

Zoonosis: An Emerging Link to Antimicrobial Resistance Under “One Health Approach”**18**

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ABSTRACT

The current state of infectious diseases has given rise to a new era in which the management and sharing of etiological agents with their effects on ecosystems is understood through the lens of "One Health." In this regard, the importance of zoonotic illnesses gives rise to serious concerns. Because of their high density and shorter generation times, the indiscriminate and increased use of antibiotics in animal agriculture puts significant pressure on the gut microbiota to acquire resistance. In this case, the gut serves as a bioreactor for the spawning of ARBs, which are then continuously discharged into other habitats. Through quorum sensing, vectors, and horizontal gene transfer events, these ARBs spread resistance genes among the natural flora. The possibility for zoonotic infections to carry ARGs that could be transmitted to humans, accounts for about 60% of infectious illnesses that affect humans. The well-known zoonotic illnesses include hemorrhagic colitis caused by *Escherichia coli*, brucellosis caused by *Brucella abortus*, ovine tuberculosis caused by *Mycobacterium tuberculosis*, and anthrax caused by *Bacillus anthracis*. Similar to this, the majority of antibiotics are not entirely broken down before being released into the food chain where they bioaccumulate and impact different ecological niches. Antibiotics have an environmental persistence duration ranging from less than one day to 3466 days. This review has covered the effects of antibiotic misuse in cattle as well as their future in different ecological niches. Additional information is provided about the persistence of antibiotics and their biodegradation in the environment using various abiotic and biotic methods. To manage the development of antimicrobial resistance (AMR) in the environment and, eventually, to humans through food webs, comprehensive surveillance systems for zoonotic diseases, including ARB transmission, prevention, and control measures, as well as knowledge on personnel hygiene, should be built.

Keywords: Antibiotic resistance, antimicrobial resistance, Livestock, Zoonosis, Half-lives of antibiotic, Gut microbiome

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1. INTRODUCTION

In recent years, the management of human health has encountered new challenges. The global concern primarily revolves around emergence of novel opportunistic pathogens and drug resistance among existing pathogens. These emerging diseases have transcended geographical boundaries, permeating various environments. The evolving hypothesis postulates that the altered disease patterns are a result of pathogenic determinants proliferating within ecosystems, exploiting any available biological host. Among these hosts, animals stand out as the most prevalent. Animals' gastrointestinal tracts harbor diverse microbial communities that collaborate to enhance their host's well-being (Purohit 2018). By spreading their resistant genes to other gut pathogens, drug-resistant pathogens disrupt the community structure when they are introduced to the gut microbiome. Opportunistic infections spread from animals to humans with the help of direct contact (zoonoses) or vectors, having an adverse effect on human health. The intricate connection between humans and animals through ecosystems has prompted the adoption of the "one health" approach.

The global increase in concern lies in the transmission of diseases from animals to humans through the zoonotic route. Zoonotic diseases have the potential to trigger sporadic disease outbreaks, novel epidemics, or remain geographically limited occurrences. The "one health" paradigm includes the thorough management of all elements causing the introduction of novel zoonotic illnesses. This approach interconnects animal health, human health, and environment. The one health strategy must be used due to the rise in antibiotic resistance among humans, which is spread via zoonotic infections. Managing zoonotic diseases through the one health approach requires collaborative efforts from multidisciplinary teams consisting of mammalogists, entomologists, ecologists, ornithologists, physicians, and epidemiologists ensuring successful investigations.

A substantial change in human health resulted from the discovery of antibiotics in the early 1900s, which helped to save countless lives. Antibiotics are complex substances that obstruct the growth of microorganisms through a number of mechanisms, including alterations to cell membranes, antimetabolite effects, hindrance of cell wall synthesis, disruption of protein synthesis, competitive antagonism, and inhibition of nucleic acid synthesis. Antibiotics are used in livestock and animal husbandry to prevent infectious diseases and increase the meat and dairy production. Furthermore, they are employed to facilitate substantial increases in animal growth and weight. Despite the advantages of antibiotics, the unregulated utilization of these agents and their release into the environment raise significant concerns (Parmar A et al. 2018). (Fig. 1)

