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Review

Problems of conventional disinfection and new sterilization methods for antibiotic resistance control

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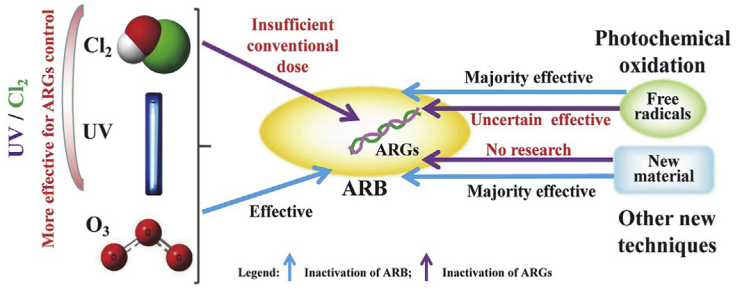
HIGHLIGHTS

- Chlorination was deficient in attaining antibiotic resistance control.
- Main disinfection problem was insufficient control of ARGs.
- Optimizing photochemical oxidation for ARGs is essential.
- UV/chlorine showed greater potential for controlling ARGs.
- Inactivation studies for ARB are inadequate.

GRAPHICAL ABSTRACT



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ABSTRACT

The problem of bacterial antibiotic resistance has attracted considerable research attention, and the effects of water treatment on antibiotic resistant bacteria (ARB) and antibiotic resistance genes (ARGs) are being increasingly investigated. As an indispensable part of the water treatment process, disinfection plays an important role in controlling antibiotic resistance. At present, there were many studies on the effects of conventional and new sterilization methods on ARB and ARGs. However, there is a lack of literature relating to the limitations of conventional methods and analysis of new techniques. Therefore, this review focuses on analyzing the deficiencies of conventional disinfection and the development of new methods for antibiotic resistance control to guide future research. Firstly, we analyzed the effects and drawbacks of conventional disinfection methods, such as chlorine (Cl), ultraviolet (UV) and ozone on antibiotic resistance control. Secondly, we discuss the research progress and shortcomings of new sterilization methods in antibiotic resistance. Finally, we propose suggestions for future research directions. There is an urgent need for new effective and low-cost sterilization methods. Disinfection via UV and chlorine in combination, UV/chlorine showed greater potential for controlling ARGs.

Contents

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1. Introduction

The extensive use of antibiotics has led to the problem of bacterial antibiotic resistance (Calero-Caceres and Muniesa, 2016). Through the expression of antibiotic resistance genes (ARGs) in cells, antibiotic resistant bacteria (ARB) have developed antibiotic resistance by synthesizing the corresponding antibiotic resistant protein (Blair et al., 2015). The molecular mechanisms include prevention of access to target (reduced permeability and increased efflux), changes in antibiotic targets by mutation, modification or protection of targets and direct modification of antibiotics (inactivation of antibiotics by hydrolysis or transfer of a chemical group). Reports showed that in the European Union and the European Economic Area, approximately 33,000 patients died due to infection with ARB in 2015 (Cassini et al., 2019). It was estimated that bacterial antibiotic resistance could cause 10 million deaths and a financial burden of about 100 trillion dollars by 2050 (Sanganyado and Gwenzi, 2019). In 2010, New Delhi metallo-β-lactamase 1 (NDM-1) super-bacteria, which is resistant to almost all antibiotics, was found in India, Britain, Pakistan, and once human beings were infected with these pathogens, the mortality rate was very high (Kumarasamy et al., 2010). Then NDM-1 bacteria has also been detected in Europe, Australia, North America, Africa, and Asia (Moellering, 2010; Chen et al., 2011; Cornaglia et al., 2011; Walsh et al., 2011). Thus, ARGs are regarded as a contaminant of emerging concern in the environment, attracting global attention (Pruden et al., 2006).

ARB and ARGs are widely distributed in surface water, groundwater, sewage treatment plants and other water environments (Gao et al., 2012; Czekalski et al., 2014; Li et al., 2015; Zhang et al., 2015a; Lorenzo et al., 2018). Moreover, ARGs can be transmitted in the aquatic environment through vertical and horizontal transfer mechanisms, including conjugation, transduction and transformation (Dodd, 2012; Qiu et al., 2012). Conjugation is the exchange of ARGs by “mated” pairs between the metabolically active donor and recipient bacterial cells. In contrast, transduction or transformation occurs when the recipient with active metabolism is infected by phage (transduction) or the recipient actively acquires foreign DNA (transformation), and the recipient then incorporates the genes into its chromosome. ARGs can spread between the same or different kinds of bacteria through horizontal transfer and which is the primary mechanism for bacteria to gain antibiotic resistance or even multiple antibiotic resistance. Certain, bacteria can directly acquire free ARGs in the aquatic environment through transformation. Thus, the horizontal transfer of ARGs poses a threat to human health (Finks et al., 2009; Sommer et al., 2009; Dodd, 2012). Although ARGs are harmful to health only when expressed in bacteria to produce corresponding proteins and are considered less of a threat than ARB, the control of ARGs is indispensable.

Water supply and sewage treatment systems should be aimed at ensuring the safety of human water use and maintaining the ecological balance. Although ARB and ARGs are not currently included in water treatment control indicators, the impact of water supply and wastewater treatment processes on ARB and ARGs has attracted extensive attention from researchers (Karkman et al., 2018; Sanganyado and Gwenzi, 2019). Disinfection is the final process to ensure water safety in water treatment, and is aimed at killing pathogenic microorganisms in water. Therefore, disinfection technology plays a significant role in controlling antibiotic resistance (Sharma et al., 2016).

Although the conventional disinfection methods, including chlorine (Cl), ultraviolet (UV) and ozone, remove ARB and ARGs, these methods are limited and do not guarantee effluent safety in terms of bacterial antibiotic resistance (More details were shown later.) (Guo et al., 2015; Zhang et al., 2015b; Alexander et al., 2016). Therefore, researchers hope to establish new sterilization methods to remove ARB and ARGs, such as photocatalysis, new materials, combined disinfection process, which have achieved positive results (Jimenez-Tototzintle et al., 2018; Michael-Kordatou et al., 2018). At present, few studies have summarized the defects of conventional disinfection systems. Sanganyado and Gwenzi (2019) reviewed the impact of specific disinfection methods on antibiotic resistance; their comments on the new sterilization technology were limited, especially in terms of the heterogeneous photocatalysis. They focused on the review of control effects and mechanisms, and disinfection was one part of this review. As such, there was a lack of critique and limited analysis regarding the deficiencies of conventional disinfection and new sterilization technologies. Similarly, Sharma et al. (2016) reviewed control strategies for antibiotic resistance, but did not provide sufficient critique of these strategies, and offered limited comments on disinfection (use of UV/chlorine). Michael-Kordatou et al. (2018) reviewed the effects of advanced oxidation on ARB and ARGs, with a focus on the removal effect and mechanism rather than on the limitations of this method. The review did not evaluate the use of UV/chlorine. Thus, there is an introduction to the shortcomings of conventional disinfection to illustrate the necessity of studying new sterilization technology. In our review, we provide a comprehensive evaluation of the limitations of conventional disinfection in terms of antibiotic resistance control. A thorough understanding of the limitations of conventional and new sterilization techniques is essential to estimate the risk of antibiotic resistance in effluent, and to guide future research.

