Chapter 18
Recent Advances in Treatment Technologies for Antibiotics and Antimicrobial Resistance Genes

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Abstract Various water and waste treatment technologies are gaining attention for having great potential to curb antimicrobial resistance (AMR) dissemination in the environment. Most of the treatment technologies treat AMR by being able to degrade antimicrobial resistance genes (ARGs), lyse antimicrobial resistant bacteria (ARBs) and/ or oxidize the antibiotics whose presence in the environmental matrices contribute in the development and spread of AMR. A number of treatment technologies like aerobic and anaerobic digestion, membrane bioreactors, composting, nanoparticles and some disinfection-based mechanisms have already been evaluated, at industrial scale, for treating the antibiotics and associated ARBs and ARGs. These technologies, at present, are in use from the perspective of waste management and/or alternative energy but their place in formulating a broad and comprehensive strategy for controlling the spread of AMR in clinical and environmental systems has

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M. Z. Hashmi (ed.), *Antibiotics and Antimicrobial Resistance Genes*, Emerging Contaminants and Associated Treatment Technologies,
https://doi.org/10.1007/978-3-030-40422-2_18

been realized. This chapter summarizes some of the important treatment technologies, illustrating their key features and efficacy in treating AMR. Studies that provide alternative views about the contributions of various treatment technologies in selecting resistant bacteria and genes are also highlighted in this chapter.

Keywords Recent advances · Treatment technologies · Antibiotics · Antimicrobial resistance genes

18.1 Introduction

Antibiotic resistance has started becoming a public health and safety concern worldwide (Roca et al. 2015). The worldwide escalation of antibiotic consumption and subsequent resistance is also a serious concern for the environment. The development and subsequent increase in the dissemination of AMR is already endangering the therapeutic efficacy of antibiotics and subsequently increasing the rates of treatment failures. All of this may, ultimately, lead to prolonged and persistent infections causing increased morbidity and mortality (Li and Webster 2018). The need for combating AMR through improved versions of current methods and development of new innovative technologies has already been realised. Scientific community is exploring different methodologies to decipher the intricate trends of ARGs persistence and dissemination in order to formulate strategies for curbing the dissemination of AMR (Li et al. 2015, Munir et al. 2017, Waseem et al. 2019). Implications are still present in developing and utilizing new techniques for AMR analysis (Williams et al. 2017). Different water and waste management treatment technologies have been evaluated by the researchers in order to gauge their impact on removing resistant microbes and associated ARGs particularly from the environmental matrices. Some of the selected treatment technologies with a great potential to be utilized on large scale for treatment of AMR have been described below.

18.2 Anaerobic Digestion

Anaerobic digestion is a complex series of microbial processes in which biological sludge (and other organic material) break down and biogas is produced in the absence of oxygen. Although the major advantages of AD are reduction in emission of greenhouse gases and renewable energy production (Zaks et al. 2011), it can also be used as a treatment technology for reducing ARGs in various environmental matrices (Ma et al. 2011). Diverse views are present on the removal efficiencies of AD (Waseem et al. 2017b). Some studies have suggested thermophilic AD to be efficient in removing ARGs (Sun et al. 2016; Xu et al. 2018), and others have reported mesophilic anaerobic digestion can reduce potential pathogens along with ARGs but a chemical oxidation process is required for enhancing the reduction efficiency (Ihara et al. 2013). Similarly, some physicochemical pre-treatments before AD are also reported to enhance the ARGs removal efficiency of the anaerobic digestion process (Tong et al. 2016). There are also reports of selected removal of ARGs, during AD, on the basis of resistance mechanisms (Sui et al. 2016). Apart from directly mitigating the dissemination of ARGs from the sludge into the environment, AD can also indirectly control the accumulation of ARGs by direct degradation of antibiotics. Enhanced and faster degradation of antibiotics can be achieved during thermophilic digestion as compared to mesophilic anaerobic digestion (Massé et al. 2014).

The underlying processes which can influence the removal of ARGs during anaerobic sludge digestion are not yet completely understood. There is a dire need to keep in mind that the primary purpose of anaerobic digestion is methane production and not pathogens and/ or resistance mitigation. Addition of graphene oxide (GO) in the concentration of 500 mg/L has reportedly enhanced the reduction of resistant genes from 33.7% in control to 40.2% in the treatment group during the digestion of swine manure, but the addition of GO has also reduced the biogas-producing capability of the anaerobic digester by 17.1% (Zhang et al. 2017). The process optimization is generally performed to keep anaerobic digestion process stable and biogas production optimum. Anaerobic digestion can also face process instability due to lack of optimization in operational parameters, which in turn can also influence antimicrobial resistance genes survival in the digesters. Sudden changes in substrate loading and/or addition of exogenous compounds are believed to be one of the main causes of the process instability (Ferguson et al. 2016). Studies have highlighted that the substrate shock—sudden addition of large amount of carbon source—is often responsible for the process imbalance, causing organic acids build-up which can ultimately lead towards inhibition of biogas production (Chen et al. 2012). Effects of various operational parameters on antimicrobial resistance remain to be elucidative. It is perhaps due to these reasons that there is still a reluctance in the broader adoption of this technology.

