Environmental Research 136 (2015) 108–119

Contents lists available at ScienceDirect

Environmental Research

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

Environmental impact of pharmaceuticals from Portuguese wastewaters: geographical and seasonal occurrence, removal and risk assessment

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ARTICLE INFO

Article history:
Received 19 May 2014
Received in revised form
2 September 2014
Accepted 5 September 2014

Keywords:
Environmental contaminants
Pharmaceuticals
Municipal wastewaters
Occurrence and fate
Seasonal variation
Environmental risk assessment

ABSTRACT

The occurrence, fate, geographical and seasonal influence and environmental risk assessment of eleven of the most consumed pharmaceuticals in Portugal were studied in wastewater treatment plants (WWTPs) influents and (WWI) and effluents (WWE). WWI and WWE samples, from two sampling campaigns (spring and summer), in 2013, were evaluated in 15 different WWTPs across the country, by solid phase extraction (SPE) and liquid chromatography coupled with tandem mass detection (LC–MS-MS).

Lipid regulators were the most frequently found in WWI and WWE (184.1 and 22.3 mg/day/1000 inhab., respectively), followed by anti-inflammatories (1339.4 and 15.0 mg/day/1000 inhab., respectively), and antibiotics (330.7 and 68.6 mg/day/1000 inhab., respectively). Anxiolytics were the least detected with 3.3 and 3.4 mg/day/1000 inhab. in WWI and WWE, respectively.

The mass loads, both in WWI and WWE, were higher in summer than those found during the spring season, being remarkable the high values registered in a region where population triplicates in this time of the year. The mean removal efficiency achieved was of 94.5%, nonetheless, between the different therapeutic groups, as well as within each group, important variations in removal were observed, going from not eliminated to 100%. In the summer higher efficiencies were observed regarding lipid regulators and antibiotics.

Furthermore, an important outcome was the evaluation, by means of risk quotients (RQs), of the potential ecotoxicological risk posed by the selected pharmaceuticals to different aquatic organisms, exposed to the effluents studied. Ciprofloxacin, bezafibrate, gemfibrozil, simvastatin and diclofenac showed RQs higher than one, being expected that these pharmaceuticals might pose a threat to the three trophic levels (algae, daphnids and fish) evaluated. These results highlight the importance of these monitoring studies, as required by the Directive 2013/39/EU, in order to minimize their aquatic environmental contamination and support future prioritization measures.

1. Introduction

Human pharmaceuticals represent a group of widely used chemicals that contaminate the environment. Albeit in trace amounts, they are of concern since they are designed to perform a biological effect. Moreover, given their continuous introduction into the environment, their environmental impact, both as stressors and as agents of change, is of great importance (Mompelat et al., 2009).

Worldwide has been recognized the environmental impact of medicinal products. Although no legal limits have been established in water, relevant legislation and regulatory guidance has been issued by the European Union (EU) (Verlicchi et al., 2014). The Water Framework Directive (WFD) (Directive 2000/60/CE), establishes the priority substances in the policies of the water domain of the EU (Afonso-Olivares et al., 2013; Vazquez-Roig et al., 2011), whereas, the Directive 2001/83/EC, as amended by the Directive 2004/27/EC, requires an evaluation of the potential environmental risks to be performed for every new marketing

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http://dx.doi.org/10.1016/j.envres.2014.09.041
0013-9351/

Table 1
Therapeutics groups, characteristics, CAS number and national sales for the selected pharmaceuticals.

Therapeutic group	Pharmaceutical	Molecular formula	Molecular weight	CAS no.	National sales by package
Anxiolytics and hypnotics	Alprazolam	$C_{17}H_{13}ClN_4$	308.8	28981-97-7	2,384,299
	Lorazepam	$C_{15}H_{10}N_2Cl_2O_2$	321.2	846-49-1	1,947,305
	Zolpidem	$C_{19}H_{21}N_3O$	307.4	82626-48-0	1,089,029
Antibiotics	Azithromycin	$C_{38}H_{72}N_2O_{12}$	749	83905-01-5	944,513
	Ciprofloxacin	$C_{17}H_{18}FN_3O_3$	331.4	85721-33-1	618,465
Lipid regulators	Bezafibrate	$C_{19}H_{20}ClNO_4$	361.8	41859-67-0	41,450
	Gemfibrozil	$C_{15}H_{22}O_3$	250.3	25812-30-0	n.a.
	Simvastatin	$C_{25}H_{38}O_5$	418.6	79902-63-9	3,440,703
Anti-Inflammatories and/or analgesics	Diclofenac	$C_{14}H_{10}Cl_2NNaO_2$	318.1	15307-79-6	1,295,809
	Ibuprofen	$C_{13}H_{18}O_2$	206.3	15687-27-1	2,063,414
	Paracetamol	$C_8H_9NO_2$	151.2	103-90-2	3,239,035

n.a. – Not available.

authorization. In January 2012, the EU published a report regarding the revision of the Directive 2000/60/CE, and several new substances were proposed, including diclofenac (European Commission 2012). Moreover, directive 2013/39/EU sets a watch list, that includes three pharmaceuticals, being one of them diclofenac, and requires relevant monitoring data from each member state, in order to minimize their aquatic environmental contamination and support future prioritization measures.

