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DOI:

[10.1016/j.scitotenv.2017.12.059](https://doi.org/10.1016/j.scitotenv.2017.12.059)

Document Version

Accepted author manuscript

[Link to publication record in Manchester Research Explorer](#)

Citation for published version (APA):

Tarpani, R. R. Z., & Azapagic, A. (2018). A methodology for estimating concentrations of pharmaceuticals and personal care products (PPCPs) in wastewater treatment plants and in freshwaters. *Science of the Total Environment*, 622-623, 1417-1430. <https://doi.org/10.1016/j.scitotenv.2017.12.059>

Published in:

Science of the Total Environment

Citing this paper

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A methodology for estimating concentrations of pharmaceuticals and personal care products (PPCPs) in wastewater treatment plants and in freshwaters

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Abstract

Despite an increasing number of studies on pharmaceuticals and personal care products (PPCPs), data on their concentrations in the environment are still scant. This is due to many factors, including great variability in usage and physicochemical properties of these compounds, which contribute to their widespread presence and complex behaviour, particularly in the aquatic environment. The main pathway for their discharge into the waterways is through wastewater treatment plants (WWTPs), which are inefficient in removing many of PPCP compounds. Therefore, aiming to contribute to a better understanding of the role that WWTPs play in the presence of PPCPs in the environment, this paper proposes a new method for estimating the expected concentrations of these compounds in WWTP influents, effluents and sludge, as well as their expected discharge and related concentrations in freshwaters. The proposed method can assist with future eco-toxicological and environmental risk assessments as well as the development of policies and regulation related to PPCP compounds.

Keywords: *freshwater pollution; pharmaceutical and personal care products; predicted environmental concentration; sewage sludge; wastewater treatment.*

1. Introduction

The environmental presence of compounds from pharmaceuticals and personal care products (PPCPs) has been increasing over the years as a result of the growing consumption of PPCPs associated with the aging population, advances in disease treatments and expansion of health care systems (Hill & Chu 2009, Liu & Wong 2013). One of the main routes for PPCPs to reach the environment is wastewater treatment plants (WWTPs) which are ineffective in removing these chemicals, unless advanced treatment methods are used (Michael et al. 2013, Ratola et al. 2012, Verlicchi & Zambello 2015). As a result, effluents discharged into the waterways can contain significant amounts of these compounds and can eventually reach potable water, particularly through freshwaters and groundwater. In some cases, PPCPs are present in potable water at concentrations found in the environment, indicating that conventional drinking water treatment plants are also ineffective in removing them (Carmona et al. 2014, Luo et al. 2014). As a consequence, concerns have been raised about the fate of PPCPs in the environment and their potential health effects over a long-term exposure through drinking water. This is particularly important given a great diversity of these compounds and the synergism among their metabolites, interactions with other compounds or their degradation products (Benotti et al. 2009, Kumar & Xagorarakis 2010). Recognising the importance of PPCPs in the environment, the European Directive 2013/39/EU defined a watch list for EU-wide monitoring for the following eight compounds: 2-Ethylhexyl 4-methoxycinnamate, 17-Alpha-ethinylestradiol (EE2), 17-Beta-estradiol (E2), Azithromycin, Clarithromycin, Diclofenac, Erythromycin, and Estrone (E1) (European Commission 2015).

However, data on the discharge of PPCPs from WWTPs and on their concentrations in the environment exhibit great variability, leading to inconclusive results (Blair et al. 2015, Boxall et al. 2014, Luo et al. 2014, Verlicchi & Zambello 2015, Verlicchi et al. 2012). This is not surprising,

given the large number of variables involved, including consumption of PPCPs, their influent concentration in WWTPs, sewage composition and plant operating parameters. As a result, there are many data gaps (Petrie et al. 2015) warranting further studies on the contribution that wastewater treatment has on the presence of PPCPs in the environment.

While the effects of these chemicals on the environment and human health are still subject of ongoing research, it is generally accepted that they could cause detrimental effects on wildlife owing to their eco-toxicological properties, even without considering the metabolites and synergetic effects (Cleuvers 2003, Fent et al. 2006, Martín et al. 2012, Verlicchi et al. 2012, Yazdankhah et al. 2006). Although the creation of metabolites is high for many compounds, a significant number of PPCP compounds are environmentally persistent and difficult to remove once in the environment (Farré et al. 2008, Kagle et al. 2009, Löffler et al. 2005, Xu et al. 2009).

