PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY A MATHEMATICAL, PHYSICAL & ENGINEERING SCIENCES

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Phil. Trans. R. Soc. A 2009 **367**, 3979-4003
doi: 10.1098/rsta.2009.0105

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Phil. Trans. R. Soc. A (2009) **367**, 3979–4003
doi:10.1098/rsta.2009.0105

Review

Fate and removal of pharmaceuticals and illicit drugs in conventional and membrane bioreactor wastewater treatment plants and by riverbank filtration

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Pharmaceutically active compounds (PhACs) and drugs of abuse (DAs) are two important groups of emerging environmental contaminants that have raised an increasing interest in the scientific community. A number of studies revealed their presence in the environment. This is mainly due to the fact that some compounds are not efficiently removed during wastewater treatment processes, being able to reach surface and groundwater and subsequently, drinking waters.

This paper reviews the data regarding the levels of pharmaceuticals and illicit drugs detected in wastewaters and gives an overview of their removal by conventional treatment technologies (applying activated sludge) as well as advanced treatments such as membrane bioreactor. The paper also gives an overview of bank filtration practices at managed aquifer recharge sites and discusses the potential of this approach to mitigate the contamination by PhACs and DAs.

Keywords: pharmaceutically active compounds; drugs of abuse; conventional activated sludge treatment; membrane bioreactor; river bank filtration

1. Introduction

Pharmaceutically active substances (PhACs) and drugs of abuse (DAs) are two classes of new so-called 'emerging' contaminants that have raised great concern in the last years. Their significance as trace environmental pollutants in waterways is due to several reasons: (i) the continuous introduction via

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One contribution of 12 to a Theme Issue 'Emerging chemical contaminants in water and wastewater'.

effluents from sewage treatment facilities and from septic tanks; (ii) they are developed with the intention of performing a biological effect; (iii) they often have the same type of physico-chemical behaviour as other harmful xenobiotics (persistence in order to avoid the substance to be inactive before having a curing effect, and lipophilicity in order to be able to pass membranes); (iv) some pharmaceutical substances are used by man in rather large quantities (i.e. similar to those of many pesticides). Numerous studies revealed their presence in wastewaters, as well as surface, ground and drinking water. This is mainly due to the fact that some compounds are not efficiently removed during wastewater treatment processes, being able to reach surface and groundwater and, subsequently, drinking waters. Although conventional wastewater treatment plants (WWTPs) can effectively reduce carbon and nitrogen content of raw sewage, the removal of pharmaceutical residues and DAs is often insufficient and WWTP effluents are frequently pointed out as the main source of these microcontaminants.

The objective of this paper is to summarize the data regarding the levels of pharmaceuticals and illicit drugs detected in wastewaters and to give an overview of their removal by conventional treatment technologies (applying activated sludge; CAS) as well as advanced treatments such as membrane bioreactor (MBR) and riverbank filtration practices at managed aquifer recharge sites.

2. Sources and levels of pharmaceuticals and illicit drugs in wastewaters

Due to their continuous input into the aquatic media through wastewater as a main point-source, PhACs and DAs are considered to be 'pseudo-persistent' contaminants. In a proper evaluation of persistency of a certain compound both transformation of a compound in the environment and its supply rate should be taken into consideration. Estimations of pharmaceutical concentration in sewage have been usually performed by back-calculating the total prescribed mass from prescription rate data (number of defined daily doses) and excretion rates, partitioning, biodegradation and the potential hydrolysis of conjugates (Montforts 2001). However, predictions based on annual sales of drugs are likely to underestimate the loads of PhACs in the influents of WWTPs. As shown by Bound & Voulvoulis (2006), the accuracy of predicted environmental concentrations is hindered by a shortage of data, both relating to over-the-counter (OTC) sales of drugs and their fate in WWTPs. In their study, the measured environmental concentrations were considerably higher than predicted, suggesting that the areas sampled deviated from the model proposed by the EMEA (2005). This could be due to regional variations in usage or differences in WWTP capabilities.

The ubiquity of drugs is related to specific sales and practices in each country. For example, antihistamines, analgesics and antidepressants are the families of drugs with major consumption in Spain, according to the National Health System. Indeed, in a comprehensive study by Gros *et al.* (2007), the highest influent loads from seven WWTPs were found for non-steroidal anti-inflammatory drugs (NSAIDs), lipid regulators, β-blockers and histamine H_1- and H_2-receptor antagonists. Total load of 29 monitored pharmaceuticals ranged from 1 to 5 g d^{-1} per 1000 inhabitants for influent wastewater. The results of a study in six

WWTPs conducted in Italy (Castiglioni *et al.* 2006*a*) indicated high inputs of antibiotics sulphamethoxazole, ofloxacin and ciprofloxacin, β-blocker atenolol, antihistaminic ranitidine, diuretics furosemide and hydrochlorothiazide, and NSAID ibuprofen. Another factor to consider is the outbreak of certain diseases, such as the case of pandemic of avian influenza, that would lead, as predicted for selected US and UK catchments, to high concentrations of antiviral drugs (especially of oseltamivir carboxylate (OC), the main metabolite of tamiflu). Concentrations of OC in catchments with low flow and high populations are predicted to be more than $20\,\mathrm{mg\,l^{-1}}$, which may affect the function and stability of WWTP (Singer *et al.* 2007, 2008).

Under normal conditions, the inputs of PhACs are generally considered to be constant and widely distributed. However, for some pharmaceuticals (i.e. antibiotics) differences between winter and summer influent loads were noted, probably because of higher attenuation in summer and less use of pharmaceuticals (Miao *et al.* 2004; Castiglioni *et al.* 2006*a*). On the other hand, for other drugs (e.g. β-blockers, diuretics and anti-ulcer drugs) no seasonal variability was observed.

The most ubiquitous drugs in WWTP influents are summarized in table 1, together with their concentration ranges reported in the literature.

Generally, the highest concentrations are commonly reported for NSAIDs, which could be attributed to their wide consumption because they can be purchased without medical prescription (i.e. OTC drugs). For example, ibuprofen is usually detected at very high concentrations (in $\mu\mathrm{g\,l^{-1}}$; Nakada *et al.* 2006; Radjenovic *et al.* 2007; Santos *et al.* 2007; Terzic *et al.* 2008). Although the percentage of elimination of this drug is very high, it is still detected in rivers downstream WWTPs due to a very high usage in human medicine. Other very popular pain killers are acetaminophen (paracetamol) and aspirin (acetyl-salicylic acid). Besides these OTC drugs, pharmaceuticals ubiquitous in raw sewage are also prescription drugs such as β-blockers (Vieno *et al.* 2006; Gros *et al.* 2007; Radjenovic *et al.* 2007). Atenolol seems to be the most frequently found β-blocker worldwide in WWTP influents (Castiglioni *et al.* 2006*a*; Nikolai *et al.* 2006). Numerous studies also revealed substantial presence of antibiotics in the environment, due to their widespread consumption in human and veterinary medicine. For example, Gros *et al.* (2007) found the macrolide azithromycin, the sulphonamide sulphamethoxazole and trimethoprim in all samples analysed at seven Spanish WWTPs and at considerable loads, followed by the macrolide erythromycin and the fluoroquinolone ofloxacin. The anti-epileptic drug carbamazepine is one of the most prominent drugs with a long history of clinical usage, and it is frequently found in the environment (Clara *et al.* 2004*a*,*b*; Gros *et al.* 2007; Radjenovic *et al.* 2007). This drug has proved to be very recalcitrant, as it bypasses sewage treatment. Lipid regulators are ordinarily applied drugs in clinical practice, and they are used to lower the level of cholesterol and regulate the metabolism of lipids. In all countries with developed medical care, X-ray contrast media can be expected to be present at appreciable quantities in sewage water. Clara *et al.* (2005) detected iopromide at a mean concentration of $3.84\,\mu\mathrm{g\,l^{-1}}$ in the influent of a WWTP receiving hospital wastewater, while in WWTPs without a hospital within their drainage area this contrast media was not present. Iodinated X-ray contrast media are proved to contribute significantly to the total absorbable organic