An opposite point of view regarding the role of anaerobic digestion also exists among the scientific community. People are seeing the anaerobic digesters as a major source of antibiotic resistance dissemination into the environment, as studies have reported that the sludge contribution in releasing ARGs into the environment is more than the effluent wastewater (Calero-Cáceres et al. 2014). The presence of antibiotics and/or residual compounds can also select various antibiotic resistance genes in the digester. For example, risk of ARGs dispersal was increased when arsanilic acid is present in relatively higher concentrations (650 mg/kg) during anaerobic digestion (Sun et al. 2017). More emphasis is needed on the treatment processes of sludge for mitigating the spread of resistant bacteria and ARGs; therefore, further in-depth investigations into the use of anaerobic digesters for curbing antimicrobial resistance is required. Changes in design of anaerobic digesters to include physicochemical pre-treatments for enhancing cell lysis and extracellular DNA degradation may also be warranted.

18.3 Aerobic Digestion

In aerobic digestion microorganisms break down complex organic molecules in the presence of oxygen. In wastewater treatment plants (WWTPs), the process of aerobic digestion is also referred as activated sludge treatment. The major purpose of aerobic digestion is reduction of volume of sewage sludge during the process of sewage treatment. Being one of the integral parts of wastewater treatment systems, the efficacy of aerobic digestion as ARGs removal technology has been critically evaluated. Like anaerobic digestion, the ARGs removal efficiencies during activated sludge treatment are also variable (Waseem et al. 2018a). A study investigating the reduction of ARGs in municipal wastewater solids had concluded that the process of aerobic digestion can substantially decrease the abundance of ARGs but the rates of ARGs reduction are on the individual ARG under investigation and reactor design (batch vs continuous flow) (Burch et al. 2013). Other operational conditions and influent qualities are important drivers behind inconsistent removal efficiencies of aerobic digestion. For example, a study by Neyestani and colleagues has reported that presence of high antibiotics concentration, longer solid retention times (SRTs) and thermophilic conditions could increase the AMR in activated sludge systems (Neyestani et al. 2017b). Another study evaluating the effects of thermophilic aerobic digestion on 23 ARGs, 4 metal-resistant genes MRGs, *int1* and 16S rRNA gene has concluded that increased temperature decreased in ARGs due to reduction in overall resistome and bacterial diversity in sewage sludge (Thermophilic aerobic digestion). Another study has also confirmed that the longer SRTs during aerobic digestion can result in a 40% increase in the prevalence of ARBs in the presence of extracellular constituents. The authors of the study have suggested that either the antibiotic-resistant bacteria were positively selected and/or the results came out as false positive (Neyestani et al. 2017a).

Residual sub-inhibitory concentrations can play a vital role in the selection of ARGs in the environment. There are many reported instances where activated sludge digestion has not been able to clear the antibiotics completely from the biological sludge (Khan et al. 2017). A group of researchers, for example, has investigated the concentrations of nine selected antibiotics utilizing liquid chromatography tandem mass spectrometry in treated and reclaimed wastewater. Conventional activated sludge process has significantly reduced the antibiotic concentrations (>50%), during the experiments, but the complete elimination of the antibiotics was not attained (Kulkarni et al. 2017). Similarly an activated sludge floc can cause the sorption of the antibiotics and can bring bacteria and antibiotics in the vicinity of each other which may cause positive selection of resistant bacteria (Louvet et al. 2017).

Aerobic digestion could serve as a critical step in designing of wastewater treatment technologies for mitigation of ARGs into the environment; therefore, effective assessment about the influence of activated sludge process on AMR is essentially needed. Further research in investigating the role of aerobic digestion for reducing ARGs, ARBs and antibiotics will be useful for environmental engineers in comparing the advantages and limitations of this technology with other treatment technologies.

