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Review

Removal of antibiotic-resistant genes during drinking water treatment: A review

Tuqiao Zhang[1], *Kunyuan Lv*[1], *Qingxiao Lu*[2], *Lili Wang*[3], *Xiaowei Liu*[1,2,*]

[1] *Zhejiang Key Laboratory of Drinking Water Safety and Distribution Technology, Zhejiang University, Hangzhou 310058, China*

[2] *Ocean College, Zhejiang University, Hangzhou 310058, China*

[3] *Environmental Engineering, Jiyang College of Zhejiang A & F University, Zhuji 311800, China*

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ABSTRACT

Once contaminate the drinking water source, antibiotic resistance genes (ARGs) will propagate in drinking water systems and pose a serious risk to human health. Therefore, the drinking water treatment processes (DWTPs) are critical to manage the risks posed by ARGs. This study summarizes the prevalence of ARGs in raw water sources and treated drinking water worldwide. In addition, the removal efficiency of ARGs and related mechanisms by different DWTPs are reviewed. Abiotic and biotic factors that affect ARGs elimination are also discussed. The data on presence of ARGs in drinking water help come to the conclusion that ARGs pollution is prevalent and deserves a high priority. Generally, DWTPs indeed achieve ARGs removal, but some biological treatment processes such as biological activated carbon filtration may promote antibiotic resistance due to the enrichment of ARGs in the biofilm. The finding that disinfection and membrane filtration are superior to other DWTPs adds weight to the advice that DWTPs should adopt multiple disinfection barriers, as well as keep sufficient chlorine residuals to inhibit re-growth of ARGs during subsequent distribution. Mechanistically, DWTPs obtain direct and inderect ARGs reduction through DNA damage and interception of host bacterias of ARGs. Thus, escaping of intracellular ARGs to extracellular environment, induced by DWTPs, should be advoided. This review provides the theoretical support for developping efficient reduction technologies of ARGs. Future study should focus on ARGs controlling in terms of transmissibility or persistence through DWTPs due to their biological related nature and ubiquitous presence of biofilm in the treatment unit.

Introduction

Antibiotic disposal into the environment enhances selective pressures that lead to the emergence, proliferation, and prevalence of antibiotic resistant bacteria (ARB) and antibiotic resistance genes (ARGs) (Luo and Zhou, 2008; Su et al., 2014).

* Corresponding author.
E-mail: liuxiaowei@zju.edu.cn (X. Liu).

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Most of the antibiotics currently in use can acquire their corresponding ARB from the environment (Xu et al., 2011). Furthermore, ARGs can be transmitted within and between species through vertical gene transfer (VGT) and horizontal gene transfer (HGT) (Dodd, 2012; Li et al., 2019; Lu et al., 2020). After bacterial death, intracellular ARGs are released into the environment where they exist for extended periods of time. Notably, ARGs can be transferred to other non-bacterial organisms, including human beings, to inhibit their susceptibilities to antibiotics (Li et al., 2018b). Due to the antibiotic resistance imposed by ARGs and their threat to environmental safety and human health, they have been recognized as emerging environmental contaminants (Pruden et al., 2006).

Various ARGs at different concentration have been detected in air (Gibbs et al., 2004; Xie et al., 2019; Zhang et al., 2019b), soil (Lu and Lu, 2019; Zhao et al., 2017), medical wastewater (Szekeres et al., 2017), aquaculture wastewater (Chen et al., 2017), surface water (Dang et al., 2017; Stange et al., 2019b; Yang et al., 2018), and drinking water (Fernando et al., 2016; Gomes Freitas et al., 2017). Drinking water is an important potential route of ARGs exposure to humans. Therefore, limiting ARGs and their spread in drinking water systems is vital for human health. It is difficult and costly to decrease the concentration levels of ARGs in source waters and to renovate water distribution networks for drinking water systems. A reliable way of controlling ARGs in drinking water is through the interception or stabilization function of waterworks. Therefore, it is necessary to summarize how and why the currently applied drinking water treatment technologies remove ARGs.

This work reviews the presence of ARGs in drinking water, removal efficiency and mechanism of ARGs by different treatment processes in waterworks, and influencing factors on ARGs elimination based on the latest literature. The route discussed in this paper begins from the abondance of ARGs in raw source water, finished water of waterworks, and tap water, to draw a general picture of how waterworks in ARGs removal. Then the removal efficiency of ARGs for specific treatment process (coagulation/sedimentation, clarification, ozonation, biological activated carbon filtration, membrane filtration, and disinfection) is discussed, followed by the analysis of related mechanism. Finally, special attention is given to the abiotic and abiotic factors influencing the reduction of ARGs from the perspective of how waterworks minimize the induction of ARGs generation and promotion of ARGs propagation brought by drinking water treatment processes themselves.

1. ARGs in raw water sources and treated drinking water

Antibiotic resistance genes in drinking water have been attributed to raw water sources. Six ARGs were detected in raw water sources of Michigan and Ohio in America (Xi et al., 2009). In another study which conducted in Louisiana, the raw water sources of were found to contain *sul1* and *tetA* genes (Scott et al., 2015). Studies conducted in other countries including Nigeria (Adesoji et al., 2017), Canada (Fernando et al., 2016), Korea (Son et al., 2018), Japan (Nguyen et al., 2019), Tanzania (Lyimo et al., 2016), Poland (Koniuszewska et al., 2020), Germany (Stoll et al., 2012; Voigt et al., al.,2020), Australia (Stoll et al., 2012), UK (Dhanji et al., 2011), India (Ahammad et al., 2014), France (Laroche et al., 2009), and Russia (Sazykin et al., 2019) also discovered the presence of ARGs in raw water sources. In China, aminoglycoside, β-lactam, sulfonamide, FCA (fluroquinolone, quinolone, florfenicol, chloramphenicol, and amphenicol), macrolide-lincosamide-streptogramin B (MLSB), other/efflux, vancomycin and tetracycline resistance genes were found in the Qiantang river (Xu et al., 2016). Seventeen ARGs were detected in the Yellow river of China (Lu et al., 2018). The economically developed regions of China exhibited worse outcomes regarding ARGs in drinking water source. For example, 27 ARGs were detected in raw water in Pearl River Delta (Su et al., 2018). The presence of ARGs in raw water sources worldwide is summarized in Table 1.

Naturally, the ARG pollution of drinking water source will spread to the treated drinking water. Numerous studies have revealed that the ARGs were detected in treated drinking water including finished water of waterworks, water in drinking water distribution system, tap water, cistern water of residential building, and spring (Table 1). The bad news is the frequent detection of ARGs in tap water which directly contacts with consumers. In Poland, Canada, and California, *bla, sul, tet, amp* and *erm* resistance genes were detected in tap water. In Singapore and China, 265 ARGs belonging to 17 different types were found in tap water obtained from several cities (Ma et al., 2019). Among these ARGs, multidrug, bacitracin, and aminoglycoside resistance genes were the most dominant. Twenty-four ARGs were also found in tap water collected from 71 cities of 31 provincial level administrative regions of China (Zhang et al., 2020). Among the ARGs, those conferring resistance to sulfonamides exhibited the highest distribution and abundance followed by those conferring resistance to aminoglycosides and tetracyclines. The fact that ARGs are frequently detected in raw water sources and treated drinking water after waterworks indicates that ARGs pollution in drinking water is universal and deserves a high priority.

2. The efficiency of ARGs removal during the drinking water treatment processes

Drinking water treatment processes include pretreatment processes (pre-oxidation, biological pretreatment, adsorption pretreatment with powder activated carbon, etc.), conventional treatment processes, and advanced treatment processes. When the removal targets are suspended matters, colloidal substances, bacterias, and viruses, conventional treatment processes (i.e., coagulation/sedimentation, clarification, sand filtration, and disinfection) are suggested. If there are micropollutants such as ammonia, pesticides, and heavy metals in the raw water, conventional treatment processes are recommended to run with assistance of advanced treatment processes (granular activated carbon adsorption, granular activated carbon adsorption combined with sand filtration, BAC, O_3-BAC, membrane filtration etc.). Table 2 lists mainstream drinking water treatment processes in different contries. Up to now, conventional treatment processes still play a major role in the production of drinking water aroud the world, and

Table 1 – Presence of ARGs in raw source water and drinking water worldwide.

Source	Region	ARGs Type	Abundance (copies/L)	Refs.
Raw source water	Louisiana (America)	*sul1, tetA*	Unknown	Scott et al. (2015)
	Michigan and Ohio (America)	*bla*$_{TEM}$, *bla*$_{SHV}$, *sul1, sul2, cat, cmr*	10^2–10^6	Xi et al. (2009)
	America	*sul1, sul2, intl1*	10^{-5}–10^{-2} (Relative abundance)	Rocha et al. (2019)
	Lake Michigan (America)	*Sul1, sul2, mexB, acrA, acrB, qacH, intl1*	10^6–10^8	Kappell et al. (2019)
	Southwestern Nigeria	*sul1, sul2*	Unknown	Adesoji et al. (2017)
	Island Lake Region of Manitoba (Canada)	*ampC, tetA, mecA*	1–7 (opy No./ng DNA)	Fernando et al. (2016)
	Cheongju and Cheonan (Korea)	*tetA, tetX, sul1, ermB, ermC, qnrS, aac(6′)-lb-cr, floR, bla*$_{TEM}$, *bla*$_{SHV}$, *oqxA, intl1*	10^3–10^{11}	Son et al. (2018)
	Tama River and Lake Kasumigaura (Japan)	*bla*$_{TEM}$, *sul1, tetA, ere(A), intl1*	10^4–10^9	Nguyen et al. (2019)
	Northern Tanzania	*bla*$_{TEM-1}$, *bla*$_{CTX-M}$, bla$_{SHV-1}$, *tetA, tetB*	Unknown	Lyimo et al. (2016)
	River Thames (London, UK)	*bla*$_{CTX-M-14}$	Unknown	Dhanji et al. (2011)
	Pilica river (Poland)	β-lactam, tetracycline, MLS, fluoroquinolones and sulfonamide resistance genes	Unknown	Koniuszewska et al. (2011); (Koniuszewska et al., 2020)
	River Brisbane, Rhine and Danube (Australia and Germany)	Sulfonamide, trimethoprim, β-lactam, aminoglycosides, chloramphenicol, tetracycline, macrolide, glycopeptide resistance genes	Unknown	Stoll et al. (2012)
	Germany	*bla*$_{OXA-58}$,*mcr*	Unknown	Voigt et al. (2020)
	Ganges river (India)	*bla*$_{NDM-1}$, *bla*$_{OXA}$, *tetM, tetW, tetQ*	10^3–10^9	Ahammad et al. (2014)
	Seine (France)	*intI1*and *intI2*	Unknown	Laroche et al. (2009)
	Don River (Russia)	*OXA-48, VanB and CTX-M*	Unknown	(Sazykin et al., 2019)
	Qiantang river (Hangzhou, China)	Aminoglycosides, β-lactams, sulfonamides, FCA, MLSB, other/efflux, vancomycin and tetracycline resistance genes	10^7–10^{10}	Xu et al. (2016)
	Pearl River (Guangzhou, China)	Sulfonamides, tetracycline, chloramphenicol, quinolones and macrolides resistance genes	10^4–10^{11}	Su et al. (2018)
	Tai lake (China)	*sul1, sul2, tetC, tetG, tetX, tetA, tetB, tetO, tetM, tetW*	10^3–10^9	Guo et al. (2014)
	Yellow River (Lanzhou, Yinchuan, Hohhot, Zhengzhou, Jinan, Dongying, China)	Aminoglycosides, macrolide, tetracycline, sulfonamides resistance genes	$<10^8$	Lu et al. (2018)
Finished water of DWTP	Qiantang river (Hangzhou, China)	Aminoglycosides, β-lactams, sulfonamides, FCA, MLSB, other/efflux, vancomycin and tetracycline resistance genes	10^5–10^8	Xu et al. (2016)
	Pearl River (Guangzhou, China)	Sulfonamides, tetracycline, chloramphenicol, quinolones and macrolides resistance genes	10^4–10^{10}	Su et al. (2018)
	Tai Lake (China)	*sul1, sul2, tetC, tetG, tetX, tetA, tetB, tetO, tetM, tetW*	$<10^8$	Guo et al. (2014)
	Yellow River (Lanzhou, Yinchuan, Hohhot, Zhengzhou, Jinan, Dongying, China)	Aminoglycosides, macrolide, tetracycline, sulfonamides resistance genes	$<10^7$	Lu et al. (2018)
	Wrocław (Poland)	*bla*$_{NDM}$, *qnrS, qacH, intl1, bla*$_{TEM}$, *ampC, tolA*	Unknown	Siedlecka et al. (2020)

