply (Su *et al.,* 2023). Freshwater bivalve molluscs may harbor multidrug-resistant Escherichia coli, and it can be transmitted to human populations through the food chain. It is proof that water creatures can be the agents to spread antibiotic resistance. Filter-feeding bivalve molluscs, including molluscs and clams, may feed on bacteria and other harmful chemicals found in water. If humans eat such bivalve molluscs that they acquired from contaminated water, they may be exposed to multidrug-resistant *E. coli*. It may lead to colonization, infection, and spread of antibiotic resistance (Martins *et al.,* 2024). Utilizing polluted water for irrigation may leave ARB on fresh vegetables and fruits that may deteriorate human health if we consume such polluted food. Irrigation water containing ARB and ARGs may transmit such resistance characteristics to fresh vegetables and fruits, potentially subjecting individuals to danger when consuming such polluted food. ARB presence on fresh vegetables may increase the likelihood of bacteria multiplying, resulting in infections, and transmission of antibiotic resistance to additional bacteria that may infect human beings (O'Flaherty *et al.,* 2018).

Water as a Pathway for Transmission: Release of ARB and ARG into the waterbody by WWTP effluent results in their spread and potential transmission to humans through water, directly compromising human health. Infected water sources, comprising drinking water, recreational water bodies, and water for irrigation, may be a mode of human exposure to ARB and ARG. Ingestion of infected water, either directly or through consumption of infected edibles, may seed ARB into the human gut, potentially leading to colonization and infection. Exposure to ARB through recreational water bodies, for instance, through bathing with or swimming through water bodies, may similarly increase the risk of skin and soft tissue infections (Zou *et al.,* 2019). The presence of pharmaceutical contaminants in water sources, usually at trace levels, can result in a series of negative health effects on human beings, including endocrine disruption, developmental anomalies, and promotion of antibiotic resistance.

Pathways of Human Exposure: Humans can come into contact with agricultural soils through breathing, dermal contact, or consumption of vegetables that may be infected with ARB and ARGs, thus creating various human exposure routes to antibiotic resistance in agricultural settings. Agricultural soils can become polluted with ARB and ARGs through various pathways, including the

use of manure, sewage sludge, and irrigation water. People can become exposed to the contaminants through dust inhalation, dermal contact with the soil, or vegetables grown from the polluted soils. It is thus important to adopt Prevention and Control Measures to minimize contamination of agricultural soils with ARB and ARGs to ensure human health security (Jampani *et al.,* 2023). Contact with animals that are farmed intensively is a possible means of transmission of ARB to humans, mostly in communities where humans live in close contact with animals. Animals that are farmed on intensively farmed farms can be infected with ARB in their gut after antibiotics are administered to the livestock feed, and intensive stocking of animals. Humans who work for or live in close contact with such farms can be infected with ARB after direct contact with animals, inhalation of dust aerosols, or eating infected foods. This puts a lot of importance on the need to implement measures that decrease the administration of antibiotics for farms that have livestock and decrease transmission of ARB from animals to humans (Rousham *et al.,* 2021). In coastal areas, recreational water activities can put people and wildlife at risk for antibiotic-resistant diseases. This shows that there is a chance of coming into contact with antibiotic resistance in places where people have fun. Coastal water may be contaminated with antibiotic-resistant bacteria and genes through several routes, including wastewater discharge, stormwater runoff, and agricultural runoff. People engaging in recreational water sports, like swimming, surfing, and boating, can be exposed to these contaminants by consuming them, coming into contact with them, or breathing them in.

Risk to aquatic organisms and ecological functions

Effects of ecotoxicology on the environment: Waterborne drugs are toxic to aquatic organisms, impacting the physiology of aquatic organisms and jeopardizing the health of water environments. Waterborne drugs induce many adverse effects on inhabitants of water, including interfering with hormones, issues of reproduction, and alteration of behavior. Such issues may be at trace levels, and at such a level, they could be potentially detrimental to the survival and health of inhabitants of water (Szarka *et al.,* 2024). The occurrence of pharmaceutical impurities in water will result in impaired physiological functions and reproductive injury in aquatic organisms, thus posing a threat to the long-term sustainability of aquatic populations. Microplastics in aquatic ecosystems will act differently from natural particles, hosting particular populations of bacteria and potentially modifying the structure and functioning of microbial communities (Kock *et al.,* 2023). Antibiotic contamination may co-select for multiple resistances in aquatic environments; the ecological role of ARGs becomes increasingly complicated, and even more so, potentially leading to the development of multidrug-resistant bacteria. Pharmaceuticals may have an effect on wildlife, affecting aquatic ecosystems and possibly the fine balance of the ecosystem (Herriz *et al.,* 2021).

