



Mini Review

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Antibiotic Resistant Genes in Various Environments



Hyun Min Jang¹ and Eunsung Kan^{1,2*}

¹Texas A&M AgriLife Research Center, USA

²Department of Wildlife, Sustainability and Ecosystem Sciences, Tarleton State University, USA

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*Corresponding author: Eunsung Kan, Texas A&M AgriLife Research Center, 1229 North US Highway 281, Stephenville, TX 76401, USA.

Abstract

This mini-review addresses occurrence, fate, mechanisms and possible remediation of antibiotic resistant genes in various environments. While antibiotic resistant genes are widely spread via multiple mechanisms, they often cause various diseases and significantly influence on human health. Wastewater treatment plants among various environmental matrices are considered as the main reservoir of antibiotic resistant genes. Current wastewater treatment technologies have revealed the limitations for effective treatment of antibiotic resistance at wastewater treatment plants. Thus, innovative and cost-effective means to reduce antibiotic resistance in wastewater needs to be developed.

Keywords: Antibiotics; Antibiotic resistance genes; Human health; Human bacterial pathogens

Abbreviations: ARGs: Antibiotic Resistance Genes; HGT: Horizontal Gene Transfer; WWTPs: Wastewater Treatment Plants; CWs: Constructed Wetlands

Introduction

Since the penicillin was discovered by Fleming [1], over 250 different antibiotics are registered for use in human and veterinary medicine [2]. A lot of antibiotics including tetracyclines, quinolones and sulfonamides have been extensively used for the prevention and treatment of human and animal diseases [3]. However, low metabolic efficiencies of antibiotics have led to negative effects on human and animal health. As reported by Daughton & Ternes [4], most of the ingested antibiotics were excreted through urines and feces [5]. The undigested antibiotics were released to groundwater, wastewater, surface water and soil [6,7], while they often caused biotoxicity and antibiotic resistance in environments.

Unlike other pharmaceutical compounds, antibiotics are selectively act on bacteria via various mechanisms [8]. For example, antibiotics can inhibit the synthesis of cell wall and enzyme as well as protein [9]. However, some bacteria can be intrinsically resistant to one or multiple antibiotics through following molecular mechanisms [10]:

- Changes in antibiotic targets by mutation.
- Modification of targets.
- Direct modification of antibiotics.
- Prevention of access to target (e.g., efflux pump). All genes related to the antibiotic resistance are called "Antibiotic resistance genes (ARGs)".

In ecosystems, ARGs can persist over many generations and enable to proliferate by not only vertical transfer but also horizontal

gene transfer (HGT) such as conjugation and transduction [11]. Accordingly, more recent attention has focused on the fate of ARGs in environment due to it is undoubtedly threaten human and animal health directly [12,13]. For instance, in US, at least 23,000 people die each year as a direct result of these antibiotic-resistant infections [14].

Several extensive literatures have reported the fate of ARGs in various environment matrices such as soil [15-18], ocean [19,20], river [21,22], and wastewater treatment plants (WWTPs) [23,24]. Among them, WWTPs is one of the largest reservoirs of ARGs and plays a significant role in the proliferation of ARGs to the environment [25-27]. Especially, environmental conditions including high microbial density and diversity in WWTPs may promote the HGT of ARGs with abundant mobile genetic elements [28]. Recent studies have revealed that the negative effects of effluent from WWTPs on received environments [29,30]. For this reason, tertiary process which may present an opportunity to minimize the expose of ARGs to the environment and ultimately reduce the risk of antibiotic-resistant infections in human [11,31].

Several methods have been proposed for the removal of various antibiotics from water: biological treatment, advanced oxidation, membrane separation, and adsorption [32-38]. Unfortunately, these conventional water treatment processes do not remove antibiotics completely owing to the low concentrations and bio-refractory properties of these contaminants [39,40]. Current biological treatments use the most economical means available, but they require a prolonged period of time to degrade antibiotics. Poor and inconsistent removal efficiencies of antibiotics are

another drawback [41,42]. Advanced oxidation methods (e.g., using ozone, H₂O₂/UV, Fenton oxidation [Fe/H₂O₂] and photocatalytic oxidation) remove emerging contaminant by utilizing strongly oxidizing hydroxy radicals [43-49]. Although these systems can achieve complete degradation of antibiotics [50,51], the short lifetime of the hydroxyl radicals necessitates the use of large amounts of oxidant to degrade trace levels of contaminants, which in turn degrades other organic compounds and generates metabolites of unknown toxicity [32,52]. Membrane separation is a promising technology for removal of micropollutants in water, however, it easily suffers from (bio)fouling problems which could result in unexpected interruption of contaminant treatment.

Interestingly, DNA and RNA can be damaged when it is exposed to hydroxy radicals [53]. In this respect, ozone, chlorination and photocatalytic oxidation have been applied for the removal of ARGs [54]. In addition, some studies were also extended to UV irradiation for the removal of ARGs [3,55]. For instance, Zhuang et al. [56], reported that 2.98 -3.24, 2.48 - 2.74 and 1.68 - 2.55 log reductions of ARGs were achieved by chlorination (dose of 160mg/L with contact time of 120min), UV irradiation (UV dose of 12,477mJ/cm²) and ozonation (ozonation dose of 177.6mg/L), respectively. Although the ozone, chlorination and UV processes showed high removal of ARGs in a short time, they require high costs associated with energy and chemical consumption, maintenance and equipment. Recently, constructed wetlands (CWs) has been applied for the removal of antibiotics as well as ARGs due to its lower cost, easy operation and less maintenance requirements. In a positive sense, Huang et al. [57], reported that the removal efficiencies of ARGs in swine wastewater were greatly reduced with their removal efficiency ranging from 58 to 99.9% after vertical up-flow CWs treatment. However, increase in ARGs (e.g., tetracycline and sulfonamide resistance genes) was observed after horizontal and vertical subsurface flow CWs [58]. Thus, further study is needed to investigate the relationship between the operating conditions and ARGs in CWs as well as other treatment processes [59,60].

Discussion

A growing evidence indicates the importance of proper control of ARGs in WWTPs. However, there is still insufficient information available regarding the tertiary processes which can effectively remove the ARGs in effluent of WWTPs. More cost effective and efficient treatment processes for complete control of ARGs in wastewater should be developed along with detailed mechanisms and biotoxicity. In addition, long-term tracing of ARGs in the receiving environment (e.g., river and soil) after tertiary processes should be conducted since the regulation of level of ARGs is still questionable.

Conclusion

A lot of antibiotics have been released to various environments and led to develop antibiotic resistance causing serious health problems. Particularly, antibiotic resistant genes (ARGs) are widely spread over soil, water and air via multiple mechanisms

while negatively influencing on human health. Since wastewater treatment plants are the major sink of ARGs, various remediation technologies such as ultraviolet light, ozone, chlorination and biological treatment have been applied to reduction of ARGs in wastewater. However, these technologies have shown limitations to effectively remove ARGs in wastewater. Therefore, innovative and cost-effective technologies for reduction of ARGs in wastewater need to be developed.

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