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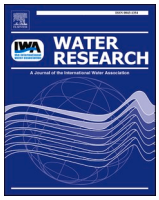

Chlorination-induced spread of antibiotic resistance genes in drinking water systems

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ABSTRACT

Chlorine, the most widely utilized disinfectant for drinking water globally, has recently been implicated in facilitating the spread of antibiotic resistance genes (ARGs), raising concerns about its underestimated environmental and ecological risks. However, given the current fragmented research focus and results, a comprehensive understanding of the potential mechanisms and influencing factors behind chlorination-promoted ARGs transmission in drinking water systems is crucial. This work is the first to systematically review the variations in abundance, transmission mechanisms, influencing factors, and mitigation strategies related to ARGs during the chlorination process. The results indicated that chlorination could induce genetic mutations and promote horizontal gene transfer through multiple pathways, including increased reactive oxygen species, enhanced membrane permeability, stimulation of the SOS response, and activation of efflux pumps. In addition, this work delves into significant discoveries regarding the factors affecting ARG transmission in drinking water, such as chlorine concentration, reaction time, disinfection byproducts, pipe materials, biofilms, and the water matrix. A series of effective strategies from water source to point-of-use were proposed aimed at mitigating ARGs transmission risks in the drinking water system. Finally, we address existing challenges and outline future research directions to overcome these bottlenecks. Overall, this review aims to advance our understanding of the role of chlorination in the dissemination of ARGs and to inspire innovative research ideas for optimizing disinfection techniques, minimizing the risks of antibiotic resistance transmission, and enhancing the safety of drinking water.

1. Introduction

Antibiotic resistance has emerged as one of the top ten global public health crises. Statistics show that antibiotic-resistant bacteria (ARB) are responsible for over 25,000 deaths annually in Europe and affect more than 2.8 million people in the United States, resulting in over 35,000 fatalities each year (Zheng et al., 2022). Unfortunately, both ARB and antibiotic resistance genes (ARGs) have been identified in drinking water, which considered a critical vector for the transmission of antibiotic resistance from the environment to humans (Lubick, 2011). The occurrence of ARGs in drinking water systems poses significant health risks, including heightened virulence and pathogenicity, which can lead to disease outbreaks and higher rates of sickness, hospitalizations, and mortality (Liang et al., 2022). Moreover, research have shown that beta-lactam resistance genes are notably more prevalent in tap water compared to treated water, emphasizing the imperative to curb their dissemination (Xu et al., 2016).

Disinfection acts as the most effective barrier for the physicochemical eradication of microorganisms in drinking water systems. It is an essential step in the water treatment process, eliminating waterborne pathogens within drinking water distribution systems (DWDS) and maintaining water quality. The application of disinfectants and the consistent management of residual disinfectant levels throughout the DWDS prevent the resurgence and spread of pathogenic microorganisms (Zheng et al., 2024). Currently, chlorination remains the method of choice in the drinking water treatment sector due to its affordability,

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operational simplicity, and high efficacy. Chlorine exerts its disinfecting effects primarily through the activity of hypochlorite and hypochlorous ions, which irreversibly oxidize proteins, leading to enzyme deactivation and cell death (Terhalle et al., 2018). Chlorination is crucial for maintaining drinking water safety by preventing microbial contamination, including ARB and ARGs, and has also proven effective in controlling and managing COVID-19 (Choi et al., 2021a; Choi et al., 2021b). Theoretically, disinfection processes should help reduce, or even eliminate ARB and associated ARGs. However, instead of complete inhibition or removal, disinfection processes, along with residual disinfectants and their by-products, may alter cellular activities, disrupt microbial interactions and genetic exchanges, ultimately compromising treatment efficiency (Li et al., 2019).

Recent studies have increasingly documented the unintended impacts of various disinfection methods on the drinking water microbiome. Notably, an increase in both intracellular ARGs (iARGs) and extracellular ARGs (eARGs) was observed following chlorination in a full-scale drinking water treatment plant (Liu et al., 2018). Although a specific concentration of residual chlorine is maintained in the distribution pipelines to guarantee the microbiological safety of drinking water, several ARGs, pathogenic bacteria and ARB belonging to genera such as *Acinetobacter, Burkholderia*, and *Pseudomonas,* have still been detected, raising significant concerns due to their high resistance to chlorine (Delafont et al., 2014; Han et al., 2020). Those ARGs and ARB that escape chlorination and remain in tap water, can undergo horizontal gene transfer into gut microorganisms, thereby enabling gut bacteria to acquire antibiotic resistance (McInnes et al., 2020; Wang et al., 2024a). Most gut bacteria maintain a symbiotic or commensal relationship with the human host, playing critical roles in digestion, immune regulation, and nutrient absorption (McInnes et al., 2020). However, the acquisition of ARGs can disrupt this balance, potentially converting commensal bacteria into opportunistic pathogens and posing a potential risk to public health, particularly in immunocompromised individuals or during gut dysbiosis. Despite the critical importance of accurately assessing the public health risks posed by antibiotic resistance in drinking water, there remains a lack of comprehensive understanding regarding the mechanisms and pathways that facilitate the transfer of ARGs during chlorination in water treatment and distribution networks. Gaining insight into the sources of ARGs, the underlying mechanisms of their spread, and the influence of both anthropogenic and environmental factors on their emergence in aquatic environments could help guide the development of innovative strategies for monitoring, controlling, and mitigating the proliferation and persistence of ARGs in chlorinated drinking water systems.

Therefore, the objectives of this study were to: (1) systematically summarize the effects and potential mechanisms of chlorination on the ARGs spread, (2) analyze the key factors influencing the ARGs proliferation during the chlorination process, (3) propose feasible control strategies to reduce ARGs transmission in DWDS, and (4) explore future research directions for controlling antibiotic resistance in DWDS.

2. Overview of the impacts of chlorination on antibiotic resistance transmission

2.1. Variation in diversity and abundance of ARGs

Following chlorination, the absolute abundance of both eARGs and iARGs decreased, with eARGs showing higher removal efficiency compared to iARGs (Li et al., 2023a). This indicates that chlorination effectively inactivated ARB and degraded ARGs, particularly in the extracellular environment, where eARGs are more vulnerable to oxidative damage (Li et al., 2023a). Despite the absolute ARGs concentrations decreased after chlorination, the relative abundance of both eARGs and iARGs increased significantly (Jia et al., 2015; Li et al., 2023a). The relative abundance of eARGs and iARGs was calculated as the ratio of their absolute abundance to the abundance of extracellular and intracellular 16S rRNA genes, respectively (Li et al., 2023a). This standardization accounts for microbial biomass, providing a more meaningful comparison across samples. Specifically, several eARGs, including those associated with chloramphenicol and β-lactam resistance, remained high-level after chlorination, with certain eARGs, such as those for erythromycin, tetracycline, chloramphenicol, and β-lactam resistance genes, exhibiting a notable increase in the relative abundance (Li et al., 2023a). Similarly, iARGs relatively to bacitracin, polymyxin, and fosfomycin also increased markedly (Jia et al., 2015). The increase in relative abundance of ARGs, despite reductions in their absolute abundance, indicates that treatment processes like chlorination may enrich resistant bacterial subpopulations, highlighting the selective pressures that favor ARG persistence (Xu et al., 2016).

Following chlorination with free chlorine at concentrations of 2–4 mg/L, the relative abundance of ARGs increased, while the diversity of ARGs exhibited contrasting trends between particle-associated and free-living fractions (Jia et al., 2024). Specifically, the diversity of ARGs in the free-living portion increased, primarily due to the absence of a protective particle barrier, which rendered microbes more susceptible to direct exposure to free chlorine-induced oxidative stress (Jia et al., 2024). This exposure triggered specific adaptive responses, including the overexpression of efflux pumps and activation of stress-response mechanisms, enhancing microbial survival while facilitating the release and acquisition of ARGs (Jia et al., 2024). Conversely, in particle-associated microbes, both the subtype number and Shannon index of ARGs decreased, possibly because the particles provided a protective barrier and nutrients that mitigated the stress from free chlorine (Jia et al., 2024). Regarding specific ARG types, in the free-living fraction, chlorination with free chlorine notably enriched multidrug resistance genes, followed by beta-lactam and tetracycline resistance genes (Jia et al., 2024). These changes were accompanied by increased prevalence of resistance mechanisms such as efflux pumps, enzymatic inactivation, and antibiotic target alteration, with efflux pumps emerging as the dominant mechanism after chlorination with free chlorine (Jia et al., 2024). In contrast, in the particle-associated fraction, chlorination with free chlorine led to a reduction in genes conferring resistance to multidrug, bacitracin, chloramphenicol, and aminoglycosides (Jia et al., 2024).

2.2. Variation in the abundance of mobile genetic elements

Similar to the trends observed in ARGs, the abundance of various mobile genetic elements (MGEs), including integrons, insertion sequences, and plasmids increased significantly after chlorination with free chlorine (Wang et al., 2024b; Zhang et al., 2019a). This increase was particularly notable in the free-living portion of microbial communities, where it was substantially higher than in the particle-associated portion, following chlorination with free chlorine at a concentration of 2–4 mg/L (Jia et al., 2024). Further analysis revealed that transposons and insertion sequences are the primary components of MGEs in the free-living portion after chlorination with free chlorine at a concentration of 2–4 mg/L (Wang et al., 2024b). This increase could be attributed to the enhanced activity of enzymes like transposase and integrase, which facilitate the mobility of these genetic elements (Jia et al., 2024). Moreover, in the free-living portion, a stronger correlation was observed between the abundance of MGEs and various ARGs, such as *bacA, catB*, and *tolC*, in comparison with the particle-associated portion (Wang et al., 2024b). This observation underscores the critical role of the free-living portion in facilitating higher horizontal gene transfer of ARGs. The elevated abundance of MGEs in the free-living portion might enhance the mobility of ARGs, potentially promoting the transmission of resistance genes from non-pathogenic to pathogenic bacteria and thereby increasing health risk (Wang et al., 2024b). Besides, free chlorine could facilitate the plasmid transfer from donor cells to acceptor cells in a concentration-dependent manner (Li and Zhang, 2023). Apart from plasmid conjugation, other study also reported that free chlorine at

practically relevant concentrations (as low as 0.5 mg/L) facilitated the transformation of plasmid-encoded ARGs in the recipient *A. baylyi* (Zhang et al., 2021).

2.3. Enrichment of antibiotic resistance genes host bacteria

Closed correlations between target ARGs and bacterial community composition were observed in the Mantel test, suggesting that bacterial phylogeny mediates ARG host types and plays a key role in antibiotic resistance dissemination in water supply networks treated with free chlorine (Jia et al., 2020; Ke et al., 2023a). Considering that shifts in bacterial communities are known to drive alterations in the resistome, the co-occurrence patterns between ARGs and bacterial taxa, evidenced by similar abundance trends, emphasize specific microbial hosts as critical contributors to ARG proliferation (Jia et al., 2020; Su et al., 2018). These findings highlight the importance of identifying key bacterial taxa associated with ARGs to inform mitigation strategies. By targeting high-risk bacterial hosts through optimized disinfection techniques or combining physical and chemical treatments, it is possible to reduce the spread of ARGs. Furthermore, the integration of bacterial phylogeny into water treatment monitoring systems can enhance early detection of ARG hotspots, providing a proactive approach to managing antibiotic resistance in water supply networks.

