Science of the Total Environment 500–501 (2014) 250–269

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Review

Fluoroquinolone antibiotics: An emerging class of environmental micropollutants

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HIGHLIGHTS

- Fluoroquinolones (FQs) are important environmental emerging micropollutants.
- Overview of environmentally relevant FQ physical–chemical properties
- Use, sources and pathways of FQs to the environment
- Concentration data of FQs in different environmental matrices
- Tentative ecological risk assessment by means of hazard quotients

ARTICLE INFO

Article history:
Received 16 July 2014
Received in revised form 21 August 2014
Accepted 21 August 2014
Available online 16 September 2014

Editor: D. Barcelo

Keywords:
Fluoroquinolones
Antibiotics
Pharmaceuticals
Environment
Water

ABSTRACT

The aim of this review paper is to provide a comprehensive overview of different chemical and environmental aspects concerning fluoroquinolone antibiotics as emerging contaminants. A literature survey has been performed based on 204 papers from 1998 to mid-2013, resulting in a dataset consisting out of 4100 data points related to physical–chemical properties, environmental occurrence, removal efficiencies, and ecotoxicological data.

In a first part, an overview is given on relevant physical–chemical parameters to better understand the behavior of fluoroquinolones during wastewater treatment and in the environment. Secondly, the route of these antibiotics after their application in both human and veterinary surroundings is discussed. Thirdly, the occurrence of fluoroquinolone residues is discussed for different environmental matrices. The final part of this review provides a tentative risk assessment of fluoroquinolone compounds and their transformation products in surface waters by means of hazard quotients.

Overall, this review shows that fluoroquinolone antibiotics have a wide spread use and that their behavior during wastewater treatment is complex with an incomplete removal. As a result, it is observed that these biorecalcitrant compounds are present in different environmental matrices at potentially hazardous concentrations for the aquatic environment. The latter calls for actions on both the consumption as well as the wastewater treatment aspect to diminish the discharge of these biological active compounds.

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Abbreviations: BAF, bioaccumulation factor; CEC, cation exchange capacity; CIP, ciprofloxacin; DANO, danofloxacin; DI, difloxacin; ECDC, European Centre for Disease Prevention and Control; ENRO, enrofloxacin; ESAC, European Surveillance for Antimicrobial Consumption; FLU, flumequine; FQ, fluoroquinolone; GATI, gatifloxacin; HQ, hazard quotient; LEVO, levofloxacin; LOME, lomefloxacin; LOQ, limit of quantification; MARBO, marbofloxacin; MEC, measured environmental concentration; MOX, moxifloxacin; NOR, norfloxacin; OFL, ofloxacin; PEFL, pefloxacin; PNEC, predicted no effect concentration; RE, removal efficiency; SARA, sarafloxacin; SPAR, sparfloxacin; WWTP, wastewater treatment plant.

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http://dx.doi.org/10.1016/j.scitotenv.2014.08.075
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1. Introduction

At date, more than 5000 different pharmaceutical compounds intended for human and veterinary applications are used worldwide (Dorival-García et al., 2013a). Despite their benefits, a growing concern about potential adverse impacts on biota and human health has emerged as a result of their continuous release into the environment (Allen et al., 2010; Fent et al., 2006; Jones et al., 2004; Kümmerer, 2009a; Michael et al., 2013; Rizzo et al., 2013; Tijani et al., 2013).

Pharmaceuticals are a broad group of compounds divided into different classes, such as analgesics and anti-inflammatory drugs, antibiotics, anti-epileptics, beta-blockers, contrast media, cytostatics, hormones, antidepressants, disinfectants and antiseptics, among others. Recent reviews provide a general overview on the exposure routes and the occurrence of pharmaceutical residues in the environment (Fatta-Kassinos et al., 2011; Gavrilescu and Caliman, 2009; Kümmerer, 2009a; Tijani et al., 2013) and in wastewater treatment plants (WWTPs) (Miège et al., 2009; Verlicchi et al., 2012a). Other reviews particularly focus on one specific class of pharmaceuticals, such as antiviral drugs (Jain et al., 2013), psychiatric pharmaceuticals (Calisto and Esteves, 2009), anti-inflammatory and analgesic pharmaceuticals (Ziylan and Ince, 2011), and antibiotics (Du and Liu, 2012; Kemper, 2008; Kümmerer, 2009b,c; Michael et al., 2013; Segura et al., 2009; Seifrtová et al., 2009; Thiele-Bruhn, 2003) covering different topics, including detection techniques, occurrence in the environment, ecotoxicity, and treatment by biological systems.

