



## Determination of sorption of seventy five pharmaceuticals in sewage sludge

Hörsing, Maritha; Ledin, Anna; Grabic, Roman; Fick, Jerker; Tysklind, Mats; Jansen, Jes la Cour; Andersen, Henrik Rasmus

*Published in:*  
Water Research

*Link to article, DOI:*  
[10.1016/j.watres.2011.05.033](https://doi.org/10.1016/j.watres.2011.05.033)

*Publication date:*  
2011

[Link back to DTU Orbit](#)

### *Citation (APA):*

Hörsing, M., Ledin, A., Grabic, R., Fick, J., Tysklind, M., Jansen, J. L. C., & Andersen, H. R. (2011). Determination of sorption of seventy five pharmaceuticals in sewage sludge. *Water Research*, 45(15), 4470-4482. <https://doi.org/10.1016/j.watres.2011.05.033>

---

### General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Please cite this article as: Hörsing, M., Ledin, A., Grabic, R., Fick, J., Tysklind, M., la Cour Jansen, J., Andersen, H.R. Determination of sorption of seventy five pharmaceuticals in sewage sludge, Water Research (2011), doi: 10.1016/j.watres.2011.05.033  
Water research 45 (2011) 4470-4482

## **Determination of sorption coefficients for seventy five pharmaceuticals in sewage sludge**

Maritha Hörsing<sup>a1\*</sup>, Anna Ledin<sup>a,1</sup>, Roman Grabic<sup>b,2</sup>, Jerker Fick<sup>b</sup>, Mats Tysklind<sup>b</sup>, Jes la Cour Jansen<sup>c</sup> and Henrik R. Andersen<sup>a</sup>

<sup>a</sup> Department of Environmental Engineering, Technical University of Denmark, B113, DK-2800 Kgs Lyngby, Denmark

<sup>b</sup> Department of Chemistry, Umeå University, SE-901 87 Umeå, Sweden

<sup>c</sup> Water and Environmental Engineering at Department of Chemical Engineering, Lund University, P.O. Box 124, SE-221 00 Lund, Sweden

\* Corresponding author. E-mail address [Maritha.Horsing@chemeng.lth.se](mailto:Maritha.Horsing@chemeng.lth.se) (M. Hörsing)

Phone number: +46462228212

---

Present address: <sup>1</sup> Water and Environmental Engineering at Department of Chemical Engineering, Lund University, P.O. Box 124, SE-221 00 Lund, Sweden

<sup>2</sup> University of South Bohemia in Ceske Budejovice, Faculty of Fisheries and Protection of Waters, South Bohemian Research Center of Aquaculture and Biodiversity of Hydrocenoses, Zátíší 728/II CZ 389 25 Vodňany, Czech Republic.

## ABSTRACT

Sorption of 75 active pharmaceutical ingredients (APIs) to three different types of sludge (primary sludge, secondary sludge with short and long sludge age respectively) was investigated. To obtain the sorption isotherms batch studies with the APIs mixture were performed in four nominal concentrations to water containing 1 g of sludge. The range of APIs concentrations was between  $\text{ng L}^{-1}$  to  $\mu\text{g L}^{-1}$  which is found in the wastewater effluent. Isotherms were obtained for approximately 45 of the APIs, providing distribution coefficients for linear ( $K_d$ ), Freundlich ( $K_f$ ) and Langmuir ( $K_L$ ) isotherms.  $K_d$ ,  $K_f$  and  $K_L$  ranging between  $71\text{-}3.8\times 10^4$ ,  $1.1\times 10^{-5}\text{-}61$  and  $9.2\times 10^{-6}\text{-}1.1\times 10^{-3}\text{L g}^{-1}$ , respectively. The obtained coefficients were applied to estimate the fraction of API in the water phase (see Abstract Graphic). For 37 of the 75 the APIs predicted presence in the liquid phase was estimated to  $> 80\%$ . 24 APIs were estimated to be present in the liquid phase between 20 - 80 %, and 14 APIs were found to have  $< 20\%$  presence in the liquid phase, i.e. high affinity towards sludge. Furthermore, the effect of pH at values 6, 7 and 8 was evaluated using one way ANOVA-test. A significant difference in  $K_d$ s due to pH changes was found for 6 of the APIs (variation 10-20%).

### *Keywords:*

Distribution coefficients ( $K_d$ )

Pharmaceuticals

Sorption isotherms

Sludge

Wastewater treatment plant (WWTP)

NOMENCLATURE See Table S1, supplementary data.

## **1. Introduction**

The presence of human and veterinary pharmaceuticals in the environment has been recognized as a potential environmental threat (Ternes et al., 2002). After their use, pharmaceuticals are either excreted unchanged or as metabolites via urine and faeces or are washed off and subsequently reach a wastewater treatment plant (WWTP) via the sewage system. The active pharmaceutical ingredients (APIs) are designed to have pharmacological effects at low concentrations, which have led to concerns regarding their distribution in aquatic environments and potential non-wanted biological effects in different organisms.

APIs have been found in several environmental compartments such as waste, surface and ground waters (Calisto and Esteves, 2009; Fick et al., 2009; Gabet-Giraud et al., 2010; Lindberg et al., 2010), as well as in sludge and sediments (Ternes et al., 2002; Andersen et al., 2003). Sorption of APIs to sludge, during wastewater treatment processes in which sludge is separated from the wastewater stream may be an important factor for the removal of non-biodegradable pharmaceuticals from WWTPs.

Solid matter is separated from wastewater during treatment. After the separation of incoming particles, the remaining organic material is generally biologically removed in an activated sludge system. After treatment, sludge is separated from the treated water by a second sedimentation step. If extended nitrogen removal is required, biological nitrogen removal is implemented. In colder regions, nitrogen removal is not needed and only biological oxygen demand (BOD) is removed. Thus the sludge age can be shorter. The pH of wastewater during the treatment process is typically close to 7, within the range of 6.0-8.0 which likely results in minor property changes. Surveys in which  $pK_a$  (acid- ionization constant) have been determined, reported  $pK_a$  values of

5.3 and 9.5 for dissolved organic matter (DOM) in the sludge (Wang et al., 1998) and 6.1 for sludge particles (Wang et al., 2000). For the APIs however, the pH may change the effect of sorption, especially for APIs with  $pK_a$  or  $pK_b$  (base-ionization constant) within pH range of 6-8. The effect of pH on the sorption of APIs has been discussed by other studies (Ternes et al., 2004; Jones et al., 2006; Carballa et al., 2008) but without firm conclusions. However, studies have shown that for acidic compounds, such as Ibuprofen and Diclofenac the distribution between water and solid phase is affected by pH changes. At pH 4, which is below the pH values found in WWTP, the distribution coefficient ( $K_d$ ) increased compared to the  $K_d$  obtained at the pH 7 (Urase and Kikuta, 2005).  $K_d$  may be experimentally determined or calculated from the octanol-water distribution coefficient ( $K_{ow}$ ). Stuer-Lauridsen et al., (2000) provides thoroughly described estimations of  $K_d$  based on  $K_{ow}$  where  $pK_a$  and the fraction of organic carbon are considered. Also Radjenović et al., (2009) calculated  $K_d$  values for APIs ranging between 0.4-16 859 L kg<sup>-1</sup>. Experimental determination of  $K_d$  may be conducted in continuous or batch experiments. In order to obtain  $K_d$  values during continuous experiments several different parameters need to be known, such as the order of biodegradation, rate of sorption and rate of desorption. In batch experiments, biodegradation is eliminated by adding sodium azide or some other toxic substance, however the ion strength changes which may affect the APIs sorption. A third option is to freeze dry the sludge gently, this will preserve the tertiary structure of the sludge. Thereafter heat the sludge to 103°C in order to sterilize the sludge. This procedure was used by Andersen et al, (2005). In a continuous experiment  $K_d$  values were determined for antiepileptic, antiphlogistic, antibiotic, estrogens, contrast medium. (Carballa et al., 2008) However, these studies cover a rather low number of the APIs available on the market and the experimentally obtained  $K_d$  values ranges from negligibly to log  $K_d$  4.43 (Carballa et al., 2008).

The objective of this study was to experimentally determine  $K_d$  values for 75 selected APIs. The  $K_d$  values were obtained from sorption isotherms in three different types of sludge, primary sludge, and secondary sludge with long and short sludge age, respectively. The obtained  $K_d$  values were used to estimate the removal of APIs by sorption to sludge in WWTPs. Furthermore, the influence on sorption caused by normal pH variations (pH 6-8) found in WWTPs was investigated. This study was based on a straightforward approach using fixed nominal concentrations of each API in water mixed with a known amount of sterilized sludge in order to determine the sorption distribution coefficients.

## **2. Materials and methods**

### **2.1. Sludge**

Sludge was collected from three WWTPs which were representative of WWTPs in Sweden and other industrialised countries for treatment of municipal wastewater.

Primary sludge was collected from Avedøre WWTP, which treats wastewater corresponding to 275 000 person equivalents (PE) from 10 municipalities in the southern part of Greater Copenhagen, Denmark. It was chosen since it was possible to collect primary sludge without contamination from internal recirculation of secondary sludge. Suspended solids (SS) and volatile suspended solid (VSS) were 43 and 35 g L<sup>-1</sup>, respectively. Secondary sludge with a long sludge age and nitrification was collected from Klagshamn WWTP. This plant treats municipal wastewater corresponding to about 60 000 PE from the southern part of Malmö City, Sweden and a nearby municipality. The plant uses primary precipitation and nitrification in activated sludge (sludge content 3 g L<sup>-1</sup>). SS and VSS were 4 and 3 g L<sup>-1</sup>, respectively. Denitrification took place in a post-denitrifying, moving bed biofilm reactor. Biological sludge with short sludge

age was collected from Sjölanda WWTP. This is typical for plants in the north and in many inland cities in Sweden. The plant treats wastewater corresponding to approximately 315 000 PE from Malmö city, Sweden and surrounding municipalities. The plant was operated with combined primary and simultaneous precipitations. Removal of organic matter took place in a highly loaded activated sludge plant where sludge was collected (sludge content  $6 \text{ g L}^{-1}$ ). SS and VSS were  $8$  and  $6 \text{ g L}^{-1}$ , respectively. Nitrification took place in a fixed bed trickling filter and denitrification in a moving bed biofilm reactor.

Each portion of sludge was washed twice with tap water, decanted in order to remove water soluble constituents and frozen at  $-18^\circ\text{C}$  after sample collection. The sludge was gently freeze dried in order to preserve the structure and sterilized by heating at  $103^\circ\text{C}$  for minimum 3 h.

## 2.2. Experimental design

Nominal concentrations of the 75 APIs (see Table 1) included in the experiments were chosen based on the solubility, limit of quantification (LOQ) and linear range of the analytical method (Grabic et al., unpublished data; Fick et al., 2009). Volatilisation was considered and Henry's Law constant ( $K_H$ ; Table S2 supplementary data) was calculated EPI Suite software HenryWin v3.10. All APIs had a  $K_H < 9 \times 10^{-7} \text{ Atm}\cdot\text{m}^3\text{mol}^{-1}$ , therefore volatilisation would be insignificant, since only compounds with  $K_H > 3 \times 10^{-3}$  are considered to be volatile (Ternes and Joss, 2008). The aim was to get four API equilibriums with water concentration ( $C_w$ ;  $\text{g L}^{-1}$ ) in the range of 90 % of the starting concentration ( $C_0$ ;  $\text{g L}^{-1}$ ) and the LOQ. The water solubility should be larger than the starting concentration;  $C_w \ll C_0$ ;  $\text{LOQ} < C_w$ . Sludge concentration in the experiments was  $1 \text{ g/L}$ , with exception for one sludge where it was increased to  $10$  and  $50 \text{ g L}^{-1}$  (Table 1). The  $1 \text{ g L}^{-1}$  sludge density was about 5- to 10-fold more than the realistic sludge production that can occur in a WWTP which ensures that APIs that adsorb significantly to sludge in a real

WWTP also would be removed significantly from the water phase in the batch experiment which was the basis for determining a  $K_d$ -value, while low sorbing APIs  $K_d$ s will not be determined

A stock solution including the 75 API of  $0.1\text{g}\times\text{L}^{-1}$  was prepared in MeOH from which the four MeOH stock solutions of 0.4, 2.0, 10.0 and  $50.0\text{ ng }\mu\text{L}^{-1}$  were prepared, respectively. These stock solutions suited the design (Table 1) and were theoretically determined to fit the criteria for the present study. Böhm and During (2010) showed that there was no significant difference between determination of the distribution coefficient  $K_{\text{DOC}}$  for single compounds or mixtures.