Although lower Shannon index and Chao index were observed in the microbial community after chlorination with free chlorine, indicating that the residual chlorine obviously decreased the diversity and richness of bacterial community in drinking water (Ke et al., 2024; Shi et al., 2013). However, the relative abundance of various chlorine-tolerant bacteria, such as *Pseudomonas, Sphingomonas, Polaromonas*, and *Acinetobacter*, was observed to increase notably (Hwang et al., 2012; Jia et al., 2015). These bacteria were found to carry genes encoding resistance-nodulation-cell division superfamily (RND) transport systems, ATP-binding cassette (ABC) efflux pump genes, and major facilitator superfamily (MFS) efflux systems, indicating their identity as ARGs hosts under treatment with free chlorine (Jia et al., 2015; Jia et al., 2019).

Interestingly, most of the above enriched bacteria were found to belong to *Proteobacteria* and *Actinobacteria*, indicating the dominance status of two phyla in drinking water treated with free chlorine (Schmeisser et al., 2003; Shi et al., 2013). A metagenomic analysis of biofilm found that *Proteobacteria* were recognized as connectors of the microbial ecological networks in the drinking water system treated with free chlorine (Ke et al., 2023b; Ke et al., 2024; Ke et al., 2023c). The above phenomenon may be attributed to the fact that *Proteobacteria* possess an additional outer lipid membrane, specifically the outer membrane characteristic of Gram-negative bacteria. This outer membrane, composed of lipopolysaccharides, phospholipids, and proteins, serves as a robust barrier against external stressors. The unique structure of the outer membrane effectively limits the penetration of chlorinated disinfectants into bacterial cells, thereby enhancing their survival in treated water systemswhich can effectively hinder the penetration of chlorinated disinfectants into the bacterial cells (Varghese and Balachandran, 2021; Wang et al., 2023). *Actinobacteria* form exospores in nutrient-limited environments induced by disinfectants, thereby protecting their genetic material from adverse external conditions (Beskrovnaya et al., 2021). Besides, the number of nodes, edges, and average degrees were observed to decrease after chlorination, indicating that the disinfection decreased the microbial community network complexity and community stability (Ke et al., 2024). Moreover, it is notable that the chlorination increased the positive interaction proportions of community networks, suggesting that microbes tended to collaborate in resisting environmental stress, which may facilitate the ARGs spread (Ke et al., 2024).

3. Potential mechanisms of chlorination promote the spread of ARGs

Fig. 1 illustrates the potential mechanisms by which chlorination promotes the spread of ARGs. Firstly, chlorination can induce genetic mutations, creating favorable conditions for ARG dissemination. Secondly, it can activate drug efflux pumps by up-regulating functional genes, thereby enhancing the bacterial ability to expel antibiotics. Thirdly, chlorination leads to increased cell membrane permeability, resulting in improved transformation efficiency and facilitating horizontal gene transfer. Lastly, chlorination enhances conjugation through an enhanced SOS response, accelerating the spread of ARGs among bacterial populations. These mechanisms collectively contribute to the increased dissemination of ARGs during chlorination processes.

3.1. Genetic mutations

Genetic mutation serves as the primary mechanism by which bacteria acquire antibiotic resistance, involving the development of resistance through base substitutions or frameshift mutations in specific genes (Lv et al., 2014; Walsh, 2000). Both chlorination with free chlorine at concentrations of 0.34–0.63 mg/L and certain disinfection byproducts (DBPs), such as iodoacetic acid, bromoacetic acid, and dibromoacetic acid, have been shown to significantly increase the mutation rate (Li et al., 2016; Zeng et al., 2015). These processes primarily induce oxidative stress responses, leading to the generation of reactive oxygen species (ROS), which cause DNA damage through oxidative alterations to nucleotide bases or crosslink formation (Feng et al., 2021; Wang et al., 2024c). Elevated ROS levels can cause DNA damage through oxidative alterations to nucleotide bases or by inducing the formation of crosslinks, thereby activating the error-prone SOS response mechanism in bacteria (Feng et al., 2021). This response facilitates an increase in chromosomal mutations, including base substitutions and frameshifts, which are critical pathways through which bacteria acquire antibiotic resistance (Feng et al., 2021).

Additionally, chlorination with free chlorine at a concentration of 0.3 mg/L could up-regulate the *rpoS* gene, a stress-response sigma factor, which subsequently increases the expression of small RNA *SdsR* (Li et al., 2016; Zhang et al., 2017). The elevated levels of *SdsR* bind to and inhibit the translation of *MutS* mRNA, a message crucial for the production of *MutS* protein that corrects DNA replication errors (Gutierrez et al., 2013). This significant reduction in *MutS* protein levels impairs the cell's ability to repair replication-associated errors, leading to an elevated mutation frequency and promoting the emergence of antibiotic-resistant phenotypes (Gutierrez et al., 2013; Zhang et al., 2017). Similarly, DBPs alter the expression of genes involved in DNA damage repair (e.g., *recA* and *lexA*) and oxidative stress response (e.g., *soxR, soxS, marR*, and *sodC*), contributing to increased mutation rates via similar pathways (Li et al., 2016). Prolonged exposure to sub-MIC levels of DBPs can also cause mutations in chromosomal replication-related genes, such as *proS* (prolyl-tRNA synthetase) and *gyrA* (DNA gyrase), leading to resistance against antibiotics like amoxicillin and ciprofloxacin (Li et al., 2016). Notably, both chlorination and DBPs increase the frequency of mutations that accumulate gradually through small-step changes. These mutations, often associated with minimal fitness costs, facilitate the development and spread of antibiotic resistance within bacterial populations (Feng et al., 2021).

3.2. Activating the drug efflux pump by up-regulating the functional genes

Chlorination with free chlorine at a concentration of 2–4 mg/L can enhance antibiotic resistance in bacteria by promoting the expression of drug efflux pumps, which become the dominant resistance mechanism in the free-living portion after chlorination (Jia et al., 2024). Structurally, an efflux pump is composed of four main components, including an outer membrane protein, a periplasmic adaptor protein, an inner

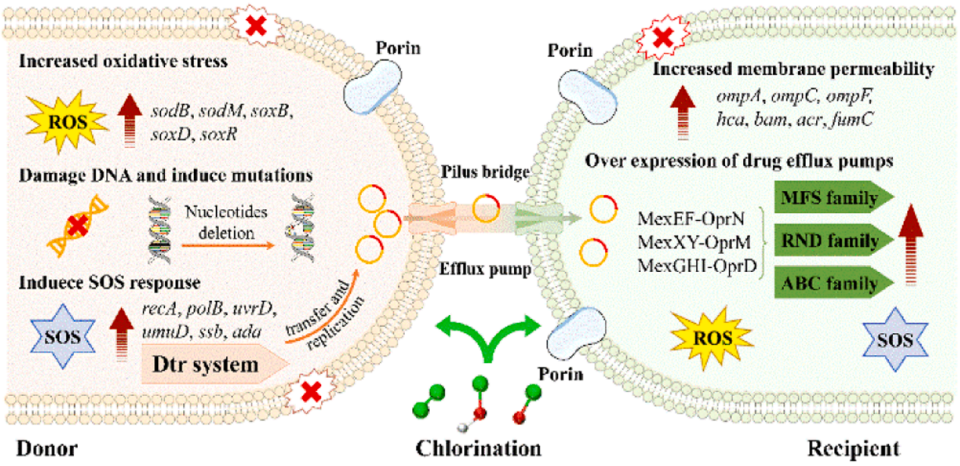

Fig. 1. The molecular mechanisms of chlorination promote the spread of ARGs.

membrane transporter, and a transmembrane channel (Adefisoye and Olaniran, 2022). Based on secondary structure, energy source, amino acid homology, and size, active efflux systems are categorized into five distinct families. These families include the ABC, MFS, RND, small multidrug resistance family, and multi antimicrobial extrusion protein family (Adefisoye and Olaniran, 2022; Rahman et al., 2017). As illustrated in Fig. 2, interactions between the outer and inner membranes and the periplasmic protein maintain the duct in a closed configuration. Activation occurs when a substance, such as an antibiotic, binds to the inner membrane protein, initiating a cascade of biochemical reactions that ultimately open the channel and expel the drug molecules. The energy required for this process is derived from different mechanisms depending on the efflux pump family. SMR, MATE, MFS, and RND families use the electrochemical gradient across the bacterial membrane, while the ABC family relies on ATP hydrolysis (Rahman et al., 2017).

Previous study indicates that following exposure to 4 mg/L sodium hypochlorite, the expression of several key efflux pump genes, especially those associated with the RND family, such as *mexE, mexF,* and *oprN* (Hou et al., 2019). These pumps are capable of expelling a broad spectrum of antibiotics, such as tetracyclines, fluoroquinolones, macrolides, novobiocin, sulfonamides, and methicillin (Lamarche and Déziel, 2011; Lister et al., 2009). For example, overexpression of the *MexEF-OprN* efflux pump is associated with enhanced resistance to chloramphenicol,

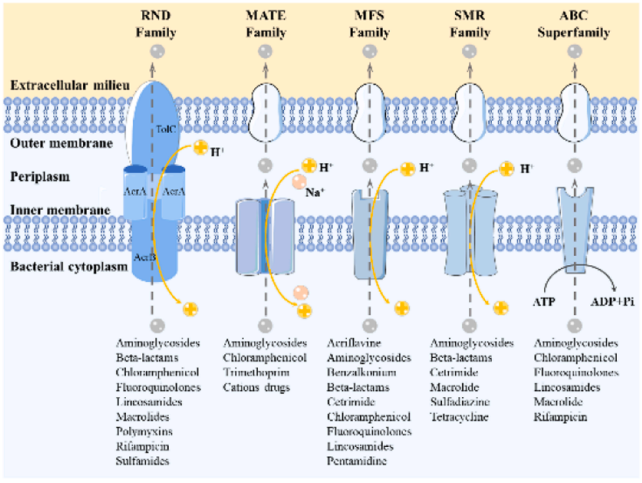

Fig. 2. Schematic diagram of the multidrug efflux pump systems Reprinted with permission from ref Adefisoye and Olaniran (2022) Copyright 2022 Elsevier.

fluoroquinolones, and triclosan (Hou et al., 2019; Ni et al., 2020a). Additionally, ABC family pumps, which were also upregulated following exposure to 4 mg/L sodium hypochlorite, utilize the free energy from ATP hydrolysis to export a broad spectrum of substrates, enhancing resistance to antibiotics (Hou et al., 2019). These pumps not only extrude traditional antimicrobial agents but also non-antibiotic substances like heavy metals, biocides, and organic solvents, showing broad-spectrum cross-resistance (Gnanadhas et al., 2013).

3.3. *Improved transformation induced by increased cell membrane permeability*

The bacterial outer membrane serves as a critical barrier to horizontal gene transfer (Luo et al., 2023). However, studies have indicated that subinhibitory concentrations of free chlorine (0.1–1 mg/L) increase membrane permeability by disrupting the membrane structure, thereby facilitating the transfer of plasmid DNA from donor to recipient through conjugation mechanisms (Zhang et al., 2017). Specifically, free chlorine oxidizes amino acids within the phospholipid bilayer and peptidoglycan, altering the structural and functional integrity of these components and thus increasing the permeability (Ramseier et al., 2011; Xu et al., 2018). Transmission electron micrographs have shown that chlorination with sodium hypochlorite at a CT value of 20 mg active Cl·min/L causes holes and wrinkles on the surfaces of conjugative cells, in contrast to the smooth and intact surfaces of non-chlorinated cells, indicating the disruptive effects of chlorine on bacterial surface structures (Guo et al., 2015).