18.4 Membrane Bioreactors

Membrane bioreactors (MBRs) have also emerged as a promising and sustainable technology for the treatment of AMR in municipal and industrial wastewater (Fig. 18.1) (Aslam et al. 2017). It is important to understand the fundamental processes responsible for proliferation of ARGs in MBR systems so that efficient removal mechanism can be developed. In MBRs, foulant layer plays a very important role in the removal of ARGs whereas transmembrane pressure contributes in the removal of ARBs. Various aerobic and anaerobic MBRs have been employed in different studies and their contaminant removal efficiencies have also been evaluated. Role and contribution of membrane fouling, in reducing ARGs from WWTP effluents, is widely discussed in the literature. An anaerobic MBR, for example, has been employed highlighting the impact of membrane fouling on ARBs and ARGs removal; membrane fouling was found to be positively correlated with the removal of ARGs (Cheng and Hong 2017). A different anaerobic MBR treatment was able to remove selected ARGs and *int*1 in the range of 3.3–3.6 log units. In this case anaerobic MBR treatment had also decreased the biomass significantly as depicted by the reduction in the concentration of the housekeeping gene (Kappell et al. 2018). Another study, evaluating the repercussions of antibiotics presence on membrane fouling, has measured the ARGs removal capacity of anoxic/aerobic membrane bioreactor (A/O-MBR) (Zhu et al. 2018). Membrane fouling acted as an additional barrier that effectually stopped the flow of ARGs across the membrane.

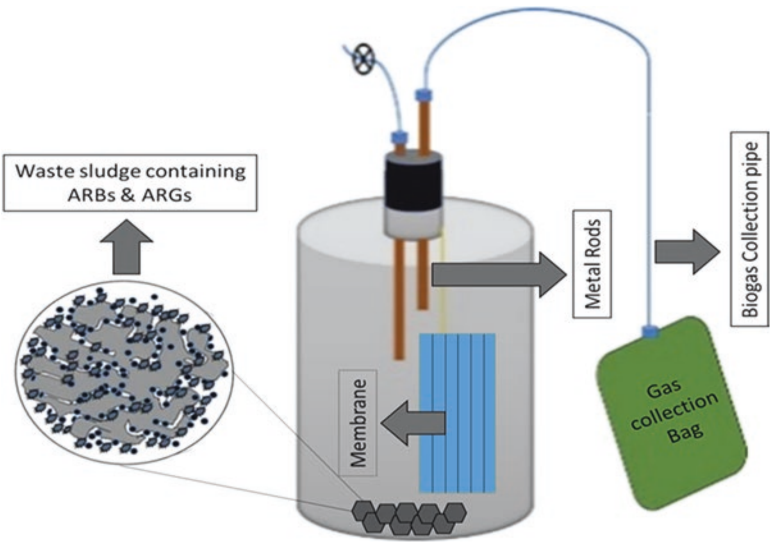

Fig. 18.1 Schematic diagram of a working membrane anaerobic digester for the treatment of ARGs and ARBs

Different treatment technologies, sometimes, are synergistically applied for the enhancement of AMR removal. Karaolia et al. (2017) have investigated the performance of a small-scale MBR combined together with a solar fenton oxidation system. The integrated system was able to remove >99% of bacteria, and the antibiotic removal efficiency was also improved. However, the integrated process was unable to remove some selected ARGs. In fact, few ARGs proliferated after 180 min of treatment. One probable reason for this increase of ARGs is the release of intracellular ARGs to the outside environment, after the treatment, as a result of bacterial cell lysis.

MBRs, particularly anaerobic ones, can play an important role in future plans for efficient AMR reduction from wastewater because they don't require any intensive energy demanding oxygen transfer and can also synthesize biogas during wastewater treatment. Filtration performance of MBRs can be substantially increased or decreased by variations in membrane fouling. Membrane fouling, on the other hand, is also viewed as a major drawback halting the general adoption of application of MBRs for treating AMR because it can reduce the lifespan of the membranes resulting in a considerable increase in operation costs.

18.5 Disinfection-Based Treatment Technologies

Disinfection is the process of inactivation and/or killing of microorganisms (>99%) from the inanimate objects. Various physical and chemical disinfection processes have been employed for tackling AMR in different environmental matrices (Di Cesare et al. 2016; Shi et al. 2013). Environmental cleaning and disinfection can play a role in curbing the spread of various resistant bacterial species like vancomycin-resistant *enterococci* (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA) (Carling and Huang 2013). Routine cleaning and disinfection of inanimate objects in patient rooms was associated with a significant reduction in MRSA, VRE, and *Clostridium difficile* infections in a hospital in Canada (Alfa et al. 2015). Surface disinfectants like hydrogen peroxide kills the pathogen by oxidative cellular destruction. The process is instantaneous, and occurs on multiple non-specific target sites making it challenging for the bacterial pathogen to develop resistance against surface disinfectants.