Ecosystem Function Disruption: Spread and development of antibiotic resistance in aquatic ecosystems can disturb ecosystem processes, such that changes in nutrient cycling, decomposition rates, and other important processes may be possible. Changes in microbial community structure through contamination with antibiotics can alter nutrient cycling and other important processes, which can destabilize the balance of aquatic ecosystems. Presence of ARB and ARGs in aquatic ecosystems can reduce the effectiveness of control activities and jeopardize the health of the ecosystem as a whole, therefore underscoring the importance of integrated management to offset antibiotic resistance (Tong *et al.,* 2024).

A single health viewpoint that connects humans, animals, and environments

The Interdependence of Health Domains: Antimicrobial resistance is a significant One Health concern. It reveals how intimately intertwined individuals, animals, plants, and their common environments are. It identifies the need for an integrated approach to dealing with the complex issue. The One Health concern recognizes that human, animal, and environmental health are intimately connected. It emphasizes examining how those sectors interrelate when addressing health issues (Ugbo *et al.,* 2025). For instance, the application of antibiotics in animal husbandry can result in the development of ARB, which can subsequently be transferred to human beings via the food chain or by direct contact with animals. Likewise, contamination of the environment with antibiotics and other contaminants can lead to the development and transmission of antibiotic resistance. Combating AMR demands an interdisciplinary and coordinated effort, merging human, animal, and environmental health

principles, and thus focusing attention on intersectoral collaboration to fight antibiotic resistance effectively (Perveen *et al.,* 2022).

AMR Transmission from Animals to Humans: Antimicrobial application to animals results in the spread and shedding of antimicrobial-resistant bacteria that directly and indirectly infect humans, thus underscoring the potential for animals to be the origin of the resistance of humans to antibiotics. The absence of gene barriers for all species supports the application of an ecological approach to dealing with effects of antimicrobial application to human disease, thus underscoring the need for consideration of the wider ecological context when dealing with resistance to antibiotics. Antibiotic resistance from animals to humans can be transmitted by various routes, including by food, water, and manure application to food crops' soils, thus underscoring the varied routes by which resistance to antibiotics can be transmitted from animals to humans (Cesare *et al.,* 2016).

Human Health and Environmental Reservoirs: The development and spread of bacteria resistant to antibiotics are influenced by environmental factors. It facilitates the spread of resistance genes to people and acts as a gene storage unit for them. That implies that we must evaluate those risks carefully (Bengtsson-Palme *et al.,* 2018). The One Health policy exemplifies the way humans and the environment influence each other. It reveals that we must collaborate to address antibiotic resistance among humans and the environment (Wako *et al.,* 2022).

STRATEGIES FOR MITIGATION

In order to prevent drug-induced antibiotic resistance, one needs to have specific plans that look at sources of drugs in the environment and medicinal practice. There must be monitoring, risk analysis, and means of minimizing risks put together under an environmental plan. Plans involve taking fewer antibiotics from the beginning, developing better wastewater treatment technologies, boosting laws and regulations, and launching long-term monitoring projects. Both of these are a combined approach to preventing drug resistance from drugs. This section demonstrates key practices that can be implemented to minimize the environmental and health dangers of releasing antibiotics:

Methods for Preventing and Controlling Sources: Restricting the use of antibiotics in agriculture is a direct means of limiting environmental ARGs and ARB. Improved husbandry, like low animal numbers and proper feeding, can lower antibiotic usage in farming. Increased regulation of medical and agricultural use of antibiotics must be employed to lower the spread of antibiotic resistance. This can be realized through activities like the establishment of antibiotic stewardship programs in healthcare facilities, the prohibition of the use of antibiotics for non-therapeutic reasons in agriculture, and the encouragement of responsible use of drugs (Aslam *et al.,* 2021). Shifting to green alternatives for drugs and cosmetics can minimize use from the beginning. It requires a shift towards green chemistry concepts in the production and design of PPCPs, and consumers' increased awareness and demand for green products. Increasing public knowledge concerning those issues is quite crucial for promoting the appropriate use of antibiotics and decreasing the pressure responsible for resistance. It can be achieved through various means, such as mass media campaigns for public health, educational activities, and media relations. Educating citizens to dispose of unused drugs in appropriate ways can prevent environmental pollution. Inefficient disposal of unused drugs is considered the chief reason for pharmaceutical pollution, resulting in damage to the environment and the dissemination of AMR (Salmanov *et al.,* 2018). Encouraging the preference for food products that are produced without unnecessary use of drugs can transform the way farmers operate. Citizens can make farmers change the way they operate by demanding food products that are produced without unnecessary use of drugs. All these steps address the fundamental issue of drug pollution even before it enters the wastewater treatment works.

