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Fate and distribution of pharmaceuticals in wastewater and sewage sludge of the conventional activated sludge (CAS) and advanced membrane bioreactor (MBR) treatment

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ABSTRACT

In this paper we report on the performances of full-scale conventional activated sludge (CAS) treatment and two pilot-scale membrane bioreactors (MBRs) in eliminating various pharmaceutically active compounds (PhACs) belonging to different therapeutic groups and with diverse physico-chemical properties. Both aqueous and solid phases were analysed for the presence of 31 pharmaceuticals included in the analytical method. The most ubiquitous contaminants in the sewage water were analgesics and anti-inflammatory drugs ibuprofen (14.6–31.3 μg/L) and acetaminophen (7.1–11.4 μg/L), antibiotic ofloxacin (0.89–31.7 μg/L), lipid regulators gemfibrozil (2.0–5.9 μg/L) and bezafibrate (1.9–29.8 μg/L), β-blocker atenolol (0.84–2.8 μg/L), hypoglycaemic agent glibenclamide (0.12–15.9 μg/L) and a diuretic hydrochlorothiazide (2.3–4.8 μg/L). Also, several pharmaceuticals such as ibuprofen, ketoprofen, diclofenac, ofloxacin and azithromycin were detected in sewage sludge at concentrations up to 741.1, 336.3, 380.7, 454.7 and 299.6 ng/g dry weight. Two pilot-scale MBRs exhibited enhanced elimination of several pharmaceutical residues poorly removed by the CAS treatment (e.g., mefenamic acid, indomethacin, diclofenac, propyphenazone, pravastatin, gemfibrozil), whereas in some cases more stable operation of one of the MBR reactors at prolonged SRT proved to be detrimental for the elimination of some compounds (e.g., β-blockers, ranitidine, famotidine, erythromycin). Moreover, the anti-epileptic drug carbamazepine and diuretic hydrochlorothiazide by-passed all three treatments investigated.

Furthermore, sorption to sewage sludge in the MBRs as well as in the entire treatment line of a full-scale WWTP is discussed for the encountered analytes. Among the pharmaceuticals encountered in sewage sludge, sorption to sludge could be a relevant removal pathway only for several compounds (i.e., mefenamic acid, propranolol, and loratidine). Especially in the case of loratidine the experimentally determined sorption coefficients (K_ds) were in the range 2214–3321 L/kg (mean). The results obtained for the solid phase indicated that MBR wastewater treatment yielding higher biodegradation rate could reduce

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the load of pollutants in the sludge. Also, the overall output load in the aqueous and solid phase of the investigated WWTP was calculated, indicating that none of the residual pharmaceuticals initially detected in the sewage sludge were degraded during the anaerobic digestion. Out of the 26 pharmaceutical residues passing through the WWTP, 20 were ultimately detected in the treated sludge that is further applied on farmland.

1. Introduction

The escalating population growth and intensified agricultural and industrial activity has raised concerns not only in water-scarce regions but also in developed countries.

The reuse of treated water imposes as the most adequate solution for the future sustainable water cycle management. One of the key issues in wastewater recycling is the emerging problem of micropollutants such as pharmaceuticals, hormones, fragrances and personal care products (PCPs). Pharmaceutically active compounds (PhACs) represent an overgrowing portion of trace organic contaminants in the urban aquatic environment that after human consumption reach wastewater treatment plant (WWTP) in metabolised and/or unmetabolised from. WWTPs are frequently pointed out as main points of discharge of PhACs (Castiglioni et al., 2006; Ternes, 1998; Radjenović et al., 2007; Lindqvist et al., 2005; Carballa et al., 2004). The presence of PhACs in surface, drinking and wastewaters is well documented in literature (Castiglioni et al., 2006; Ternes, 1998; Kolpin et al., 2002; Joss et al., 2005). Furthermore, farmland application of sewage represents another input of PhACs into the environment (Golet et al., 2003).

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 membrane bioreactor (MBR). The MBR technology integrates biological degradation of organic matter present in wastewater with membrane filtration, thus surpassing the limitations of the conventional activated sludge (CAS) treatment (e.g., limited operational solids retention time (SRT), sludge settling characteristics). At prolonged SRT applied in an MBR the biomass growth is not restricted to fast-growing and floc-forming microorganisms, whereas the dispersed bacteria can develop. As far as PhACs are concerned, there have been several studies that proved their more complete elimination in MBR treating municipal wastewater (Radjenović et al., 2007; Lesjean et al., 2005; Göbel et al., 2007., Kimura et al., 2007). Moreover, in a recent study of Pérez and Barceló (2008) a 56% of elimination of human metabolite of diclofenac, 4′-hydroxydiclofenac, was observed in a laboratory-scale MBR, versus only 26% in CAS treatment.

The fate of a certain pharmaceutical in a complex system of WWTP will depend on various parameters (e.g., applied SRT, hydraulic retention time (HRT), temperature, pH, biomass concentration, compound's polarity, biodegradability, cation-exchange properties). During sewage treatment pharmaceutical residues can be removed from the aqueous phase either through abiotic processes (e.g., sorption, isomerisation/epimerisation, hydrolytic degradation) or by biotic transformation/degradation. The majority of studies on the removal of PhACs in WWTPs were focused on the aqueous phase, whereas their load in the corresponding solid phase was often neglected. However, PhACs can absorb onto bacterial lipid structure and fat fraction of the sewage sludge through hydrophobic interactions (e.g., aliphatic and aromatic groups), adsorb onto often negatively charged polysaccharide structures on the outside of bacterial cells through electrostatic interactions (e.g., amino groups), and/or they can bind chemically to bacterial proteins and nucleic acids (Meakins et al., 1994). Moreover, other mechanisms such as hydrogen bonding, ion exchange and surface complexation may intervene in the sorption process (Tolls, 2001). There has been some work conducted on the occurrence of PhACs in sewage sludge (Göbel et al., 2005; Ternes et al., 2005). Some authors tried to estimate separately contributions of adsorption and biodegradation to the removal of PhACs in CAS and MBR treatments based on literature values for solid–water distribution coefficients (K_d) or by direct measurements of the adsorbed and dissolved amounts of pharmaceuticals in batch experiments (Kimura et al., 2007; Clara et al., 2005; Joss et al., 2006; Urase and Kikuta, 2005).

