Science of the Total Environment 612 (2018) 649–659

Contents lists available at ScienceDirect

Science of the Total Environment

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

Occurrence, distribution and environmental risk of pharmaceutically active compounds (PhACs) in coastal and ocean waters from the Gulf of Cadiz (SW Spain)

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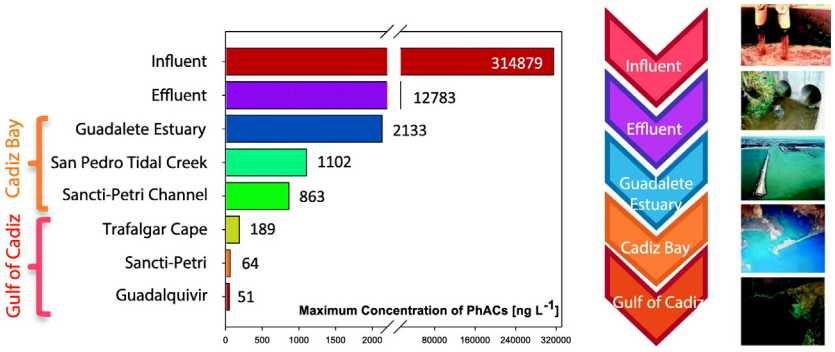
HIGHLIGHTS

- Carbamazepine, furosemide and hydrochlorothiazide persisted during wastewater treatment.
- Conservative behaviour along Guadalete Estuary was observed for specific PhACs.
- 5 out of 45 antibiotics were found in open sea transects at levels up to 5 ng L^{-1}.
- Preliminary risk assessment shows that PhACs pose no risk in offshore waters.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 31 December 2016
Received in revised form 28 August 2017
Accepted 28 August 2017
Available online xxxx

Editor: D. Barcelo

Keywords:
Pharmaceuticals
Antibiotics
Seawater
Wastewater
Environmental risk assessment

ABSTRACT

In this study, we have evaluated the occurrence and distribution of 78 pharmaceuticals in different aquatic marine environments from the Gulf of Cadiz (SW Spain) for the first time. The obtained results revealed that pharmaceuticals were present in seawater at total concentrations ranging 61–2133 and 16–189 ng L^{-1} in coastal and oceanic transects, respectively. Potential marine pollution hotspots were observed in enclosed or semi-enclosed water bodies (Cadiz Bay), showing concentrations that were one or two orders of magnitude higher than in the open ocean. The presence of these chemicals in local sewage treatment plants (STPs), one of the main contamination sources, was also assessed, revealing total concentrations of up to 23 μg L^{-1} in effluents. PhACs with the highest detection frequencies and concentrations in the sampling region were analgesics and anti-inflammatories followed by antibiotics in the case of samples from Cadiz Bay or caffeine in oceanic seawater samples. Risk quotients, expressed as ratios between the measured environmental concentration (MEC) and the predicted no-effect concentrations (PNEC) were higher than 1 for two compounds (gemfibrozil and ofloxacin) in effluent of Jerez de la Frontera sewage treatment plant (STP). No high environmental risk was detected in both coastal and oceanic sampling areas, although the information available about the effects of these chemicals on marine biota is still very limited and negative effects on non-target species cannot be discarded.

1. Introduction

Pharmaceutically active compounds (PhACs) have the ability to prevent, diagnose or treat infections and diseases in humans and animals,

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http://dx.doi.org/10.1016/j.scitotenv.2017.08.279
0048-9697/

and to correct or modify organic functions (Daughton and Ternes, 1999). After oral administration, some PhACs are metabolized, while others remain intact before being excreted. These pharmaceuticals and their metabolites enter wastewater and go through municipal sewage treatment plants (STPs). However, removal of many PhACs during the wastewater treatment process is inefficient, and some PhACs are also directly released into the environment after use in aquaculture and animal feeds (Ternes et al., 1999). Hence, PhACs are considered emerging contaminants, compounds that have become of increasing concern in recent years as they have been identified in the environment at trace levels and their effects are mainly unknown (McEneff et al., 2015). As an example, antibiotics may have the potential to cause ecological harm in organisms and to select for antibiotic resistance genes (ARGs) in bacterial populations (Kümmerer, 2004).

The highest PhAC concentrations in aquatic settings are usually measured in rivers impacted by domestic, industrial and hospital wastewater effluents. Indeed, pharmaceutical compounds are frequently detected in STP effluents and receiving surface waters in concentrations ranging from a few pg to several μg L^{-1} (López-Serna et al., 2011; Gros et al., 2012). Among the PhACs, analgesics and anti-inflammatories are often predominant followed by antibiotics and the antiepileptic carbamazepine (Gros et al., 2007; Santos et al., 2007). In contrast, comparable analytical data from marine environments are scarce. So far, Alygizakis et al. (2016) studied the occurrence and spatial distribution of 158 pharmaceuticals and illicit drugs in seawater from the Eastern Mediterranean Sea (Saronikos Gulf and Elefsis Bay in central Aegean Sea), confirming the presence of 38 target compounds. Among them, 15 substances (caffeine, tramadol, salicylic acid, lidocaine, amoxicillin, carbamazepine, amisulpride, niflumic acid, norvenlafaxine, paracetamol, EDDP, diclofenac, mefenamic acid, citalopram and sulpiride) were detected at concentrations higher than 50 ng L^{-1}. A similar study was performed by Weigel et al. (2002), who measured concentrations of seven classes of PhACs in the North Sea and coastal areas of UK, Netherlands, Denmark, and Norway ranging from 0.03 to 16.1 ng L^{-1}. Fifteen different PhACs could be found in seawater samples from Jamaica Bay (NY, USA) by Benotti and Brownawell (2007). The highest levels of most identified compounds were generally <100 ng L^{-1}, except for caffeine, cotinine, nicotine, nifedipine, paraxanthine, and albuterol, which were detected at the highest concentrations inside the bay (> 1000 ng L^{-1}). Zhang et al. (2013) analyzed eleven classes of antibiotics in seawater from the Bohai Sea and the Yellow Sea (China). All target compounds were detected, with a predominance of erythromycin, sulfamethoxazole and trimethoprim (between 0.1 and 16.6 ng L^{-1}). Another recent study (Moreno-González et al., 2015) evaluated the distribution of pharmaceuticals in seawater at Mar Menor lagoon (Spain), finding 20 out of 42 analytes (mostly drugs for treating cardiovascular diseases) at concentrations higher than the method limits of quantification (mLOQ). The results reported in the literature suggest that the presence of pharmaceutical compounds can be detected in the coastline environment due to the STP effluents discharging or terrestrial input, but the concentrations of these compounds are generally below the detection limit in the open sea environment owing to the dilution effect and degradation processes.