Upgrade of wastewater treatment plants: Use of advanced wastewater treatment technologies before discharge can avoid hazardous pharmaceutical pollutants. Standard wastewater treatment plants (WWTPs) commonly are not effective for the elimination of pharmaceutical pollutants, including antibiotics and antibiotic resistance genes (ARGs). Advanced treatment technologies, including activated carbon adsorption, advanced oxidation processes (AOPs), membrane filtration or bioreactors, and ozonation, can be used to eliminate these pollutants more effectively before discharge into the environment (Hammerum *et al.,* 2014).

Technologies like biodegradation, adsorption, and chemical changes can help remove antibiotic-resistant bacteria (ARB) and antibiotic resistance genes (ARGs) in wastewater treatment plants (WWTPs). Biodegradation uses tiny living things called microorganisms to break down harmful organic waste, including medicines, into safer substances. Adsorption uses materials like activated carbon to catch and remove pollutants from wastewater. Chemical changes use reactions to turn harmful pollutants into less toxic or easier-to-remove substances. Advanced oxidation processes (AOPs) are good options for breaking down pollution and preventing it, but specific uses may not be available in some areas. Changing how WWTPs work to improve the removal of ARB and ARGs is very important. More studies are needed to find the best treatment methods for improving WWTP design and operations. Regular checks on pharmaceuticals and other new pollutants in the environment are very important (Osabuohien *et al.*, 2021). Application of systematic elimination technologies of pharmaceuticals through algae immobilization methods as a cost-effective, efficient, and viable alternative technology. Algae immobilization methods represent a potential strategy for the elimination of pharmaceuticals from wastewater. Algae immobilization methods involve the immobilization of algae cells in a firm matrix, e.g., polymer material or gel matrix, to enable their repeated use and efficacy for pollutant elimination. Algae can be utilized to remove pharmaceuticals from wastewater through various removal mechanisms such as biosorption, bioaccumulation, and biodegradation (Szopiska *et al.*, 2022).

New technologies for remediation: Novel methods such as bioadsorption, nanomaterials, and phytoremediation hold potential as low-cost and sustainable remediation technologies. Bioadsorbents, including sawdust, prawn shell waste, algae, and fungi, exhibit exceptional affinity for traces of antibiotics and can efficiently remove them from water. These are cheap, easily obtained, and eco-friendly materials that represent a promising alternative to traditional adsorbents like activated carbon. Using bioadsorbents can allow for achieving remarkable removal efficiency for traces of antibiotics from water, while at the same time cutting down the cost and environmental footprint of treatment. Microalgae, Terminalia catappa leaf, and siris seed pods demonstrated remarkable removal efficacy for antibiotics including tetracycline, dicloxacillin, and nitromidazole. Microalgae are phototrophic microorganisms that can efficiently remove various pollutants from water, including antibiotics. Terminalia catappa leaf and siris seed pods are agricultural waste materials that also demonstrated potential to be used as bio adsorbents for the removal of antibiotics. Bio adsorption focuses not only on targeting ARGs and antibiotic-resistant bacteria, but also eliminates traces of antibiotics (Baguma *et al.*, 2023). Nanomaterials, such as nanoparticles and nanofibers, possess distinctive characteristics that enable them to efficiently remove pollutants from water. Nano-zero-valent iron (nZVI) and nano-copper (CuONPs) can be used as nano-sized adsorbents to reduce levofloxacin from water samples and antibiotic-resistant genes. The constructed nZVI and CuONPs can be recycled several times and are cheap and environmentally friendly (Obaid *et al.*, 2023). Phytoremediation, whereby plants are used to clean up pollutants, can be economical and environmentally friendly. Constructed wetlands can be constructed to remove pharmaceutical pollutants and antibiotic-resistant genes from wastewater (Sardar *et al.*, 2023).

Frameworks for policies and regulations: We must establish regulations for the top AR levels of pharmaceutical waste to diminish ARG's contribution to AMR. It is crucial to establish these regulations and ensure they are enforced and functioning effectively. Developing environmental guidelines for purchasing and payment mechanisms can promote the adoption of safe and green mechanisms (Pant *et al.*, 2022).