(*continued on next page*)

Table 1 (*continued*)

Source	Region	ARGs Type	Abundance (copies/L)	Refs.
Tap water	Michigan and Ohio (America)	bla_{TEM}, bla_{SHV}, *sul1*, *sul2*, *cat*, *cmr*	10^3–10^9	Xi et al. (2009)
	America	*tetA*, *sul1*	10^{-4}–10^{-2} (Relative abundance)	Rocha et al. (2019)
	Hangzhou (China)	Aminoglycosides, β-lactams, sulfonamides, FCA, MLSB, other/efflux, vancomycin and tetracycline resistance genes	$<10^8$	Xu et al. (2016)
	Guangzhou (China)	Sulfonamides, tetracycline, chloramphenicol, quinolones and macrolides resistance genes	10^4–10^8	Su et al. (2018)
	71 cities (China)	Integration, quinolones, tetracycline, aminoglycosides, β-lactam and macrolides resistance genes	$<10^7$ (Total ARGs)	Zhang et al. (2020)
	Singapore and China (Hong Kong, Nanning, Jinzhong, Qingdao, Wugang, Shanghai, Linyi, Botou, Xigaze, Fujin, Yinchuan)	Multidrug, bacitracins, MLS, β-lactam, aminoglycosides, sulfonamide, fosmidomycin, tetracycline, rifamycin, vaconmycin, polymixin, trimethoprim, kasugamycin, quinolone, chloramphenicol, fosfomycin, puromycin resistance genes	4×10^{-2}–10° (Copies/cell)	Ma et al. (2019)
	Wrocław (Poland)	bla_{TEM}, bla_{NDM}, *qnrB*, *qnrC*, *tetA*, *sul1*, *sul2*, *ermB*, *intl1*	Unknown	Siedlecka et al. (2020)
	Island Lake Region of Manitoba (Canada)	*ampC*, *tetA*	1–2.5 (opy No./ng DNA)	Fernando et al. (2016)
	California (Los Angeles, San Diego, Bakersfield, Fresno)	Bla_{SHV}, *sul1*	$<10^7$	Echeverria-Palencia et al. (2017)
	Scotland	*sul1 and sul2*	Unknown	Khan et al. (2016)
	Northern Tanzania	bla_{TEM}-1, bla_{CTX-M}, bla_{SHV-1}, *tetA*, *tetB*	Unknown	Lyimo et al. (2016)
	Cajamarca (Peru)	$bla_{CTX-M-3}$	Unknown	Larson et al. (2019)
	Dhaka (Bangladesh)	$bla_{CTX-M-15}$, bla_{CMY-2}, *qnrS*, *qnrB*	Unknown	Talukdar et al. (2013)
Cistern water of residential building	Manitoba (Canada)	$bla_{SHV,}$, bla_{TEM}, bla_{CTX-M}, bla_{OXA-1}, bla_{CYM-2}, bla_{KPC}, bla_{OXA-48}, bla_{NDM}	Unknown	Mi et al. (2019)
Spring	Portugal	bla_{L1}	Unknown	Henriques et al. (2012)

the most popular advanced treatment processes are O_3-BAC and membrane filtration.

2.1. *Pretreatment processes*

The pretreatment processes are aimed at changing the nature and improving the treatability of pollutants by physical, chemical, and biological methods so that they can be effectively removed in the subsequent treatment process. Common raw water pretreatment processes include chemical oxidation, biodegradation, pH adjustment, precipitation among others. The existing reports regarding the removal of ARGs during the pretreatment process involve the pre-oxidation process that occurs before the coagulation/ precipitation or clarification processes. Therefore, this study laid much emphasis on the removal efficiency of ARGs during the pre-oxidation process.

2.1.1. *Pre-chlorination*

Pre-chlorination is the oldest and most common pre-oxidation method in waterworks. This technology utilizes active chlorine (hypochlorous acid, chlorine dioxide, chloramine) to oxidize and enhance the removal of pollutants (algae, iron, manganese, colloidal particles, etc.). In a previous study, it was found that after pre-chlorination in waterworks W, the absolute abundance of *sul1*, *sul2*, *tetG* and *tetA* genes were reduced by more than 1.7 log, while *tetO*, *tetM* and *tetW* genes were difficult to be eliminated even though their concentrations were low (Guo et al., 2014). However, the relative abundance of sulfonamide and tetracycline ARGs increased at least 1 log after pre-chlorination in waterworks W.

2.1.2. *Pre-ozonation*

The ozonation technology has been applied in water treatment procedures since the 1970s. This process enhances the

Table 2 – Mainstream drinking water treatment processes in different contries.

Countries	Common drinking water treatment processes	Refs.
UK	Surface water→Pre-ozonation→Coagulation→Sedimentation→Sand filtration→O_3/BAC→Chlorine disinfection	Xu et al. (2004); (Xu, 2004)
Netherlands	Surface water→Coagulation→Sedimentation→disinfection (UV, O_3, UV/H_2O_2)→Activated carbon filtration→Sand filtration	van Dooremalen et al. (2020)
Germany	Ground water→Aeration→Sand filtration	Zhang (2010)
France	Groundwater/ Surface water→Coagulation→Sedimentation→Sand filtration→O_3/BAC→Disinfection	Wang (2006)
Israel and Saudi Arabia	Seawater→Pre-chlorination→Coagulation→Sedimentation→Sand filtration→Multistage flash/ Reverse osmosis→Disinfection	Al-Mutaz (1996); Al-Jaseem et al. (2016); Zhao et al. (2010)
Singapore	(1) Reclaimed water→Micro filtration→Reverse osmosis→Ultraviolet (2) Seawater→Coagulation→Sedimentation→Sand filtration/Ultra filtration→Reverse osmosis	Bai et al. (2020), Tong et al., 2007
China	Surface water→Coagulation→Sedimentation→Sand filtration→Chlorine disinfection	China Urban Water Association, 2019
Japan	Surface water→Rapid sand filtration→O_3/BAC→Chlorine disinfection	(Japan Water Works Association, 2017)
USA	Surface water→Coagulation→Sedimentation→Sand filtration→O_3/BAC→Chlorine disinfection	Yao et al. (2013)
Australia	(1) Surface water→Coagulation→Sedimentation→Sand filtration→Chlorine disinfection (2) Seawater→Pre-chlorination→Coagulation→Sedimentation→Sand filtration→Reverse osmosis→Chlorine disinfection	(El Saliby et al., 2009); Chen (2003)
South Africa	Surface water→Coagulation→Sedimentation→Sand filtration→Chlorine disinfection	Wang et al. (2017)

removal of pollutants by oxidizing ozone molecules and free radicals (such as hydroxyl radicals, superoxide radicals, etc.) generated by ozone chain decomposition. The ozonation process can be classified into pre-ozonation and post-ozonation phases. The former is usually applied in the pretreatment of raw water while the latter is applied in advanced treatments.

Pre-ozonation of two waterworks located in Suzhou City, China, exhibited a poor reduction of total ARGs (Guo et al., 2014). Most of the ARGs were recalcitrant with small fluctuations. The absolute abundance of *tetX* gene was the only one that was reduced by approximately 1.8 log in one of the two waterworks. Another study documented that the pre-ozonation process slightly reduced the relative abundance of ARGs including aminoglycoside, β-lactam, sulfonamide, FCA, MLSB, other/efflux, vancomycin and tetracycline resistance genes but, increased absolute abundance of these ARGs (Xu et al., 2016). The poor reduction in ARGs may be attributed to the competitive consumption of the coexisting matrix constituents such as natural organic matter.

2.2. Conventional drinking water treatment processes

The conventional drinking water treatment processes in waterworks involve coagulation/sedimentation, sand filtration and chlorine/UV disinfection. Coagulation and sedimentation are two independent processes, while clarification integrates the two processes. During flocculation, impurities such as colloids, suspended solids, microorganisms, heavy metals, and organic pollutants in the raw water are aggregated into flocs that then settle down by gravity. The supernatant then flows into the sand filter and the residual tiny suspended matter, organic matter, and bacteria are further removed. Finally, the treated water is disinfected to further remove residual pathogenic microorganisms.

2.2.1. *Coagulation/sedimentation and clarification*

Zhang et al. (2016b) found that the coagulation and sedimentation processes of a waterworks in the Yangtze River Delta suppressed the absolute abundance of ARGs about 0.9 log. Other studies on waterworks located in the Yangtze River Delta and Qiantang Delta documented that coagulation/sedimentation and clarification units decreased the absolute abundance of most ARGs to a limited extent (Guo et al., 2014; Xu et al., 2016). Wang et al. (2019) reported that the absolute abundance of MCR-1 and NDM-1 increased by 0.42 log and 0.28 log respectively after flocculation. The sedimentation unite of two waterworks in Guangzhou, China, showed that, in one of them, the absolute abundance of most ARGs was increased while the absolute abundance was reduced in the other (Su et al., 2018). Hu et al. (2019) in their study documented that the total absolute abundance of ARGs was effectively reduced (1.6 log) by coagulation and sedimentation unites of a waterworks in East China.