Due to higher dilution in marine waters, the concentrations of PhACs are expected to be low compared to freshwater settings and wastewater and, thus, direct effects of single pharmaceutical substances are assumed to be minor or negligible (Pomati et al., 2008). However, it is essential to establish the environmental risk posed to marine organisms by mixtures of these compounds and to assess long-term effects. This is encouraged due to the rising usage of PhACs and the occurrence of these compounds in effluents from STPs, which has led recently to new legal requirements and guidelines in the USA (EPA, 1998) and EU (ECB, 2003). In addition to these criteria, the environmental risk has recently become a matter of increasing research (Hernando et al., 2006; Park and Choi, 2008). The ecotoxicological hazard assessment of PhACs is mostly based on laboratory studies. As an example, Park and Choi (2008) evaluated eleven commonly used antibiotics, including sulfonamides, tetracyclines, aminoglycosides, fluoroquinolones, and β-lactams, for their acute and chronic aquatic toxicities using different standard test organisms (*Vibrio fischeri*, *Daphnia magna*, *Moina macrocopa*, and *Oryzias latipes*). Only 1 class out of 5 showed low toxicity (β-lactams) whereas the rest of the tested antibiotics presented intermediate or acute toxicity at concentrations between 0.03 and 150 mg L^{-1}. Many comprehensive review studies indicate that the concentration levels of PhACs often detected in STP effluents and the receiving waters could threaten some aquatic organisms (Hernando et al., 2006; Claessens et al., 2013). Bioaccumulation is also possible for some specific compounds. As an example, Moreno-González et al. (2016) recently analyzed 20 PhACs in cockle (*Cerastodema glaucum*), noble pen shell (*Pinna nobilis*), sea snail (*Murex trunculus*), golden grey mullet (*Liza aurata*) and black goby (*Gobius niger*) in the Mar Menor lagoon (Spain), finding 8 of these compounds at low concentrations (ng g^{-1}). Hydrochlorothiazide and carbamazepine were detected in all species. Further research including monitoring and detailed toxicological tests at environmentally relevant concentrations are, however, still required for a better assessment of the potential ecological risk of most PhACs, especially in the marine environment, where there is less information.

The current work aims at broadening the knowledge about the occurrence of pharmaceuticals in coastal areas affected by sewage discharges (as most focus has been done on assessing surface freshwater quality) through the determination of the occurrence, distribution and potential environmental risk of a wide selection of PhACs in different locations situated in the Gulf of Cadiz. This is an area of special interest because it is adjacent to the Strait of Gibraltar, which connects the Atlantic Ocean and the Mediterranean Sea, allowing the exchange of water and organisms between the two water bodies. The levels of PhACs in this zone, and the subsequent exposure of organisms to complex mixtures that could decrease their fitness and affect the quality of the different ecosystems in this region, are still unknown. Pharmaceuticals included in this study comprise a group of 78 compounds belonging to different therapeutic categories including analgesics, antiinflammatories, lipid regulators, antibiotic, etc. They were selected taking into account their high consumption and their previous detection in freshwater and terrestrial environments in previous studies (Pérez-Carrera et al., 2010; Corada-Fernández et al., 2015; Baena-Nogueras et al., 2016; Díaz-Garduño et al., 2017). Current EU legislation has included some of them, such as diclofenac and several macrolide antibiotics (erythromycin, clarithromycin and azithromycin), in the first watch list under the Environmental Quality Standards Directive (2008/105/EC) (European Commission, 2015). The main objectives of this research were to provide baseline contamination data of these chemicals in both coastal and ocean waters in the region, as well as to identify the influence of PhAC sources, mostly related to sewage discharges from local STPs and other activities such as aquaculture. To this end, three different types of water samples were analyzed: (i) influent and effluent wastewater samples from a local STP (Jerez de la Frontera), (ii) three transects at different coastal aquatic systems (estuaries and tidal creeks at Cadiz Bay) and (iii) three transects in open ocean along the Gulf of Cadiz (from the Strait of Gibraltar towards the mouth of the main watercourse in the region, Guadalquivir River). Later, a preliminary environmental risk assessment was performed for those PhACs that were detected and for which ecotoxicological data towards aquatic species were available.

2. Materials and methods

2.1. Sampling areas and sample collection

The study area and sampling sites are shown in Fig. 1 and Table S1 (Supplementary material). Twenty-four hour composite wastewater samples (influent and effluent) were collected during summer months