Surveillance and Monitoring Initiatives: Regularly surveying water bodies, soil, and sediments for ARGs and drug pollutants is important. We require sophisticated techniques to detect and quantify environmental samples for drug contaminants. Detection and quantifying these drug contaminants involve the use of sophisticated techniques such as liquid chromatography-mass spectrometry (LC-MS) and gas chromatography-mass spectrometry (GC-MS) (Hamad and El-Sesy, 2023). These techniques can detect and quantify drug compounds at extremely low concentrations, enabling us to detect even minor levels of pollution. Employing sophisticated techniques is necessary for us to adequately comprehend the effects of drug pollutants upon the environment and monitor whether solutions are effective. An ongoing

program of monitoring can give us information to determine whether mitigation measures can be successful. Installing monitoring systems to detect the emergence and spread of antibiotic-resistant bacteria is worthwhile. Sharing information to track trends in resistance to antibiotics can allow us to respond as a collective. The use of ecological risk assessment allows us to assess how pharmaceutical pollutants could affect ecosystems. It is important that we conduct long-term studies to determine whether deployed solutions can be sustained for the long term. Such studies must be used to look at the success of the intervention over the long term, as well as economic and social effects. The research findings must be used to inform future policy decisions and ensure that mitigation measures can be sustained for the long term (Asaduzzaman, 2018).

Alternative tactics: Include immunomodulatory treatments, antimicrobial peptides, and phage therapy. Exploring the use of bacteriophages (phages) rather than antibiotics to cure bacterial infections. Phage therapy is specific to certain bacteria, thus reducing the possibility of developing resistance to antibiotics. More studies are required to improve phage therapy and fix potential problems such as phage resistance. Designing antimicrobial peptides (AMPs) as a new strategy to combat drug-resistant bacteria. AMPs have the ability to lyse bacterial membranes and function against numerous different bacteria. More work is being conducted to stabilize the AMPs and enhance their effectiveness. Investigating immunomodulatory treatments to enhance the body's resistance to bacterial infection. Vaccinating farm animals and fish with affordable vaccines for common farm animal diseases can curb the use of antibiotics. Such treatments can be utilized to counter the use of antibiotics and resistance to drugs (Arora, 2025).

Future Perspective

Investigation of mechanisms by which pharmaceutical contaminants trigger horizontal gene transfer, including mechanisms of enhanced membrane permeability, plasmid transfer gene induction, and SOS response of the antibiotic resistance genes. Investigation of the role of microbial populations in ARG transmission across various environments. Microbial communities are instrumental in ARG spread. Exploration of the influence of non-antibiotic substances on AMR plasmid conjugation by clinical isolates (Huang *et al.*, 2022). Improved analytical techniques for the identification of pharmaceutical pollutants in water systems. Effective analytical techniques are required for the identification and quantification of pharmaceutical pollutants in water systems. Additional research must be performed to improve more sensitive, selective, and economical analytical techniques for monitoring the pollutants. Investigation of the application of nanotechnology and biotechnology for pollution cleanup. Investigating innovative materials and techniques for the removal of ARGs and antibiotic-resistant bacteria from wastewater. Carrying out long-term experiments to evaluate the ecological and health effects of pharmaceutical pollutants and antibiotic resistance. Testing the efficacy of mitigation measures in curbing these effects. Employing a broad-based approach towards understanding the interplay between pharmaceutical pollutants, antibiotic resistance, and environmental health (Alav and Buckner, 2023).

CONCLUSION

The use of antibiotics has been a significant part of medical history, bringing about a major change in how bacterial infections are treated. Antibiotics help us to fight disease, but their overuse and misuse have caused antibiotic resistance to increase rapidly. This means that bacteria have learned how to survive against these medicines, which shows a symptom of imbalance between ecological and human activity. Pharmaceutical effluents entering water and soil are not only chemical contaminants but active drivers of microbial evolution, which reshape microbial community networks that are still poorly understood. Understanding that resistance not only represents a medical emergency but also an environmental policy issue changes the way it could be handled. Environmental regions, which are frequently ignored in antibiotic management plans, serve as secret stores where resistance genes collect and spread, and that's what makes the problem. In order to solve this issue, industrial management and wastewater treatment must be considered as an ethical responsibility to protect shared resources instead of technological difficulties. Future strategies need to close the gap between environmentally friendly pharmaceutical techniques, public wellness policy, and microbial ecology. Preserving antibiotics against environmental deterioration isn't just a scientific

necessity, but also a responsibility to future generations.

Abbreviations

AR- Antibiotic resistance
ARG- Antibiotic Resistance gene
ARB- Antibiotic-resistant bacteria
AMR - Antimicrobial Resistance
WHO - World Health Organization
MDR - Multidrug-resistant
CDC - Centers for Disease Control
API - Active Pharmaceutical Ingredients
WWTP - Wastewater treatment plants
ESBL - Extended-spectrum beta-lactamase
MSW - Municipal Solid Waste
HGT - Horizontal gene transfer
MGE - Mobile genetic elements
CRE - Carbapenem-resistant Enterobacteriaceae
AOP - Advanced Oxidation Processes
(LC-MS) - Liquid Chromatography-Mass Spectrometry
GC-MS - Gas Chromatography-Mass Spectrometry
AMP- Antimicrobial Peptides

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