Environmental behavior and impacts of antibiotics

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Abstract. Antibiotics are widely used to treat or prevent human and animal diseases, as well as to promote the growth of animals in livestock breeding and aquaculture. As a type of antibacterial drugs, antibiotics have been widely applied in human/animal disease prevention, disease treatment, animal husbandry and aquaculture, etc. A majority of antibiotics introduced into human/animal cannot be utilized directly, leading to the result that more than 85% antibiotics were discharged into the environment. Once antibiotics enter the ecosystems, they could influence the evolution of the community structure, which according affect the ecological function of aquatic environment. Correspondingly, antibiotic resistant bacteria (ARB) have been found, which is threatening ecological safety and human health. In this review, five parts were discussed in detail: (1) the source of antibiotics in the environment; (2) the determination of antibiotics and antibiotic resistance genes (ARGs) in the environment; (3) the spatial distribution of antibiotics and in the environment; (4) the fate of antibiotics in the environment; (5) the toxicological effects of antibiotics. Moreover, the existing problems and future research directions are proposed.

Introduction

Antibiotics are defined as drugs of natural, semisynthetic or synthetic origin with antibacterial, antifungal or antiparasitic activity. Until now, antibiotics have been applied in treating and preventing human and animal diseases as one of the most effective drug treatments. However, antibiotics could also induce ARB, becoming the important environmental pollutants. Large amounts of antibiotics introduced into human/animal cannot be utilized directly, leading to the result that more than 85% antibiotics were discharged into the environment in the form of treated or untreated wastewater [1].

However, the inappropriate use of antibiotics has caused serious environmental pollution recently. In pathogenicity and environmental microbiology, the proliferation and development of antibiotic resistance have been a public health problem [2]. Antibiotics with the characteristics of persistent and difficult biodegradability have the potential harm to human, land and sea creatures. More severely, the use of antibiotics could induce the development of antibiotic resistant bacteria and ARGs. Feces are used as fertilizer from animal feeding could also be a potential source of environmental antibiotic contamination [3].

The Use of Antibiotics

Generally speaking, the antibiotics are mainly used in both human and veterinary medicine. With the development of living standards, people will pay more attention to their own health. At present, antibiotics are also abused in hospital for pharmaceutical purpose.

For a long time, the abuse of antibiotics in China has been one of the most serious environmental problems in the world. In developed countries in Europe and the United States, the use of antibiotics could reach to about 10% of all drugs, while the hospitals in China accounted for at least 30%.

In addition, the use of antibiotics can effectively treat the infections and prevent the health of animals. In the process of poultry production, the reasonable use of antibiotics could promote the growth of poultry quickly. It was reported that the United States had supplied about 11,200 tons of veterinary antibiotics in production, such as pigs, cattle or others. Besides, the similar situation was also occurred in Africa, Europe, New Zealand and other countries [4].

Sources and Pathways for Antibiotic Residues in the Environment

Antibiotics in the environment have many sources which are animal husbandry, factory emissions, pharmaceuticals, aquaculture, etc. After consumption, antibiotics are usually excreted and are metabolized only partially via feces or urine (figure 1).

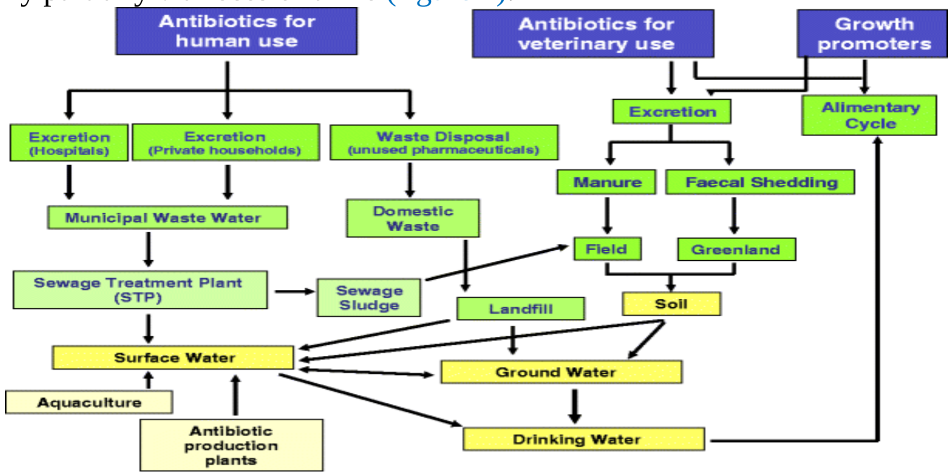

Fig.1 Sources and pathways for antibiotic residues in the environment[5]