In this study, the inactivation effect and the mechanism of conventional disinfection methods (Cl, UV, and ozone) on ARB and ARGs are reviewed, and the drawbacks are analyzed. Next, the progress in research into new sterilization methods for antibiotic resistance are discussed, and future research directions are proposed. The UV/chlorine combined disinfection method might be a more potential means of controlling ARGs as it is efficient and low-cost. (The types of water of differenet disinfection are described in Table 2, and Supplementary Information Table S1 and Table S2).

2. Conventional disinfection for antibiotic resistance control

2.1. Chlorination and chloramination

Chlorine is one of the most widely used disinfection methods (Guo et al., 2015). It has a powerful inactivation effect on ARB, but its damage effect on ARGs is considered inadequate (Sharma et al., 2016). The amount of ARB decreased by 3.8–5.6 log with 0.5 mg/L (30 min) free chlorine, while ARGs only decreased by 0.8–2.8 log, which indicated that the inactivation effect of chlorine on ARB was significantly higher than that of ARGs. With a reduction in the chlorine dosage, the ARGs removal efficiency decreased. (Stange et al., 2019). In one study, chlorine disinfection [631–710 (mg·min) Cl_2/L] increased the abundance of extracellular ARGs (eARGs) by up to 3.8 times and intracellular ARGs (iARGs) by 7.8 times (Liu et al., 2018). The removal effect of free chlorine on ARGs was stronger than that of chloramine. As a result, when there is higher ammonia nitrogen in the water, the formation of chloramine reduces the free chlorine , which is not conducive to ARGs removal (Yoon et al., 2017). The chlorine disinfection thus had a limited effect on ARGs removal. The chlorine inactivation kinetics (pH = 7) also showed that the chlorine inactivation rate of ARGs [$k = 1.0 (\pm 0.1) \times 10^{-1}$–$3.1 (\pm 0.2) \times 10^{-1}$ L/(mg × min)] was evidently lower than that of ARB [$k = 8.7 (\pm 0.9) \times 10^{1}$ L/(mg × min)] and cell membrane [$k = 3.8 (\pm 0.5) \times 10^{1}$ L/(mg × min)] (Yoon et al., 2017). This indicates the limitation of chlorine in controlling ARGs, and similar conclusions have been reached in other studies (Yuan et al., 2015; Furukawa et al., 2017).

Jia et al. (2015) indicated that chlorine disinfection could lead to changes in bacterial communities, and noticeably increase the total relative abundance of 15 ARGs types (including multidrug, bacitracin, aminoglycoside, sulfonamide, M-L-S, chloramphenicol, β-lactam, tetracycline, polymyxin, fosmidomycin, vancomycin, trimethoprim, quinolone, fosfomycin, and others). Chlorine-resistant bacterias carry multiple resistance genes and are the dominant species in chlorine disinfection, increasing the abundance of ARGs. This indicates that the use of chlorine in disinfection is inadequate. A low dose of chlorine (up to 4 mg Cl_2/L) within 10 min significantly increased the frequency of ARGs conjugation transfer by 2–5 times, and only when the chlorine dose was as high as 8 mg Cl_2/L within 10 min, the chlorine disinfection inhibited ARGs conjugation transfer by inactivating a large number of bacteria (Guo et al., 2015). However, the disinfection CT values do not reach 80 mg Cl_2 min/L in many water treatment plants. Another study showed that 3–30 mg Cl_2 min/L free chlorine and 3–30 mg Cl_2 min/L chloramine increased the conjugative transfer frequency by 3.4–6.4 and 1.9–7.5 folds, respectively, and no transconjugants were detected with exposure to 300 mg Cl_2 min/L free chlorine and 300 mg Cl_2 min/L chloramine (Zhang et al., 2017). The low-dose oxidant could not kill ARB completely, while the reactive oxygen species (ROS) produced increased the permeability of the bacterial cell membrane, which made it easier to establish the gene transfer channel between the donor and the recipient bacteria through the pilus. At the same time, the gene expression involved in the conjugation transfer increased, and the corresponding protein synthesis increased, promoting conjugation transfer. Some ARB may regenerate and reactivate in the secondary wastewater after chlorine disinfection. The ARB was treated for 10 min with 2.0 mg Cl_2/L, and the resuscitation rate of chloramphenicol-resistant bacteria was greater than 50% (Huang et al., 2011). The ARB resuscitation might threaten the safety of the wastewater. The drug efflux pump is a type of protein in the bacterial cell membrane, through which bacteria can pump intracellular antibiotics out of the cell, reducing the drug concentration in the cell and causing antibiotic resistance. Overexpression of the efflux pump would increase the synthesis of these proteins and enhance the antibiotic resistance of bacteria (Blair et al., 2015). Culturable chlorine-damaged *Pseudomonas aeruginosa* produced by chlorine disinfection could overexpress the efflux pump mechanism under oxidative stress, thus enhancing its resistance to antibiotics. Under the action of 4 mg/L sodium hypochlorite (half lethal dose), the resistance of *Pseudomonas aeruginosa* to ceftazidime, chloramphenicol and ampicillin increased by 1.4–5.6 times (Hou et al., 2019). Thus, chlorine disinfection under specific conditions might improve the resistance of ARB to antibiotics and harm human health.

In summary, chlorine has limited removal effects on ARB and ARGs, and main five aspects are summarized in Fig. S1. The chlorine disinfection has a weak removal effect on specific bacteria, such as chlorine-resistant ARB, and increases the relative abundance of ARGs. The chlorine disinfection (especially chloramine) has an inferior removal effect on ARGs ARB, and there is abundant ARGs residues after chlorine disinfection. The chlorine dose in most water treatment plants is insufficient, which may increase the horizontal transfer frequency of ARGs in water. The regeneration and reactivation of bacteria after chlorine disinfection threatens the safety of wastewater. The oxidative stress induced by chlorine disinfection can lead to overexpression of the antibiotic resistance mechanism of ARB, and temporarily improve the antibiotic resistance of ARB. In general, the control of ARGs using chlorine is not adequate.

2.2. UV

UV radiation has been used for disinfection due to its broad-spectrum sterilization ability. However, due to complex and diverse substances in the treated water and economic restrictions, the dosage of UV dose not guarantee the complete inactivation of ARGs. Moreover, UV has no lasting residual disinfection ability, and there may be photoreactivation and dark repair, limiting the effectiveness of this disinfection method.

Table 1 lists the removal effects of UV on ARB and ARGs. The removal effect of UV on ARB was much stronger than that of ARGs. There was effective removal of ARGs only when the dose of UV exceeded 100 mJ/cm^2. With a UV dose of less than 100 mJ/cm^2, the ARB removal rate (>2 log), but the ARGs removal rate was inadequate (<2 log). increasing the ARGs residues in the effluent of the wastewater plants. The residual ARGs could enter pathogenic microorganisms through transformation and transduction in the water environment, posing a threat to human health.

