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Drug residues in urban water: A database for ecotoxicological risk management

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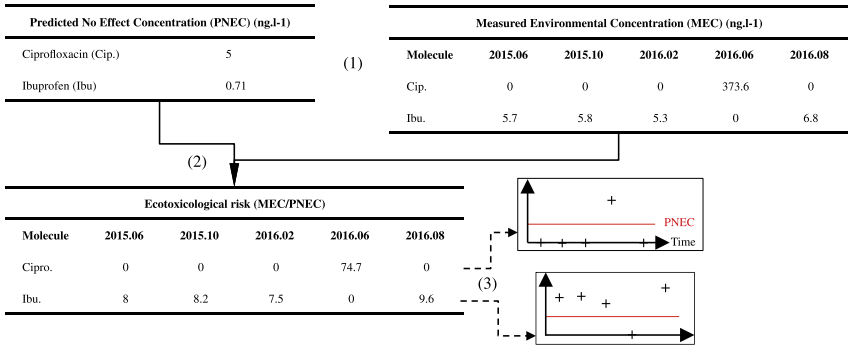
HIGHLIGHTS

- Medicines rise adverse effects on various trophic levels of aquatic organisms.
- Data grouping and homogenisation will facilitate ecotoxicological risks management.
- The occurrence of some medicines in the river generated environmental risks.
- 70% of drugs with environmental risks in the river were found downstream WWTP.

GRAPHICAL ABSTRACT



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ABSTRACT

Human-use drug residues (DR) are only partially eliminated by waste water treatment plants (WWTPs), so that residual amounts can reach natural waters and cause environmental hazards. In order to properly manage these hazards in the aquatic environment, a database is made available that integrates the concentration ranges for DR, which cause adverse effects for aquatic organisms, and the temporal variations of the ecotoxicological risks.
To implement this database for the ecotoxicological risk assessment (ERA database), the required information for each DR is the predicted no effect concentrations (PNECs), along with the predicted environmental concentrations (PECs). The risk assessment is based on the ratio between the PNECs and the PECs. Adverse effect data or PNECs have been found in the publicly available literature for 45 substances. These ecotoxicity test data have been extracted from 125 different sources. This ERA database contains 1157 adverse effect data and 287 PNECs. The efficiency of this ERA database was tested with a data set coming from a simultaneous survey of WWTPs and the natural environment. In this data set, 26 DR were searched for in two WWTPs and in the river. On five sampling dates, concentrations measured in the river for 10 DR could pose environmental problems of which 7 were measured only downstream of WWTP outlets. From scientific literature and measurements, data implementation with unit homogenisation in a single database facilitates the actual ecotoxicological risk assessment, and may be useful for further risk coming from data arising from the future field survey. Moreover, the accumulation of a large ecotoxicity data set in a single database should not only improve knowledge of higher risk molecules but also supply an objective tool to help the rapid and efficient evaluation of the risk.

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1. Introduction

DR occurrence in WWTP effluents has been highlighted since the 70s (Hignite and Azarnoff, 1977). The improvement of analytical techniques now allows the quantification of DR in the natural environment with concentrations ranging from $ng \cdot l^{-1}$ to $\mu g \cdot l^{-1}$ (Daughton and Ternes, 1999; Jorgensen and Halling-Sorensen, 2000; Kümmerer, 2001). More than 600 active substances have been detected in natural waters on a global scale (Weber et al., 2014) and the measured concentrations vary according to molecules and countries (Hughes et al., 2013). Surface water is probably the natural environment most impacted by these residues, but the presence of medicines is also cited in groundwater (Lopez-Serna et al., 2013), in drinking water (Fick et al., 2009; ANSES, 2011) and in soils (Kümmerer, 2004; Vazquez-Roig et al., 2012).

Nowadays, the DR occurrence in aquatic environments and the related hazards are better assessed due to wide improvement of the technology. These DR are found in almost all continental water bodies with environmental concentrations, and WWTPs have been identified as the main route of DR arrival in natural waters. These molecules can come from:

- human medicines, with domestic and hospital use;
- veterinary medicines, with domestic and agricultural use;
- DR production by the chemical-pharmaceutical industries.