Table 1. Occurrence of pharmaceutical residues in wastewater treatment plants influents.

compound	influent concentration ($\mu g\,l^{-1}$)	reference
analgesics and anti-inflammatory drugs		
ibuprofen	53.48–373.11; 150.73[a]	Santos *et al.* (2007)
	0.381–1.13; 0.672[b]	Nakada *et al.* (2006)
	2.6–5.7	Carballa *et al.* (2004)
	8.45[a]; 16.5[c]	Lishman *et al.* (2006)
	23.4[a]	Vieno *et al.* (2005)
	34–168; 84[a]	Gómez *et al.* (2007)
ketoprofen	0.108–0.369; 0.208[b]	Nakada *et al.* (2006)
	0.146[a]; 0.289[c]	Lishman *et al.* (2006)
	2.9[a]	Vieno *et al.* (2005)
	0.57[c]	Tauxe-Wuersch *et al.* (2005)
	0.16–0.97; 0.451[a]	Gros *et al.* (2006)
naproxen	0.038–0.23; 0.1[b]	Nakada *et al.* (2006)
	1.8–4.6	Carballa *et al.* (2004)
	8.6[a]	Vieno *et al.* (2005)
	5.58[a]; 17.1[c]	Lishman *et al.* (2006)
diclofenac	0.204[a]; 1.01[c]	Lishman *et al.* (2006)
	0.46[a]	Vieno *et al.* (2005)
	3.25[a]; 4.114[a]; 3.19[a]; 1.4[a]; 0.905[a]	Clara *et al.* (2005)
	0.05–0.54; 0.25[a]	Gros *et al.* (2006)
	2.94[c]	Tauxe-Wuersch *et al.* (2005)
indomethacin	0.23[a]; 0.64[c]	Lishman *et al.* (2006)
	n.d.	Gros *et al.* (2006)
acetyl-salicylic acid	0.47–19.4; 5.49[b]	Nakada *et al.* (2006)
salicylic acid	13.7[a]; 27.8[c]	Lishman *et al.* (2006)
acetaminophen	0.13–26.09; 10.194[a]	Gros *et al.* (2006)
	29–246; 134[a]	Gómez *et al.* (2007)
lipid regulator and cholesterol lowering statin drugs		
gemfibrozil	0.453[a]; 0.965[c]	Lishman *et al.* (2006)
	n.d.–0.36; 0.155[a]	Gros *et al.* (2006)
bezafibrate	2.2[a]	Vieno *et al.* (2005)
	1.96[a]; 2.014[a]; 6.84[a]; 7.6[a]; 1.55[a]	Clara *et al.* (2005)
	n.d.–0.05; 0.023[a]	Gros *et al.* (2006)
clofibric acid	n.d.–0.11; 0.072[a]	Gros *et al.* (2006)
	0.36[c]	Tauxe-Wuersch *et al.* (2005)
psychiatric drugs		
carbamazepine	0.015–0.27; 0.054[b]	Nakada *et al.* (2006)
	1.85[a]; 1.2[a]; 0.704[a]; 0.67[a]; 0.325[a]	Clara *et al.* (2005)
	n.d.–0.95; 0.42[a]	Gros *et al.* (2006)
	0.12–0.31; 0.15[a]	Gómez *et al.* (2007)
antibiotics		
sulphamethoxazole	n.d.–0.87; 0.59[a]	Gros *et al.* (2006)
ofloxacin	n.d.	Gros *et al.* (2006)
ciprofloxacin	3.8[b]; 4.6[c]	Watkinson *et al.* (2007)
norfloxacin	0.17[b]; 0.21[c]	Watkinson *et al.* (2007)

(*Continued.*)

Table 1. (*Continued.*)

compound	influent concentration ($\mu g\,l^{-1}$)	reference
trimethoprim	0.34[b]; 0.93[c]	Watkinson *et al.* (2007)
	n.d.–4.22; 1.172[a]	Gros *et al.* (2006)
antihistamines		
ranitidine	n.d.–0.29; 0.188[a]	Gros *et al.* (2006)
β-blockers		
atenolol	n.d.–0.74; 0.395[a]	Gros *et al.* (2006)
	(0.971 ± 0.03)[a]	MacLeod *et al.* (2007)
metoprolol	(0.411 ± 0.015)[a]	MacLeod *et al.* (2007)
sotalol	0.12–0.2; 0.167[a]	Gros *et al.* (2006)
	(0.529 ± 0.01)[a]	MacLeod *et al.* (2007)
propranolol	0.08–0.29; 0.168[a]	Gros *et al.* (2006)
	(0.01 ± 0.001)[a]	MacLeod *et al.* (2007)
X-ray contrast media		
iopromide	6.0–7.0	Carballa *et al.* (2004)
	(7.5 ± 1.5)[a]	Ternes & Hirsch (2000)
diatrizoate	(3.3 ± 0.7)[a]	Ternes & Hirsch (2000)
iopamidol	(4.3 ± 0.9)[a]	Ternes & Hirsch (2000)

[a]Mean.
[b]Median.
[c]Maximum concentrations.

iodine in clinical wastewaters; up to $130\,\mu g\,l^{-1}$ of iodine in the influent of municipal WWTP in Berlin, and $10\,mg\,l^{-1}$ was detected in hospital sewage (Oleksy-Frenzel *et al.* 2000).

According to the World Drug Report 2007, DA usage seems to be stabilized now after the increasing trends observed over a decade; however, the amount of people who still use illicit drugs each year globally accounts for 200 million (UNODC 2007). Similar to pharmaceuticals, these substances are considered to be 'pseudo-persistent' in the environment, thus they have become a group of emerging environmental contaminants of interest. DAs reach aquatic systems mainly through sewage water. After drug ingestion, diverse proportions of the parent compound, conjugated forms and metabolites are excreted via urine and flushed towards municipal WWTPs. Some of them are not efficiently removed at WWTPs and reach the aquatic environment via WWTP effluents, which is their main release pathway, as direct disposal is not a common practice. Neither their fate in the aquatic environment nor their potential toxicological or cumulative effects on the aquatic ecosystems have yet been studied.

Since 2004 several authors have developed analytical methodologies based on liquid chromatography-tandem mass spectrometry (LC-MS/MS) to evaluate the occurrence of DAs in sewage and natural waters: (Jones-Lepp *et al.* 2004; Zuccato *et al.* 2005; Castiglioni *et al.* 2006*b*; Hummel *et al.* 2006; Boleda *et al.* 2007; Bones *et al.* 2007; Huerta-Fontela *et al.* 2007; Kasprzyk-Hordern *et al.* 2007, 2008; Gheorghe *et al.* 2008; Postigo *et al.* 2008*a*; Zuccato *et al.* 2008). These methods have been appropriately validated in terms of linearity,

Table 2. Occurrence of DAs and metabolites in wastewater treatment plant influents and effluents.