The majority of antibiotics introduced into human and animal bodies undergo incomplete metabolism, leading to the release of unmetabolized forms into the environment. These unmetabolized compounds are expelled from the body and find their way into the environment through sewage sludge, municipal wastewater, and animal manure. The heightened presence of antibiotics across diverse environments exerts selective pressure, fostering the growth of antimicrobial-resistant bacteria (ARBs). This growth triggers antimicrobial resistance (AMR) within the indigenous microbiome and alters the sensitivity of bacterial populations (Parmar KM et al. 2017). Environmental Antibiotics bring about modifications in the

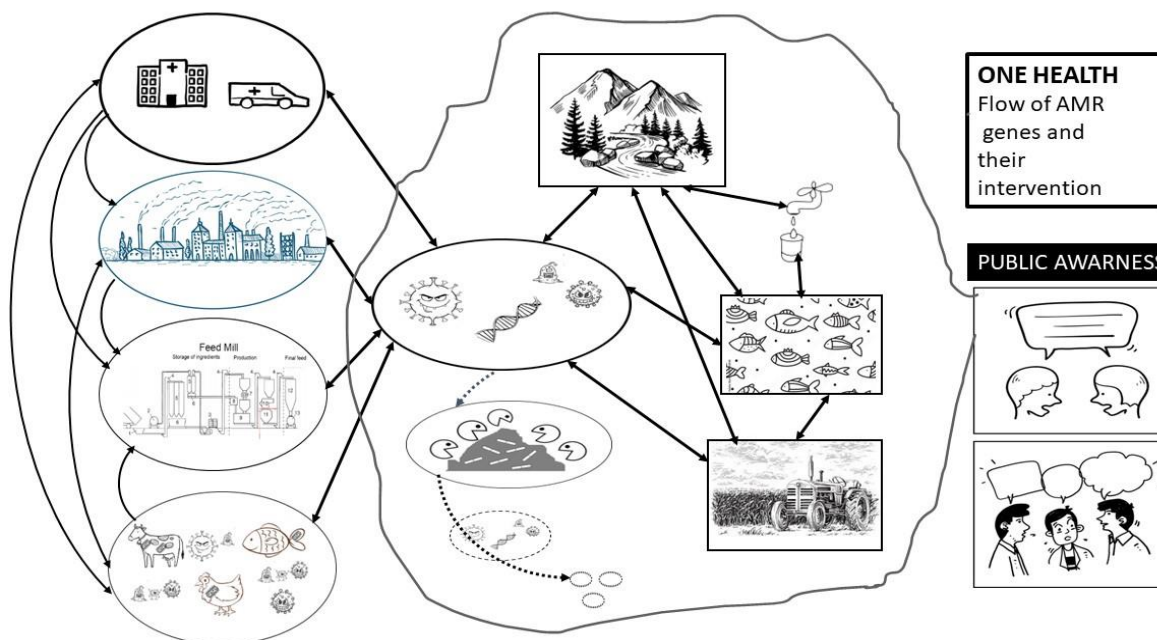


Fig. 1: Diagram showing the movement of resistance genes in the environment and how the "One Health" approach can be used to control it. ARB breeding hotspots are connected by a black solid line, and the bioremediation strategy in the environment is shown by a dotted line.

genetic composition of bacteria that results in the proliferation of antibiotic resistance genes (ARGs). These ARGs are transferred via mobile genetic elements (MGEs) like transposons, genomic islands, and plasmids to other microbial populations, consequently amplifying the prevalence of ARBs within the environment and these ARBs can develop into potent zoonotic pathogens, contributing to severe infections within the global human population.

The utilization of antibiotics in the treatment of animals used for food production is fostering the emergence of ARBs among both zoonotic pathogens and normal bacterial communities. The correlation between AMR and the occurrence of illnesses in animals and humans is a significant concern within modern medical practices. Despite the ongoing comprehensive research concerning zoonotic pathogens, the effective regulation and management of antimicrobial agents, combined with their careful use by humans, still lack appropriate measures. Additionally, the practice of using antibiotics in manure for agricultural purposes leads to the dissemination of antibiotics into various ecological niches, including water and soil. Antibiotics from the soil can leach into water bodies, and thus becoming distributed throughout different ecological environments. The dispersal of antibiotic resistance within the environment is recognized as a global threat, and AMR has attained paramount importance within the recent approach of One Health framework introduced by the World Bank (Thakur and Gray 2019). This One Health approach to AMR encompasses considerations for wildlife, environment, and the aquaculture. The approach recognizes the pivotal roles that various sectors play in the advancement and proliferation of AMR, concentrating efforts on actionable and impactful research.

