Chapter 19
Treatment Technologies for Removal of Antibiotics, Antibiotic Resistance Bacteria and Antibiotic-Resistant Genes

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Abstract This chapter describes current knowledge on the selected eco-friendly strategies for the treatment of main sources (manure and wastewater) of antibiotics, antibiotic resistance genes (ARGs) and antibiotic resistance bacteria (ARB), including bacteria pathogenic for humans and animals, also those mentioned on the WHO list of antibiotic-resistant priority pathogens. In the first part, known and used methods for manure treatment, like thermophilic composting and digestion, are described. In the second part, established methods of wastewater treatment (anaerobic-aerobic bioreactors, constructed wetlands, coagulation, membrane filtration and disinfection processes) as well as those tested only in a laboratory or small scale requiring further investigation (nanomaterials and biochar). The chapter concludes by highlighting the importance to develop effective treatment methods, management strategies and prevention activities, to eliminate or reduce the risk of the release of antibiotics, ARGs and ARB to the environment from manure and wastewater.

Keywords Antimicrobial resistance · Antibiotic resistance bacteria · Antibiotic resistance genes · Manure treatment methods · Wastewater treatment strategies

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19.1 Introduction

The knowledge about entry routes of antibiotics and antimicrobial resistance in the environment and the associated risks to humans and animals demonstrates an important, difficult yet urgent problem to be solved (Chaps. 1, 6 and 14). Many of the currently applied treatment methods applied for treatment of wastewaters and manure have been proven to have limited effectiveness in the elimination of antibiotics, ARB and ARGs. Therefore, it is extremely important to develop effective treatment strategies, especially for manure and municipal sewage, to eliminate or at least reduce the risk of the release of antibiotics, ARG and ARB to the environment. It is in these environments, referred to as hot spots, that the highest concentrations of antibiotics belonging to all known groups are detected, as well as bacteria from the list of antibiotic-resistant priority pathogens published by the WHO.

The following sections present current knowledge on selected treatment strategies applied for the treatment of manure and wastewater with regard to their removal of ARB and ARGs. Some of these treatment methods are already established and used in full-scale applications like anaerobic-aerobic bioreactors, constructed wetlands, coagulation, membrane filtration or disinfection processes (for wastewater), and thermophilic composting or anaerobic digestion (for manure). Others are either emerging or have only been tested in a laboratory or on a small scale such as use of nanomaterials and biochar.

19.2 Treatment Strategies

19.2.1 Manure Treatment Strategies

Animal manures are usually a mixture of faeces, urine, discarded bedding, and waste feed but with variable water content. Therefore, some manure treatment technologies can be more suitable than others to handle manure depending on if they are in solid, semi-solid, slurry, or liquid forms. The treatment technologies of manure are applied for different reasons: emissions reduction (including bioaerosols, NH3, odours); to reduce nutrients prior to soil, like nitrogen (N) and phosphorus (P); in order to liquefy and unify the form of manure and volume reduction and energy recovery; to get rid of pathogenic bacteria and ultimately antibiotics and other drugs or chemical compounds that may be a contamination of manure. Thermophilic composting and anaerobic digestion, which can facilitate the degradation of antibiotics and the reduction of ARG in animal manures (Pruden et al. 2013; Szogi et al. 2015; Youngquist et al. 2016), are discussed.

