A Review of the Reasons for Increasing the Antibiotic-Resistant Bacteria Presence in Drinking Water

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ABSTRACT

Water purification included the elimination of pathogenic organisms and the reduction of suspended substances in water, which was obtained by conventional methods of disinfection and filtration. But today, due to the increase in all kinds of pollution to water sources, the common methods are not fully able to properly purify water. Based on the results obtained from various studies, drinking water disinfection can increase antibiotic-resistant bacteria in water environments. Water treatment may extend antibiotic resistance in bacteria, and systems of water distribution may serve as a vital reservoir for antibiotic resistance spread to opportunistic pathogens. Treatment processes of drinking water cannot remove all ARGs from sources of drinking water, thus, supply systems of drinking water may be a primary release of ARGs route from the environment to the host, which poses potential hazards to human health. It is also known that some bacteria number increases with the chlorine increase in drinking water and the water purification process can not eliminate all antibiotics from drinking water. Therefore, it is essential to obtain more information about the frequency and amount of bacteria with antibiotic-resistant mutations. In this review article, the studies done on drinking water treatment, as well as the introduction of antibiotics used in everyday life through sewage and production effluents and their impact on the health of human society.

Keywords: Bacteria, Drinking water, Pathogenic organisms, Antibiotic-resistant

INTRODUCTION

Examining the quality and health of drinking water has always been one of the important issues in public health. According to the WHO (World Health Organization), potable and accessible water is important for public health, drinking, food production, domestic use, and recreational purposes. Improving water sanitation and appropriate management of water resources can increase the economic growth of countries and help reduce poverty (WHO, 2014). Drinking water quality is evaluated by physical, chemical, biological, and organic tests. Water can be consumed only if the concentration of the components is within its standards, taking into account the maximum daily consumption over time, the nature of the pollutants, and the degree of toxicity of that water (Petraccia *et al.*, 2006; Quattrini *et al.*, 2016). Water before entering the distribution systems, is disinfected to kill microorganisms. However, some bacteria can reproduce in the water due to the resistance to disinfectants and the presence of a small amount of degradable organic matter required by bacteria (Ashbolt, 2004; Gwimbi *et al.*, 2019; Shayo *et al.*, 2023).

Pathogenic organisms that are transmitted through drinking water are mostly of fecal origin, so they are named enteric pathogens (Ashbolt, 2001; Wen *et al.*, 2020). The discharge of urban, agricultural, and industrial wastewater into waterways jeopardizes public health, and as a result, the amount of environmental and pathogenic pollution increases (Alipour *et al.*, 2014; Ibekwe *et al.*, 2023). Human and animal infectious bacteria continuously enter the water system through sewage (Baquero *et al.*, 2008; Larsson & Flach, 2022; Kulik *et al.*, 2023). Bathing in recreational water contaminated with feces increases the risk of transmitting infectious diseases, including gastrointestinal diseases, skin infections, and eye and ear diseases (Alipour *et al.*, 2014) and there is also an increase in health risk. Antibiotic-resistant bacteria and antimicrobial resistance genes (AMR) in feces can enter water sources with treated or untreated wastewater this is also true for drinking, bathing, washing, and other uses (WHO, 2014). Blue is also increasing (Schwartz *et al.*, 2003; Fernando *et al.*, 2016) contained in the water to be transferred to the body. In the urban water cycle context, bacteria that can reside in various types of water are of specific importance to assess the possible spread of antimicrobial resistance (Figueira *et al.*, 2011; Piotrowska *et al.*, 2017; Milligan *et al.*, 2023). Apart from untouched places in mountain ranges, before the water passes through agricultural or metropolitan areas, it is hard to find a place where antibiotics are not detected in the water (Yang & Carlson, 2003; Morina & Franklin, 2023).

The marine environment is considered a vital reservoir of ARB (Antibiotic Resistance Bacteria) and ARG (Antibiotic Resistance Genes) (Zhang *et al.*, 2009; Singh *et al.*, 2022) and antibiotics in the marine ecosystem have caused two concerns about the existence of ARB and ARG. The major issue is the possible toxicity of ARB and ARG substances to aquatic animals and humans through treated wastewater. In addition, there is greater concern that the antibiotics released in the environment are related to the pathogenic bacteria emergence that are

resistant to high amounts of these drugs. This paper is a review of the studies done on the treatment of drinking water, as well as the introduction of antibiotics utilized in everyday life through sewage and production effluents and their effect on the health of human society.

