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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).

Table 5
Measured concentrations of PPs in effluent samples expressed in ng L^{-1} (nd: not determined).

Sampling date	04 July 07	13 July 07	24 July 07	27 July 07	31 July 07	28 August 07	06 Feb. 08	08 Feb. 08	LR eff. from 2 STPs Rabiet et al. (2006)	HN eff. from 3 STPs Togola and Budzinski, (2007)	IF eff. STP Paffoni et al. (2006)	RA eff. from 2 STPs Andreozzi et al. (2003)
NOR	107 ± 5	129 ± 23	157 ± 9	247 ± 24	48 ± 7	<5.2	nd	nd	–	–	–	50–80
ACE	91 ± 10	115 ± 17	82 ± 3	92 ± 5	94 ± 3	94 ± 2	192 ± 2	145 ± 2	–	–	–	80–130
PROP	486 ± 26	560 ± 23	179 ± 4	187 ± 17	267 ± 14	160 ± 3	405 ± 4	291 ± 3	–	–	190	10–40
IFO	<3.8	<3.8	<3.8	<3.8	<3.8	<3.8	<3.8	<3.8	–	–	<50	–
PRAV	<7.7	<7.7	<7.7	<7.7	<7.7	<7.7	<7.7	<7.7	–	–	–	–
CAR	1492 ± 66	1519 ± 35	1106 ± 19	1097 ± 114	1573 ± 34	1075 ± 19	667 ± 10	326 ± 3	157–293	30–2520	1020	980–1200
LOR	130 ± 8	196 ± 7	86 ± 1	88 ± 6	114 ± 6	93 ± 2	39 ± 1	31 ± 1	–		–	–
TAM	53 ± 3	83 ± 44	102 ± 7	97 ± 2	<5.8	<5.8	<5.8	<5.8	–		–	–
DIC	388 ± 8	409 ± 14	148 ± 3	164 ± 19	161 ± 6	214 ± 4	399 ± 4	320 ± 4	211–486	25–920	810	250–410
IBU	45 ± 2	67 ± 9	61 ± 2	61 ± 1	23 ± 2	47 ± 1	67 ± 2	58 ± 2	18–219	<5.8–200	600	20–1820
FEN	23 ± 2	15 ± 2	24 + 3	23 ± 0	<5.5	46 ± 1	<5.5	<5.5	–		310	20–120

LR Languedoc–Roussillon; HN Haute Normandie; IF Ile de France; RA Rhône-Alpes.

The mass-spectrometric detection was performed on a micromass Quattro micro™ (Waters) mass spectrometer equipped with electrospray, using multi-reaction monitoring (MRM) mode that detected the daughter ions of $m = z$.

The analytical method was characterized for the investigated pharmaceutical products. The detection using LC-MS/MS in MRM mode resulted in a low noise level and improved sensitivity (Andreozzi et al., 2003). This was particularly important for analysis of the pharmaceuticals in the real wastewater samples (Petrovic et al., 2005).

Table 3 gives the corresponding SPE recovery, limit of detection and limit of quantification.

For the majority of PPs, the absolute recoveries obtained in this study are sufficiently high (>60%) for the current purpose and are in agreement with published data (Hilton and Thomas, 2003). Recoveries for norfloxacin (47%), pravastatin (38%) and ibuprofen (53%), were reproducible (R.S.D. <10%) and sufficient for use in environmental monitoring.

2.4. Calculation of PECs

Besse and Garric (2007, 2008) have adapted the equation from the model proposed by the EMEA guideline (2006),with the aim of developing a prioritization approach to the identification of pharmaceuticals for human use that should be monitored in French surface waters. For surface waters the described equation is as follows:

$$\mathrm{PECsurfacewater}\left(\mathrm{ng\,L^{-1}}\right) = \frac{\mathrm{consumption} \times \mathrm{Fexcreta} \times \mathrm{Fstp}}{\mathrm{WWinhab} \times \mathrm{hab} \times \mathrm{Dilution} \times 365}.$$

With:

Consumption (ng $year^{-1}$) quantity of active molecule consumed over 1 year in a defined zone (generally a country);
Fexcreta excretion fraction of the unchanged active molecule;
Fstp fraction of the drug that enters surface waters (STP efficiency);
WWinhab volume of wastewater per person per day (default of 200 L $inhab^{-1}$ day^{-1});
hab number of inhabitants in the defined zone;
Dilution dilution factor from WWTP effluents to surface water (default value of 10, (EMEA, 2006).