19.2.1.1 Thermophilic Composting of Manure

There are a lot of interest in composting manures for several reasons: to reduce bulk, concentrate nutrients, reduce odour, kill pathogens and weed seeds, and have a stabilized product for transport to the fields providing a source of slow release nutrients (Westerman and Bicudo 2005). There are several methods for composting manures: passive composting, aerated composting, windrow composting. in-vessel composting and vermicomposting. Those interested, I refer to the relevant, professional literature devoted to this. In addition, composting manure has also been shown to degrade antibiotics effectively, thus limiting the transfer of antibiotics to cultivated soil after its application (Kim et al. 2012; Selvam et al. 2012a, b). Literature data indicated that composting eliminates on average 50–70% of some antibiotics. In Sharma et al. (2009) was investigated how the composting process during 18 weeks will affect the reduction of total *E. coli*, *E. coli* resistant to ampicillin and tetracycline; and selection tetracycline (tet) and erythromycin resistance methylase (erm) genes. The compost windrows were prepared using manure collected from cattle (*Bos Taurus L.*) fed tylosin, chlortetracycline-sulphamethazine, and from control cattle (no antimicrobials). It was observed that just after two weeks (where the temperature was still relatively low—55 °C) composting reduced high initial levels of total *E.coli* and *E. coli* resistant to ampicillin and tetracycline. The tet and erm genes significantly decreased after 18 weeks of composting process (Sharma et al. 2009). In the other study was determined the effect of adding chlortetracycline, tylosin, and monensin to horse manure on distribution ARG. The manures, with and without antibiotics, were subjected to high-intensity management (sample 1) by composting or low-intensity management (sample 2). The samples were monitored for antibiotic concentrations and levels of tetracycline ARG [tet(W) and tet(O)] using quantitative real-time polymerase chain reaction. All three antibiotics dissipated more rapidly in sample 1 of manure, with twice shorter half-lives compared to sample 2 of manure (Storteboom et al. 2007). It was also shown that composting of pig manure resulted in decrease of cultivated aerobic heterotrophic erythromycin-resistant bacteria and tetracycline-resistant bacteria by more than 4 and 7 logs, respectively. Among six classes each of erm and tet genes quantified by class-specific real-time PCR assays, the abundance of erm(A), erm(C), erm(F), erm(T), erm(X), tet(G), tet(M), tet(O), tet(T), and tet(W) declined marginally during the first 17 days, but then within 31 days of the composting treatment dramatically decreased (Wang et al. 2012). Analysis of these results indicates that, antibiotic degradation to mainly occur only during the thermophilic phase over the first 2 weeks, and efficiency of degradation process depends on both duration and temperature. All treatments used during composting as watering, aeration, and turning significantly accelerate antibiotic degradation (Storteboom et al. 2007). The assessment of composting effectiveness is very difficult due to the lack of large-scale research, and not only on a laboratory scale. Only one work shows the reduction of the amount of antibiotic resistance genes (ARGs) in three types of animal (bovine, chicken, and pig) manure after industrial composting (Qian et al. 2018). The authors of this work explain this result suggesting that different animal species had significant effects on the diversity, abundance, and persistence of ARGs, and hence these differences. Other study on composting showed that the manure composting process is more effective with addition of mushroom biochar compared to addition of rice straw biochar (Cui et al. 2016). In this work, tetracycline (tetA, tetB, tetL, tetM, tetW, tetQ, tetO and tetX), sulfonamide (sul1 and sul2), chloramphenicol (fexA, floR, cmlA, cfr and fexB) resistance genes, and integrase gene (intI1) were studied in lab-scale chicken manure composting test. The average removal rate of ARGs was 0.86 log units and was dependent on the biochar used and the presence of heavy metals. In the other research work, Guo et al. (2017) have analysed the effects of superabsorbent polymers (15 mg/kg) on the abundances of antibiotic resistance genes, mobile genetic elements, and the bacterial community during swine manure composting. After 35 days of composting, the abundances of ARGs and MGEs decreased to a different extent, and were more efficient in removing tetW, dfrA7, ermX, aac(6¢)-ib-cr and MGEs which exceeded 90% (Guo et al. 2017). Until now, research has also shown that there are ARBs and ARGs that even become persistent after composting (McKinney et al. 2010; Sharma et al. 2009), and ARGs can persist even in the absence of selection pressure (Johnsen et al. 2011).

19.2.1.2 Digestion of Manure

A new field of application for animal manure is in biogas plants. This method is not widely used but has a large development potential due to the possibility of production environmentally friendly energy (Nkoa 2014). As demonstrated in the studies of Mohring et al. (2009) such antibiotics as sulphadiazine, sulphamerazine, sulphamethoxazole, sulphadimethoxine, and trimethoprim were nearly completely eliminated during a 5-week fermentation process while sulphathiazole, sulphamethazine, and sulphamethoxypyridazine showed persistence. Noteworthy, sulphonamides and tetracyclines are frequently used veterinary pharmaceuticals in animal husbandry. Yet, despite the risk of their reintroduction in the environment, fermentation residues are often used as fertilizers on agricultural fields. Thus, the effective fermentation process may be an efficient way to reduce the load of selected veterinary antibiotics preventing their way into the environment. However, comparative studies indicate that the aerobic process removed some of the antibiotics (e.g. sulphamethoxazole and oxytetracycline) more effectively than anaerobic incubation of dairy lagoon water or composting process (Pei et al. 2007; Wang et al. 2012).

19.2.2 Wastewater Treatment Strategies

A proper treatment of wastewater is essential before its discharge into natural water reservoirs (e.g. rivers, lake) or before the water is reused. Choosing and applying the right treatment strategies allows to prevent the spread of ARB and ARGs into the environment. An analysis of numerous publications indicates that the high amount of antibiotics, ARB and ARGs are released into the wastewater that may promote their dissemination into natural environments (Rizzo et al. 2013). Emerging microbial pathogens and increasing antibiotic resistance among emerging microbial pathogens is a global public health issue which has been recognized internationally (EU 2011; WHO 2015; UN 2016; EU 2017).