Outer membrane proteins (OMPs), such as OmpA, OmpC, and OmpF, are integral components of Gram-negative bacterial membranes and play crucial roles in regulating exchanges between bacteria and their environment (Wang et al., 2020). These proteins are encoded by the *ompA, ompC*, and *ompF* genes, respectively, and their expression influences key bacterial functions (Zhu et al., 2023a). OmpA, a 36 kDa monomeric protein, serves as a structural component of the outer membrane and contributes to bacterial adherence, invasion, and immune response activation (Zhou et al., 2024). In contrast, OmpC (40 kDa) and OmpF (42 kDa) are proteins that form water channels, aiding in the regulation of osmotic pressure and membrane permeability under environmental stress (Zhou et al., 2024). OmpA and OmpC, are reported to facilitate the passive diffusion of molecules smaller than 500–600 Da, contributing to membrane permeability and enabling processes like plasmid transfer, which is critical for horizontal gene transfer (Zhang et al., 2017; Zhu et al., 2023a). Free chlorine exposure has been demonstrated to enhance the expression of these OMPs genes, further increasing membrane permeability and facilitating the transfer of ARGs (Zhang et al., 2017).

This enhanced permeability allows greater leakage of cellular contents, including plasmids, thus increasing transformation frequencies (Bai et al., 2024; Jin et al., 2020), and also enables chlorine-resistant bacteria such as *Escherichia coli* and *Salmonella Aberdeen* to acquire transferable plasmids from deceased donors or environmental sources. For instance, chlorination with sodium hypochlorite at low doses of 5–40 mg active Cl·min/L significantly increased the conjugative transfer frequency by 2- to 5-fold (Guo et al., 2015), leading to a substantially higher proportion of iARG in post-disinfection water compared to pre-disinfection water (Jin et al., 2020). Therefore, the augmented membrane permeability leads to elevated transformation frequencies of ARGs during chlorination (Zhai et al., 2022).

3.4. Enhanced conjugation promoted by improved SOS response

ROS include a variety of chemical compounds produced by the incomplete reduction of oxygen, including superoxide anion ($O_2{\cdot}^-$), hydrogen peroxide (H_2O_2), hydroxyl radical (·OH), and singlet oxygen ($^1O_2$), formed through one-electron, two-electron, and three-electron reductions, respectively (Feng et al., 2021; Zhang et al., 2022a). Free chlorine can stimulate significant ROS production during bacterial inactivation (Guo et al., 2023), which in turn triggers the SOS response, a bacterial global emergency repair system activated by DNA damage, to restore genetic stability (Crane et al., 2021; Feng et al., 2021). This SOS response has been shown to enhance the horizontal transfer of ARGs, including integrative conjugative elements among Vibrio cholerae populations (Beaber et al., 2004). Previous research has demonstrated that exposure to free chlorine (0.3 mg/L) up-regulates the expression of genes associated with the SOS response, such as *yebG, recX, polB, uvrD*, and *ada* (Zhang et al., 2017). Enhanced expression of *umuC* and *umuD* genes is known to increase the frequency of ARGs conjugation (Cao et al., 2024). Additionally, the SOS response regulates the expression of the *intI1* gene, which encodes an integrase that exhibits increased activity during DNA damage-induced SOS responses (Shi et al., 2022). This upregulation of integrase enhances the activity of class 1 integrons, allowing them to integrate new resistance genes more effectively and facilitating the spread of ARGs across bacterial communities (Shi et al., 2022).

4. Affecting factors of chlorination on the ARGs proliferation

4.1. Chlorine concentration and reaction time

The inactivation of ARGs in drinking water is significantly influenced by both the dosage of chlorine used and the duration of exposure. The efficacy of chlorine in water treatment is typically measured by the CT value, which represents the product of the disinfectant concentration and the contact time with water. Although high CT values can fragment isolated plasmid DNA and reduce bacterial counts, including those encoding for 16S rRNA, they do not necessarily reduce the transfer or survival of ARGs. While high-dose chlorination generally demonstrates higher removal rates of ARGs compared to low-dose treatments, certain ARGs types like bacitracin- and polymyxin-ARGs become enriched, particularly in total microbial populations (Ma et al., 2022). This indicates that while chlorine effectively reduces overall microbial load, it may also exert selective pressure on bacteria that possess or can acquire resistance traits, thereby enhancing the spread of specific ARGs. The duration of chlorine exposure also critically affects outcomes. As shown in Fig. 3, longer exposure times at effective dosages can significantly reduce bacterial populations, including those harboring ARGs. However, prolonged exposure might select for chlorine-resistant bacteria or biofilms capable of harboring and spreading ARGs even in the presence of disinfectants (Ke et al., 2024).

At sub-inhibitory concentrations, particularly at distribution system endpoints, chlorine can inadvertently enhance horizontal gene transfer of ARGs. These lower concentrations stress bacteria without killing them, resulting in increased membrane permeability and elevated intracellular ROS production (Wang et al., 2024c). This physiological alteration facilitates plasmid transfer and also affects the SOS response, promoting the acquisition and dissemination of ARGs through mechanisms such as transformation and conjugation (Cai et al., 2021). For example, previous studies have demonstrated that a sub-inhibitory dose of chlorine (5–40 mg active Cl·min/L) significantly increased the conjugative transfer frequency by 2- to 5-fold (Guo et al., 2015), which is attributed to enhanced membrane permeability and the stimulation of conjugative pili on donor cells. Furthermore, this treatment upregulates the mRNA expression levels of type IV secretion system (T4SS) proteins, including *vir4D, vir5B*, and *vir10B* (Wang et al., 2020). Thus, sub-inhibitory chlorination is prone to influence the conjugation of ARGs by stimulating the generation of intracellular ROS, which subsequently impacts the SOS response, membrane permeability, transcription of genes associated with conjugation, and the development of pili (Zhang et al., 2015).

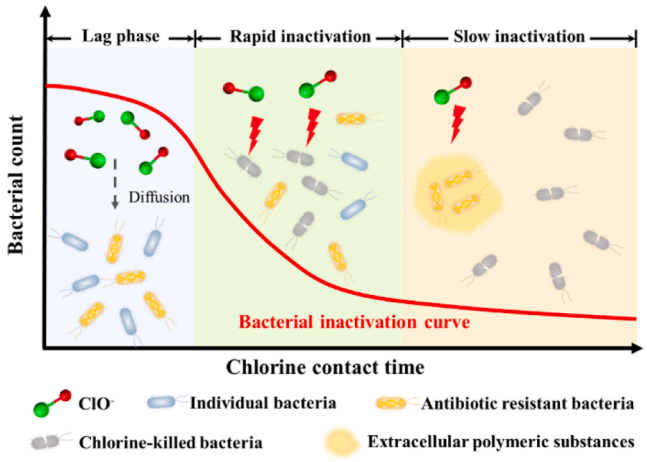

Fig. 3. Schematic diagram of the bacterial inactivation process.

4.2. Disinfection byproducts

During disinfection, chlorine-based disinfectants react with organic compounds in drinking water through oxidation, electrophilic addition, and substitution reactions, leading to the formation of various disinfection byproducts (DBPs) such as trihalomethanes, haloacetic acids, mutagen X, and nitrosamines (Fig. 4) (Ding et al., 2024). Although the concentrations of DBPs in chlorinated drinking water systems are typically maintained below the minimum inhibitory concentration (sub-MIC), prolonged low-level exposure can exert selective pressure on microbial communities, favoring the survival and proliferation of resistant strains while gradually eliminating susceptible ones. This selective pressure enhances the risk of spreading ARGs and ARB, thereby amplifying the overall threat of antibiotic resistance. Notably, higher concentrations of DBPs correlate with increased antibiotic resistance (Lv et al., 2014).

Certain DBPs, including iodoacetic acid, bromoacetic acid, and dibromoacetic acid, can further enhance mutation rates by modulating oxidative stress and SOS response pathways, thereby promoting antibiotic resistance. Additionally, despite the infrequent occurrence of horizontal gene transfer and co-selection due to a lack of ARGs, heavy metals, and disinfectants in drinking water, the mutagenic activity induced by DBPs could be the primary mechanism for developing antibiotic resistance (Feng et al., 2021; Lv et al., 2014).. Long-term exposure to sub-MIC levels of DBPs will likely induce a high frequency of mutations, favoring the accumulation of a broader range of multiple small-step mutations (Li et al., 2016). Moreover, sub-MIC levels of DBPs can also increase cell membrane permeability and regulate the

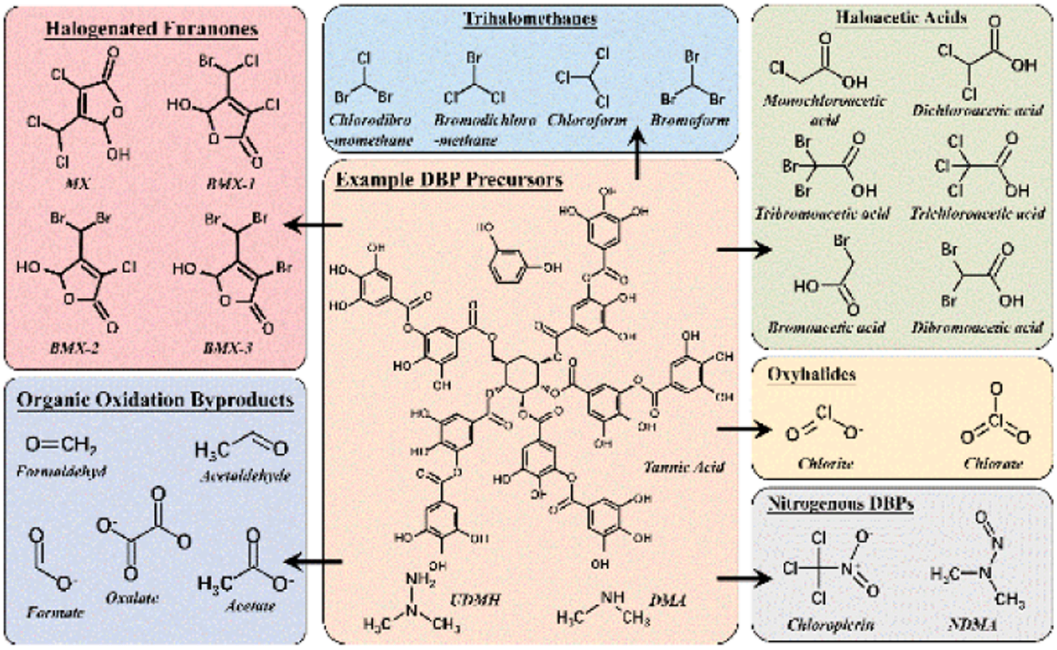

Fig. 4. Typical DBPs produced from chlorination process during drinking water treatment process, Reprinted with permission from Mayer and Ryan (2019), Copyright 2019, Springer.

expression of genes related to conjugative transfer, thereby accelerating the horizontal transfer of ARGs (Li and Gu, 2019). To date, over 1000 types of DBPs have been identified, existing as mixtures in drinking water (Renau et al., 1999). The total concentration of these DBPs can reach sub-μg/L or low- to mid-μg/L levels, and a growing body of evidence highlights their mutagenic properties (Lv et al., 2014; Richardson, 2003). Therefore, it is hypothesized that the synergistic effects of these DBP mixtures at environmentally relevant low concentrations may have a more significant impact on the selection of antibiotic resistance compared to individual DBP entities.