2. THE ONE HEALTH STRATEGY TO TACKLE WIDESPREAD RESISTANCE

AMR can have fatal consequences, yet the implementation of effective strategies to counter AMR remains intricate. Deciphering the pattern of AMR is challenging because of its intricate, multifaceted ecological,

and interconnected characteristics. Addressing the extensive resistance requires decisions made by individuals and societies, which must prioritize the judicious use of antimicrobial products across various sectors. Gaining a comprehensive understanding of the intricate AMR landscape necessitates holistic oversight involving multi-sectoral teams comprising healthcare professionals, environmental experts, stakeholders, and veterinarians. One Health approach emphasizes interdisciplinary collaboration among researchers, policymakers, and leaders operating at regional, local, national, and the international levels (Binot et al. 2015). It aims to enhance health outcomes for humans, animals, and the environment. The mitigation of epidemic infections associated with AMR is a central focus of the "one health" strategy. This approach interconnects diverse sectors engaged in comprehending the AMR challenge and devising effective solutions, including the establishment of appropriate usage guidelines and the provision of effective risk communication. Furthermore, dissemination of AMR poses another challenge, necessitating a broader exploration of bacterial transmission among human hosts, both domestic and wild animals, and the corresponding environments in which genes of resistant bacteria can propagate.

The management of AMR under the one health approach involves considering various factors, including

1. The establishment of regulations and guidelines for the prudent use of diverse antimicrobial classes in both human and animal health.
2. Comprehending the environmental dissemination of AMR through mediums such as water, air, and soil, which harbor resistant bacteria and ARGs and serve as pathways for AMR transmission between human and animal populations.
3. The implementation of innovative and established solutions using novel technologies to quantify AMR across domains like herd management and animal husbandry.
4. Effective communication strategies to raise awareness of consumer about the risks related to AMR dissemination from sources such as food production, and other non-human origins.

The grasp of zoonotic-mediated AMR is a universal concern that spans the food animal producers, scientific community, patients, healthcare professionals, and consumers. In order to sustain the judicious use of antibiotics in both human and animal medicine, the "One Health" approach employs a variety of strategies to curb the cross-border and zoonotic propagation of AMR.

3. ZOONOTIC PATHOGENS AS VECTORS OF ANTIMICROBIAL RESISTANCE (AMR)

Over the previous years, both human and animal health have faced challenges stemming from environmental pollution, AMR, and chronic diseases, consequencing in elevated morbidity and mortality rates (Kalia et al. 2014). The emergence and dissemination of zoonoses, epidemics, and epizootics have underscored the heightened health risks on a global scale, emphasizing the significance of comprehending the interface between humans and animals in the transfer of infectious agents. Many of these infectious diseases are regarded as severe health concerns originating from a zoonotic source. As defined by the WHO, the zoonotic diseases, or zoonoses, refer to "any disease or infection that is naturally transmitted between vertebrate animals and humans." These diseases can be caused by viruses, fungi, bacteria, parasites, or prions. Currently, there are approximately 200 recognized zoonoses, with some confined to specific geographic regions and others having a global distribution. Zoonotic pathogen transmission occurs through various routes, including ingestion, inhalation, and other means that lead to mucous membrane contamination. Furthermore, zoonotic pathogens can be transmitted through dietary habits involving undercooked animal tissue, unpasteurized milk, dairy products, seafood, and contaminated vegetables. Several other well-documented zoonotic diseases include anthrax, animal influenza, bovine tuberculosis (BTB), brucellosis, hemorrhagic colitis, zoonotic diphtheria, rabies, and Q fever.

The prevalence of zoonotic diseases is the outcome of intricate interactions among various factors, encompassing biological, genetic, political, social, ecological, environmental, and physical aspects. Zoonotic pathogens are accountable for over 60% of infectious diseases in humans. Within this group, ARBs represent one of the most prevalent zoonotic pathogens that can be found widely within the environment. These bacteria exhibit a short generation time and are subject to intense selection pressure from the host immunity and antimicrobial agents. Consequently, these bacterial communities undergo notable evolutionary changes, impacting human health by their interactions with pathogen-host spp., serving as infection reservoirs. Specific bacteria, such as *Proteus mirabilis*, *Pseudomonas fluorescens*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Staphylococcus* species, have demonstrated resistance against certain antibiotics (Hathroubi et al. 2018). The one health approach underscores the direct correlation between the emergence of ARBs and the escalated use of antibiotics within the farm animal and aquaculture sectors.