The objective of this study was to determine the distribution of selected PhACs between wastewater and sewage sludge in WWTP Terrassa (Barcelona, Spain). In total 36 flow-proportional composite samples of wastewater and 35 grab samples of different types of sewage sludge produced along the treatment were analysed. The performances of full-scale CAS treatment and two pilot-scale MBRs in eliminating pharmaceutical residues from wastewater were compared. From the measured concentrations of pharmaceuticals in the collected sludge samples and their corresponding supernatants, sorption capacities of primary, secondary activated and MBR sludge were estimated. Finally, total aqueous and solid phase output loads of WWTP Terrassa were determined.

2. Experimental

2.1. Materials and standards

All analytical standards of pharmaceuticals used were of high purity grade (>90%). Detailed information on the providers of analytical reference standards can be obtained elsewhere (Gros et al., 2006).

Isotopically labelled compounds used as internal standards were ^{13}C-phenacetin obtained from Sigma-Aldrich, mecoprop-d_3 from Dr. Ehrenstorfer (Augsburg, Germany), ibuprofen-d_3, atenolol-d_7 and carbamazepine-d_{10} from CDN

Isotopes (Quebec, Canada), and diazepam-d_5 and phenobarbitol-d_3 from Cerilliant (Texas, United States).

All solvents (methanol, acetonitrile and water) were HPLC-grade and were purchased from Merck (Darmstadt, Germany), as well as hydrochloric acid (HCl, 37%), ammonium-acetate (NH_4Ac) and acetic acid (HAc). Nitrogen for drying 99.99% of purity was from Air Liquide (Spain).

2.2. Wastewater treatment plant Terrassa

WWTP Terrassa is located approximately 21 km of Barcelona (Spain) and it has a total treatment capacity of 277,000 equivalent inhabitants. Flow diagram of the wastewater and sludge treatment line in the WWTP Terrassa with two pilot-scale MBRs is illustrated in Fig. 1. Wastewater treated is a mixture of municipal and industrial wastewater (mostly pharmaceutical and textile industry). The treatment consists of a pre-treatment, preliminary treatment, primary sedimentation unit and a secondary (biological) treatment. Pre-treated wastewater goes through a physical process of settling in a primary clarifier. Secondary treatment (i.e., CAS treatment) consists of a pre-denitrification (anaerobic) and nitrification (aerobic) tank, and two secondary clarifiers. The HRT for the CAS treatment in WWTP Terrassa, calculated for an average daily flow (i.e., 42,000 m^3/day), is approximately 11.5 h. During the performed sampling campaign, WWTP Terrassa was operating with SRT of approximately 10 days. Some activated sludge from the secondary sedimentation unit is returned to the inlet of the primary clarifier, whereas the remaining fraction of secondary sludge is being combined with the primary sludge and further treated (i.e., thickened, dewatered and anaerobically digested). In the anaerobic digester, the biosolids are stabilized during approximately 30 days period at 34 °C. The treated sludge is then shipped from the WWTP for the direct application to agricultural fields.

2.3. Membrane bioreactors (MBRs)

The two pilot-scale MBRs were operating in parallel with CAS treatment (i.e., aeration tank and secondary settling tanks). One MBR was equipped with hollow-fibre (HF) ultra-filtration (UF) membranes (nominal porosity 0.05 μm) purchased from Koch Membrane Systems, Wilmington, Massachusetts, USA. The other MBR operated with micro-filtration (MF) flat-sheet (FS) membrane module (Kubota, Osaka, Japan) with nominal porosity of 0.4 μm. The HF and FS MBR were operating with HRTs of 7.2 and 15 h, respectively. Their mixed liquor suspended solids concentrations were measured to be in the range of 1.4–8.4 and 6.7–26 g/L for HF and FS MBR, respectively. Both MBRs had external membrane module configuration, whereas the reactor volumes were 3.6 m^3 and 4.7 m^3 for HF and FS MBR system, respectively. The temperature inside the reactor was 20 ± 2 °C during the whole sampling campaign.

2.4. Sampling and sample preparation

The sampling campaign was done during March and April, 2007. All wastewater samples were taken as flow-proportional composite samples, using automated samplers that collected defined volumes every hour over a 24-h period. For the sample collection were used amber glass bottles pre-rinsed with ultra-pure water. The sampling points indicated in Fig. 1 correspond to the: 1) primary sedimentation tank effluent, as the influent of the conventional treatment and membrane bioreactors (sampling point, s.p. 1), 2) CAS effluent (s.p. 2), 3) HF MBR effluent (s.p. 3), and 4) FS MBR effluent (s.p. 4). In total 36 samples were analysed, i.e., 9 for each type of sewage. The samples were filtered immediately upon the arrival to the laboratory through 1 μm glass fibre filters followed by 0.45 μm nylon membrane filters purchased from Whatman (England). All target compounds were extracted in one single extraction step, according to the previously published analytical method (Gros et al., 2006). For this purpose was used a Baker vacuum system (J.T. Baker, The Netherlands) and Oasis HLB cartridges (60 mg, 3 ml) from Waters Corporation (Milford, MA), previously conditioned at neutral pH with 5 ml of methanol followed by 5 ml of deionised water (HPLC-grade). According to the type of the samples 100 ml of wastewater was extracted for the influent of CAS and MBRs, and 200 ml of effluent wastewater. The elution was performed two times with 4 ml of methanol at a flow of 1 ml min^{-1}. The extracts were then

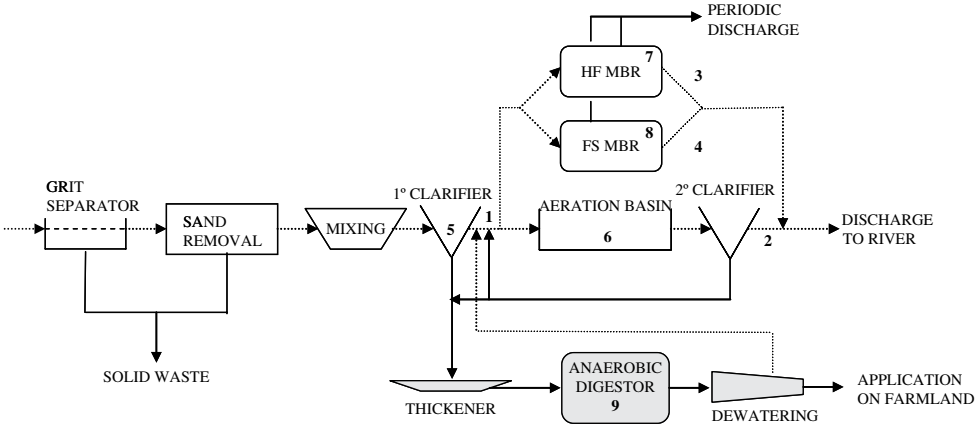

Fig. 1 – Flow diagram showing the process train for wastewater and sludge handling in the full-scale activated sludge treatment plant studied. Numbers indicate the sampling locations for sludge and wastewater.

evaporated under a nitrogen stream and reconstituted with 1 mL of methanol–water mixture (25:75, v/v).