4.3. Pipe materials

Once treated drinking water enters the distribution network, it can

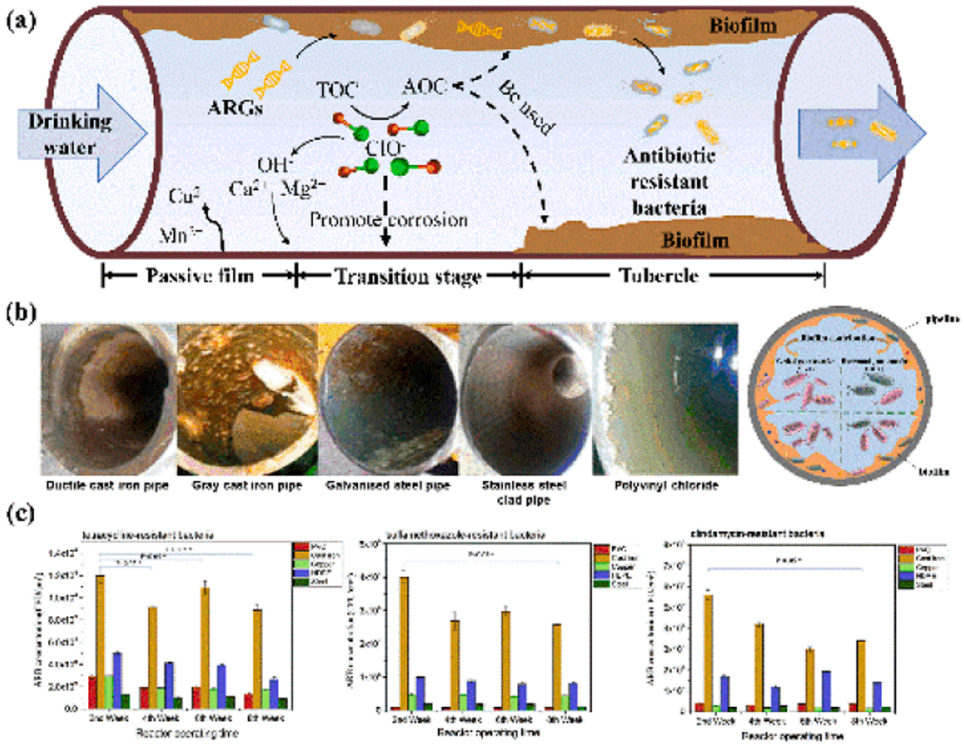

Fig. 5. (a) Schematic diagram of the effects of metal pipes and corrosion products on ARGs in DWDS. (b) Biofilm growth on different pipe materials. Reprinted with permission from Ren et al. (2015), Copyright 2015, Springer. (c) Variation of ARB concentrations in biofilm with different pipe materials. Reprinted with permission from Zhang et al. (2018), Copyright 2018, Elsevier.

remain in the pipes for hours to days before reaching consumers. During this time, the material of the pipes plays a crucial role in influencing the spread of ARGs in chlorinated water systems (Kimbell et al., 2020; Liao et al., 2022). Common pipe materials such as ductile iron, polyethylene, polyvinyl chloride, stainless steel, and cast iron, significantly impact the migration and transformation of ARGs (Barton et al., 2019; Zhang et al., 2022b).

Metal pipes, especially those made of cast iron, tend to consume more chlorine due to corrosion (Fig. 5(a) and (b)). This reduces residual disinfectant levels, permitting increased microbial growth and ARGs proliferation (Yin et al., 2023). The metal ions released and the corrosion products formed, even at sub-inhibitory concentrations, can co-select for ARGs and metal resistance genes, promoting horizontal gene transfer and resistance through mechanisms such as increased cell membrane permeability and the SOS response (Kimbell et al., 2020). For example, copper ions (Cu^{2+}) and copper oxide (CuO) nanoparticles can enhance the conjugative transfer of ARGs by increasing cell membrane permeability and altering the expression of genes related to conjugation, such as *korA, korB*, and *trbA* (Folvarska et al., 2024). Copper corrosion products also increase the abundance of ARGs like *sul1, qacEΔ1*, and *intI1*, potentially enhancing bacterial conjugation and stress response (Folvarska et al., 2024).

Iron pipes, though also subject to corrosion, have a lesser impact on the propagation of ARGs compared to copper and lead (Kimbell et al., 2020; Zhang et al., 2023a). However, as displayed in Fig. 5(c), iron corrosion products still contribute to biofilm formation, which can harbor resistant bacteria and provide a habitat for ARGs (Yin et al., 2023). Cast iron pipes are particularly prone to biofilm development and microbial growth, thereby increasing the risk of ARGs transmission and associated microbial risks (Yin et al., 2023). In contrast, stainless steel pipes exhibit reduced biofilm formation and lower microbial risks, making them less conducive to the spread of ARGs (Yin et al., 2023).

Plastic pipes, such as polyethylene and polyvinyl chloride, could prevent the release of metal ions and minimize the release of organic nutrients due to their non-metallic nature. The smoother surfaces of these pipes also lead to less biofilm formation, reducing opportunities for ARGs dissemination (Zhu et al., 2023b). Additionally, plastic pipes maintain higher residual levels of disinfectants like chlorine, which can suppress the growth of resistant bacteria, although it may select for chlorine-resistant strains. However, it should be noted that the chlorination and environmental conditions (e.g., freeze-thaw cycles) could accelerate microplastics generation and the chemicals leaching from plastic pipes, which not only increase the abundance of pathogenic bacteria but also enhance the risk of ARGs dissemination (Yang et al., 2024).

4.4. Biofilms formation

Biofilms in DWDS serve as reservoirs and facilitators for the spread of ARGs, harboring various potential ARGs carriers such as *Hirschia, Terrimonas*, and *Bacillus*, which reside within the biofilm matrix (Li et al., 2023b). Biofilms are composed of microbial communities and extracellular polymeric substances like polysaccharides, proteins, and DNA, constituting over 95% of the total biomass in the DWDS (Li et al., 2023b; Zhang et al., 2024).

As shown in Fig. 6, the extracellular polymeric substances matrix provides nutrients for the bacteria, and also acts as a protective barrier, reducing the penetration of disinfectants such as chlorine, thereby safeguarding the bacteria within the biofilm from environmental stressors (Siedlecka et al., 2021; Zhang et al., 2023b). This protective mechanism decreases bacterial sensitivity to antibiotics and disinfectants, enhancing resistance. As a result, bacteria in biofilms exhibit greater resistance to external stresses such as chlorine disinfectants compared to planktonic bacteria (Zhang et al., 2023c).

Moreover, biofilms facilitate the horizontal gene transfer of ARGs by promoting cell-to-cell communication through quorum sensing (Zhang et al., 2024; Zhu et al., 2020). The dense cell population within biofilms significantly increases the efficiency of plasmid transfer - up to 700 times greater than that of free-living cells in the aqueous phase (Angles et al., 1993; Li et al., 2023b). This close proximity and high cell density enable the spread of ARGs among resistant bacteria and potentially to susceptible microbes and opportunistic pathogens (Zhang et al., 2024). It has been observed that the communities and ARG-carrying bacteria in the inner layers of biofilms in systems treated with sodium hypochlorite at a free chlorine concentration of 2 mg/L are more diverse than those on the surface, indicating higher risks of ARGs spread (Li et al., 2023b).

During chlorination, biofilm detachment is a significant pathway for ARGs dissemination (Liu et al., 2016; Zhang et al., 2018). External shear forces or disinfectant exposure can weaken the biofilm structure, leading to the release of resistant bacteria and ARGs into the water (Zhang et al., 2018). This release elevates the concentration of ARB in the water, potentially facilitating the further spread of ARGs (Zhang et al., 2018).

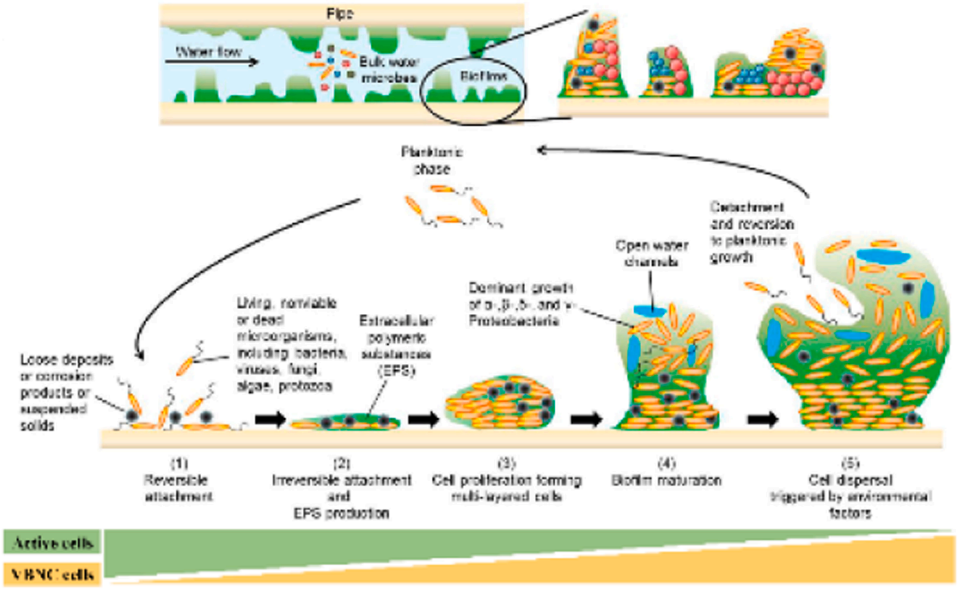

Fig. 6. Biofilm life cycle in DWDS. Reprinted with permission from Liu et al. (2016), Copyright 2016, American Chemical Society.

Detached biofilm fragments and eARGs can be taken up by surviving bacteria in the water through natural transformation, forming new resistant populations (Liang et al., 2022; Zhang et al., 2023a).

4.5. Other micropollutants

Micropollutants in water, such as plastic additives (e.g., antioxidants, flame retardants, plasticizers), pharmaceutical residues (like the fluoroquinolone antibiotic ciprofloxacin), and other chemicals that leach into water from various sources, significantly impact the spread of ARGs during chlorination processes (Yang et al., 2024). Specifically, dimethyl phthalate and perfluorooctanoic acid could induce biofilms formation ubiquitous in distribution pipes, potentially leading to secondary pollution of drinking water (Wu et al., 2023; Yin et al., 2023). These micropollutants can increase the generation of ROS in bacterial cells (Chen et al., 2022; Yin et al., 2023). The induced ROS could damage cellular components and increase cell membrane permeability, facilitating horizontal gene transfer of ARGs by allowing genetic material, including plasmids and ARGs, to move more easily between cells. The presence of bromide and iodide ions can further exacerbate this effect by forming additional halogenated compounds during chlorination, intensifying oxidative stress and promoting ARGs transfer (Zhai et al., 2022). Additionally, micropollutants can upregulate genes involved in oxidative stress responses (e.g., *rpoS* gene) and membrane proteins (e.g., *ompC* gene), both of which are critical for bacterial survival under stress and for the transfer of genetic material (Zhai et al., 2022). This upregulation can be triggered by the interaction of micropollutants with chlorine, further enhancing the transfer of ARGs. Besides, ciprofloxacin residues in water can react with chlorine to form products that promote the growth of bacterial genera such as *Helicobacter* and *Sphingomonas* in DWDSs, while also increasing the expression of efflux pump and quinolone resistance genes (Wang et al., 2017a).