ARBs enter the human gut via zoonotic disease transmission, leading to disruptions in the natural gut diversity. Zoonotic pathogens harboring ARGs are introduced into the body of humans, where they can transfer these resistance genes to the gut microbiome, thereby causing disturbances in the ecosystem of gut. Moreover, the ARGs or ARBs are expelled from the body of human and find their way into the environment either through the soil or municipal wastewater. These ARG genes from the soil or wastewater are then transmitted to ARBs, which enter the food web, affecting animal health, and perpetuating the ARB transmission cycle (Hathroubi et al. 2018).

4. ZOONOTIC PATHOGENS AND THEIR ANTIBIOTIC RESISTANCE

The One Health strategy highlights that the majority of animals acting as reservoirs for the zoonotic diseases, are domesticated and frequently interact with humans. Animal husbandry is an integral component of agricultural economy, and holds significant importance in sustaining the rural population's livelihood. This practice supplies milk, meat, eggs, and wool that have direct interactions with human population. Potential for zoonotic disease transmission from animals to humans is particularly elevated in the context of animal husbandry. Despite the substantial risks associated with zoonotic diseases, livestock continues to play a pivotal role in the income of numerous farmers, as well as in providing nutrition for households and contributing to the consumption of animal products.

It has been shown that the ARGs, which are passed to the human population upon infection, have recently been found to be present in a number of zoonotic diseases. The misuse of antibiotics is thought to be a contributing factor in the rise of ARGs in zoonotic diseases (Dafale et al. 2016; Yadav et al. 2019). In the context of animal husbandry, even when only certain animals show clinical symptoms, entire herds are often treated with antibiotics to prevent disease transmission within the herd. This practice, known as metaphylaxis, involves administering high doses of antibiotics for a short duration. In contrast, prophylaxis involves incorporating antibiotics into feed at lower doses over an extended period, typically spanning several weeks. While animals may not exhibit clinical symptoms during this period, the risk of infection remains. The imprudent use of antibiotics subject's pathogens to selective pressure, leading to antibiotic resistance even at sub-therapeutic antimicrobial concentrations. Bacterial species acquire resistance through various mechanisms, including mutation, changes in cell permeability, drug efflux, quorum sensing and horizontal gene transfer. The increased prevalence of resistant bacteria in the intestinal flora of swine, chickens, and other agricultural animals has been related to the transmission of ARGs and the excessive use of antibiotics. The close contact between farmers, workers, and animals greatly increases the likelihood of ARB transmission. Numerous routes facilitate the transmission of zoonotic pathogens between humans and animals, with the food chain being the most probable pathway. Humans face a

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significant risk of exposure to ARBs originating from animals through the consumption of products like milk, meat, eggs, and protein. The ARBs are particularly likely in raw, less processed, or fermented foods with higher microbial loads. The presence of pathogenic bacteria in animal-derived foods creates a concerning scenario within the human gut, leading to the emergence of the resistant strains in the humans (Kalia and Purohit 2011; Dafale et al. 2015).

5. LIVESTOCK AS POTENTIAL RESERVOIRS FOR ANTIBIOTIC RESISTANCE

Threats posed by zoonotic diseases have escalated as a result of their adaptation to antibiotic resistance. Methicillin-resistant *Staphylococcus* (MRSA) strains that have emerged from farm animals, including CC93 in Denmark, ST 130 across Europe, and ST398 in the Netherlands, have been seen to spread among human populations (Chang et al. 2015). Concerns about animals acting as reservoirs for illnesses that could evolve to spread among humans are brought up by the possibility of zoonotic transmission. Research has indicated a correlation between antibiotic usage in food animals and a rise in ARBs in humans. The importance of fluoroquinolones, a class of antibiotics frequently used to treat infectious illnesses, has been highlighted (Dafale et al. 2015). Fluoroquinolone-resistant *Campylobacter* infections were reported by Barza and Travers (Barza and Travers 2002), who linked them to an overuse of the drugs in animals. Following this, the Food and Drug Administration (FDA) of the United States determined that chicken eating was directly related to fluoroquinolone-resistant *Campylobacter* in people. This result finally helped to justify the US decision to stop using fluoroquinolones on poultry (Pereira et al. 2018).

