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Toxicological impacts of antibiotics on aquatic micro-organisms: A mini-review

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ABSTRACT

Antibiotics are found globally in the environment at trace levels due to their extensive consumption, which raises concerns about the effects they can have on non-target organisms, especially environmental micro-organisms. So far the majority of studies have focused on different aspects of antibiotic resistance or on analyzing the occurrence, fate, and removal of antibiotics from hospital and municipal wastewaters. Little attention has been paid to ecotoxicological effects of antibiotics on aquatic micro-organisms although they play a critical role in most ecosystems and they are potentially sensitive to these substances. Here we review the current state of research on the toxicological impacts of antibiotics to aquatic micro-organisms, including proteobacteria, cyanobacteria, algae and bacteria commonly present in biological wastewater treatment processes. We focus on antibiotics that are poorly removed during wastewater treatment and thus end up in surface waters. We critically discuss and compare the available analytical methods and test organisms based on effect concentrations and identify the knowledge gaps and future challenges. We conclude that, in general, cyanobacteria and ammonium oxidizing bacteria are the most sensitive micro-organisms to antibiotics. It is important to include chronic tests in ecotoxicological assessment, because acute tests are not always appropriate in case of low sensitivity (for example for proteobacteria). However, the issue of rapid development of antibiotic resistance should be regarded in chronic testing. Furthermore, the application of other species of bacteria and endpoints should be considered in the future, not forgetting the mixture effect and bacterial community studies. Due to differences in the sensitivity of different test organisms to individual antibiotic substances, the application of several bioassays with varying test organisms would provide more comprehensive data for the risk assessment of antibiotics. Regardless of the growing concerns related to antibiotics in the environment, there are still evident knowledge gaps related to antibiotics, as there is only limited or no ecotoxicological data on many potentially harmful antibiotics.

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1. Introduction

Today water security is one of the most pressing global issues due to the growing demand for limited water resources. The release of antibiotics in an aquatic environment at trace concentrations is among the major concerns of water researchers. Antibiotics were invented almost 90 years ago, and since then they have revolutionized human medicine. Today, antibiotics play a crucial role in the management of infectious disease, and they are consumed extensively in human and veterinary medicine and aquaculture. In addition to therapeutic applications, antibiotics are used for non-therapeutic purposes, for example to promote the growth of cattle, hogs, and poultry (Sarmah et al., 2006; Kümmerer, 2009). The use of antibiotics as growth-promoters is prohibited in the EU in 2006, but they are still used in other parts of the world such as China and India (Ronquillo and Hernandez, 2017). Due to their extensive consumption, antibiotics are ubiquitous and they have been detected in various ecosystems from terrestrial to aquatic environments (Yang and Carlson, 2003; Kümmerer, 2009; Martinez, 2009; Leung et al., 2012; Alygizakis et al., 2016). The advantages of antibiotics in healthcare are undisputed; however the bioactive properties of antibiotics and their presence in the environment at trace levels raise concerns about their toxicity to non-target organisms. Fundamentally, antibiotics were designed to be effective towards micro-organisms, due to which they are likely the most antibiotic-sensitive group of organisms, making them of particular interest (Brandt et al., 2015).

According to the reported data based on population estimates, the main origin of environmental pollution by human antibiotics is the diffuse contribution of the general public sewage plants. Antibiotic substances are not fully metabolized in the body, and residues of the antibiotics excreted with urine and feces end up at wastewater treatment plants (Ternes, 1998; Zuccato et al., 2010). Municipal wastewaters are a major source of antibiotics, as only 10–25% of antibiotics consumed by people come directly from hospitals (Kümmerer, 2009). Due to the continuous discharge of antibiotics, they are typically found in the environment in the low ng/L or μg/L range (Ternes, 1998; Kümmerer, 2009; Santos et al., 2010). Moreover, some of the antibiotics are poorly biodegradable and thus they can be persistent in the environment, and their toxic properties toward micro-organisms can remain even at trace levels (Kümmerer et al., 2000; Brown et al., 2006). The monitoring of harmful substances is currently based on chemical analytics from collected samples, however the complex nature of environmental samples, low concentrations, the dilution effect, and partial transformation of the parent compounds make the detection of antibiotics challenging. Indirect toxicological methods can provide additional knowledge on water quality and insight on mixture effects (González-Pleiter et al., 2013; Marx et al., 2015).