compound	STP influent ($ng\,l^{-1}$)	STP effluent ($ng\,l^{-1}$)	reference
cocainics			
cocaine	225[a], 79[b]	47[a], 17[b]	Huerta-Fontela *et al.* (2007)
	(421.4 ± 83.3)[b], (218.4 ± 58.4)[b]	<0.99 (10.7 ± 3.2)[b]	Castiglioni *et al.* (2006*a*,*b*)
	(489 ± 117)[b]	n.d. (138 ± 20)[b]	Bones *et al.* (2007)
	42–120; 80.25[b]	—	Zuccato *et al.* (2005)
	(860.9 ± 213.6)[b]; 502.3[b]	(6.2 ± 3.65)[b]; 73.9[b]	Postigo *et al.* (2008*a*)
	4–4700; 200[c]	1–100; 10[c]	Huerta-Fontela *et al.* (2008)
	22–678; 204.6[b]	—	Gheorghe *et al.* (2008)
	526	149	Kasprzyk-Hordern *et al.* (2008)
benzoylecgonine	2307[a], 810[b]	928[a], 216[b]	Huerta-Fontela *et al.* (2007)
	(1132.1 ± 197.2)[b], (547.4 ± 169.4)[b]	<0.92; (100.3 ± 28.6)[b]	Castiglioni *et al.* (2006*a*,*b*)
	(290 ± 11)[b]	n.d. (22 ± 4)[b]; (31 ± 18)[b]	Bones *et al.* (2007)
	390–750; 550[b]	—	Zuccato *et al.* (2005)
	78	49	Hummel *et al.* (2006)
	(4225.7 ± 1142.8)[b]; 1456.7[b]	(30.3 ± 17.6)[b]; 196.0[b]	Postigo *et al.* (2008*a*)
	9–7500; 1100[c]	1–500; 90[c]	Huerta-Fontela *et al.* (2008)
	82–1898; 752.5[b]	—	Gheorghe *et al.* (2008)
	1229	1597	Kasprzyk-Hordern *et al.* (2008)
nor-benzoylecgonine	(36.6 ± 7.8)[b], (18.8 ± 5.6)[b]	<0.56 (7.5 ± 2.9)[b]	Castiglioni *et al.* (2006*a*,*b*)
cocaethylene	(11.5 ± 5.1)[b], (5.9 ± 2.6)[b]	<0.66 (0.2 ± 0.5)[b]	Castiglioni *et al.* (2006*a*,*b*)
	(77.5 ± 33.2)[b]; 78.5[b]	(1.71 ± 1.2)[b]; 4.2[b]	Postigo *et al.* (2008*a*)
nor-cocaine	(13.7 ± 5.3)[b]; (4.3 ± 0.9)[b]	<0.67 (0.7 ± 0.5)[b]	Castiglioni *et al.* (2006*a*,*b*)
opiates			
heroin	n.d.; 2.4[b]	n.d.; 1.2[b]	Postigo *et al.* (2008*a*)
	<20.0	<20.0	Boleda *et al.* (2007)

(*Continued.*)

Table 2. (*Continued.*)

compound	STP influent ($ng\,l^{-1}$)	STP effluent ($ng\,l^{-1}$)	reference
morphine	$(83.3 \pm 11.8)^{b}$; $(204.4 \pm 49.9)^{b}$	<3.2 $(55.4 \pm 11.1)^{b}$	Castiglioni *et al.* (2006*a*,*b*)
	n.d	n.d. $(452 \pm 86)^{b}$, $(874 \pm 86)^{b}$	Bones *et al.* (2007)
	820^{a}; 310^{c}	110^{a}; 40^{c}	Hummel *et al.* (2006)
	$(162.9 \pm 20.0)^{b}$; 68.1^{b}	$(21.8 \pm 3.0)^{b}$; 20.1^{b}	Postigo *et al.* (2008*a*)
	$<7.1 - 96.7$	$<7.1 - 81.1$	Boleda *et al.* (2007)
nor-morphine	<25	$<25 - 30.7$	Boleda *et al.* (2007)
6-monoacetyl morphine	$(11.8 \pm 8.5)^{b}$; $(10.4 \pm 4.8)^{b}$	<3.08	Castiglioni *et al.* (2006*a*,*b*)
	$(12.8 \pm 3.1)^{b}$; 8.4^{b}	$(3.6 \pm 0.5)^{b}$; 2.5^{b}	Postigo *et al.* (2008*a*)
	<3.1	<3.1	Boleda *et al.* (2007)
morphine-3β-D-glucuronide	$(2.5 \pm 7.1)^{b}$; $(18.1 \pm 30)^{b}$	<0.48	Castiglioni *et al.* (2006*a*,*b*)
methadone	$(11.6 \pm 1.7)^{b}$; $(49.7 \pm 9.6)^{b}$	$(9.1 \pm 0.5)^{b}$; $(36.2 \pm 2.8)^{b}$	Castiglioni *et al.* (2006*a*,*b*)
	4–23.9	4–24.7	Boleda *et al.* (2007)
2-ethylidene-1,5-dimethyl-3, 3-di-phenylpyrrolidine	$(19.8 \pm 3.1)^{b}$; $(91.3 \pm 19.2)^{b}$	$(22.6 \pm 0.6)^{b}$; $(72.1 \pm 8.7)^{b}$	Castiglioni *et al.* (2006*a*,*b*)
	n.d.	n.d. $(206 \pm 10)^{b}$	Bones *et al.* (2007)
	4.5–41.3	4.9–56.7	Boleda *et al.* (2007)
amphetamine-like compounds			
amphetamine	15	<1	Huerta-Fontela *et al.* (2007)
	$(14.7 \pm 10.6)^{b}$; <5.4	<2.8	Castiglioni *et al.* (2006*a*,*b*)
	$(41.1 \pm 9.1)^{b}$; 20.8^{b}	$(0.45 \pm 0.1)^{b}$; 2.2^{b}	Postigo *et al.* (2008*a*)
	3–668; 207^{c}	4–210; 28^{c}	Huerta-Fontela *et al.* (2008)
	5236	127	Kasprzyk-Hordern *et al.* (2008)
methamphetamine	$(16.2 \pm 7.1)^{b}$; <3.7	$(3.5 \pm 2)^{b}$; <1.11	Castiglioni *et al.* (2006*a*,*b*)
	$(18.2 \pm 5.8)^{b}$; 4.8^{b}	$(6.3 \pm 0.6)^{b}$; 2.1^{b}	Postigo *et al.* (2008*a*)
	n.d.	n.d.	Huerta-Fontela *et al.* (2007)
	3–277; 6^{c}	3–90; 6^{c}	Huerta-Fontela *et al.* (2008)

(*Continued.*)

Table 2. (*Continued.*)