Drinking water treatment

In the past, water treatment aimed to decrease suspended substances and remove pathogenic organisms in water, which was obtained by conventional methods of disinfection and filtration. But currently, with the increase in the concentration of fine particles, nitrogen compounds, organic and inorganic substances, and heavy metals in water sources, the normal methods are not fully able for proper water purification, and it is necessary to use new methods and processes for this operation. **Figure 1** shows water pollution/percentage of studies sources (Antwi *et al*., 2021; Lin *et al*., 2022).
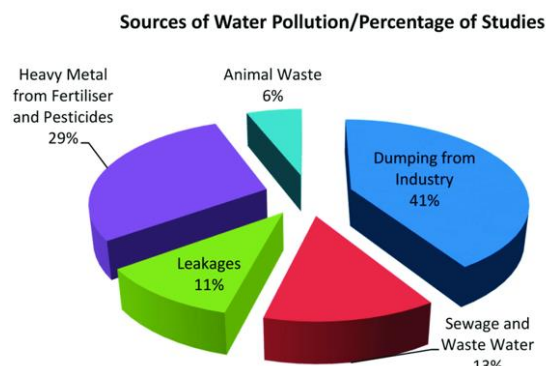

Figure 1. Water pollution/percentage of studies sources.

The effect of purifying drinking water (traditionally using chlorination and filtration) to eliminate bacterial pathogens such as the agent of typhoid fevers (*Salmonella paratyphi* and *Salmonella typhi*), and cholera (Vibrio cholerae), the fecal
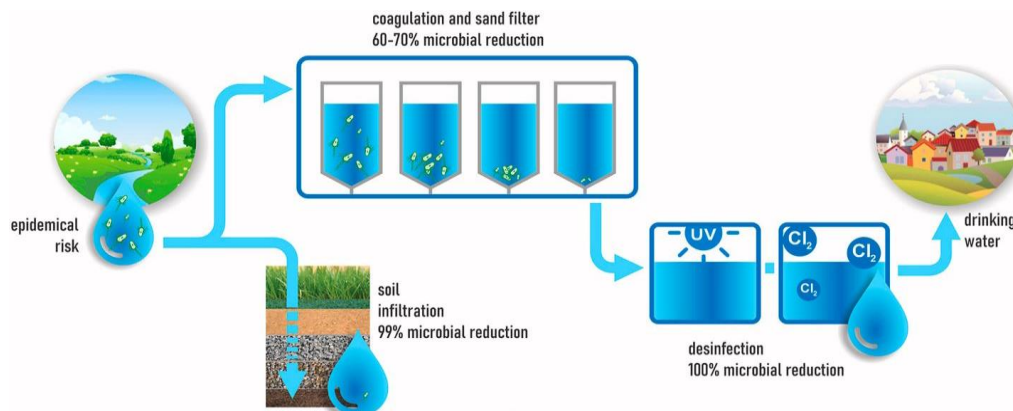
indicator bacterium Escherichia coli, which the feces of some reptiles and all warm-blooded animals are well characterized (Edberg *et al*., 2000). However, many enteric pathogens behave differently, especially concerning resistance to disinfectants and environmental conditions (Ashbolt, 2001).

Studies have shown that the use of chlorine to disinfect drinking water can cause an increase in antibiotic-resistant bacteria in water environments. This was confirmed in the study of Ribas *et al*. (2000). The water purification process cannot completely remove antibiotics from drinking water, and the water purification process can not eliminate antibiotics from drinking water (Figueira *et al*., 2011).

Resistance to some antibiotics has been reported in tap water and during water treatment, water treatment may raise the surviving bacteria antibiotic resistance, and systems of water distribution may be a vital reservoir for the spread of antibiotic resistance act on opportunistic pathogens (Xi *et al*., 2009). Treatment processes of drinking water cannot remove all ARGs from sources of drinking water. Thus, supply systems of drinking water may be a primary route of ARG diffusion from the environment to the host, which poses potential risks to human health (Han *et al*., 2020).