Concurrently with wastewater sampling, sewage sludge samples were taken once per week as grab samples during 7 weeks, whereas five different types of sewage sludge were sampled: 1) primary sewage sludge (i.e., from the primary sedimentation unit) (s.p. 5), 2) activated sludge (i.e., secondary sludge proceeding from the aeration basin of CAS treatment) (s.p. 6), 3) sewage sludge proceeding from the HF MBR (s.p. 7), 4) sewage sludge proceeding from the FS MBR (s.p. 8), and 5) treated sewage sludge (s.p. 9). In total 35 biosolid samples were analysed (i.e., 7 for each type of sewage sludge). In Fig. 1 all sampling locations for sewage sludge and wastewater are indicated with numbers 5–9. The 4 L volumes of activated sludge samples were taken in polypropylene bottles, and centrifuged immediately upon the arrival to the laboratory (Mixtasel, P Selecta) and freeze-dried (LioAlfa 6, Telstar) at −40 °C and with 0.044 bar vacuum, wrapped in aluminium paper and stored at −20 °C until the analysis. Approximately 300 g of treated (i.e., digested and dehydrated) sludge was sampled, and was wrapped in aluminium paper and stored at −20 °C until the analysis. Besides the solid phase for each sludge sample except for the treated, dehydrated and digested sludge, 100 mL of corresponding supernatant samples was analysed as described for the aqueous samples, in order to determine K_d coefficients. Freeze-dried sludge was extracted with a water–methanol mixture (2:1, v/v) at 100 °C using a Dionex accelerated solvent extractor (ASE) 200 (Dionex, Idstein, Germany) by a previously developed method (Radjenović et al., in press). Sludge extracts were diluted with water to reduce the methanol content below 5% and subsequently enriched on Oasis HLB cartridges (200 mg, 6 ml).

2.5. *Chemical analysis*

LC analysis was performed using a Waters 2690 HPLC system (Milford, MA, USA) coupled to a Micromass Quattro (Manchester, UK) triple quadrupole (QqQ) mass spectrometer, equipped with a Z-spray electrospray interface. Chromatographic separation was achieved with a Purospher Star RP-18 endcapped column (125 × 2.0 mm, particle size 5 μm) and a C_{18} guard column, both supplied by Merck (Darmstadt, Germany). The concentrations of selected pharmaceuticals in sludge and water samples were determined by the previously developed analytical methods (Gros et al., 2006; Radjenović et al., in press).

Method detection limits (MDLs) and method quantification limits (MQLs) for the analysed samples were calculated by a signal-to-noise ratio (S/N) 3 and 10, respectively. MQLs determined for wastewater were in the range 1.2–139.0 ng/L for the primary effluent, 1.1–84.7 ng/L for the MBR and CAS effluents, and 1.5–94.3 ng/L for sludge supernatants. MQLs in sludge samples were varying from 0.04 to 86.5 ng/g d.w., whereas in the case of ibuprofen, diclofenac and indomethacin they were significantly higher (i.e., up to 120.6, 163.7 and 258.5 ng/g d.w.).

Recoveries of the method for wastewater and sewage sludge were determined by analysing fortified samples of each type of wastewater and sludge spiked in triplicate to 1 μg/L and 200 ng/g dry weight (d.w.), respectively. The recoveries determined for wastewater were in the range from 35.4 to 127%, whereas generally they were over 70%. On the other side, the method yielded recoveries for the sludge phase from 3.2 (ranitidine) to 129.9% (diclofenac), whereas they were greater than 60% for the majority of compounds. The recoveries of some compounds were varying strongly depending on the sludge matrix (e.g., 29.2–93.0% for gemfibrozil), whereas for ranitidine and fluoxetine they were found to be low for the optimised conditions (i.e., around 30%). Furthermore, the intra- and inter-day precisions of the method optimised for the extraction and analysis of sludge were in the range 0.1–15.3% and 0.9–17.4% R.S.D., respectively.

In order to compensate matrix effects from sample matrices internal standard calibration, adequate dilution of sample extracts as well as standard addition method in the case of sewage sludge were applied, which has been described in detail elsewhere (Gros et al., 2006; Radjenović et al., in press).

3. Results and discussion

3.1. *Biological performances of CAS and MBRs*

In Table 1 are summarized parameters of CAS, HF and FS MBR reactors such as total suspended solids (TSS) and volatile suspended solids (VSS), as well as the content of TSS, VSS, free ammonia nitrogen (NH_4), chemical oxygen demand (COD) and biological oxygen demand (BOD_5) in the effluents of these three treatments. The TSS concentration measured during the sampling campaign in the HF MBR (i.e., mean 2180 mg/L) is very similar to the one measured in the aeration basin of CAS

Table 1 – Comparison of biological performances of the full-scale conventional activated sludge (CAS) and pilot-scale hollow-fibre (HF) and flat-sheet (FS) membrane bioreactor (MBR). The concentrations are given as ranges with the mean values ($n = 15$) presented in brackets, measured in the period of sampling campaign.

	CAS	HF MBR	FS MBR
TSS (reactor), mg/L	2450–2679 (2500)	1350–8390 (2180)	6740–25920 (13090)
VSS (reactor), mg/L	2130–2330 (2175)	1160–6800 (1810)	5320–20120 (10260)
TSS (effluent), mg/L	9–53 (20)	0.4–2.8 (1.5)	0.4–3.5 (2)
NH_4 (effluent), mg/L	7–43 (30)	0–12.8 (0.4)	0–44.6 (0.8)
COD (effluent), mg/L	58–159 (88)	6–163 (40.5)	6–122 (31)
BOD_5 (effluent), mg/L	7–52 (15)	1–10 (4)	1–8 (4)

(i.e., mean 2500 mg/L). This was a consequence of strong foaming experienced in the HF MBR during the sampling campaign that led to frequent sludge wasting, thus the TSS concentration inside this reactor was lower than the desired value. On the other side, FS MBR was operating at TSS concentration of up to 25.9 g/L. Nevertheless, HF MBR provided an effluent of the same quality as FS MBR in terms of ammonia and COD/BOD_5 removal (see Table 1).