4.6. Water matrix parameters

Water matrix parameters, including temperature, pH and Ca^{2+}, have been reported to obviously influenced the abundance of eARGs (Li et al., 2023a). Specifically, DWDS, typically located underground, still experience temperature variations, especially in regions with multiple seasons. The temperature range in DWDS bulk water in temperate regions typically varies from 15 to 20 °C during summer and 4 to 10 °C throughout winter in temperate regions (Ahmad et al., 2020). In summer, the higher temperature promotes bacterial regrowth, biofilms formation and ARGs transformation in tap water (Hao et al., 2019; Zhang et al., 2024). The higher temperature was positively correlated with the prevalence of aminoglycoside ARGs and sulfonamide ARGs (Ke et al., 2023a), while the extracellular *ermB, blaTEM* and $\sum$*β-lactam* exhibited significant negative correlations with temperature [89]. Previous studies have demonstrated that higher temperatures significantly increase conjugative transfer frequencies, primarily due to elevated ATP levels and enhanced electron transport chain activity, which provide the energy required for DNA replication, transfer, and cell bridging (Zhao et al., 2025). Additionally, elevated temperatures induce ROS accumulation, triggering the SOS response that enhances bacterial resilience and facilitates horizontal gene transfer of ARGs (Zhao et al., 2025). Concurrently, the upregulation of conjugative transfer-related genes (e.g., *traJ, fimA*), efflux pump genes, and quorum sensing-related genes under higher temperatures further amplifies the risk of ARG transfer (Zhao et al., 2025). While residual chlorine inhibits bacterial activity and reduces membrane permeability to suppress ARG dissemination, these effects are markedly diminished at elevated temperatures. In contrast, during the winter months, the temperature is reported to exert minimal influence on biofilm stability (Rilstone et al., 2021). However, it is notable that at lower temperatures around 4 °C, SOS responses are triggered, selectively enhancing the survival of resistant organisms, while bacteria begin producing cold shock proteins (Miller et al., 2014; Rilstone et al., 2021).

In addition, pH levels, within the typical drinking water range of 6.5–8.5, play a critical role in determining the fate of ARGs during chlorination by influencing the chemical forms and reactivity of chlorine. At pH 6.5–7.5, hypochlorous acid (HOCl), with its strong oxidizing potential, predominates, enhancing the efficiency of ARG removal (Chen et al., 2023a). In contrast, at pH 7.5–8.5, hypochlorite ions (OCl^-) become more prevalent, leading to reduced oxidative efficiency by scavenging reactive radicals such as hydroxyl radicals, thereby limiting ARG degradation (Chen et al., 2023a). These pH-dependent variations also affect the transformation frequency of plasmid vectors like RP4, which peaks at neutral pH (~7) but declines under more acidic or alkaline conditions (Jin et al., 2020), likely due to the impact of pH on plasmid stability and bacterial membrane permeability. Additionally, at pH 6.5–7.5, chloride ions promote the formation of dichloride radicals ($Cl_2\cdot^-$), which exhibit selective reactivity toward specific target genes (Zhang et al., 2019b). However, these radicals become less prevalent under alkaline conditions, further reducing ARG removal efficiency. Different ARGs showed varying responses to pH changes, impacting their stability and mobility within the water system (Jin et al., 2020). The extracellular *tetC, qnrA, cat* and $\sum$*Tetracycline* resistance genes were negatively associated with pH, while the extracellular *sul1, qnrS, cmr,* $\sum$*Sulfonamide,* $\sum$*Chloramphenicol* resistance genes were positively correlated with pH (Li et al., 2023a). Ca^{2+} is one of the most common competence-inducing agents that can increase the transformation frequency of released plasmid *RP4* from killed ARB into viable chlorine-injured bacteria (Jin et al., 2020). It is widely believed to induce the formation of pore-like structures on the cell surface, allowing intact double-stranded DNA to pass through (Hasegawa et al., 2018). These findings highlight the complexity of environmental factors influencing ARG dynamics, as they result from the combined effects of various elements, such as temperature, pH, and calcium ion concentration. Therefore, managing ARGs requires a comprehensive consideration of these interactions.

5. Prospects for reducing ARGs transformation in the chlorinated water systems

5.1. Strengthening water source protection

A fundamental step in reducing ARGs spread is the protection of source water. Water utilities should establish water source reservoirs that are separately and strictly controlled. Despite the previously great efforts, ARGs contamination in groundwater and rivers has been widely affected due to large-scale wastewater discharge and insufficient regulation (Wang et al., 2024a). Compared to river water intake, water from reservoirs has been shown to contain lower levels of ARGs (Wang et al., 2024a). As shown in Fig. 7, drinking water reservoirs, typically located along local rivers and natural lakes, are specialized water supply reservoirs with stringent environmental protections, including barbed wire installation, limitations on local livestock farming and discouragement of non-resident settlements. Moreover, implementing source control measures in hotspot areas of the catchment, such as biofilters, can significantly reduce the transport of ARGs to drinking water reservoirs (Boehm et al., 2020; Huang et al., 2023). Biofilters are particularly effective in reducing organic and microbial loads in reservoirs, lowering natural organic matter (NOM) levels and the associated risk of DBP formation during disinfection. NOM acts as a precursor for DBPs. By decreasing NOM concentrations, the need for high chlorine doses is minimized, thus reducing DBP formation and the selective pressure for ARGs proliferation.

5.2. Optimizing drinking water disinfection procedures

Water treatment facilities are tasked with optimizing their disinfection processes by precisely controlling the dosage and contact time of

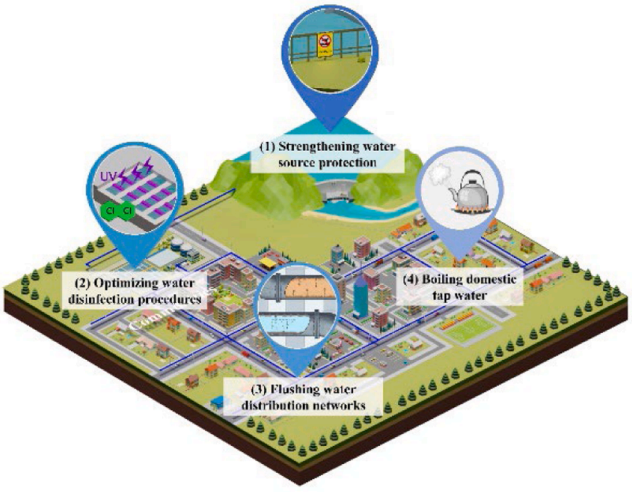

Fig. 7. Proposed strategies to mitigate chlorination-induced ARGs in drinking water systems.

chlorine to strike a balance between maximizing bactericidal efficacy and minimizing the selection pressure for ARGs. Continuous monitoring and adjustment of chlorine levels are essential to ensure effective microbial inactivation without the overuse of chemicals. Implementing real-time monitoring systems provides the necessary data to dynamically fine-tune these parameters, optimizing chlorine dosing and contact times to ensure efficient disinfection with minimal DBP production. By controlling DBPs, the potential for ARG transformation is also reduced. Moreover, adopting a multi-stage disinfection strategy can further reduce the risk of ARGs proliferation. Initial pre-treatment methods, such as enhanced coagulation and ozonation, effectively remove large organic molecules from the water, preparing it for subsequent chlorination (Liu et al., 2012; Ni et al., 2020b). This step is critical as it reduces the formation of DBPs when chlorine reacts with organic matter, thereby lowering the potential for ARGs dissemination (Badawy et al., 2012; Wang et al., 2017b).

However, relying solely on chlorination has limitations. It has been found to increase pollution from both eARGs and iARGs, and facilitate the horizontal gene transfer of ARGs across different bacterial genera. To address these challenges, a more effective strategy for ARG removal may involve combined methods, such as sequential UV/chlorine disinfection, which offers a promising supplement to traditional chlorination practices. UV disinfection directly damages bacterial nucleic acids, preventing the replication of genetic information, thus addressing the limitations of chlorine alone (Zhang et al., 2019b). Moreover, ultraviolet irradiation significantly reduces the transformation potential of free eARGs, effectively addressing the limitations of chlorination (Yuan et al., 2022). Integrating UV and chlorine disinfection allows for the use of lower doses of chlorine, achieving desired disinfection levels more efficiently (Chen et al., 2023b). This integrated approach reduces operational costs while minimizing the formation of DBPs, making it a safer and more economical option for water treatment (Sun et al., 2023). By adopting these strategies, water treatment facilities can enhance the safety and quality of drinking water while reducing the risk of antibiotic resistance emergence.

5.3. Mitigating transmission risks in water distribution networks

Biofilms in water distribution networks pose significant risks for secondary contamination and the spread of ARB in drinking water. To mitigate these risks, it is crucial to select appropriate pipe materials that hinder biofilm development and to consider upgrading aging infrastructure with antibacterial or innovative materials that reduce bacterial adhesion and mitigate chlorine decay (Ling et al., 2018). Additionally, managing flow-rate variations and implementing routine management practices such as periodic physical flushing, pigging to remove sediments, and air-water scouring, are essential strategies. Moreover, precise flushing of smaller-diameter pipes in distal locations of water systems, which harbor higher cell counts, rather than flushing the entire building, can prevent water stagnation and minimize waste (Ling et al., 2018). Such targeted interventions are crucial for preventing biofilm formation and ensuring the effectiveness of disinfection measures throughout the network (Liu et al., 2016; Oliveira et al., 2024). Ensuring drinking water safety at the endpoints of supply systems, such as in buildings, is crucial to minimize the spread of ARGs. Regular disinfection of secondary water supply facilities, like rooftop water tanks, is highly recommended. UV and ozone disinfection are highly effective for secondary water supply systems, offering significant advantages such as short contact times, absence of residual chlorine, and avoidance of harmful DBPs. These methods ensure effective microbial inactivation while simultaneously reducing DBP formation and ARG dissemination risks, enhancing the overall safety and quality of distributed water.

5.4. Point-of-use ARGs removal by boiling water

At the user end, point-of-use disinfection at the household level may be warranted to mitigate potential health risks associated with ARGs. Among various disinfection methods, boiling water has shown a broader spectrum and more efficient bactericidal capabilities and ARGs removal than chlorination and pasteurization. Although the heating process below 80 °C may lead to the release of iARGs, temperatures above 90 °C effectively eliminate both intracellular and extracellular ARGs (Wan et al., 2022). The underlying mechanism involves high temperatures causing DNA denaturation, which affects DNA biological activity and reduces the risk of horizontal gene transfer of ARGs. These findings underscore that boiling water provides greater safety in addressing ARGs as a novel contaminant compared to chlorination. While boiling water requires higher energy consumption, advancements in energy technology could potentially offset this drawback. Given its effective disinfection performance and the ease of obtaining the necessary hardware, boiling is particularly suitable for promotion in developing countries and economically disadvantaged areas (Sanganyado and Gwenzi, 2019).