18.5.1 Chlorination

Chlorination is the most popular disinfection process for treating aquatic environments due to its effectiveness and availability. The number of systems employing free chlorine as a disinfectant is an order of magnitude greater than alternate disinfection technologies (AWWA 2017). Yuan and colleagues have recently studied the fates of nine ARBs and eight selected ARGs providing bacterial resistance to erythromycin and tetracycline during wastewater chlorination. A chlorine dose ranging from 15 to 300 milligrams-minutes per litre (mg-min/L) was able to remove 60%

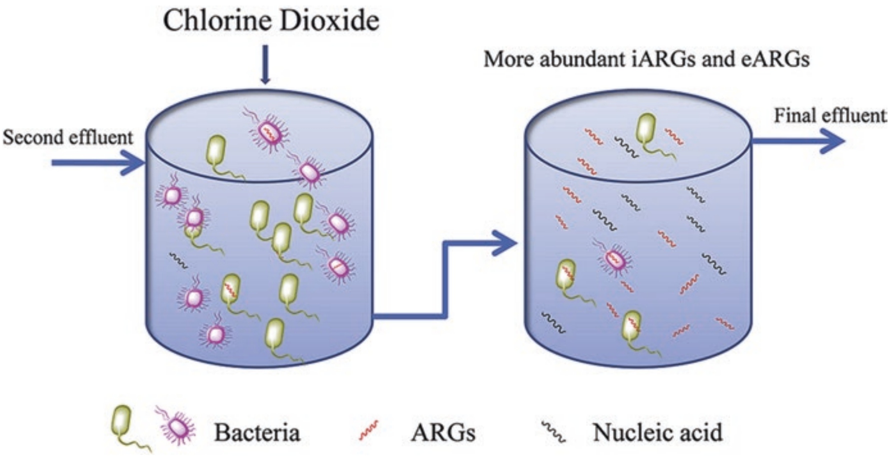

Fig. 18.2 Chlorine dioxide treatment more efficiently treating ARBs than ARGs (Liu et al. 2018) Reprinted from Water Research,136, Liu et al., Chlorine disinfection increases both intracellular and extracellular antibiotic resistance genes in a full-scale wastewater treatment plant, 131–136, Copyright (2018), with permission from Elsevier

and 20% of the ARGs, respectively. All resistant bacteria were inactivated with the chlorine dose of only 15 mg-min/L except sulphadiazine- and erythromycin-resistant bacteria which required an additional dosage of 60 mg-min/L (Yuan et al. 2015). Another group of scientists evaluated the chlorination impact on the removal of 282 ARGs from secondary effluent of a WWTP. A total of 4 mg of chlorine per litre with a contact time of 30 min was capable of reducing the ARGs abundance by 2.4–3.4 folds (Lin et al. 2016). A contact time of 10 min with a relatively higher chlorine concentration of 75 mg/L was also able to inactivate 90% of ARBs and 78.8% of pB10 plasmid in a different study (Pak et al. 2016). However a constant and long-term application of chlorine can also increase the environmental spread of AMR. Liu et al. (2018) have monitored the effects of chlorine disinfection, for a year, on intracellular and extracellular ARGs and found that ARGs were increased by 3.8-folds and 7.8-folds, respectively, thus enhancing the risk of AMR in the environment (Fig. 18.2). Apart from chlorination, potential of other relatively mature disinfectant treatment technologies like ozone and UV treatment for AMR elimination have also been investigated by researchers.

18.5.2 Ozone

Ozone is a strong disinfectant and oxidant which can be a promising choice for inactivating resistant microorganisms. Contact time is considered very critical for the ozone treatment. Addition of various catalysts like persulphate and monopursulphate can also significantly reduce the contact time for the treatment of ARGs