There are about 80% often partially metabolized in organisms and excreted as the primary compounds or metabolites into the environment via feces and urine. After consumption, antibiotics are discharged into the urban sewage treatment plants (STPs), which cannot be effectively removed from environment [6]. Once antibiotics enter in the environment, the inactive drug, and including metabolites, they could be transported and degraded. Effluents from the STPs are released into surface waters and ground waters, which may cause the pollution of drinking water.

Antibiotics have attracted a great deal of attention during the last decade, especially in the field of animal husbandry and aquaculture. Extensive use of veterinary antibiotics in livestock breeding increases risk that these compounds ends up in the environment when metabolites are used as fertilizer. There are some overdue without formal handling of antibiotic drugs directly into the trash, besides, pharmaceutical wastewater directly discharged into the aquatic environment, which could cause pollution.

Detection Methods

At present, some different standard methods have been developed to determine the concentration of antibiotics in the aquatic environment, activated sludge, and sediments samples. Due to the polar nature, thermal stability and low volatility of these antibiotics, they need derivatization before detection. Thus, liquid chromatography (LC) has become the technique of solution for multiclass methods, particularly when coupled to mass spectrometry (MS) and tandem MS (LC-MS-MS), the LC-MS^2 allowing improved selectivity and sensitivity in much more complex matrices [7]. Despite these characteristics, due to the relatively low antibiotic concentration levels predicted in most food and water samples, the main detection need a preconcentration step, for sample extraction procedures, before analysis. The final target analytes are detected by LC-MS-MS. Solid phase extraction is usually performed in offline mode, while online provides a choice for samples. Future trendencies in the application of LC-MS-based techniques to multiclass antibiotic methods are also proposed.

The Current Status of Antibiotics Contamination

Because of the large application amount of antibiotics and their wide distribution, they can be detected in STPs, soils, sediments, and biological samples, and even in drinking water. Among them, the detection of high frequency of antibiotics has macrolides, quinolones, sulfonamides, tetracycline.

Current Situation of Antibiotics Pollution in Water Environment. At present, the STPs, hospital, aquaculture and pharmaceutical manufactures wastewater have been detected in the existence of a majority of antibiotics with the concentration from μg • L^{-1} to mg • L^{-1}. In 2009, Hojosa et al.[8] found that the influent concentration was 46.0 μg •L^{-1} and the effluent concentration was 30.0 μg • L^{-1} for amoxicillin in STPs in Spain. In 2006, Watkinson et al. [9] reported that the ciprofloxacin (CIP) concentration in Australia of detection for influent concentration was 3.80 μg • L^{-1} and the effluent concentration was 0.64 μg • L^{-1}, respectively.

Pollution Status of Antibiotics in Sludge and Sediments. Part of the antibiotic entering the STPs enters the surface water with the effluent, and the other part also enters into the activated sludge during the treatment process. In addition, a large number of the antibiotics in the surface water will transport into the sediments, leading to the accumulation effect of antibiotics which cannot be degraded in sediments and activated sludge. In 2008, Zhou et al. [10] found that the concentrations of the NOR and oxytetracycline in Liaohe basin in China ranged from not detection to 120μg • kg^{-1} and from not detection to 76.6 μg • kg^{-1}, respectively. In 2004, Lindberg et al. [11] found that the concentrations of the CIP in activated sludge samples in Sweden ranged from 5500 to 6300 μg • kg^{-1}.

The Degradation of Antibiotics in the Environment

The degradation of antibiotics in the environment could be classified as biodegradation and abiotic degradation. Non-biodegradation includes chemical degradation, photodegradation and hydrolysis.

Antibiotics Removal in STPs. As far as our knowledge, the STPs which become the point source of enriched antibiotics cannot completely remove all antibiotics. In a study by Gan et al. [12] investigations were conducted in sludge and sewage from a STP in southwestern China regarding the behavior and fate of typical antibiotics. Results showed that biotransformation and degradation were the main removal mechanisms. For quinolone antibiotics and azithromycin, sludge sorption was also a removal way (sludge sorption accounted for 9.35%~26.96% of the influent water load).