6. Conclusions and perspectives

Following chlorination treatment, the drinking water system frequently experiences an increase in the relative abundances of ARGs, as well as a rise in mobile genetic elements and the resistant bacteria. As highlighted in this reviewed, chlorination may enhance cell membrane permeability, activate efflux pumps, raise ROS levels, and trigger the SOS response, contributing to elevated rates of gene mutation and horizontal gene transfer, thereby promoting the spread of resistance genes. Several critical factors influencing the effects of chlorination on ARGs dissemination are summarized, including chlorine concentration and reaction time, the presence of disinfection byproducts, pipe materials, biofilm formation, and water matrix. To effectively mitigate the spread of ARGs, a range of strategies have been proposed, such as strengthening water source protection, optimizing disinfection procedures, reducing transmission risks within water distribution networks, and implementing point-of-use ARGs removal by boiling water. Nevertheless, the rapid detection methods for resistance genes are still lack, and several knowledge gaps remain in terms of the complex interactions between chlorine and ARGs under different chlorination conditions, as well as the uncertain public health impacts related to chlorine-promoted ARGs dissemination.

To better safeguard public health, several challenging yet promising topics warrant further exploration, as outlined below:

(1) While techniques such as qPCR and metagenomic sequencing have made significant progress in detecting ARGs, they remain limited by their complexity, time-consuming processes, and the need for specialized laboratory facilities, hindering their application for real-time monitoring in urban water systems (van Belkum et al., 2020), (Xue et al., 2024). Future research should prioritize the development of real-time and in-situ detection methods. Simplifying current techniques and reducing detection time, as well as establishing standardized protocols capable of simultaneously detecting multiple ARGs and contaminants, will enhance the accuracy and efficiency of water quality monitoring.

(2) Current research on chlorination and ARGs often focuses on immediate disinfection outcomes, but it fails to capture the complex and variable environmental conditions that influence ARG spread in real-world water systems (Choi et al., 2021b; Sahulka et al., 2021). Traditional experimental approaches struggle to replicate these dynamic conditions, leading to a gap between lab results and field applicability. Future research should focus on integrating machine learning, which could integrate various factors like water pH, temperature, and contaminant levels, to develop predictive models to optimize chlorination strategies, helping to reduce ARG propagation and improve water treatment effectiveness.

(3) Although numerous studies have investigated the impact of chlorination on ARG dissemination, there is still a lack of direct epidemiological data linking these processes to human health risks (Sanganyado and Gwenzi, 2019). To address this gap, future efforts should focus on long-term monitoring of water quality and associated health outcomes, particularly with regard to the effects of chlorination over time. Developing priority lists for high-risk ARGs and bacterial species involved in horizontal gene transfer, such as *E. coli, Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*, will be essential for establishing risk assessment standards and safeguarding public health against antibiotic resistance in drinking water systems.

CRediT authorship contribution statement

Weixin Zhao: Conceptualization, Methodology, Writing – original draft, Writing – review & editing. **Yanan Hou:** Writing – review & editing. **Liangliang Wei:** Writing – review & editing. **Wei Wei:** Writing – review & editing. **Kefeng Zhang:** Writing – review & editing. **Haoran Duan:** Writing – review & editing, Investigation. **Bing-Jie Ni:** Supervision, Writing – review & editing, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

Adefisoye, M.A., Olaniran, A.O., 2022. Does chlorination promote antimicrobial resistance in waterborne pathogens? Mechanistic insight into co-resistance and its implication for public health. Antibiotics 11 (5), 564.

Ahmad, J.I., Liu, G., van der Wielen, P.W.J.J., Medema, G., Peter Van Der Hoek, J., 2020. Effects of cold recovery technology on the microbial drinking water quality in unchlorinated distribution systems. Environ. Res. 183, 109175.

Angles, M.L., Marshall, K.C., Goodman, A.E., 1993. Plasmid transfer between marine bacteria in the aqueous phase and biofilms in reactor microcosms. Appl. Environ. Microbiol. 59 (3), 843–850.

Badawy, M.I., Gad-Allah, T.A., Ali, M.E.M., Yoon, Y., 2012. Minimization of the formation of disinfection by-products. Chemosphere 89 (3), 235–240.

Bai, C., Cai, Y., Sun, T., Li, G., Wang, W., Wong, P.K., An, T., 2024. Mechanism of antibiotic resistance spread during sub-lethal ozonation of antibiotic-resistant bacteria with different resistance targets. Water Res. 259, 121837.

Barton, N.A., Farewell, T.S., Hallett, S.H., Acland, T.F., 2019. Improving pipe failure predictions: factors affecting pipe failure in drinking water networks. Water Res. 164, 114926.

Beaber, J.W., Hochhut, B., Waldor, M.K., 2004. SOS response promotes horizontal dissemination of antibiotic resistance genes. Nature 427 (6969), 72–74.

Beskrovnaya, P., Fakih, D., Morneau, I., Hashimi, A., Guadarrama, B.D., Xing, S., Nanci, A., Huan, T., Tocheva, E.I., 2021. No endospore formation confirmed in members of the phylum proteobacteria. Appl. Environ. Microbiol. 87 (5), e2312–e2320.

Boehm, A.B., Bell, C.D., Fitzgerald, N.J.M., Gallo, E., Higgins, C.P., Hogue, T.S., Luthy, R. G., Portmann, A.C., Ulrich, B.A., Wolfand, J.M., 2020. Biochar-augmented biofilters to improve pollutant removal from stormwater—can they improve receiving water quality? Environ. Sci. 6 (6), 1520–1537.

Cai, Y., Sun, T., Li, G., An, T., 2021. Traditional and emerging water disinfection technologies challenging the control of antibiotic-resistant bacteria and antibiotic resistance genes. ACS ES&T Eng. 1 (7), 1046–1064.

Cao, J., Xue, B., Yang, S., Yang, X., Zhang, X., Qiu, Z., Shen, Z., Wang, J., 2024. Chlorite and bromate alter the conjugative transfer of antibiotic resistance genes: co-regulation of oxidative stress and energy supply. J. Hazard. Mater. 471, 134257.

Chen, C., Fang, Y., Cui, X., Zhou, D., 2022. Effects of trace PFOA on microbial community and metabolisms: microbial selectivity, regulations and risks. Water Res. 226, 119273.

Chen, T., Cevallos, D., Hurtado, A., Mackey, E., Wang, C., Hofmann, R., 2023a. Predicting chlorine demand by peracetic acid in drinking water treatment. Water Res. 243, 120361.

Chen, X., Chen, Z., Ngo, H.H., Mao, Y., Cao, K., Shi, Q., Lu, Y., Hu, H., 2023b. Comparison of inactivation characteristics between Gram-positive and Gram-negative bacteria in water by synergistic UV and chlorine disinfection. Environ. Pollut. 333, 122007.

Choi, H., Chatterjee, P., Lichtfouse, E., Martel, J.A., Hwang, M., Jinadatha, C., Sharma, V. K., 2021a. Classical and alternative disinfection strategies to control the COVID-19 virus in healthcare facilities: a review. Environ. Chem. Lett. 19 (3), 1945–1951.

Choi, Y., He, H., Dodd, M.C., Lee, Y., 2021b. Degradation kinetics of antibiotic resistance gene mecA of methicillin-resistant *Staphylococcus aureus* (MRSA) during water disinfection with chlorine, ozone, and ultraviolet light. Environ. Sci. Technol. 55 (4), 2541–2552.

Crane, J.K., Alvarado, C.L., Sutton, M.D., 2021. Role of the SOS response in the generation of antibiotic resistance in vivo. Antimicrob. Agents. Chemother. 65 (7), 10–1128.

Delafont, V., Mougari, F., Cambau, E., Joyeux, M., Bouchon, D., Héchard, Y., Moulin, L., 2014. First evidence of amoebae–mycobacteria association in drinking water network. Environ. Sci. Technol. 48 (20), 11872–11882.

Ding, Y., Sun, Q., Lin, Y., Ping, Q., Peng, N., Wang, L., Li, Y., 2024. Application of artificial intelligence in (waste) water disinfection: emphasizing the regulation of disinfection by-products formation and residues prediction. Water Res. 253, 121267.

Feng, G., Huang, H., Chen, Y., 2021. Effects of emerging pollutants on the occurrence and transfer of antibiotic resistance genes: a review. J. Hazard. Mater. 420, 126602.

Folvarska, V., Thomson, S.M., Lu, Z., Adelgren, M., Schmidt, A., Newton, R.J., Wang, Y., McNamara, P.J., 2024. The effects of lead, copper, and iron corrosion products on antibiotic resistant bacteria and antibiotic resistance genes. Environ. Sci. 3 (6), 808–818.

Gnanadhas, D.P., Marathe, S.A., Chakravortty, D., 2013. Biocides—resistance, cross-resistance mechanisms and assessment. Expert Opin. Investig. Drugs 22 (2), 191–206.

Guo, J., Wang, B., Qiu, X., Ren, S., Wang, Y., 2023. Improvement of chlorination and sterilization of pathogenic bacteria by natural products. J. Hazard. Mater. Adv. 10, 100318.

Guo, M., Yuan, Q., Yang, J., 2015. Distinguishing effects of ultraviolet exposure and chlorination on the horizontal transfer of antibiotic resistance genes in municipal wastewater. Environ. Sci. Technol. 49 (9), 5771–5778.

Gutierrez, A., Laureti, L., Crussard, S., Abida, H., Rodríguez-Rojas, A., Blázquez, J., Baharoglu, Z., Mazel, D., Darfeuille, F., Vogel, J., Matic, I., 2013. β-lactam antibiotics promote bacterial mutagenesis via an RpoS-mediated reduction in replication fidelity. Nat. Commun. 4 (1), 1610.

Han, Z., An, W., Yang, M., Zhang, Y., 2020. Assessing the impact of source water on tap water bacterial communities in 46 drinking water supply systems in China. Water Res. 172, 115469.

Hao, H., Shi, D., Yang, D., Yang, Z., Qiu, Z., Liu, W., Shen, Z., Yin, J., Wang, H., Li, J., Wang, H., Jin, M., 2019. Profiling of intracellular and extracellular antibiotic resistance genes in tap water. J. Hazard. Mater. 365, 340–345.

Hasegawa, H., Suzuki, E., Maeda, S., 2018. Horizontal plasmid transfer by transformation in *Escherichia coli*: environmental factors and possible mechanisms. Front. Microbiol. 9, 2365.

Hou, A., Yang, D., Miao, J., Shi, D., Yin, J., Yang, Z., Shen, Z., Wang, H., Qiu, Z., Liu, W., Li, J., Jin, M., 2019. Chlorine injury enhances antibiotic resistance in *Pseudomonas aeruginosa* through over expression of drug efflux pumps. Water Res. 156, 366–371.

Huang, Y., Zhang, J., Ren, Z., Xiang, W., Sifat, I., Zhang, W., Zhu, J., Li, B., 2023. Next generation decentralized water systems: a water-energy-infrastructure-human nexus (WEIHN) approach. Environ. Sci. 9 (10), 2446–2471.