Prokaryotes are likely the most sensitive environmental organisms to antibiotics because antimicrobial agents are efficient inhibitors of bacterial growth (Martinez, 2009; Brandt et al., 2015). The present mini-review focuses on the toxicological impact of antibiotics which are most often passed through municipal wastewater treatment plants (WWTPs) and remain at detectable concentrations in aquatic environments with possible effects on prokaryotic microorganisms and micro-algae. Several methods for evaluating the toxicity of antimicrobial agents are currently available, and different bioassays using representative organisms of aquatic ecosystems have been used to assess the ecotoxicity (Wollenberger et al., 2000; Isidori et al., 2005; Robinson et al., 2005; Kim et al., 2007; González-Pleiter et al., 2013; Yasser and Adli, 2015).

Cyanobacteria are an essential group of prokaryotic organisms in the aquatic ecosystems: they represent the majority of phytoplankton mass and contribute largely to the total free oxygen production and carbon dioxide fixation in marine and terrestrial habitats. Many of them are also able to fix atmospheric nitrogen (Mitsui et al., 1986; Berman-Frank et al., 2003). Thereby inhibitory effects of antibiotics on cyanobacteria have been under the scrutiny of the researchers (Baquero et al., 2008; Guo et al., 2016). In addition to cyanobacteria, green algae have been applied to study the toxic effects of antibiotics on aquatic ecosystems (Isidori et al., 2005; Ando et al., 2007; De Liguoro et al., 2012; Kolar et al., 2014; Baumann et al., 2015). Algae are a vital part of the food chain in aquatic environments, forming a substantial share of the total biomass and therefore relevant for ecotoxicological studies. Another important group is proteobacteria. Proteobacteria can be divided into five subgroups (alpha-, beta-, delta-, gamma-, and epsilon-), including marine microorganisms as well as bacteria participating in the wastewater treatment processes, particularly ammonium and nitrite oxidizing and nitrogen fixating bacteria, and also bioluminescent bacteria (Kersters et al., 2006).

So far, the majority of the studies have focused on studying different aspects of antibiotic resistance. Additionally the occurrence, fate, and removal of antibiotics from hospital and municipal wastewaters have been studied extensively. Markedly, the ecotoxicological effects of antibiotics on aquatic micro-organisms have received less attention despite their significant role in different ecosystems. This mini-review provides an overview on antibiotics of high ecotoxicological concern based on their toxicological properties to aquatic micro-organisms, frequent detection in environmental samples and high potential for accumulation in natural waters. The existing analytical methods and effect concentrations for the most commonly applied micro-organisms for antibiotic effect studies are summarized and the current state of research is discussed with emphasis on the existing knowledge gaps and future perspectives. The issue of antibiotic resistance is left out of the scope of the study.

2. Antibiotics of high ecotoxicological concern

Not all of the antibiotics found in environmental samples are harmful, and the real challenge is to identify the ones that actually pose a risk in the environment from the complex sample mixtures. Some antibiotics are consumed more than others, and penicillins, sulphonamides, macrolides, and quinolones form the largest share of antibiotics consumed by humans globally (Kümmerer, 2009). However, it is very difficult to assess which compounds are potentially toxic, since for several compounds there is no comprehensive ecotoxicological data available, if any. In addition to toxicological data, parameters such as persistence and detection frequency should be considered. Table 1 lists antibiotics that can be considered of high ecotoxicological concern. The compounds were selected based on different parameters: large consumption, frequent detection in environmental samples, persistence, and toxic effects detected at low concentrations. Regardless of the wastewater treatment processes, these antibiotics still enter the environment through effluents because WWTPs are not specifically designed for the removal of these substances (Batt et al., 2007; Watkinson et al., 2007; Luo et al., 2014). Antibiotics from different chemical structure classes were selected. Presented in the table are maximum concentrations (μg/L) detected in environmental water samples (surface waters or ground water) and wastewater effluents. Median or mean concentrations are presented if this information was given in the reference.

Based on the maximum environmental concentrations reported in the literature, the highest concentrations have been measured for enrofloxacin (ENR), ciprofloxacin (CIP), norfloxacin (NOR), sulfamethoxazole (SMX), trimethoprim (TMP), azithromycin (AZM), erythromycin (ERY, ERY-H_2O), chlortetracycline (CTC) and oxyte-