Artificial media was used in the study for the water phase (Berg and Nyholm, 1996), modified as described by Andersen et al. (2005). Fundamentally, the artificial sewage was a phosphate-buffered mineral media containing  $\text{Ca}^{2+}$ ,  $\text{K}^+$ ,  $\text{Mg}^{2+}$ ,  $\text{Na}^+$ ,  $\text{Cl}^-$  and  $\text{SO}_4^{2-}$ .

Sludge was added to 1 L borosilicate glass bottles. In order to inhibit microbial growth oxygen was removed by purging with  $\text{N}_{2(g)}$  for 1 min and  $\text{Na}_2\text{SO}_3$  was added to a final concentration of  $50\text{ mg L}^{-1}$  to each bottle. The bottles were left on stirring in the dark at  $+4\text{ }^\circ\text{C}$  in order for the sludge to rehydrate. After 12 h,  $200\text{ }\mu\text{L}$  of the API stock solutions of 0.4, 2.0, 10.0 or  $50.0\text{ ng }\mu\text{L}^{-1}$  were added to the bottles using a Hamilton syringe giving the final concentrations presented in Table 1. The bottles were left on stirring in the dark at  $+4\text{ }^\circ\text{C}$  for 12 h. Experiments were performed at three pH values (Table 1). The pH 7.0 was chosen based on a typical pH in WWTPs and pH 6.0 and 8.0 were based on low and high values from WWTPs. Control batches without APIs in the sludge and standard APIs solutions were prepared (Table 1).



**Table 1.** The experimental set up, including API concentrations, pH sludge concentration and the number of bottles per blank/zero sludge/sludge. From each bottle triplicate solid phase extractions (SPE) were made.

	API conc. ( $\mu\text{g}\times\text{L}^{-1}$ )				pH	Sludge conc. ( $\text{g}\times\text{L}^{-1}$ )	No. of bottles
	0	0.08	0.4	2			
Blank for each sludge	0				7	1	3
No sludge	0.08	0.4	2	10	7	0	4
Primary sludge Avedøre	0.08	0.4	2	10	7	1	4
Secondary sludge short sludge age Sjölunda	0.08	0.4	2	10	7	1	4
	10					10	1
	10					50	1
Secondary sludge long sludge age Klagshamm	10				6	1	1
	0.08	0.4	2	10	7		4
	10				8		1

**Table 2.** Sorption isotherms obtained during sorption to primary sludge. P is the significance that the linear model has a better fit than another model tested, the model tested was Freundlich and Langmuir.

	Linear model		Freundlich model				Langmuir model			
	$K_d$ $\text{L kg}^{-1}$	$R^2$ %	$K_f$ $\text{L g}^{-1}$	n	$R^2$ %	P %	$\tau_{\text{MAX}}$ $\text{L g}^{-1}$	$K_L$	$R^2$ %	P %
Afluzosin	$1.8\times 10^3$	99	2.7	1.1	99	42	$5.5\times 10^4$	$3.7\times 10^{-5}$	99	31
Amityriptiline	$4.1\times 10^3$	98	3.1	0.96	98	70	no fit			
Atenolol	$4.6\times 10^2$	88	4.0	1.3	91	17	$5.7\times 10^3$	$1.4\times 10^{-4}$	90	18
Atracurium	$3.5\times 10^2$	100	0.24	0.96	100	40	no fit			
Azelastine	$6.4\times 10^3$	82	46	1.4	86	11	$2.0\times 10^4$	$5.8\times 10^{-4}$	89	3.5
Biperiden	$8.2\times 10^2$	88	1.3	1.1	88	83	$2.4\times 10^4$	$4.6\times 10^{-5}$	89	46
Bupropion	85	98	$4.8\times 10^{-3}$	0.76	99	0.99	no fit			
Chloprothixene	$3.8\times 10^4$	98	8.3	0.77	99	0.98	no fit			
Citalopram	$5.4\times 10^2$	76	0.97	1.1	76	83	$1.0\times 10^4$	$6.7\times 10^{-5}$	7.7	59
Clomipramine	$1.7\times 10^4$	99	7.6	0.88	99	8.5	no fit			
Clonazepam	$5.7\times 10^2$	96	0.10	0.84	96	33	no fit			
Clotrimazol	$3.2\times 10^4$	91	19.0	0.92	92	59	no fit			
Cyproheptadine	$1.1\times 10^4$	98	2.2	0.81	91	30	no fit			
Desloratidine	$3.7\times 10^3$	99	1.9	0.92	100	17	no fit			
Dicycloverin	$1.4\times 10^3$	92	1.2	0.98	94	90	$6.2\times 10^4$	$2.7\times 10^{-5}$	94	66
Donepezil	$3.6\times 10^3$	96	10.4	1.2	96	21	$1.9\times 10^4$	$2.6\times 10^{-4}$	97	7.3
Duloxetine	$1.3\times 10^4$	77	30.8	1.2	78	53	$1.6\times 10^4$	$1.1\times 10^{-3}$	79	37
Etonogestrel	no fit						no fit			
Ezetimibe	$2.3\times 10^3$	97	$4.9\times 10^{-2}$	0.68	99	1.1	no fit			
Fexofenadine	$2.7\times 10^3$	82	$1.1\times 10^{-5}$	0.38	94	0.15	no fit			
Fluoxetine	$1.0\times 10^4$	99	2.7	0.83	99	3.6	no fit			
Flutamide	$1.5\times 10^3$	88	0.13	0.77	90	27	no fit			
Glibenclamide	$3.6\times 10^3$	77	no fit				no fit			
Glimepiride	$2.1\times 10^3$	92	$1.9\times 10^{-3}$	0.53	97	0.8	no fit			
Haloperidol	$1.0\times 10^4$	76	60.9	1.4	80	21	$1.5\times 10^4$	$1.2\times 10^{-3}$	81	12
Hydroxyzine	$1.2\times 10^3$	98	3.2	1.1	99	14	$1.9\times 10^4$	$8.3\times 10^{-5}$	99	16
Irbesartan	$7.0\times 10^2$	92	$1.5\times 10^{-2}$	0.70	93	19	no fit			
Ketoconazole	$9.7\times 10^3$	88	1.6	0.79	90	30	no fit			
Loperamide	$1.4\times 10^4$	98	0.60	0.69	99	0.04	no fit			
Maprotiline	$6.7\times 10^3$	99	1.7	0.83	100	0.05	no fit			
Megesterol	no fit						no fit			
Mianserin	$3.0\times 10^3$	81	12.5	1.2	83	36	$1.6\times 10^4$	$2.9\times 10^{-4}$	85	17

Nefazodone	1.4×10 <sup>4</sup>	98	2.7	0.79	99	4.0	no fit				
Oxazepam	7.9×10 <sup>2</sup>	90	0.80	1.0	90	99	2.1×10 <sup>4</sup>	4.3×10 <sup>-5</sup>	90	71	
Paroxetine	1.4×10 <sup>4</sup>	96	5.6	0.87	97	28	no fit				
Pizotifen	4.7×10 <sup>3</sup>	100	no fit				no fit				
Progesterone	7.5×10 <sup>2</sup>	98	0.18	0.86	99	14	no fit				
Repaglinide	1.7×10 <sup>2</sup>	94	1.4	1.3	95	19	7.6×10 <sup>3</sup>	2.8×10 <sup>-5</sup>	94	53	
Risperidone	1.9×10 <sup>3</sup>	99	3.1	1.1	99	36	3.2×10 <sup>4</sup>	7.0×10 <sup>-5</sup>	99	17	
Sertraline	3.5×10 <sup>4</sup>	97	4.1	0.72	99	0.4	no fit				
Sulfamethoxazol	3.2×10 <sup>2</sup>	77	0.91	1.1	77	79	8.6×10 <sup>3</sup>	5.4×10 <sup>-5</sup>	78	58	
Telmisartan	1.3×10 <sup>3</sup>	100	0.86	0.95	100	51	no fit				
Tramadol	1.1×10 <sup>2</sup>	94	4.9×10 <sup>-4</sup>	0.63	96	3.3	no fit				
Trimethoprim	3.9×10 <sup>2</sup>	98	0.43	1.0	98	91	3.7×10 <sup>4</sup>	1.1×10 <sup>-5</sup>	98	73	
Verapamil	1.8×10 <sup>3</sup>	99	1.1	0.94	99	26	no fit				

**Table 3.** Sorption isotherms obtained during sorption to secondary sludge long sludge age P is the significance that the linear model has a better fit than another model tested, the model tested was Freundlich and Langmuir.

	Linear model		Freundlich model				Langmuir model			
	K <sub>d</sub> (L kg <sup>-1</sup> )	R <sup>2</sup> (%)	K <sub>f</sub> (L g <sup>-1</sup> )	n	R <sup>2</sup> (%)	P (%)	τ <sub>MAX</sub> (L g <sup>-1</sup> )	K <sub>L</sub>	R (%)	P (%)
Afluzosin	1.2×10 <sup>3</sup>	100	2.2	1.1	100	4.0	3.7×10 <sup>4</sup>	4.0×10 <sup>-5</sup>	100	1.3
Alprazolam	7.4×10 <sup>2</sup>	94	1.6×10 <sup>-2</sup>	0.69	96	4.6	no fit			
Amitryptiline	2.8×10 <sup>3</sup>	99	1.9	0.95	100	40	no fit			
Atenolol	1.6×10 <sup>3</sup>	94	22	1.5	99	0.0	7.8×10 <sup>3</sup>	4.9×10 <sup>-4</sup>	99	0.0
Atracurium	4.7×10 <sup>2</sup>	100	0.37	0.97	100	40	no fit			
Azelastine	2.0×10 <sup>3</sup>	99	3.2	1.1	99	31	5.8×10 <sup>4</sup>	3.9×10 <sup>-5</sup>	99	22
Biperiden	7.5×10 <sup>2</sup>	98	0.13	0.84	98	7.7	no fit			
Bisoprolol	1.1×10 <sup>2</sup>	-4.4	46	3.0	68	0.14	9.9×10 <sup>2</sup>	1.3×10 <sup>-3</sup>	86	0.0
Bupropion	1.4×10 <sup>2</sup>	99	0.35	1.1	100	4.2	5.3×10 <sup>3</sup>	3.5×10 <sup>-5</sup>	100	1.4
Chloprothixene	2.0×10 <sup>4</sup>	98	9.4	0.89	99	14	no fit			
Citalopram	2.1×10 <sup>2</sup>	94	0.90	1.2	95	25	3.8×10 <sup>3</sup>	8.1×10 <sup>-5</sup>	95	20
Clomipramine	6.7×10 <sup>3</sup>	100	3.4	0.91	100	1.4	no fit			
Clotrimazol	3.4×10 <sup>4</sup>	96	4.5	0.73	98	2.2	no fit			
Cyproheptadine	3.6×10 <sup>3</sup>	100	3.7	1.0	100	93	no fit			
Desloratidine	2.9×10 <sup>3</sup>	100	2.1	0.96	100	40	no fit			
Dicycloverin	1.7×10 <sup>3</sup>	99	0.50	0.88	99	13	no fit			
Donepezil	9.7×10 <sup>2</sup>	99	4.6	1.2	100	0.0	1.0×10 <sup>4</sup>	1.5×10 <sup>-4</sup>	100	0.0
Duloxetine	2.9×10 <sup>3</sup>	98	2.8	1.0	98	98	no fit			
Eprosartan	71	93	0.43	1.2	94	38	1.8×10 <sup>3</sup>	6.6×10 <sup>-5</sup>	94	32
Estradiol	no fit				0.0					
Etonogestrel	no fit				0.0					
Ezetimibe	3.0×10 <sup>3</sup>	96	3.0×10 <sup>-2</sup>	0.63	99	0.0	no fit			
Fexofenadine	3.6×10 <sup>2</sup>	95	0.2	0.93	96	74	no fit			
Fluoxetine	6.0×10 <sup>3</sup>	99	1.3	0.83	100	0.80	no fit			
Flutamide	7.5×10 <sup>2</sup>	90	1.5×10 <sup>-4</sup>	0.50	96	0.13	no fit			
Glibenclamide	1.3×10 <sup>3</sup>	93	0.2	0.82	99	8.2	no fit			
Glimepiride	9.6×10 <sup>2</sup>	99	0.2	0.83	99	11	no fit			
Haloperidol	2.9×10 <sup>3</sup>	98	3.5	1.0	98	78	1.1×10 <sup>5</sup>	2.8×10 <sup>-5</sup>	98	76
Hydroxyzine	7.2×10 <sup>2</sup>	98	0.54	0.97	98	68	no fit			
Irbesartan	9.4×10 <sup>2</sup>	94	5.3×10 <sup>-4</sup>	0.54	97	1.2	no fit			
Ibuprofen	3.6×10 <sup>2</sup>	91	1.6×10 <sup>-2</sup>	0.73	94	38	no fit			
Ketoconazole	8.5×10 <sup>3</sup>	91	0.70	0.73	95	0.8	no fit			