Antibiotics are more and more a focus point of research due to their high detection frequency in the environment and the increasing bacterial resistance formation (Bouki et al., 2013; Kümmerer, 2009b,c; Rizzo et al., 2013). Reviews on one specific subgroup of antibiotics are scarce. Hruska and Franek (2012) recently discussed the environmental occurrence of sulfonamides, and Speltini et al. (2010) mainly focused on sample preparation and detection methods for fluoroquinolones (FQs) in environmental matrices. To date, no recent comprehensive review on the occurrence of FQs in different environmental matrices has been published. A last update has been given by Sukul and Spiteller (2007), who present a rather broad overview including a brief description of the environmental occurrence of FQ compounds.

FQs are of interest, since they are wide spectrum antibacterials with an increasing use in hospitals, households, and veterinary applications (Adriaenssens et al., 2011; BelVetSac, 2011; Grave et al., 2012). They are the third largest group of antibiotics accounting for 17% of the global market share with a sale of 7.1 billion US dollars in 2009 (Hamad, 2010).

FQ antibiotics are excreted unmetabolized up to 70% and, when released in the environment, they can promote resistance formation on microbial populations. A significant increase in FQ bacterial resistance between 2007 and 2010 is observed by the European Surveillance for Antimicrobial Consumption (ESAC) (ESAC, 2010). Moreover, the presence of these pseudo-persistent compounds in the environment can induce toxic effects on aquatic organisms (Robinson et al., 2005). The lack of biodegradation and high adsorption affinity results in long residence times in the environment, with reported half-life times of 10.6 days in surface water (Andreozzi et al., 2003) and up to 580 days in soil matrices (Rosendahl et al., 2012).

The main goal of this paper is to compile a comprehensive review on the FQ structure, use, classes, sources, pathways, occurrence, fate and behavior, and ecotoxicity of these emerging micropollutants in different environmental matrices. An extensive literature survey is performed, including manuscripts from 1998 to mid-2013, which report physical–chemical properties, removal efficiencies (RE) after wastewater treatment, and environmental FQ concentrations above the limit of quantification (LOQ), yielding a dataset of 4100 data points from over 200 references.

The paper is structured as follows. First, the chemical structure and therapeutic use of the FQs detected in the environment are presented in Section 2. Section 3 summarizes published information on physical–chemical properties relevant for the fate and behavior of FQs in the environment. Main sources and pathways of FQ compounds to the environment are discussed in Section 4 and Section 5, respectively, where Section 6 deals with the occurrence of FQs in different environmental matrices. The environmental fate and behavior of FQs are presented in Section 7, while the final section (Section 8) deals with ecological effects of FQs and their transformation products in both solid and aqueous matrices. A schematic outline and the link between the different sections are presented in Fig. 1.

2. Chemical structure and therapeutic use

Nalidixic acid, discovered in 1962 as a by-product of anti-malaria research, is the parent compound of the quinolone antibiotic class and has a narrow antibacterial spectrum. Until the development of flumequine (FLU), none of the earlier synthesized compounds had offered any significant therapeutic improvements (Appelbaum and Hunter, 2000).

FLU is the first monofluorinated quinolone, from which the subgroup of the FQs has been arised. The addition of fluorine resulted into an increased antibacterial spectrum, indicating that a structural modification of the '4-quinolone' skeleton (Table 1 Top) could improve the activity. This marked the beginning of intensive chemical synthesis efforts to refine structure–activity relationships, optimize pharmacokinetics, and reduce toxicity and drugs interactions. The addition of different R_1, R_7 and R_8 groups created new and more effective FQ compounds