There are differences in the epidemiology of vancomycin resistance components between Europe and the USA. The gastrointestinal microbiome of healthy individuals and livestock animals in Europe has been found to have *Enterococcus faecium* expressing the *vanA* resistance gene (VRGs), however in the United States, neither healthy humans nor livestock animals had been found to contain this organism until 2008. This discrepancy was anticipated due to the extensive utilization of avoparcin in European agricultural practices since the 1970s, while this glycopeptide had never been authorized for agricultural use in the United States. It has been proven that avoparcin exerts selective pressure favoring the establishment of VRGs in mice by conferring cross-resistance to vancomycin (Birkegård et al. 2019). ARBs have several opportunities to colonize the human environment and to infect humans when VRGs are present in animals. Molecular and epidemiological studies have demonstrated the similarity between VRGs-containing organisms isolated from both animals and humans, confirming the potential for the transmission of VRGs. A thorough understanding of zoonotic pathogens, transmission of disease, control measures, and prevention is indispensable for individuals working with livestock. This knowledge is essential to mitigate zoonotic diseases as occupational hazards, contributing to the prevention and control of such diseases in both human and animal populations.

6. TRANSMISSION OF ANTIBIOTIC RESISTANCE GENES FROM LIVESTOCK

Zoonotic AMR pathogens can move from farm animals and affect humans through the consumption of food or water that has been contaminated, as well as through direct contact with animals. In the various stages and processes of the food production chain, there are opportunities for the transfer of ARBs. Physical environment, including soil, water, and air, significantly contributes to the transfer of ARBs from animals. Within a farm setting, there is a potential for the direct movement of the resistant bacteria among animals within the same herd and those in close proximity. Additionally, interactions between farmers and their animals can also facilitate the transmission of resistant

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bacteria. Moreover, when animals consume water, feed, or waste contaminated with ARBs, the likelihood of transfer increases (Barton 2014). Several instances of ARBs in livestock have been recorded by numerous researchers. These instances encompass bacteria that produce extended-spectrum beta-lactamases (ESBLs), vancomycin-resistant *Enterococcus*, methicillin-resistant *Staphylococcus aureus* (MRSA), *E. coli*, and multidrug-resistant *Salmonella* (Barton 2014). Other ARGs, such as plasmid-mediated colistin resistance, *Klebsiella pneumoniae* carbapenemase-2, and New Delhi Metallo- β -lactamase-1 found in the livestock animals, pose threats to both human and animal health (Liu et al. 2016; Tafaj et al. 2019).

In the livestock industry, inappropriate antibiotic usage contributes to the rise of the specific resistant bacteria. The extent of antibiotic use correlates directly with specific resistance level observed in commensal *E. coli* isolates from poultry, cattle, and swine. Metagenomic data has also demonstrated that the imprudent administration of antibiotics to animals leads to resistance development in the commensal microbial populations of human (Chang et al. 2015). Vounba et al. (2019) reported instances where use of 3rd generation cephalosporins in poultry led to human fatalities caused by the resistant *E. coli*. The GIT of animals functions as a notable reservoir for ARBs. It is well established that bacteria can transfer genes within the same species or between different species through mechanisms such as phagocytic transduction, natural transformation, and plasmid transfer. Resistance genes for sulfonamides, quinolones, tetracycline, aminoglycosides, β -lactams, and vancomycin have been identified in animals. ARBs and ARGs perpetually circulate within soil, plants, animals, and contribute to the spread of resistant microorganisms among diverse living organisms.

7. VECTOR BORNE ZOONOTIC DISEASES

Most instances of zoonotic diseases characterized by antibiotic resistance are often perceived as resulting from direct contact between the host and recipient. The intricate interplay among the resistant pathogen, the host, and humans is frequently influenced by vector-borne diseases, introducing unforeseen complexities. Compared to directly transmitted antibiotic-resistant infections, vector-borne zoonotic diseases (VBZDs) represent a sizable category of zoonotic illnesses with an increasing occurrence rate. Since VBZDs make for 22% of all newly developing infectious illnesses in humans, they are disproportionately prevalent (Jones et al. 2008). The main vectors of these diseases are hematophagous or blood-feeding arthropods. Mites, ticks, flies, and mosquitoes make up more than 90% of the vectors that cause emergent VBZDs. Ticks like *Ixodes* and *Amblyomma* transmit a number of common bacterial illnesses, including ehrlichiosis, Rocky Mountain spotted fever, and Lyme disease.