3.2. *Occurrence of PhACs in the primary effluent*

Among the encountered PhACs, the highest concentrations in the primary effluent, i.e., influent of the full-scale CAS and pilot-scale MBR treatments were found for analgesic drugs ibuprofen (14.6–31.3 μg/L) and acetaminophen (7.1–11.4 μg/L), lipid regulators gemfibrozil (2.0–5.9 μg/L) and bezafibrate (1.9–29.8 μg/L), β-blocker atenolol (0.84–2.8 μg/L), antibiotic ofloxacin (0.89–31.7 μg/L), hypoglycaemic agent glibenclamide (0.12–15.9 μg/L) a diuretic hydrochlorothiazide (2.3–4.8 μg/L). Table 2 shows the MQLs and concentration ranges with their mean values for PhACs encountered in the primary effluent. The values of MQLs are slightly higher for some analgesic and anti-inflammatory drugs than the ones reported in literature (Carballa et al., 2004; Clara et al., 2005), whereas the lowest MQLs were observed for β-blockers and anti-histamines, similar to the previously reported results for the detection on HPLC–QqQ mass spectrometer (Lee et al., 2007; Gros et al, 2006).

Table 2 – Method quantification limits (MQLs) and concentration ranges in the primary effluent of the encountered pharmaceuticals, with their mean values ($n = 9$).

Compound	MQL, ng/L	c (Primary effluent), μg/L	
		Range	Mean
Analgesics and anti-inflammatory drugs			
Ibuprofen	115.3	14.6–31.3	21.7
Naproxen	65.1	0.13–0.67	0.463
Ketoprofen	139.0	0.70–1.2	1.08
Diclofenac	96.2	1.0–1.6	1.32
Mefenamic acid	5.3	0.80–1.2	1.07
Propyphenazone	4.8	0.046–0.097	0.065
Acetaminophen	75.3	7.1–11.4	9.90
Indomethacin	134.7	0.66–1.0	0.875
Anti-histamines			
Ranitidine	8.2	0.072–0.54	0.347
Loratidine	12.7	0.015–0.043	0.028
Famotidine	1.2	0.027–0.14	0.080
Anti-epileptic drug			
Carbamazepine	15.8	0.054–0.22	0.156
Psychiatric drugs			
Fluoxetine	32.5	0.12–2.3	0.573
Antibiotics			
Erythromycin	12.8	0.32–2.7	0.82
Sulfamethoxazole	1.7	0.25–1.3	0.093
Ofloxacin	21.5	0.89–31.7	10.5
Trimethoprim	5.5	0.15–0.43	0.204
ß-blockers			
Atenolol	8.2	0.84–2.8	2.0
Sotalol	9.2	0.17–0.85	0.509
Metoprolol	2.3	0.026–0.063	0.039
Propranolol	8.6	0.108–1.13	0.292
Hypoglycaemic agents			
Glibenclamide	25.8	0.12–15.9	9.89
Lipid regulator and cholesterol lowering statin drugs			
Gemfibrozil	11.5	2.0–5.9	3.08
Bezafibrate	15.6	1.9–29.8	14.9
Pravastatin	47.3	0.46–1.5	0.886
Diuretics			
Hydrochlorothiazide	17.3	2.3–4.8	2.74

3.3. *Removal of PhACs from the aqueous phase and sorption to sewage sludge*

Estimated removals of the encountered pharmaceutical residues from the aqueous phase during CAS, FS and HF MBR treatment were calculated as mean values with their relative standard deviations (R.S.D.) and presented in Table 3. Possible errors in estimation could have been made since only filtered sewage water was analysed, without considering the content of pharmaceuticals sorbed onto the particulate matter.

Almost complete removal of anti-inflammatory drugs ibuprofen and acetaminophen from the aqueous phase was observed regardless of the type of treatment applied. Also, incomplete removal of naproxen in CAS (70%) was enhanced to around 90% in HF and FS MBR. This is in accordance with previously published studies on MBR and CAS performance (Radjenović et al., 2007; Kimura et al., 2007; Quintana et al., 2005; Joss et al., 2006). Based on the literature data (Joss et al., 2006; Ternes et al., 2004; Jones et al., 2006) no sorption onto the sewage sludge would be expected for these two compounds. Considering the negatively charged state of analgesic drugs at the neutral pH of the primary clarifier and aerated tanks, electrostatic repulsion with the negatively charged groups of activated sludge would be expected. However, acetaminophen and ibuprofen were detected at relatively high concentrations in the primary, activated and treated sewage sludge (see Fig. 2). Nevertheless, adsorption of PhACs onto the sludge can be influenced by intermolecular forces such as Van der Waals forces. Kulshrestha et al. (2004) noted that oxytetracycline can sorb onto the sludge even in the form of zwitterion, which implies that hydrophobic interactions with sludge matrix can occur despite the presence of ionic charges and/or low octanol–water partition coefficient ($\log K_{OW}$) of trace organic pollutants.

Mefenamic acid, indomethacin and diclofenac were not eliminated during CAS treatment. The two MBRs achieved only partial removals of mefenamic acid (35–41%) and indomethacin (~40%), whereas the elimination of diclofenac was significantly enhanced to around 65%. For mefenamic acid the removal in CAS treatment reported in literature varies between 29 and 70%, whereas MBR treatment operating at prolonged long SRT (>2 months) can be expected to enhance its elimination (Radjenović et al., 2007; Kimura et al., 2007). The biodegradability of indomethacin was estimated to be rather low in batch experiments with CAS and MBR sludge (Joss et al., 2006). As far as the biodegradability of diclofenac is

Table 3 – Mean removals ($n = 9$)of selected pharmaceuticals from the aqueous phase, with their relative standards deviations (R.S.D.s) in CAS, FS and HF MBRs treatments in wastewater treatment plant (WWTP) Terrassa.