Levonorgestrel	$2.6 \times 10^2$	61	18	$1.9 \times 10^3$	81	1.4	$1.9 \times 10^3$	$6.6 \times 10^{-4}$	87	0.23
Loperamide	$5.5 \times 10^3$	97	0.53	0.77	98	0.83	no fit			
Maprotiline	$4.5 \times 10^3$	99	0.65	0.79	100	0.05	no fit			
Medroxyprogesterone	$1.7 \times 10^2$	42	15	2.1	56	11	$1.3 \times 10^3$	$6.4 \times 10^{-4}$	60	6.1
Megesterol	$5.9 \times 10^2$	82	6.7	1.4	85	16	$5.3 \times 10^3$	$2.4 \times 10^{-4}$	87	7.1
Mianserin	$9.1 \times 10^2$	99	1.4	1.1	99	45	$2.6 \times 10^4$	$4.0 \times 10^{-5}$	99	29
Nefazodone	$8.3 \times 10^3$	96	0.96	0.76	98	1.6	no fit			
Orphenadrine	$6.4 \times 10^2$	99	0.12	0.84	98	2.6	no fit			
Oxazepam	$1.1 \times 10^3$	87	11	1.4	91	9.2	$6.5 \times 10^3$	$3.6 \times 10^{-4}$	92	5.2
Paroxetine	$8.3 \times 10^3$	97	0.63	0.73	98	0.07	no fit			
Pizotifen	$3.1 \times 10^3$	100	1.9	0.94	100	26	no fit			
Progesterone	$1.1 \times 10^3$	87	8.6	1.3	90	17	$7.4 \times 10^3$	$2.9 \times 10^{-4}$	92	5.4
Repaglinide	$2.1 \times 10^2$	17	10	1.8	98	0.0	$2.7 \times 10^3$	$2.8 \times 10^{-4}$	99	0.0
Risperidone	$6.5 \times 10^2$	98	2.8	1.2	99	1.1	$8.9 \times 10^3$	$1.2 \times 10^{-4}$	99	0.15
Sertraline	$1.7 \times 10^4$	92	1.3	0.71	97	1.3	no fit			
Sotalol	$3.6 \times 10^2$	99	0.56	1.1	99	35	$1.3 \times 10^4$	$3.3 \times 10^{-5}$	99	14
Sulfamethoxazol	$3.7 \times 10^2$	96	$5.2 \times 10^{-3}$	0.68	98	5.6	no fit			
Telmisartan	no fit									
Tramadol	$1.9 \times 10^2$	99	$9.0 \times 10^{-2}$	0.92	99	39	no fit			
Trimethoprim	$4.2 \times 10^2$	99	0.18	0.91	99	16	no fit			
Venlafaxine	$1.0 \times 10^2$	85	0.77	1.3	86	32	$2.1 \times 10^3$	$7.9 \times 10^{-5}$	0.0	25
Verapamil	$4.0 \times 10^2$	84	20	1.8	96	0.0	$3.3 \times 10^3$	$4.3 \times 10^{-4}$	98	0.0

**Table 4.** Sorption isotherms obtained during sorption to secondary sludge short sludge age. P is the significance that the linear model has a better fit than another model tested, the model tested was Freundlich and Langmuir.

	Linear model		Freundlich model				Langmuir model			
	$K_d$ ( $L \text{ kg}^{-1}$ )	$R^2$ (%)	$K_f$ ( $L \text{ g}^{-1}$ )	n	$R^2$ (%)	P (%)	$\tau_{MAX}$ ( $L \text{ g}^{-1}$ )	$K_L$	$R^2$ (%)	P (%)
Alprazolam	$4.3 \times 10^2$	80	no fit							
Amitryptiline	$2.8 \times 10^3$	96	$4.2 \times 10^{-2}$	0.66	98	0.27	no fit			
Atenolol	$1.9 \times 10^3$	100	no fit							
Atracurium	$6.1 \times 10^2$	98	$2.9 \times 10^{-2}$	0.73	99	0.1				
Azelastine	$1.4 \times 10^3$	96	$1.7 \times 10^{-2}$	0.65	99	0.0	no fit			
Biperiden	$8.4 \times 10^2$	96	0.13	0.82	96	26	no fit			
Bisoprolol	94	64	7.5	2.0	79.6	2.0	$1.1 \times 10^3$	$3.4 \times 10^{-4}$	81	1.2
Bupropion	$2.0 \times 10^2$	97	$1.9 \times 10^{-2}$	0.79	98	6.2	no fit			
Chloprothixene	no fit									
Clomipramine	$7.3 \times 10^3$	88	$6.0 \times 10^{-3}$	0.49	97	0.0	no fit			
Clotrimazol	no fit									
Cyproheptadine	$5.3 \times 10^3$	97	0.23	0.70	99	0.0	no fit			
Desloratidine	$3.2 \times 10^3$	96	0.10	0.69	99	0.22	no fit			
Dicycloverin	$1.7 \times 10^3$	97	0.11	0.75	98	3.1	no fit			
Diltiazem	$4.4 \times 10^2$	100	0.65	1.0	100	35	$5.2 \times 10^4$	$9.2 \times 10^{-6}$	100	27
Duloxetine	$3.2 \times 10^3$	80	$1.7 \times 10^{-5}$	0.37	99	0.0	no fit			
Estradiol	$2.3 \times 10^2$	72	0.16	0.97	72	93	$1.6 \times 10^4$	$1.6 \times 10^{-5}$	72	85
Etonogestrel	$2.4 \times 10^2$	73	0.11	0.92	73	87	no fit			
Ezetimibe	$8.5 \times 10^3$	87	0.72	0.98	87	91	$9.4 \times 10^4$	$1.0 \times 10^{-4}$	87	65
Fexofenadine	$6.7 \times 10^2$	94	$2.5 \times 10^{-3}$	0.60	98	0.54	no fit			
Fluoxetine	$5.7 \times 10^3$	91	$1.4 \times 10^{-3}$	0.47	99	0.0	no fit			
Flutamide	$1.2 \times 10^3$	93	$1.6 \times 10^{-4}$	0.49	99	0.0	no fit			

Glibenclamide	$2.3 \times 10^3$	97	0.16	0.75	98	1.2	no fit		
Glimepiride	$2.6 \times 10^3$	94	$9.1 \times 10^{-2}$	0.70	94	2.0	no fit		
Haloperidol	$1.7 \times 10^3$	98	0.90	1.0	96	75	no fit		
Hydroxyzine	$6.0 \times 10^2$	95	0.27	0.91	95	56	no fit		
Irbesartan	no fit								
Ibuprofen	$2.0 \times 10^2$	80	1.1	1.3	81	62	$2.4 \times 10^3$	$1.3 \times 10^{-4}$	82 56
Ketoconazole	no fit								
Levonorgestrel	no fit								
Loperamide	$1.1 \times 10^4$	91	0.16	0.62	96	0.88	no fit		
Maprotiline	$3.9 \times 10^3$	91	$9.3 \times 10^{-2}$	0.66	95	3.1	no fit		
Medroxyprogesterone	$2.5 \times 10^2$	96	0.46	1.1	96	65	$9.7 \times 10^3$	$3.0 \times 10^{-5}$	96 59
Megesterol	$8.3 \times 10^2$	86	0.30	0.89	86	66	no fit		
Mianserin	$5.2 \times 10^2$	94	$6.6 \times 10^{-2}$	0.80	95	22	no fit		
Nefazodone	$8.9 \times 10^3$	92	$3.0 \times 10^{-2}$	0.54	99	0.0	no fit		
Orphenadrine	$5.4 \times 10^2$	98	0.17	0.88	98	25	no fit		
Oxazepam	$1.6 \times 10^3$	97	3.1	1.1	97	40	$2.3 \times 10^4$	$8.7 \times 10^{-5}$	98 33
Paroxetine	$8.6 \times 10^3$	82	$5.6 \times 10^{-5}$	0.37	98	0.0	no fit		
Pizotifen	$3.1 \times 10^3$	98	0.20	0.74	1005	0.0	no fit		
Progesterone	$1.1 \times 10^3$	96	0.21	0.83	96	20	no fit		
Repaglinide	$5.1 \times 10^2$	98	1.3	1.1	98	28	$2.5 \times 10^4$	$2.4 \times 10^{-5}$	98 44
Risperidone	$3.3 \times 10^2$	98	0.15	0.92	98	45	no fit		
Sertraline	no fit								
Sotalol	$7.4 \times 10^2$	99	0.22	0.87	99	6.3	no fit		
Sulfamethoxazol	$2.8 \times 10^2$	95	no fit				no fit		
Telmisartan	no fit								
Trimethoprim	$2.8 \times 10^2$	98	$1.3 \times 10^{-2}$	0.75	100	0.15	no fit		
Verapamil	$6.3 \times 10^2$	96	0.90	1.0	96	75	$3.3 \times 10^4$	$2.1 \times 10^{-5}$	96 63

### 2.3. Extraction and chromatography

Triplicate extractions were made from each 1 L borosilicate glass bottle. After 12 h of stirring, the samples were allowed to stand for 30 minutes in order to let the sludge settle. In order to remove particles, the liquid phase was decanted and filtered through a glass microfiber filters (GC/F; VWR Denmark). In the filtered samples (100 g) a surrogate standard mixture was added followed by solid phase extraction using OASIS HLB (6cc, Waters, Sweden). A detailed description of sample preparation and analyses employing the LC-MS/MS methodology reported in Grabic et al., (unpublished data) and Fick et al., (2009) may be found as supplementary data S1.

## 2.4. Data analysis

The measured concentrations of APIs in the water phase ( $C_0$ ) where no sludge was added and when sludge was added ( $C_w$ ) and SS were used to calculate  $C_s$  as follows in each experimental replicate:

$$C_s = (C_0 - C_w)/SS \quad (\text{Eq. 1})$$

The sorption isotherms define the equilibrium between the concentration of a chemical in aqueous and solid phases (Schwarzenbach et al., 2003). With batch sorption experiments including multiple concentrations, sorption isotherms may be constructed, from which the solid-water distribution coefficients can be determined. Three equations are used here to describe the sorption isotherms; linear (Eq. 2), Freundlich (Eq. 3) and Langmuir (Eq. 4).  $C_s$  is the concentration sorbed to the sludge ( $\text{g kg}^{-1}$ ) and  $K_d$  is the linear sorption constant.  $K_f$  is the Freundlich coefficient and  $n$  is the Freundlich exponent.  $\tau$  represents the total number of surface sites per mass of sorbent and  $K_L$  is the Langmuir coefficient.

$$\text{Linear } C_s = K_d * C_w \quad (\text{Eq. 2})$$

$$\text{Freundlich } C_s = K_f * C_w^{\frac{1}{n}} \quad (\text{Eq. 3})$$

$$\text{Langmuir } C_s = \frac{\tau_{\max} * K_L * C_w}{1 + K_L * C_w} \quad (\text{Eq. 4})$$

The linear isotherm is the simplest case where the affinity of the API remains constant over the concentration interval. The Langmuir isotherm may have the best fit in cases where the sorbent becomes saturated at higher concentrations of API. Freundlich, is commonly employed to describe experimentally obtained sorption data (Schwarzenbach et al., 2003).

The software GraphPad Prism 5 for Windows (GraphPad Software, Inc.) was used for data evaluation, using a 95 % confidence interval for the best fit sorption isotherms. The two hypotheses tested were whether the linear isotherm was a better fit than the Freundlich isotherm, and whether the linear was a better fit compared to Langmuir isotherm. Furthermore, in order to qualify as the best fit the  $R^2$ -value for the curve should be  $>0.7$ , otherwise no fit was made.

## 2.5. Estimation of the sorbed fraction

The estimation of the sorbed fraction of each API was made by employing the obtained  $K_d$ -values (Table 2 to 4). In those cases where both Freundlich and Langmuir isotherms were found to have a better fit than the linear, the one with the best significance was chosen as the best fit. For the APIs where the Freundlich or Langmuir isotherm gave the best fit (see Table 2 to 4),  $K_d$ -values were calculated for a water concentration of  $1 \mu\text{g L}^{-1}$ . The fraction of the APIs at equilibrium for a given sludge concentration ( $SS$ ;  $\text{kg L}^{-1}$ ) was calculated using the  $K_d$ -values ( $\text{L kg}^{-1}$ ) according to equation 5.

$$\text{Sorbed fraction (F}_S) = 1 - F_w = \frac{C_s}{C_w + SS \times C_s} = \frac{SS \times K_d}{1 + SS \times K_d} \quad (\text{Eq. 5})$$

Furthermore, if the mass of the sludge removed from the WWTP per volume of treated sewage ( $RESS$ ;  $\text{kg L}^{-1}$ ) is known, the fraction of the total APIs load into the activate sludge tank which would not be lost either by degradation or stripping, but that will be removed at equilibrium can be calculated as shown in equation 6.

$$\text{Removed fraction (F}_R) = \frac{RESS \times K_d}{1 + RESS \times K_d} \quad (\text{Eq. 6})$$

The sludge production from treatment of municipal sewage can be considered reasonably constant irrespective of the methods of treatment. Based on Henze et al. (2002) the typical

amounts of sludge removed from a WWTP can be calculated for primary and secondary sludge. For a WWPT with 2 h of settling time, the removal of primary sludge was estimated to  $210 \text{ g m}^{-3}$  of treated wastewater. In order to estimate the removal of secondary sludge, the yield coefficient for a low load treatment plant was employed giving a removal of  $110 \text{ g m}^{-3}$  for the secondary sludge. The corresponding value for a high load treatment plant would be  $165 \text{ g m}^{-3}$ .