UV has a significant inactivation effect on various ARB, but this effect is selective. UV disinfection led to a reduction in the abundance of bacteria resistant to erythromycin, cefalexin, gentamicin and ciprofloxacin, while the proportion of ARB resistant to rifampicin, sulfadiazine, vancomycin, tetracycline, and chloramphenicol increased in the wastewater (Guo et al., 2013). This indicates that UV may lead to an increase (2%–28%) in the abundance of specific ARB. UV (<10 mJ/cm^2) could remove some ARB, but the horizontal transfer frequency of ARGs did not change significantly. The ARGs horizontal transfer was inhibited only when the UV dose exceeded 10 mJ/cm^2(Guo et al., 2015). Due to the complexity of substances in

Table 1
Inactivation of ARGs by UV.

Target ARB	Target ARGs	UV dose (mJ/cm^2)	ARB log inactivation	ARGs log inactivation	Reference
E.coli, *E. faecium*	*tetA, ampC, ermB, vanA*	60	4.8−5.5	0−1.0	Stange et al. (2019)
E.coli *P. aeru- ginosa*	*tetA, bla- TEM1, sul1, mph(A)*	3−200	3.8−6.6(3−7 mJ/cm^2 UV dose)	0.1−1.2 (20−200 mJ/cm^2 UV dose)	Destiani and Templeton (2019)
E.coli	*tetA, sul1, bla- TEM* et al.	20−400	4.2−6.0 (20−80 mJ/cm^2 UV dose)	0.3−2.4 (40−400 mJ/cm^2 UV dose)	Zheng et al. (2017)
Methicillin-resistant S. aureus (MRSA), vancomycin resistant Enterococcus faecalis (VRE), E. coli, P. aeru- ginosa	*ampC, mecA, tetA, vanA*	10−400	0.2−5.0 (10−20 mJ/cm^2 UV dose)	0.5−3.2 (50−400 mJ/cm^2 UV dose)	McKinney and Pruden (2012)

the treated water, a larger dose of UV is usually required, but most wastewater plants do not meet this requirement (Guo et al., 2015). The viable but non-culturable (VBNC) bacteria is a group of bacteria that has some biological activities, but do not grow, reproduce, or form colonies by conventional culture methods. Photoreactivation is that UV forms cyclobutane pyrimidine dimers in DNA, which blocks the normal replication of genes, leading to the inactivation of bacteria. However, during photoreactivation, the lysozyme in bacteria can reactivate the inactivated bacteria under the action of far ultraviolet or visible light. When the DNA of cells exposed to ultraviolet light is repaired without the reaction of visible light, and the proliferation ability is restored, this is referred to as dark repair. VBNC bacteria produced after UV disinfection could be reactivated by photoreactivation and dark repair, and could maintain the same horizontal transfer ability as those of non-UV disinfected bacteria (Guo and Kong, 2019). This indicates that UV disinfection has no lasting residual disinfection ability, and there can be bacterial resurrection. Thus, UV disinfection does not guarantee the safety of the treated effluent.

Above all, although the mechanism of UV disinfection is damage to DNA, the inactivation effect of UV on ARGs was much lower than that of ARB. At present, the effective dosage of UV (<10 mg/L) used in some water plants is insufficient to control ARGs and their transfer (Guo et al., 2015). The selectivity of UV disinfection to ARB and ARGs might lead to an increase in specific ARB ratios. Furthermore, the problems of photoreactivation and dark repair associated with the use of UV might lead to the reactivation of ARB. Therefore, there is a need for new sterilization technologies to ensure the safety of the treated effluent.

2.3. Ozonation

As a strong oxidant (Hembach et al., 2019), ozone sterilizes completely through acteriolysis (at a sufficient dose), has no residue, no photoreactivation and no dark repair. It is globally recognized as a green, broad-spectrum and efficient disinfectant. However, because of the high cost and lack of lasting disinfection effect, it is seldom used for disinfection in large water treatment plants. There are few studies on the effects of ozone on bacterial antibiotic resistance, so there is only a brief introduction and analysis.

Zhuang et al. (2015) reported that, during ozonation, ARGs removal efficiency was lower than that of *16S rDNA* (*intI1* < *sul1* < *tetG* < *16S rDNA*) during ozonation, increasing the relative abundance of ARGs. The ARGs were reduced by 1.68−2.55 log from 177.6 mg/L O_3 complete response disinfection. This indicates that completely removing ARGs requires very high doses of ozone (over 177.6 mg/L). Another report showed that 50 mg/L O_3 might reduce ARB by 4.0 log, *16S rDNA* by 2.1 log, *intI1* by 2.0 log, *blaTEM* and *qnrS* approach the limit of quantity, while *vanA* and *sul1* reductions were reduced below the limit of detection. Moreover, all the ARB and ARGs, except for *qnrS*, reached pretreatment levels after 3 days of storage (Sousa et al., 2017). Conventional clarification wastewater was treated using ozone (0.9 g/g DOC). The test results showed that a strong removal effect for ARB was achieved, and *ermB* was reduced by 2.0 log, while the abundance of *vanA* and *blaVIM* increased (Alexander et al., 2016), which indicated that a lower concentration of ozone had particular selectivity for ARGs.

Ozone removed both ARB and ARGs, but there was insufficient removal of certain ARGs. The required dosage of ozone for ARGs removal exceeded 177.6 mg/L. After analysis, the cost of ARGs removal by ozone disinfection was much higher than chlorine disinfection. When the chlorine dose was 40 mg/L and the exposure time was 60 min, the inactivation efficiency of ARGs could reach 1.65−2.28 log, and the cost was high enough (0.041 yuan/m^3) (Zhuang et al., 2015). Therefore, it is unrealistic to use ozone disinfection in large water plants to control antibiotic resistance. Ozone disinfection required a CT value of 31 and 33 mg min/L for 2 log ARB and ARGs reduction respectively, while Ozone with persulfate required 15.9 and 18.5 mg min/L and ozone with monopersulfate needed 12 and 14.5 mg min/L (Oh et al., 2014). It is possible to improve disinfection efficiency and to reduce cost by using ozone combined with other materials for advanced oxidation disinfection, which could become the direction of future research.

3. New sterilization methods for antibiotic resistance control

The results of the analysis show that widely used conventional disinfection methods (chlorine, UV and ozone) might not adequately control the risk of bacterial antibiotic resistance in water treatment. Many researchers hope to find new and more efficient disinfection methods to remove ARB and ARGs. Recently, research is focusing on novel nano-materials and photochemical oxidation technology (including photocatalytic oxidation and photo-induced oxidation) with strong oxidation ability (The effects of photochemical oxidation on ARB and ARGs are shown in Table 2). Moreover, the combination of UV/chlorine is more widely accepted by researchers due to the effectiveness of sterilization.

3.1. Photocatalytic oxidation

Photocatalytic oxidation includes homogeneous and heterogeneous photocatalysis. Homogeneous photocatalysis refers to the reactants in the same phase, either gas, liquid or solid. In contrast, heterogeneous photocatalysis occurs the reactants that are not in the same state and the reaction process occurs at the interface (Michael-Kordatou et al., 2018).

Heterogeneous photocatalysis mainly inactivates ARB by producing free radical and ROS (Sunada et al., 2003) which attack the cell membrane and wall (Gogniat et al., 2006), damage the DNA

Table 2
Effects of photochemical oxidation on ARB and ARGs [Adapted from Michael-Kordatou et al. (2018)].