Compound	Elimination from the aqueous phase (%)		
	CAS	FS MBR	HF MBR
Analgesics and anti-inflammatory drugs			
Ibuprofen	99.1 ± 1.8	99.2 ± 1.8	99.5 ± 1.6
Naproxen	71.8 ± 14.3	90.7 ± 3.2	91.6 ± 8.1
Ketoprofen	54.6 ± 19.7	43.9 ± 27.7	44.0 ± 20.6
Diclofenac	21.8 ± 28.5	65.8 ± 13.1	62.6 ± 18.3
Mefenamic acid	n.e.	40.5 ± 23.7	35.5 ± 28.3
Propyphenazone	37.6 ± 10.8	64.5 ± 16.0	60.7 ± 18.7
Acetaminophen	99.9 ± 0.1)	99.8 ± 0.2	99.9 ± 0.1
Indomethacin	n.e.	41.4 ± 20.6	39.7 ± 26.2
Anti-histamines			
Ranitidine	24.7 ± 44.9	44.2 ± 29.6	29.5 ± 47.9
Loratidine	15.0 ± 43.9	n.e.	33.5 ± 52.2
Famotidine	60.1 ± 22.3	64.6 ± 24.5	47.4 ± 63.0
Anti-epileptic drug			
Carbamazepine	n.e.	n.e.	n.e.
Psychiatric drugs			
Fluoxetine	33.1 ± 28.9	98.0 ± 1.9	98.0 ± 1.6
Antibiotics			
Erythromycin	35.4 ± 50.5	43.0 ± 51.5	25.2 ± 108.9
Sulfamethoxazole	73.8 ± 12.7	80.8 ± 12.2	78.3 ± 13.9
Ofloxacin	75.8 ± 13.8	95.2 ± 2.8	91.3 ± 10.8
Trimethoprim	40.4 ± 25.4	66.7 ± 20.6	47.5 ± 22.5
ß-blockers			
Atenolol	61.2 ± 18.6	76.7 ± 12.6	69.5 ± 12.5
Sotalol	21.4 ± 31.5	53.1 ± 24.1	30.4 ± 25.3
Metoprolol	24.7 ± 44.9	44.2 ± 29.6	29.5 ± 47.9
Propranolol	58.8 ± 24.5	77.6 ± 12.2	65.5 ± 22.4
Hypoglycaemic agents			
Glibenclamide	46.1 ± 40.8	95.6 ± 4.4	82.2 ± 28.6
Lipid regulator and cholesterol lowering statin drugs			
Gemfibrozil	n.e.	42.2 ± 36.7	32.5 ± 49.3
Bezafibrate	80.8 ± 20.9	90.3 ± 10.1	88.2 ± 15.3
Pravastatin	59.4 ± 16.2	86.1 ± 9.1	83.1 ± 12.5
Diuretics			
Hydrochlorothiazide	n.e.	n.e.	n.e.

n.e.: no elimination, defined for the mean elimination efficiency less than 10%.

concerned, no biotic transformation was observed in batch experiments performed by various authors (Quintana et al., 2005; Joss et al., 2006), whereas Urase and Kikuta, 2005 reported slow biodegradation. There is a great discrepancy in the literature data for the removal of diclofenac in WWTPs (i.e., 0–69%) (Ternes, 1998; Radjenović et al., 2007; Lindqvist et al., 2005). The differences in sludge age, as well as the composition of sludge and wastewater are probably the reason for such results. On the other side, Kimura et al. (2007) reported an increased adsorption capacity of MBR sludge for diclofenac when compared to the sludge collected from WWTP, which was assumed to be due to greater available surface area. In our study the K_d was estimated to be somewhat higher for the sludge from the MBRs, although it is probably primarily removed by biodegradation mechanism. The highest solid phase concentrations of diclofenac were detected in the primary sludge (see Fig. 2).

Propyphenazone exhibited a rather poor removal in the conventional treatment that was meliorated in the MBRs (i.e., 37.6 and 60.7–64.5%, respectively). In the previously conducted experiment with the laboratory-scale MBR, around 60% elimination was observed (Radjenović et al., 2007). Ketoprofen was attenuated up to 55% in the CAS process whereas in the MBR this percentage was slightly lower (44%). The results of Quintana et al. (2005) from the batch trials with activated sludge indicated that ketoprofen could serve as a sole substrate for the microbial growth, which could imply its high biodegradability. On the other side, slow biodegradation of ketoprofen was reported in other laboratory experiments (Joss et al., 2006; Urase and Kikuta, 2005). Comparative studies of MBR and CAS (Radjenović et al., 2007; Kimura et al., 2007) showed that the elimination of this drug is enhanced in the MBR treatment, probably due to better adaptation of microorganisms.

The β-blockers atenolol and propranolol were removed in WWTP Terrassa with around 60% efficiency, whereas sotalol and metoprolol meagrely passed the CAS treatment untransformed. While CAS and HF MBR exhibited similar performances, FS MBR managed to slightly improve the elimination of these compounds (i.e., 44–78%). The reported removals in literature of β-blockers atenolol, metoprolol, propranolol and sotalol in WWTPs range from <10 to 46, <10 to 83, 0 to 96 and 15 to 36% (Castiglioni et al., 2006; Ternes, 1998; Radjenović et al., 2007; Lee et al., 2007; Paxéus, 2004; Alder et al., 2005). Their removal in WWTP is most probably achieved through stereoselective biological degradation (Nikolai et al., 2006; Maurer et al., 2007). Maurer et al. (2007) observed faster biodegradation of β-blockers with MBR sludge, whereas sorption was identified as possible removal pathway only for propranolol.

As far as elimination of antibiotics from the aqueous phase is considered, the worst performance of the two MBRs and CAS was observed for the elimination of erythromycin (see Table 3). The poor removal of erythromycin has been reported for CAS (Radjenović et al., 2007; Göbel et al., 2007), whereas laboratory-scale MBR was capable of 67% elimination (Radjenović et al., 2007). However, pilot-scale MBRs did not show any significant enhancement in its removal. Trimethoprim was removed during the conventional treatment with around 40% efficiency, whereas in the FS and HF MBR this percentage was 66.7 and 47.5%, respectively. Trimethoprim was considered recalcitrant to the activated sludge bacteria (Lindberg et al., 2006), although its degradation by the slow-growing nitrifying bacteria was observed (Pérez et al., 2005). The removals of ofloxacin and sulfamethoxazole achieved in CAS were around 75%, whereas in the FS and HF MBR it was more complete (80–90%). The low removal of sulfamethoxazole have been previously reported by several authors, possibly due to the cleavage of its human metabolite N^4-acetylsulfamethoxazole in WWTPs (Radjenović et al., 2007; Göbel et al., 2005; Lindberg et al., 2006). The reported removals of ofloxacin vary from 24 to 86% (Radjenović et al.,

