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Ecotoxicological risk assessment linked to the discharge by hospitals of bio-accumulative pharmaceuticals into aquatic media: The case of mitotane

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HIGHLIGHTS

- Bioaccumulative pharmaceuticals are present in hospital wastewater.
- Bioaccumulation can result in an increased risk for aquatic organisms.
- A specific approach have been developed to assess this risk.
- It has been applied to mitotane, a bioaccumulative drug commonly used in hospitals.
- An important risk is obtained with this pollutant for the studied scenario.

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ABSTRACT

The release of hospital wastewater into the urban sewer networks contributes to the general contamination of aquatic media by pharmaceutical residues. These residues include bio-accumulative pharmaceuticals that lead to increased risk for ecosystems because they can concentrate in organisms and food chains, and therefore reach toxic levels. In order to assess the ecotoxicological risks linked to this particular category of residues, we have developed a specific method, by combining a theoretical calculation of pollutant concentrations in organisms to estimate Body Residue (BR), and ecotoxicity biomarkers in fish cell lines, enabling the calculation of a Critical Body Residue (CBR). This method finally results in the calculation of a specific risk quotient (Qb = BR/CBR), characterizing the risk linked to this type of pollutant. This method was applied to mitotane, a bio-accumulative pharmaceutical typically found in hospital wastewater, in the framework of an exposure scenario corresponding to the discharge of all the hospital wastewaters into the Rhone River which flows through the city of Lyon, France. This approach leads to risk quotients (Qb and Qbg) much higher than those found with the classical approach, i.e. Q = PEC/PNEC (Predictive Environmental Concentration/Predictive Non Effect Concentration) = 0.0006. This difference in the appreciation of risk is important when using cytotoxicity as the criterion for measuring the toxicity of mitotane (Qb = 0.056) and it is even greater when the criterion used is genotoxicity (Qbg = 6.8). This study must be now consolidated by taking the biomagnification of the pharmaceuticals into consideration.

1. Introduction

Hospitals use a large variety of chemicals such as pharmaceuticals, radionuclides, disinfectants and detergents for health care, diagnostics, disinfection and research (Kümmerer et al., 1998). After application, some of these substances and non-metabolized drugs excreted by patients are found in hospital wastewaters (Kümmerer, 2001; Langford and Thomas, 2009), and generally reach the municipal sewer network without preliminary treatment (Emmanuel et al., 2004). Thus pollutants from hospitals have been found in WWTP effluents (Brown et al., 2006; Langford and Thomas, 2009) as well as in surface waters (Sprehe et al., 2001). Among these pollutants, pharmaceuticals occupy a special place and are subject to an increasing number of studies (Langford and Thomas, 2009; Ort et al., 2010; Escher et al., 2011; Sim et al., 2011). These pharmaceuticals include bio-accumulative drugs that present a specific risk for aquatic ecosystems, because of their ability to concentrate in the organisms forming the trophic chain. A recent

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study showed that 15–20% of medicines used in hospitals are potentially bio-accumulative (Jean et al., 2012). Consequently, priority has been given to the study of 14 pharmaceuticals (Jean et al., 2012). In order to better assess the impact of these molecules on aquatic ecosystems, it is now necessary to elaborate a specific Ecological Risk Assessment methodology adapted to the discharge of these molecules into natural media.

In this article we present: (i) the steps involved in a specific methodology to assess ecological risks linked to the release of bio-accumulative pharmaceuticals in natural media, (ii) the result of its application to mitotane, one of the 14 bio-accumulative pharmaceuticals selected by Jean et al. in 2012, in a hospital discharge scenario in a large French city (case study).

2. Development of the specific ERA methodology

Our specific ERA (Ecological Risk Assessment) methodology has been developed according to the four steps defined by the United States *Environmental Protection Agency* (USE EPA) in its "Guidelines for Ecological Risk Assessment" (US EPA, 1998) (Fig. 1). This methodological framework corresponds to the international reference regarding ERA.

2.1. Formulation of the problem

The problem formulation phase is fundamental. It comprises the description of the scenario studied, the definition of priority objectives, and the formulation of the conceptual model (US EPA, 1998).