Hwang, C., Ling, F., Andersen, G.L., LeChevallier, M.W., Liu, W., 2012. Microbial community dynamics of an urban drinking water distribution system subjected to

phases of chloramination and chlorination treatments. Appl. Environ. Microbiol. 78 (22), 7856–7865.
Jia, S., Bian, K., Shi, P., Ye, L., Liu, C., 2020. Metagenomic profiling of antibiotic resistance genes and their associations with bacterial community during multiple disinfection regimes in a full-scale drinking water treatment plant. Water Res. 176, 115721.
Jia, S., Shi, P., Hu, Q., Li, B., Zhang, T., Zhang, X., 2015. Bacterial community shift drives antibiotic resistance promotion during drinking water chlorination. Environ. Sci. Technol. 49 (20), 12271–12279.
Jia, S., Wang, S., Zhuang, Y., Gao, L., Zhang, X., Ye, L., Zhang, X., Shi, P., 2024. Free-living lifestyle preferences drive the antibiotic resistance promotion during drinking water chlorination. Water Res. 249, 120922.
Jia, S., Wu, J., Ye, L., Zhao, F., Li, T., Zhang, X., 2019. Metagenomic assembly provides a deep insight into the antibiotic resistome alteration induced by drinking water chlorination and its correlations with bacterial host changes. J. Hazard. Mater. 379, 120841.
Jin, M., Liu, L., Wang, D., Yang, D., Liu, W., Yin, J., Yang, Z., Wang, H., Qiu, Z., Shen, Z., Shi, D., Li, H., Guo, J., Li, J., 2020. Chlorine disinfection promotes the exchange of antibiotic resistance genes across bacterial genera by natural transformation. ISME J. 14 (7), 1847–1856.
Ke, Y., Sun, W., Jing, Z., Zhu, Y., Zhao, Z., Xie, S., 2023a. Antibiotic resistome alteration along a full-scale drinking water supply system deciphered by metagenome assembly: regulated by seasonality, mobile gene elements and antibiotic resistant gene hosts. Sci. Total Environ. 862, 160887.
Ke, Y., Sun, W., Chen, X., Zhu, Y., Guo, X., Yan, W., Xie, S., 2023b. Seasonality determines the variations of biofilm microbiome and antibiotic resistome in a pilot-scale chlorinated drinking water distribution system deciphered by metagenome assembly. Environ. Sci. Technol. 57 (31), 11430–11441.
Ke, Y., Sun, W., Jing, Z., Zhao, Z., Xie, S., 2023c. Seasonal variations of microbial community and antibiotic resistome in a suburb drinking water distribution system in a northern Chinese city. J. Environ. Sci. 127, 714–725.
Ke, Y., Sun, W., Chen, Z., Zhu, Y., Chen, X., Yan, S., Li, Y., Xie, S., 2024. Effects of disinfectant type and dosage on biofilm's activity, viability, microbiome and antibiotic resistome in bench-scale drinking water distribution systems. Water Res. 249, 120958.
Kimbell, L.K., Wang, Y., McNamara, P.J., 2020. The impact of metal pipe materials, corrosion products, and corrosion inhibitors on antibiotic resistance in drinking water distribution systems. Appl. Microbiol. Biotechnol. 104 (18), 7673–7688.
Lamarche, M.G., Déziel, E., 2011. MexEF-OprN efflux pump exports the *Pseudomonas* quinolone signal (PQS) precursor HHQ (4-hydroxy-2-heptylquinoline). PLoS One 6 (9), e24310.
Li, D., Gu, A.Z., 2019. Antimicrobial resistance: a new threat from disinfection byproducts and disinfection of drinking water? Curr. Opin. Environ. Sci. Health 7, 83–91.
Li, D., Zeng, S., He, M., Gu, A.Z., 2016. Water disinfection byproducts induce antibiotic resistance-role of environmental pollutants in resistance phenomena. Environ. Sci. Technol. 50 (6), 3193–3201.
Li, L., Zhang, T., 2023. Plasmid-mediated antibiotic resistance gene transfer under environmental stresses: insights from laboratory-based studies. Sci. Total Environ. 887, 163870.
Li, R.A., McDonald, J.A., Sathasivan, A., Khan, S.J., 2019. Disinfectant residual stability leading to disinfectant decay and by-product formation in drinking water distribution systems: a systematic review. Water Res. 153, 335–348.
Li, S., Niu, Z., Wang, M., Zhang, Y., 2023a. The occurrence and variations of extracellular antibiotic resistance genes in drinking water supply system: a potential risk to our health. J. Clean. Prod. 402, 136714.
Li, S., Niu, Z., Zhang, Y., 2023b. The prevalence of extra- and intra- cellular antibiotic resistance genes and the relationship with bacterial community in different layers of biofilm in the simulated drinking water pipelines. J. Water Process. Eng. 53, 103780.
Liang, Y., Li, H., Chen, Z., Yang, Y., Shi, D., Chen, T., Yang, D., Yin, J., Zhou, S., Cheng, C., Shao, Y., Li, J., Jin, M., 2022. Spatial behavior and source tracking of extracellular antibiotic resistance genes in a chlorinated drinking water distribution system. J. Hazard. Mater. 425, 127942.
Liao, P., Zhang, T., Fang, L., Jiang, R., Wu, G., 2022. Chlorine decay and disinfection by-products transformation under booster chlorination conditions: a pilot-scale study. Sci. Total Environ. 851, 158115.
Ling, F., Whitaker, R., LeChevallier, M.W., Liu, W., 2018. Drinking water microbiome assembly induced by water stagnation. ISME J. 12 (6), 1520–1531.
Lister, P.D., Wolter, D.J., Hanson, N.D., 2009. Antibacterial-resistant *Pseudomonas aeruginosa*: clinical impact and complex regulation of chromosomally encoded resistance mechanisms. Clin. Microbiol. Rev. 22 (4), 582–610.
Liu, H., Liu, R., Tian, C., Jiang, H., Liu, X., Zhang, R., Qu, J., 2012. Removal of natural organic matter for controlling disinfection by-products formation by enhanced coagulation: a case study. Sep. Purif. Technol. 84, 41–45.
Liu, S., Gunawan, C., Barraud, N., Rice, S.A., Harry, E.J., Amal, R., 2016. Understanding, monitoring, and controlling biofilm growth in drinking water distribution systems. Environ. Sci. Technol. 50 (17), 8954–8976.
Liu, S., Qu, H., Yang, D., Hu, H., Liu, W., Qiu, Z., Hou, A., Guo, J., Li, J., Shen, Z., Jin, M., 2018. Chlorine disinfection increases both intracellular and extracellular antibiotic resistance genes in a full-scale wastewater treatment plant. Water Res. 136, 131–136.
Lubick, N., 2011. Antibiotic resistance shows up in India's drinking water. Nature, 218. https://doi.org/10.1038/news.2011.218.
Luo, T., Dai, X., Chen, Z., Wu, L., Wei, W., Xu, Q., Ni, B., 2023. Different microplastics distinctively enriched the antibiotic resistance genes in anaerobic sludge digestion through shifting specific hosts and promoting horizontal gene flow. Water Res. 228, 119356.
Lv, L., Jiang, T., Zhang, S., Yu, X., 2014. Exposure to mutagenic disinfection byproducts leads to increase of antibiotic resistance in *Pseudomonas aeruginosa*. Environ. Sci. Technol. 48 (14), 8188–8195.
Ma, L., Yang, H., Guan, L., Liu, X., Zhang, T., 2022. Risks of antibiotic resistance genes and antimicrobial resistance under chlorination disinfection with public health concerns. Environ. Int. 158, 106978.
Mayer, B.K., Ryan, D.R., 2019. Applications of Advanced Oxidation Processes (AOPs) in Drinking Water Treatment. Springer International Publishing, Cham, pp. 345–386.
McInnes, R.S., McCallum, G.E., Lamberte, L.E., van Schaik, W., 2020. Horizontal transfer of antibiotic resistance genes in the human gut microbiome. Curr. Opin. Microbiol. 53, 35–43.
Miller, J.H., Novak, J.T., Knocke, W.R., Pruden, A., 2014. Elevation of antibiotic resistance genes at cold temperatures: implications for winter storage of sludge and biosolids. Lett. Appl. Microbiol. 59 (6), 587–593.
Ni, B., Yan, X., Dai, X., Liu, Z., Wei, W., Wu, S., Xu, Q., Sun, J., 2020a. Ferrate effectively removes antibiotic resistance genes from wastewater through combined effect of microbial DNA damage and coagulation. Water Res. 185, 116273.
Ni, B., Zeng, S., Wei, W., Dai, X., Sun, J., 2020b. Impact of roxithromycin on waste activated sludge anaerobic digestion: methane production, carbon transformation and antibiotic resistance genes. Sci. Total Environ. 703, 134899.
Oliveira, I.M., Gomes, I.B., Simões, L.C., Simões, M., 2024. A review of research advances on disinfection strategies for biofilm control in drinking water distribution systems. Water Res. 253, 121273.
Rahman, T., Yarnall, B., Doyle, D.A., 2017. Efflux drug transporters at the forefront of antimicrobial resistance. Eur. Biophys. J. 46 (7), 647–653.
Ramseier, M.K., von Gunten, U., Freihofer, P., Hammes, F., 2011. Kinetics of membrane damage to high (HNA) and low (LNA) nucleic acid bacterial clusters in drinking water by ozone, chlorine, chlorine dioxide, monochloramine, ferrate(VI), and permanganate. Water Res. 45 (3), 1490–1500.
Ren, H., Wang, W., Liu, Y., Liu, S., Lou, L., Cheng, D., He, X., Zhou, X., Qiu, S., Fu, L., Liu, J., Hu, B., 2015. Pyrosequencing analysis of bacterial communities in biofilms from different pipe materials in a city drinking water distribution system of East China. Appl. Microbiol. Biotechnol. 99 (24), 10713–10724.
Renau, T.E., Léger, R., Flamme, E.M., Sangalang, J., She, M.W., Yen, R., Gannon, C.L., Griffith, D., Chamberland, S., Lomovskaya, O., Hecker, S.J., Lee, V.J., Ohta, T., Nakayama, K., 1999. Inhibitors of efflux pumps in *Pseudomonas aeruginosa* potentiate the activity of the fluoroquinolone antibacterial levofloxacin. J. Med. Chem. 42 (24), 4928–4931.
Richardson, S.D., 2003. Disinfection by-products and other emerging contaminants in drinking water. Trac Trends Anal. Chem. 22 (10), 666–684.
Rilstone, V., Vignale, L., Craddock, J., Cushing, A., Filion, Y., Champagne, P., 2021. The role of antibiotics and heavy metals on the development, promotion, and dissemination of antimicrobial resistance in drinking water biofilms. Chemosphere 282, 131048.
Sahulka, S.Q., Bhattarai, B., Bhattacharjee, A.S., Tanner, W., Mahar, R.B., Goel, R., 2021. Differences in chlorine and peracetic acid disinfection kinetics of *Enterococcus faecalis* and *Escherichia fergusonii* and their susceptible strains based on gene expressions and genomics. Water Res. 203, 117480.
Sanganyado, E., Gwenzi, W., 2019. Antibiotic resistance in drinking water systems: occurrence, removal, and human health risks. Sci. Total Environ. 669, 785–797.
Schmeisser, C., Stöckigt, C., Raasch, C., Wingender, J., Timmis, K.N., Wenderoth, D.F., Flemming, H.C., Liesegang, H., Schmitz, R.A., Jaeger, K.E., Streit, W.R., 2003. Metagenome survey of biofilms in drinking-water networks. Appl. Environ. Microbiol. 69 (12), 7298–7309.
Shi, P., Jia, S., Zhang, X., Zhang, T., Cheng, S., Li, A., 2013. Metagenomic insights into chlorination effects on microbial antibiotic resistance in drinking water. Water Res. 47 (1), 111–120.
Shi, X., Xia, Y., Wei, W., Ni, B., 2022. Accelerated spread of antibiotic resistance genes (ARGs) induced by non-antibiotic conditions: roles and mechanisms. Water Res. 224, 119060.
Siedlecka, A., Wolf-Baca, M., Piekarska, K., 2021. Microbial communities of biofilms developed in a chlorinated drinking water distribution system: a field study of antibiotic resistance and biodiversity. Sci. Total Environ. 774, 145113.
Su, H., Liu, Y., Pan, C., Chen, J., He, L., Ying, G., 2018. Persistence of antibiotic resistance genes and bacterial community changes in drinking water treatment system: from drinking water source to tap water. Sci. Total Environ. 616–617, 453–461.
Sun, W., Dong, H., Wang, Y., Duan, S., Ji, W., Huang, H., Gu, J., Qiang, Z., 2023. Ultraviolet (UV)-based advanced oxidation processes for micropollutant abatement in water treatment: gains and problems. J. Environ. Chem. Eng. 11 (5), 110425.
Terhalle, J., Kaiser, P., Jütte, M., Buss, J., Yasar, S., Marks, R., Uhlmann, H., Schmidt, T. C., Lutze, H.V., 2018. Chlorine dioxide—pollutant transformation and formation of hypochlorous acid as a secondary oxidant. Environ. Sci. Technol. 52 (17), 9964–9971.
van Belkum, A., Burnham, C.D., Rossen, J.W.A., Mallard, F., Rochas, O., Dunne, W.M., 2020. Innovative and rapid antimicrobial susceptibility testing systems. Nat. Rev. Microbiol. 18 (5), 299–311.
Varghese, M., Balachandran, M., 2021. Antibacterial efficiency of carbon dots against Gram-positive and Gram-negative bacteria: a review. J. Environ. Chem. Eng. 9 (6), 106821.
Walsh, C., 2000. Molecular mechanisms that confer antibacterial drug resistance. Nature 406 (6797), 775–781.
Wan, K., Zheng, S., Ye, C., Hu, D., Zhang, Y., Dao, H., Chen, S., Yu, X., 2022. Ancient oriental wisdom still works: removing ARGs in drinking water by boiling as compared to chlorination. Water Res. 209, 117902.