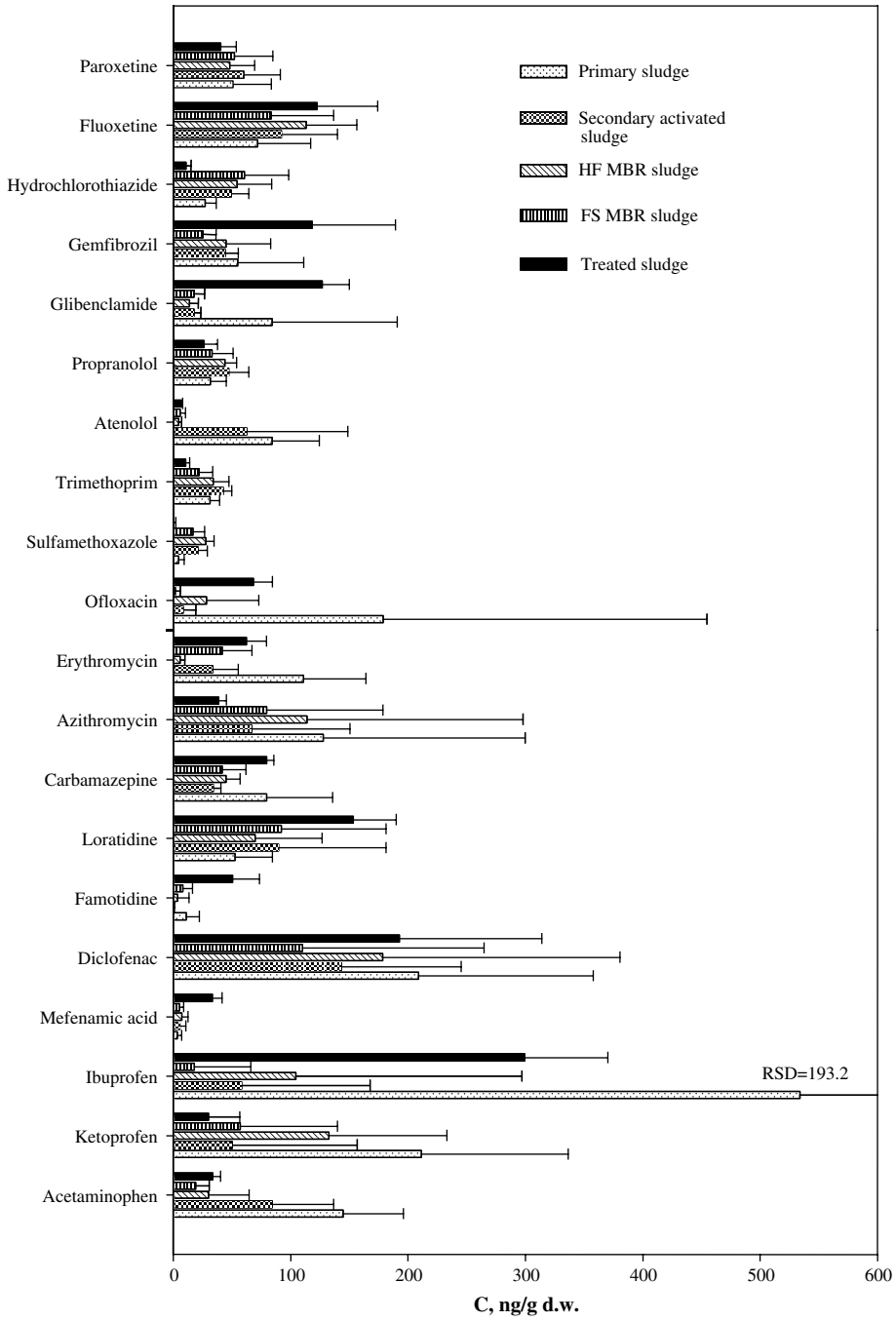

Fig. 2 – Mean concentrations of the PhACs encountered in the primary, secondary activated, FS and HF MBR and treated sludge in WWTP Terrassa, with their R.S.D.s.

2007; Lindberg et al., 2006). Also, antibiotics could be expected to sorb onto negatively charged surface of sewage sludge through ionic interactions. Azithromycin, erythromycin, sulfamethoxazole, ofloxacin and trimethoprim were encountered in the sludge at low ng/g concentration level (see Fig. 2), whereas the concentrations measured are similar to the ones reported in a study of Göbel et al. (2005).

The anti-epileptic drug carbamazepine and diuretic hydrochlorothiazide by-passed all three treatments investigated, frequently with the treated effluent concentrations higher than the influent ones. The poor removal of carbamazepine in both CAS and MBR systems were previously observed by many researchers (Castiglioni et al., 2006; Radjenović et al., 2007; Clara et al., 2005). They could be a consequence of conjugation/deconjugation processes that occur during the activated sludge treatment. For example, Miao et al. (2005) found that the aqueous fraction of hydroxylated human metabolites of carbamazepine augmented during the wastewater treatment, since their conjugated forms present in the influent are cleaved back into the free form by microbial

activity. Although previously observed eliminations of hydrochlorothiazide in MBR were around 66% (Radjenović et al., 2007) and in CAS from 0 to 77% (Castiglioni et al., 2006; Radjenović et al., 2007), in this study it was not removed at all.

Among the lipid regulators and cholesterol lowering statin drugs, gemfibrozil was not removed at all during CAS treatment, while its elimination in MBRs was slightly improved to around 30–40%. Bezafibrate had a very satisfactory removal in CAS (i.e., 80%), while the pilot-scale reactors achieved a 90% removal of this drug. The degradation of pravastatin was also enhanced from 60% in CAS to around 85% in MBRs. For gemfibrozil and bezafibrate very high and uniform removal was observed for a laboratory-scale MBR (Radjenović et al., 2007). Clara et al. (2005) reported over 90% removal of bezafibrate in WWTP.

The removal of anti-histamines ranitidine, famotidine and loratidine in the conventional treatment was rather poor (i.e., 15.0–60.1%) and unstable. FS MBR attained somewhat improved elimination of ranitidine, while for loratidine its performance was worsened. Strong variance in the aqueous concentrations of loratidine such as higher effluent than influent concentrations could be produced by adsorption/desorption processes since it was detected in the sewage sludge samples (see Fig. 2). The removals of hypoglycaemic drug glibenclamide and psychiatric drug fluoxetine were incomplete in CAS treatment (46.1 and 33%%, respectively), while the MBRs significantly enhanced their elimination to around 82–98.

