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Presence of antibiotic residues in various environmental compartments of Shandong province in eastern China: Its potential for resistance development and ecological and human risk

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ABSTRACT

Objectives: To investigate the occurrence of antibiotic residues in different types of environmental samples including water samples in rural Shandong province, China. Further, to characterize the potential ecological risk for development of antibiotic resistance in the environment, and the potential direct human health risk of exposure to antibiotics via drinking water and vegetables.

Methods: Environmental samples (n = 214) (river water, waste water, drinking water, sediments, manure, soil and edible parts of vegetables) were collected in twelve villages in Shandong province in eastern China. High performance liquid chromatography–tandem mass spectrometry (HPLC–MS/MS) was used to determine the concentration of antibiotic residues. The ratio of the measured environmental concentrations (MEC) to the predicted no-effect concentrations (PNEC) was used to evaluate the ecological risk (risk quotient, RQ) for development of antibiotic resistance. The potential risks to human health through exposure to antibiotics in drinking water were assessed by comparing measured environmental concentrations (MEC) and predicted no-effect concentration in drinking water ($PNEC_{DW}$), and in vegetables by comparing estimated daily intake (EDI) to ADI.

Results: Sulfapyridine, sulfamethoxazole, ciprofloxacin, enrofloxacin, levofloxacin, norfloxacin, chloramphenicol, florfenicol, doxycycline, and metronidazole were detected at concentrations ranging between 0.3 and 3.9 ng/L in river water, 1.3 and 12.5 ng/L in waste water, 0.5 and 21.4 ng/L in drinking water, 0.31 and 1.21 μg/kg in river sediment, 0.82 and 1.91 μg/kg in pig manure, 0.1 and 11.68 μg/kg in outlet sediment, 0.5 and 2.5 μg/kg in soil, and 6.3 and 27.2 μg/kg in vegetables. The RQs for resistance development were > 1 for enrofloxacin, levofloxacin, and ranged between 0.1 and 1 for ciprofloxacin. MECs/$PNEC_{DW}$ ratios were < 1 from exposure to antibiotics through drinking water for both adults and children. EDI/ADI ratios were < 0.1 from exposure to antibiotics by vegetable consumption.

Conclusions: Antibiotic pollutants were ubiquitous in various environmental compartments of Shandong province of China. Risk estimates indicated a potential for the measured levels of enrofloxacin, levofloxacin and ciprofloxacin in waste water to pose an ecological risk for resistance selection, and further studies are needed to validate this finding. The investigated antibiotics did not appear to pose an appreciable direct human health risk from environmental exposure through drinking water or vegetables consumption. However, they might still pose a risk for resistance development.

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1. Introduction

Antibiotics are widely used to treat and prevent infectious diseases in humans and animals, to improve growth rate and feed efficiency in animals, and they are also used in agriculture and aquaculture (Cabello, 2006; FDA, 2009; McEwen and Fedorka-Cray, 2002; McManus et al., 2002). After administration of antibiotics, a significant fraction is released into different environmental compartments (Zhou et al., 2013). Between 30% and 90% of all antibiotics used in humans and animals are excreted unchanged or as active metabolites into the environment via urine and feces (Jjemba, 2006; Lienert et al., 2007).

The consumption of antibiotics is increasing in many countries resulting in their detection in surface water (Roberts and Thomas, 2006; Zhang et al., 2011), groundwater, drinking water (Fick et al., 2009; López-Serna et al., 2013; Standley et al., 2008; Teijon et al., 2010), municipal sewage (Lindberg et al., 2010), soil, vegetables (Christian et al., 2003; Li et al., 2014), sediment (Pei et al., 2006) and sludge (Göbel et al., 2005; Lindberg et al., 2010) around the world. The types and concentrations of antibiotics detected in the environment varies between and within countries, depending on patterns of antibiotic use, environmental parameters, and the environmental behaviors of different antibiotics (e.g. adsorption, biodegradation, photodegradation) (Díaz-Cruz et al., 2003; Kümmerer, 2009a; Li and Zhang, 2010).

China is one of the world's largest producers and consumers of antibiotics. Antibiotics are widely used for treatment of infectious diseases in humans and livestock, and are also used as prophylaxis and growth promoters for the latter. Research showed that in China approximately 92,700 tons of antibiotic were consumed in 2013. Of this 48% were consumed by humans, and the rest by animals. Approximately 46% of the antibiotics were ultimately released into rivers through sewage effluent with the remaining to land through manure and sludge land spreading (Zhang et al., 2015). As one example, three classes of antibiotics including tetracycline, sulfonamide and quinolone were detected from a sewage treatment plant and its effluent receiving river in Beijing China. These same antibiotics were also detected in the secondary effluent at levels of 195, 2001 and 3866 ng/L, respectively, which were higher than in the receiving river water (Xu et al., 2015). The results of another study revealed the presence of chloramphenicol, sulfonamides and tetracyclines at concentration ranges of 3.27–17.85, 5.85–33.37 and 4.54–24.66 mg/kg respectively in animal manures and agricultural soils adjacent to feedlots in Shanghai (Ji et al., 2012).