Based on the research conducted on the change of the bacterial community in drinking water during chlorination, it was found that at the level of genus, chlorination can eliminate Methylophilus, Limnobacter, Polynucleobacter, and Methylotenera, while increasing the Pseudomonas relative abundance, Acidvorax, Sphingomonas, Pletomonas, and Andibacterium in drinking water. It was also found that overall bacterial community patterns were significantly changed by chlorination. Analysis of potential hosts revealed that Pseudomonas is the main latent host of persistent ARGs. Genes of resistance to several drugs are dominant in drinking water and their relative frequency increases to a great extent after chlorination (Jia *et al*., 2015). **Figure 2** shows the different stages impact of the water treatment process on the bacteria number.

Figure 2. The effect of different stages of the process of water treatment on the bacteria number.

Antibiotic resistance

Antibiotic resistance is the occurrence of a specific feature in a microorganism that makes it not affected by antibiotic drugs. If it was previously sensitive to the mentioned drug, this resistance makes that drug no longer cause death or stop the growth of the microorganism. In recent years, antibiotics have

been widely utilized in bacterial infection treatment in animals and humans, as well as increased promoters in agriculture. The increase in antibiotic-resistant species in various environments causes problems in the optional treatment of bacterial infections. The occurrence of bacterial resistance in aquatic environments has been reported in many different studies.

Therefore, many researchers consider water environments, especially sewage, as the main recipient of intestinal bacteria, a favorable place for many bacteria to become resistant to various types of antibiotics. Because in such an environment, the transfer of resistant genes takes place well between different bacterial species due to the high food load and micro load (Le *et al.*, 2018; Manaia *et al.*, 2018).

Today, antibiotics play a vital role in livestock industries and modern agriculture, and their utilization is increasing in many developed countries. One of the most important utilization of antibiotics in recent years is to increase the growth and effectiveness of feed for healthy animals. Indiscriminate use or lack of a correct antibiotic use pattern is considered one of the main challenges in antibiotic resistance emergence (Sarmah *et al.*, 2006). The emergence of antibiotic-resistant bacteria is usual in areas where antibiotics are utilized, in addition, antibiotic-resistant bacteria are increasingly observed in environments of aquatic. The prevalent use of antibiotics in animal husbandry and hospitals indicates selective conditions

that affect bacteria. Animal husbandry causes the entry of resistant bacteria into the soil through liquid and solid manure (Aarestrup *et al.*, 1996).

In addition, several studies documented the presence of VRE (vancomycin-resistant enterococci) in the individual's stools who had neither been recently hospitalized nor received antibiotics (Sarmah *et al.*, 2006). VRE has been reported in the feces of healthy animals, animal products, and livestock in sewage and surface water. VRE can cause infections in immunocompromised and weak patients, which are hard to treat due to the high resistance of these bacteria (Bates, 1997; Harwood *et al.*, 2001; Iversen *et al.*, 2002).