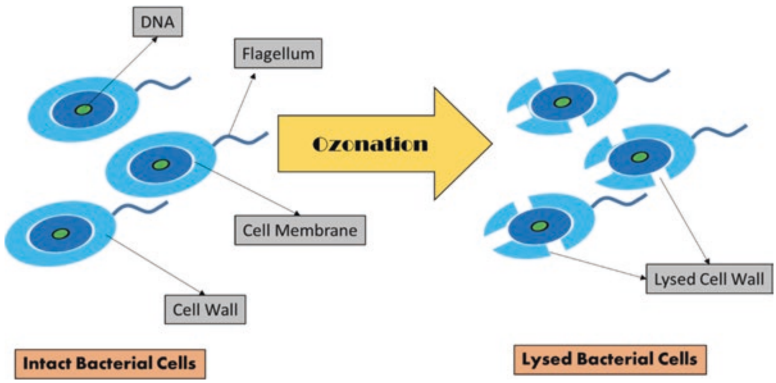

Fig. 18.3 Ozone's antibacterial action killing the ARBs by cell wall lysis

(Oh et al. 2014). Diverse trends in ARGs abundance in response to ozone treatment could be due to selective shifts among different bacterial groups within a community. Such diverse trends of ozone on ARGs were highlighted in wastewater where a concentration of 0.9 ± 0.1 g ozone per 1 g of dissolved organic content (DOC) was employed for treating wastewater. Although the ozone treatment was able to reduce *ermB* by two orders of the magnitude but at the same time two other resistant genes (*vanA, blaVIM*) increased within the survived bacterial population (Alexander et al. 2016). Ozone disinfection has better influence on resistant bacteria as compared to ARGs as ozone treatment of only 15 min was able to completely remove erythromycin and ertapenem *E. coli* in urban wastewater effluents (Michael-Kordatou et al. 2017). Ozone has the potential to degrade the bacterial cell wall (Fig. 18.3). It can also be employed for the degradation of various antibiotics and hence can also play an indirect role for the reduction of AMR in wastewaters (Ben et al. 2012; Lange et al. 2006).

18.5.3 UV

The impact of UV disinfection on various ARGs, ARBs and antibiotics have also been investigated in different studies. Increase in UV doses have been linked with the exponential decrease in ARGs in the effluent of a WWTP (Zheng et al. 2017). In most of the studies, strong oxidants like H_2O_2 have also been employed along with UV to enhance the treatment capability of UV. Degradation kinetics and transformation products of trimethoprim and sulphamethoxazole with UV, UV/H_2O_2 and UV peroxydisulphate treatments were explored in synthetic and hydrolysed urine (Zhang et al. 2016). Ferro and colleagues have reported the successful implementation of a UV/H_2O_2 disinfection treatment process on coliforms isolated from wastewater. Although the process had significantly inactivated the coliforms including the resistant *E. coli*, resistant genes including *blaTEM*, *qnrS* and *tetW* survived even

4 h of treatment process (Ferro et al. 2016). UV disinfection treatment can also negatively impact the human health by increasing the risk which it can pose during the use of reclaimed wastewater. A UV dose of 20 mJ/cm^2, for example, has initially inactivated tetracycline-resistant (3.0 log) and other heterotrophic bacteria (>4.0 log) but bacterial population reactivated during a dark repair period. Abundance of tetracycline-resistant bacteria was increased after reactivation due to more rigorous inactivation of non-resistant heterotrophic bacteria (Huang et al. 2016). There are also concerns that transduction by bacteriophages can be induced with the help of UV treatment, which in turn can enhance the transferability potential of ARGs among bacterial populations (Torres-Barceló, 2018).

Overall, disinfection treatment processes can decrease bacterial susceptibility and develop cross-resistance to therapeutically important antibiotics (Webber et al. 2006). Studies have shown sublethal concentrations of disinfectants can trigger resistance mechanism in bacteria (Buffet-Bataillon et al. 2012). Similarly, many different studies have also reported the role of disinfection by products in induction of AMR (Li et al. 2016, Lü et al. 2015). Evidence is available in literature to support both the viewpoints about the pros and cons of disinfectants for curbing the dissemination of AMR. Further research is required to decipher the intricate relationship between various disinfection mechanisms and AMR to conclude the usefulness of disinfection as an effective and sustainable AMR treatment technology.

18.6 Nanoparticles to Control Antibiotic Resistance

Metal nanoparticles (NPs) have emerged as a new tool to cope the antibiotic resistance due to their excellent antibacterial activities against deadly bacterial infections (Rai et al. 2009). Nanoparticle-based strategies are more effective in controlling ARBs and ARGs than conventional approaches. Silver, titanium, copper, zinc and iron are the metals extensively used in nanoparticle-based antimicrobial studies. Among all the nanomaterials, silver has been extensively used in various medicinal compounds such as bhasmas and Ayurveda used to treat numerous bacterial infections since time immemorial (Sharma et al. 2009). Antibacterial activities of silver nanoparticles (AgNPs) are due to their extremely minute size rendering them high surface area to volume ratio, which increase the contact area with microbes. Moreover, AgNPs enhance the chemical and biological activities and has the potential to target numerous bacterial structures (Fig. 18.4). Generally, metal nanoparticles disturb the physiology of cell membrane such as permeability and respiration (Xiu et al. 2012). Furthermore, AgNPs can bind with sulphur-containing amino acids and phosphorous-containing nucleotides, thus destroying the major molecular machinery of bacteria (Zheng et al. 2018).