Currently, predictions on the presence of PPCPs in WWTPs and freshwaters are largely based on prescription or sales data and disregard dilution and other operating parameters in WWTP plants. This approach is unreliable due to many factors, including incomplete sales data, fluctuations in consumption patterns and differing conditions in WWTP plants (Celle-jeanton et al. 2014, Oosterhuis et al. 2013, Verlicchi et al. 2014). Therefore, the following aspects require further attention (Shannon et al. 2008; Siemens et al. 2008; Bolong et al. 2009; Christensen et al. 2009; Miège et al. 2009; Walters et al. 2010; Gottschall et al. 2012):

- determining concentrations of PPCPs in WWTP influents;
- determining concentrations in the effluent after the secondary treatment in WWTPs at which advanced treatment methods should be used to reduce the impact on the environment or to enable wastewater reuse;
- identifying safe levels of discharge of these substances from WWTPs; and
- determining the necessity for monitoring the effluents and sludge for the presence of certain PPCP compounds.

In an attempt to address some of these research challenges and inform policy, this work proposes a new methodology for estimating expected concentrations of PPCPs in WWTP influents, effluents and sludge, based on data from direct measurements available in literature. These estimates are then used to predict concentrations of target compounds in freshwaters. The proposed method can assist future eco-toxicological and environmental risk assessments as well as development of policies and regulation related to PPCP compounds.

2. Methodology

The proposed methodology involves the following four steps:

1. selection of target PPCPs and data collection;
2. estimation of the influx of PPCPs into WWTPs and their removal efficiencies;
3. estimation of concentration ranges of PPCPs in WWTPs; and
4. estimation of expected concentrations of PPCPs in freshwaters.

These steps are described in the next sections.

2.1. Selection of target PPCP compounds and data collection

The first step of the methodology involves selection of target PPCPs from over 3,000 compounds currently used in Europe alone (Daughton & Ternes 1999; Roig 2010; World Health Organization 2004). In this work, the target compounds have been selected based on data availability, environmental risks they pose, their different physicochemical properties (and hence different behaviour during wastewater treatment) and inclusion in the European watch list. As a result, the following 14 PPCP substances ubiquitous in WWTPs are considered (Radjenović et al. 2009; Jelic et al. 2011; Petrie et al. 2015):

- analgesics: acetaminophen, diclofenac and ibuprofen;
- antibiotics: erythromycin, trimethoprim and sulfamethoxazole;
- beta blockers: metoprolol;
- lipid regulators: gemfibrozil and bezafibrate;
- psychiatric drugs: carbamazepine;
- hormones: estrone and 17 β -estradiol;
- antiseptics: triclosan; and
- stimulants: caffeine.

To enable estimation of the parameters in steps 2-4 of the methodology, the following data need to be collected based on the actual WWTPs and measurements:

- influent and effluent concentrations of the target PPCPs;
- wastewater influent into WWTPs; and
- population served by WWTPs.

As part of this research, the above data were collected from the literature for 81 full-scale WWTPs in different countries, spanning a range of operating parameters and treatment types. These data are summarised in Table 1, sorted by the region, starting with the countries in North America and followed by those in Asia, Europe and, finally, Australia.

Table 1 Target PPCPs in wastewater treatment plants in different countries

Location of WWTP (Source of data)	Compounds and their average concentrations in WWTP (influent; effluent) ($\mu\text{g/L}$)	Influent water flow (m^3/d)	Population served (no. of inhabitants)	Treatment type
US (Gao et al. 2012)	Sulfamethoxazole (1.10; 0.10) Carbamazepine (0.10; 0.20) Caffeine (42.0; 0.70)	45,400	Not stated	Activated sludge
US (Conkle et al. 2008)	Acetaminophen (39.3; 0.02) Ibuprofen (9.92; 0.08) Sulfamethoxazole (4.09; 0.31) Metoprolol (0.21; 0.02) Gemfibrozil (1.65; 1.82) Carbamazepine (0.06; 0.09) Caffeine (25.6; 0.03)	7,200	Not stated	Constructed wetland
US (Thomas & Foster 2005)	Diclofenac (0.47; ~0.0) Ibuprofen (9.50; 0.02) Triclosan (3.00; 0.08) Caffeine (43.8; 0.04)	11,300	194,000	Activated sludge
US (Batt et al. 2007)	Trimethoprim (7.90; 0.26) Sulfamethoxazole (2.80; 0.63)	113,562	Not stated	Activated sludge + sand filter
US (Yang et al. 2011)	Acetaminophen (80.0; 0.05) Diclofenac (0.22; 0.01) Ibuprofen (11.0; 0.06) Trimethoprim (0.61; 0.28) Erythromycin (0.34; 0.27) Sulfamethoxazole (2.60; 0.42) Carbamazepine (0.23; 0.25) Triclosan (0.47; 0.02) Caffeine (80.0; 0.07)	227,000	Not stated	Membrane bioreactor
Canada (Lishman et al. 2006)	Diclofenac (0.20; 0.19) Ibuprofen (8.45; 0.38) Gemfibrozil (0.45; 0.25) Estrone (0.03; 0.01) Triclosan (1.93; 0.11)	202,133	Not stated	Several ^a
Canada (Atkinson et al. 2012)	Estrone (0.05; 0.10) 17 β -estradiol (0.05; 0.003)	422,000	786,130	Activated sludge
South Korea (Behera et al. 2011)	Acetaminophen (7.50; 0.01) Diclofenac (0.15; 0.02) Ibuprofen (2.20; 0.15) Trimethoprim (0.20; 0.04) Sulfamethoxazole (0.09; 0.09)	451,000	1,100,000	Several ^b