In a wastewater treatment plant (WWTP), many pathogenic bacteria resistant to antibiotics have been identified, including multidrug resistant (MDR) listed on the antibiotic-resistant “priority pathogens list” (Table 1.2, Chap. 1). The treatment methods applied to prevent the spread of ARB and ARGs into the environment should be able to destroy DNA and inactivate pathogens and the other ARB in the sewage. The selected methods like biological treatment reactors, constructed wetlands, membrane filtration, coagulation, biochar or nanomaterials, with a potential to limit a spread of AMR, are further discussed in this section.

19.2.2.1 Biological Treatment Reactors

Anaerobic–aerobic sequence (AAS) bioreactors combine anaerobic pre-treatment with aerobic post-treatment of anaerobic effluent. Like other anaerobic and aerobic bioreactors, AAS are low energy and environmentally friendly strategies and have a potential to remove ARB and ARGs. Fate of ARG in anaerobic, aerobic and AAS bioreactors was studied with metagenomic approaches (Christgen et al. 2015). For 6 months, five reactor configurations were monitored for treatment performance, energy use, and ARG abundance and diversity. The obtained results showed that AAS was more efficient compared with aerobic and anaerobic units. ARGs reductions were achieved in over 85% in AAS compared to 83% in aerobic and 62% in anaerobic conditions. In the other WWTP with the anaerobic/anoxic/aerobic membrane bioreactor (MBR) process the variation of ARGs [tet(G), tet(W), tet(X), sul(1), and intI(1)] in the influent and effluent of each treatment unit has been evaluated (Du et al. 2014). The results of these studies allow to conclude that anaerobic and anoxic conditions are more suitable to remove ARGs compared to aerobic conditions. It seems that in anaerobic conditions, the propagation of resistance genes is inhibited because microorganisms have lower bioactivity in these conditions. In another study, occurrence of tetracycline-resistant and sulphonamide-resistant bacteria, as well as three genes [sul(1), tet(W), and tet(O)], was monitored in the effluent of five WWTPs (Munir et al. 2011). The ARGs and ARB removal level was highest in MBR (from 2.6-log to 7.1-log) compared with activated sludge, oxidative ditch and rotatory biological contactors (from 2.4-log to 4.6-log). For comparison, in conventional WWTPs, the number of bacteria in the effluent decreases compared to the influent but there is still a significant number of ARBs whose resistance profile changes. An example may be the work on the level analysis of resistance to beta-lactams of *Aeromonas* spp. (Piotrowska et al. 2017). Five of the β-lactamases families (blaTEM, blaOXA, blaFOX, blaV EB, and cphA) were identified in all three isolation sites (influent, activated sludge and effluent). Most of the tested strains had a MDR phenotype (68%) and 62% of the isolates from all three points of the WWTP carry plasmids and some of them coding blaFOX-4-like and blaGES genes. These results strongly suggest that WWTPs are hotspots of ARB and ARGs dissemination. Additionally, *Aeromonas* spp. are referred to as important vectors of ARGs in the environment (Berendonk et al. 2015; Piotrowska and Popowska 2014). The metagenomic study was also proven co-occurrence of ARGs and human bacterial pathogens in municipal sewage sludge digesters and poor performance in their treatment (Ju et al. 2016). In result of 323 ARGs and 83 human bacterial pathogens studied, it was found that most ARGs and a minor proportion of HBPs (mainly *Collinsella aerofaciens*, *Streptococcus salivarius* and *Gordonia bronchialis*) could not be removed by anaerobic digestion. It was also shown that ARGs of multidrug and macrolide-lincosamide-streptogramin tended to co-occur more with human bacterial pathogens. The metagenomic sequencing approach was applied also by Guo et al. (2017) to determine the occurrence, abundance and diversity of ARGs and MGEs in a full-scale WWTP treating domestic wastewater. The activated and digested sludge were a source of ARGs and different MGEs including plasmids, transposons, integrons (intI1) and insertion sequences (e.g. ISSsp4, ISMsa21 and ISMba16) responsible for horizontal transfer of resistance genes. The findings also corroborate the hypothesis that WWTPs are hotspots of ARGs and MGEs. It evidently points to biological risk of post-digestion sludge in disseminating antibiotic resistance and pathogenicity.

These studies strongly indicate that the use of only biological treatment in WWTP is not sufficient to limit the flow of ARB to the environment. However, when biological treatment is applied together in combination with membrane-based technologies (e.g. MBR), better ARG removal efficiency can be achieved.

19.2.2.2 The Man-Made Wetlands

Constructed Wetlands (CWs) are small semi-aquatic ecosystems that use natural processes, and which can be used as alternative approaches for treatment of municipal, industrial and agricultural wastewaters. In man-made systems, these wetlands are artificially created and are typically long, narrow trenches or channels. CWs have been used as a green technology to treat various wastewaters and offer a low-energy, and less-operational-requirements alternative to conventional treatment systems but are land-intensive as large areas are required (Wu et al. 2014, 2015a, b).

