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Pharmaceuticals and iodinated contrast media in a hospital wastewater: A case study to analyse their presence and characterise their environmental risk and hazard

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ABSTRACT

This work analyses the presence of twenty-five pharmaceutical compounds belonging to seven different therapeutic groups and one iodinated contrast media (ICM) in a Spanish medium-size hospital located in the Valencia Region. Analysis of the target compounds in the hospital wastewater was performed by means of solid phase extraction (SPE) followed by liquid chromatography-tandem mass spectrometry analysis (HPLC-MS/MS). A screening level risk assessment combining the measured environmental concentrations (MECs) with dose-response data based on Predicted No Effect Concentration (PNEC) was also applied to estimate Hazard Quotients (HQs) for the compounds investigated. Additionally, the environmental hazard associated to the various compounds measured was assessed through the calculation of the Persistence, Bioaccumulation and Toxicity (PBT) Index, which categorizes compounds according to their environmentally damaging characteristics. The results of the study showed the presence of twenty-four out of the twenty-six compounds analysed at individual concentrations ranging from 5 ng L^{-1} to 2 mg L^{-1}. The highest concentrations corresponded to the ICM iomeprol, found at levels between 424 and 2093 μg L^{-1}, the analgesic acetaminophen (15–44 μg L^{-1}), the diuretic (DIU) furosemide (6–15 μg L^{-1}), and the antibiotics (ABIs) ofloxacin and trimethoprim (2–5 μg L^{-1}). The lowest levels corresponded to the anti-inflammatory propyphenazone, found at concentrations between 5 and 44 ng L^{-1}. Differences in terms of concentrations of the analysed compounds have been observed in all the therapeutic groups when comparing the results obtained in this and other recent studies carried out in hospitals with different characteristics from different geographical areas and in different seasons. The screening level risk assessment performed in raw water from the hospital effluent showed that the analgesics and anti-inflammatories (AAFs) acetaminophen, diclofenac, ibuprofen and naproxen, the antibiotics (ABIs) clarithromycin, ofloxacin and trimethoprim, and the β-blocker (BBL) propranolol were present at concentrations leading to HQ values higher than 10, thus indicating high risk. When applying a

Abbreviations: AAF, analgesics and anti-inflammatory; ABI, antibiotic; AF, assessment factor; AEMPS, Spanish Agency for Medicines and Medical Devices; API, active pharmaceutical ingredient; BBL, β-Blocker; CAS, chemical abstracts service; DDD, defined daily dose; DIU, diuretic; EC50, median effective concentration; ECOSAR, ecological structure activity relationship; EMEA, European Medicines Agency; EP, emerging pollutant; EPSAR, Organization for water sanitation. Valencia Region; ERA, environmental risk assessment; EU, European Union; HPLC, high performance liquid chromatography; HQ, hazard quotient; ICM, iodinated contrast media; IS, internal standard; L(E)C50, median lethal (effective) concentration; LIR, lipid regulator; MDL, method detection limit; MEC, measured environmental concentration; MQL, method quantification limit; MRM, multiple reaction monitoring; MS/MS, tandem mass spectrometry; MS, mass spectrometry; N.A., not analysed; N.AV., not available; N.D., not detected; NI, negative ion; NOEC, no observed effect concentration; OECD, Organisation for Economic Co-operation and Development; PBT, Persistence, Bioaccumulation and Toxicity; PDE, Phosphodiesterase; PEC, predicted environmental concentration; PET, polyethylene terephthalate; PI, positive ion; PNEC, predicted no effect concentration; PVI, PDE-V inhibitor; PDT, Psychiatric drugs treatment; QSAR, quantitative structure-activity relationship; Rt, retention time; SPE, solid phase extraction; TU, toxic unit; US EPA, United States Environmental Protection Agency; WHO, World Health Organization; WWTP, wastewater treatment plant.

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factor to take into account potential dilution and degradation processes, only the compound ibuprofen showed a HQ higher than 1. Likewise, the cumulative HQ or Toxic Units (TUs) calculated in the raw water for each of the therapeutic groups studied showed that these three classes of drugs were at concentrations high enough to potentially generate high risk to aquatic organisms while taking into account possible dilution and degradation processes only one of them, the AAFs can be considered to represent high risk. Finally, the environmental hazard assessment performed showed that the AAFs diclofenac and ibuprofen and the ABI clarithromycin have the highest, maximum value of 9 of PBT Index due to their inherent environmentally damaging characteristics of persistence, bioaccumulation and toxicity.

The methodology followed in the present case study can be taken as a novel approach to classify and categorize pharmaceuticals on the basis of their occurrence in hospital effluents, their derived environmental risks, and their associated environmental hazard. This classification becomes important because it can be used as a model or orientation for hospitals in the process of developing environmentally sustainable policies and as an argument to justify the adoption of advanced, specific treatments for hospital effluents before being discharged into the public sewage system.