Antibiotics are widely utilized as food additives to protect human and animal health or to increase the animal's growth rate. Most antibiotics are excreted unchanged in the environment. Therefore, the concern about the possible effect of antibiotic residues in the environment of aquatic has been increasing in recent years (Kouchesfahani *et al.*, 2015). Bacteria have various mechanisms to neutralize antibiotics **(Figure 3)**.
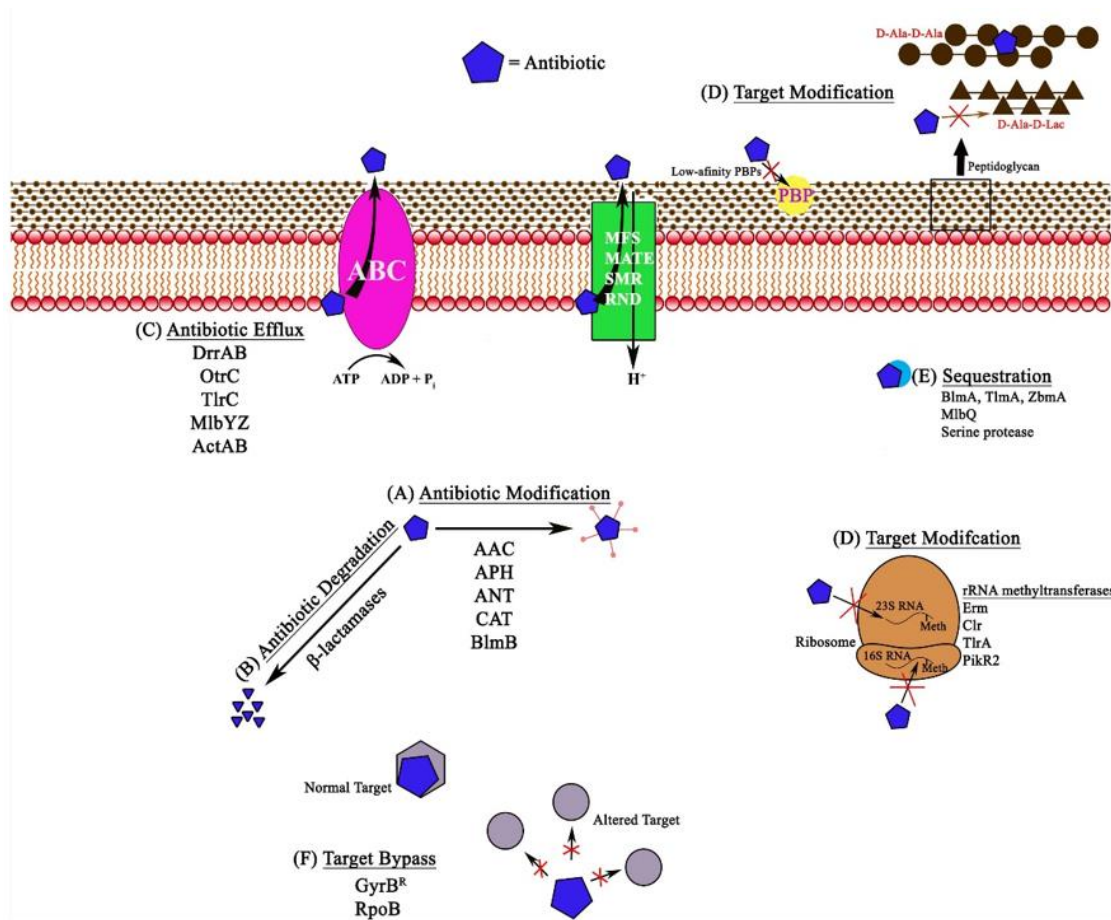

Figure 3. Antibiotic Resistance Mechanisms in Bacteria.

Genes encoding this mechanism. Defenses are located in the extrachromosomal plasmids or on bacterial chromosomes and are transferred to the next generation (vertical gene transfer). Genetic factors (such as plasmids) can also be exchanged among different bacteria (horizontal gene transfer) (Davison, 1999).

In water distribution systems, the main focus of treatment facilities is the microbial quality of drinking water. Antibiotics

used are not always completely metabolized in the body and are mostly transferred to the environment. The trace levels presence of antibiotics ARBs and ARGs in source water and wastewater can greatly affect public health and this issue is important for the industry of drinking water (Bergeron *et al.*, 2015). Bacteria antibiotic resistance indicates a global health issue that needs a better understanding of the ARB (antibiotic-

resistant bacteria) fate in aquatic environments and their spread in the supply system of water and groundwater supplies that are infected with antibiotics and antibiotic-resistant genes (ARG).

Current processes of water treatment cannot remove all antibiotics in drinking water. In addition, horizontal transfer of ARGs among microbes in the supply system of water can simplify the spread and emergence of antibiotic resistance in human health and drinking water (Bai *et al.*, 2015). Antibiotic-resistant genes as emerging environmental pollutants are a vital concern related to the development and spread of antibiotic resistance. The environment of aquatic is known as a vital reservoir of bacteria and antibiotic-resistant genes.