In this study, PEC values (ng L^{-1}) were calculated for STP effluents (PEC_{Eff}) and surface waters (PEC_{Sw}), using the equation above. PEC_{Eff} was derived from PEC_{Sw} without dilution factor. Consumption was calculated from CNAMTS statistical data (MEDICAM, 2006). This set of data considers medicine paid for by the French social health care system (CPAM) and excludes over-the-counter products. It was assumed that the entire amount of each product sold was consumed and that the predicted consumed amount was evenly distributed over the year and throughout the French population (62.9 millions inhabitants in 2006).

Fexcreta and Fstp were extracted from data based on an extensive literature review (Besse and Garric, 2007) and when data were not available in this source from others studies (Kummerer et al., 1997; Tauxe Würsch, 2005; Vieno et al., 2006; Lee et al., 2007; Lienert et al., 2007; Radjenovic et al., 2007; Watkinson et al., 2007). Fexcreta values are those determined by Besse and Garric (2007) when available for the studied drugs. They include the proportion of the unchanged active molecule excreted in urine and/or in faeces and the proportion of the parent molecule excreted as conjugates, assuming that they are cleaved in the environment to the parent drug (Ayscough et al., 2000).

Fstp is defined as (1-STP removal fraction). In the case of acebutolol for which a wide range of values of the fraction removed by STPs is available, Fstp was calculated as the average of these. For tamoxifen and lorazepam for which data were not reported in the literature, a default value of 1 (worse case scenario) was applied.

WWinhab was set at 200 L $inhabitant^{-1}$ day^{-1}. The dilution of the STP effluent to surface water depends on local conditions. In our study, it was calculated with reference to the concentrations of carbamazepine in water samples, assuming that no degradation of carbamazepine occurs in the environment (Clara et al., 2004).

Table 4 gathers all the data required for the PEC_{Eff} calculation.

3. Results and discussion

3.1. Occurrence of pharmaceuticals in Alès STP effluent and Gardon River

Concentrations of pharmaceuticals found in this study are presented in Table 5. Literature data for some other French STPs have been added for comparison.

3.1.1. Alès STP effluent

Data from this sampling campaign show that 4 compounds are predominant in Alès effluent — carbamazepine, diclofenac, acebutolol and propranolol. The range of concentrations varied from100 ng L^{-1} to 1500 ng L^{-1}. On the whole, these results are in accordance with concentrations in Rhône-Alpes STPs (Andreozzi et al., 2003), Ile

Table 6
PPs concentrations in the Gardon River (ng L^{-1}).

Sampling date	13 July 07	27 July 07	31 July 07	08 Feb. 08
NOR	17 ± 3	<5.2	11 ± 1	<5.2
ACE	12 ± 3	21 ± 3	36 ± 2	39 ± 2
PROP	96 ± 23	52 ± 6	113 ± 2	81 ± 4
IFO	<3.8	<3.8	<3.8	<3.8
PRAV	<7.7	<7.7	<7.7	<7.7
CAR	320 ± 54	372 ± 68	675 ± 15	105 ± 3
LOR	39 ± 8	29 ± 6	34 ± 1	9 ± 1
TAM	22 ± 10	25 ± 4	<5.8	<5.8
DIC	69 ± 20	45 ± 4	65 ± 2	107 ± 5
IBU	11 ± 5	14 ± 1	5 ± 1	26 ± 1
FEN	8 ± 3	16 ± 1	<5.5	<5.5