Reaction conditions	Water for reaction	Target ARB/ARGs	Results	Reference
Heterogeneous photocatalysis				
P25 TiO_2 (0.05−2 g/L); time: 10 −60 min three light sources : (i) a wide spectrum 250 W lamp, (ii) the same lamp equipped with a filter to simulate solar radiation, and (iii) a 125 W black light fluorescent lamp.	Wastewater samples from the effluent of the biological treatment process.	*E. coli* resistant to: ciprofloxacin, cefuroxime, tetracycline, vancomycin.	99.76% ARB reduction after 10 min 250 W lamp irradiation at 0.10 g/L TiO_2.	Rizzo et al. (2014a)
P25 TiO_2 (0.0625 and 0.125 g/L); time: 15−80 min; UVA irradiation (400 μW/cm2 and 800 μW/cm2).	90 μL bacterial culture [Luria-Bertani (LB) broth, Tryptic Soy Broth, or Mueller Hinton broth] mixed with 30 μL of TiO2 suspensions.	Methicillin resistant *S.aureus* (MRSA), multi-drug resistant *Acinetobacter baumannii* (MDRAB), and vancomycin resistant *Enterococcus faecalis* (VRE).	1-3 log ARB reduction by TiO_2 in the presence of UVA.	Tsai et al. (2010)
Synthetic anatase TiO_2 thin films loaded on quartz plates; UV_{254} (6, 12, 120 mJ/cm^2).	Phosphate-buffered saline solution (PBS), and nature water sampled from drinking water source in Beijing	MRSA, multi-antibiotic resistant *Pseudomonas aeruginosa; mecA, ampC.*	4.5−5.0 log ARB reduction with 6 or 12 mJ/cm^2 UV, and 5.5−5.8 log ARGs reduction with 120 mJ/cm^2 UV.	Guo et al. (2017a)
Photocatalytic ozonation (P25 TiO_2-coated glass Raschig rings); time: 0−180 min; ozone at a constant inlet concentration (50 g N/m^3); two 10 W LEDs (λ = 382 nm);	Wastewater samples collected after activated sludge biological treatment, and surface water	Total heterotrophs, *Enterococcus*, and *Enterobacteria*, resistant to ciprofloxacin, gentamicin, meropenem; *sul1, qnrS, blaTEM, intl1*	ARB, *16S rDNA*, fungi and *intl1* increased to pretreatment level after 3 days, except the ARGs (*blaTEM, qnrS and sul1*)	Moreira et al. (2016)
P25 TiO_2 (1.0 g/L); time: 60 min; 4 UVA LEDs (9W).	Wastewater collected from the effluent of the secondary settling tank.	*E. coli* and *Enterococci* resistant to azithromycin, trimethoprim, ofloxacin, sulfamethoxazole.	Approximately 2.0 log ARB reduction, the value of ARB increased to pretreatment level after 3 days	Biancullo et al. (2019)
Aeroxide P25 TiO_2, immobilized TiO_2 stirred tank reactor; time: 180 min; UVA (9 W, λ = 370 nm, 80 W/m^2).	Distilled water and autoclaved secondary effluent from wastewater plant	*E. coli* resistant to rifampicin and chloramphenicol.	Reduced 2.5 ARB by 2.5 log, increased Gene pair conjugant numbers by four times, the value of ARB increased to pretreatment level after 24 h.	Dunlop et al. (2015)
Nitrogen (N) -doped TiO_2 (0.025 and 0.5 g/L); time: 10−60 min; natural or simulated solar irradiation (250 W).	Wastewater samples were taken from the effluent of the biological process (activated sludge).	*E. coli* resistant to ciprofloxacin, cefuroxime, tetracycline, vancomycin.	Total inactivation of ARB reached within 60 min irradiation under optimum photocatalyst capacity (0.2 g/L).	Rizzo et al. (2014b)
P25 TiO_2 modified polyvinylidene fluoride (PVDF, with a molecular weight cutoff of 100 kDa) membrane; time: 60 min; UV_{254} (12 μW/cm^2).	Secondary wastewater effluent prefiltered through filter paper (pore size of 80−120 μm) to remove large particulates and suspended matters.	Heterotrophic bacteria resistant to chloramphenicol, tetracycline, and sulfadiazine; *floR, tetC , tetW, tetQ, sul1, sul2, intl1 , intl2,* and *intl3.*	Completely intercept ARB; reduced ARGs by ~98%.	Ren et al. (2018)
Mn- and Co-doped P25 TiO_2 (0.04 wt% Mn/Co:TiO_2); time: 30 −90 min; natural or simulated solar irradiation (150 W).	Wastewater inoculated with *K. pneumoniae* cells	*K. pneumonia* resistant to, ampicillin, cefaclor, sulfamethoxazol, tetracycline; *tetA*, *tetM*, *sul1*, *blaTEM*, and *ampC.*	Reduced ARB by 4−6 log with 90 min; resistance of surviving cells after treatment remained at high levels, reflecting the abundance of the corresponding target ARGs.	Venieri et al. (2017)
TiO_2-reduced graphene oxide (0.10 g/L); time: 60−180min laboratory-scale solar simulator (63 W/m^2).	Real MBR-treated wastewater effluent.	*E. coli* resistant to sulfamethoxazole, erythromycin, clarithromycin; *sul1*, *ampC*, *ermB, mecA* and *ecfX.*	Complete bacterial inactivation was observed after 120 min of treatment; no *E. coli* regrowth observed after 180 min; removed *ampC* and *ecfX* by 0.5−2.3 log but not sul1, *ermB* and *23S rRNA* genes.	Karaolia et al. (2018)
Cerium-doped zinc oxide (Ce−ZnO) photocatalyst in the immobilized form on a metallic support (0.04:1 Ce:Zn atom-to atom ratio); time: 180 min; two Osram Dulux®L BL UVA 18W/78.	Wastewater from the secondary clarifier of an urban wastewater treatment plant (UWWTP); 0.85% physiological saline.	*E. coli* resistant to ofloxacin and azithromycin; *Pseudomonas aeruginosa* resistant to ofloxacin and ciprofloxacin.	Reduced ARB by up to 4.0 log with 38 cm^2 photocatalyst coated discs and 36 W UVA.	Zammit et al. (2019)
Titanium Tetraisopropoxide (TTIP) based thin-film coated photocatalyst immobilized with parallel plate reactor (PPL); time: 180 and 240 min; UVA (0.90 mw/cm^2).	0.8% physiological saline.	*E. faecalis, E. coli and* resistant to ampicillin, cefaclor, clarithromycin - erythromycin and amikacin.	Reduced *E. faecalis* by 99% removal after 180 min and 99.9% removal after 240 min.	Ozkal et al. (2019)
Metal-free photocatalyst graphitic carbon nitride (g-C_3N_4) (5 g/L); time: 60 min; UVA (15.23 mW/cm^2) and visible light (131.74 mW/cm^2)	Wastewater from secondary effluents of wastewater treatment plant (WWTP), and PBS. 0.9% physiological saline.	Heterotrophic bacteria resistant to ciprofloxacin, norfloxacin, ofloxacin, and sulfamethoxazole.	Reduced ARB by up to 1.26 log.	Ding et al. (2019)

