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Discharge of pharmaceutical products (PPs) through a conventional biological sewage treatment plant: MECs vs PECs?

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ABSTRACT

Pharmaceuticals for human use are consumed in significant quantities and their occurrence in aquatic systems has been reported by a number of authors. In the context of environmental risk assessment, there is an increasing interest in evaluating the discharge of pharmaceutical products to surface waters through sewage treatment plants (STP). This case study was carried out on a conventional biological treatment plant (Alès, France) and focused on a set of eleven drugs representing the main therapeutic classes. Measured environmental concentrations (MECs) range from the low ng L^{-1} to 1.5 μg L^{-1} in effluent and up to few hundred ng L^{-1} in receiving surface waters. There is a good agreement between MEC and predicted environmental concentration (PEC) values for seven of the eleven investigated drugs in STP effluent. There is not such a good match between PEC and MEC values in surface waters, and this highlights the limits of this approach, at the local scale.

1. Introduction

The presence of pharmaceuticals has been reported in many studies in Europe since the 1980s, (Richardson and Bowron, 1985; Andreozzi et al., 2003; Kummerer, 2004; Nikolaou et al., 2007; Radjenovic et al., 2007). Recent works have demonstrated that elimination of many pharmaceuticals in sewage treatment plants (STP) is often incomplete (Ternes, 1998; Heberer, 2002; Jones et al., 2005; Joss et al., 2005; Ternes et al., 2005; Castiglioni et al., 2006; Paffoni et al., 2006; Gros et al., 2007). Consequently, variable concentrations of pharmaceuticals ranging from ng L^{-1} to μg L^{-1} have been detected in surface waters (Gros et al., 2006; Paffoni et al., 2006; Roberts and Thomas, 2006; Togola and Budzinski, 2007) and groundwaters (Ellis, 2006; Rabiet et al., 2006). Moreover, some compounds have been found in drinking water (Ternes et al., 2002; Stackelberg et al., 2007).

This wide range of pharmaceuticals reaching the aquatic environment could impact on exposed organisms (Cleuvers, 2003; Webb, 2004; Williams, 2005; Crane et al., 2006; Fent et al., 2006). Consequently there is a need for environmental risk assessment of pharmaceutical products. In Europe, specific guidelines are recommended for the environmental assessment of medicinal products. Currently, the environmental risk assessment (ERA) of pharmaceuticals for human use is based on the guidelines of the European Agency for the Evaluation of Medicinal Products (EMEA, 2006). A tiered approach is described for human medicines. The first tier consists of deriving a crude predicted environmental concentration (PEC) in surface waters. In this phase, the calculation is based on assumptions such as no metabolism, biodegradation or retention of the drug which lead to worst case estimates of risk. If the predicted PEC is above 10 ng L^{-1}, aquatic fate and effect studies using OECD tests have to be conducted in higher tier risk assessment phases.

PEC values provide important information for the prioritization of PPs for environmental monitoring strategies. Nevertheless, assumptions made during the calculation of PEC values may introduce some uncertainty. Thus, the relevance of PEC vs MEC (measured environmental concentration) can be considered, especially at a local scale where the pattern of consumption could differ from the national one.

This paper presents the study of a conventional biological treatment plant, located in Alès (France) where an evaluation of the discharge of a set of 11 pharmaceutical products in the Gardon River has been carried out. In a first step, measured concentrations are reported for each investigated pharmaceutical product for Alès STP effluent (MEC_{Eff}) and the related receiving medium (MEC_{Sw}). Then, corresponding PEC values (PEC_{Eff} and PEC_{Sw}) were calculated using the equation described by Besse and Garric (2007), adapted from the EMEA guideline (2006). Finally, PEC and MEC values are compared and the relevance of PEC values is assessed according to the PEC/MEC ratio.

2. Materials and methods

2.1. Sampling sites

Alès is located in Languedoc Roussillon region, in the south of France. Alès STP serves a population of 55,000 inhabitants. This low capacity conventional activated sludge process also collects effluents from hospital and industrial facilities (Table 1).

24-h averaged flow proportional STP effluents samples were collected between June 2007 and February 2008. Over the same period,

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Table 1
Alès STP characteristics.

Capacity (Eq Hab)	90,000
Served population (Inhab)	55,000
Median flow rate (m^3 day^{-1})	11,000
Influent BOD_5 (mg O_2 L^{-1})	300
Received sewage	Domestic
	Industrial
	Hospital
Treatment processes	Primary settling
	Activated sludge with prolonged aeration;
	Nitrification/denitrification;
	Phosphate removal
	Low load
Receiving medium	Gardon River

spot samples were taken in the Gardon River, 10 m downstream of the discharge point.

All samples were stored at 4 °C prior to laboratory treatment on the same day.