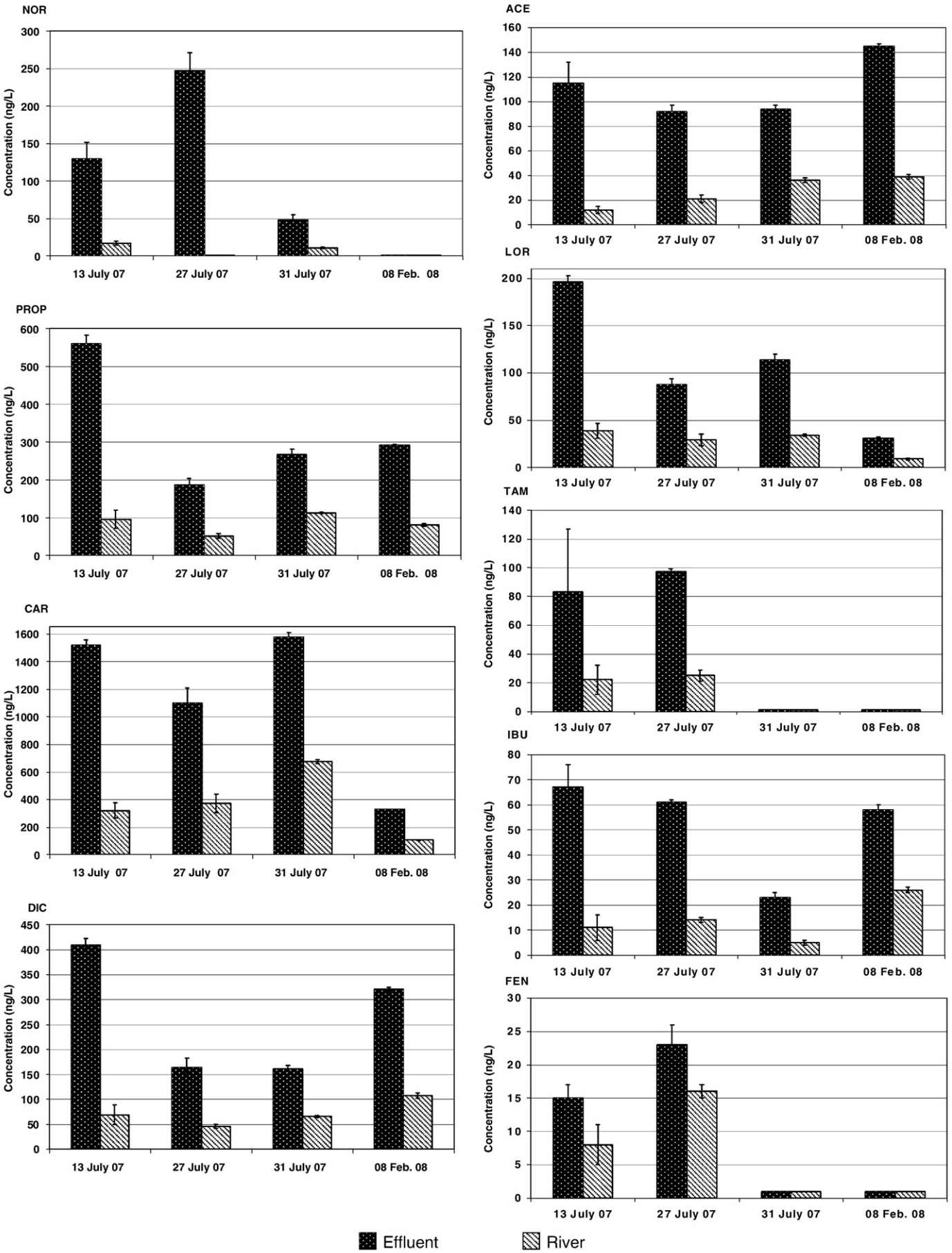

Fig. 1. Measured concentrations of PPs in effluent from the STP at Alès and in the Gardon River.

Table 7
Calculated predicted concentrations in effluent, PEC_{Eff} (without dilution factor), in surface water PEC_{Sw} and MEC (ng L^{-1}).