### **3. Results and discussion**

#### **3.1 Sludge properties**

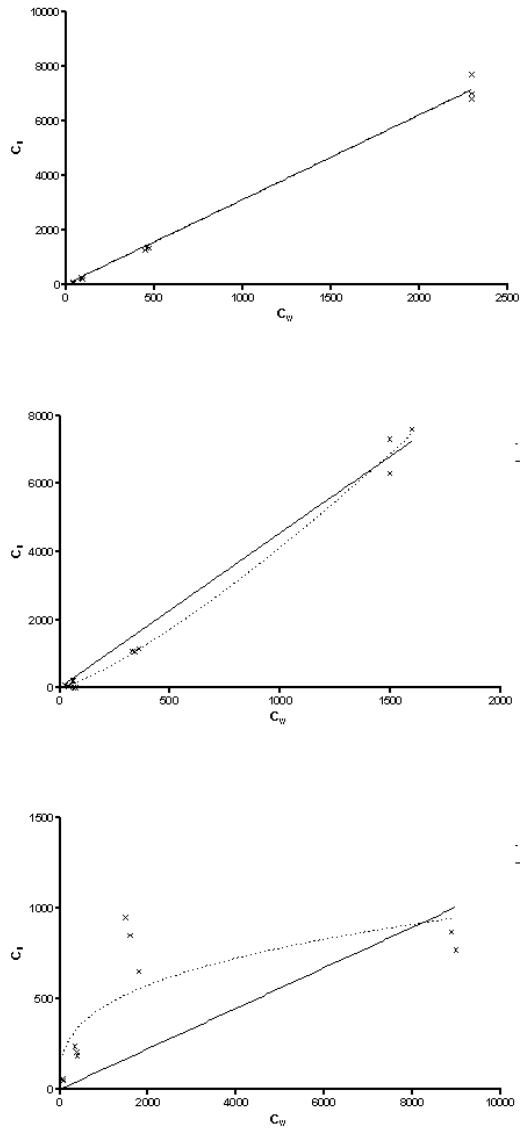
An ocular inspection of the freeze dried sludge showed that the primary sludge may be described as wadding, whereas the two types of secondary sludge had an appearance as instant coffee. The ocular differences between the different types of sludge may be due to their origin. Primary sludge settable particles of wastewater include faeces, toilet paper particles of food, and secondary sludge consist of bacteria biomass and biopolymers created by bacteria. It is likely that the mainly plant/wood derived primary sludge has different densities of functional groups and aromatic rings compared to the bacteria derived secondary sludge.

#### **3.2 Sorption isotherms**

Due to analytical limitations and the experimental conditions it was possible to determine sorption isotherms for 44-52 APIs (Table 2 to 4) out of the 75 APIs (Table S2). The linearly obtained  $K_d$  values ranged from 85 to 38 400, 199 to 11 340 and 71 to 34 050  $\text{L kg}^{-1}$  for primary sludge, secondary sludge with short sludge age and secondary sludge with long sludge age, respectively.

The sorption isotherm with the best fit was predominantly linear followed by the Freundlich isotherm (Table 2 to 4) within the studied concentration range ( $0.08\text{-}10 \mu\text{g L}^{-1}$ ). Examples of the

obtained isotherms are shown in Figure 1. Table 2 to 4 presents for  $1 \text{ g L}^{-1}$  sludge the obtained distribution coefficients, Freundlich coefficient, Freundlich exponent,  $\tau_{\max}$  and Langmuir coefficient in the cases where the isotherms fitted these isotherm descriptions. Table 2 to 4 exhibit the order of significance for each hypothesis tested.



**Figure 1.** Example of the obtained sorption isotherms. From the top Pizotifen linear isotherm, second Maprotiline Freundlich isotherm and at the bottom Bisoprolol Langmuir isotherm.



The isotherms coefficients did not change significantly even at the higher sludge densities (Table S3). The average difference between the  $K_d$ 's obtained from  $1 \text{ g L}^{-1}$  sludge compared to the  $K_d$  obtained, when  $10$  and  $50 \text{ g L}^{-1}$  sludge was 4%.

### 3.3 Sorption results and literature comparison

As mentioned before for some of the APIs the sorption isotherms were not obtained under our experimental conditions, possibly because of strong sorption to the glass surface of the bottle and/or the water surface. These APIs were Amiodiarone, Bromocriptine, Chlorpromazine, Clemastine, Dihydroergotamin, Fluphenazine, Levomepromazine, Meclozine, Miconazole, Perphenazine, Prometazine, Roxithromycine and Tamoxifen.

The experimental design of the present study and the LOQ in the present matrixes for the individual APIs measured, provides the limits of  $K_d$ . The highest  $K_d$  that could be obtained within the concentration range  $0.08 - 10 \mu\text{g L}^{-1}$  and given the median LOQ,  $8 \text{ ng L}^{-1}$  was  $1.2 \times 10^6 \text{ L kg}^{-1}$ . However, if the LOQ was low ( $1 \text{ ng L}^{-1}$ ) or high ( $170 \text{ ng L}^{-1}$ ), the highest  $K_d$  could be expected within the range from  $5 \times 10^4$  to  $1 \times 10^7 \text{ L kg}^{-1}$ . Furthermore, assuming that at least 10% was required to be sorbed in order to determine a  $K_d$  value the lowest  $K_d$  value obtained within the present study was  $100 \text{ L kg}^{-1}$ .

Thirteen of the APIs exhibited so low sorption on the sludge that a sorption isotherm was impossible to determine. The low sorbing APIs were Buprenorphine, Cilazapril, Carbamazepine, Codeine, Diclofenac, Estrone, Flecainide, Fluconazole, Metoprolol, Naloxone and Rosuvastatine, Tramadol and Venlafaxine in all three sludge. For the following APIs their sorption vary between each type of sludge. APIs which specifically exhibited low sorption for the primary sludge were Bisoprolol, Diltiazem, Eprosartan, Estradiol, Ibuprofen, Levonorgestrel,

Medroxyprogesterone, Orphenadrine and Sotalol. The obtained  $K_d$  values for the APIs above ranged in the two secondary sludge between 71 and 740 L kg<sup>-1</sup> (Table 3 and 4). APIs which specifically exhibited low sorption for the sludge with short sludge age were Alfuzosin, Citalopram, Clonazepam, Donepezil and Eprosartan. Finally for the secondary sludge with long sludge age the low sorbing APIs were the APIs Clonazepam and Diltiazem, generally the  $K_d$  values obtained for these APIs were low in the other sludge types.

Several of the  $K_d$  values obtained in other studies would in comparison with the present study be below or around the lowest  $K_d$  values that could be obtained. Examples of such APIs are Codeine (Wick et al., 2009) and Estrone, (Andersen et al., 2005; Carballa et al., 2008). Further low  $K_d$  values were reported by Ternes et al. (2004) with Carbamazepine in primary and secondary sludge <20 and 1.2 L kg<sup>-1</sup> and Ibuprofen <20 and 7.1 L kg<sup>-1</sup>, respectively. Results from Carballa et al. (2008) and Joss et al., (2005) supported these findings. Abegglen et al., (2009) reports  $K_d$  values from experiments with secondary sludge from membrane bioreactors for Carbamazepine and Ibuprofen which both were found to have low sorption (<75 L kg<sup>-1</sup>). Calculated  $K_d$  values for primary and secondary sludge were in the same range for Ibuprofen 9.5 and 0 L kg<sup>-1</sup>, respectively, whereas for Carbamazepine they were 10 to 100 times higher (314 and 135 L kg<sup>-1</sup>; Radjenović et al., 2009). Urase and Kikuta (2005) evaluated the sorption and degradation of APIs. Two of the APIs included were Ibuprofen and Carbamazepine, which were found to have  $K_d$  values of 80 and 66 L kg<sup>-1</sup>, respectively at pH 6.7 (Urase and Kikuta; 2005). In the present study Ibuprofen had a weak sorption in the two secondary sludge, which resulted in low  $K_d$  values, 200 and 360 L kg<sup>-1</sup>, obtained from the short and long sludge age, respectively, the reason may be due to the differently performed experiments. Contrary to the present study Ternes et al. (2004) report for Diclofenac the  $K_d$  value 459 L kg<sup>-1</sup> for primary sludge which is

within the limits of the present study but no sorption isotherm could be obtained, whereas for secondary sludge the authors report  $16 \text{ L kg}^{-1}$  which was outside the limits for the present study. Also Joss et al., (2005) report values for Diclofenac in the same range for both sludges. Carballa et al. (2008) reported values ranging between  $19\text{-}158 \text{ L kg}^{-1}$  which would be out of the limits for the present study. Radjenović et al. (2009) calculated the  $K_d$  value for Diclofenac for primary and secondary sludge at 194 and 118, respectively. Based on this, Diclofenac appears to have higher affinity for the primary sludge. One explanation could be the difference in pH values (Ternes et al., (2004)). However, in the present study Diclofenac was not among those APIs for which pH was affecting its sorption (see below section 3.4 and Table 5). The  $K_d$  values obtained in this study for Sulfamethoxazole (Table 2 to 4) were in the same order as those reported in Göbel et al. (2005) for activated sludge. Abegglen et al., (2009) and Carballa et al., (2009) found the  $K_d$  of Sulfamethoxazole to be one order of magnitude lower compared to the present study, and Radjenović et al. (2009) reported two order of magnitude lower  $K_d$  values. Another contradictory study of Sulfamethoxazole come from Wu et al. (2009) whom claimed sorption to be too weak, but also reported  $K_d$  for other antibiotics in the same level as found here for Sulfamethoxazole. Sulfamethoxazole has been reported to be photosensitive (e.g. Zhou and Moore, 1994; Trovó et al., 2009; Ryan et al., 2010). In the present study precautions were taken against photo-degradation. Depending on how different sorption studies have been carried out and precautions taken against photo-degradation throughout the whole experiment, including the extracts, photo-degradation might be an explanation to the diverging  $K_d$  results. The  $K_d$  values obtained in this study for Trimetoprim (Table 2 to 4) were in the same order as those reported in Göbel et al. (2005) for activated sludge. Also Radjenović et al. (2009), and Abegglen et al., (2009) found  $K_d$  for Trimetoprim to be in the same order of magnitude. The  $K_d$  obtained by

Radjenović et al. (2009) for Atenolol and Glibenclamide was one order of magnitude lower compared to those presented in this study (Table 2 to 4). In addition, Maurer et al (2007) obtained even lower  $K_d$  values below  $40 \text{ L kg}^{-1}$  for Atenolol, Sotalol, Metoprolol. Roxithromycin was included in the study conducted by Abegglen et al., (2009) where the authors determined  $K_d$  to be  $570 \text{ L kg}^{-1}$  which is almost 6 times higher than the one reported by Ternes et al., (2004). In the present study Roxithromycin was among those APIs for which no sorption isotherm could be obtained. However, the main differences were found between primary and secondary sludge and not between the two secondary types of sludge. It may therefore be assumed that the explanation can be derived from the origin of the sludge type. Primary sludge originate from particles found in wastewater e.g. much of it is derived from toilet paper and other plant matter found in food waste and secondary sludge mainly contains settled bacteria and biopolymers created by the bacteria. Based on the origin of the sludge it is likely that the sorption of different APIs structures can vary between the sludge types.

Influence of temperature on sorption is not well studied and the temperature may not always be reported in sorption studies. The effect of temperature was studied by Zeng et al., (2009) who found the difference in  $K_d$  between 10, 20 and 30 °C was 20-25%. The  $K_d$  values obtained in the present study may thus have somewhat higher  $K_d$ -values in comparison with other studies conducted at 10 or 20 °C.

### **3.4 Effect of pH on sorption**

In the present study, 20 out of 50 APIs were found to have a significant difference in their mean  $K_d$  values obtained in the secondary sludge with long sludge age between pH values 6, 7 and 8 (Table 5). By employing one way ANOVA-test, with Tukeys post-test at 95 % confidence level, the significant difference within the pH range of WWTPs was determined and identified.