2.2.2. *Sand filtration*

Several studies have been performed to ascertain the efficiency of ARGs removal by sand filtration. In one of them, it was found that sand filtration reduced the absolute abundance of ARGs and effectively decreased the relative abundance of ARGs (Zhang et al., 2016b). Due to the difficulties of cutting down the relative abundance, it was suggested that sand filtration be listed as a control technology for ARGs. Another two works also inclined to this view that sand filtration could remove ARGs effectively (Su et al., 2018; Zheng et al., 2018). However, different outcomes were obtained from other studies. Two studies announced that the absolute abundance of ARGs decreased while the relative abundance increased after sand filtration (Guo et al., 2014; Xu et al., 2016). Another study declared that sand filtration was powerless to significantly reduce the relative and absolute abundance of MCR-1 and NDM-1 (Wang et al., 2019). In addition, the total absolute abundance of ARGs was shown not to have changed after flowing through the sand filter following flocculation/coagulation+sedimentation or pre-zonation +flocculation+sedimentation processes (Hu et al., 2019).

2.2.3. *Chlorine disinfection*

Chlorination is an effective process for reducing the concentration of ARGs. The removal rate of ARGs has been positively correlated with the CT value of chlorine (chlorine dosage × contact reaction time) (Destiani and Templeton, 2019; Stange et al., 2019a). Besides remarkable abatement of absolute abundance, raising of chlorine dose yielded a remarkable reduction of ARGs types (Lin et al., 2016a). Compared to ARB, ARGs are more difficult to remove. At the chlorine dose of 0.25 mg/L, the inactivation of ARB reached 5.1 log. However, only 0.4–0.5 log ARGs removal was attained (Stange et al., 2019a). It has also been shown that chlorination is effective and superior compared to the other water treatment processes (Guo et al., 2014; Xu et al., 2016). Nevertheless, the selective enrichment of some ARGs due to chlorination needs further studies (Guo et al., 2014; Shi et al., 2013; Xu et al., 2016; Zheng et al., 2018).

2.2.4. *Ultraviolet disinfection*

Ultraviolet disinfection has been shown to be inferior to chlorination with regards to ARGs removal. Utilizing multiple antibiotic resistant *E. coli* and *P. aeruginosa* as test bacteria, a UV_{254} fluence of 200 mJ/cm^2 resulted in 1.2 log ARGs reduction while chlorination at a lower dose (30 mg/L•min) achieved 1.7 log reduction (Destiani and Templeton, 2019). An increase in the UV dose over the suggested values (40–200 mJ/cm^2) did not enhance the reduction efficiency. For instance, a UV_{254} dose of 600 mJ/cm^2 inhibited ARGs hosting in *E. faecium* by 0.33 log (Stange et al., 2019a) while the dose of 400 mJ/cm^2 slightly enhanced the elimination of ARGs hosting in SER2 strain and MAR SER6–1 strain compared to the UV_{254} dose of 200 mJ/cm^2 (Zhang et al., 2017a). Because of its lack of continuous disinfection abilities, UV is normally used in tandem with chlorination (Zhu and Chen, 2013). The combination of UV disinfection and chlorination exhibited a better ARGs removal performance compared to chlorination or UV disinfection alone (Destiani and Templeton, 2019; Zhang et al., 2019c, 2015).

2.3. *Advanced drinking water treatment processes*

Advanced treatment processes (ATPs) are performed after the conventional treatment processes to further improve water quality. ATPs decrease the levels of the remaining pollutants including natural organic matter, micro-polluted organic matter, and pathogenic microorganisms. Ozonation, in combination with biological activated carbon (O_3/BAC) and membrane filtration are the two widely used ATPs in waterworks. The membrane filtration process includes microfiltration (MF), ultrafiltration (UF), nanofiltration (NF), and reverse osmosis (RO). The most common membrane filtration processes in waterworks are UF and RO (Slipko et al., 2019). UF effectively removes macromolecular organics, suspended solids, colloids, bacteria, and viruses from water, thereby providing the possibility of removing ARB and ARGs (Fan et al., 2013; Jiang et al., 2003; Krzeminski et al., 2020).

2.3.1. *Post-ozonation*

Reduction in the concentration of ARGs by post-ozonation, has not been conclusively studied. Studies have documented an increased absolute abundance of several ARGs (*tetA, tetM, tetW, cfr, cmlA, qnrB, qnrS*) after post-ozonation (Su et al., 2018). However, a decreased absolute abundance of target ARGs after post-ozonation has also been documented (Xu et al., 2016; Zheng et al., 2018). Guo et al. (2018) reported that in waterworks JS and JG, post-ozonation exhibited a significantly positive contribution towards the reduction in the absolute concentrations of ARGs and a negative contribution towards the reduction in the relative abundance of tetracycline resistance genes. Furthermore, post-ozonation in waterworks SX exhibited a little effect on the relative and absolute abundance of ARGs. Post-ozonation in waterworks W significantly reduced both relative and absolute abundance of ARGs.

2.3.2. *Biological activated carbon process*

The BAC process utilizes the adsorptive ability of activated carbon and the biodegradation ability of biofilm on the activated carbon surface to remove pollutants. The ARGs removal efficiency by the BAC process differs among different waterworks. In four waterworks (waterworks W, waterworks SX, waterworks JS, and waterworks JG) in the Yangtze River Delta (Guo et al., 2014), it was found that 80%−90% target ARGs in waterworks W and SX were enriched by BAC while the ARGs could not be detected by qPCR in waterworks JS after the BAC process. In waterworks JG, *tetO, tetM*, and *tetW* genes were the only ones whose absolute abundance decreased by less than 1 log, *tetC* gene increased by about 1.27 log while the other ARGs were slightly decreased. This enrichment effect (increase of relative abundance) by the BAC process has also been documented by other studies (Xu et al., 2016; Zheng et al., 2018). The BAC process can also change the type of ARGs. A previous study showed that after treatment by the BAC process, the ARGs type increased from 84 to 159 (Zheng et al., 2018).

2.3.3. *Membrane filtration process*

The membrane filtration process including UF, NF, and RO processes exhibited a good performance in ARGs elimination when a proper membrane molecular weight cut off (MWCO) was selected. Guo et al. (2014) showed that UF membranes with MWCO 20–100 KDa in waterworks was unable to effectively eliminate ARGs. Instead, the abundance of most ARGs in the effluent increased by varying degrees. In bench scale tests, UF, NF, and RO processes performed well in the elimination of plasmid-encoded ARGs dispersed in ultrapure water. The plasmid removal rate increased with a decrease in membrane MWCO (Krzeminski et al., 2020). The UF membrane with 1 KDa MWCO can intercept more than 2 log plasmids. For the

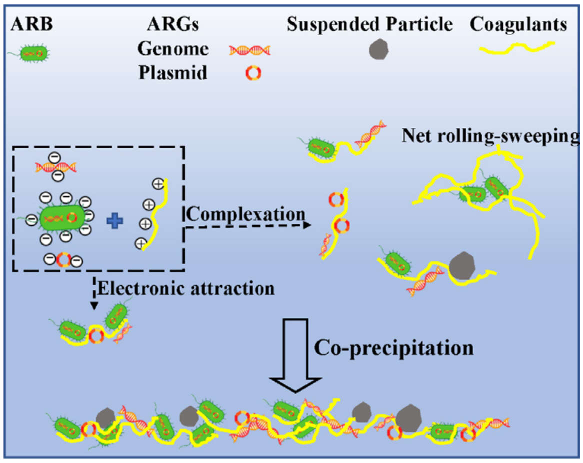

Fig. 1 – Mechanism of ARGs reduction during coagulation/sedimentation or clarification treament.

UF membrane with MWCO 300 KDa, only 23% of the plasmid (0.07 μm) was retained (Slipko et al., 2019). When the MWCO of the membrane (UF, NF, and RO) was less than 5 KDa, more than 99.80% aqueous plasmids and linear DNA carrying ARGs were removed.

3. Removal mechanisms of ARGs by different drinking water treatment processes

3.1. *Coagulation/sedimentation and clarification processes*

Most ARGs are carried by ARB. Coagulation/sedimentation and clarification processes achieve a reduction of intracellular ARGs by removing ARBs through electrostatic attraction (negatively charged viruses + positively charged iron/aluminum oxyhydroxide floc particles) (Zhang et al., 2016b). Extracellular ARGs can be directly bound to hydrolyzed coagulants and settled with flocs (Fig. 1). Thus, background constituents, coagulant types, extracellular ARGs fragment size, and ARB type can influence ARGs removal (Zhuang et al., 2014). Notably, if the vigorous hydraulic agitation caused the sedimentation sludge containing ARGs resuspend, the abundance of ARGs in the effluent may increase (Hu et al., 2019).

3.2. *Sand filtration*

Sand filtration removes ARGs through the contact adhesion effect (Fig. 2). This is attributed to the small size of ARB and free ARGs when compared to the pore size of the filter bed (Su et al., 2018). In long-term operation of the sand filter, biofilms grow on the surface of filter materials. Biofilms facilitate HGT of ARGs. However, in a nutrient-poor environment, ARB are prone to losing resistant plasmids and may therefore grow with a gradual loss of antibiotic resistance (Griffiths et al., 1990). Aging biofilms fall off from the surface of the filter media, enter into the bulk water and increase the abundance of ARGs (Wang et al., 2017b).

3.3. *Ozonation process*

The mechanism of ARGs reduction by ozonation process is presented in Fig. 3. Ozone is a strong oxidant with an oxidation potential of 2.07 V. It can decompose through chain reactions to generate hydroxyl radicals (HO•) that are non-selective and strongly oxidative. Ozone and HO• can damage extracellular DNA molecules in water (Fan, 2017; Qu et al., 2013). However, concerning intracellular DNA, water background components, cell wall/membrane molecules, and cytoplasmic constituents may take precedence over DNA molecules to consume ozone and HO• (Zhang et al., 2019c). Ozone is strongly reactive in the presence of amino acids and unsaturated carbon-carbon bonds in proteins, peptidoglycans and lipids. Therefore, it causes functional failures of cell wall/membrane (such as cell permeability increase) and ARGs-carrying DNA, or destroys their structure (Dodd, 2012; Ren et al., 2011). The destruction of the cell wall/membrane causes transformations of intracellular ARGs to extracellular ARGs. The latter exhibits a better chance coming into contact with ozone and HO•, leading to a more efficient removal of ARGs.

The reactions between intracellular ARGs with ozone and its secondary oxidant HO• cannot be initiated until the oxidants penetrate into the cell and achieve a certain cumulative concentration. Higher ozone doses may, therefore, be needed. Studies have shown that increasing the exposure time and ozone dose to a certain range enhances the elimination of ARGs (Iakovides et al., 2019; Oh et al., 2014; Sousa et al., 2017; Stange et al., 2019a). This mechanism can be used to explain why the pre-ozonation process (0.3˜0.6 O_3 mg/L) is less effective than the post-ozonation process (1.5˜1.7 O_3 mg/L) (Xu et al., 2016). However, some studies found that increasing the ozone dose does not enhance the efficiency of ARGs removal (Zheng et al., 2017). In addition, some studies found that the ozonation process increased the absolute abundance of ARGs in the effluent (Guo et al., 2014; Su et al., 2018). Su et al. (2018) speculated that the regulatory locus *soxRS* induced the increase in antibiotic resistance of ARB under the selective pressure of ozone.