DR are new emerging molecules that occur in natural water with potential effects on natural biodiversity. Most ecotoxicological studies showed *in vitro* or *in vivo* impact on several aquatic organisms (Pascoe et al., 2003; Parrott and Blunt, 2005; Martinović et al., 2007; Stanley et al., 2007; Quinn et al., 2008). Environmental effects of the focusing substances should be characterised by PNECs which are calculated by applying an assessment factor (AF) to the standard ecotoxicity test results (Medical Products Agency, 2004). The AF is an expression of the degree of uncertainty in the extrapolation from the test data on a limited number of species to the actual environment (EMA, 2006, p. 200). Organisms recommended by regulation for the ecotoxicological tests are algae, crustaceans and fish (European Chemicals Bureau, 2003). These tests allow the estimation of the PNECs that represent the threshold not to be exceeded to get no effect on the living biota in the natural environment. The PNECs should preferably be obtained from long-term ecotoxicity tests. If long-term data are lacking, short-term ecotoxicity data may be used. AF value depends on the confidence with which PNECs can be derived from the available data. This confidence increases if the concentrations are obtained from ecotoxicity tests, named ecotoxicity data, available for organisms with trophic levels, taxonomic groups and lifestyles representing various feeding strategies. Thus, lower AF values can be used with larger and more relevant datasets than the base-set data. To illustrate, when only short-term toxicity data are available, an AF of 1,000 will be applied to the lowest concentration available irrespective of whether or not the species tested is a standard test organism (EMEA, 2006). A lower assessment factor, from 10 to 100, will be applied to the lowest concentration derived in long-term tests (EMEA, 2006).

This potential ecotoxicological risk related to the presence of DR in aquatic environments is estimated by comparison with the river exposure to DR, and this risk is characterised by the ratio between the predicted environmental concentrations (PECs) or the measured environmental concentrations (MECs), and the environmental hazard estimated by PNECs (Straub, 2002; EMA, 2006; FASS and LIF, 2012).

Despite a considerable number of studies on environmental exposure and tools on varied chemical substance ecotoxicity, such as AIIDA (Payet, 2013), ECOTOX-US EPA ("EPA: Welcome to ECOTOX", n.d.) and the Sweden environmental classification for pharmaceuticals (Environmentally Classified Pharmaceuticals 2014–2015, 2014), there is no tool to monitor environmental risk by linking exposure, as indicated by MECs or PECs, and hazard, as indicated by PNECs. Furthermore, the additional information about temporal variation of DR natural risk appears significant due to previous demonstration of a higher risk period during the year. A better understanding of the distinct behaviour of these emerging molecules during the last part of their life cycle in both sewage and the natural environment should lead to improvement of their management strategy. In particular, the observation of the DR concentration variations and the related environmental risk according to time should allow the identification of the period of higher risk when vigilance should be increased. The aim of this study is to gather exposure and hazard information together in a single database with a number of DR high enough to identify different types of behaviour. The gathering of a large number of ecotoxicity data in a single database, with ecotoxicity information fed by scientific literature, should promote objective decision making on this sensitive topic of DR management. With an application of this database in case studies that take into account the temporal dynamic of these DR. It is assumed that the merging database could be used as the support for management decisions, through the identification of time period and molecule, allowing the establishment of management priorities.

2. Materials and methods

2.1. ERA database description

The ERA database was created with the relational database management system available in open source, Postgresql, and the programming interface, Datagrip, which is a multi-engine database environment developed by the Jetbrains company.

Nowadays, this ERA database contains thirteen tables. Some of them are devoted to hazard assessment with the help of PNECs or toxicity data and others to exposure assessment by using PECs or MECs. Crossing these tables allows the estimation of the ecotoxicological risks. Table 1 presents the different tables contained in this ERA database. Structured query language (SQL) is used to manage the ERA database. Toxicity data are presented in the same unit allowing homogeneity and comparison between them.

The ERA database is structured according to Datagrip principles using tables and establishing relations between them. These tables are interconnected through primary and foreign keys, which correspond to similar columns between two tables. The overall organisation of the ERA database is shown in Fig. 1 the arrow direction indicates the link between a foreign key (column where the arrow starts), and a primary key (the same column in another table, where the arrow ends). For example, concerning the tables "sites" and "analyses", the link is allowed by the "idsite" column, which exists in these two tables. The "idsite" is the primary key for the first one and the foreign key for the second one.

In this ERA database, the tables which inform about DR hazard are: "moleculesproperties", "pnec" and "toxicity". For the exposure there are: "river", "wwtp" and "middleproperties". Thus, the specific tables that are linked to the estimation of risks are the tables "pnec", "toxicity", "river", and "wwtp", "moleculesproperties" and "middleproperties". This last table allows understanding of DR behaviour in the aquatic environment.

The following tables present general information: "sites", "samples", "analyses", "molecules", "references", "sampling" and "analyticalmethodology". It means they will not be used directly for risk assessment.

2.2. PNECs and ecotoxicity data recovery from literature

Ecotoxicity data, which usually estimate xenobiotic toxicity on living organisms, could be expressed with different indicators such as effective concentration on 10%, 25% and 50% of the population (EC_{10}, EC_{25} and EC_{50}), the inhibitory concentration on 50% of the population (IC_{50}), the lethal concentration on 50% of the population (LC_{50}), the no