compound	STP influent ($ng\,l^{-1}$)	STP effluent ($ng\,l^{-1}$)	reference
3,4-methylenedioxy-methamphetamine	91[a]; 49[b]	67[a]; 41[b]	Huerta-Fontela *et al.* (2007)
	(14.2 ± 14.5)[b]; (13.6 ± 12.6)[b]	(4.4 ± 3.7)[b]; (5.1 ± 3)[b]	Castiglioni *et al.* (2006*b*)
	(133.6 ± 29.8)[b]; 135.13[b]	(82.1 ± 22.2)[b]; 148.2[b]	Postigo *et al.* (2008*a*)
	2–598; 43[c]	2–267; 56[c]	Huerta-Fontela *et al.* (2008)
3,4-methylenedioxy-ethamphetamine	27[a]; 28[b]	<2.1	Huerta-Fontela *et al.* (2007)
	(1.5 ± 3.8)[b]; <4.19	<1.64	Castiglioni *et al.* (2006*b*)
	6–114; 28[c]	12	Huerta-Fontela *et al.* (2008)
3,4-methylenedioxy-amphetamine	(4.6 ± 7.3)[b]; <8.7	(1.1 ± 1.5)[b]; (0.9 ± 1.9)[b]	Castiglioni *et al.* (2006*b*)
	n.d.	n.d.	Huerta-Fontela *et al.* (2007)
	3–266; 86[c]	1–200; 22[c]	Huerta-Fontela *et al.* (2008)
LSD			
lysergic acid diethylamide	(2.8 ± 1.2)[b]; 2.9[b]	(0.3 ± 0.2)[b]; 1.6	Postigo *et al.* (2008*a*)
	n.d.	n.d.	Huerta-Fontela *et al.* (2007)
2-oxo-3-hydroxy-LSD (O-H-LSD)	(5.6 ± 12.1)[b]; 3.4[b]	(0.7 ± 0.3)[b]; 0.8.	Postigo *et al.* (2008*a*)
N-desmethyl-LSD	(4.3 ± 1.8)[b]; 13.5[b]	(0.6 ± 0.5)[b]; 2.3[b]	Postigo *et al.* (2008*a*)
cannabinoids			
Δ9−tetra-hydrocannabinol	n.d.; 14.24[b]	n.d.; 25.1[b]	Postigo *et al.* (2008*a*)
	$<8.3 - 31.5$	<8.3	Boleda *et al.* (2007)
11-nor-9-carboxy-Δ9-THC	(62.7 ± 5)[b]; (91.2 ± 24.7)[b]	<0.94 (7.2 ± 3.7)[b]	Castiglioni *et al.* (2006*b*)
	(4.3 ± 7.8)[b]; 21.03[b]	(8.4 ± 3.8)[b]; 11.23[b]	Postigo *et al.* (2008*a*)
	$<12.5 - 96.2$	<12.5	Boleda *et al.* (2007)
11-hydroxy-THC (OH-THC)	(8.4 ± 2.1)[b]; 46.3[b]	(4.8 ± 1.9)[b]; 15.03[b]	Postigo *et al.* (2008*a*)

[a]Maximum concentration.
[b]Mean.
[c]Median.

sensitivity, precision and accuracy and, since most of them rely on the use of two selected reaction monitoring transitions per compound and deuterated standards for quantification by the internal standard method, the methods are also highly selective and reliable (Postigo *et al.* 2008*b*). The target DAs and metabolites studied so far belong to five different classes: cocainics, amphetamine-like compounds, opiates, cannabinoids and lysergics. However, due to their recent identification as water contaminants (the first report of their presence in water dates from 2004 (Jones-Lepp *et al.* 2004), data on their occurrence in wastewater are still scarce. Table 2 summarizes the mean concentration values reported so far in the peer-reviewed literature. These values correspond to both influent and effluent wastewater samples collected from several European WWTPs located in Spain (Boleda *et al.* 2007; Huerta-Fontela *et al.* 2007, 2008; Postigo *et al.* 2008*a*), Ireland (Bones *et al.* 2007), Italy (Zuccato *et al.* 2005; Castiglioni *et al.* 2006*b*), Switzerland (Castiglioni *et al.* 2006*b*), Belgium (Gheorghe *et al.* 2008), United Kingdom (Kasprzyk-Hordern *et al.* 2008) and Germany (Hummel *et al.* 2006).

The ubiquity of the different target compounds is directly related to local patterns of drug abuse. The highest loads are usually reported for two cocainic compounds, namely cocaine (CO) and its main metabolite benzoylecgonine (BE), that are commonly detected at the high nanograms per litre or even the micrograms per litre level. The highest concentrations have been found in influent waters collected at a WWTP located in Catalonia (Spain), where cocaine and BE, an inactive metabolite of cocaine, were present at maximum concentrations of 4700 and 7500 $\mathrm{ng\,l^{-1}}$ (Huerta-Fontela *et al.* 2008). Other cocaine metabolites, namely cocaethylene, nor-cocaine and nor-benzoylecgonine, have been investigated by some authors, but their levels have always been below 100 $\mathrm{ng\,l^{-1}}$ in influent waste waters.

Overall, opioids are present in water at lower concentrations than BE and CO. Morphine (MOR), which has medical applications, is the opioid found at the highest levels in WWTPs. Deconjugation of its major urinary metabolite in waste water (morphine-3β-D-glucuronide, M3G) and degradation of other opioids (e.g. heroin (HER) and its metabolite 6-acetylmorphine (6ACM)) may contribute to increased MOR concentration in water, since these compounds often go undetected or are detected at low concentrations, below 20 $\mathrm{ng\,l^{-1}}$ (Castiglioni *et al.* 2006*b*; Boleda *et al.* 2007; Postigo *et al.* 2008*a*). Regarding methadone—the long-acting opioid agonist used for treating acute and chronic pain and for detoxification treatment of opioid addiction—is commonly present in sewage waters at lower levels than its pharmacologically inactive metabolite, 2-ethylidene-1,5-dimethyl-3,3-di-phenylpyrrolidine (EDDP) (Castiglioni *et al.* 2006*b*; Boleda *et al.* 2007; Bones *et al.* 2007).

Amphetamine-like compounds, so-called 'designer drugs' (3,4-methylenedioxymethamphetamine (MDMA or 'Ecstasy'), *N*-methyl-1-(1,3-benzodioxol-5-yl)-2-butanamine (MBDB or 'Eden'), 3,4-methylenedioxyethamphetamine (MDEA or 'Eve') and 3,4-methylenedioxyamphetamine (MDA or 'Love pills'), have frequently been detected at the nanograms per litre level in the different WWTPs studied. In the light of the reported results summarized in table 1, amphetamine (AM) and methamphetamine (MA) are usually present at lower concentrations than MDMA. Only high levels of AM (5236 $\mathrm{ng\,l^{-1}}$) were found in influent sewage water collected at a WWTP in Wales, surpassing the levels found for BE and CO in the same sample (Kasprzyk-Hordern *et al.* 2008).

Concerning lysergic acid diethylamide (LSD) and its metabolites *N*-demethyl-LSD (nor-LSD and nor-iso LSD) and 2-oxo-3-hydroxy-LSD (O-H-LSD), absence or very low concentrations have been reported in influent samples. These results are in line with the very low doses of LSD needed to produce an effect compared with those needed in the case of other drugs (micrograms versus milligrams), as LSD is the most potent psychoactive drug known to date.

The presence of Δ^9-tetrahydrocannabinol (THC), which is the most psychologically active constituent of cannabis (the most widely used illicit drug), in influent sewage waters has been observed insignificantly when compared with that of its metabolites since THC is extensively metabolized before excretion. 11-Nor-9-carboxy-D9-tetrahydrocannabinol (nor-THC) and 11-hydroxy-D9-tetrahydrocannabinol (OH-THC) have been found at levels below 100 and 50 $\mathrm{ng\,l^{-1}}$, respectively.

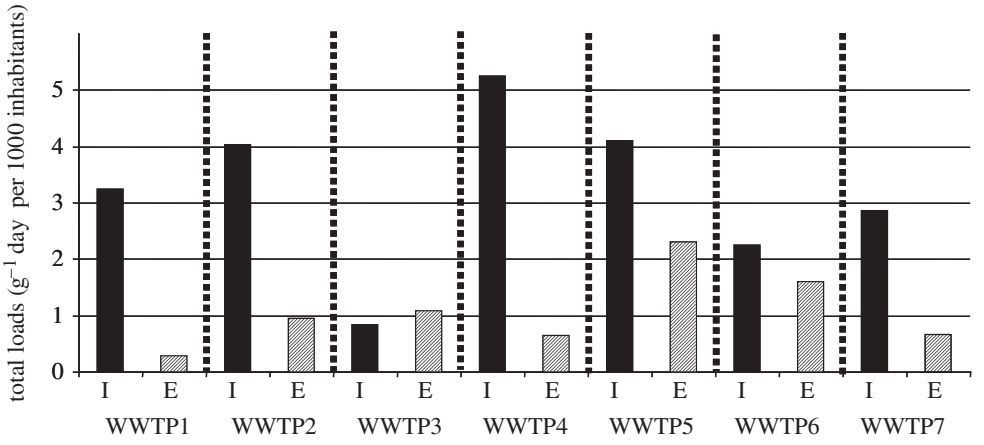
Measured values of DAs in sewage waters provide real-time data to estimate drug abuse at the community level. This strategy was first proposed by Daughton (2001) in 2001 and implemented 4 years later by Zuccato *et al.* (2005) to estimate cocaine abuse in the north of Italy. Such estimations, obtained in a fairly cheap and anonymous way (avoiding potential privacy conflicts), are useful to adopt immediate measures to fight drug abuse.