Wang, H., Hu, C., Liu, L., Xing, X., 2017a. Interaction of ciprofloxacin chlorination products with bacteria in drinking water distribution systems. J. Hazard. Mater. 339, 174–181.
Wang, F., Gao, B., Yue, Q., Bu, F., Shen, X., 2017b. Effects of ozonation, powdered activated carbon adsorption, and coagulation on the removal of disinfection by-product precursors in reservoir water. Environ. Sci. Pollut. Res. 24 (21), 17945–17954.
Wang, H., Wang, J., Li, S., Ding, G., Wang, K., Zhuang, T., Huang, X., Wang, X., 2020. Synergistic effect of UV/chlorine in bacterial inactivation, resistance gene removal, and gene conjugative transfer blocking. Water Res. 185, 116290.
Wang, M., Zhang, Y., Niu, Z., Miao, Q., Fu, W., 2023. Study on the distribution characteristics and metabolic mechanism of chlorine-resistant bacteria in indoor water supply networks. Environ. Pollut. 328, 121640.
Wang, S., Nie, W., Gu, Q., Wang, X., Yang, D., Li, H., Wang, P., Liao, W., Huang, J., Yuan, Q., Zhou, S., Ahmad, I., Kotaro, K., Chen, G., Zhu, B., 2024a. Spread of antibiotic resistance genes in drinking water reservoirs: insights from a deep metagenomic study using a curated database. Water Res. 256, 121572.
Wang, S., Zhuang, Y., Gao, L., Huang, H., Zhang, X., Jia, S., Shi, P., Zhang, X., 2024b. Deciphering the dynamics and driving mechanisms of high-risk antibiotic resistome in size-fractionated bacterial community during drinking water chlorination via metagenomic analysis. J. Hazard. Mater. 466, 133572.
Wang, S., Shao, Z., Chen, G., Lin, B., Li, D., Chen, J., 2024c. Assessment of chlorine and hydrogen peroxide on airborne bacteria: disinfection efficiency and induction of antibiotic resistance. J. Hazard. Mater. 474, 134697.
Wu, J., Zhou, J., Liu, D., Wu, J., He, R., Cheng, Z., Li, H., Li, W., 2023. Phthalates promote dissemination of antibiotic resistance genes: an overlooked environmental risk. Environ. Sci. Technol. 57 (17), 6876–6887.
Xu, L., Ouyang, W., Qian, Y., Su, C., Su, J., Chen, H., 2016. High-throughput profiling of antibiotic resistance genes in drinking water treatment plants and distribution systems. Environ. Pollut. 213, 119–126.
Xu, L., Zhang, C., Xu, P., Wang, X.C., 2018. Mechanisms of ultraviolet disinfection and chlorination of *Escherichia coli*: culturability, membrane permeability, metabolism, and genetic damage. J. Environ. Sci. 65, 356–366.
Xue, W., Shi, X., Guo, J., Wen, S., Lin, W., He, Q., Gao, Y., Wang, R., Xu, Y., 2024. Affecting factors and mechanism of removing antibiotics and antibiotic resistance genes by nano zero-valent iron (nZVI) and modified nZVI: a critical review. Water Res. 253, 121309.
Yang, X., Zhou, Y., Xia, R., Liao, J., Liu, J., Yu, P., 2024. Microplastics and chemical leachates from plastic pipes are associated with increased virulence and antimicrobial resistance potential of drinking water microbial communities. J. Hazard. Mater. 463, 132900.
Yin, H., Wang, H., Wang, M., Shi, B., 2023. The interaction between extracellular polymeric substances and corrosion products in pipes shaped different bacterial communities and the effects of micropollutants. Water Res. 247, 120822.
Yuan, Q., Yu, P., Cheng, Y., Zuo, P., Xu, Y., Cui, Y., Luo, Y., Alvarez, P.J.J., 2022. Chlorination (but Not UV disinfection) generates cell debris that increases extracellular antibiotic resistance gene transfer via proximal adsorption to recipients and upregulated transformation genes. Environ. Sci. Technol. 56 (23), 17166–17176.
Zeng, Q., Zhang, S., Liao, J., Miao, D., Wang, X., Yang, P., Yun, L., Liu, A., Lu, W., 2015. Evaluation of genotoxic effects caused by extracts of chlorinated drinking water using a combination of three different bioassays. J. Hazard. Mater. 296, 23–29.
Zhai, H., Guo, Y., Zhang, L., Miao, Y., Wang, J., 2022. Presence of bromide and iodide promotes the horizontal transfer of antibiotic resistance genes during chlorination: a preliminary study. Sci. Total Environ. 846, 157250.
Zhang, J., Li, W., Chen, J., Qi, W., Wang, F., Zhou, Y., 2018. Impact of biofilm formation and detachment on the transmission of bacterial antibiotic resistance in drinking water distribution systems. Chemosphere 203, 368–380.
Zhang, J., Xu, Z., Chu, W., Ju, F., Jin, W., Li, P., Xiao, R., 2023a. Residual chlorine persistently changes antibiotic resistance gene composition and increases the risk of antibiotic resistance in sewer systems. Water Res. 245, 120635.
Zhang, M., Wang, Y., Bai, M., Jiang, H., Cui, R., Lin, K., Tan, C., Gao, C., Zhang, C., 2023b. Metagenomics analysis of antibiotic resistance genes, the bacterial community and virulence factor genes of fouled filters and effluents from household water purifiers in drinking water. Sci. Total Environ. 854, 158572.
Zhang, M., Zhang, L., Lin, K., Wang, Y., Xu, S., Bai, M., Jiang, H., Wang, S., Wang, Y., Zhang, C., 2023c. Influence of chlorinated disinfection by-products on transmission of antibiotic resistance genes in biofilms and water of a simulated drinking water distribution system. Environ. Eng. Res. 28 (4), 210617.
Zhang, S., Wang, Y., Lu, J., Yu, Z., Song, H., Bond, P.L., Guo, J., 2021. Chlorine disinfection facilitates natural transformation through ROS-mediated oxidative stress. ISME J. 15 (10), 2969–2985.
Zhang, H., Chang, F., Shi, P., Ye, L., Zhou, Q., Pan, Y., Li, A., 2019a. Antibiotic resistome alteration by different disinfection strategies in a full-scale drinking water treatment plant deciphered by metagenomic assembly. Environ. Sci. Technol. 53 (4), 2141–2150.
Zhang, T., Hu, Y., Jiang, L., Yao, S., Lin, K., Zhou, Y., Cui, C., 2019b. Removal of antibiotic resistance genes and control of horizontal transfer risk by UV, chlorination and UV/chlorination treatments of drinking water. Chem. Eng. J. 358, 589–597.
Zhang, T., Liao, P., Fang, L., Zhang, D., 2024. Effect of booster disinfection on the prevalence of microbial antibiotic resistance and bacterial community in a simulated drinking water distribution system. Environ. Pollut. 341, 122902.
Zhang, S., Lu, J., Wang, Y., Verstraete, W., Yuan, Z., Guo, J., 2022a. Insights of metallic nanoparticles and ions in accelerating the bacterial uptake of antibiotic resistance genes. J. Hazard. Mater. 421, 126728.
Zhang, X., Lin, T., Jiang, F., Zhang, X., Wang, S., Zhang, S., 2022b. Impact of pipe material and chlorination on the biofilm structure and microbial communities. Chemosphere 289, 133218.
Zhang, Y., Gu, A.Z., He, M., Li, D., Chen, J., 2017. Subinhibitory concentrations of disinfectants promote the horizontal transfer of multidrug resistance genes within and across genera. Environ. Sci. Technol. 51 (1), 570–580.
Zhang, Y., Zhuang, Y., Geng, J., Ren, H., Zhang, Y., Ding, L., Xu, K., 2015. Inactivation of antibiotic resistance genes in municipal wastewater effluent by chlorination and sequential UV/chlorination disinfection. Sci. Total Environ. 512–513, 125–132.
Zhao, W., Zhang, B., Zheng, S., Yan, W., Yu, X., Ye, C., 2025. High temperatures promote antibiotic resistance genes conjugative transfer under residual chlorine: mechanisms and risks. J. Hazard. Mater. 483, 136675.
Zheng, D., Yin, G., Liu, M., Hou, L., Yang, Y., Van Boeckel, T.P., Zheng, Y., Li, Y., 2022. Global biogeography and projection of soil antibiotic resistance genes. Sci. Adv. 8 (46), eabq8015.
Zheng, S., Lin, T., Chen, H., Zhang, X., Jiang, F., 2024. Impact of changes in biofilm composition response following chlorine and chloramine disinfection on nitrogenous disinfection byproduct formation and toxicity risk in drinking water distribution systems. Water Res. 253, 121331.
Zhou, Y., Zhang, G., Zhang, D., Zhu, N., Bo, J., Meng, X., Chen, Y., Qin, Y., Liu, H., Li, W., 2024. Microplastic biofilms promote the horizontal transfer of antibiotic resistance genes in estuarine environments. Mar. Environ. Res. 202, 106777.
Zhu, L., Chen, T., Xu, L., Zhou, Z., Feng, W., Liu, Y., Chen, H., 2020. Effect and mechanism of quorum sensing on horizontal transfer of multidrug plasmid RP4 in BAC biofilm. Sci. Total Environ. 698, 134236.
Zhu, S., Yang, B., Jia, Y., Yu, F., Wang, Z., Liu, Y., 2023a. Comprehensive analysis of disinfectants on the horizontal transfer of antibiotic resistance genes. J. Hazard. Mater. 453, 131428.
Zhu, Z., Xu, S., Bao, X., Shan, L., Pei, Y., Zheng, W., Yuan, Y., 2023b. Effect of outdoor pipe materials and community-intrinsic properties on biofilm formation and chlorine resistance: black sheep or team leader. J. Clean. Prod. 411, 137308.