AgNPs have been regarded as new weapon against the multidrug-resistant (MDR) bacteria. The orthodox chemical synthesis of AgNPs is rapidly becoming obsolete due to the hazardous nature, low yield and cost ineffectiveness of the process (Duan et al. 2015; Raza et al. 2016). So, people are exploring the facile, eco-

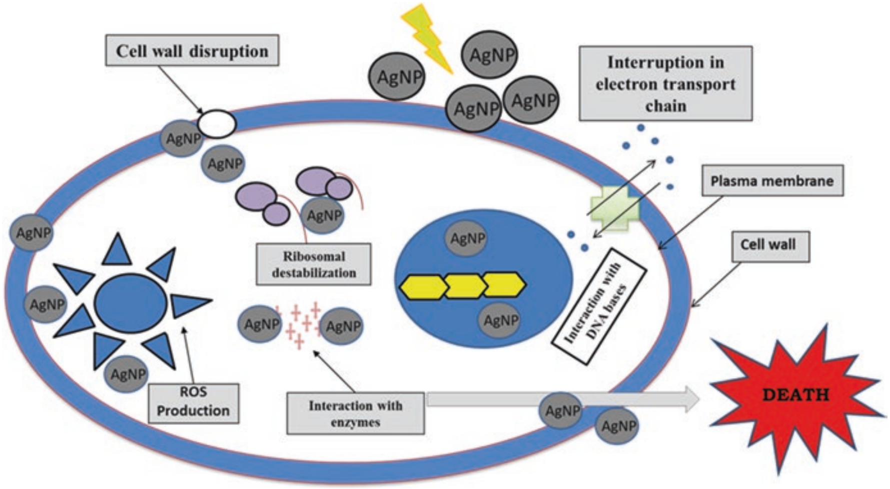

Fig. 18.4 Schematic representations of different antimicrobial mechanisms employed by silver nanoparticles against bacteria (AgNPs)

friendly and cost-effective alternative options (Shah et al. 2019). Influenced by the bio-reduction of silver ion (Ag^{+}) using microorganisms, green synthesis of AgNPs has become a timely topic (Ali et al. 2017, 2018). Although biogenic production of AgNPs has been evaluated using fungi, plants and enzymes, bacterial synthesis is considered as easy and facile fabrication (Ali et al. 2016). Silver compounds or AgNPs have been extensively used in antibacterial assessment against the both gram-positive and gram-negative pathogenic bacteria (Rana et al. 2018).

Even though metal nanoparticles have been effectively used against the antibiotic-resistant bacteria, they also pose some toxicity to mammalian cells (Park et al. 2007; Waseem et al. 2018b). Therefore, modifications and new combinations must be evaluated to minimize the toxicity of NPs. Recently, different amalgams of NPs with antibiotics, polymers, essential oils and antimicrobial peptides have been developed to reduce their toxicity (Hemaiswarya et al. 2008). The combined efficacy of AgNPs and antibiotics lessened the toxicity of both agents towards mammalian cells possibly because of lowered dosage requirements owing to synergistic antimicrobial effect. Likewise, selective/target specificity are major concerns in the use of AgNPs in targeted drug delivery and antimicrobial therapy against multidrug resistant (MDR) bacterial infections (Wang et al. 2018). A recent study combined the antibacterial potential of AgNPs with branched polyethylenimine (bPEI), a selective bacterial toxic agent, thus providing a cationic Ag-nanocluster as a potent antibacterial agent for MDR (Huma et al. 2018).