2.2. Chemicals

Eleven pharmaceutical products were investigated. Standard products were purchased from Sigma-Aldrich (purity>97% by weight, compound name abbreviations and CAS no. indicated): norfloxacin (NOR 70458-96-7), acebutolol (ACE 34381-68-5), propranolol (PROP 318-98-9), ifosfamide (IFO 3778-73-2), pravastatin (PRAV 81131-70-6), carbamazepine (CAR 298-46-4), lorazepam (LOR 846-49-1), tamoxifen (TAM 10540-29-1), diclofenac (DIC 15307-79-6), ibuprofen (IBU 15687-27-1) and fenofibrate (FEN 49562-28-9). The list of pharmaceuticals studied was selected on the basis of the leading medicinal products most frequently encountered in French STP effluents (Andreozzi et al., 2003) and widely consumed in France (CNAMTS — Direction de la stratégie des études et des statistiques (DSES-DEPP) (MEDICAM, 2006)). Some molecules such as anticancer drugs, that are dispensed only in hospitals, were added (Kummerer et al., 1997).

Solvents used for pre-treatment and chromatographic samples analysis (acetonitrile, methanol, ethyl acetate, acetone and 0.1% acetic acid water of gradient grade) were purchased from Chromasolv, Riedel-de-Haen. Standard solutions were made up in a mixture (50:50) of methanol:milliQ pure water.

2.3. Analytical method

2.3.1. Solid phase extraction

Solid phase extraction (SPE) was performed on GF/F glass-filtered HCl acidified samples (500 mL, pH 2) using STRATA™ X cartridges (200 mg/6 mL, Phenomenex, Inc). Analytes were eluted with 5 mL of ethyl acetate followed by 5 mL of a mixture (50:50 (v/v)) of ethyl acetate:acetone and finally 5 mL of a mixture (49:49:2 (v/v/v)) of ethyl acetate:acetone:ammonium hydroxide. Solvents were removed under nitrogen flow and the residue was brought to 0.5 mL using methanol.

Recovery rates from real water samples were determined by spiking samples with different known concentrations of a mixture of standards (60, 120, 250, 500 ng L^{-1} of each compound). Extracts from unspiked ultra-pure grade water, concentrated and treated as described above, were used as blanks.

Table 2
Gradient solvent program.

Time (min)	Solvent A	Solvent B
0	85	15
8	50	50
13	30	70
15	0	100
17	0	100
18	85	15
25	85	15

Table 3
Analytical method performances.

Compounds	SPE recovery (%)	Limits of detection (ng L^{-1})	Limits of quantification (ng L^{-1})
NOR	47±5	5.2	12
ACE	73±3	2.8	8.5
PROP	80±8	2	9.6
IFO	94±7	2.8	9.7
PRAV	38±2	7.7	19
CAR	93±12	0.4	0.8
LOR	84±4	1.3	4
TAM	71±4	5.8	14
DIC	80±8	0.7	2
IBU	53±4	0.3	0.5
FEN	71±6	5.5	12

2.3.2. LC-MS/MS

Pharmaceuticals were analysed by LC-MS/MS. The LC system consists of a separation module Alliance HPLC Waters 2695 equipped with a quaternary pump, a vacuum degasser and an autosampler. Chromatographic separation was performed on Ascentis C_{18} (50 mm×2.1 mm, 3 µm) reversed-phase column (Supelco, UK). Chromatographic conditions were as follows:

- Solvents A (H_2O; 0.1% HCOOH) and B (CH_3CN),
- Flow rate 0.4 mL min^{-1},
- Gradient program (Table 2).

Table 4
Reported data for calculation of PEC_{Eff}.

Compounds	Therapeutic class	Reimbursed amount[a] (kg)	Fexcreta	STP removal fraction	Fstp
Norfloxacin NOR	Fluoroquinolone antibiotic	8177	0.63[b]	0.85[c]	0.15
Acebutolol ACE	β-blockers	29862	0.57[d]	0.2–0.8[e]	0.5
Propranolol PROP		8892	0.24[d]	0.22[d]	0.78
Ifosfamide IFO	Antineoplastic	121	0.9[f]	0[g]	1
Pravastatin PRAV	Statin lipid regulator	6533	0.5[d]	0.62[h]	0.38
Carbamazepine CAR	Anti-convulsivant	22094	0.15[b]	0.19[d]	0.81
Lorazepam LOR	Anxiolytic	347	0.85[d]	–	1
Tamoxifen TAM	Anticancer agent SERM	335	0.3[f]	0[f]	1
Diclofenac DIC	Antiflogistics	15610	0.15[d]	0.27[d]	0.73
Ibuprofen IBU		139605	0.25[d]	0.96[d]	0.04
Fenofibrate FEN	Fibrate lipid regulator	53775	0.01[d]	<0.1[d]	0.9

– no data available.
[a] MEDICAM (2006).
[b] Lienert et al. (2007).
[c] Watkinson et al. (2007).
[d] Besse and Garric (2007).
[e] Vieno et al. (2006), Lee et al. (2007).
[f] Tauxe Würsch (2005).
[g] Kummerer et al. (1997).
[h] Radjenovic et al. (2007).