CWs are simple, cost efficient, and provide reduction of biochemical oxygen demand (BOD), suspended solids, nitrogen, metals, pathogens and some of the contaminants of emerging concern such as ARGs (Krzeminski et al. 2019). The following characteristics are important for ARB and ARGs removal efficiency: plant species, flow configuration and flow types including surface, horizontal subsurface and vertical subsurface flow. In this treatment solution, processes such as biodegradation, sedimentation, chemical precipitation and adsorption, and microbial interactions with BOD, solids, and nitrogen as well as plant uptake are responsible for decreasing the loadings of pollutants like nutrients, antibiotics, and ARGs (Chen et al. 2016; Wang et al. 2017). However, studies conducted during the winter and summer in the wetland construction steadily operated over 10 years have shown removal of total targeted ARGs (78% and 60% in the winter and summer, respectively, but was observed that the concentrations of ARGs (sul1, sul3, tetA, tetC, tetE, and qnrS) were increased throughout the treatment process. In this work strong positive correlations between concentrations of intI1 and ARGs were also shown. This suggests that long-used wetlands can be reservoirs of specific ARGs and that mobile genetic elements affect the dissemination of ARGs in this system (Fang et al. 2017). Chan and other researchers in 2016 studied on the elimination of ARB and ARGs in differently constructed wetland and found that removal efficiencies of total antibiotics ranged from 78 to 99%, while those of total ARGs fluctuated between 64% and 84%. It was also shown that the presence of plants was beneficial to the removal of pollutants, and the subsurface flow constructed wetland had higher pollutant removal than the surface flow constructed wetlands.

19.2.2.3 Membrane Filtration

Membrane filtration processes include microfiltration (MF), ultrafiltration (UF), nanofiltration (NF) and reverse osmosis (RO). During membrane filtration a portion of water known as permeate passes through the membrane, while the constituents larger than the membrane pores are rejected by the membrane generating a concentrated stream containing the separated salts and other pollutants. Membranes are classified according to their pore sizes and molecular weight cut-off (MWCO).

The removal of ARB is expected to be comparable to removal of bacteria not containing antibiotic resistance. This has been verified by investigating the efficiency to remove antibiotic-resistant *E. coli* from WWTP effluents and demonstrating, as expected, complete removal of viable *E. coli* below the limit of quantification (10 CFU/mL) of the plating method (Schwermer et al. 2018). MF and UF are both capable of total removal of protozoa and effective removal of bacteria with up to 4 log removals for UF (Hai et al. 2014; Pecson et al. 2017). Due to even smaller pore size, NF and RO are considered to be absolute barriers for bacteria as long as the membrane is intact (Gerba et al. 2018).

Regarding the effectiveness against ARGs, only limited data exists in the literature on the performance and effects of the membrane filtration processes (Gwenzi et al. 2018). Most of the studies focused on MBRs (Munir et al. 2011; Rizzo et al. 2013; Yang et al. 2013; Du et al. 2014; Wang et al. 2015; Zhang et al. 2015; Sun et al. 2016; Threedeach et al. 2016; Le et al. 2018; Zhu et al. 2018b), which combine biological treatment with membrane separation. Only few others have investigated MF or UF (Arkhangelsky et al. 2008, 2011; Riquelme Breazeal et al. 2013; Krzeminski et al. 2018; Slipko et al. 2018).

Riquelme Breazeal et al. (2013) demonstrated in a lab-scale UF system a reduction of *vanA* and bla_{TEM} ARGs from WWTP effluent by 0.9, 3.5 and 4.2 log for membranes with MWCO of 100, 10 and 1 kDa, respectively. The removal of plasmid-associated ARGs was attributed to membrane retention and the removal of DNA was improved by colloids present in the water. The impact of colloids was stronger at lower membrane pore size. Riquelme Breazeal et al. (2013) observed incomplete removal of plasmid, including also 1 kDa membrane, and pointed out that the effective size of DNA is smaller than predicted by molecular weight because DNA is a long, thin and flexible molecule.

In another lab-scale study with a dead-end system, authors focused on penetration of plasmid DNA through UF membranes (Arkhangelsky et al. 2008, 2011). The authors demonstrated that despite electrostatic repulsion and significant size difference between membrane pore sizes and plasmid, a circular double-stranded DNA was able to pass through the UF membrane with 20 kDa MWCO. They have speculated that at pressure exceeding 2–3 bars, under which UF, NF and RO membranes are typically operated, the DNA plasmid may be stretched allowing to penetrate through membrane pores. Although penetration mechanism is not yet fully verified, the stretching out of plasmid due to hydrodynamic pressure into long and flexible strands increases the plasmid penetration capability through the pores; the mechanism is in line with the findings of others (Thompson and Travers 2004; Marko et al. 2011). Transportation levels are supposed to be linearly correlated to transmembrane pressure (TMP).