	PEC_{Eff}	PECEff	MEC_{Eff}	PEC_{Sw}	PEC_{Sw}	PEC_{Sw}	PEC_{Sw}	Median PEC_{Sw}	Median MEC_{Sw}
		Besse and Garric (2007)	Median –maximum	July 13	July 27	July 31	Feb 08		
				DF = 4.7	*DF* = 2.9	*DF* = 2.3	*DF* = 3.1		
NOR	168	–	77.5–247	36	58	73	54	56	6
ACE	1853	–	94–192	394	639	806	598	619	29
PROP	363	535	279–560	77	125	158	117	121	89
IFO	24	–	3.8	5	8	10	8	8	3.8
PRAV	270	–	7.7	58	93	118	87	90	7.7
CAR	585	–	1101.5–1519	124	202	254	189	156	346
LOR	64	–	90.5–196	14	22	28	21	21	32
TAM	22	–	26.5–102	5	7	9	7	7	11
DIC	372	250	267–409	79	128	162	120	72	67
IBU	304	550	59.5–67	65	105	132	98	101	13
FEN	105	<180	19–46	22	36	46	34	35	4

de France (Paffoni et al., 2006) and Haute-Normandie (Togola and Budzinski, 2007). Nevertheless, it can be seen that higher concentrations of ibuprofen (highly prescribed and widely used in France) have been found in STPs in the Rhône Alpes than that in Alès. A similar observation can be made for concentrations of carbamazepine in STPs in Haute Normandie compared with that in Alès.

Diclofenac and ibuprofen concentrations in other STPs in the Languedoc-Roussillon region (Rabiet et al., 2006) were of the same order of magnitude as those in the STP in Alès. On the other hand, Rabiet and co-workers found lower concentrations of carbamazepine than those found in the current study.

Some of the PPs studied in this work (lorazepam, tamoxifen) have not been reported previously in French STP effluents. Lorazepam was found in all samples at a maximum concentration of about 200 ng L^{-1} whereas tamoxifen was present sporadically and mostly at lower concentrations (<100 ng L^{-1}). This anti cancer drug has never been reported in French STP effluents but has been found on a few occasions in British STP effluents in the same range of concentrations as observed in this study (Hilton and Thomas, 2003; Ashton et al., 2004) and at concentrations higher than 100 ng L^{-1} (Roberts and Thomas, 2006).

Ifosfamide was not detected in Alès STP, and although it was searched for in the Ile de France region it was never found above the reported detection limit of 50 ng L^{-1} (Paffoni et al., 2006). This is not surprising as this product is selectively delivered in hospitals.

In order to detect potential seasonal variation, samples were collected in July–August (6 samples) and February (2 samples). No significant variation in concentrations was observed for acebutolol, propranolol, diclofenac, ibuprofen and fenofibrate between seasons. Concentrations of carbamazepine and lorazepam decreased in winter, especially that of lorazepam. However, Castiglioni et al. (2006) reported seasonal variations in ibuprofen concentrations in an Italian STP effluent due to the seasonal variability of the load of this compound in the influent and a higher removal rate observed during summer period. It seems that the variability of PP concentrations observed in the current study does not reflect a variation in the efficiency of the Alès STP, and is more likely to be due to variations in consumption through the year.

3.1.2. Gardon River

Almost all of the PPs detected in the effluent of the STP at Alès were found in the receiving water of the Gardon River (Table 6), with concentrations modified by the dilution factor. In particular, norfloxacin, tamoxifen, and fenofibrate, which are found at very low concentrations in effluent, were reduced below detection limits.

Fig. 1 shows that concentrations of PPs are in accord with those found in STP effluent at the same date. It can be seen that measured concentrations for propranolol, carbamazepine and diclofenac can exceed 100 ng L^{-1}, the regulatory threshold value (as defined in the European water quality directives) for micro pollutants other than the priority pollutants in surface water (Paffoni et al., 2006).

3.2. Calculated PECs in Alès STP effluent and Gardon River

PEC values of the PPs in this study were calculated for the effluent (PEC_{Eff}) from the STP in Alès and for the Gardon River (PEC_{Sw}) in order to compare these with the measured concentration (MEC_{Eff} and MEC_{Sw}) for the respective compounds. PECs, and median and maximum MECs are reported in Table 7. According to the timing of the sampling event, the dilution factor of STP effluent in surface water varied between 2.3 and 4.7.

3.2.1. Effluent from the STP at Alès

The PEC was compared with the median MEC. Since ifosfamide and pravastatin were never detected in the STP effluent, median values were set to the detection limit. The ratio PEC/MEC was calculated in order to assess the relevance of PEC values (Sadezky et al., 2008). The scheme ranking is given below:

0.2<PEC/MEC<1, PEC acceptable, slightly underestimated;
1<PEC/MEC<4, PEC acceptable, slightly overestimated;
4<PEC/MEC<8, PEC significantly overestimated;
PEC/MEC>8, PEC strongly overestimated.