Despite the fact that metal NPs are the ray of hope in the war against AMR, there are some concerns that metal contamination may serve as a selective agent in the spread of antibiotic resistance and ARGs. Bacterial cells can develop metal resistance/tolerance by limiting the entry of metal into the cell envelop via synthesizing the various extracellular polymeric substances (EPS). Another important strategy is to release the siderophores in the medium, which can protect the bacteria from metal toxicity. Bio-sorption and biofilm production are also essential ways opted by bacteria to protect the metal toxicity (Giovanella et al. 2017). A recent study described that pervasive metal pressure in the environment may facilitate the proliferation of antibiotic resistance by co-selection of metal resistance genes (MRGs) and ARGs. The co-selection process can be attributed to various underlying mechanisms depending upon the type and level of contaminations as documented in literature (Baker-Austin et al. 2006). This particular interaction may result from co-resistance (different resistance determinants present on same genetic element) and cross-resistance (only one genetic element responsible for both metal and antibiotic resistance) (Li et al. 2017). Moreover, indirect and shared regulatory responses to antibiotic and metals such as biofilm development also represent a co-selection mechanism in bacteria. Environmental factors associated with the dissemination of metal NPs and antibiotics must also be considered. An important factor in emergence of combined resistance is experimentally induced co-selection using microcosms amended with an antibiotics and variety of metals, or which resulted in an increased frequency of multiple resistance phenotypes (Wang et al. 2017a). Although a direct assessment of the critical role of metals in co-selection is often hindered by the manifestation of some other anthropogenic contaminants, these studies do link contaminant exposure with elevated antibiotic resistance. Current advances in microbial physiology, genomics, and biochemistry could provide the basis for the accurate determination of important steps involved in complex metal–antibiotic resistance interactions, particularly, the relative contributions of co-resistance determinants to the fitness of bacteria in different environmental and clinical settings (Pal et al. 2017). Despite of abovementioned studies on the existence of selection mechanism of metals and antibiotics, there are still some uncertainties which must be explored to fully understand this scientific mysteries about the co-selection mechanism and influence of horizontal gene transfer in the presence of metals (Seiler and Berendonk 2012). Therefore, metal contamination represents a long-standing, widespread and recalcitrant selection pressure with both environmental and clinical importance that potentially contributes to the maintenance and spread of antibiotic resistance factors.

18.7 Constructed Wetlands

Constructed wetlands (CWs) are artificially engineered wetlands that have been employed for either the treatment of wastewater or the reclamation of an effected land (Sheoran and Sheoran 2006, Wang et al. 2017b). Poor performance of individual septic systems and higher cost associated with centralized sewer systems have paved the use of constructed wetlands to treat various environmental contaminants including ARGs, ARBs and antibiotics. Abundance and distribution dynamics of ARGs before and after treatment of municipal wastewater with constructed wetland have been evaluated by researchers. A study, for example, has reported that certain targeted resistance encoding genes *(tetA, tetB, tetM, ermB, sul1, ampC and qnrS)* were detectable in the mesocosm environment and the abundance of these genes was reduced after the remediation of wastewater in the constructed wetlands (Nõlvak et al. 2013). In addition to ARGs, mesocosm-scale constructed wetlands have also been used for the removal of antibiotics in domestic wastewater. Six CWs (mesocosm-scale) with three flow types and two different species of plants were set up to observe the removal of 8 antibiotics, 12 genes in different matrices through CWs. The removal efficiencies ranged from 75.8% to 98.6% and 63.5% to 84.00% for antibiotics and ARGs, respectively, where the presence of plants played an important role for removal of pollutants and other substrates (Chen et al. 2016). Another study reported the volcanic CWs with vertical flow cemetery in the removal of ARGs including three *tet* genes and 16S rRNA from swine wastewater which is reduced by 50% and affected by the nature of wetland medium (Liu et al. 2013).

Water remediation is often considered as a time-requiring process which in certain cases can take months and years. Concentrations of ARGs were also monitored over a period of 10 years in an integrated surface flow constructed wetland (ICW) where domestic sewage was the primary source of ARGs contribution, and 77.8% and 59.5% removal rates were determined in the winter and summer seasons, respectively. Significant correlations were observed between *intI*1 and many ARGs, signifying the role of mobile genetic elements dissemination of ARGs in an ICW (Fang et al. 2017). Constructed wetlands have also been employed to check their potential in the removal of antibiotic resistance bacteria from the saline aquaculture effluents. A study suggested that the removal percentages of both the total and resistant bacteria were relatively fewer and unstable during the first week of experiment in the CWs microcosms, stabilizing after the third week of the treatment to attain the maximum removal values of around 96% (Bôto et al. 2016). In another comparative study, percentages of antibiotic resistance bacteria were found to be similar in constructed wetlands and conventional wastewater treatment, and the abundance of bacteria was much low in CW as in activated sludge of WWTP which means much lower ARB spread in the environment. It was also supported by faecal indicator bacteria resistance to antibiotics in experimental constructed wetlands (Sidrach-Cardona and Bécares 2013).