3.4. *Biological activated carbon process*

Biological activated carbon adsorbs and enriches antibiotics to induce the generation of ARGs (Xu et al., 2016). Activated carbon can also intercept ARGs-hosting bacteria and reduce the concentration of ARGs in the water phase. Biofilms are composed of proteins, polysaccharides, DNA, RNA, peptidoglycan, lipids, and phospholipids (Høiby et al., 2010). These compounds enhance the growth and remediation of bacteria on the biofilm. Biofilm formation is affected by quorum sensing. Quorum sensing refers to bacterial community behaviors that rely on self-induced factors (usually called signal molecules) to sense the amount or density of bacteria around them and regulate gene expression (Liu et al., 2012). For example, acyl homoserine lactones (AHLs) is a signal molecule with little effect on bacterial growth but can promote the horizontal transfer of resistant plasmids, thereby intensifying the spread of antibiotic resistance (Zheng et al., 2018). Horizontal gene transfer may also occur between the water phase and the biofilm phase (Farkas et al., 2013). Peeling off of aged biofilms

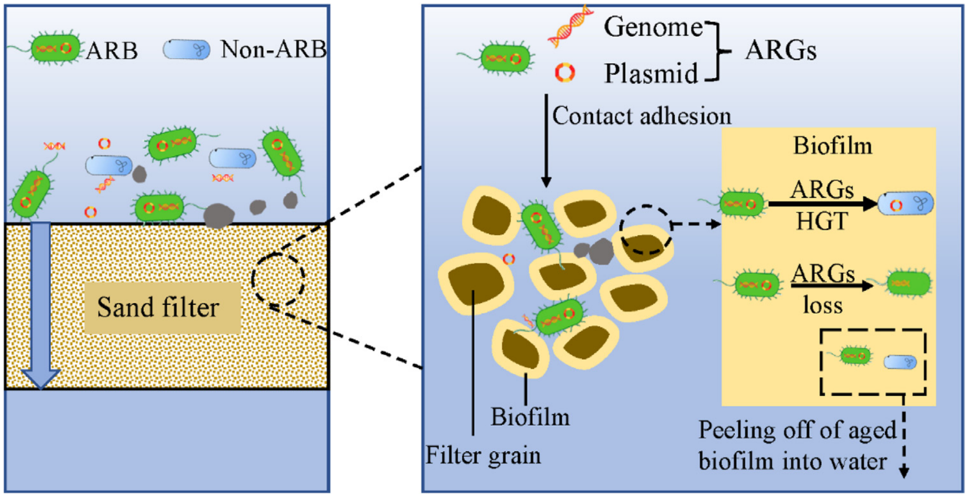

Fig. 2 – Mechanism of ARGs reduction and dissemination during sand filtration treatment.

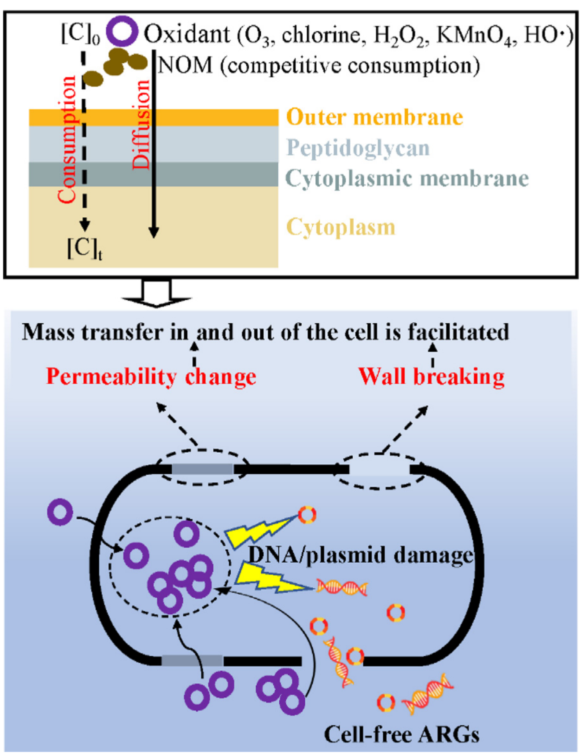

Fig. 3 – Mechanism of ARGs reduction during ozonation treatment.

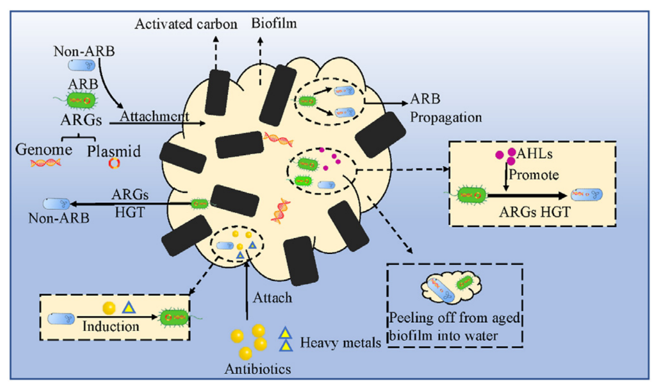

Fig. 4 – Mechanism of ARGs reduction and dissemination during BAC treatment.

into water exhibits a negative effect on the removal of ARGs removal by BAC (Hu et al., 2019). Due to the difficulties brought by the differences in feeding water quality and biofilm property in different waterworks, the current research on mechanisms of ARGs removal by BAC (Fig. 4) remains at a relatively shallow level and needs in-depth study.

3.5. *Membrane filtration process*

The membrane filtration process eliminates water pollutants through size exclusion, electrostatic effect, and diffusion effect (Ernst et al., 2000; Ganiyu et al., 2015; Taheran et al., 2016). Ultrafiltration effectively eliminates ARB and is believed to be efficient in the removal of intracellular ARGs (Lan et al., 2019). Most of the extracellular ARGs exist on mobile genetic elements (MGEs), such as transposons, integrates, and plasmids (Guo et al., 2014). Plasmids exhibit certain flexibilities in size and shape (Slipko et al., 2019). A plasmid can be stretched and elongated in the converging flow field and dovetail through pores that are smaller than its radius (Morão et al., 2011; Slipko et al., 2019). Linear DNA molecules exhibit better flexibility when compared to plasmids. This property enhances their penetration through membranes (Latulippe and Zydney, 2011). A decrease in the MWCO of the membrane reduces the ability of plasmids to pass through the membrane and enhances its interceptive success rate for ARGs. Slipko et al. (2019) documented that membranes with MWCO $\leq$ 2500 Da should be applied in the treatment of drinking water to enhance DNA interception.

In addition to the sieving effect that is associated with the membrane pore size, charge interactions between the surface of the membrane and ARGs are involved in ARGs removal mechanisms (Fig. 5). Deoxyribonucleic acid molecules are

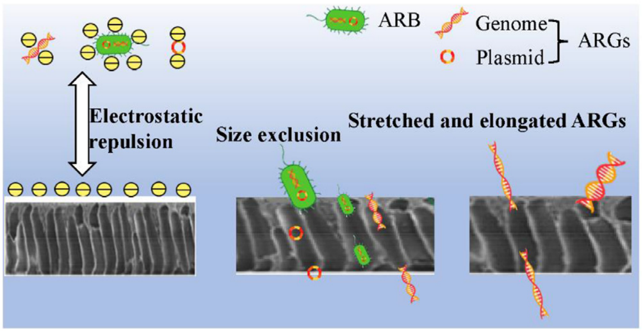

Fig. 5 – Mechanism of ARGs reduction during membrane filtration treatment.

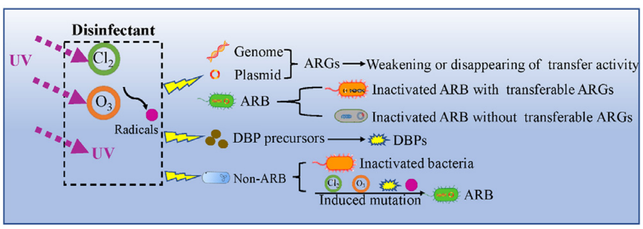

Fig. 6 – Mechanism of ARGs reduction during disinfection treatment.

negatively charged. Therefore, when the surface of the membrane is negatively charged, electrostatic repulsion enhances the retention of free DNA (Ager et al., 2009). However, an increase in driving forces such as transmembrane pressures may lead to the ARGs rejection to fall, not rise. This effect could be attributed to overcompensation of the electrostatic repulsion by the convergent flow field (Slipko et al., 2019). However, the above mentioned ARGs removal mechanism does not provide a plausible explanation for the increased ARGs abundance in the effluents from the UF process as found in some studies (Guo et al., 2014).

3.6. *Disinfection process*

The disinfection processes inactivate ARB by destroying their cellular structure or DNA (Fig. 6). However, ARGs have been known to survive in cellular debris. Chlorination is widely used because of its efficient and continuous disinfection ability (Deborde and von Gunten, 2008). Electrically neutral hypochlorous acid molecules are easily close to the negatively charged surface of the cell and diffuse into the cell. Then, the penetrated active chlorine damages bacterial enzymes and leads to a sugar metabolism disorder that inactivates bacteria. However, before the active chlorine molecules interact with enzymes and ARGs-encoding DNA, it is consumed by components of the cell wall/membrane and the cytoplasm (Dodd, 2012; Sharma et al., 2016). For efficiency in the removal of ARGs, it is important to ensure sufficient exposure to chlorine (chlorine dose × contact time) (Chen and Zhou, 2018; Dodd, 2012). This aspect is attributed to the enrichment of some types of ARGs borne in chlorine-tolerant bacteria (Huang et al., 2011; Jia et al., 2015; Shi et al., 2013; Xi et al., 2009). Co-resistance of disinfectants and antibiotics mediated by multidrug resistance efflux pumps has been associated with chlorine resistance (Yuan et al., 2015). In addition, the increased abundance of MGEs and excessive disinfectant-stimulated plasmid replication may also be attributed to the enrichment of ARGs (Shi et al., 2013). Bacteria acquire co-resistance to disinfectants and antibiotics and proliferate in clean water reservoirs to enhance the abundance of ARGs (Xu et al., 2016).

Ultraviolet light penetrates the relatively UV-transparent bacterial cell envelope and cytoplasm, where it is absorbed by the pyrimidine and purine bases that assemble into DNA and RNA. The DNA molecules of pathogenic microorganisms absorb UV light in the ranges of 200˜280 with a maximum absorption peak at 254 nm (Nebot Sanz et al., 2007). Ultraviolet damages the molecular structure of DNA by inducing the formation of pyrimidine dimers or by inducing DNA strand breakage. These effects inhibit the ability of the bacteria to reproduce and finally leads to cell death (Dodd, 2012; Nebot Sanz et al., 2007; Zhang et al., 2004). Ultraviolet irradiation can, therefore, induce direct photolytic degradation and deactivation of intracellular ARGs-encoding DNA. However, even if DNA molecules are damaged, ARGs fragments may remain intact (Stange et al., 2019a). In addition, it has been reported that a large number of spores contain traceable amounts of ARGs formed after UV disinfection (Zheng et al., 2017). Under favorable conditions the spores can develop into mature microorganisms (Michod et al., 2008).