All structures of the APIs, where the ANOVA-test indicated a significant difference between  $K_d$ s included a nitrogen atom and in many case an amine functional group and hence had basic properties. Even though the  $K_d$  values were significantly different in the pH range 6 to 8, it will not have any significant effect on the removal via sorption to sludge (in a subsequent appendix Table A1). However, Chlorpramine, Chloprothixene, Duloxetine, Fluoxetine, Levomepromazine, Loperamide, Nefazodone and Sertraline were exceptions. For these APIs the pH variation from 6 to 8 affected the fraction in the liquid phase by 10-20% (in a subsequent appendix Table A1). These APIs can be assumed to be weak bases. Carballa et al., (2008) point out that it has to be considered whether the pH value will affect sorption, as an example for Diclofenac ( $pK_a$  4.15). In the current study the variation of pH did not significantly affected the  $K_d$  for Diclofenac even though pH was 2 to 4 pH units higher than the  $pK_a$ . Fluoxetine ( $pK_a$  9.6) was in the current study shown to be affected by the pH, the difference between  $pK_a$  and the investigated pH was 2 to 4 pH units. Even though the differences between  $pK_a$  for Diclofenac and Fluoxetine was in the same range the two APIs showed different influence by changes of the pH. An investigation of the effect of pH on Naproxen and Carbamazepine, found the highest sorption was at pH 4, and no significant difference occur between pH values 6 and 8 (Maoz and Chefetz, 2010). Further investigation of the particulate fraction of the sludge found the overall  $pK_a$  to be 6.1 (Wang et al., 2000). The present study was conducted at a pH value above the  $pK_a$  for sludge. It cannot be excluded that the  $K_d$  was affected by changes caused by pH both in the API structure and the structure of the sludge since among the studied compounds were APIs containing N-groups. The APIs which did not show a significant difference in the  $K_d$ -values within the pH range 6 to 8 can be expected to be stable in their ionized and neutral form, respectively.

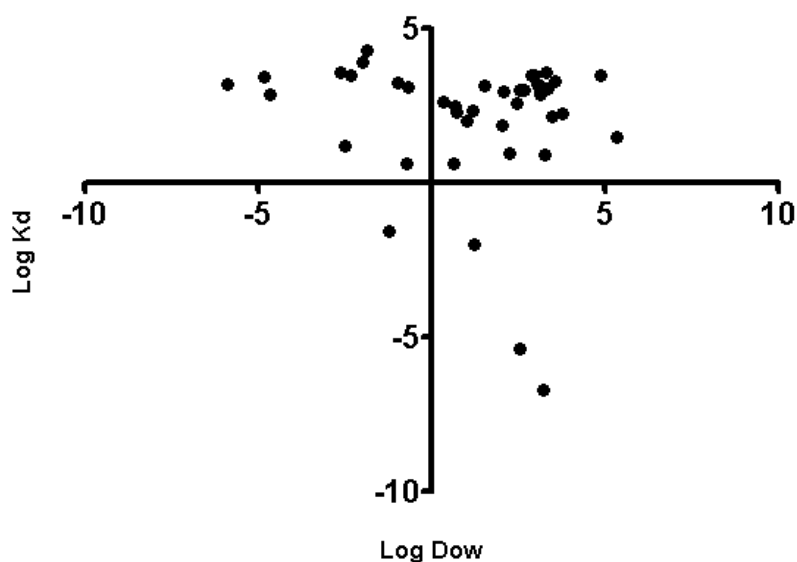
**Table 5.** Evaluating the effect of pH within the pH rang for a WWTP, pH 6-8. Average one point  $K_d$  values with standard deviation (n=3) obtained in sludge from secondary sludge long sludge age at pH 6, 7 and 8for the concentration  $10 \mu\text{g L}^{-1}$ . By employing one way ANOVA with a 95 % confidence interval was the following question asked; are the means significantly different?

	Average $K_d$				P<0,05?
	pH 6-8	pH 6	pH 7	pH 8	pH 6-8
Alfuzosin	$1.0 \pm 0.2 \times 10^3$	$12 \pm 0.4 \times 10^2$	$7.3 \pm 0.3 \times 10^2$	$11 \pm 0.5 \times 10^2$	no
Amitryptiline	$2.8 \pm 1.0 \times 10^3$	$2.8 \pm 0.2 \times 10^3$	$1.8 \pm 0.3 \times 10^3$	$4.0 \pm 0.7 \times 10^3$	yes
Atenolol	$1.6 \pm 0.2 \times 10^3$	$1.6 \pm 0.2 \times 10^3$	$1.6 \pm 0.2 \times 10^3$	$16 \pm 0.9 \times 10^2$	no
Atracurium	$4.1 \pm 0.6 \times 10^2$	$4.7 \pm 0.2 \times 10^2$	$413 \pm 20 \times 10^3$	$3.4 \pm 0.2 \times 10^2$	yes
Azelastine	$1.7 \pm 0.7 \times 10^3$	$2.0 \pm 0.1 \times 10^3$	$8.7 \pm 0.5 \times 10^2$	$2.3 \pm 0.1 \times 10^3$	yes
Biperiden	$0.8 \pm 0.2 \times 10^3$	$7.6 \pm 0.9 \times 10^2$	$0.6 \pm 0.1 \times 10^3$	$1.0 \pm 0.2 \times 10^3$	no
Bisoprolol	$1.2 \pm 0.9 \times 10^2$	$0.6 \pm 0.6 \times 10^2$	$2.1 \pm 0.9 \times 10^2$	$0.8 \pm 0.4 \times 10^2$	no
Bupropion	$1.4 \pm 0.1 \times 10^2$	$1.4 \pm 0.1 \times 10^2$	$1.4 \pm 0.2 \times 10^2$	$1.5 \pm 0.2 \times 10^2$	no
Chloprothixene	$1.9 \pm 0.8 \times 10^4$	$2.0 \pm 0.1 \times 10^4$	$10 \pm 0.7 \times 10^3$	$2.8 \pm 4.6 \times 10^4$	yes
Clomipramine	$6.6 \pm 2.4 \times 10^3$	$6.7 \pm 0.2 \times 10^3$	$3.9 \pm 0.2 \times 10^3$	$9.3 \pm 1.1 \times 10^3$	yes
Clotrimazol	$3.6 \pm 0.5 \times 10^4$	$3.6 \pm 0.5 \times 10^4$	$3.3 \pm 0.4 \times 10^4$	$4.0 \pm 0.4 \times 10^4$	no
Cyproheptadine	$3.4 \pm 1.0 \times 10^3$	$3.6 \pm 0.2 \times 10^3$	$2.1 \pm 0.1 \times 10^3$	$4.4 \pm 0.3 \times 10^3$	yes
Desloratidine	$2.9 \pm 0.5 \times 10^3$	$2.9 \pm 0.2 \times 10^3$	$2.3 \pm 0.2 \times 10^3$	$3.4 \pm 0.3 \times 10^3$	no
Diclofenac	$0.8 \pm 0.4 \times 10^3$	$8.0 \pm 0.6 \times 10^2$	$4.8 \pm 81 \times 10^2$	$1.2 \pm 0.6 \times 10^3$	no
Dicycloverin	$1.8 \pm 0.6 \times 10^3$	$1.7 \pm 0.2 \times 10^3$	$1.2 \pm 0.3 \times 10^3$	$2.4 \pm 0.5 \times 10^3$	no
Donepezil	$0.8 \pm 0.3 \times 10^3$	$9.6 \pm 0.1 \times 10^2$	$4.8 \pm 0.3 \times 10^2$	$10 \pm 0.4 \times 10^2$	no
Duloxetine	$3.0 \pm 1.2 \times 10^3$	$2.9 \pm 0.1 \times 10^3$	$1.8 \pm 0.3 \times 10^3$	$4.4 \pm 0.7 \times 10^3$	yes
Eprosartan	$0.6 \pm 0.7 \times 10^2$	$0.5 \pm 0.4 \times 10^2$	$0.6 \pm 0.9 \times 10^2$	$0.8 \pm 1.0 \times 10^2$	no
Estradiol	$0.3 \pm 0.2 \times 10^3$	$0.4 \pm 0.3 \times 10^{23}$	$0.2 \pm 0.9 \times 10^2$	$4.2 \pm 0.7 \times 10^2$	no
Ezetimibe	$3.3 \pm 0.6 \times 10^3$	$3.2 \pm 0.3 \times 10^3$	$3.0 \pm 0.6 \times 10^3$	$3.9 \pm 0.7 \times 10^3$	no
Fexofenadine	$2.7 \pm 1.4 \times 10^2$	$3.6 \pm 0.8 \times 10^2$	$3.5 \pm 0.5 \times 10^2$	$1.0 \pm 0.9 \times 10^2$	yes
Fluoxetine	$6.2 \pm 2.3 \times 10^3$	$6.1 \pm 0.4 \times 10^3$	$3.7 \pm 0.7 \times 10^3$	$8.7 \pm 1.6 \times 10^3$	yes
Flutamide	$0.8 \pm 0.1 \times 10^3$	$0.8 \pm 0.1 \times 10^3$	$0.8 \pm 0.1 \times 10^3$	$0.6 \pm 0.1 \times 10^3$	no
Glibenclamide	$1.2 \pm 0.2 \times 10^3$	$1.4 \pm 0.1 \times 10^3$	$1.1 \pm 0.1 \times 10^3$	$1.1 \pm 0.1 \times 10^3$	yes
Glimepiride	$9.4 \pm 0.8 \times 10^2$	$9.6 \pm 0.8 \times 10^2$	$0.9 \pm 0.1 \times 10^3$	$964 \pm 12$	no
Haloperidol	$2.3 \pm 0.8 \times 10^3$	$2.9 \pm 0.2 \times 10^3$	$1.2 \pm 0.1 \times 10^3$	$28 \pm 0.3 \times 10^2$	no
Hydroxyzine	$0.5 \pm 0.2 \times 10^3$	$7.1 \pm 0.9 \times 10^2$	$5.3 \pm 1.0 \times 10^2$	$0.3 \pm 0.1 \times 10^3$	yes
Irbesartan	$0.3 \pm 0.5 \times 10^3$	$0.9 \pm 0.2 \times 10^3$	$1 \pm 0$	$14 \pm 2$	yes
Levomepromazine	$2.5 \pm 1.5 \times 10^3$	$2.4 \pm 70. \times 10^3$	$1.0 \pm 0.3 \times 10^3$	$4.2 \pm 0.1 \times 10^3$	yes
Levonorgestrel	$0.1 \pm 0.2 \times 10^3$	$2.5 \pm 0.6 \times 10^2$	$7 \pm 193$	$0.2 \pm 0.1 \times 10^3$	no
Loperamide	$5.4 \pm 2.0 \times 10^3$	$5.7 \pm 0.6 \times 10^3$	$3.0 \pm 0.3 \times 10^3$	$7.3 \pm 1.2 \times 10^3$	no
Maprotiline	$4.5 \pm 1.7 \times 10^3$	$4.6 \pm 0.4 \times 10^3$	$2.7 \pm 0.4 \times 10^3$	$6.2 \pm 1.2 \times 10^3$	no
Medroxyprogesterone	$0.1 \pm 0.1 \times 10^3$	$0.2 \pm 0.1 \times 10^3$	$-0.2 \pm 0.8 \times 10^2$	$0.2 \pm 0.1 \times 10^3$	no
Megestrol	$0.5 \pm 0.3 \times 10^3$	$0.6 \pm 0.2 \times 10^3$	$0.3 \pm 0.2 \times 10^3$	$0.7 \pm 0.2 \times 10^3$	no
Mianserin	$0.6 \pm 0.2 \times 10^3$	$9.1 \pm 0.9 \times 10^2$	$404 \pm 0.3 \times 10^2$	$6.2 \pm 0.3 \times 10^2$	yes
Nefazodone	$6.4 \pm 2.2 \times 10^3$	$8.8 \pm 1.1 \times 10^3$	$6.3 \pm 0.9 \times 10^3$	$4.2 \pm 0.9 \times 10^3$	yes
Orphenadrine	$0.7 \pm 0.2 \times 10^3$	$6.5 \pm 0.5 \times 10^2$	$5.0 \pm 0.5 \times 10^2$	$8.2 \pm 0.9 \times 10^2$	yes
Oxazepam	$1.5 \pm 0.4 \times 10^3$	$1.1 \pm 0.2 \times 10^3$	$1.9 \pm 0.2 \times 10^3$	$1.6 \pm 0.3 \times 10^3$	no
Paroxetine	$8.2 \pm 3.0 \times 10^3$	$8.5 \pm 1.2 \times 10^3$	$4.9 \pm 0.8 \times 10^3$	$11 \pm 2.0 \times 10^3$	no
Pizotifen	$3.1 \pm 1.0 \times 10^3$	$3.1 \pm 0.2 \times 10^3$	$2.0 \pm 0.2 \times 10^3$	$4.3 \pm 0.6 \times 10^3$	yes
Progesterone	$1.0 \pm 0.4 \times 10^3$	$1.1 \pm 0.3 \times 10^3$	$0.6 \pm 0.1 \times 10^3$	$1.3 \pm 0.2 \times 10^3$	no
Repaglinide	$0.1 \pm 0.1 \times 10^3$	$0.1 \pm 0.1 \times 10^3$	$0.2 \pm 0.1 \times 10^3$	$0.7 \pm 1.2 \times 10^2$	no
Risperidone	$0.6 \pm 0.1 \times 10^3$	$6.5 \pm 0.6 \times 10^2$	$4.2 \pm 0.4 \times 10^2$	$6.2 \pm 0.3 \times 10^2$	no
Sertraline	$1.8 \pm 0.7 \times 10^4$	$1.8 \pm 0.2 \times 10^4$	$9.8 \pm 0.7 \times 10^3$	$2.6 \pm 0.4 \times 10^4$	yes
Sotalol	$3.0 \pm 0.6 \times 10^2$	$4.0 \pm 0.3 \times 10^2$	$2.4 \pm 0.5 \times 10^2$	$3.0 \pm 0.2 \times 10^2$	no
Sulfamethoxazol	$0.3 \pm 0.1 \times 10^3$	$0.3 \pm 0.2 \times 10^3$	$0.3 \pm 0.1 \times 10^3$	$2.7 \pm 0.8 \times 10^2$	no