3. Removal in conventional activated sludge treatment

After administration, both PhACs and DAs can be excreted as an unchanged parent compound, in the form of metabolites or as conjugates of glucuronic and sulphuric acid, primarily via urine and faeces. Their removal in conventional WWTPs is variable and dependent on the properties of the substance and on the treatment process applied and is potentially affected by several factors such as sludge retention time (SRT), hydraulic retention time (HRT) and temperature (Suárez *et al.* 2008).

(*a*) *Pharmaceuticals*

The most important pathways for removal of PhACs during wastewater treatment are biotransformation/biodegradation and abiotic removal by adsorption to the sludge. Considering the low values of Henry coefficients (K_{H}) of most of the PhACs detected in wastewater streams, stripped fractions removed by volatilization can be neglected (Joss *et al.* 2006). The efficiency of their removal at WWTP depends on their physico-chemical properties, especially hydrophobicity and biodegradability, and process operating parameters (i.e. HRT, SRT and temperature). Higher SRT will allow the enrichment of slowly growing bacteria, and hence a more diverse microbial biocenosis will be established than with lower SRT. If a PhAC is biodegradable and if this degradation can be described by Michaelis–Menten kinetics, then critical SRT can be determined below which no biological removal of a substance occurs (Clara *et al.* 2005). If a compound is present only at trace levels of concentration (nanograms per litre, lower range of micrograms per litre), it will probably be transformed by co-metabolism (i.e. mixed substrate growth), whereas specific SRT of such trace organics will depend on the maximum specific growth rate ($\mu_{\max}$) on primary substrate. The nature of microbial population can have a significant impact on the biodegradation of some



HRT (h)	32	18	8	25	10	6–10	33
RR (%)	91	76	0	88	44	29	77

Figure 1. Total loads of pharmaceuticals measured, expressed as $g\,d^{-1}$ per 1000 inhabitants, in the seven Spanish WWTPs and the RRs reported for each plant. I, influent; E, effluent; HRT, hydraulic retention time. Adapted from Gros *et al.* (2007).

persistent PhACs. For example, it was found that longer SRT that provide growth of nitrifying bacteria is favourable for degradation of antibiotic trimethoprim (Batt *et al.* 2006). Clara *et al.* (2005) reported a correlation between the observed removal of ibuprofen and bezafibrate and the operating SRT. NSAID ibuprofen is considered to be easily degraded in the environment, and removal rates (RRs) traditionally reported in the literature were in the range of 80–100%. On the other hand, HRT can more seriously affect compounds with a moderate degradation velocity leading to better elimination of such compounds at higher HRT. Figure 1 shows the total load of 29 pharmaceuticals detected in seven Spanish WWTPs, as well as the RRs for each WWTP in correlation to the HRT (Gros *et al.* 2007).

Contradictory results have been reported for the removal of NSAID diclofenac during CAS wastewater treatment. No influence of the increased SRT on its biodegradation was found (Clara *et al.* 2005). In some WWTPs attenuation of 50–70% of diclofenac was reported (Ternes 1998; Thomas & Foster 2005; Castiglioni *et al.* 2006*a*; Radjenovic *et al.* 2007). In contrast, many studies showed extremely low efficiency of conventional treatment (only 10–30% removal; Lindqvist *et al.* 2005; Joss *et al.* 2005).

Unexplained variations of concentration over time were also observed for lipid regulator bezafibrate (Lindqvist *et al.* 2005) and sulphonamide antibiotics, probably because of deconjugation processes that may occur during contact with activated sludge. For example, a significant amount of sulphamethoxazole enters WWTPs in metabolized form as N_4-acetyl-sulphamethoxazole that can be converted back to the original compound (Göbel *et al.* 2004).

Many authors reported poor elimination of the anti-epileptic drug carbamazepine (Metcalfe *et al.* 2003; Clara *et al.* 2004*a*,*b*, 2005; Joss *et al.* 2005; Radjenovic *et al.* 2007). Pharmacokinetic data indicate that only 1–2%

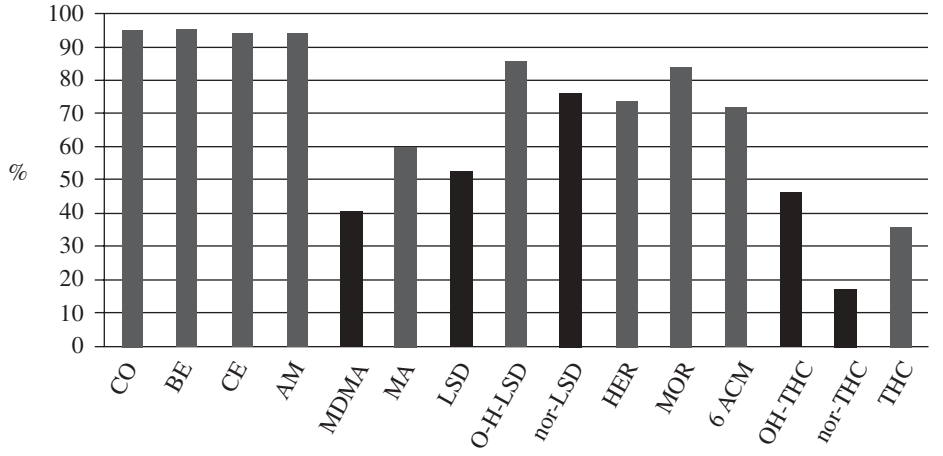


Figure 2. Average removal efficiencies (per cent) calculated for various DAs and metabolites monitored by Postigo *et al.* (2008*a*) in four Spanish WWTPs. Black bars are used to highlight analytes that have shown occasionally negative eliminations (counted as 0 removal when calculating average values).

of carbamazepine is excreted unmetabolized. However, glucuronide conjugates of carbamazepine can presumably be cleaved in the sewage, and thus increase its environmental concentrations (Ternes 1998). This is confirmed by its high ubiquity in the environment at concentration levels of several hundred nanograms per litre in different surface waters. Due to its recalcitrant nature, it can be used as an anthropogenic marker for the contamination of the aquatic environment.

(*b*) *Illicit drugs*

Efficiency of removal of DAs in WWTPs is largely unknown and should be addressed in order to control their release to the environment and avoid potential adverse effects in the aquatic ecosystem. Removal values of DAs reported so far refer to the elimination of these compounds by conventional activated sludge processes. No peer-reviewed literature on their elimination in MBRs or by river bank filtration has been found.

Most of the investigated DAs and metabolites are hydrophilic analytes; therefore they are expected to be predominantly present in the dissolved aqueous phase and to adsorb poorly onto solid particles. As an exception, cannabinoids, with octanol–water partition coefficients higher than 5, are expected to be predominantly found in sewage sludge.

The compounds investigated present different elimination rates, which differ also between WWTPs. As can be observed in table 2, concentrations of DAs and metabolites are in general lower by 1–3 orders of magnitude in effluent than in influent wastewater samples. This indicates good degradation or sorption to sludge during conventional wastewater treatment. Figure 2 summarizes the average removals calculated for various DAs and metabolites in a study conducted by Postigo *et al.* (2008*a*) in four Spanish WWTPs. As can be observed, average

eliminations varied from 17.5 per cent for THC-COOH to 96 per cent for BE. Black bars correspond to analytes that were occasionally detected at higher levels in effluent than in influent waters.