Ultraviolet /chlorination (UV/Cl_2) disinfection is characterized by the formation of non-selective HO• and selective reactive chlorine species (RCSs, including Cl•, $Cl_2\bullet^-$ and ClO•) (Fang et al., 2014; Feng et al., 2007). Before interacting with ARGs, HO• and RCSs have to pass through cell membrane and cytoplasmic components. Zhang et al. (2019c) found that RCS was more efficient than HO• due to the fast consumption of HO•. Three possible mechanisms are involved in ARGs elimination by the UV/chlorination disinfection process: i. UV irradiation damages the cell wall and cell membranes, enhancing the entry of chlorine and free radicals into the cell that then react with ARGs (Zhang et al., 2006); ii. Chlorine and free radicals damage the cell membrane and facilitates the adsorption of UV into the cells to destroy ARGs-encoding DNA molecules (Destiani and Templeton, 2019; Li et al., 2018a) and iii. cell permeability is damaged under the actions of UV/chlorine, followed by the discharge of intracellular ARGs-encoding DNA and the formation of cell-free ARGs that are degraded by UV, chlorine, and other radicals (Dodd, 2012).

4. Factors affecting the removal of ARGs during water treatment processes

4.1. *Abiotic factors*

4.1.1. *Selective pressures*

Selective pressures from antibiotics, heavy metals (Baker-Austin et al., 2006; Zhang et al., 2018a), disinfectants (Kim et al., 2018; Zhang et al., 2017b), and disinfection by-products (Li and Gu, 2019) in the water treatment process increase the risk of ARGs and ARB enrichment as well as ARGs removal. The emergence of ARGs is mainly attributed to antibiotics. Antibiotic concentration in drinking water is relatively low (usually at ng/L). These low concentrations are, therefore, difficult to induce the generation of ARGs and the selection of ARB (Lv et al., 2014). However, as mentioned earlier, the BAC process can adsorb and enrich antibiotics thereby creating a suitable environment for the development of antibiotic resistance. Heavy metals also stimulate the emergence of bacterial resistance. Ji et al. (2012) revealed that the concentration of heavy metals (copper, mercury, zinc) in the soil had a strong positive correlation with the concentration of ARGs. Yang et al. (2017) documented a similar finding after their studies in the lakes of Wuhan. Stepanauskas et al. (2006) documented that heavy metals could select for multi-drug resistant bacteria in fresh water while Zhang et al. (2018b) showed that four heavy metals including Cu(II), Ag(I), Cr(VI), and Zn(II) promote HGT of ARGs under sub-inhibitory concentrations. Due to the low concentrations of heavy metals in drinking water, it has not been established if concentrations below the recommended levels can screen for ARB.

Unlike antibiotics and heavy metals, the concentrations of disinfectants in drinking water is relatively high (usually mg/L). Chlorine disinfectants have been shown to change the bacterial community structure and enrich ARGs and ARB in drinking water plants. Chlorine reacts with humic acid, algae, and other organics to generate disinfection by-products (DBPs) while at the same time killing bacteria. Disinfection by-productsenhance bacterial resistance. Four typical DBPs, 3-chloro-4-(dichloromethyl)−5-hydroxy-2(5H)-furanone (MX), dichloroacetonitrile, potassium bromate, and dibromoacetic acid, were shown to enhance *Pseudomonas aeruginosa* PAO1 resistance to 10 antibiotics by various levels (Lv et al., 2014). These compounds enhanced antibiotic resistance by a factor of more than 10 when compared to the control. The induction of antibiotic resistance by MX was the most conspicuous and was shown to be realized through mutagenesis that enhanced the overexpression of efflux pumps. Through a similar mechanism, DBPs such as trichloroacetic acid, chlorite, iodoacetic acid, bromoacetamide, trichloroacetonitrile, and tribromonitromethane were also found to enhance bacterial resistance (Li et al., 2016; Lv et al., 2015).

Under multiple environmental selective pressures, bacteria develop co-resistance or cross-resistance (Zhang et al., 2016a). Antibiotic resistance bacteria with co-resistance to chlorine and antibiotics have been found to be the dominant strains after disinfection associated pressures (Jia et al., 2015; Shi et al., 2013). Yang et al. (2017) documented that the co-selection mechanisms of heavy metals and antibiotics promote the emergence and spread of ARGs in lake water. Therefore, more studies should be done to elucidate on co-resistance and cross-resistance.

4.1.2. *Nutrition limiting factors*

Selective pressure is the basis for maintaining bacterial resistance. When the selective pressure is high, the bacteria with plasmid encoded resistance mechanisms to the source of the pressure have a growth advantage. However, ARB require additional energy to express resistance and, therefore, lose a competitive advantage with wild-type sensitive flora. This phenomenon is referred fitness cost. Lin et al. (2016b) found that the lower the concentration of total organic carbon (TOC), the more evident the fitness cost and the faster the loss of resistant plasmids. However, the degree of fitness cost varies among different types of plasmids. This implies that fitness cost is relevant to nutritional levels besides selective pressures. Griffiths et al. (1990) reported that resistant plasmids can be partially or completely lost in a poor nutritional environment. This effect leads to a loss in the ability of bacteria to resist antibiotics. A study performed by Lin et al. (2018) found that antibiotic resistance increases fitness cost only under high nutrient conditions. Poor nutrient conditions weaken the fitness cost. This is attributed to the adaptive mutations and low relative expression of the *rpoS* gene. In addition, Wan et al. (2019) also found that decreasing the TOC concentration also increases the relative abundance of ARGs (that is, decreasing the fitness cost).

Organic carbon, nitrogen and phosphorus are nutritional factors required for bacterial growth. Ali et al. (2016) revealed that the addition of nitrogen and phosphorus to bacterial growth medium enhanced the resistance of *E. faecalis* to oxytetracycline (OXY), chloramphenicol (CHL), vancomycin and erythromycin (ERY). However, only a high dose of the nutrients led to ciprofloxacin (CIP) resistance. Studies have also observed that the abundance of ARGs in freshwater lakes or rivers is positively correlated with the concentration of nitrogen and phosphorus (Wang et al., 2020; Xi, 2018). Eutrophic water is beneficial for the propagation of ARGs. Therefore, regulating the concentrations of nitrogen and phosphorus in drinking water is important in the inhibition of the spread of drug resistance.

4.2. *Biotic factors*

4.2.1. *Biofilms*

Biofilms are composed of microorganisms and extracellular polymers (EPS). Extracellular polymers refer to polymers, proteins, and ribose substances. Extracellular polymers enhance the clustering property of biofilms and their firm adsorption on the surface of the carrier. More importantly, EPS provide a "shelter" for the microorganisms in the biofilm to resist external harm such as water shear force, antibiotic activities and oxidant effects (Fish et al., 2017; Flemming, 2009). Biofilms also exhibit advantages in biodiversity, gene pool richness, genetic exchange convenience, biocides and other stress resistance abilities, nutrients recycle, and high-density population (Flemming, 2009). These ecological advantages explain the relatively frequent ARGs transmission and ARB propagation in the biofilm.

Biofilms are common in DWTPs, especially BAC filter. Due to the ideal environment they provide and their stable structure, biofilms serve as reservoirs for the spread of ARGs and ARB. They lead to poor ARGs removal efficiency of BAC (Bai et al., 2015).

4.2.2. *Types of ARB and ARGs*

The removal efficiency of ARGs is associated with the types of ARB. When ARB resist external interference or destruction, it is difficult to eliminate the ARGs in the ARB. Jia et al. (2015) found that ARGs in chlorine-tolerant bacteria such as Methylophilus could be effectively removed by chlorination, while ARGs in strong chlorine-tolerant bacteria such as *Pseudomonas* and *Acidovorax* could survive and become the dominant species. McKinney and Pruden. (2012) documented that gram-positive ARB exhibited better tolerance to ultraviolet disinfection compared to gram-negative ARB. The small total genome sizes of the gram-positive ARB reduced the number of potential pyrimidine dimer targets, thereby leading to the low susceptibility to UV.

The nature and structure of different types of ARGs can also affect the efficiency of their removal. Xu et al. (2016) found that among the MLSB resistance genes in BAC tank effluents, the *erm* genes were easily captured by MGEs and could be readily transferred among different host bacteria compared to the other genes. This property of *erm* genes enhances their persistence in drinking water treatment flow. Destiani and Templeton. (2019) revealed that the removal efficiency of different ARGs by UV disinfection was consistent with the number of potential dimers, particularly TT dimers on each gene.

4.2.3. *Existence form of ARGs*

Antibiotic resistance genes are commonly divided into cell-carrying ARGs (intracellular ARGs) and cell-free ARGs (extracellular ARGs). Without the protection of cell walls and cell membranes, extracellular ARGs are easily damaged by UV irradiation and oxidants such as chlorine (Yoon et al., 2017). However, cell-free ARGs easily penetrate UF and RO membranes due to their small sizes compared to cell-carrying ARGs.

Environmentally, ARGs can be classified as particle-associated ARGs, biofilm-associated ARGs, and free ARGs in water (Zhang et al., 2019a). Particle-associated ARGs are easily ignored. Particles serve as “seeds” for the attachment of ARGs and ARB that lead to the formation of biofilms. Under the shield of particles and biofilms, the removal of ARGs by chlorination, ozonation, and ultraviolet irradiation is inhibited (Liu et al., 2013). However, sand and membrane filtration processes may effectively intercept particle-associated ARGs.

5. Summary and outlook

In conclusion, it is commonly accepted that drinking water treatment process, excellent in removing or seperating host bacteria of ARGs from water, is more promising on ARGs removal. The comparisons of the removal efficiency of ARGs by different water treatment processes found that: i. coagulation, sedimentation/clarification, sand filtration, and BAC filtration cannot effectively remove ARGs; ii. The effect of ozonation process is uneven; iii. The ARGs removal efficiency by membrane filtration depends on the MWCO and iv. The disinfection process is effective; however, chlorination may enrich ARGs while UV disinfection requires a high UV dosage. In contrast, a combination of UV/chlorination is more reliable.

The ARGs removal efficiency by drinking water treatment processes is influenced by diverse factors such as selective pressure, nutrition level, ARGs types and existing form, as well as processing parameters. The combined effects of various factors complicate the ARGs removal process. Generally, knowledge regarding the removal mechanisms of ARGs by different drinking water treatment processes is at the initial stages. Future studies should focus on:

(i) The removal properties and mechanisms of ARGs of different types or forms in specific drinking water treatment processes.
(ii) The effects and mechanisms of the disinfection processes and disinfection by-products on the generation and spread of various ARGs.
(iii) The post-treatment of ARGs in sludge and the concentrate from membrane filtration generated in waterworks to avoid secondary pollution.
(iv) Exploration of rapid analysis methods to quantify the transmissibility of ARGs in drinking water, rather than simple concentration evaluation.