Recently, more attention has been given to high-pressure membrane filtration such as NF and RO (Krzeminski et al. 2018; Slipko et al. 2018). Between 5.0–8.1 log reduction value (LRV) for NF and 5.3–9.5 LRV for RO were reported for ARGs removal from swine WWTP effluent (Lan et al. 2019). However, the LRVs were not calculated for NF or RO alone but for the whole treatment train of the WWTP. Krzeminski et al. (2018) demonstrated removal from ultrapure water spiked with cell-free DNA containing antibiotic resistance kanamycin and ampicillin genes by nine UF, NF, and RO membranes in a bench-scale system. The plasmid rejection varied between 2 and 7 log removal value (LRV, >99.2%) and was correlated with MWCO of the membranes. A LRV of 2 was observed for a UF membrane with MWCO of 100 kDa, between 3 and 4 LRV for a tight UF (50–1 kDa) and between 5 and 7 LRV for NF and RO membranes with MWCO below 0.4 kDa. Additionally, the membrane concentrate was effectively treated by UV-LED irradiation providing damage and inactivation of ARGs (Krzeminski et al. 2020). Slipko et al. (2018) studied nine MF, UF, NF and RO membranes in the lab-scale system feed with spiked ultrapure water or WWTP effluent. The authors reported up to 99.9% removal of free DNA by NF membrane. Due to a large pore size, the 0.3 μm MF membrane was able to remove only up to 20% of cell-free DNA. In MF and UF, the removal was attributed to size exclusion mechanism, whereas in NF and RO electrostatic repulsion also plays an important role (Slipko et al. 2019).

To conclude, membranes may be effective in reducing the risk of ARB and ARGs release and spreading of antibiotic resistance in the environment commonly providing 99.9% removal, but further investigations to verify if complete removal is achievable are needed. The separation mechanisms and factors impacting removal (i.e., feed composition, membrane properties, operating conditions) as well as concentrate treatment methods need to be addressed. Furthermore, the possible contribution of membrane filtration to conditions that induce the SOS response in bacteria potentially leading to an increased mutation rate in bacteria should be evaluated (Karkman et al. 2018).

19.2.2.4 Coagulation

Coagulation/flocculation has been extensively used in wastewater treatment and drinking water production for removal of particles, natural organic matter, but also pathogens, heavy metals and phosphorous (Alexander et al. 2012). Through addition of a coagulant agent, electrical charges of small particles are neutralized during coagulation causing particles agglomeration. Flocculation promotes particle collision and growth of flocs, resulting in the formation of larger particles for easier separation from water during sedimentation or filtration (Bratby 2016). Coagulation can remove ARGs through electric-double-layer compression, charge neutralization, adsorption, and/or entrapment (Li et al. 2017; Yuan et al. 2019).

Although there are studies on antibiotics removal by coagulation (Choi et al. 2008; Alexander et al. 2012), there exist very few studies that have focused on ARG removal from wastewater by coagulation. Li et al. (2017) evaluated the potential of the jar-test coagulation for removal of two sulphonamide resistance genes (sulI and sulII), three tetracycline resistance genes (tetO, tetW and tetQ), and the class 1 integron (intI1 gene) from treated wastewater. Coagulation with $FeCl_3$ and polyferric chloride (PFC) resulted in removal of various ARGs between 0.5-log and 3.1-log reductions. Removal of ARGs was dependent on the coagulant type and dose, and was significantly correlated with the removal of dissolved NH_3-N and DOC suggesting that the co-removal of DOC, NH3-N, and ARGs could play a role.

Lee et al. (2017) studied changes in 12 ARGs which confer resistance to tetracycline (tetX, tetM, tetA), sulphonamide (sul1, sul2), macrolide (ermB, ermC), quinolone (qnrD, qnrS) and β–lactam (blaTEM, blaSHV, blaCTX) in two full-scale WWTPs treating municipal and industrial wastewater. Four of the ARGs (ermC, qnrS, blaSHV, and blaCTX) were not detected in the samples. Regarding coagulation process, contrasting results were observed between two WWTPs using polyaluminium chloride (PAC) as a coagulant. At one, tet, sul and bla ARGs were reduced by 48%, 75%, and 44%, respectively. At second WWTP, tet decreased by 76% whereas sul and bla increased by 36% and 152%, respectively. The difference in the reduction of ARGs was attributed to larger usage of coagulant at the plant with higher effectiveness.

Yuan et al. (2019) studied fate of five ARGs (sulI, sulII, tetO, tetQ, tetW) and class 1 integrase (intI1) in a full-scale WWTP treating municipal and industrial wastewater. Polyferric chloride (30–45 mg/L) was used as a coagulant. Coagulation was essential for the removal of the ARGs providing between 0.48-log and 1.86-log in terms of the absolute abundance. Among the five investigated genes, the lowest removal was observed for sulII.