2.1.1. Description of the scenario studied

This description presents the different environmental targets potentially reached by the pollutants present in the hospital wastewater and the different related exposure pathways. Here, the main pathway of exposure concerns the discharge of the hospital wastewater into the urban wastewater, then into the WWTP, then into the river. Characterising the level of exposure of the target organisms therefore requires the assessment of the respective flows of the hospital wastewater, of the urban wastewater and of the river, in order to calculate the percentage of hospital wastewater in the river. This permits calculating the PEC (Predicted Environmental Concentration) and assessing the BR (Body Residue, i.e. the pollutant concentration in the body of the species studied). These flows can vary through a season, and even during the course of a day for urban and hospital wastewaters (Boillot et al., 2008). With concern being given to aquatic organisms, we sought to evaluate the ecotoxicological risk for the most "critical" period, i.e. that corresponding to the maximum hospital discharge when the river is at its minimum flow level. Taking into account the bio-physico-chemical specificities of bio-accumulative molecules, we considered that the treatment of pollutants in the WWTP was non-significant regarding their elimination, which is a reasonably pessimistic assumption.

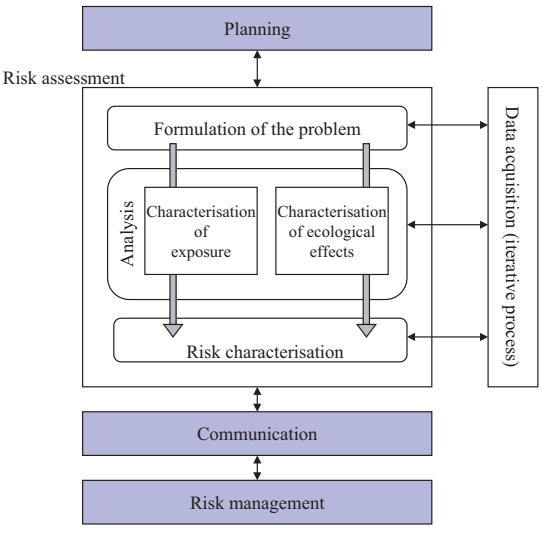

Fig. 1. General diagram of Ecological Risk Assessment (US EPA, 1998).

2.1.2. Definition of the priority objectives

In view of the scenario set out, the general objective of the assessment was the following: "the discharge of bio-accumulative pharmaceuticals into the public drainage system, then into the WWTP and then into the river, should not lead to effects on the organisms in the river, given their ecological, economic and societal importance". Within this general objective, the decision was taken to first privilege the preservation of pelagic organisms living in the water column. This approach should be completed at a later stage by a risk assessment for organisms living in the sediment, given their contribution to the global ecological functioning of the river.

2.1.3. Formulation of the conceptual model

Fig. 2 summarises the different elements of the conceptual model, such as they emerge from previous formulations, and defines the sections dealt with in what follows.

3. Materials and methods

3.1. Characterisation of the exposure

The characterisation of exposure aims at determining the spatial-temporal contact between pollutants and target populations (US EPA, 1998). It includes the analysis of sources of pollutants, the transfer of the latter from their sources, and the distribution of pollutants in the environment. This analysis can be performed by using theoretical models of pollutant transfer and/or experimental results (Perrodin et al., 2011). This phase results in the determination of the PEC (Predicted Environmental Concentration).

3.1.1. Calculation of pharmaceutical concentrations in hospital wastewater

The concentration in hospital effluents is linked to the consumption of pharmaceuticals, modified by the excreted fraction, and the water consumption of the hospital of the town studied, calculated during the same period (Mullot et al., 2010).

$$\text{Effluent concentration} = \text{Quantity consumed} \times \text{Rate excreted}/\text{Volume of effluent}$$

3.1.2. Calculation of the pharmaceutical concentration in the river (PEC)

The pharmaceutical concentration in the river (PEC) is obtained by dividing the initial concentration of the hospital effluent by the dilution factor of this effluent in the sewer network of the city studied, then by the dilution factor of the latter in the river. This is carried out taking into account the conclusions of the "formulation of the problem" phase which follows: (i) there is no reduction of the bio-accumulative pharmaceutical load into the WWTP, (ii) the dilution calculation in the river is performed during the most unfavourable period, i.e. when the river is at its minimum flow level.

3.1.3. Calculation of the pharmaceutical concentration in the fish (BR)

The Body Residue (BR) corresponds to the product of the PEC multiplied by the BioConcentration Factor (BCF) (BR = PEC × BCF).