Table 8 presents classification of the investigated compounds.

As consumption data were available only for prescribed medicines, the calculated PEC_{Eff} are likely to be underestimated, in comparison with PEC values given by Besse and Garric (2007) which take into account over the counter drugs. Nevertheless, a rather good agreement was observed between PEC_{Eff} and MEC_{Eff} for 2/3 of the PPs investigated. For the remaining compounds an overestimation is observed. It is very likely that in the case of ibuprofen, a proportion of the prescribed drug is not consumed and is therefore not introduced into the wastewater. In the cases of fenofibrate, acebutolol and pravastatin, that are markedly overestimated, the difference could be related to pattern consumption. These drugs are probably less prescribed in the studied region, with reference to the national average consumption. Moreover, it is known that cardiovascular diseases are less common in the south than in other regions of France (DREES, 2000).

3.2.2. Gardon River, surface water

Median PEC_{Sw} and MEC_{Sw} were compared using the same approach as was used for the STP effluent. Table 9 presents PEC vs MEC values.

As for effluent from the STP, PEC_{Sw} and MEC_{Sw} are in good agreement for carbamazepine, lorazepam, tamoxifen propranolol, diclofenac and ifosfamide. On the other hand, drugs for which PEC_{Eff}/MEC_{Eff}>4 are strongly overestimated. Nevertheless, norfloxacin, a highly polar fluoroquinolone antibiotic (Ternes et al., 2004), shows a different behaviour. Indeed, despite a good agreement between PEC_{Eff} and MEC_{Eff}, the PEC_{Sw} differs greatly from the MEC_{Sw}. This result could be explained by an additional elimination occurring in the STP, possibly due to sorption phenomenon either in sludge during sewage treatment or in the river.

4. Conclusion

The main objective of this study was to compare PEC and MEC values in order to assess their relevance in STP effluent and surface water at a local scale in Alès, a city in Languedoc Roussillon region. The reliability of the PEC is a key point for the assessment of

Table 8
PEC_{Eff} vs MEC_{Eff} for effluent from the STP in Alès.

0.2<PEC/MEC<1	1<PEC/MEC<4	4<PEC/MEC<8	PEC/MEC>8
Carbamazepine	Propranolol	Ibuprofen	Acebutolol
Lorazepam	Diclofenac	Fenofibrate	Pravastatin
Tamoxifen	Norfloxacin		
Ifosfamide			

Table 9
PEC_{Sw} vs MEC_{Sw} for surface water from the Gardon River.

0.2<PEC/MEC<1	1<PEC/MEC<4	PEC/MEC>8
Carbamazepine	Propranolol	Ibuprofen
Lorazepam	Diclofenac	Fenofibrate
Tamoxifen	Ifosfamide	Norfloxacin
		Acebutolol
		Pravastatin

environmental risk for aquatic systems. Eleven drugs representing the main therapeutic classes were investigated, and included lorazepam, pravastatin and tamoxifen for which no data are available in France. Lorazepam was detected in effluent from the Alès STP at concentrations up to 200 ng L^{-1}. Tamoxifen was found sporadically and pravastatin was not detected. All pharmaceuticals products occurring in the effluent were detected in the receiving water of the Gardon River. The dilution of the STP effluent in the receiving water body was set to roughly 3, a rather low value in comparison with the EMEA default value of 10, but more adapted to conditions in the south of France. Further calculation of the PEC is based on assumptions such as an evenly distributed usage over time and space, and this may not be appropriate depending on local conditions.

The predicted concentrations of PPs in STP effluent were found to be in good agreement with measured concentrations for seven of the eleven molecules investigated. For the others, an overestimation was observed, and this could be related to local patterns of consumption. The comparison of PEC with MEC for surface water highlights the differences between these and those found in the effluent from the STP. It may be that the mechanisms leading to lowered concentrations of PPs in surface waters could include transformation processes.

Many of the variables used in the calculation of PECs can be associated with poorly defined uncertainties. Differences can be particularly marked where local conditions are markedly different from assumed average values, and although PEC values can be used as a first approximation, MEC values, when available, should be preferred in ERAs.

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