With the widespread utilization of antibiotics in the agricultural industry and veterinary and human medicine, ARGs have been identified in various environments such as DWTPS (drinking water treatment plants), MWTPS (municipal wastewater treatment plants), river surface water, and water from storage tanks. Evidence shows that ARBs and ARCs are transferred from source water to refilled water in drinking water systems. Since fresh water is obtained from DWTPS, the prevalence of ARGs in systems of drinking water can be a latent threat to public health (Lu *et al.*, 2018). In this regard, in recent years, research has been conducted on the antibiotic resistance of bacteria in water sources and the transfer of resistant genes to humans through drinking water **(Figure 4)**.
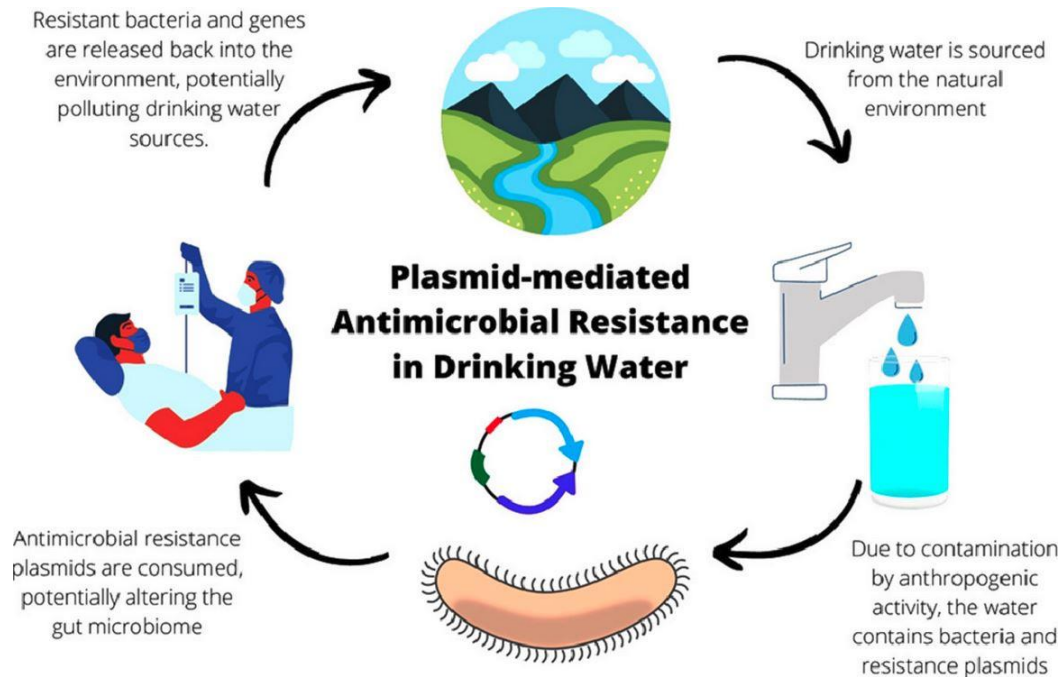

Figure 4. Plasmid-mediated antimicrobial resistance in drinking water.

Bergeron *et al*. (2015) stated that antibacterial resistance in water and freshwater sources showed that water sources have ARB. The presence of STRAN16 in urban water was also confirmed (Bergeron *et al.*, 2015). Xi *et al.*'s (2009) investigation on antibiotic resistance in drinking water and water distribution systems showed that ARB and ARCS are present in all treated water samples (Xi *et al.*, 2009).

RESULTS AND DISCUSSION

Due to the increasing population and the development of industries and the increase in the pollution of freshwater sources, access to safe and suitable water has become a serious crisis in most countries. The life-giving effect of water on development and life on the one hand and the increase in population and the growth of agricultural, domestic, and industrial uses and the lack of this vital substance in arid and semi-arid countries on the other hand have led to the optimal use of water for various purposes of drinking, health, and agriculture should cause the authorities to worry and the use of packaged water should be considered as a serious solution in

the implementation of the fair water law. Due to the increasing shortage of water, it is necessary to protect water to prevent its wastage and damage to human health and the environment. Epidemiological knowledge states that consumption of contaminated water directly (drinking) or indirectly (contact) can endanger human health and cause disease. Many disease agents that cause water pollution are microorganisms that are transmitted through human and animal waste. In addition to the mentioned cases, today the presence of antibiotic-resistant bacteria and genes, and resistance in water is important from different aspects. Their persistence and spread in nature lead to an increase in infection with these pathogens. Also, the spread of antibiotic-resistant bacteria and genes may increase the reservoir of drug-resistant genes in the environment and lead to the transfer of these genes to other pathogenic bacteria. Due to the indiscriminate use of beta-lactam antibiotics such as penicillins, cephalosporins, and carbapenems (used to treat Pseudomonas infections), *Pseudomonas aeruginosa* has become resistant to them. Recent studies have shown that there are different types of antibiotic resistance genes (ARG) in drinking water around the world (Jia *et al.*, 2015). Metallobetalactamase-