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REFERENCES

Adesoji, A.T., Ogunjobi, A.A., Olatoye, I.O., 2017. Characterization of integrons and sulfonamide resistance genes among bacteria from drinking water distribution systems in Southwestern Nigeria. Chemotherapy 62, 34–42.
Ager, K., Latulippe, D.R., Zydney, A.L., 2009. Plasmid DNA transmission through charged ultrafiltration membranes. J. Membr. Sci. 344, 123–128.
Ahammad, Z.S., Sreekrishnan, T.R., Hands, C.L., Knapp, C.W., Graham, D.W., 2014. Increased waterborne blaNDM-1 resistance gene abundances associated with seasonal human pilgrimages to the upper Ganges river. Environ. Sci. Technol. 48, 3014–3020.
Ali, L., Wang, Y.Q., Zhang, J., Ajmal, M., Xiao, Z.R., Wu, J.R., et al., 2016. Nutrient-induced antibiotic resistance in Enterococcus faecalis in the eutrophic environment. J. Glob. Antimicrob. Resist. 7, 78–83.
Al-Jaseem, Q.K., Almasoud, F.I., Ababneh, A.M., Al-Hobaib, A.S., 2016. Radiological assessment of water treatment processes in a water treatment plant in Saudi Arabia: water and sludge radium content, radon air concentrations and dose rates. Sci. Total Environ. 563-564, 1030–1036.
Al-Mutaz, I.S., 1996. A comparative study of RO and MSF desalination plants. Desalination 106, 99–106.
Bai, X.H., Ma, X.L., Xu, F.M., Li, J., Zhang, H., Xiao, X., 2015. The drinking water treatment process as a potential source of affecting the bacterial antibiotic resistance. Sci. Total Environ. 533, 24–31.
Bai, Y., Shan, F., Zhu, Y., Yao, Xu, J., Yi, Wu, Y., et al., 2020. Long-term performance and economic evaluation of full-scale MF and RO process – A case study of the changi NEWater Project Phase 2 in Singapore. Water Cycle 1, 128–135.
Baker-Austin, C., Wright, M.S., Stepanauskas, R., McArthur, J.V., 2006. Co-selection of antibiotic and metal resistance. Trends Microbiol. 14, 176–182.

Chen, C.Q., Zheng, L., Zhou, J.L., Zhao, H., 2017. Persistence and risk of antibiotic residues and antibiotic resistance genes in major mariculture sites in Southeast China. Sci. Total Environ. 580, 1175–1184.
Chen, L., Zhou, G.Z., 2018. Removal techniques of antibiotic resistant bacteria and resistant genes in sewage. Ecol. Environ. Sci. 27, 2163–2169.
Chen, Y.P., 2003. Experience of studying and training in Australian Water Supply Company. Water Wastewater. Eng. 12, 14–16.
China Urban Water Association, 2019. Annual Report of Chinese Urban Water Utilities (2019). China Architecture & Building Press Book.
Dang, B.J., Mao, D.Q., Xu, Y., Luo, Y., 2017. Conjugative multi-resistant plasmids in Haihe River and their impacts on the abundance and spatial distribution of antibiotic resistance genes. Water Res. 111, 81–91.
Deborde, M., von Gunten, U., 2008. Reactions of chlorine with inorganic and organic compounds during water treatment—Kinetics and mechanisms: a critical review. Water Res. 42, 13–51.
Destiani, R., Templeton, M.R., 2019. Chlorination and ultraviolet disinfection of antibiotic-resistant bacteria and antibiotic resistance genes in drinking water. AIMS Environ. Sci. 6, 222–241.
Dhanji, H., Murphy, N.M., Akhigbe, C., Doumith, M., Hope, R., Livermore, D.M., et al., 2011. Isolation of fluoroquinolone-resistant O25b:H4-ST131 Escherichia coli with CTX-M-14 extended-spectrum β-lactamase from UK river water. J. Antimicrob. Chemother. 66, 512–516.
Dodd, M.C., 2012. Potential impacts of disinfection processes on elimination and deactivation of antibiotic resistance genes during water and wastewater treatment. J. Environ. Monit. 14, 1754–1771.
Echeverria-Palencia, C.M., Thulsiraj, V., Tran, N., Ericksen, C.A., Melendez, I., Sanchez, M.G., et al., 2017. Disparate antibiotic resistance gene quantities revealed across 4 major cities in California: a survey in drinking water, air, and soil at 24 public parks. ACS Omega 2, 2255–2263.
El Saliby, I., Okour, Y., Shon, H.K., Kandasamy, J., Kim, I.S., 2009. Desalination plants in Australia, review and facts. Desalination 247, 1–14.
Ernst, M., Bismarck, A., Springer, J., Jekel, M., 2000. Zeta-potential and rejection rates of a polyethersulfone nanofiltration membrane in single salt solutions. J. Membr. Sci. 165, 251–259.
Fan, X.J., Zhang, X.H., Su, Z.J., Bai, Z.Q., Qu, Z.J., 2013. Application of ultrafiltration technology in drinking water treatment plants in China. Chin. Water Wastewater. 29, 64–70.
Fan, X.S., 2017. The research progress in DNA damage induced by hydroxyl radicals. J. Biol. 34, 80–84.
Fang, J., Fu, Y., Shang, C., 2014. The roles of reactive species in micropollutant degradation in the UV/free chlorine System. Environ. Sci. Technol. 48, 1859–1868.
Farkas, A., Butiuc-Keul, A., Ciatarâş, D., Neamţu, C., Crăciunaş, C., Podar, D., et al., 2013. Microbiological contamination and resistance genes in biofilms occurring during the drinking water treatment process. Sci. Total Environ. 443, 932–938.
Feng, Y.G., Smith, D.W., Bolton, J.R., 2007. Photolysis of aqueous free chlorine species (HOCl and OCl-) with 254 nm ultraviolet light. J. Environ. Eng. Sci. 6, 277–284.
Fernando, D.M., Tun, H.M., Poole, J., Patidar, R., Li, R., Mi, R., et al., 2016. Detection of antibiotic resistance genes in source and drinking water samples from a first nations community in Canada. Appl. Environ. Microbiol. 82, 4767.
Fish, K., Osborn, A.M., Boxall, J.B., 2017. Biofilm structures (EPS and bacterial communities) in drinking water distribution systems are conditioned by hydraulics and influence discolouration. Sci. Total Environ. 593-594, 571–580.
Flemming, H.-.C., 2009. Why Microorganisms Live in Biofilms and the Problem of Biofouling. In: Flemming, H.-C., Murthy, P.S., Venkatesan, R., Cooksey, K. (Eds.), Marine and Industrial Biofouling. Springer, Berlin, Heidelberg, pp. 3–12.
Ganiyu, S.O., van Hullebusch, E.D., Cretin, M., Esposito, G., Oturan, M.A., 2015. Coupling of membrane filtration and advanced oxidation processes for removal of pharmaceutical residues: a critical review. Sep. Purif. Technol. 156, 891–914.
Gibbs, S.G., Green, C.F., Tarwater, P.M., Scarpino, P.V., 2004. Airborne antibiotic resistant and nonresistant bacteria and fungi recovered from two swine herd confined animal feeding operations. J.Occup.Environ. Hyg. 1, 699–706.
Freitas, Gomes, D., Silva, R., R.D., Bataus, L.A.M., Barbosa, M.S., da Silva Bitencourt Braga, C.A., Carneiro, L.C., 2017. Bacteriological water quality in school's drinking fountains and detection antibiotic resistance genes. Microbiol. Antimicrob. 16, 5.
Griffiths, R.P., Moyer, C.L., Caldwell, B.A., Ye, C., Morita, R.Y., 1990. Long-term starvation-induced loss of antibiotic resistance in bacteria. Microb. Ecol. 19, 251–257.
Guo, X., Li, J., Yang, F., Yang, J., Yin, D., 2014. Prevalence of sulfonamide and tetracycline resistance genes in drinking water treatment plants in the Yangtze River Delta. China. Sci. Total Environ. 493, 626–631.
Henriques, I.S., Araújo, S., Azevedo, J.S.N., Alves, M.S., Chouchani, C., Pereira, A., et al., 2012. Prevalence and diversity of Carbapenem-resistant bacteria in untreated drinking water in Portugal. Microb. Drug Resist. 18, 531–537.
Høiby, N., Bjarnsholt, T., Givskov, M., Molin, S., Ciofu, O., 2010. Antibiotic resistance of bacterial biofilms. Int. J. Antimicrob. Agents. 35, 322–332.
Hu, Y., Zhang, T., Jiang, L., Luo, Y., Yao, S., Zhang, D., et al., 2019. Occurrence and reduction of antibiotic resistance genes in conventional and advanced drinking water treatment processes. Sci. Total Environ. 669, 777–784.
Huang, J.J., Hu, H.Y., Tang, F., Li, Y., Lu, S.Q., Lu, Y., 2011. Inactivation and reactivation of antibiotic-resistant bacteria by chlorination in secondary effluents of a municipal wastewater treatment plant. Water Res. 45, 2775–2781.
Iakovides, I.C., Michael-Kordatou, I., Moreira, N.F.F., Ribeiro, A.R., Fernandes, T., Pereira, M.F.R., et al., 2019. Continuous ozonation of urban wastewater: removal of antibiotics, antibiotic-resistant Escherichia coli and antibiotic resistance genes and phytotoxicity. Water Res. 159, 333–347.
Japan Water Works Association, 2017. Water Supply in Japan 2017. Available: http://www.jwwa.or.jp/english/index.html. Accessed November 28, 2020.
Ji, X.L., Shen, Q.H., Liu, F., Ma, J., Xu, G., Wang, Y.L., et al., 2012. Antibiotic resistance gene abundances associated with antibiotics and heavy metals in animal manures and agricultural soils adjacent to feedlots in Shanghai. China. J. Hazard. Mater. 235-236, 178–185.
Jia, S.Y., Shi, P., Hu, Q., Li, B., Zhang, T., Zhang, X.X., 2015. Bacterial community shift drives antibiotic resistance promotion during drinking water chlorination. Environ. Sci. Technol. 49, 12271–12279.
Jiang, S.J., Shi, C.E., Jiang, Z.X., 2003. Approach on feasibility of application of membrane technology in drinking water disinfection. Chongqing Environ. Sci. 25, 52–54 +45.
Kappell, A.D., Harrison, K.R., McNamara, P.J., 2019. Effects of zinc orthophosphate on the antibiotic resistant bacterial community of a source water used for drinking water treatment. Environ. Sci.: Water Res. Technol. 5, 1523–1534.
Khan, S., Knapp, C.W., Beattie, T.K., 2016. Antibiotic resistant bacteria found in municipal drinking water. Environmental Processes 3, 541–552.
Kim, M., Weigand, M.R., Oh, S., Hatt, J.K., Krishnan, R., Tezel, U., et al., 2018. Widely used Benzalkonium Chloride disinfectants