(*continued on next page*)

Table 2 (*continued*)

Reaction conditions	Water for reaction	Target ARB/ARGs	Results	Reference
Tetrapodal zinc oxide (T-ZnO) photocatalyst (1 g/L); time: 3 −12 h; UVA (4W, λ = 365 nm)		*E. coli* resistant to ampicillin; *Amp* in pUC19 plasmid.	ARB was inactivated up to 94% after 3 h and most ARB was inactivated after 12 h, the pUC19 plasmids in inactivated *E. coli* were not damaged, based on the results of gel electrophoresis.	Hwangbo et al. (2019)
Homogeneous photocatalysis				
Fe^{2+}/H_2O_2 was 0.033, 0.05, 0.067, 0.1, 0.2 and 0.5, pH = 3 and 7; time: 120 min; dark Fenton.	Wastewater from secondary effluents.	*sul1, tetX, tetG, intI1.*	With increasing Fe^{2+}/H_2O_2 molar ratio from 0.033 to 0.1, ARGs removal increased considerably; at pH = 3 and 7, the removals of *sul1* was 3.8 and 3.2 respectively.	Zhang et al. (2016)
Fe^{2+} (5 mg/L), H_2O_2 (50 mg/L), pH = 2.8; time: 240min; natural solar irradiation.	Wastewater from membrane bioreactor (MBR) effluent.	*E. coli*, *P. aeruginosa* and *Klebsiella* spp. resistant to erythromycin, clarithromycin, sulfamethoxazole; *ermB, sul1, mecA, ampC, Enc, ecfX.*	Reduced most ARB after 240 min; total DNA concentration was reduced by 97%, but *sul1* and *ermB* were still present after treatment.	Karaolia et al. (2017)
Photo-induced oxidation				
H_2O_2 (0.5 mmol/L), UVA (250W, λ = 340−450 nm), Time:45 min.	Surface water samples collected from the Tusciano river.	*E. coli* resistant to ciprofloxacin, ampicillin, and tetracycline.	Reduced ARB by 6 log with 45 min.	Miranda et al. (2016)
H_2O_2 (0.01 mol/L), UVC (16W, λ = 254 nm), Time:45 min.	Wastewater from secondary effluents.	*sul1, tetX, tetG, intI1.*	1.9 log 16 S rDNA, 2.0 log intI1, 2.3 log tetX, 1.7 log tetG and 1.6 log sul1 reductions were achieved.	Zhang et al. (2016)
H_2O_2 (20 mg/L), solar light (Q_{uv} = 40 kJ/L)	Wastewater from secondary effluents.	*Fecal coliforms* and *Enterococci* resistant to tetracycline and ciprofloxacin; *intI1* , *qnrS* , bla_{CTX-M} , *sul1* , bla_{TEM} and *vanA.*	Reduced ARB by up to 5.0 log, ARGs log average reduction of 1 value, except for bla_{CTX-M} (3 log reduction), ARB and ARGs (except bla_{CTX-M} and bla_{TEM}) increased to pre-processing level after 3 days.	Moreira et al. (2018)
UVA (250 W, λ = 320−450 nm, 0 -2.5×10^4 μW s/cm^2), H_2O_2 (20 mg/L).	Wastewater from secondary effluents.	*E. coli* resistant to ampicillin, ciprofloxacin, and tetracycline; bla_{TEM}, *qnrS, tetW.*	Removed almost all ARB and iARGs within 90 min; but eARGs remained.	Ferro et al. (2016)
Peracetic acid (PAA) (0.075−20 mg/L), sunlight (Within 30 min), UVC (33.7 W/m^2 for Wastewater, 99.7 W/m^2 for groundwater)	Wastewater taken after biological process and groundwater from a borehole.	*E. coli* resistant to sulfamethoxazole.	1 and 2 mg/L PAA reduced ARB by 4 and 5 log respectively after 15 min sunlight; total ARB inactivation was achieved in a few minutes for 0.15 mg/L PAA (2 min UVC) and 0.2 mg/L PAA (4 min UVC).	Rizzo et al. (2019)
Peroxymonosulfate (PMS, 1 −20 mg/L), time: 30 min, UVC (100 μW/cm^2).	PBS.	*Pseudomonas* sp. resistant to sulfonamide; *sul1* and *intI1.*	1 mg/L PMS removed 5.3 log ARB, 20 mg/L PMS removed 2.9 log *sul1* and 3.4 log *int.*	Hu et al. (2019)

(Dalrymple et al., 2010), lead to lipid peroxidation (Alrousan et al., 2009), oxidation of proteins and polysaccharides (Malato et al., 2009), and increases cell membrane permeability (Kambala and Naidu, 2009), causing substances to flow out of the cells. TiO_2 is the most widely used catalyst in heterogeneous photocatalysis. TiO_2 photocatalysis could effectively prevent ARB from entering the water environment and improve disinfection (Rizzo et al., 2014a). Suitable operating conditions to optimize photocatalysis inactivation efficiency are required. For example, optimizing the optical thickness of the reactor would could improve the disinfection rate. Optical thickness was introduced to explain the rates of disinfection (Rizzo et al., 2014a). When the photocatalyst loading was 0.1 g TiO_2/L, and the thickness was close to 6 (Puma and Brucato, 2007), the highest photocatalytic activity and inactivation rate (99.76%) of *E.coli* was achieved. TiO_2 with UVA effectively removed antibiotic resistant microbes 1−3 log in suspension (Tsai et al., 2010). Based on the strong inactivation ability of photocatalysis to ARB, studies on ARGs have emerged. TiO_2 photocatalysis with UVC could effectively remove ARB and ARGs (including eARGs and iARGs) approximately 4.5−5.0 log and 5.5−5.8 log respectively (Guo et al., 2017a). The ARB reduction was achieved by TiO_2 photocatalysis using 6 or 12 mJ/cm^2 UVC, but 4.7 log *ampC* and 5.8 log *mecA* reduction were accomplished with 120 mJ/cm^2 UVC dose. However, this UV dose is too high for conventional water supply and wastewater plants.

Some studies indicate the deficiencies of TiO_2 photocatalysis for antibiotic resistance control. Immobilized TiO_2 with UVA-LED photocatalytic ozonation was used to remove micro-pollutants, ARB and ARGs, but ARB (resistant to gentamicin, ciprofloxacin and meropenem), *16S rDNA*, fungi and *intI1* increased to pretreatment levels after 3 days, except the ARGs (*blaTEM*, *qnrS* and *sul1*) (Moreira et al., 2016). Another study showed that TiO_2-photocatalytic treatment with UVA-LEDs effectively removed antibiotics and ARB, but ARB increased to pretreatment level after 3 days (Biancullo et al., 2019). Similarly, Dunlop et al. (2015) found that TiO_2 photocatalytic disinfection (PCD) could effectively inactivate ARB, but there was ARB revival after disinfection. Moreover, the horizontal transfer frequency of ARGs increased by PCD over 180 min. Only when PCD has completely deactivated ARB can the regeneration of ARB and horizontal transfer of ARGs be inhibited. Overall, the UV dose, the reactivation of ARB and horizontal transfer control are problems that must be addressed in terms of TiO_2 photocatalysis.