The fate and removal of ARB and ARGs was also studied during drinking water treatment (Guo et al. 2014; Bai et al. 2015; Xu et al. 2016). With regard to ARBs, the antibiotic resistance rates of bacteria did not increase during coagulation and sedimentation (Bai et al. 2015). With regard to ARGs, Guo et al. (2014) studied removal of ten sulphonamide (sulI, sulII) and tetracycline (tetC, tetG, tetX, tetA, tetB, tetO, tetM, tetW) resistance genes as well as 16S-rRNA genes in seven DWTPs. The relative abundance of ARGs was not changed significantly by coagulation process during drinking water production. The removal of different ARGs at two DWTPs varied, based on absolute abundance, between 0.2 and 0.7 LRV for coagulation/flocculation process and between 0.3 and 1.0 LRV for coagulation/flocculation followed by sedimentation (Xu et al. 2016).

Concluding, coagulations seem to be effective technology for ARG reduction in WWTPs, but studies should be devoted to optimizing coagulation process for enhanced ARG removal. The effectiveness of coagulation for ARG reduction in DWTPs is somewhat smaller and varies between the studies, and thus requires more investigation.

19.2.2.5 Biochar

Biochar is a porous carbon-rich product, which can be produced by pyrolysis of high organic content materials (biomass) such as sludge, algae, and waste from different sources and sectors, e.g. industrial, livestock, agricultural, household and garden. Biochar has been typically applied as a soil amendment to improve soil quality or for carbon sequestration. But, due to strong adsorption capacity, biochar can be also used for organic, inorganic and microbial contaminants removal from water and/or control in soils (Beesley et al. 2011; Gwenzi et al. 2017). Biochar can stabilize heavy metals in the contaminated soils, leading to a significant reduction in crop uptake of heavy metals (by reducing their bioavailability, but also phytotoxicity). It may regulate the concentration of organic pollutants in contaminated soils and consequently may affect other processes such as bioavailability, degradation, leaching, and volatilization of contaminants (Zhang et al. 2013).

However, until now, biochar research focused on AMR was predominantly concentrated on the applications related to soil, manure and solid waste, whereas studies on wastewater are scarce. Sun et al. (2018) assessed the effect of biochar on ARGs when applied to the organic solid produced during anaerobic digestion of wastewater. The authors studied resistance genes of tetracycline (tetA, tetB/P, tetC, tetE, tetG, tetM, tetO, tetQ, tetT, tetW, and tetX), sulphonamide (sul1, sul2 and dfrA7), fluoroquinolone (aac(6′)-Ib-cr, qnrA, parC, qnrC, and qnrS), macrolide (ermB, ermF, ermQ, and ermX), as well as mobile genetic elements (intI1, intI2, ISCR1, and Tn916/1545) in lab-scale anaerobic digestion experiments with cattle manure. The relative abundance was decreased for 5–7 out of 13 ARGs but the results were inconsistent. In another study, the type of wastewater used for irrigation of soil was of importance for the biochar effect. When piggery wastewater was used, after initial decrease, the relative abundance increased again suggesting that the effect of biochar on tet and sul genes in soil was time-dependent (Cui et al. 2018).

Application of biochar to a contaminated soil decreased the uptake of sulphonamides, ARB enrichment and abundance of sulI and sulII genes in lettuce tissues during lettuce pot experiment (Ye et al. 2016). The ARGs levels, based on absolute abundance, were at least 1-log lower for lettuce tissues (roots and leaves) and between 0.2 and 0.8 log lower in the soil with 0.5% (w/w) biochar amendment. Furthermore, biochar was also found effective in controlling soil antibiotics, ARB, and ARGs disseminate to the edible part of potato (Jiao et al. 2018). In a study with ARGs of tetracycline (tetC, tetG, tetW, and tetX), sulfonamide (sul1 and sul2), and macrolide (ermF and ermX), ARGs levels were decreased in soil and lettuce tissues after biochar application in the lettuce pot experiments (Duan et al. 2017). The relative abundances of ARGs were reduced by 44%, 43%, and 52% in soil, roots, and lettuce leaves, respectively. Bacterial community influenced the variations in ARGs and intI1. However, due to high abundance of intI1 in soil and lettuce tissue, the spread of ARGs via horizontal gene transfer cannot be excluded. According to another pot experiment, the absolute abundance of ARGs decreased in non-planted soil after biochar application. Yet, biochar alone was reported to be insufficient to decrease ARGs level in planted soil and crops (Chen et al. 2018). Authors suggested maintaining or increasing diversity of bacterial community in soil as possibly more effective measure in mitigating ARG spread and accumulation. In addition, biochar weakened the effect caused by struvite application on intI1 ARG cassettes in soil, indicating biochar capability to mitigate the spread of resistance determinants from soils to vegetables (An et al. 2018).