8. DYNAMICS AND DRIVERS OF VECTOR BORNE DISEASES

Vector-borne diseases are influenced by multiple factors that facilitate the transmission of infection from the original host to the recipient. A significant driver of vector-borne diseases is the reduction in host abundance. This phenomenon has been closely linked to a decline in rodent populations, which serves as the primary host, causing *Yersinia pestis* to transition to human populations through vectors as an alternative host (Jones et al. 2008). Environmental changes and human activities stand as crucial factors that shape the dynamics of vector-borne diseases. Over the past three decades, vector-borne zoonotic diseases (VBZDs) have extensively emerged in new geographical areas. The emergence of VBZDs primarily results from the pathogen's shift from its original host to humans due to human-induced activities. While local environmental changes like urbanization and deforestation play a role in local regions, trade and travel are the primary drivers of events in new regions. In order to treat patients

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and promote behaviors that lower the risk of infection, doctors and public health officials must work together to control vector-borne zoonotic illnesses. In order to combat the ecological factors that drive the spread of disease, urban planners, disease ecologists, and medical entomologists must all work together to help direct the growth and restoration of ecological communities and put vector control strategies into place.

9. QUORUM SENSING

By accumulating multiple genotypic and phenotypic mechanisms that confer resistance against widely used antibiotics, bacterial populations are evolving into superbugs. Quorum sensing (QS), which enables microorganisms to interact using tiny signal molecules, is one such method (Kalia et al. 2019). In order to create biofilms that enable bacteria to withstand antibiotic dosages up to 1000 times higher, QS relies on the cell density phenomenon. By producing dangerous molecules through QS regulation and circumventing defensive mechanisms, resistant bacteria use information exchange to spread infectious diseases among animals and people (Kalia 2013). A promising approach is Quorum Sensing Inhibition (QSI), which involves inhibiting the QS process.

Quorum sensing inhibitors (QSIs) exert their effects through diverse mechanisms, encompassing:

1. Halting the synthesis of signal molecules
2. Enzymatically breaking down signal molecules
3. Competing with signal molecules for receptor binding sites
4. Disrupting the binding of signal molecules to gene promoters, thus inhibiting gene expression
5. Scavenging autoinducers through antibodies and macromolecules like cyclodextrins (Fetzner 2015).

QSIs come from a variety of sources and have shown promise as anti-pathogenic substances (Dafale et al. 2016). It has been shown that some enzymes, including as lactonases, acylases, oxidoreductases, and lactonases with properties similar to phosphotriesterase, can degrade QS signal molecules (Fetzner 2015). It is known that a variety of plants produce QSIs that either weaken QS signals or compete with them for signal receptors. *Emblica officinalis*, *Curcuma longa*, *cinnamon*, grapefruit, *Medicago truncatula*, and other edible fruits and plants have all demonstrated usefulness as extracts against diseases brought on by plant pathogens. By concentrating on the QS signaling pathway, a QSI reduces the pathogenicity of pathogenic bacteria that are resistant to it. It's important to note that QSI doesn't necessarily affect bacterial growth (Koul et al. 2016; Koul and Kalia 2017), but rather impedes the establishment of a bacterial community among resistant pathogens. Therefore, the combined application of QSIs and antibiotics holds promise as an approach for treatment.

10. FATE OF ANTIBIOTICS IN ENVIRONMENT

Non-metabolized antibiotics are consistently released in the environment, including water and soil, from sources such as veterinary practices, hospital waste, pharmaceutical industries, poultry and dairy operations, households, and municipal waste disposal (Cycoń et al. 2019), posing pollution concerns. Antibiotics are frequently identified in various aquatic settings like rivers, groundwater, and lakes, originating from wastewater treatment plants (WWTPs), surface runoff, or aquacultural activities. Due to the fact that they acquire unmetabolized antibiotics through wastewater from various sources, WWTPs are acknowledged as important nodes for the evolution of ARBs and ARGs (Kapley et al. 2016). A few nanograms to milligrams of antibiotics per kilogram of soil are also discovered in soil, in addition to water bodies (Jiang et al. 2010). Sewage sludge, manure, and locations where there are livestock populations are the main causes of antibiotic presence in soil.