can promote antibiotic resistance. Appl. Environ. Microbiol. 84, e01201 -01218.
Koniuszewska, I., Korzeniewska, E., Harnisz, M., Kiedrzyńska, E., Kiedrzyński, M., Czatzkowska, M., et al., 2020. The occurrence of antibiotic-resistance genes in the Pilica River. Poland. Ecohydrol. Hydrobiol. 20, 1–11.
Krzeminski, P., Feys, E., Anglès d'Auriac, M., Wennberg, A.C., Umar, M., Schwermer, C.U., et al., 2020. Combined membrane filtration and 265 nm UV irradiation for effective removal of cell free antibiotic resistance genes from feed water and concentrate. J. Membr. Sci. 598, 117676.
Lan, L.H., Kong, X.W., Sun, H.X., Li, C.W., Liu, D.Z., 2019. High removal efficiency of antibiotic resistance genes in swine wastewater via nanofiltration and reverse osmosis processes. J. Environ. Manag. 231, 439–445.
Laroche, E., Pawlak, B., Berthe, T., Skurnik, D., Petit, F., 2009. Occurrence of antibiotic resistance and class 1, 2 and 3 integrons in Escherichia coli isolated from a densely populated estuary (Seine, France). FEMS Microbiol. Ecol. 68, 118–130.
Larson, A., Hartinger, S.M., Riveros, M., Salmon-Mulanovich, G., Hattendorf, J., Verastegui, H., et al., 2019. Antibiotic-Resistant Escherichia coli in drinking water samples from rural andean households in Cajamarca, Peru. Am. J. Trop. Med. Hyg. 100, 1363–1368.
Latulippe, D.R., Zydney, A.L., 2011. Separation of plasmid DNA isoforms by highly converging flow through small membrane pores. J. Colloid Interface Sci. 357, 548–553.
Li, B., Qiu, Y., Song, Y., Lin, H., Yin, H., 2019. Dissecting horizontal and vertical gene transfer of antibiotic resistance plasmid in bacterial community using microfluidics. Environ. Int. 131, 105007.
Li, D., Gu, A.Z., 2019. Antimicrobial resistance: a new threat from disinfection byproducts and disinfection of drinking water? Environ. Sci. Health. 7, 83–91.
Li, D., Zeng, S.Y., He, M., Gu, A.Z., 2016. Water disinfection byproducts induce antibiotic resistance-role of environmental pollutants in resistance phenomena. Environ. Sci. Technol. 50, 3193–3201.
Li, G.Q., Huo, Z.Y., Wu, Q.Y., Lu, Y., Hu, H.Y., 2018a. Synergistic effect of combined UV-LED and chlorine treatment on Bacillus subtilis spore inactivation. Sci. Total Environ. 639, 1233–1240.
Li, J.M., Li, X., Zhang, S.T., 2018b. Effect of disinfection process on removal of antibiotic resistance genes (ARGs) in water body. Water Purif. Technol. 37, 10–16.
Lin, W.F., Chen, S., Wan, K., Wang, C.M., Lin, H.R., Yu, X., 2016b. Effects of low-level nutrition and trace antibiotics on the fitness cost of plasmids bearing antibiotic resistance. Environ.Sci 37, 3224–3228.
Lin, W.F., Zeng, J., Wan, K., Lv, L., Guo, L.Z., Li, X., et al., 2018. Reduction of the fitness cost of antibiotic resistance caused by chromosomal mutations under poor nutrient conditions. Environ. Int. 120, 63–71.
Lin, W., Zhang, M., Zhang, S., Yu, X., 2016a. Can chlorination co-select antibiotic-resistance genes? Chemosphere 156, 412–419.
Liu, G., Ling, F.Q., Magic-Knezev, A., Liu, W.T., Verberk, J.Q., Van Dijk, J.C., 2013. Quantification and identification of particle-associated bacteria in unchlorinated drinking water from three treatment plants by cultivation-independent methods. Water Res. 47, 3523–3533.
Liu, L., Tan, X.J., Jia, A.Q., 2012. Relationship between bacterial quorum sensing and biofilm formation—A review. Acta Microbiol. Sin. 52, 271–278.
Lu, J.Y., Tian, Z., Yu, J.W., Yang, M., Zhang, Y., 2018. Distribution and abundance of antibiotic resistance genes in sand settling reservoirs and drinking water treatment plants across the Yellow river. China. Water. 10.
Lu, J., Zhang, Y.X., Wu, J., Wang, J.H., Cai, Y., 2020. Fate of antibiotic resistance genes in reclaimed water reuse system with integrated membrane process. J. Hazard. Mater. 382, 121025.
Lu, X.M., Lu, P.Z., 2019. Distribution of antibiotic resistance genes in soil amended using Azolla imbricata and its driving mechanisms. Sci. Total Environ. 692, 422–431.
Luo, Y., Zhou, Q.X., 2008. Antibiotic resistance genes(ARGs)as emerging pollutants. Acta Sci. Circum. 28, 1499–1505.
Lv, L., Jiang, T., Zhang, S.H., Yu, X., 2014. Exposure to mutagenic disinfection byproducts leads to increase of antibiotic resistance in Pseudomonas aeruginosa. Environ. Sci. Technol. 48, 8188–8195.
Lv, L., Yu, X., Xu, Q., Ye, C.S., 2015. Induction of bacterial antibiotic resistance by mutagenic halogenated nitrogenous disinfection byproducts. Environ. Pollut. 205, 291–298.
Lyimo, B., Buza, J., Subbiah, M., Smith, W., Call, D.R., 2016. Comparison of antibiotic resistant Escherichia coli obtained from drinking water sources in northern Tanzania: a cross-sectional study. BMC Microbiol. 16, 254.
Ma, L., Li, B., Zhang, T., 2019. New insights into antibiotic resistome in drinking water and management perspectives: a metagenomic based study of small-sized microbes. Water Res. 152, 191–201.
McKinney, C.W., Pruden, A., 2012. Ultraviolet disinfection of antibiotic resistant bacteria and their antibiotic resistance genes in water and wastewater. Environ. Sci. Technol. 46, 13393–13400.
Mi, R.D., Patidar, R., Farenhorst, A., Cai, Z., Sepehri, S., Khafipour, E., et al., 2019. Detection of fecal bacteria and antibiotic resistance genes in drinking water collected from three First Nations communities in Manitoba, Canada. FEMS Microbiol. Lett. 366.
Michod, R.E., Bernstein, H., Nedelcu, A.M., 2008. Adaptive value of sex in microbial pathogens. Infect. Genet. Evol. 8, 267–285.
Morão, A.M., Nunes, J.C., Sousa, F., Pessoa de Amorim, M.T., Escobar, I.C., Queiroz, J.A., 2011. Ultrafiltration of supercoiled plasmid DNA: modeling and application. J. Membr. Sci. 378, 280–289.
Nebot Sanz, E., Salcedo Dávila, I., Andrade Balao, J.A., Quiroga Alonso, J.M., 2007. Modelling of reactivation after UV disinfection: effect of UV-C dose on subsequent photoreactivation and dark repair. Water Res. 41, 3141–3151.
Nguyen, T.N., Kasuga, I., Liu, M., Katayama, H., 2019. Occurrence of antibiotic resistance genes as emerging contaminants in watersheds of Tama River and Lake Kasumigaura in Japan. IOP Conf. Series: Earth Environ. Sci. 266, 012003.
Oh, J., Salcedo, D.E., Medriano, C.A., Kim, S., 2014. Comparison of different disinfection processes in the effective removal of antibiotic-resistant bacteria and genes. J. Environ. Sci. 26, 1238–1242.
Pruden, A., Pei, R., Storteboom, H., Carlson, K.H., 2006. Antibiotic resistance genes as emerging contaminants: Studies in northern Colorado. Environ. Sci. Technol. 40, 7445–7450.
Qu, Y.J., Wan, F., Gao, N.Y., Chu, W.H., Jiang, J., 2013. Research on control of disinfection by-products by ozone and ozone-based advanced oxidation processes. Water Wastewater. Eng. 49, 166–172.
Ren, H.W., Cai, X., Zhu, Y., Liu, Y., Zhou, Y.Y., 2011. Research and development of ozone disinfection. Water Wastewater. Eng. 47, 207–211.
Rocha, J., Fernandes, T., Riquelme, M.V., Zhu, N., Pruden, A., Manaia, C.M., 2019. Comparison of culture- and quantitative PCR-based indicators of antibiotic resistance in wastewater, recycled water, and tap water. Int. J. Environ. Res. Public Health 16, 4217.
Sazykin, I.S., Seliverstova, E.Y., Khmelevtsova, L.E., Azhogina, N., Kudeevskaya, E.M., Khammami, M.I., et al., 2019. Occurrence of