In recent years, has been observed an increased and chronic consumption of several medicines all across the world. In Portugal the highest prescription and consumption regard, among others, alprazolam, lorazepam and zolpidem (anxiolytics and hypnotics), azithromycin and ciprofloxacin (antibiotics), simvastatin, bezafibrate and gemfibrozil (lipid regulators), and ibuprofen, diclofenac and paracetamol (non-steroidal anti-inflammatories and analgesics) (INFARMED, 2011) (Table 1). As their use cannot be avoided, a sound risk assessment of their presence in the environment is a key problem. The selected pharmaceuticals were chosen within each group by the ranking of national sales, by package, in 2011 (INFARMED, 2011) (Table 1).

The main source of pharmaceuticals residues in the aquatic environment is from human excretion, consequently, the widespread presence of pharmaceuticals in environmental samples is most likely to occur from wastewaters treatment plants (WWTPs), which incompletely remove these compounds. Pharmaceuticals are then released into the environment as parent compounds, metabolites, as well as transformation products formed during water treatments, by biodegradation, photolysis or hydrolysis (Petrovic and Barceló, 2007), leading to the contamination of surface waters, seawaters, groundwater and some drinking waters. Nevertheless, there are also other pathways of aquatic contaminations such as sewage overflow, aquaculture, and leaching from agricultural fields resulting from the spreading of manure and presence of livestock (Al Aukidy et al., 2012; Bueno et al., 2012; Fick and Söderström, 2009; Focazio et al., 2004; Jelic, 2012; Kümmerer, 2010; Nikolaou et al., 2007; Seifrtová et al., 2008).

Heavy contamination pressures from extensive urban activities characterize the Portuguese coast and main rivers that might lead to high aquatic contamination levels and consequent environmental and human exposure. Although the concentrations of pharmaceuticals in influents (WWI) and effluents (WWE) of WWTPs are routinely monitored in many countries, there is little knowledge on pharmaceuticals occurrence/fate, and their environmental exposure profile in Portugal (Loos et al., 2012; Salgado et al., 2012; Santos et al., 2013; Sousa et al., 2011). Moreover, their sources of contamination may be influenced by different geographical patterns of pharmaceuticals consumption, and important fluctuations due to seasonal variations might also occur.

These are important issues for an integrated management of the possible environmental risk assessment, which is essential for the implementation of minimizing measures. Frequently, a pragmatic approach for identifying hazards or prioritizing critical substances has been made (EMA, 2006), but this concept is not sufficiently precise for an accurate assessment of pharmaceuticals risk. Nevertheless, information on real measured concentrations of pharmaceuticals in the environmental aquatic compartment, allows a good insight into human exposure.

The key driving force of this study was to perform, for the first time, a nationwide environmental contamination mapping of the above mentioned 11 pharmaceuticals, in 15 WWTPs from 5 different Portuguese regions, in order to evaluate geographical/national contamination patterns and to assess vulnerable areas. Moreover, we aimed to assess seasonal influence, in spring and summer seasons, and WWTPs removal efficiency. Furthermore, an important outcome was the evaluation of the potential ecotoxicological risk posed by these pharmaceuticals to different aquatic organisms, when exposed to the studied WWEs, allowing a better understanding of the environmental risk in the Portuguese context.

2. Materials and methods

2.1. Sampling site and collection

WWIs and WWEs of 15 different WWTPs, located in 5 Portuguese regions, North, Center, Lisbon and Tagus Valley, Alentejo and Algarve (Fig. 1), were collected. These WWTPs are designed for 6850 to 756,000 population equivalents, representing 26.1% of the national population (10,526,700, in 2012). With average flow rates ranging between 349 and 140,000 m^3 per day, these facilities have their discharge points in the main Portuguese rivers and Atlantic Ocean. They treat domestic, hospital and industrial wastewaters, operating with secondary or tertiary treatments, as described in Table 2.

Sampling campaigns, carried out in 2013, were performed during two sampling periods; between 14 May/04 June – spring, and 11 July/14 August – summer, one sample by sampling site (WWI and WWE) for each season. The characterization of WWIs and WWEs, for the different sampling periods, is shown in Table S1 (Supporting information). WWIs and WWEs samples were collected in high-density polyethylene containers previously rinsed with bi-distilled water, as time proportional 24-h composite samples. Samples, kept refrigerated (4 °C) during the transport to the laboratory, upon reception, were frozen and stored at −20 °C until analysis.