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Antibiotics are continuously being introduced into the environment, exposing aquatic and soil species to them. Through gene mutations or horizontal gene transfer from other resistant germs, environmental microbes may gain resistance to these particular medicines. Antibiotics entering different water bodies and soil pose serious dangers to human health and also harm numerous biological ecosystems, even at low amounts. Antibiotic use and distribution contribute to the growth and ubiquity of ARGs worldwide. Severe infections are linked to the ongoing growth in ARG and ARB strains.

Following a cycle of bioaccumulation, partial biotransformation, and slow deposition in soil or water, antibiotics diffuse from sources into the environment (Binot et al. 2015). Antibiotics naturally persist in the environment, which causes them to build up at higher quantities and spread farther. Although certain antibiotics, like penicillins, are easily degraded, others, including fluoroquinolones, macrolides, and tetracyclines, demonstrate greater persistence because of their longer half-lives, enabling them to stay in the environment for longer periods of time (Nimonkar et al. 2019). The environmental half-lives of antibiotics range from 1 to 3466 days. According to Walter et al. (Walters et al. 2010), azithromycin had half-lives ranging from 408 to 3466 days and ofloxacin had half-lives ranging from 866 to 1733 days in a sand clay loam in the United States. Notably, even antibiotics within the same groups can have differing half-lives, potentially influenced by varying conditions, compositions, and soil variations. The degradation of antibiotics in the soil is often impacted by diverse functional groups, which exhibit a wide range of half-lives in the soil. The extended persistence of antibiotics in the environment provides ample time for genetic changes to occur in bacteria residing within their respective niches.

11. DIFFERENT APPROACHES FOR ANTIBIOTIC DEGRADATION

The increased use of antibiotics and their release into the environment affect the biological processes that affect water quality. Therefore, controlling the formation of novel resistant strains and ARGs depends on the degradation of antibiotics. Antibiotics undergo degradation through both non-biological (abiotic) and biological processes. This degradation is facilitated by various methods, including bioelectrochemical approaches, hydrolysis, mechanisms involving adsorption, metal-assisted photolysis, oxidation, as well as reduction.

12. PHYSICO-CHEMICAL DEGRADATION OF ANTIBIOTIC

The abiotic degradation is predominantly influenced by the molecular structure of antibiotics and physicochemical properties. For instance, β -lactams are more susceptible to hydrolytic degradation compared to sulfonamides and macrolides. The degradation of fluoroquinolone antibiotics primarily occurs through photo-degradation. In a study by Wajahat et al. 2019, two methods were investigated for the degradation of commonly used antibiotic ciprofloxacin: anatase-facilitated photocatalysis and ozonation. Their findings indicated that the photocatalysis process resulted in a higher degradation rate in comparison to ozonation. The treatment of wastewater through UV radiation and chlorination aids in decontaminating wastewater, thereby reducing the antibiotic levels. Natural polysaccharide chemical conjugates can be used to suppress the growth of resistant bacteria, halting the proliferation of ARBs and ARGs, in addition to degrading antibiotics. A process known as adsorption and desorption of antibiotics occurs in the soil when drugs bind to particles and produce complexes that reduce their antibacterial effectiveness. In this sorption process, the soil's pH and water-retentiveness both play significant roles. For instance, sulfonamides, an antibiotic, may shift from their cationic form to neutral

and anionic forms as they are absorbed by the soil. Degradation of abiotic antibiotics is influenced by a number of physical and chemical factors. Abiotic treatment may be hindered by changes in salt concentration, pH, and the presence of other substances in the system. In such circumstances, biotic activities that employ microbes may be crucial in eliminating lingering antibiotics from the environment.

13. DEGRADATION OF ANTIBIOTIC THROUGH BIOAUGMENTATION

Antibiotics are broken down through the metabolic processes of bacteria during biotic degradation. ARGs are the main component of microorganisms that take part in the bioremediation of antibiotics, as emphasized in reference (Purohit et al. 2016). ARGs effectively break down the parent antibiotic or its functional groups, releasing byproducts in the process. Antibiotics can be successfully removed from industrial effluents via the bioaugmentation technique. Antibiotics have been extensively removed from soil and wastewater using bacterial strains. For instance, *Labrys portucalensis F11* and *Rhodococcus sp. FP1* were used by (Maia et al. 2018) to break down routinely used antibiotics like Ofloxacin and Levofloxacin (Walters et al. 2010). Similar to this, it has been reported that bioaugmentation of a membrane bioreactor with *Achromobacter dentrificans* improves the elimination of sulfamethoxazole (Leng et al. 2017).