Based on the research of TiO_2 photocatalysis, more complex photocatalysts have been synthesized to improve photocatalytic efficiency. It was reported that the synthesized N-doped TiO_2 photocatalyst could be used for photocatalytic disinfection under sunlight. Using the optimum photocatalyst capacity (0.2 g/L) the

kinetic experiments showed that total inactivation of ARB could be reached with 60 min irradiation (Rizzo et al., 2014b), and this could be successfully applied in small UWWTPs. In the same way, a TiO_2-modified polyvinylidene fluoride (PVDF) membrane could completely intercept ARB and showed significant photocatalytic deactivation of integrons and ARGs. The ARGs (*floR*, *sul1*, and *sul2*) removal rate of the membrane under UV was close to 98%, and the ARGs removal efficiency in the genome was higher than that in the plasmid (Ren et al., 2018). The membrane could also effectively inhibit the conjugative transfer of ARGs. Furthermore, the TiO_2-modified PVDF membrane antifouling performance was sufficient, and this method could be used in wastewater treatment.

Synthetic photocatalysis also has limitations in terms of bacterial antibiotic resistance control. Mn- and Co-doped TiO_2 photocatalysis is an effective disinfectant (Venieri et al., 2017), and it inactivats ARB 4–6 log under simulated sunlight conditions, but ARB resistance to antibiotics increased after disinfection. Another study found that composite photocatalysts using TiO_2-reduced graphene oxide (TiO_2-rGO) (under solar radiation) had a significant removal effect on antibiotics and ARB, and the ARB would not regenerate within 24 h after the reaction time, which exceeded 180 min (Karaolia et al., 2018). However, TiO_2-reduced graphene oxide could only remove *ampC* and *ecfX* of *Pseudomonas aeruginosa* effectively, and had no inactivation effect on other ARGs. Those all showed that the inactivation effect of the photocatalytic material on ARGs was minimal and the safety of the treated effluent cannot be guaranteed in terms of antibiotic resistance.

The effect of photocatalysis on antibiotic resistance is disputed in various studies. Photocatalysis with UVC ($\lambda \approx 254$ nm) (Guo et al., 2017a) was more effective for ARGs inactivation due to the stronger DNA damage, and photocatalysis with UVA (Biancullo et al., 2019) under certain conditions was not sufficient for antibiotic resistance control, which might partly be due to the stronger DNA damage of UVC itself. Thus, treatment effects vary across photocatalytic materials and parameters. The efficiency of PCD can be improved by optimizing reaction parameters and synthesizing more efficient materials.

Besides TiO_2, there are other photocatalytic materials used to control bacterial antibiotic resistance. Ce–ZnO (Zammit et al., 2019), immobilized photocatalysis with parallel plate reactor (PPL) (Ozkal et al., 2019) and graphitic carbon nitride (metal-free photocatalyst, g-C_3N_4) (Ding et al., 2019) all showed inactivation ability to ARB. However, there is no research on their impact on ARGs. Drug-resistant *E. coli* were inactivated under low intensity UV within 6 h by ZnO-assisted photocatalytic degradation (Hwangbo et al., 2019), but plasmids containing ARGs were still not removed and a higher UV dose was needed to damage the plasmid DNA (pUC19) structure. More attention should be paid to new photocatalytic materials disinfection for ARGs.

Overall, heterogeneous photocatalysis can remove ARB, but the inactivation effect of ARGs is controversial. The removal of micropollutants, ARB and ARGs, is influenced by various parameters. Current research results indicate that there are challenges in removing multiple pollutants simultaneously using heterogeneous photocatalysis (Moreira et al., 2016; Karaolia et al., 2018; Biancullo et al., 2019). Specific synthetic materials under specific conditions had better removal effects on specific pollutants, but the removal effect on other contaminants might be insufficient. Therefore, to control antibiotic resistance, it is essential to find the specific materials and appropriate parameters for ARGs control. In addition, ARB regeneration needed to be considered.

Homogeneous photocatalysis, is mainly the photo-Fenton method. Photo-Fenton is a kind of advanced oxidation technology, which produces a series of free radicals such as ·OH with high reaction activity through the interaction of a catalyst, hydrogen peroxide, and light, to remove organic pollutants in water by oxidation (Du et al., 2020). The ROS is a single electron reduction product of oxygen in vivo, generated by the electron leaking out of the respiratory chain and consuming about 2% oxygen before the electron is transferred to the terminal oxidase, including $O2\cdot^-$, H_2O_2, and ·OH (Sun et al., 2019). Photo-Fenton can also produce ROS on bacteria (Anjem and Imlay, 2012) to destroy cell structure (Diao et al., 2004), and damage DNA (Giannakis et al., 2016a, 2016b), base or ribose moieties (Imlay, 2015). Solar light and solar photo-Fenton effectively inactivated ARB, while solar photo-Fenton was more effective, and sufficient time disinfection could inhibit ARB regeneration (Giannakis et al., 2018). A reduction in ARGs (2.3–4.6 log) was achieved by Fenton oxidation, and many parameters, such as pH, H_2O_2 concentration, Fe^{2+}/H_2O_2 molar ratios and reaction time, could influence the target genes removal (Zhang et al., 2016). However, the membrane bioreactor using solar Fenton oxidation had a significant removal effect on antibiotics, ARB and total DNA. In contrast, the removal effect on ARGs (*sul1* and *ermB*) was insufficient (Karaolia et al., 2017).

There is less research on the ARG removal effectiveness of the Fenton method. The Fenton method had better removal effect on ARGs in the absence of a light source. There are significant differences between various reaction systems. Thus, further research into the effect of Fenton and photo-Fenton on ARGs removal is needed.

3.2. Photo-induced oxidation (UV or solar light source)

Photo-induced oxidation mainly includes H_2O_2/UV and solar-H_2O_2. It inactivates bacteria due to UV self-sterilization (Eischeid et al., 2009) and H_2O_2 oxidation (minimal) (Lee et al., 2015). Free radicals, produced by advanced oxidation processes (AOPs), blocks DNA replication through strong oxidation (Michod et al., 2008). Miranda et al. (2016) found that the heterogeneous photocatalytic process was much slower than the H_2O_2/UV process (UVA), and a 6.0 log reduction in ARB was achieved with 45 min treatment. Zhang et al. (2016) also indicated that 1.9 log *16S rDNA*, 2.0 log *intI1*, 2.3 log *tetX*, 1.7 log *tetG* and 1.6 log *sul1* reductions were achieved by the UV/H_2O_2 (UV_{254}) process. Some different points were put forward. A highly dispersed nanometer TiO2 with an average particle sizfe of 25 nm (P25) was produced by Degussa in Germany (Moreira et al., 2018). It was reported that photo-Fenton, solar-H_2O_2, and heterogeneous photocatalysis all effectively removed ARB and ARGs, and among these, P25/H_2O_2 and solar-H_2O_2 were the most effective treatments to reduce ARGs abundance. However, the abundance of ARGs would increase to pretreatment levels after 3 days (Moreira et al., 2018). Similarly, iARGs were removed by UV/H_2O_2 ($\lambda = 320–450$ nm), but eARGs could not be effectively reduced, cauing ARGs to be released into the water environment after bacterial death and increasing the risk of ARGs transfer (Ferro et al., 2016). Thus, UV/H_2O_2 (UV_{254}) removal of ARGs (1.9 log average reduction) was much better than UV/H_2O_2 ($\lambda = 320–450$ nm) (<1.0 log average reduction) and solar-H_2O_2 (1.0 log average reduction). This could be attributed to the more significant damage to DNA by UV_{254}. The inactivation effect of photo-induced oxidation (with H_2O_2) on ARGs partly depends on the light source. Although $UV_{320\text{-}450}$ might achieve greater removal of organic pollutants (Li et al., 2019), its removal effect on ARGs is insufficient. The removal effect of solar light source was also inadequate, and the parameters need to be optimized.