Overall, cocainic compounds have shown high removal percentages. Huerta-Fontela *et al.* (2008) reported a removal higher than 88 per cent for cocaine and benzoylecgonine after investigation of several WWTPs located in Catalonia (Spain). Good elimination of benzoylecgonine (93%) was also observed by Bones *et al.* (2007) in an Irish WWTP; however, a worse value was reported for cocaine (72%). The results obtained by Postigo *et al.* (2008*a*) indicate an average elimination of 95 per cent for CO, BE and cocaethylene. In this study, removals ranging from 67 to almost 100 per cent, from 69 to almost 100 per cent and from 66 to 98 per cent were observed for cocaine, benzoylecgonine and cocaethylene, respectively.

Overall, lower removals compared with cocainic compounds have been observed for opioids. Average removals of 72, 74 and 86 per cent have been calculated from the results reported by Postigo *et al.* (2008*a*) for 6ACM, HER and MOR, respectively. Good removal of MOR was also observed by Hummel *et al.* (2006), as MOR concentration was reduced by a factor of 8 from influent to effluent waters. However, according to the results published by Boleda *et al.* (2007), the average MOR elimination in various Spanish WWTPs reached only 38 per cent, and the rest of the studied opioids (nor-MOR, methadone, EDDP, HER and 6ACM) were not or very poorly eliminated, showing two of the WWTPs investigated had higher concentrations for methadone and EDDP in effluent than in influent waters. MOR is excreted in urine mainly as glucuronide metabolites; however, cleavage of the conjugated molecules in wastewater is likely to occur in the light of the low levels found for M3G (the only conjugated compound studied) in comparison with those usually detected for MOR (Castiglioni *et al.* 2006*b*).

Removal of amphetamine-like compounds (AM, MA, MDMA, MDA) in Spanish WWTPs was between 40 and 99 per cent according to Huerta-Fontela *et al.* (2008) and 65 per cent on average according to Postigo *et al.* (2008*a*). Among all investigated amphetamine-like compounds, MDMA provides the worst elimination values and the highest loads of this type of analytes in effluent samples, with occasionally higher values in effluent than in influent samples (Postigo *et al.* 2008*a*). Also, negative eliminations, in this case for MDA, have been reported by Castiglioni *et al.* (2006*b*) and Huerta-Fontela *et al.* (2008), which could be related to *N*-demethylation processes of MDMA during wastewater treatment.

The results reported by Postigo *et al.* (2008*a*) for LSD and its metabolites point at an average removal of 72 per cent; with variations from 45 to almost 100 per cent depending on the compound and WWTP, and occasionally higher (in the low nanograms per litre range) concentrations in effluent than in influent waters.

Concerning cannabinoids, a metabolite of THC, namely nor-THC, has been observed to be poorly removed by conventional wastewater treatment processes, as several authors have reported higher levels in effluent waters than in influents (Boleda *et al.* 2007; Postigo *et al.* 2008*a*). This phenomenon has been less frequently observed for the other investigated THC metabolite (OH-THC); however, removals under 50 per cent have usually been reported for this compound and the parent drug THC.

4. Removal by membrane bioreactor wastewater treatment

The upgrading of WWTPs and implementation of sustainable technologies impose as possible solutions for the safe reclamation of high-quality treated effluent. One of the advanced technologies that has been gaining interest over the last 25 years is MBR. The MBR technology integrates biological degradation of organic matter present in wastewater with membrane filtration, thus surpassing the limitations of the conventional CAS treatment (e.g. limited operational SRT, sludge-settling characteristics). MBR has become a technically and economically feasible alternative for water and wastewater treatment, especially because of high SRTs achieved within compact reactor volumes. Due to high biomass concentration the degradation rate is higher, and also specialists are grown for problematic compounds. Therefore, MBR sludge is expected to have higher biodegradation potential for trace organic contaminants for several reasons: more diversified microbial population, better acclimation of micro-organisms to substrate and larger fraction of active biomass.

Several studies (Lesjean *et al.* 2005; Quintana *et al.* 2005; Göbel *et al.* 2007; Radjenovic *et al.* 2007; Reif *et al.* 2008) confirmed an advantage of MBR over CAS when reduction of pharmaceutical residues is concerned. For most of the investigated PhACs, MBR effluent concentrations were usually significantly lower than in the effluent of a conventional treatment. They are removed from wastewater during membrane treatment by sorption, degradation or a combination of both. Better removal of readily biodegradable micropollutants in the MBR could be due to a smaller flock size of sludge, which enhances mass transfer by diffusion and therefore increases the elimination. Considering the composition of sludge originating from an MBR (specialized micro-organisms, large portion of active biomass in suspended solids) improved removal is to be expected. In general, no relationship has been found so far between the structures of micropollutants and their removal during wastewater treatments.

Radjenovic *et al.* (2007, submitted) found improved removal of the majority of target compounds (figure 3). Kimura *et al.* (2005) reported greater attenuation of influent concentrations of ketoprofen, mefenamic acid and naproxen, which was explained by better adaptation of MBR microbial consortia to these compounds. Lesjean *et al.* (2005) also correlated an improved removal in the MBR to the enrichment of specialized micro-organisms.

MBR technology is generally considered as suitable for the treatment of wastewater containing refractory compounds. However, some compounds such as the anti-epileptic drug carbamazepine pass through both WWTPs and MBRs without any reduction. Moreover, in many cases significantly higher concentrations in the effluent were recorded, which could be explained by the presence of input conjugate compounds of carbamazepine that are being retransformed during treatment into the original compounds. NSAID diclofenac and the lipid regulator clofibric acid were also found to be slightly recalcitrant pharmaceutical residues in some studies. Kimura *et al.* (2005) related the persistence of diclofenac and clofibric acid in both MBR and CAS processes to the presence of chlorine in their structures, which makes them barely degradable. González *et al.* (2006) also suggested that faster diminution of diclofenac was because of better acclimation of micro-organisms to the MBR influent water. Radjenovic *et al.* (2007) noted a significant improvement in the removal of