Telmisartan	$0.8 \pm 0.4 \times 10^3$	$1.0 \pm 0.1 \times 10^3$	$0.9 \pm 0.4 \times 10^3$	$0.4 \pm 0.2 \times 10^3$	no
Trimetoprim	$3.5 \pm 0.7 \times 10^2$	$4.3 \pm 0.3 \times 10^2$	$348 \pm 9$	$2.8 \pm 0.2 \times 10^2$	yes
Venlafaxine	$0.5 \pm 0.6 \times 10^2$	$1.0 \pm 0.4 \times 10^2$	$-6 \pm 21$	$0.6 \pm 0.4 \times 10^2$	no
Verapamil	$4.0 \pm 0.8 \times 10^2$	$3.8 \pm 0.7 \times 10^2$	$3.6 \pm 0.8 \times 10^2$	$0.4 \pm 0.1 \times 10^3$	yes

### 3.5 Correlation of sorption with $K_{ow}$

An illustration of the absence of correlation between  $\log D_{ow}$  (calculated) and  $\log K_d$ -values is shown in Figure 2. The calculation of  $\log D_{ow}$  was based on calculated values of  $\log K_{ow}$  using KOWIN and calculated  $pK_a$  values presented by Manallack (2009).  $\log D_{ow}$  was for acidic compounds calculated according to  $D_{ow} = K_{ow} + 1 / (1 + 10^{(pH - pK_a)})$  and for basic compounds  $D_{ow} = K_{ow} + (1 / (1 + 10^{(pK_a - pH)}))$ . To estimate the sorption behavior based only on  $\log D_{ow}$  gives an incorrect sequence when compared and put in relation to other compounds. A few examples to illustrate the difficulties include Atenolol  $\log K_d$  3.6 and  $\log D_{ow}$  -2.6 and Bisoprolol  $\log K_d$  3.1 and  $\log D_{ow}$  -0.7, with the calculated  $pK_a$  9.6 and 9.5, respectively. However, using  $\log D_{ow}$  to predict the tendency of sorption for Glimpiride and Ibuprofen with the  $\log D_{ow}$  2.7 and 2.0, respectively, using  $pK_a$  5.0 and 4.3, respectively would give the impression that Glimperide could be expected to have higher affinity to sludge than Ibuprofen. The experimentally determined  $\log K_d$  (3.0 and 2.6, respectively) values obtained in the present study confirm such a hypothesis. However, applying the same hypothesis for Estradiol and Ezetimibe with the same  $\log K_{ow}$  3.94 but with respect to  $pK_a$  (9.72 and 10.3) the  $\log D_{ow}$  would be 0.67 and 1.22, respectively, the tendency would be that Ezetimibe would have higher affinity to sludge. But the results from the present study imply the opposite,  $\log K_d$  2.47 and  $\log K_d$ -1.98, respectively. Even though efforts have been made to calculate the  $K_d$  based on  $K_{ow}$  with respect to  $pK_a$  values, the inherent properties of the APIs and the sludge will need multiple descriptors to get close to experimentally derived  $K_d$ -values.



**Figure 2.** The plot illustrates that for majoring of the APIs in this study it was not possible estimate their sorption behavior based on  $\log D_{ow}$ .

### 3.7 Consequence of sorption for the fate of APIs

In order to estimate the removal (see Materials and methods 2.5) of APIs that were not lost from degradation or stripping but due to sorption in the WWTP process, the obtained  $K_d$  values were employed to estimate the fraction of API in the water phase (see Fig. 3; Table S4). The  $K_d$  values obtained from the primary sludge and secondary sludge with long sludge age were used for the estimation. However, the difference from the other secondary sludge was not larger than 6 percentage points with the median at 4 percentage points. Therefore, the results can be considered to be similar. Figure 3 presents the predicted distribution between the water and sludge of APIs based on the determined  $K_d$ s and selected typical primary and secondary sludge outputs from the WWTP. All APIs detected, and hence the APIs for which no sorption isotherms were determined are included (both those with too low sorption and those with too strong



sorption for the experimental design used). Figure 3 includes 37 APIs which mainly are present in the water phase at >80%. For 15 of the APIs, the sorption was so strong that the fraction in the water phase was 20% or less. For 13 of those, sorption was too strong that isotherms were not obtained. The estimated water fraction for the APIs showed that they could be distributed from 100 % in the water phase to 13% in the water phase (see Fig. 3).

Earlier investigations of APIs removal in activated sludge (Göbel et al., 2005) distinguished between different treatments steps in the WWTP. For Sulfamethoxazole and Trimetoprim the API removed by sorption can be compared with the present study. Göbel et al. (2005) found 1.5% and 4% as total removal of these compounds to primary and secondary sludge, respectively. The removal of those compounds was in this study approximately 10% (see Fig. 3) for both APIs. Ra et al. (2008) presents the removal for Estradiol, Diclofenac and Ibuprofen which were in the same range as in the present study, see Figure 3.

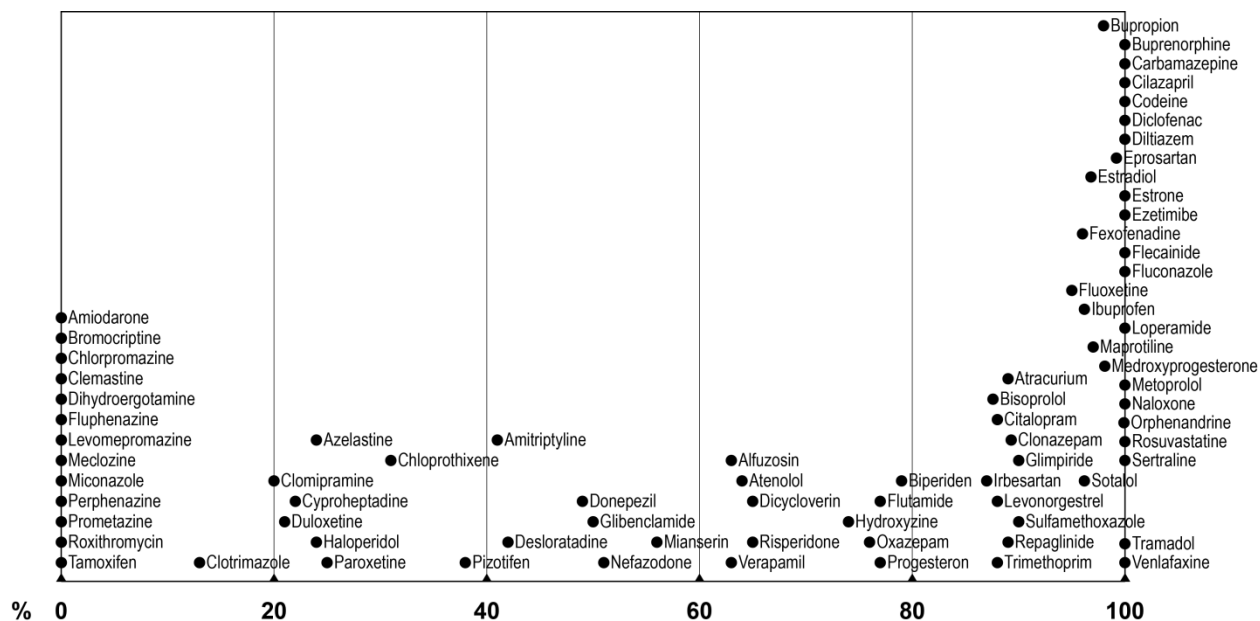


Figure 3. Estimated fraction, i.e. the fraction of the total APIs load into the activated sludge tank which isn't lost either by degradation or stripping, of the API in the water phase based on

experimentally determined sorption isotherms obtained by using primary and secondary sludge. For further information see supplementary data Figure S1.

#### **4. Conclusion**

In this study experimentally derived sorption isotherms are presented along with the corresponding obtained  $K_d$  values. The obtained  $K_d$  values were used in order to estimate the removal of the APIs in the WWTPs due to sorption to sludge.

The major findings from this study are:

- Experimentally derived  $K_d$  values and sorption isotherms for 52 APIs.
- For 13 APIs sorption to sludge was stronger than  $1.2 \times 10^6 \text{ L kg}^{-1}$
- For 10 APIs sorption to sludge was less than  $100 \text{ L kg}^{-1}$ .
- The estimation of removal due to sorption (in the absence of degradation and stripping) demonstrated that for 31 APIs were fractioned >80% of the initial concentration would be recovered in the liquid phase.
- 15 APIs have high affinity towards the sludge, i.e. <20% of the initial concentration would be found in the liquid phase. These APIs will therefore mainly be removed from the wastewater with the sludge, unless they are biodegraded significantly during treatment.

#### **Acknowledgment**

We gratefully acknowledge Mrs. Marika Wennberg at Klagshamn WWTP, Mrs. Maria Mases at Sjölanda WWTP and Mr. Thomas Guildal at Avedøre WWTP, for information regarding the WWTPs and assistance when sludge was collected. The present study was part of the

*MistraPharma* project, and was supported by the Foundation for Strategic Environmental Research (MISTRA) and for the post doc scholarship to Maritha Hörsing granted by The Swedish Research Council for Environment, Agricultural Sciences and Spatial Planning (FORMAS). The authors' are grateful to Dr. Maria G. Antoniou (DTU-Environment) for the editorial assistance of the manuscript.

## REFERENCES

Abegglen, C., Joss, A., McArdell, C.S., Fink, G., Schlüsener, M.P., Ternes, T.A., Siegrist, H. The fate of selected micropollutants in a single-house MBR. *Water Research* 43(7), 2036-2046.

Andersen, H.R., Siegrist, H., Halling-Sørensen, b., Ternes, T. (2003) Fate of esterogens in a municipal sewage treatment plant. *Environ. Sci. Technol.* 37(18), 4021-4026.

Andersen, H.R., Hansen, M., Kjølholt, Stuer-Lauridsen, F., Ternes, T., Halling-Sørensen, B. (2005) Assessment of the importance of sorption for steroid esterogens removal during activated sludge treatment. *Chemosphere* 61(1), 139-146.

Berg, U.T., Nyholm, N. Biodegradability simulation studies in semicontinuous activated sludge reactors with low ( $\mu\text{g/L}$ ) and standard (ppm range) chemical concentrations. *Chemosphere* 33(4), 711-735.

Böhm, L., During, R-A., (2010) Partitioning of polycyclic musk compounds in soil and aquatic environment - experimental determination of  $K_{\text{DOC}}$ . *J Soils Sediments* 10(4), 708–713.

Calisto, V., Esteves, V.I., (2009) Psychiatric pharmaceuticals in the environment. *Chemosphere* 77(10), 1257-1274.

Carballa, M., Fink, G., Omil, F., Lema, J., Ternes, T. (2008) Determination of the solid-water distribution coefficient ( $K_d$ ) for pharmaceuticals, esterogenes and musk fragrances in digested sludge. *Water research* 42(1-2), 287-295.

Fick J., Söderström H., Lindberg R.H., Phan C., Tysklind M., Larsson D.G. J. (2009) Contamination of surface, ground and drinking water from pharmaceutical production. *Environm. Toxicol. Chem.*, 28(12), 2522-2527

Gabet-Giraud, V., Miège, C., Choubert, J.M., Martin Ruel, S., Coquery, M. (2010) Occurrence and removal of estrogens and beta blockers by various processes in wastewater treatment plants. *Science of the total environment* 408(19), 4257-4269.