antibiotic resistance genes in sewages of Rostov-on-Don and lower Don River. Theor. Appl. Ecol. 4, 76–82.
Scott, B., Raj, B., Rajkumar, N., Angie, C., Gary, L., 2015. Presence of antibiotic resistant bacteria and antibiotic resistance genes in raw source water and treated drinking water. Int. Biodeterior. Biodegrad. 102, 370–374.
Sharma, V.K., Johnson, N., Cizmas, L., McDonald, T.J., Kim, H., 2016. A review of the influence of treatment strategies on antibiotic resistant bacteria and antibiotic resistance genes. Chemosphere 150, 702–714.
Shi, P., Jia, S., Zhang, X.X., Zhang, T., Cheng, S., Li, A., 2013. Metagenomic insights into chlorination effects on microbial antibiotic resistance in drinking water. Water Res. 47, 111–120.
Siedlecka, A., Wolf-Baca, M., Piekarska, K., 2020. Spatiotemporal changes of antibiotic resistance and bacterial communities in drinking water distribution system in Wrocław. Water 12, 2601.
Slipko, K., Reif, D., Wögerbauer, M., Hufnagl, P., Krampe, J., Kreuzinger, N., 2019. Removal of extracellular free DNA and antibiotic resistance genes from water and wastewater by membranes ranging from microfiltration to reverse osmosis. Water Res. 164, 114916.
Son, D.-i., Aleta, P., Park, M., Yoon, H., Cho, K.H., Kim, Y.M., et al., 2018. Seasonal changes in antibiotic resistance genes in rivers and reservoirs in South Korea. J. Environ. Qual. 47, 1079–1085.
Sousa, J.M., Macedo, G., Pedrosa, M., Becerra-Castro, C., Castro-Silva, S., Pereira, M.F.R., et al., 2017. Ozonation and UV254 nm radiation for the removal of microorganisms and antibiotic resistance genes from urban wastewater. J. Hazard. Mater. 323, 434–441.
Stange, C., Sidhu, J.P.S., Toze, S., Tiehm, A., 2019a. Comparative removal of antibiotic resistance genes during chlorination, ozonation, and UV treatment. Int. J. Hyg. Environ. Health. 222, 541–548.
Stange, C., Yin, D., Xu, T., Guo, X., Schäfer, C., Tiehm, A., 2019b. Distribution of clinically relevant antibiotic resistance genes in Lake Tai. China. Sci. Total Environ. 655, 337–346.
Stepanauskas, R., Glenn, T.C., Jagoe, C.H., Tuckfield, R.C., Lindell, A.H., King, C.J., et al., 2006. Coselection for microbial resistance to metals and antibiotics in freshwater microcosms. Environ. Microbiol. 8, 1510–1514.
Stoll, C., Sidhu, J.P.S., Tiehm, A., Toze, S., 2012. Prevalence of clinically relevant antibiotic resistance genes in surface water samples collected from Germany and Australia. Environ. Sci. Technol. 46, 9716–9726.
Su, H.C., Liu, Y.S., Pan, C.G., Chen, J., He, L.Y., Ying, G.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.
Su, J.Q., Huang, F., Zhu, Y.G., 2014. Antibiotic resistance genes in the environment. Biodivers. Sci. 21, 481–487.
Szekeres, E., Baricz, A., Chiriac, C.M., Farkas, A., Opris, O., Soran, M.L., et al., 2017. Abundance of antibiotics, antibiotic resistance genes and bacterial community composition in wastewater effluents from different Romanian hospitals. Environ. Pollut. 225, 304–315.
Taheran, M., Brar, S.K., Verma, M., Surampalli, R.Y., Zhang, T.C., Valero, J.R., 2016. Membrane processes for removal of pharmaceutically active compounds (PhACs) from water and wastewaters. Sci. Total Environ. 547, 60–77.
Talukdar, P.K., Rahman, M., Rahman, M., Nabi, A., Islam, Z., Hoque, M.M., et al., 2013. Antimicrobial Resistance, Virulence Factors and Genetic Diversity of Escherichia coli Isolates from Household Water Supply in Dhaka, Bangladesh. PLOS One 8, e61090.
Tong, J.Z., Bhat, Gireesh-Babu, Ge, W.T., 2009. Introduction of design basis, operation date&background for Singsping Sea Water Desalination Plant, Singapore. In: the Third Seminar on Application of Membrane Separation Technology in Metallurgical Industry (in Chinese). Shandong, China, pp. 9–12.
van Dooremalen, W.T.M., Learbuch, K.L.G., Morré, S.A., van der Wielen, P.W.J.J., Ammerdorffer, A., 2020. Limited presence of Waddlia chondrophila in drinking water systems in the Netherlands. New Microbes New Infect 34, 100635.
Voigt, A.M., Ciorba, P., Döhla, M., Exner, M., Felder, C., Lenz-Plet, F., et al., 2020. The investigation of antibiotic residues, antibiotic resistance genes and antibiotic-resistant organisms in a drinking water reservoir system in Germany. Int. J. Hyg. Environ. Health. 224, 113449.
Wan, K., Zhang, M.L., Ye, C.S., Lin, W.F., Guo, L.Z., Chen, S., et al., 2019. Organic carbon: an overlooked factor that determines the antibiotic resistome in drinking water sand filter biofilm. Environ. Int. 125, 117–124.
Wang, H., 2006. Comparison Study of Drinking Water Quality Management in China and France. Tongji University, Shanghai, China.
Wang, J.X., Qi, X.J., Wang, H.T., 2017a. Application situation of natural flocculant and drinking water quality for water supply in some areas of Africa. Water Purif. 36, 35–40.
Wang, R.N., Zhang, Y., Cao, Z.H., Wang, X.Y., Ma, B., Wu, W.B., et al., 2019. Occurrence of super antibiotic resistance genes in the downstream of the Yangtze River in China: prevalence and antibiotic resistance profiles. Sci. Total Environ. 651, 1946–1957.
Wang, S.L., Wang, L., Zhou, H., Wang, Y.J., Xu, M.Y., Zhang, M.L., et al., 2017b. An overview on antibiotic resistance genes in drinking water systems. Environ. Chem. 36, 229–240.
Wang, Z., Han, M.Z., Li, E., Liu, X., Wei, H.M., Yang, C., et al., 2020. Distribution of antibiotic resistance genes in an agriculturally disturbed lake in China: their links with microbial communities, antibiotics, and water quality. J. Hazard. Mater. 393, 122426.
Xi, C., Zhang, Y., Marrs, C.F., Ye, W., Simon, C., Foxman, B., et al., 2009. Prevalence of antibiotic resistance in drinking water treatment and distribution systems. Appl. Environ. Microbiol. 75, 5714–5718.
Xi, H., 2018. Study of the Spatio-Temporal Distribution of Antibiotic Resistance Genes and Related Influential Factors in Typical Urban Water of Shanghai. East China Normal University, Shanghai, China.
Xie, J.W., Jin, L., He, T.T., Chen, B.W., Luo, X.S., Feng, B.H., et al., 2019. Bacteria and antibiotic resistance genes (ARGs) in PM2.5 from China: implications for human exposure. Environ. Sci. Technol. 53, 963–972.
Xu, C.Y., Su, J.Q., Yan, Q.P., Ma, Y., 2011. Research progresses of antibiotic resistomics. Nat. Sci. J. Hainan Univ. 29, 188–192.
Xu, J.L., 2004. British drinking water quality standard and advanced treatment technology (in Chinese). Shanghai Water 02, 39–41.
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.
Yang, Y.X., Shi, W.J., Lu, S., Liu, J., Liang, H., Yang, Y., et al., 2018. Prevalence of antibiotic resistance genes in bacteriophage DNA fraction from Funan River water in Sichuan. China. Sci. Total Environ. 626, 835–841.
Yang, Y., Xu, C., Cao, X., Lin, H., Wang, J., 2017. Antibiotic resistance genes in surface water of eutrophic urban lakes are related to heavy metals, antibiotics, lake morphology and anthropic impact. Ecotoxicology 26, 831–840.
Yao, H., Zhang, S.C., Zhou, X.L., Wang, C.R., 2013. Process design and water purification efficiency of one water treatment plant in America. Chin. J. Environ. Eng. 02, 422–426.

Yoon, Y., Chung, H.J., Wen Di, D.Y., Dodd, M.C., Hur, H.G., Lee, Y., 2017. Inactivation efficiency of plasmid-encoded antibiotic resistance genes during water treatment with chlorine, UV, and UV/H_2O_2. Water Res. 123, 783–793.
Yuan, Q.B., Guo, M.T., Yang, J., 2015. Fate of antibiotic resistant bacteria and genes during wastewater chlorination: implication for antibiotic resistance control. PLoS One 10, e0119403.
Zhang, C.M., Xu, L.M., Wang, X.C., Zhuang, K., Liu, Q.Q., 2017a. Effects of ultraviolet disinfection on antibiotic-resistant Escherichia coli from wastewater: inactivation, antibiotic resistance profiles and antibiotic resistance genes. J. Appl. Microbiol. 123, 295–306.
Zhang, C., Zhang, X., Lv, D.M., Xiao, W.X., 2004. Theoretical research on ultraviolet desinfection. Water Wastewater Eng 30, 21–24.
Zhang, J.Q., Xu, Y., Luo, Y., Mao, D.Q., 2016a. Co-selection mechanisms of bacterial resistance to heavy metals and antibiotics. J. Agro-Environ. Sci. 35, 409–418.
Zhang, K., Xin, R., Zhao, Z., Ma, Y.Z., Zhang, Y., Niu, Z.G., 2020. Antibiotic resistance genes in drinking water of China: occurrence, distribution and influencing factors. Ecotoxicol. Environ. Saf. 188, 109837.
Zhang, M.L., Chen, L.H., Ye, C.S., Yu, X., 2018a. Co-selection of antibiotic resistance via copper shock loading on bacteria from a drinking water bio-filter. Environ. Pollut. 233, 132–141.
Zhang, M., Wang, L., Xu, M., Zhou, H., Wang, S., Wang, Y., et al., 2019a. Selective antibiotic resistance genes in multiphase samples during biofilm growth in a simulated drinking water distribution system: occurrence, correlation and low-pressure ultraviolet removal. Sci. Total Environ. 649, 146–155.
Zhang, N.X., 2010. On water supply in Germany. Shanxi Architecture 36, 161–162.
Zhang, S., Lin, W., Yu, X., 2016b. Effects of full-scale advanced water treatment on antibiotic resistance genes in the Yangtze Delta area in China. FEMS Microbiol. Ecol. 92 fiw065.
Zhang, T.Y., Hu, Y.R., Jiang, L., Yao, S.J., Lin, K.F., Zhou, Y.B., et al., 2019c. 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., Li, X.Y., Wang, M.F., Chen, H.X., Yang, Y., Chen, Q.l., et al., 2019b. Time-resolved spread of antibiotic resistance genes in highly polluted air. Environ. Int. 127, 333–339.
Zhang, Y.J., Liu, W.J., Zhang, L., 2006. Synergistic Disinfection of Bacillus subtilis Spores by UV Irradiation and Chlorine. Environ. Sci. 27, 329–332.
Zhang, Y., Gu, A.Z., Cen, T.Y., Li, X.Y., He, M., Li, D., et al., 2018b. Sub-inhibitory concentrations of heavy metals facilitate the horizontal transfer of plasmid-mediated antibiotic resistance genes in water environment. Environ. Pollut. 237, 74–82.
Zhang, Y., Gu, A.Z., He, M., Li, D., Chen, J., 2017b. Subinhibitory concentrations of disinfectants promote the horizontal transfer of multidrug resistance genes within and across Genera. Environ. Sci. Technol. 51, 570–580.
Zhang, Y., Zhuang, Y., Geng, J., Ren, H., Zhang, Y., Ding, L., et al., 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, X., Ding, M.L., Chen, X.H., Chen, C., 2010. Application of reverse osmosis to Ashkelon seawater desalination project in Israel. Chin. Water Wastewater. 26, 81–84.
Zhao, X., Wang, J.H., Zhu, L.S., Ge, W.L., Wang, J., 2017. Environmental analysis of typical antibiotic-resistant bacteria and ARGs in farmland soil chronically fertilized with chicken manure. Sci. Total Environ. 593-594, 10–17.
Zheng, J., Chen, T., Chen, H., 2018. Antibiotic resistome promotion in drinking water during biological activated carbon treatment: is it influenced by quorum sensing? Sci. Total Environ. 612, 1–8.
Zheng, J., Su, C., Zhou, J., Xu, L., Qian, Y., Chen, H., 2017. Effects and mechanisms of ultraviolet, chlorination, and ozone disinfection on antibiotic resistance genes in secondary effluents of municipal wastewater treatment plants. Chem. Eng. J. 317, 309–316.
Zhu, Y., Chen, W.G., 2013. Application of combined disinfection technology of UV radiation and chlorine in third waterworks in Shiyan city. Chin. Water Wastewater. 29, 56–59.
Zhuang, Y., Ren, H.Q., Geng, J.J., Zhang, Y., Ding, L.L., Xu, K., 2014. Removal of antibiotic resistant genes in municipal wastewater with coagulation method. Chin. J. Environ. Sci. 8, 5105–5110.