3.4. Estimation of K_d coefficients

Based on the measured concentrations of pharmaceuticals in the sludge and in the corresponding supernatants of each grab sample, K_d coefficients were calculated by the formula:

$$K_{d,\ \mathrm{sludge-wastewater}} = \frac{C}{C_{i,\mathrm{dissolved}}} \times 10^3,$$

where K_d is expressed in L/kg, $C_{i,\mathrm{sorbed}}$ is a concentration of pharmaceutical measured in the solid phase (ng/g d.w.) and $C_{i,\mathrm{dissolved}}$ is the one measured in the aqueous (i.e., supernatant) phase (ng/L). The K_d values obtained for the primary, secondary activated, HF MBR and FS MBR sludge are presented in Table 4. It should be stressed out that these K_d values are given only as rough estimates, considering a possible non-equilibrium state in the samples and the inhomogeneity of sewage sludge. Also, neither for the aqueous nor for the solid phase conjugated forms or metabolites were included in the analysis.

From the values calculated for K_d coefficients in Table 4 it can be concluded that for most of the encountered pharmaceuticals removal by sorption will be a minor removal pathway in the overall mass balance of wastewater treatment (i.e., $K_d < 500$ L/kg) (Ternes et al., 2004). For anti-inflammatory drugs the calculated K_d values for anti-inflammatory drugs were relatively low, and only in the case of mefenamic acid sorption to the sludge could be a relevant removal pathway.

Table 4 – Summary of mean values ($n = 7$) for sorption coefficient (K_d) with their R.S.D.s calculated from the sludge and supernatant concentrations, and comparison with literature values presented as mean or ranges.

Compound	Calculated K_d (L/kg)				Literature values of K_d (L/kg)		
	Primary	Second. act.	FS MBR	HF MBR	Primary	Second. act.	Digested
Ibuprofen	9.5 ± 3.1	0.0	0.0	n.d.	[1] < 20[m]	[1] 7.1 ± 2.0[m] [3] 72–1265[m] [4] 453, 2.02[p], 251[m] [5] 453.8[p]	[2] 20.0–44.3[m]
Ketoprofen	226 ± 180	16 ± 39	72 ± 111	165 ± 272		[3] 13–444[p] [5] 217.2[p]	[2] 10.8–36.5[m]
Diclofenac	194 ± 134	118 ± 95	197 ± 255	321 ± 402	[1] 459 ± 32[m]	[1] 16 ± 3 [m] [3] 16–701 [m] [5] 0.72[p]	[2] 36.9–72.4 [m]
Acetaminophen	6.7 ± 6.2	1160 ± 692	126 ± 68	238 ± 255		[4] 0.4, 0.43[p]	
Mefenamic acid	294 ± 379	434 ± 304	495 ± 290	537 ± 507		[5] 18,916.98[p]	
Gemfibrozil	23 ± 23	19.3 ± 9.3	18.7 ± 4.8	27.8 ± 11.1		[3] 75–1106[m]	
Carbamazepine	314 ± 205	135 ± 39	194 ± 94	164 ± 49	[1] < 20[m]	[1] 1.2 ± 0.5[m] [3] 28–66[m] [5] 25.5[p]	[2] 20.2–56.4[m]
Loratidine	2336 ± 851	3321 ± 3345	3058 ± 1974	2214 ± 958			
Erythromycin	309 ± 272	74 ± 54	183 ± 133	11.4 ± 6.4		[5] 164.8[p]	
Trimethoprim	427 ± 238	253 ± 37	225 ± 87	320 ± 117		[6] 157–375[m]	
Atenolol	95 ± 60	64 ± 88	5.9 ± 4.4	40 ± 50		[5] 0.21[p], [7] < 40 L/kg$^{m}_{COD}$	
Propranolol	641 ± 478	366 ± 138	298 ± 165	375 ± 111		[7] 320 ± 58 L/kg$^{m}_{COD}$	
Hydrochloroth.	25.8 ± 14.4	20.2 ± 3.4	23.5 ± 12.6	22.3 ± 12.5		[4] 0.1, 0.0555[p]	
Glibenclamide	282 ± 307	239 ± 146	315 ± 169	142 ± 81			
Sulfamethoxaz.	3.2 ± 4.5	77 ± 60	60 ± 49	63 ± 42		[6] 114–400[m]	[2] 5.8–61.5[m]

m: measured value, p: predicted value.
[1] Ternes et al., 2004; [2] Carballa et al., 2008; [3] Urase and Kikuta, 2005; [4] Stuer-Lauridsen et al., 2000; [5] Jones et al., 2002; [6] Göbel et al., 2005; [7] Maurer et al., 2007.

Moreover, Jones et al. (2006) indicated that sorption could be a possible elimination pathway of this pharmaceutical in a WWTP. The extremely high value for K_d of acetaminophen for the secondary activated sludge (i.e., $K_d = 1160.1 \pm 691.8$ L/kg) can rather be assigned to a very fast biodegradation that outcompeted the sorption process and led to very low concentrations measured in the aqueous phase, than to the high sorption potential of this sludge. Among β-blockers the K_d was estimated to be relatively high only for propranolol in the primary sludge (i.e., 640.7 ± 478.0 L/kg), which could be interpreted by the lipophilic interactions with sludge particles. As far as antibiotics are concerned, for trimethoprim and erythromycin higher sorption potential was estimated for the primary sludge, whereas for sulfamethoxazole very low K_d values were obtained. Also, estimated K_d value of carbamazepine for the primary sludge (i.e., 314.2 ± 204.7 L/kg) might indicate that this sludge will be more enriched with carbamazepine than the biologically active one, although the results of EU POSEIDON project (http://poseidon.bafg.de) indicated that carbamazepine does not adsorb onto the sludge. From the investigated PhACs, anti-histaminic drug loratidine was the only compound for which sorption can be considered as a significant removal pathway in WWTPs, since the K_d coefficients were calculated to be extremely high for all types of sewage sludge analysed (see Table 4).

Generally all drugs encountered in the sewage sludge exhibited the same tendency of greater enrichment in the primary sludge when compared to the activated sludge. For several pharmaceuticals, the lowest concentrations were observed for the FS MBR sludge (e.g., paroxetine, fluoxetine, gemfibrozil, propranolol, atenolol, trimethoprim, acetaminophen, ketoprofen, ibuprofen, diclofenac) that was operating at prolonged SRT and high TSS concentration. This pattern of lower FS MBR sludge concentrations repeated for most of other pharmaceuticals encountered, and it could be explained as a consequence of either:

1) lower sorption potential of FS MBR sludge, which is generally not in accordance with the calculated K_d values from Table 4, and/or
2) higher biodegradation potential of FS MBR sludge, thus leaving less amount of soluble compound available for sorption onto the sludge.