Grabic, R., Fick, J., Lindberg, R.H., Fedorova, G., Tysklind, M. (Unpublished data) Multi-residue method for trace level determination of pharmaceuticals in environmental samples by liquid chromatography coupled to triple quadrupole mass spectrometry.

Göbel, A., Thomasen, A., Mcardell, C.S., Joss, A., Giger, W. (2005) Occurrence and sorption behavior of sulfonamides, macrolides, and Trimetoprim in activated sludge treatment. *Environ. Sci. Technol.* 39(11), 3981-3989.

Henze, M., Harremoës, P., Arvin, E., Jansen, J.la C. (2002) *Wastewater treatment: biological and chemical processes*. Förstner, U., Murphy, R.J., Rulkens, W.H. (editors). 430p, Springer, Berlin.

Jones, O.A.H., Voulvoulis, N., Lester, J.N. (2006) Partitioning behavior of five pharmaceutical compounds to activated sludge and river sediment. *Arch. Environ. Contam. Toxicol.* 50(3), 297-305.

Joss, A., Keller, E., Alder, A.C., Göbel, A., McArdell, C.S., Ternes, T., Siegrist, H. (2005) Removal of pharmaceuticals and fragrances in biological wastewater treatment. *Water Research* 39 (14), 3139-3152.

Lindberg R., Fick J., Tysklind M. (2010) Screening of antimycotics in Swedish sewage treatment plants – Waters and sludge. *Water Res.*, 44(2), 649-657.

Manallack, D.T. (2009) The acid-base profile of a contemporary set of drugs: implications for drug discovery. *SAR and QSAR in environmental research* 20(7-8), 611-655.

- Maoz, A., Chefetz, B. (2010) Sorption of the pharmaceuticals carbamazepine and naproxen to dissolved organic matter: Role of structural fractions. *Water research* 44(3), 981-989.
- Maurer, M., Escher, B.I., Richle, P., Schaffner, N., Alder, A.C. (2007) Elimination of  $\beta$ -blockers in sewage treatment plants. *Water research* 41(3), 1614-1622
- Ra, J. S., Oh, S-Y., Lee, B.C., Kim, S.D. (2008) The effect of suspended particles coated by humic acid on the toxicity of pharmaceuticals, estrogens, and phenolic compounds. *Environment International* 34(2), 184–192.
- Radjenović, J., Petrović, M., Barceló, D. (2009) Fate and distribution of pharmaceuticals in wastewater and sewage sludge of the conventional activated sludge (CAS) and advanced membrane bioreactor (MBR) treatment. *Water research* 43(3), 831-841.
- Ryan, C.C., Tan, D.T., Arnold, W.A. (2010) Direct and indirect photolysis of sulfamethoxazole and trimetoprim in wastewater treatment plant effluent. *Water Research* 45(3), 1280-1286.
- Stuer-Lauridsen, F., Birkved, M., Hansen, L.P., Holten Lützhøft, H.-C., Halling-Sørensen, B. (2000) Environmental risk assessment of human pharmaceuticals in Denmark after normal therapeutic use. *Chemosphere* 40(7), 783-793
- Schwarzenbach, R.P. Gschwend P.M. Imboden, D.M. (2003). *Environmental Organic Chemistry*, Wiley & Sons, Inc, Hoboken, New Jersey.
- Ternes, T., Meisenheimer, M., McDowell, D., Sacher, F., Brauch, H-J., Haist-Gulde, B., Preuss, G., Wilme, U., Zulei-Seibert, N. (2002) Removal of Pharmaceuticals during drinking water treatment. *Environ. Sci. Technol.* 36(17), 3855-3863.

- Ternes, T., Herrmann, N., Boners, M., Knacker, T., Siegrist, H., Joss, A. (2004) A rapid method to measure the solid—water distribution coefficient ( $K_d$ ) for pharmaceuticals and fragrances in sewage sludge. *Water Research* 38(19), 4075–4084.
- Ternes, T., Joss, A. (Editors; 2008) *Human Pharmaceuticals, Hormones and Fragrances: The Challenge of Micropollutants in Urban Water Management*, IWA Publishing.
- Trovó, A.G., Nogueira, R.F.P., Agüera, A., Frenandez-Alba, A.R., Sirtori, C., Malato, S. (2009) Degradation of sulfamethoxazole in water by solar photo-Fenton. Chemical and toxicological evaluation. *Water Research* 43(16), 3922-3931.
- Uruse, T., Kikuta, T. (2005) Separate estimation of adsorption and degradation of pharmaceutical substances and estrogens in the activated sludge process. *Water Research* 39(7), 1289-1300.
- Wang, J., Huang, C.P., Allen, H.E., Takiyama, L.R., Poesponegoro, I., Poesponegoro, H., Pirestani, D. (1998) Acid Characteristics of dissolved organic matter in wastewater. *Water Environment Research* 70(5), 1041-1048.
- Wang, J., Huang, C.P., Allen, H.E. (2000) Surface physical-chemical characteristics of sludge particulates. *Water Environment Research* 72(5), 545-553
- Wick, A., Fink., G., Joss., A., Siegrist., H., Ternes, T.A. (2009) Fate of beta blockers and psycho-active drugs in conventional wastewater treatment. *Water Research* 43(4) 1060-1074.
- Wu, C., Spongberg, A.L., Witter, J.D. (2009) Sorption and biodegradation of selected antibiotics in biosolids. *Journal of Environmental Science and Health, Part A* 44(5), 454- 461.
- Zeng, Q., Li, Y., Gu, G. (2009) Effect of temperature on the sorption of 17 $\alpha$ -ethinylestradiol to aerobic and anaerobic sludge. *International conference on energy and environmental technology*.

Zhou, W., Moore, D.E. (1994) Photochemical decomposition of sulfamethoxazole. *International Journal of Pharmaceutics*, 110(1), 55-63.



## ***Supplementary information***

### **S1. Supplementary information regarding sample extraction and analyses using LC-MS/MS.**

The filters used in order to remove particles from the water phase were rinsed once in MeOH followed by deionized water before use. The filtered samples were adjusted to pH 3 with a strong phosphate buffer. As surrogate standards, a mixture of 13 <sup>13</sup>C and <sup>2</sup>D labelled APIs was employed, containing Amytriptyline, Carbamazepine, Ciprofloxacin, 17β-Ethinylestradiol (EE2), Fluoxetine, Ibuprofen, Oxazepam, Promethazine, Risperidone, Sulfamethoxazole, Tamoxifen, Tramadol and Trimetoprim. The samples were extracted employing solid phase extraction (SPE), Oasis HLB 6cc/200 mg, 30μm (Waters, Sweden). Before loading the samples, the cartridges were solvated and conditioned as follows; 5 mL EtAc followed by 5 mL MeOH and 5 mL acidified water pH 3. The cartridges were freeze dried over night and thereafter stored in a freezer at -20°C until analysis was performed. The cartridges were eluted with 5 mL MeOH followed by 2 mL EtAc, extracts were evaporated to dryness and the solvent was changed to 30 % MeOH with 0.1 % formic acid before analysis by LC-MS/MS. The same methodology as that reported in Grabic et al. (unpublished data), Fick et al., (2009) was used for this analysis. Hence, detailed information on chromatographic settings, mass transitions, collision energies, scan times, mass spectrometric settings, etc. can be found there. In short, a triple stage quadrupole MS/MS TSQ Quantum Ultra EMR (Thermo Fisher Scientific, San Jose, CA, USA) coupled with an Accela LC pump (Thermo Fisher Scientific, San Jose, CA, USA) and a PAL HTC autosampler (CTC Analytics AG, Zwingen, Switzerland) were used as analytical system. 20 μL of the sample was loaded onto a Hypersil GOLD aQ TM column (50 mm x 2.1 mm ID x 5 μm particles, Thermo Fisher Scientific, San Jose, CA, USA) preceded by a guard column. A gradient of flow and

MeOH and ACN in water (all solvents buffered by 0.1% formic acid) was used for elution of analytes. Both heated electrospray (HESI) and atmospheric pressure photoionization (APPI) in positive and negative ion modes were used for ionisation of target compounds. Both first and third quadrupoles were operated at resolution 0.7 FMWH, and two or three selected reaction monitoring (SRM) transitions were monitored for each analyte. SRM is an analogue to the more common monitoring method, single ion monitoring (SIM) in standard mass spectrometry. With SRM, the ion monitored in the first step is required to form a given fragment through a selected reaction in order to be positively identified. Samples were quantified using the SRM method. Several calibration standards covering all concentration ranges were measured before, in the middle and at the end of sample sequences. The maximum difference between results at quantification and qualification mass transition was set to 30% as criterion for positive identification.

Table S1 NOMENCLATURE

---

API	active pharmaceutical ingredient
APPI	atmospheric pressure photoionization
$C_0$	measured concentrations of API in the water phase without sludge
$C_s$	calculate concentration of APIs sorbed to the sludge
$C_w$	measured concentrations of API in the water phase
DOM	dissolved organic matter
GC/F	glass microfiber filter
HESI	heated electro spray ionisation
$K_d$	distribution coefficient
$K_{DOC}$	distribution coefficient dissolved organic carbon
LC-MS/MS	liquid chromatography coupled with tandem mass selective detector
LOQ	limit of quantification
n	Freundlich exponent
PE	person equivalents
SIM	single ion monitoring
SPE	solid phase extraction
SRM	selected reaction monitoring
SS	suspended solids
RESS	mass of the sludge removed
$\tau_{max}$	the total number of surface sites per mass of sorbent
VSS	volatile suspended solid

**Table S2.** Presenting the APIs included in the present study and the calculated Henry's Law constant ( $K_H$ ;  $\text{Atm m}^3 \text{mol}^{-1}$ )

Alfuzosin	$9.5 \times 10^{-20}$	Dihydroergotamine	$1.1 \times 10^{-26}$	Medroxyprogesterone	$1.3 \times 10^{-8}$
Amiodarone	$1.8 \times 10^{-12}$	Diltiazem	$8.6 \times 10^{-17}$	Metoprolol	$1.4 \times 10^{-13}$
Amitriptyline	$6.8 \times 10^{-8}$	Donepezil	$1.2 \times 10^{-12}$	Mianserin	$8.1 \times 10^{-10}$
Atenolol	$1.4 \times 10^{-18}$	Duloxetine	$5.4 \times 10^{-10}$	Miconazole	$2.4 \times 10^{-9}$
Atracurium	$2.0 \times 10^{-35}$	Eprosartan	$5.6 \times 10^{-17}$	Naloxone	$5.4 \times 10^{-19}$
Azelastine	$2.6 \times 10^{-13}$	Estradiol	$3.6 \times 10^{-11}$	Nefazodone	$1.5 \times 10^{-17}$
Biperiden	$2.5 \times 10^{-10}$	Estrone	$3.8 \times 10^{-10}$	Orphenadrine	$4.1 \times 10^{-9}$
Bisoprolol	$2.9 \times 10^{-15}$	Ezetimibe	$4.4 \times 10^{-18}$	Oxazepam	$5.5 \times 10^{-10}$
Bromocriptine	$1.1 \times 10^{-25}$	Fexofenadine	$1.2 \times 10^{-18}$	Paroxetine	$1.1 \times 10^{-11}$
Buprenorphine	$7.8 \times 10^{-18}$	Fecainide	$5.8 \times 10^{-13}$	Perphenazine	$5.2 \times 10^{-18}$
Bupropion	$1.0 \times 10^{-7}$	Fluconazole	$1.0 \times 10^{-13}$	Pizotifen	$2.6 \times 10^{-8}$
Carbamazepine	$1.1 \times 10^{-10}$	Fluoxetine	$8.9 \times 10^{-8}$	Progesterone	$6.5 \times 10^{-8}$
Chlorpromazine	$3.7 \times 10^{-10}$	Fluphenazine	$6.1 \times 10^{-17}$	Promethazine	$5.0 \times 10^{-10}$
Chlorprothixene	$2.5 \times 10^{-9}$	Flutamide	$3.7 \times 10^{-10}$	Repaglinide	$1.3 \times 10^{-17}$
Cilazapril	$1.8 \times 10^{-18}$	Glibenclamide	$7.6 \times 10^{-19}$	Risperidone	$2.2 \times 10^{-16}$
Citalopram	$2.7 \times 10^{-11}$	Glimepiride	$1.4 \times 10^{-21}$	Rosuvastatin	$1.5 \times 10^{-16}$
Clemastine	$3.8 \times 10^{-9}$	Haloperidol	$2.3 \times 10^{-14}$	Roxithromycin	$5.0 \times 10^{-31}$
Clomipramine	$7.5 \times 10^{-9}$	Hydroxyzine	$3.9 \times 10^{-17}$	Sertraline	$5.1 \times 10^{-8}$
Clonazepam	$7.0 \times 10^{-13}$	Ibuprofen	$1.5 \times 10^{-7}$	Sotalol	$2.5 \times 10^{-14}$
Clotrimazole	$3.1 \times 10^{-8}$	Irbesartan	$7.0 \times 10^{-15}$	Sulfamethoxazole	$9.6 \times 10^{-13}$
Codeine	$7.6 \times 10^{-14}$	Levomepromazine	$3.9 \times 10^{-11}$	Tamoxifen	$4.5 \times 10^{-10}$
Cyproheptadine	$9.2 \times 10^{-9}$	Levonorgestrel	$7.7 \times 10^{-10}$	Tramadol	$1.5 \times 10^{-11}$
Desloratadine	$2.1 \times 10^{-11}$	Loperamide	$6.9 \times 10^{-19}$	Trimethoprim	$2.4 \times 10^{-14}$
Diclofenac	$4.7 \times 10^{-12}$	Maprotiline	$8.0 \times 10^{-8}$	Venlafaxine	$2.0 \times 10^{-11}$
Dicycloverine	$8.9 \times 10^{-7}$	Meclozine	$4.6 \times 10^{-12}$	Verapamil	$8.8 \times 10^{-15}$