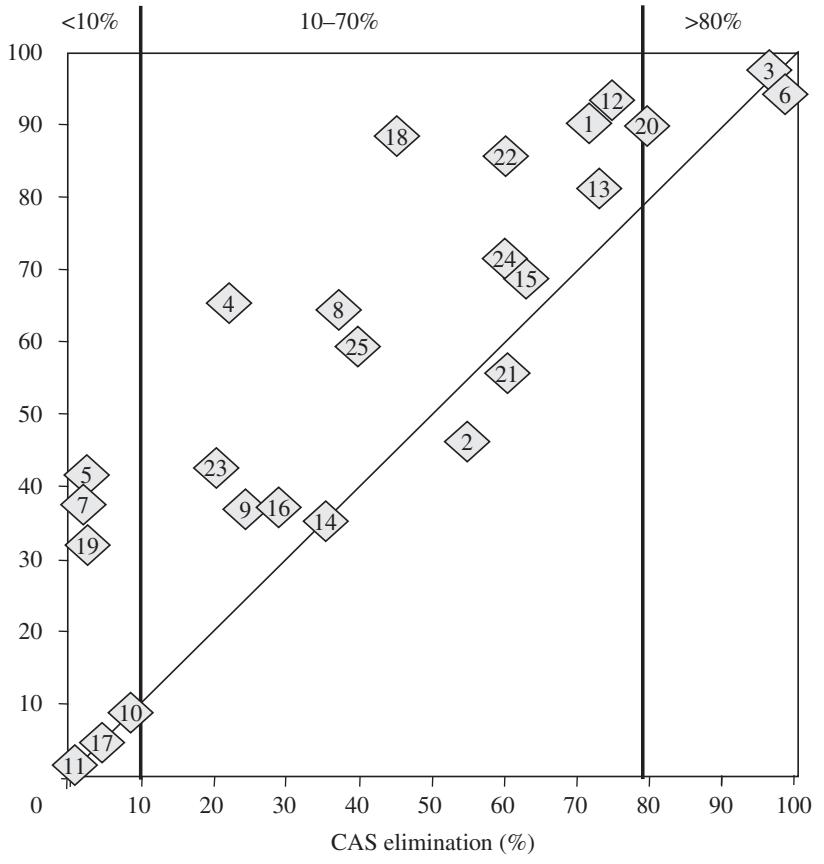


Figure 3. Comparison of the mean removal of encountered pharmaceuticals in full-scale CAS and pilot-scale MBRs. The eliminations presented for MBR are given as mean values of the removal of each compound obtained in two pilot-scale MBR (one with hollow fibre membrane and another with flat-sheets). 1, naproxen; 2, ketoprofen; 3, ibuprofen; 4, diclofenac; 5, indomethacin; 6, acetaminophen; 7, mefenamic acid; 8, propyphenazone; 9, ranitidine; 10, loratidine; 11, carbamazepine; 12, ofloxacin; 13, sulphamethoxazole; 14, erythromycin; 15, atenolol; 16, metoprolol; 17, hydrochlorothiazide; 18, glibenclamide; 19, gemfibrozil; 20, bezafibrate; 21, famotidine; 22, pravastatin; 23, sotalol; 24, propranolol; 25, trimethoprim. Adapted from Radjenovic *et al.* (2008).

these compounds when using an MBR unit. Eliminations in MBR of diclofenac and clofibric acid were 87 and 72 per cent, compared with 50 and 28 per cent found in CAS, respectively. Besides possible changes in microbial consortia during adaptation to wastewater contaminants, another explanation for the better performance of MBR could be its enhanced elimination by sorption. Since sorption processes are relevant for diclofenac (Suárez *et al.* 2008), and keeping in mind that MBR sludge has higher organic matter content which means higher sorption potential, the amount of the adsorbed compound can be expected to be greater than in the CAS system.

Theoretically, the increase in SRT should have a positive influence on the biodegradation of organic micropollutants. In a study of Göbel *et al.* (2007), a clear increase in attenuation percentages was observed at sludge ages of

60–80 days for the antibiotics trimethoprim, azithromycin, erythromycin and clarythromycin, whereas higher reduction of roxythromycin occurred already at 33 days SRT. Drastic improvement in the elimination of mefenamic acid was also observed for the laboratory-scale MBR operating with long SRT (greater than two months; Radjenovic *et al.* 2007). Kimura *et al.* (2007) noticed an improvement in the MBR operating with extremely aged sludge (i.e. SRT = 65 days) where 90 per cent elimination was achieved, which was assigned mainly to the biodegradation removal pathway. However, Joss *et al.* (2005) found no improvement in degradation of roxythromycin and some other PhACs with increased SRT. They noted a comparable performance of CAS and a pilot-scale MBR process run in parallel regarding removals of several selected PhACs (i.e. ibuprofen, naproxen, diclofenac, carbamazepine and roxythromycin).

5. Removal by riverbank filtration

At present, surface water is certainly not enough to cope with the water requirement for agricultural, industrial, recreational and drinking purposes. In this context, the usage of groundwater has become essential; therefore, their quality and quantity has to be carefully managed. Induced recharge of aquifers can guarantee a sustainable level of groundwater, while strict quality control of waters intended for recharge will minimize contamination of both the groundwater and the aquifer area. However, all water resources available are threatened by multiple sources of contamination from the extended use of chemicals worldwide. In this respect, the environmental occurrence of organic micropollutants such as pesticides, pharmaceuticals, industrial chemicals and their metabolites has experienced fast-growing interest (Heberer 2002; Hiemstra *et al.* 2003).

Bank filtration is a type of filtration that purifies water by passing the water through the banks of a river or lake. It is then extracted by wells located some distance away from the water body. This purifying approach has been in use in Europe, especially in Germany along the Rhine, since the 1870s. Major facilities also exist in many other countries, including the USA, where Nebraska is leading the use of such facilities.

In this section an overview of the pharmaceutical and illicit drug residues found to be present in the waters involved in bank-filtration practices at managed aquifer recharge sites as well as the potential of this approach as an efficient method for the mitigation of such pollutants is presented.

(*a*) *Groundwater contamination*

Aquifer systems as environmental compartments are substantially different from other aqueous systems. Long residence times, low temperatures, low degrees of dilution and decreased microbial population are factors favouring the long-term fate of organic micro-contaminants in groundwater. The primary concern regarding contaminants input is the removal of pathogenic micro-organisms; however, trace metals and organic compounds are also important issues. When organic contaminants are introduced into an aquifer, they will either move with the water or be adsorbed on the solid surfaces. Whenever retained contaminants do not break down they will accumulate in the aquifer. This accumulation may have long-term impacts.

Reclaiming an aquifer that has been contaminated is a difficult, long and expensive process; therefore, a prerequisite of induced recharge is that it should not risk the quality of the groundwater resource. It is well known that hydrogeology influences the fate and transport of organic micro-contaminants. Factors such as depth to water table, sediment porosity and permeability, and groundwater flow control how fast and to what extent contaminants make their way from the recharge point to the recovery point. Geochemical and nutrient conditions also drive the fate of organics into the aquifer, with low dissolved oxygen/low nutrient conditions favouring long-term persistence.

(*b*) *Fate*

Surface water used for the infiltration at bank filtration sites is often contaminated with pharmaceutical residues and their metabolites as a consequence of discharges from municipal WWTP effluents, where they are not effectively removed (Verstraeten *et al.* 2002). In a recent review (Díaz-Cruz & Barceló 2008), an overview of the pharmaceuticals, pesticides and industrial chemicals found to be present in infiltrated and ground waters was published. Table 3 lists some of the most frequently detected pharmaceuticals in surface waters that are transferred to the aquifer area and the supply water.

The transport and fate of six pharmaceuticals belonging to different prescription classes, carbamazepine, primidone, bezafibrate, indomethacine, diclofenac and propyphenazone, and two drug metabolites, clofibric acid, and 1-acetyl-1-methyl-2-dimethyl-oxamoyl-2-phenylhydrazide (AMDOPH; a metabolite of dimethylaminophenazone), were detected in waters from recharging ponds and control wells and six of them persisted in the drinking water supply in bank-filtration sites in Berlin (Germany), replenishing groundwater from lakes Tegel and Vannsee (Heberer *et al.* 2004; table 3).

Heberer *et al.* (2008) recently evaluated the behaviour of antibiotic residues during bank filtration in Berlin. Anhydroerothromycin, clindamycin and sulphamethoxazole were the three analytes detected in the filtrate out of the seven antibiotics detected in the surface water used for recharge. Only sulphamethoxazole was further detected in the abstracted water. A higher mean concentration of 118 ng l^{-1} sulphamethoxazole has been reported in the drinking water extracted from the production well in a recharge facility at Lake Tegel (Grünheid *et al.* 2005). The analgesic diclofenac (Heberer *et al.* 1997; Sacher & Brauch 2000) and the lipid regulator bezafibrate (Heberer *et al.* 2001) were also detected in ground water at low concentrations.