Approximately 50% of hospital outpatients in China were reported to be prescribed antibiotics, out of which, 74.7% were prescribed one antibiotic, and 25.3% were prescribed two or more antibiotics (Yin et al., 2013). Cephalexin, amoxicillin, ofloxacin, tetracycline, and norfloxacin were the top five antibiotics used for humans in 2013 in China (Zhang et al., 2015). With the implementation of the human medical system reform, the antibiotic consumption in outpatient and inpatient has likely declined.

Consumption of veterinary antibiotics increased from 46% in 2007 to 52% in 2013, totaling approximately 84,240 tons (Van Boeckel et al., 2015). Alternative strategies for the control of bacterial infections, such as optimizing the living conditions of livestock with respect to hygiene and sanitation, are required to reduce antibiotic consumption in animals in China.

Previous investigations on antibiotics in surface water of the Pearl River Delta, Yellow River, Haihe River, and Bohai Bay (Luo et al., 2011; Xu et al., 2007a, 2007b; Xu et al., 2009; Zou et al., 2011) provide evidence that China has problems of antibiotic pollution in aquatic environments.

Significant attention is being paid to the presence of antibiotic residues in the environment because of their potential adverse effects on ecosystems and human health. Specifically, antibiotic residues are likely to lead to the development and spread of antibiotic resistant bacteria/resistance genes (Martínez, 2008; Martinez, 2009; Stålsby Lundborg and Tamhankar, 2017). The transfer of resistant bacteria/resistance genes is favored by the presence of antibiotic residues in the environment over a long period, as selection can occur at very low concentrations (Gullberg et al., 2011, 2014). Moreover, the natural environment has been identified as a pathway by which transmission of antibiotic resistance to humans and animals might occur. Thus, animal, human, plant pathogens and other bacteria in different compartments of the environment share a common pool of resistance determinants that can be exchanged (Davies and Davies, 2010; Kümmerer, 2009b; Su et al., 2017). This common pool of resistance determinants may, therefore, pose a health threat to humans and animals (Purohit et al., 2017). Worldwide, the occurrence and spread of antibiotic resistant bacteria/resistance genes are a pressing public health problem (UN, 2016). High rates of common infections caused by resistant bacteria have been found in countries in all WHO regions, including China (WHO, 2014).Thus, antibiotic resistance has become a serious and growing threat to modern medicine, and is considered as one of the leading health concerns of the 21st century (UN, 2016).

In recognition of these concerns, the objectives of this study were to investigate the occurrence of antibiotic residues in different types of environmental samples including water samples in rural eastern China, and to characterize the ecological risk for development of resistance to antibiotics in the environment as well as the potential human health risk of exposure to antibiotics via drinking water and vegetables.

2. Methods

2.1. Setting

The study was conducted in twelve villages in Shandong province in eastern China. The province has a population of 96 million in 17 cities and 140 counties, of which around half are rural. The locations of sampling sites in villages (A–L) are illustrated in Fig. 1.

2.2. Environmental sample collection

Environmental samples (n = 214) were collected from the twelve villages, over six consecutive days in July 2015. The samples consisted of different types of water (well, surface, tap and waste water), sediments, pig (*Sus scrofa domesticus*) manure, soil and parts of the vegetables that are edible for humans (Table S1).

In each village, at least two households with animal breeding were included in the study. In each household, one sample each was taken from one human and one animal drinking water container. If for humans and animals different drinking water sources were used e.g. well water for animals and tap water for humans, then both would be sampled. If human and animals used the same drinking water only one drinking water sample was taken. In addition, waste water, manure, and outlet sediments were also sampled from the same household. If the village was near the river, water and sediment from river was sampled. For vegetables, different types of edible parts such as cucumber, tomato, lettuces and kidney beans etc. (Table S1) was sampled.

In sterile glass bottles, one liter of water or 30 g of river sediment or soil were collected. For vegetables, 30 g of vegetable samples were collected in plastic bags. The samples were directly placed in cool-boxes with ice-bags (~4 °C), and remained in the field for 1–3 h (depending on the local logistics). After the sample collection was complete, the samples were transported with ice-bags by car (4 h) to Shandong University (SDU) for further analysis. Thus, during the whole time from sample collection to its reaching the SDU laboratory, the samples remained in cool boxes containing ice-bags (~4 °C). The numbers of samples per sample type are presented in Fig. S1.

2.3. Antibiotic residue analysis

Target compounds were selected based on their usage in humans and animals in China, particularly in the target area, as well as their