In one particular study, the abundance and removal of sulphonamides and tetracycline were also examined other than ARGs using wetland plants *(Phragmites autralis)* under microcosm adsorption, biodegradation and sunlight photodegradation mechanisms. The study suggested that the physiochemical properties of plants play an important role in the removal of antibiotics. The average removal efficiencies of other selected antibiotics in this study were found to be 85% (SMA), 81.86% (SH), 49.43% (SHZ), 29.47% (CTC) and 22.26% (EFX) (Choi et al. 2016). Some CWs studies have also reported inconsistent removal of ARGs. A constructed wetland treatment study has reported inefficient removal of ARGs whereas successful removal of nutrients, suspended solids, pharmaceuticals and micro-pollutants was reported by the same wetland (Anderson et al. 2013). Another study encountered the continuous supply of antibiotics in constructed wetland to determine the antibiotic removal efficiency by CW and evaluate resistance development and expression profiling. It suggested that short-term treatment of CW with antibiotics has no observed impacts on antibiotic resistance genes (Berglund et al. 2014).

18.8 Composting

Composting can also be an effective approach for mitigating the risk of AMR propagation via environmental routes. It can serve as a powerful treatment technique for curtailing ARGs, ARBs and residues of antibiotics. Aerobic composting has been reported to significantly reduce the ARGs and MGEs in cattle manure. In a 120-day-long microcosm incubation experiment, the abundance and diversity of resistome in manure-treated soils were significantly higher than those in compost-treated soils (Gou et al. 2018). Recently, researchers have found that removal of AMR can be significantly enhanced by increasing the temperature during composting in a 3-week-long experiment. Hyper-thermophilic composting is also better able to reduce the half-life of ARGs and MGEs as compared to conventional composting (0.8–1.3 vs. 1.9–4 days) (Liao et al. 2018). The major advantage of compositing is that it can be easily transformed into bigger industrial scale technology. Addition of biochar can also influence the removal capacity of ARGs during composting. Impacts of rice straw biochar and mushroom biochar on the behaviour of ARGs in a lab scale chicken manure compost were investigated by Cui and colleagues. Mushroom biochar had positively influenced the ARGs removal while addition of rice straw biochar had decreased the ARGs removal capacity of compost treatment (Cui et al. 2016) (Fig. 18.5).

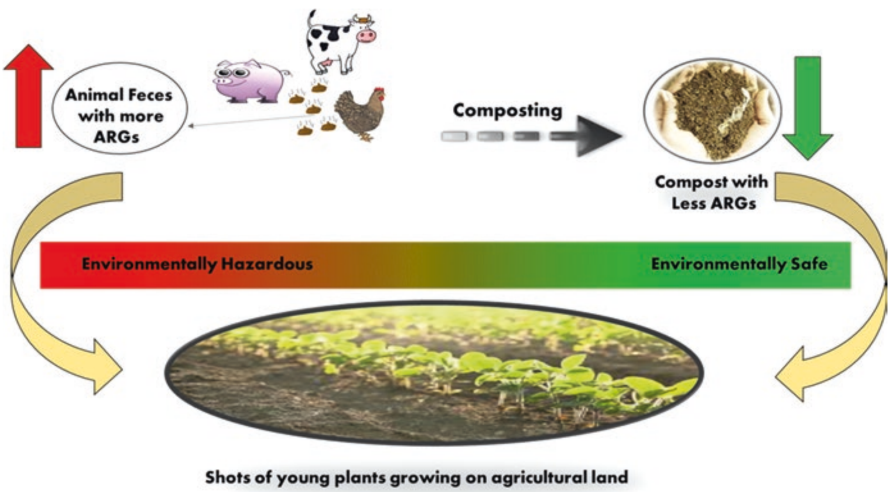

Fig. 18.5 Pictorial depiction of composting reducing ARGs in animal manure

Some researchers advocate against composting because they believe that ARGs are disseminated into the environment from animal faeces and even the treated manure can contribute significantly in the dispersion of ARGs into the environment. Reducing or eliminating compost, however, is not a viable option because traditional composting actually helps the agricultural sector to have less dependence on chemical fertilizers. This in turn could produce healthier and more environmentally friendly food, but we have to make it safe in the context of dissemination of ARGs and ABRs in the agricultural settings.

18.9 Conclusion

As the pace of new antibiotic development is not keeping up with the development and dissemination of AMR, the need for the development and validation of treatment technologies is realized greatly. Many of the reported treatment technologies are yet not yet able to achieve complete elimination of ARGs, ARBs and antibiotic residues. Thus, only treatment technologies alone cannot fully tackle the problem of AMR spread in the environment, so they should, instead, be a part of a broader and comprehensive AMR control strategy. Bioinformatics approaches for identifying the AMR risk should be explored (Waseem et al. 2017a, b). Other integrated approaches like rational prescription of the existing antibiotics, AMR stewardship programmes, controlled discharge of antibiotic resistance waste, on-site analysis of AMR and strict infection control along with the already developed potential treatment technologies are required for designing and implementing an efficacious and sustainable strategy to win the war against the ever-increasing threat of AMR.

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