In addition to H_2O_2, other materials have been used in photo-induced oxidation. It was reported that photo-driven (solar and UVC) advanced oxidation process (AOP) using peracetic acid (PAA) had significant inactivation efficiency in terms of ARB, but the reaction parameters for the simultaneous removal of ARB and antibiotics must be optimized (Rizzo et al., 2019). The UVC-activated

peroxymonosulfate (UVC/PMS) process was used to remove sulfonamide antibiotic resistant bacteria. Within 30 min, 100 μW/cm^2 UVC/1 mg/L PMS removed 5.3 log ARB with an initial concentration of 10^8 CFU/mL, but UVC (100 μW/cm^2)/PMS (20 mg/L) was needed to inactivate 2.9 log *sul1* and 3.4 log *int1* (Hu et al., 2019). The study indicated that the removal of ARGs by UVC/PMS was less effective than that of ARB, but more effective than using UVC alone (Hu et al., 2019). However, another study indicated that H_2O_2/UVC, PMS/UVC and PMS/Fe(II)/UVC showed less effective removal of ARGs compared to using UVC alone. It could be ascribed that the competition between oxidants and DNA in UV photon absorption could reduce the direct DNA photolysis (Rodriguez-Chueca et al., 2019).Different test parameters, test ARB and test ARGs might lead to different results. More in-depth research is needed in this regard.

As summarized in Fig. S2, photochemical oxidation (photocatalytic and photo-induced oxidation) had a significant inactivation effect on ARB, and sufficient disinfection time could avoid ARB regeneration. However, the removal of ARGs varied based on the different materials and methods used. Some synthetic photocatalytic materials effectively inactivate ARGs. The simultaneous and effective removal of micro-pollutants (such as antibiotics), ARB, and ARGs is challenging, pointing to the need for separation and individual treatment. The control of ARGs must be considered in photochemical oxidation disinfection to reduce the risk of antibiotic resistance. More cost-effective, specific, and efficient materials for gene control must be developed to reduce ARGs and their transfer in the water environment.

3.3. UV/chlorine

UV/chlorine is a type of photo-induced oxidation and deserves a separate discussion as a novel method for the removal of antibiotic resistance. In contrast to conventional AOP (UV/H_2O_2), UV/chlorine cam produce the hydroxyl radical (·OH) and reactive chlorine species radicals (RCS), including ClOH·$^-$, Cl·, Cl_2·$^-$ and ClO·. The generation mechanism of RCS is shown in Fig. S3. Furthermore, UV/chlorine requires 30–75% less energy to produce free radicals than UV/H_2O_2, since the molar absorption coefficient (254 nm) of H_2O_2 is 19 M^{-1} cm^{-1}, and it is much lower than those of OCl^- (66 M^{-1} cm^{-1}) and HOCl (59 M^{-1} cm^{-1}) (Watts and Linden, 2007; Sichel et al., 2011). Micro-pollutants in water, including endocrine disrupters, taste and odor compounds, antibiotics, e.g. sulfamethoxazole (SMX), caj be effectively degraded by UV/chlorine (Qin et al., 2014; Wang et al., 2015; Dong et al., 2017; Guo et al., 2017b). Research on the effect of UV/chlorine on bacterial antibiotic resistance is also under way.

The control of ARGs by chlorine and UV disinfection alone is insufficient at the conventional dose. With UV/Chlorine treatment, synergistic effects on target genes were 0.006–0.31 log with varying operating parameters (62.4, 124.8, 249.5 mJ/cm^2 UV dose, and 5, 15, 25, 30 mg Cl_2/L within 30 min) (Zhang et al., 2015b). The UV reduced the demand for chlorine and the potential for the formation of disinfection by-products (DBPs). The superiority of UV/chlorine is obvious, and other studies have achieved similar results. Destiani and Templeton (2019) reported that *bla-TEM1*, *tetA*, *sul1* and *mphA* were inactivated approximately 1.7 log by 30 (mg·min)/L chlorine, while only 1.2 log genes reduction was achieved by 200 mJ/cm^2 UV, but over 2 log reduction of all tested ARGs was achieved by the combination of 200 mJ/cm^2 UV followed by 2 mg/L chlorine.

The using of chlorination after continuous ultraviolet disinfection effectively reduces ARGs and the synergistic effect on ARGs increases the removal rate by 0.01–0.62 log compared to the use of chlorine disinfection alone (Destiani and Templeton, 2019). The mechanism of UV/chlorine inactivation of ARGs was proposed by Zhang et al. (2019b). A higher removal efficiency of ARGs (more than 3.50 log of *sul1* ; more than 4.00 log of *inti1*) was achieved by UV/chlorine (UV intensity: 200 μW/cm^2, free chlorine: 20 mg Cl_2/L, pH: 7.0, time: 10min). Nitrobenzene (NB) was used as quenching agent to remove ·OH, but once ·OH was removed, the removal rate of ARGs did not decrease significantly. It indicated that among the generated free radicals, only RCS (Cl·, Cl^2·- and ClO·) could promote the degradation of target genes, while ·OH did not play a role in genes inactivation (Zhang et al., 2019b). ·OH could damage genes, but was easily consumed by other substances in advance because of its strong non-selective oxidation ability. The RCS free radicals have more significant potential to react with target genes than to be consumed by other components in ARB cells due to selective oxidation ability. The specific mechanism is shown in Fig. 1. Lower pH is more conducive to ARGs removal in UV/chlorine disinfection. The RCS is a unique product of UV/chlorine, and its removal of ARGs is stronger than ·OH. Thus, UV/chlorine showed more significant potential for controlling ARGs, but there are limited studies in this regard, and the real effects need to be further verified.

UV and chlorine are the most commonly used disinfection methods. Therefore, the application of UV/chlorine combined disinfection method is straightforward. Meantime, UV/chlorine also shows its superiority in ARGs control. To guarantee the practicability and safety of this disinfection method in realistic water treatment, there is an urgent need for further research in terms of water pollution, DBPs, and economic challenges. In addition, as a kind of alternative source of UV, UV light emitting diodes (UV-LEDs) have become the focus of research due to its durability, flexibility of design, ability to tailor the emission spectrum, no chemical risk,

Fig. 1. ARGs removal mechanism of free radicals (·OH and RCS).

Table 3
Comparison between treatment processes.