Biodegradation of PhACs is influenced by desorption of pharmaceutical from the sludge matrix and by microbial activity, and the final outcome will depend on the balance between these two processes. Vice versa, the adsorption/desorption processes occurring under real conditions of WWTP will depend on the combination of different degradation rates in solid and aqueous phase. As stressed out at the beginning of Section 3, the MBR equipped with HF membranes had to be subjected to frequent sludge wasting due to the problems with foaming and bulking. This possibly influenced the biodegradation capacity of HF MBR sludge, which led to the higher concentrations of PhACs measured in the effluent and sludge produced in this pilot-scale reactor. As can be seen from Table 3 for some compounds (e.g., anti-histaminics, β-blockers, trimethoprim) significantly lower removals were obtained in the HF MBR than in the FS MBR reactor, which was probably a consequence of the lower operating SRT in the HF MBR.

The K_d values of treated sludge could not be estimated, but relatively high concentrations of ibuprofen, diclofenac, loratidine, glibenclamide, fluoxetine and gemfibrozil were encountered (see Fig. 2). Moreover, the encountered PhACs were found to be quite stable under methanogenic anaerobic conditions in the sludge digesters, since all compounds detected in the primary sludge were ultimately present in the dehydrated and anaerobically digested biosolids.

Table 5 – Output loads of the encountered pharmaceuticals in the treated effluent and sludge of WWTP Terrassa, presented as ranges, with their mean values in brackets ($n = 9$ for the aqueous and $n = 7$ for the solid phase).

Compound	Effluent load (g/day)	Treated sludge (g/day)
Analgesics and anti-inflammatory drugs		
Ibuprofen	bMDL-71.7 (bMDL)	7.0–15.2 (12.1)
Naproxen	1.0–12.0 (5.1)	n.d.
Ketoprofen	7.4 –28.1 (23.3)	bMDL-2.7 (bMQL)
Diclofenac	15.0–63.6 (46.5)	bMQL-17.0 (6.4)
Mefenamic acid	30.9–54.1 (48.6)	0.8–1.6 (1.5)
Propyphenazone	1.3–2.1 (1.6)	n.d.
Acetaminophen	0.3–2.9 (0.7)	0.9–1.7 (1.4)
Indomethacin	25.5–43.4 (40.1)	n.d.
Anti-histamines		
Ranitidine	4.4–9.1 (8.0)	n.d.
Loratidine	0.5–1.2 (0.9)	4.2–8.1 (5.7)
Famotidine	0.6–1.4 (1.0)	bMQL-3.2 (2.0)
Anti-epileptic drug		
Carbamazepine	2.7–27.6 (7.1)	2.9–3.6 (3.1)
Psychiatric drugs		
Fluoxetine	4.2–15.8 (13.0)	3.0–7.8 (4.2)
Paroxetine	n.d.	1.1–2.3 (1.5)
Antibiotics		
Erythromycin	14.1–37.9 (13.7)	1.5–3.1 (2.8)
Azythromycin	n.q.	1.3–1.9 (1.6)
Sulfamethoxazole	0.8–20.0 (13.6)	n.d.
Ofloxacin	2.1–267.2 (49.4)	1.8–3.5 (2.8)
Trimethoprim	1.9–5.7 (5.4)	bMQL-0.5 (0.4)
β-blockers		
Atenolol	2.2–50.8 (41.1)	bMQL-0.3 (0.3)
Sotalol	1.9–24.9 (19.3)	bMQL-1.0 (0.7)
Metoprolol	0.2–1.7 (1.0)	n.d.
Propranolol	1.3–4.7 (3.9)	0.6–1.7 (1.0)
Hypoglycaemic agents		
Glibenclamide	1.3–718.6 (203.9)	3.8–6.3 (5.0)
Lipid regulator and cholesterol lowering statin drugs		
Gemfibrozil	78.1–225.7 (183.2)	bMQL-7.4 (5.4)
Bezafibrate	27.4–48.1 (43.2)	1.3–3.3 (1.7)
Pravastatin	10.5–19.1 (13.2)	n.d.
Diuretics		
Hydrochlorothiazide	76.6–121.6 (106.2)	0.3–0.7 (0.4)

n.d.: not detected, n.q.: not quantifiable.

3.5. *Overall mass output loads*

In Table 5 are reported output aqueous and solid phase mass loads of WWTP Terrassa. Output mass loads were derived from the average daily flow of wastewater and average monthly production of treated sludge (42,000 m^3/day and 1200 t/month, respectively). For most of the pharmaceutical residues the portion wasted with the treated sludge into the environment was negligible compared to the aqueous fraction. Only in some cases the contribution of sludge load to the overall environmental load of WWTP could be more significant. For example, the output daily mass loads of ibuprofen, diclofenac and fluoxetine in the treated sludge could reach up to around 20–50% of their loads in the treated sewage leaving the plant. Nevertheless, considering that the treated sludge from WWTP Terrassa is directly employed as agricultural fertilizer, it represents a source of continuous contamination of terrestrial environment by PhACs.

4. Conclusions

The results have demonstrated that MBR technology generally outperforms the CAS treatment in removing PhACs from wastewater (see Figure S1, Supplementary data).

The elimination of some compounds that showed recalcitrant for the CAS treatment such as mefenamic acid, indomethacin, diclofenac, and gemfibrozil was significantly improved in the MBRs up to around 40, 40, 65, 32–42%. Based on the estimated K_ds, sorption was found to be a minor removal pathway for most of the investigated PhACs, whereas it could have a more significant contribution in the case of propranolol, mefenamic acid and particularly loratidine (mean $K_d = 2214–3321$ L/kg). Nevertheless, the measured concentrations in the solid phase indicate that sewage sludge will be enriched not only in hydrophobic compounds, but also in compounds like negatively charged analgesic drugs and positively charged β-blockers. Furthermore, PhACs tended to sorb less onto the aged MBR sludge than the primary and secondary activated sludge, possibly as a consequence of its higher biodegradation potential.

From the aspect of the excess sludge produced, advanced MBR technology would be attractive concept not only in terms of the cost reduction of sludge treatment due to its lowered production, but also because it diminishes the environmental impact of wastewater treatment since the MBR sludge is less contaminated with PhACs than the sludge produced during the conventional treatment. The amount of PhACs sorbed onto sewage sludge may increase the environmental risk of these micropollutants, since they can become bioavailable when conditions for desorption are created.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.watres.2008.11.043.

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