Biochar was also reported to help adsorb heavy metals, reduce their availability, and subsequently contribute to reduce the selective pressure on ARB (Ezzariai et al. 2018). Therefore, biochar seems to be an effective amendment for reducing the abundances of antibiotics, ARB, and ARGs in soils. But large-scale trials are required to verify lab-scale findings before implementation. Furthermore, as reversible adsorption can occur, the desorption of contaminants adsorbed onto biochar should be carefully investigated (Safaei Khorram et al. 2016). Nevertheless, the clear attractiveness of biochar is in the possibility of using low-cost waste materials to minimize the bioavailability of ARB and ARGs for plant uptake and reduce the transfer of ARB and ARGs from the soil to plant (Piña et al. 2018). Consequently, by reducing uptake of ARB and ARGs by irrigated crops, biochar may help in restricting entry into the food chain.

19.2.2.6 Nanomaterials

Due to physical, chemical, and biological properties, nanomaterials are increasingly being used, or considered to be used, not only in medical but also in different water treatment applications. Nanotechnology and water treatment have attracted considerable attention of the research community. Among other topics, one of the frequently researched aspects is nanoparticles (NPs) with antibacterial properties. Until now, a vast number of inorganic, organic and hybrid NPs have been frequently proposed: silver (Ag), gold (Au), iron oxide (Fe_3O_4), titanium oxide (TiO_2), copper oxide (CuO), magnesium oxide (MgO), zinc oxide (ZnO), nitric oxide (NO) releasing NPs, chitosan, fullerenes, carbon nanotubes (CNTs), graphene oxide (GO), reduced graphene (rGO), Polyethylenimine (PEI), quaternary ammonium compounds and nanoemulsion (Li et al. 2008; Hajipour et al. 2012; Moritz and Geszke-Moritz 2013; Yousefi et al. 2017). In addition, composites of NPs have been proposed to utilize a synergistic effect of different NPs. For example, superparamagnetic iron oxide NPs with conjugation of iron, zinc, and silver was effective inhibitor of antibiotic-resistant biofilms formation (Taylor et al. 2012).

Addition of silver nanoparticles (Ag NPs) to anaerobic digester treating a mixture of WWTP primary sludge and wasted activated sludge has not decreased the absolute or relative copy numbers of ARGs of tetracycline (tetO, tetW), sulphonamide (sulI, sulII) and intI1 (Miller et al. 2013). The anaerobic digestion itself reduces (1–2 log) but does not provide complete removal of ARGs. Thermophilic anaerobic digestions have been more effective towards reduction of tetracycline genes and digester operating conditions influence bacterial community composition and prevalence of ARGs.

Graphene, a two-dimensional carbon nanomaterial, has been intensively studied in the last years and GO has been considered to be an effective adsorbent (Liu 2012) and carrier for genes (Feng et al. 2011a, b). However, GO alone had a limited effect on ARB inactivation and on levels of tetracycline (tetA) and kanamycin (aphA) resistance genes (Guo and Zhang 2017). Only under high GO concentrations (>10 mg/L) relative abundance decreased suggesting that resistant plasmid damage was possible. In addition, GO promoted the conjugative transfer of ARGs which was GO concentration dependant.

On the other hand, GO nanosheets showed high efficiency in removal of four ARGs (tetA, sul2, ermB and ampC) in a cyclic (c-DNA) and double-stranded (ds-DNA) form, when applied for removal of ARGs spiked to a river water (Yu et al. 2017). For the cyclic DNA, the LRV were 1.2, 1.6, 1.7, and 2.0 for c-tetA, c-sul2, c-ermB, and c-ampC, respectively. For the double-stranded DNA, the removal rates were generally higher and the LRV were 2.1, 0.7, 2.5 and 2.3 for ds-tetA, ds-sul2, ds-ermB and ds-ampC, respectively. After 5 regeneration cycles of GO nanosheets, the removal ability of c-ARGs and ds-ARGs decreased less than 40%.

Combination of gold, graphene oxide and cobalt oxide hollow sphere (Au/GO-Co3O4) acted as inhibitor for tetracycline-resistant genes (tetA) limiting its replication/damaging its bioactivities (Yu et al. 2018). Au/GO-Co3O4 showed excellent binding effect towards tetA. The short (210 bp) DNA fragments were easier removed than the long (bacteria content after cracking) DNA fragments. The removal depended on composite concentration and was in range of 1.5–4.6 log for short DNA fragments, and in range of 1–3.6 log for long DNA fragments. The authors concluded that damage of tet-ARGs in water was due to combined effects of the composites properties, released ions from Au/GO-Co3O4, and coated gold NPs.