Treatment processes	Main mechanisms	Main advantages and disadvantages	ARGs removal effects	Reference
Chlorina- tion and chlorami- nation	Strong oxidation of hypochlorite damages bacterial membrane, and release substances such as protein, RNA and DNA.	Simple operation and low cost. DBPS, poor DNA removal effect,and the presence of chlorine resistant bacteria.	0.8−2.8 log *tetA*, *ampC*, *vanA*, *sul1*,and *int1* reduction.	(Stange et al., 2019) (Zhang et al., 2015b)
UV	UV radiation can destroy DNA and RNA to sterilize and can produce free radicals that damage cells, DNA, RNA, and proteins.	Broad-spectrum sterilization ability. photoreactivation and dark repair, difficult to achieve sufficient dose.	0−1.0 log *tetA*, *ampC*, *vanA*, *sul1* reduction by 60 mJ/m^2 UV.	Stange et al. (2019)
Ozonation	Direct ozonation destroys microbial organism structure and it can produce free radicals, such as ·OH, that destroys cell structure.	Sterilize completely, no residue, no photoreactivation and no dark repair. Large investment, high cost (difficult to achieve sufficient dose), and no lasting disinfection effect.	1.68−2.55 log *intI1*, *sul1*, *tetG* reduction from 177.6 mg/L O_3 complete response disinfection.	Zhuang et al. (2015)
Photoche-mical oxidation	Mainly produce free radicals, such as ·OH, that attacks cell membrane, and DNA.	Nontoxic; strong oxidation, thorough sterilization; mild reaction conditions. Complex operation, not enough mature technology, insufficient utilization of light source.	5.5−5.8 log *mecA*, *ampC* reduction with 120 mJ/cm^2 UV.	Guo et al. (2017a)
UV/Chlorine	UV, and chlorine have individual disinfection effects, and it can produce free radicals (especially RCS which selectively destroy DNA).	Simple operation, Strong removal effect of RCS on ARGs. Few related studies, DBPs, insufficient UV utilization, the specific mechanism is still unclear and the results are unconvincing.	More than 3.50 log of *sul1*, more than 4.00 log of *inti1* was achieved by UV/chlorine (UV intensity: 200 μW/cm^2, free chlorine: 20 mg Cl_2/L, pH: 7.0, time: 10min).	Zhang et al. (2019b)

and no warm-up period (Umar et al., 2019). Therefore, UV-LEDs/chlorine might further improve the disinfection efficiency for ARGs control.

3.4. Other new sterilization techniques

With the development of science, there are many other materials with high oxidation ability which may have the potential to be used as a disinfectant. In recent years, iron oxide nanoparticles have attracted much attention due to their magnetic separation, biocompatibility, and the solubility of a large number of reactive surface groups. ARB was effectively removed without biofilm formation by synthesized iron-oxide-activated bioactive-prodigiosin-conjugated carbon composite ($[Ac]_F$@Fe_3O_4−PG), through damage of the ARB membrane by the cationic ($[Ac]_F$@Fe_3O_4−PG) surface charge neutralization, and bacterial death caused by the ROS (Arivizhivendhan et al., 2019). The material could be reused and had long-term antimicrobial activity. A biological disinfectant is prepared using plant extracts, microbial polypeptides, biological enzymes, and so on. Nisin is a biological disinfectant and polypeptide produced by Streptococcus lactis, and is composed of 34 amino acid residues with a molecular weight of about 3500 Da (da). Nisin can inhibit most Gram-positive bacteria and has a strong inhibitory effect on spores of Bacillus (Kanchanapally et al., 2015). Syntheticthe nisin antimicrobial peptides attached to a graphene oxide membrane were used to inactivated *methicillin-resistant Staphylococcus aureus* (MRSA), to achieve almost 100% effect (Kanchanapally et al., 2015). Biological disinfectants have strong antimicrobial activity, do not cause secondary pollution of water, and are mainly used in food disinfection because of their high cost. Future research could focus on the effective and economical means of using biological disinfectants in water treatment and disinfection.

The inactivation of antibiotic resistant *E. coli* (7.9 log) could be achieved by the Fe^{2+}/peroxydisulfate (PDS) coupled process and galvanic cell (Fe^{2+}/PDS, GFP) electrolysis treatment (Zhang et al., 2019a). Peracetic acid (PAA) is a strong oxidant which can efficiently inactivate bacteria, viruses, and fungi, producing little mutagenic or toxic by-products. Thus, 2.3 log reduction of ampicillin-resistant bacteria was achieved with 20 mg/L PAA for 10 min. However, tetracycline-resistant bacteria could not be efficiently removed, and there was over 10 fold bacterial regrowth (tetracycline- and chloramphenicol-resistant bacteria) with 2 or 5 mg/L PAA for 10 min compared to untreated wastewater sample after 22 h (Huang et al., 2013). This indicates that PAA alone is not sufficient to remove ARB effectively and must be used in conjunction with other materials (Rizzo et al., 2019).

In summary, there is little research on bacterial drug resistance using other new sterilization techniques. To date, the studies have focused on the removal of ARB, rather than ARGs. Therefore, future research on the control of bacterial antibiotic resistance must consider the effect on ARGs.

4. Comparison between treatment processes

A comparison between treatment processes is provided in Table 3. The treatment processes mentioned in this review have a more significant effect on the removal of ARB compared to that of ARGs. Zhuang et al. (2015) compared the removal efficiency and cost of chlorine, UV, and ozone for ARGs removal and found that the cost of ozone was prohibitive and selected chlorine as the best method. In traditional disinfection, chlorine may be the best process to control ARGs, but there are numerous shortcomings. New sterilization technologies also have advantages and disadvantages, and photocatalytic oxidation currently cannot be widely used in the water treatment disinfection. There are few cost-effective disinfection options, and the best solution may be to remove antibiotic resistance at the source to reduce the costs of disinfection.

5. Conclusions and prospects

Conventional disinfection has a better control effect on ARB. However, the control effect on ARGs is weak due to insufficient dosage, which dose not guarantee the safety of the treated effluent.

ARGs in water transfer faster than ARB, and the control of ARGs is essential. Research should focus on addressing the challenges of disinfection on bacterial antibiotic resistance, mainly in relation to control of ARGs. Currently, research into the effect of new sterilization methods on antibiotic resistance is still relatively scarce, the findings are inconsistent, and most studies indicate that the removal of ARGs is less effective than that of ARB. Photochemical oxidation disinfection has potential, but studies on the simultaneous removal of micro-pollutants, ARB and ARGs show ineffective removal of ARGs, and the current research methods are still inadequate to be applied in practice. Thus, it is important to find particularly specific, economical and efficient new materials to remove ARGs and control its transfer in water.

For new sterilization materials such as peracetic acid, there are few studies on the control of ARGs, and further investigations are needed., On the basis of this review, the UV/chlorine combined disinfection technology shows more significant potential for controlling ARGs. However, there are few studies in this field and the actual effect must be further verified. Further studies are needed to optimize the parameters and to improve the treatment effect and economic benefits. Considering the inevitable formation of chloramine in actual disinfection, the effect of UV/chloramine on antibiotic resistance requires further study. In addition, UV-LEDs/chlorine should be explored and the formation of DBPs after UV/chlorine needs to be further studied.

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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Appendix A. Supplementary data

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