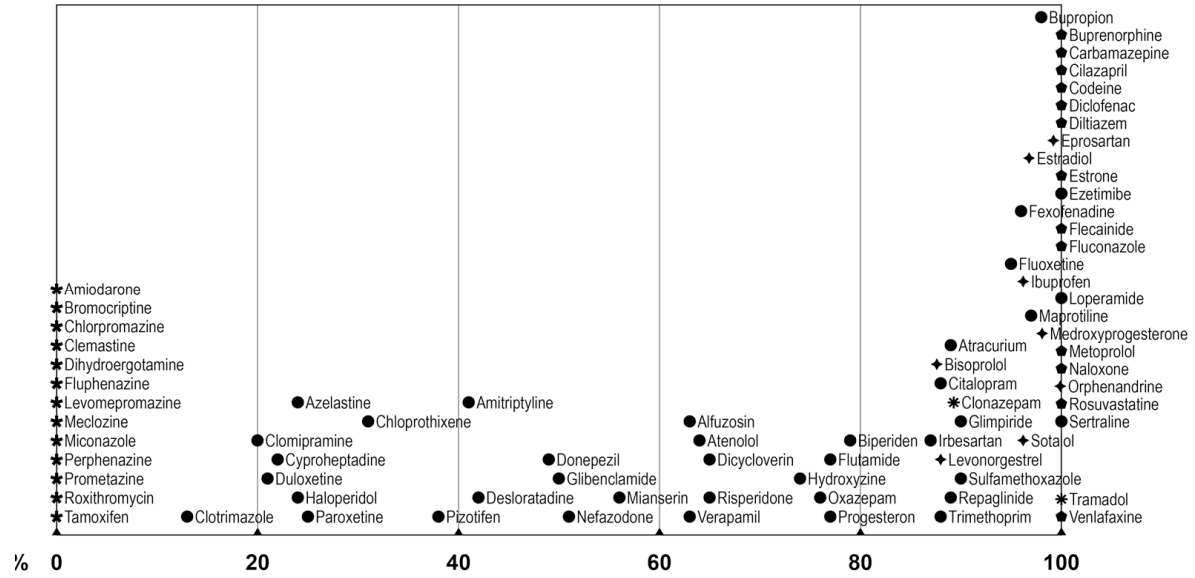
**Table S3.** Sorption isotherms obtained during sorption to secondary sludge short sludge age, including 1, 10 and 50 g sludge. P is the significance that the linear model has a better fit than another model tested, the model tested was Freundlich and Langmuir.

	Linear		Freundlich				Langmuir			
	$K_d$	$R^2$ (%)	$K_f$	n	$R^2$ (%)	P (%)	$\tau_{MAX}$	$K_L$	$R^2$ (%)	P (%)
Alfuzosin	$3.5 \times 10^2$	73	$1.2 \times 10^{-5}$	0.4	98	0.23	no fit			
Alprazolam	$3.1 \times 10^2$	55	$1.6 \times 10^{-8}$	0.3	77	0.25	no fit			
Amitryptiline	$2.7 \times 10^3$	91	$3.3 \times 10^{-2}$	0.6	98	0.01	no fit			
Atracurium	$5.5 \times 10^2$	89	$1.5 \times 10^{-3}$	0.6	98	0.01	no fit			
Azelastine	$1.4 \times 10^3$	96	$9.4 \times 10^{-2}$	0.8	97	0.72	no fit			
Biperiden	$8.0 \times 10^2$	91	$2.9 \times 10^{-2}$	0.7	95	0.52	no fit			
Bromocriptine	$7.7 \times 10^3$	75	$5.4 \times 10^{-6}$	0.3	92	0.01	no fit			
Buprenorphine	9.6E+01	71	no fit				no fit			
Bupropion	$1.9 \times 10^2$	96	$2.6 \times 10^{-2}$	0.8	97	0.60	no fit			
Chlorpromazine	$8.8 \times 10^3$	72	$3.9 \times 10^{-8}$	0.2	94	0.01	no fit			
Clemastine	$7.6 \times 10^3$	91	$3.2 \times 10^{-2}$	0.6	97	0.02	no fit			
Clomipramine	$7.1 \times 10^3$	86	$1.4 \times 10^{-2}$	0.5	97	0.01	no fit			
Clonazepam	$2.9 \times 10^2$	66	no fit				no fit			
Cyproheptadine	$5.3 \times 10^3$	97	0.4	0.7	99	0.01	no fit			
Desloratidine	$3.0 \times 10^3$	90	$2.9 \times 10^{-2}$	0.6	97	0.01	no fit			
Dicycloverin	$1.7 \times 10^3$	95	$9.0 \times 10^{-2}$	0.7	98	0.05	no fit			
Diltiazem	$4.2 \times 10^2$	96	$3.4 \times 10^{-2}$	0.8	98	0.15	no fit			
Duloxetine	$3.2 \times 10^3$	84	$2.6 \times 10^{-5}$	0.4	97	0.01	no fit			
Estradiol	$2.3 \times 10^2$	70	0.3	1.0	70	87	$1.4 \times 10^4$	$1.8 \times 10^{-5}$	71	75
Etonogestrel	$2.4 \times 10^2$	72	0.4	1.1	72	80	$1.2 \times 10^4$	$2.3 \times 10^{-5}$	72	78
Ezetimibe	$8.5 \times 10^3$	87	7.2	1.0	87	89	no fit			
Fexofenadine	$6.6 \times 10^2$	93	$2.7 \times 10^{-3}$	0.6	98	0.03	no fit			
Finasteride	$8.1 \times 10^2$	77	no fit				no fit			
Fluoxetine	$5.3 \times 10^3$	86	$3.8 \times 10^{-3}$	0.5	99	0.01	no fit			
Flutamide	$1.2 \times 10^3$	94	$1.7 \times 10^{-2}$	0.7	97	0.21	no fit			
Glibenclamide	$2.2 \times 10^3$	93	$3.2 \times 10^{-2}$	0.7	97	0.03	no fit			
Haloperidol	$1.7 \times 10^3$	98	no fit				no fit			
Hydroxyzine	$5.9 \times 10^2$	93	0.1	0.8	94	6.9	no fit			
Levomepromazine	$3.8 \times 10^3$	96	0.3	0.7	99	0.02	no fit			
Loperamid	$1.1 \times 10^4$	91	0.3	0.7	95	0.58	no fit			
Maprotiline	$3.7 \times 10^3$	89	$7.9 \times 10^{-2}$	0.7	95	0.06	no fit			
Medroxyprogesterone	$2.5 \times 10^2$	92	0.6	1.1	92	41	$1.3 \times 10^4$	$2.1 \times 10^{-5}$	92	64
Megestrol	$8.2 \times 10^2$	86	0.2	0.9	86	39	no fit			
Mianserin	$5.3 \times 10^2$	91	0.6	1.0	91	88	no fit			
Nefazodone	$8.8 \times 10^3$	92	$7.4 \times 10^{-2}$	0.6	98	0.01	no fit			
Orphenadrine	$4.8 \times 10^2$	87	$2.1 \times 10^{-3}$	0.6	93	0.09	no fit			
Oxazepam	$1.6 \times 10^3$	95	no fit				no fit			
Paroxetine	$8.1 \times 10^3$	79	$1.9 \times 10^{-4}$	0.4	97	0.01	no fit			
Pizotifen	$3.0 \times 10^3$	97	0.2	0.7	99	0.01	no fit			
Progesterone	$1.0 \times 10^3$	95	0.2	0.8	96	3.3	no fit			
Promethazine	$2.8 \times 10^3$	89	$3.2 \times 10^{-2}$	0.6	96	0.03	no fit			
Sotalol	$7.1 \times 10^2$	95	$6.3 \times 10^{-2}$	0.8	98	0.09	no fit			
Telmisartan	$5.8 \times 10^2$	70	no fit				no fit			
Trihexyphenidyl	$6.8 \times 10^2$	83	$5.8 \times 10^{-4}$	0.6	92	0.04	no fit			
Trimetoprim	$2.6 \times 10^2$	91	$3.4 \times 10^{-3}$	0.7	97	0.01	no fit			
Zolpidem	$1.4 \times 10^2$	91	no fit				no fit			

**Table S4.** Based on the best fitted sorption isotherms for each API and the removal of sludge in a Swedish average WWTP the fraction of the APIs passing through the WWTP was calculated. In the case were the linear isotherm were not the best fitted a  $K_d$  value was calculated assuming an water concentration of  $1\mu\text{g L}^{-1}$ .  $F_{wP}$  = Primary sludge water fraction,  $F_{wS}$ = Secondary sludge water fraction and  $F_{wT}$ =total fraction in water.

	Primary sludge	Secondary sludge long sludge age	$F_{wP}$ (%)	$F_{wS}$ (%)	$F_{wT}$ (%)
Afluzosin	Linear	Langmuir	73	86	63
Amityptiline	Linear	Linear	54	77	41
Atenolol	Linear	Langmuir	91	70	64
Atracurium	Linear	Linear	93	95	89
Azelastine	Langmuir	Linear	29	82	24
Biperiden	Linear	Linear	85	92	79
Bupropion	Freundlich	Linear	100	98	98
Chloprothixene	Linear	Linear	97	32	31
Citalopram	Linear	Linear	90	98	88
Clomipramine	Linear	Freundlich	22	91	20
Clotrimazol	Linear	Freundlich	13	100	13
Cyproheptadine	Linear	Linear	31	72	22
Desloratidine	Linear	Linear	56	76	42
Dicycloverin	Linear	Linear	77	84	65
Donepezil	Linear	La	57	86	49
Duloxetine	Linear	Linear	28	76	21
Ezetimibe	Freundlich	Freundlich	100	100	100
Fexofenadine	Linear	Linear	100	96	96
Fluoxetine	Freundlich	Freundlich	96	99	95
Flutamide	Linear	Freundlich	77	100	77
Glibenclamide	Linear	Linear	57	87	50
Glimepiride	Freundlich	Linear	100	90	90
Haloperidol	Linear	Linear	31	76	24
Hydroxyzine	Linear	Linear	80	93	74
Irbesartan	Linear	Freundlich	87	100	87
Loperamide	Freundlich	Freundlich	100	100	100
Maprotiline	Freundlich	Freundlich	98	100	97
Mianserin	Linear	Linear	61	91	56
Nefazodone	Freundlich	Linear	98	52	51
Oxazepam	Linear	Linear	86	89	76
Paroxetine	Linear	Freundlich	25	100	25
Pizotifen	Linear	Linear	51	75	38
Progesterone	Linear	Linear	86	89	77
Repaglinide	Linear	Langmuir	97	92	89
Risperidone	Linear	Langmuir	72	90	65
Sertraline	Freundlich	Freundlich	100	100	100
Sulfamethoxazol	Linear	Linear	94	96	90
Trimethoprim	Linear	Linear	92	96	88
Verapamil	Linear	Langmuir	72	86	63

Figure S1.



**Figure S1.** Estimated fraction, i.e. the fraction of the total APIs load into the activated sludge tank

which isn't lost either by degradation or stripping, of the API in the water phase based on experimentally determined sorption isotherms. ●) experimentally determined  $K_{ds}$  for primary and secondary sludge; \*) experimentally determined  $K_{ds}$  for the primary sludge and assuming no sorption to the secondary sludge as sorption were too low to be obtained in the present experiment; ◆) experimentally determined  $K_{ds}$  for the secondary sludge and assuming no sorption to the primary sludge as sorption were too low to be obtained in the present experiment; ◆) assuming no sorption to neither one of the sludges as the sorption were too low to be obtained in the present experiment; ★) assuming high sorption due to too high sorption in the present study.