Yousefi et al. (2017) reviewed application of GO nanoparticles and its nanohybrids as antimicrobial agent. The authors concluded high antibacterial efficiency of GO due to its capability to damage cell membranes. Nevertheless, to increase the antibacterial effects of graphene oxide, functionalization of graphene surface was pointed out for future research. Another promising field are NPs in combination with other processes such as membranes (Liu et al. 2016; Ying et al. 2017; Zhu et al. 2018a) or photocatalysis (Hwangbo et al. 2019). However, although nanomaterials might be effective against antimicrobial resistance, there is a risk associated with the use of nanomaterials in water treatment (Sharma et al. 2016). Some nanomaterials, such as silver, can have toxic effects on the environment, while others may facilitate the development of antibiotic resistance. The dissemination and propagation of ARGs in aquatic environments may be enhanced, for example, by ZnO (Wang et al. 2018), nanoalumina (Al_2O_3) but also other NPs (Qiu et al. 2012). Therefore, knowledge on the impact of the NPs on potential development of the resistance and the mechanisms of ARGs transfer is needed.

Nanostructured materials (e.g. metallic, organic, carbon nanotubes) possess antimicrobial activity and may circumvent existing drug resistance mechanisms in bacteria. Additionally, due to the specific mechanism of action of nanoparticles, no resistance was observed among bacteria. In addition to their antimicrobial potential, nanoparticles may inhibit biofilm formation and other processes in bacterial cell. The studies showed that nanoparticles can inhibit the activity of bacterial efflux pumps, formation of biofilms, and interference of quorum sensing, which confirms the possibility of their use in the strategies to combat MDR bacteria (AlMatar et al. 2017; Baptista et al. 2018; Barancheshme and Munir 2018; Bassegoda et al. 2018; Katva et al. 2018; Siddiqi et al. 2018; Zaidi et al. 2017). Aruguete et al. (2013) prepared a combination of nanomaterials with antibiotics and proved they are toxic to MDR *Pseudomonas aeruginosa* strain. In many other studies, the activity of various nanoparticles on ARB in an aqueous solution was shown, e.g. methicillin or vancomycin or multidrug-resistant *Staphylococcus. aureus*; antibiotic-resistance *E. coli*, *Salmonella* spp., *Enterococcus faecalis*, *S. epidermidis*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Mycobacterium tuberculosis*, *Acinetobacter baumanii* and MDR *Streptococcus pneumoniae* (Adegboyega et al. 2014; Luo et al. 2013; Fayaz et al. 2011; Singh et al. 2014; Taylor et al. 2012; Tran et al. 2010; Qiu et al. 2012). On the other hand, as pointed out earlier, some of the nanomaterials have shown toxic effects on the proper microflora of water or soil and more importantly on plants, animals, and humans, and can also encourage the development of antibiotic resistance in the environment (Aruguete et al. 2013; Miller et al. 2013). Therefore, before widespread use of nanoparticles or nanomaterials, more information is needed concerning the mechanisms of their antimicrobial activity and their potential for influencing the development of resistance and their toxic effect. In addition, efforts should be made to develop less toxic forms of nanomaterials and innovate with the combined use of plant-based antimicrobials and nanoparticles.

19.3 Summary and Perspectives

Due to the ubiquitous antibiotic resistance in the environment, strategies for manure, wastewater, water and soil treatment that could aid in mitigating risks of dissemination and development of antimicrobial resistance in the environment are necessary.

Despite the treatment methods mentioned in this chapter and the mechanisms governing these methods are generally well-known, there are still gaps in knowledge. For example, the dominant removal mechanism governing the removal of ARGs are not yet fully explored. In particularly, the diversification of methodologies used for screening and quantification of ARGs makes the comparison of effectiveness of different treatment solutions difficult. Thus, there is an urgent need for standardization and uniformization of AMR surveillance. In addition, many of the treatment methods have been investigated in a lab- or pilot-scale, using synthetic wastewater, and/or over short operation time. Therefore, there is limited full-scale evidence on removal of ARB and ARGs and effectiveness against AMR. Moreover, altough different advanced treatment methods are being developed and proposed for ARB and ARGs removal single treatment method is likely not going to be sufficient (Rizzo et al. 2020). Due to the costs, the optimal method should be not only effective but also economical. To confirm this, it is necessary to conduct large-scale testing under real environmental conditions. Especially in the case of WWTP, further investigation of advanced treatment systems should be carried out, to discover a suitable and cost-effective method to remove ARGs and ARB from WWTP effluents.

The further development of innovative treatment approaches should be parallel to the management strategies aiming at reduced use of antimicrobials and prevention activities related to improved sanitation and access to clean water.

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