producing bacteria are mostly multi-drug resistant and cause serious infections that are hard to treat. These enzymes can hydrolyze beta-lactam antibiotics, which are mostly found in Acinetobacter and Pseudomonas bacteria. Sources of drinking water can host various ARGs and pathogenic agents due to their connection with contamination from soil, manure, and municipal and hospital wastewater. However, some bacteria can grow in water due to their resistance to disinfectants. Studies have shown that the use of chlorine to disinfect drinking water can expand antibiotic-resistant bacteria in aquatic environments **(Figure 5)**.
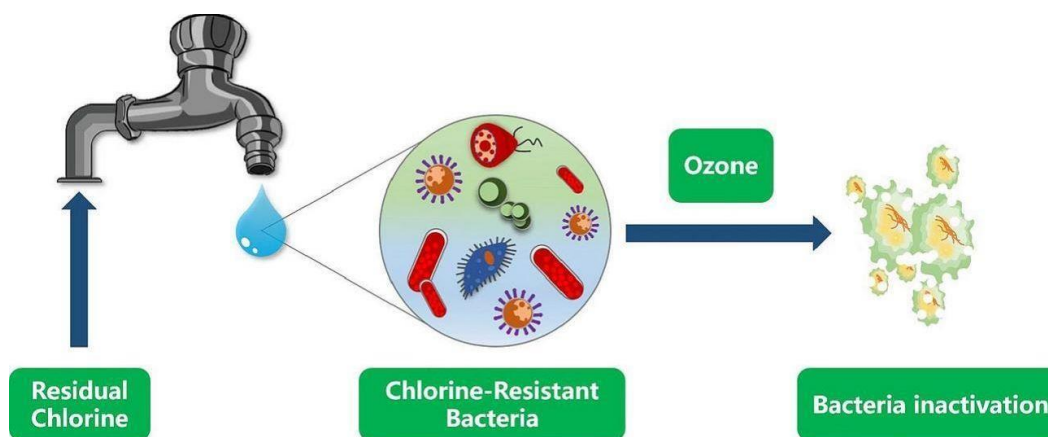

Figure 5. Chlorine-resistant bacteria in drinking water.

The existence of antibiotic-resistance genes along with several bacteria puts the health of society members at risk. In addition, antibiotic resistance has been reported in tap water and during water treatment. Water treatment may expand the antibiotic resistance of surviving bacteria, and systems of water distribution may act as a vital reservoir for antibiotic resistance spread to opportunistic pathogens (Baquero *et al.*, 2008; Mena & Gerba, 2009; Berglund *et al.*, 2023).

CONCLUSION

Considering that water (drinking and mineral) is a continuous part of the life of all people of all ages, the transmission of various pollutants in water can be a great risk to the health of different sections of society. Today, the laws necessary to control antibiotics in surface and underground water sources and drinking water are not enough, because it is assumed that their amounts in water are very low, and in the assessment of environmental risks, they did not show significant and proven effects on the environment. Therefore, obtaining more information about the frequency and amount of bacteria with antibiotic-resistant mutations seems necessary. Also, considering the dangers caused by hospital wastewater and the lack of attention to the correct disposal of such wastewater in the city, it seems that it is important to investigate how to dispose of wastewater, especially hospital wastewater. Considering the lack of sufficient studies on bacteria contaminating mineral and drinking water, and the transfer of antibiotic-resistant genes to the environment, it is necessary to investigate this issue further.

Sewage systems should be designed to consider the disinfection of bacteria present in municipal and hospital wastewater before discharging the wastewater into the aquatic ecosystem. Hence, resistance monitoring and the aquatic ecosystems' importance for the release of antibiotic resistance determinants is needed, because, in many parts of the globe, surface waters are considered endpoints for the treated/untreated effects of wastewater treatment (Devarajan *et al.*, 2017). Selecting and protecting drinking water sources is a fundamental issue in the safety of drinking water.

The results have shown that bacteria in the environment are the main cause of antibiotic resistance. The abundance of ARG is related to the opportunistic and abundant pathogens and the trend of antibiotic resistance. Therefore, protection of drinking water sources from antibiotic and biological contamination by strong policies may be practical measures to manage drinking water resources in the future. Livestock and poultry wastewater, clinical wastewater, and hospital wastewater are priority targets. Due to the high variability in antibiotic contamination in sources of drinking water, careful treatment strategies should be considered in the treatment of drinking water. Monitoring the sources of drinking water can help to determine the potential health risks of pathogens and ARGs. For the agricultural industry and government regulatory bodies to adopt effective management in this case, interdisciplinary research should be done and for this purpose, the cooperation of toxicologists, geochemists, microbiologists, organic chemists, environmental and agricultural engineers, and evaluators is needed.

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