1. Introduction

Pharmaceuticals have been recognised as emerging pollutants of concern (EPs) for the last fifteen years (Daughton and Ternes, 1999) but no legal control over their discharge and/or environmental levels has been set up yet. These compounds are designed to have biologic activity and once in the environment they can provoke undesired effects in non-target organisms and become contaminants potentially hazardous, persistent and ubiquitous. The removal efficiency of pharmaceuticals from water varies depending on the treatment used (Rivera-Utrilla et al., 2013).

Growth in pharmaceutical spending slowed down in many Organization for Economic Co-operation and Development (OECD) countries in recent years. However, for many categories of pharmaceutical drugs, the quantities consumed continue to increase, partly due to the growing demand for drugs to treat ageing-related and chronic diseases (OECD, 2013). This, jointly with the fact that analytical techniques have improved markedly in the last years to the point to allow the detection of these compounds at ng and sub-ng L^{-1} levels in environmental waters (Fatta-Kassinos et al., 2011), has reinforce the interest for them as well as the scientific efforts dedicated to investigate their occurrence and potential impact in the aquatic environment (Fatta-Kassinos et al., 2011; Verlicchi et al., 2012a).

According to the report published by Simó (2012), the Spanish consumption of most of the pharmaceutical therapeutic groups is either similar to or lower than the European average. The only pharmaceutical classes that according to this report are consumed to a greater extent in Spain are the drugs used for treatment of peptic ulcers, anxiolytics and peripheral vasodilators. Meanwhile, data provided by the OECD (OECD, 2013) on the consumption of four categories of drugs, including antihypertensives, cholesterol-lowering drugs, antidiabetics and antidepressants, indicated that in all but the latter case, the defined daily dose (DDD) per 1000 people per day was lower in Spain than in the OECD countries on average. For the antidepressants the DDD per 1000 people per day was 64 in Spain vs. 56 in the OECD. As regards antibiotics, the overall volume prescribed in the OECD countries is on average slightly higher than in Spain, with DDD per 1000 people per day of 20.5 and 20.3, respectively (OECD, 2013).

Hospitals consume large quantities of both water and pharmaceuticals per day. Minimal domestic water consumption is 100 L person^{-1} day^{-1}, whereas consumption in hospitals generally varies from 400 to 1200 L bed^{-1} day^{-1} (Perrodin et al., 2013). As regards pharmaceuticals, the types of active ingredients used in hospitals differ from those applied in other instances (Kümmerer, 2001). Although it could be expected that hospital effluents present high concentrations of pharmaceuticals due to the extensive use of all of the different therapeutic classes, few studies investigating their presence in hospital effluents have been conducted all over the world (Lindberg et al., 2004; Brown et al., 2006; Thomas et al., 2007; Lin et al., 2008; Lin and Tsai, 2009; Langford and Thomas, 2009; Watkinson et al., 2009; Sim et al., 2011; Verlicchi et al., 2012b; Almeida et al., 2013; Perrodin et al., 2013; Santos et al., 2013) and only three have addressed this issue in Spain (Gómez et al., 2006; Gómez-Canela et al. 2014; Negreira et al., 2014).

Hospital wastewaters are complex mixtures capable of generating major environmental problems, since they have been estimated to be between 5 and 15 times more toxic than classical urban effluents (Emmanuel et al., 2009). However, hospital effluents are usually discharged into the public wastewater collector system directly, without being previously treated. The analysis of hospital effluents could clarify the debate about the need for implementing water treatments for these effluents prior to their release to the public wastewater treatment plants (WWTPs) (Verlicchi et al., 2012b). This idea is reinforced by the fact that hospital effluents can contribute negatively also to the generation and spread of pathogenic microorganisms multi-resistant to antibiotics (already at the WWTPs) (De Souza et al., 2009; Kümmerer, 2009), and to the input of toxic substances into the environment with the consequent adverse effects to aquatic ecosystems (Escher et al., 2011).

Many active pharmaceutical ingredients (APIs) are recognized to be substances pharmacologically active, resistant to degradation, highly persistent in aqueous medium, and potentially able to have a negative impact on aquatic organisms and human health (Rivera-Utrilla et al., 2013). For all these reasons environmental risk assessment studies (ERA) are recommended. In a traditional ERA approach, such as that based on the calculation of hazard quotients (HQs), the predicted or measured environmental concentrations (PECs or MECs) of the pollutants are combined with data on their toxicity (usually their predicted no effect concentration (PNEC)) in order to evaluate whether the considered pollutants are likely to pose a risk for aquatic organisms in the studied context (Cooper et al., 2008).

On the other hand, in order to classify the pharmaceuticals according to their environmental hazard, it is necessary to know their inherent environmentally damaging characteristics in terms of persistence, bioaccumulation and toxicity (PBT). This criterion, environmental hazard, can be estimated by the so-called PBT index (Wennmalm and Gunnarsson, 2005). Both criteria, Environmental Risk and Environmental Hazard, should permit classifying the pharmaceuticals studied according to their potential impact to the environment, and developing enhanced monitoring programs and implementing acceptable management strategies.