Antibiotic-degrading bacteria are primarily found in anthropogenically altered habitats such soil, excrement, sludge, and seawater. In a study by Hirth et al., they added *Microbacterium sp. C448* to soil that contained sulfamethazine, and the antibiotic was reportedly degraded by 59.23% as a result (Hirth et al. 2016). Another investigation revealed that *Ochrobactrum sp.* degraded erythromycin at a rate of 97% (Zhang et al. 2017). Bioaugmentation has become a useful remediation method for antibiotics in the environment. This method plays a key role in shortening the half-life of the antibiotic by enhancing the breakdown of unwanted chemicals and completing the functions of native bacteria.

14. TRANSBOUNDARY SPREAD OF AMRS

The global dissemination of ARGs and their potential transmission between animals, humans, and environment presents a significant challenge in mitigating the threat of AMR. Notable contributors to the spread of resistance include animal farming, aquaculture industries, wastewater treatment plants, and waste generated by hospitals. ARGs can be transferred by various mechanisms, including zoonotic transmission, horizontal gene transfer, or by the environment to the opportunistic human bacteria, often facilitated by genetic elements. In addition to these factors, airborne microorganisms are frequently found to be resistant to multiple drugs, posing a significant risk of health to both animal and human populations through airborne transmission. The existence of airborne AMR has been documented in the scientific literature. For instance, Pal et al. (2016) examined the smog in Beijing and discovered the presence of a wide variety of 64.4 different types of ARGs, above levels observed in other environments (Pal et al. 2016). Tetracycline-resistant genes were found, according to Li et al. (2016), in the indoor air of human-inhabited places in Colorado (Li et al. 2016). Beta-lactam resistance genes were also found in a Californian urban park (Echeverria-Palencia et al. 2017). The distribution of airborne AMR is influenced by factors such as antibiotic usage, meteorological conditions, physicochemical parameters, and the microbial community. The efficient global transportation network and frequent human travel significantly contribute to the dissemination of airborne ARGs and ARBs across various cities. These airborne AMRs are now recognized as biological pollutants, capable of disturbing the gut flora of human and impacting the immune system when inhaled. Even in isolated areas where antibiotics are not often used, the aerial spread of AMRs exposes these areas to second-hand ARGs that have grown in other regions and been transported there.

Research in the field of airborne AMR development remains underexplored and requires attention to understand the patterns and spread of AMRs through the air.

15. CONCLUSION

Escalating environmental pollution represents a significant global threat that has garnered increased attention in recent times. In the livestock industry, the imprudent use of antibiotics fosters resistance within the gut microbiome, essentially acting as a bioreactor for cultivating pathogens. This practice elevates the likelihood of new ARGs emerging and spreading throughout the environment. Similarly, unmetabolized antibiotics are excreted into the environment, disrupting the biogeochemical cycle through the food chain.

The presence of resistant bacteria and the suppression of indigenous microorganisms lead to alterations in microbial community, nitrogen cycle, enzyme activity, and carbon assimilation. Future research efforts should prioritize the examination of antibiotic persistence, bioaugmentation, accumulation, biotransformation, and biostimulation, in the environment, as these factors heighten the risk of breeding ARBs through horizontal gene transfer (HGT) events. In pursuing these objectives, it's essential to consider the interplay between biotic and abiotic degradation processes.

Given that the animal gut serves as a significant breeding ground for antibiotic resistance, it is crucial to regulate and investigate the emerging resistance patterns using a "one health approach." This approach involves establishing an ARBs monitoring system to facilitate a timely public health response. Furthermore, the creation of a coordinated response involving numerous agencies is urgently needed. By coordinating efforts, it would be easier to communicate, deliver timely information, and spread awareness of the proper use of antibiotics in the aquaculture, animal husbandry, and agricultural sectors. These actions are anticipated to improve the environmental efficacy of both novel and existing antibiotics in addition to managing human and animal infections. Additionally, there will be a decrease in the propagation of antibiotic resistance among zoonotic diseases, which will lower the incidence of life-threatening infections in people that are resistant to treatment.

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