Hospital wastewater effluents contain, in addition to residues of typical prescription drugs, certain pharmaceutical compounds in hospital use, such as X-ray contrast media. According to Ternes & Hirsch (2000), these contrast media constitute the main fraction of the absorbable organic iodine in waters. Such compounds are very polar, persistent in the aquatic environment and have been found to be recalcitrant in wastewater treatments. Therefore, compounds such as diatrizoate, iopromide, iopamidol and amidotrizoic acid were detected up to the micrograms per litre concentration level in ground and infiltrated waters (Putschew *et al.* 2000; Sacher & Brauch 2000; Ternes & Hirsch 2000). Recently, the iodinated X-ray contrast agent iopromide has been searched for in extracted raw water from monitoring and production wells of a bank filtration site and

Table 3. Mean concentrations ($ng\,l^{-1}$) of pharmaceuticals in surface, infiltrated and supply waters when surface water is used for groundwater-enhanced recharge in drinking water supply. n.r., not reported; n.d., not detected.

compound	conc. in surface water	conc. in infiltrated water	conc. in supply water	reference
diclofenac	15[a]	< 5[a]	35[a]	Heberer *et al.* (2004)
	25[b]	30[b]	< 5[a]	
clofibric acid	40[a]	< 5[a]	50[a]	Heberer *et al.* (2004)
	60[b]	25[b]	115[b]	
propyphenazone	230[a]	170[a]	240[a]	Heberer *et al.* (2004)
	145[b]	85[a]	30[b]	
AMDOPH	355[a]	465[a]	1250[a]	Heberer *et al.* (2004)
	170[b]	115[b]	280[b]	
carbamazepine	110	110	n.r.	Brauch *et al.* (2000)
	325[a]	365[a]	60[a]	Heberer *et al.* (2004)
	330[b]	215[b]	15[b]	
primidone	55[a]	40[a]	40[a]	Heberer *et al.* (2004)
	60[b]	70[b]	10[b]	
indometazine	n.d.[a]	n.d.[a]	n.d.[a]	Heberer *et al.* (2004)
	15[b]	< 5[b]	n.d.[b]	
bezafibrate	20[a]	n.d.[a]	< 5[a]	Heberer *et al.* (2004)
	60[b]	10[b]	n.d.[b]	
iopromide	841	151	n.r.	Grünheid *et al.* (2005)
sulphamethoxazole	485	122	n.r.	Grünheid *et al.* (2005)
	151	43	2	Heberer *et al.* (2008)
acetyl-sulphamethoxazole	7	n.d.	n.d.	Heberer *et al.* (2008)
clarythromycin	8.9	n.d.	n.d.	Heberer *et al.* (2008)
roxythromycin	11	n.d.	n.d.	Heberer *et al.* (2008)
anhydroerithromycin	50	50	n.d.	Heberer *et al.* (2008)
clindamycin	31	n.d.	n.d.	Heberer *et al.* (2008)

[a]Data from Lake Tegel.
[b]Data from Lake Vannsee.

one artificial recharge site at Lake Tegel (Grünheid *et al.* 2005); however, in both production wells concentrations found were below the limit of quantification ($<20\,ng\,l^{-1}$).

(*c*) *Removal*

Several mechanisms including adsorption, dispersion and biological transformations (within the first few meters of infiltration) are the main processes driving the attenuation and fate of organic contaminants in groundwater environments during infiltration (Roberts & Valocchi 1981); however, these processes are not yet sufficiently understood. Different patterns and kinetics for the removal of the trace organic compounds can be found; however, there is a general agreement that significant improvement is achieved in the quality of the recovered waters.

Redox processes in enhanced groundwater enrichment sites are known to affect the elimination of pharmaceutical residues. These processes are known to be temperature-dependent, since these processes are in general catalysed microbially and temperature variations influence the microbial activity (Prommer & Stuyfzand 2005). Under warmer temperatures (greater than 14°C) anoxic conditions prevail, while below 14°C oxic conditions develop. Recent studies investigated the impact of the infiltration water temperature on the redox degradation of carbamazepine, phenazone and phenazone-like pharmaceuticals in Berlin. Outcomes evidenced that removal during infiltration was not observed for carbamazepine, irrespective of its redox state; meanwhile different degradation rates were shown by the rest of compounds under aerobic conditions (Greskowiak *et al.* 2006). These results are in concordance with the poor mitigation, reported by several authors, of carbamazepine and another antiepileptic drug, such as primidone, which were found to be present in ground and drinking water where infiltration was carried out (Heberer *et al.* 2001; Preuss *et al.* 2002; Mansell & Drewes 2004; Massmann *et al.* 2008*a*,*b*).

In the same study other antibiotics and X-ray contrast agents such as iopromide also show redox-dependent mitigation. Clindamycin was found to be almost completely eliminated under anoxic conditions. Sulphamethoxazole could be reduced to *ca* 25 per cent of the surface concentration by bank filtration; however, only infiltration basins were able to degrade it to half (Grünheid *et al.* 2005; Heberer *et al.* 2008). Other antibiotics investigated, namely clarythromycin, roxythromycin and anhydroerithromycin, were found to be readily removable by bank filtration, despite the redox conditions (Heberer *et al.* 2008). For the X-ray contrast medium iopromide results indicate that removal rates at both sites are around 82 and 89 per cent, respectively, which is in concordance with the rapid degradation observed under both aerobic and anoxic conditions but only partially dehalogenated under anoxic conditions observed by Grünheid *et al.* (2005) during bank filtration.

Some laboratory and field experiments on infiltration processes evidenced significant removal of diclofenac and bezafibrate in the infiltration process as a result of their tendency to be both adsorbed on the soil/sediment (Heberer *et al.* 2001, 2004; Ternes *et al.* 2007) and transformed during passage (Scheytt *et al.* 2007). According to Preuss *et al.* (2002), the elimination of bezafibrate along with diclofenac and ibuprofen would be in the range 60–80%. Clofibric acid, according to several authors, exhibited low mitigation, since little or no adsorption and only very low degradation was observed during the soil passage (Scheytt *et al.* 2001; Mersmann *et al.* 2002; Scheytt *et al.* 2007; Ternes *et al.* 2007; Massmann *et al.* 2008*a*).

6. Conclusions

Due to their beneficial health effects and economic importance, the reduction of drug inputs into the environment through restricting or banning their use is not possible. Moreover, the use of pharmaceutical compounds is expected to grow with the increasing age of the population. The only possible way is to regulate their environmental pathways, perhaps at source through labelling of medicinal products and/or developing disposal and awareness campaigns.

Another option is to add sewage treatments in hospitals, and to enhance current wastewater treatment techniques in order to eliminate such polar pollutants more efficiently.

MBR technology is considered the most promising development in microbiological wastewater treatment. Several studies clearly outlined the strong potential of MBR technology in reducing ecological risks associated with PhACs, as well as other polar micropollutants. However, MBR technology is sometimes seen as high risk and prohibitively costly compared with CAS and other more established technologies. Further improvement of the process will increase its cost-effectiveness and MBR technology is expected to play a key role in wastewater treatment in the coming years, where it may ensure enhanced elimination and biodegradation of PhACs, thus reducing the environmental risk posed by those compounds.

Bank filtration is an efficient approach for the attenuation of most pharmaceutical residues allowing a partial (propyphenazone, diclofenac, sulphamethoxazole) or a total removal (bezafibrate, indomethazine, steroids). However, special attention must be paid when residues of carbamazepine or other antiepileptic drugs, such as primidone, are present in the water intended for bank filtration, since no significant removal is observed, but just a slight decrease in the concentration as a consequence of the dilution with uncontaminated water. However, bank filtration does not guarantee the complete removal of all potential pharmaceutical residues present in the water and can be regarded as a useful tool for the pretreatment of raw water (wastewater, surface water and reclaimed water) but is not sufficient for a complete water treatment and requires further purification to produce drinking water.

This work has been supported by the EU project INNOVA-MED (INCO-CT-2006-517728) and by the Spanish Ministry of Science and Innovation Projects CTM2007-30524-E and CEMAGUA (CGL2007-64551).

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