Degradation of Pollutants in Water. Hydrolysis is one of the important ways of antibiotic degradation. For example, β-lactams have been found in the environment at very low concentrations and they are easily hydrolyzed. Boreen et al. [13] found that photodegradation rate for sulfonamide antibiotics was very slow.

Environmental Effect of Antibiotics

Problem of antibiotic resistance genes (ARGs). The use of antibiotics could lead to the emergence of ARB or ARGs, which contain the potential environment risks to humans. The environmental persistence, migration and transformation of ARGs are more detrimental than antibiotics themselves, which have attracted ever growing attention as a newly emerging environmental issue.

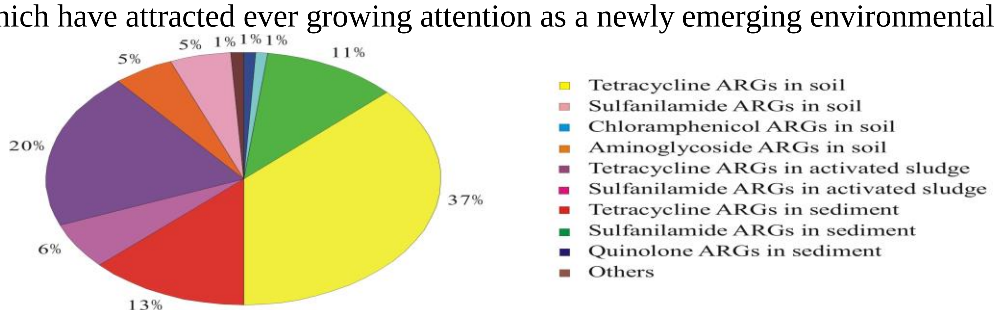

Fig.2 Research distribution for different ARGs in the soil environment of China[14]

In Figure 2, the studies about ARGs research in China from 2009 to 2014 were reviewed, and the distribution of ARGs such as soil, activated sludge and sediments were included. Analysis of soil environment showed tetracycline ARGs in soil to be in highest percentage (at least 37%), followed by tetracycline ARGs in activated sludge.

It was found that the content of ARGs in sediments was higher than that in surface water. Zhou et al. [3] reported that the concentration of ARGs in sediments was 120~2000 times higher than that in the aquatic environment in the Haihe River Basin in Tianjin. Stoll et al. [15] detected 24 resistance genes from a river basin in Europe, proving sulfonamides and streptomycin ARGs at 77~100% and 43~55%, respectively.

Ecological Toxicity of Antibiotics. The ecological toxicity of antibiotics and their metabolites in the environment are mainly as follows: (1) inhibit of plant and animal growth and development; (2) influence the community structure and ecological function, thereby affect soil fertility; (3) induce antibiotic resistant bacteria, and lead to an increasing concern about the potential environmental and public health risk.

Antibiotics on the Toxicity of Plants. Toxicity of antibiotics on plant size is dependent on the kinds of antibiotics and plants, also on the antibiotic use and soil sorption ability and so on.
Environment medium could significantly affect the toxicity of antibiotics. In 1982, Batchelder et al.[16] found that tetracycline had little effect on bean yield in the clay soil, but bean production decreased in the sandy soil.

Toxicity of Antibiotics to Animals. Previous publications have shown that tetracyclines, sulfonamides and quinolones and other antibiotics have strong soil sorption, leading to a long environment retention time. Some types of antibiotics (tylosin and oxytetracycline) showed low toxicity. Wollenberger et al. [17] reported that some of the antibiotics used in aquaculture can inhibit growth for insects and aquatic organisms, and even kill them. The studies have shown that antibiotics on aquatic invertebrates or fish had moderate toxicity. EC_{50} values after 48 hours was found in the range of 25 $mg \cdot L^{-1}$ to 500 $mg \cdot L^{-1}$ with *Daphnia magna* as the most potent.

Research and Prospects of Antibiotics

It is of great practical and theoretical significance to study the environmental behavior and ecotoxicology of antibiotics; and to establish the safety assessment and early warning system for the ecological environment of antibiotics; to protect human health and the ecological environment. In addition, we should analyze the ARGs pollution and environmental behavior with risk evaluation.

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