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Research article

Chlorination and oxidation of sulfonamides by free chlorine: Identification and behaviour of reaction products by UPLC-MS/MS

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ABSTRACT

Sulfonamides (SAs) are one class of the most widely used antibiotics around the world and have been frequently detected in municipal wastewater and surface water in recent years. Their transformation in waste water treatment plants (WWTP) and in water treatment plants (WTP), as well as, their fate and transport in the aquatic environment are of concern.

The reaction of six sulfonamides (sulfamethoxazole, sulfapyridine, sulfamethazine, sulfamerazine, sulfathiazole and sulfadiazine) with free chlorine was investigated at a laboratory scale in order to identify the main chlorination by-products. A previously validated method, liquid chromatography/mass spectrometry, was used to analyse SAs and their chlorination by-products. At room temperature, pH 6–7, reaction times of up to 2 h and an initial concentration of 2 mg/L of free chlorine, the majority of SAs suffered degradation of around 65%, with the exception of sulfamethoxazole and sulfathiazole (20%). The main reaction of SAs with free chlorine occurred in the first minute.

1. Introduction

In the last years, several pharmaceuticals have been detected in the water cycle, typically in concentrations ranging from nanograms to low micrograms per litre range. The water matrices analysed include surface waters, wastewater, groundwater and, to a lesser extent, drinking water (WHO, 2011).

Antibiotics are used in agriculture, human and animal health, for controlling bacteria, and are also incorporated into animal feed to improve growth rate and feed efficiency. It is well known that wastewaters that originate from farms and hospitals constitute one of the causes of biocontamination of environmental waters. Also, sewage and manure can contain antibiotic resistant bacteria and resistance genes, which are regarded as one of the three greatest threats to human health by the World Health Organization (WHO, 2011; Han et al., 2013; Pruden et al., 2013).

Many of these compounds appear to be relatively persistent in the aquatic environment, which can be attributed to inefficient removal in wastewater treatment plants, absence of significant attenuation in environmental waters, or due to their detection in groundwater (Benotti and Brownawell, 2007).

Due to the their low cost and relatively high efficiency against many common bacterial infections, sulfonamides (SAs) were one of the most widely used antibiotic families in the world, mainly as antibacterial veterinary drugs. This class of antibiotics is considered to be potentially toxic to aquatic organisms and eventually to humans through the food chain and drinking water (García-Galán et al., 2011). Sulfonamides were the first antimicrobials to be used in clinical practice. The development of resistant strains and the fact that they present significant toxicity have limited their therapeutic utility. The association with other antimicrobial sulfonamides, aim a synergistic effect to minimize the development of resistant strains (Infarmed, 2010).

Sulfonamides have been detected in affluent, effluents and surface waters in several studies, including Portugal (Madureira et al., 2010; Gaffney et al., 2014). In a Portuguese study, the maximum concentration of sulfamethoxazole detected in samples of the River Douro was higher than the estimated PNEC (predicted

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no-effect concentration) value (Grung et al., 2007; Madureira et al., 2010).

As illustrated in Table 1, sulfonamides contain two moieties bonded to both sides of the characteristic sulfonamide bond (sulfonamide functional group, $-NH-S(=O)_2-$), which is constituted by a sulfonyl group bonded to an amine group. The aniline moiety in *para*-connection to the sulfonyl group is present in all sulfanilamides, with variations occurring in the structures of the moiety which is bonded to the amine group.

Due to their low octanol–water partition coefficient (K_{ow}), high solubility and great stability in water, SAs can contaminate groundwater through leaching processes and therefore are very likely to be detected in water matrices.

Like other pharmaceuticals, SAs are generally better characterized than other environmental contaminants, however the effect of treatments commonly used in WTPs, is not well understood. The non-detection of the parent compound (pharmaceutical) does not imply that the treatment was efficient as some selective reactions used in WTPs, mainly chlorination and ozonation, can lead to the formation of intermediates with increased toxicity and biological activity relative to the parent compound.

The identification and study of environmental transformation products is currently the focus of great interest in environmental chemistry. With the aid of analytical techniques like GC/MS, GC-MS/MS, LC-MS/MS, LC-Q-TOF-MS, and sometimes NMR, researchers are proposing complex transformation pathways, as well as, detailed mechanisms (Moriyama et al., 2004; Radjenovic et al., 2009; Li et al., 2011; Rodriguez et al., 2013; Salgado et al., 2013).

Researchers are also combining toxicology with chemistry, in order to assess the toxicity related to the transformation products and disinfection by-products and in the identification of unknowns that can be the cause of adverse environmental effects (Richardson, 2012).

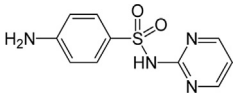
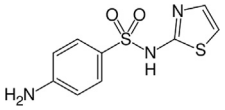
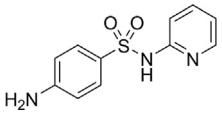
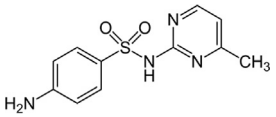
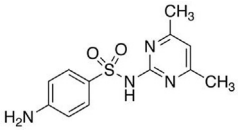
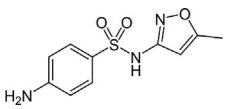
Products resulting from the reaction of some sulfonamides with chlorine were reported by several authors (Dodd and Huang, 2004; Chamberlain and Adams, 2006; Melton and Brown, 2012) that used GC/MS, LC/ESI-MS/MS, and 1H NMR to identify the chlorination by-products.

However, the method that is most widely used for the disinfection of drinking water (i.e., free chlorination with $HOCl/OCl^-$) has not been the subject of intensive research. Dodd and Huang (Dodd and Huang, 2004) studied the oxidation of one sulfonamide (sulfamethoxazole) with chlorine and estimated rate constants for both the hypochlorous acid and the hypochlorite ion. These researchers also proposed oxidation by-products and pathways based on mass spectrometry fragmentation patterns (Dodd and Huang, 2004).

The purpose of the current research was to determine the efficiency of free chlorine on the oxidation of six SAs under common conditions used in drinking water treatment plants, with by-products identification being the main scope of this study.

The SAs were rapidly transformed during the chlorination step

Table 1
Structures of sulfonamides.

Compound	Acronym	Structure	Molecular weight
Sulfadiazine	SDZ	 4-Amino-N-pyrimidin- 2-yl-benzenesulfonamide	250.28
Sulfatiazol	STZ	 4-Amino-N-(1,3-thiazol-2-yl)benzenesulfonamide	255.32
Sulfapyridine	SPD	 4-Amino-N-pyridin-2-ylbenzenesulfonamide	249.29
Sulfamerazine	SMZ	 4-Amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide	264.30
Sulfamethazine	SMT	 4-Amino-N-(4,6-dimethyl-2-pyrimidinyl)benzenesulfonamide	278.33
Sulfamethoxazole	SMX	 4-Amino-N-(5-methylisoxazol-3-yl)-benzenesulfonamide	253.28