	Metoprolol (0.005; 0.004) Gemfibrozil (0.20; 0.02) Carbamazepine (0.10; 0.08) Estrone (0.05; 0.02) 17 β -estradiol (0.004; ~0.00) Triclosan (0.55; 0.10) Caffeine (2.50; 0.02)			
South Korea (Sim et al. 2010)	Acetaminophen (8.00; ~0.00) Diclofenac (0.01; 0.01) Ibuprofen (1.00; ~0.00) Erythromycin (0.75; 0.15) Gemfibrozil (0.02; ~0.00) Carbamazepine (0.30; 0.20) Caffeine (6.00; 0.02)	1,302,100	3,600,000	Several ^c
South Korea (Choi et al. 2008)	Acetaminophen (31.9; 0.01) Trimethoprim (0.22; 0.05) Sulfamethoxazole (0.52; 0.16) Carbamazepine (0.23; 0.09) Caffeine (27.4; 0.32)	1,710,000	Not stated	Activated sludge
Japan (Nakada et al. 2006)	Ibuprofen (0.80; 0.01) Carbamazepine (0.08; 0.05) Estrone (0.04; 0.05) 17 β -estradiol (0.02; 0.01) Triclosan (0.60; 0.10)	2,785,000	4,688,000	Several ^d
Japan (Nakada et al. 2007)	Ibuprofen (0.40; 0.01) Carbamazepine (0.08; 0.03) Estrone (0.04; 0.02) 17 β -estradiol (0.02; 0.02) Triclosan (0.55; 0.12)	170,000	460,000	Activated sludge + sand filter
Japan (Hashimoto et al. 2007)	Estrone (0.03; 0.04) 17 β -estradiol (0.012; 0.002)	158,012	Not stated	Several ^c
Hong Kong (Leung et al. 2012)	Trimethoprim (0.20; 0.19) Erythromycin (1.00; 1.00) Sulfamethoxazole (0.10; 0.07)	2,081,000	5,381,900	Several ^f
Hong Kong (Xu et al. 2007)	Erythromycin (0.86; 0.74) Sulfamethoxazole (0.05; 0.03)	1,725,000	3,500,000	Modified activated sludge ^g
Hong Kong (Gulkowska et al. 2008)	Trimethoprim (0.21; 0.23) Erythromycin (0.55; 0.51)	1,377,000	3,500,000	Modified activated sludge ^g
China (Zhou et al. 2012)	Estrone (0.08; 0.012) 17 β -estradiol (0.04; 0.002)	1,000,000	2,400,000	Activated sludge
China (Sui et al. 2010)	Diclofenac (0.35; 0.20) Trimethoprim (0.30; 0.10) Metoprolol (0.10; 0.09) Gemfibrozil (0.04; 0.03) Bezafibrate (0.04; 0.01) Carbamazepine (0.15; 0.12) Caffeine (6.00; 0.01)	2,200,000	6,109,000	Several ^h
Spain (Gracia-Lor et al. 2012)	Acetaminophen (55.1; ~0.00) Diclofenac (0.53; 0.34) Ibuprofen (14.6; ~0.00) Trimethoprim (0.10; 0.09) Sulfamethoxazole (0.45; 0.05) Gemfibrozil (0.21; 0.49) Bezafibrate (0.08; 0.06)	36,000	Not stated	Activated sludge
Spain (Carballa et al. 2004)	Ibuprofen (3.70; 1.33) Sulfamethoxazole (0.58; 0.25) Estrone (0.002; 0.004)	n.a.	100,000	Activated sludge
Spain (Radjenović et al. 2009)	Acetaminophen (9.90; 0.11) Diclofenac (1.32; 1.05) Ibuprofen (21.7; 0.41) Trimethoprim (0.20; 0.12) Erythromycin (0.82; 0.54) Sulfamethoxazole (0.09; 0.02) Metoprolol (0.04; 0.03) Gemfibrozil (3.08; 3.08) Bezafibrate (14.9; 3.01) Carbamazepine (0.16; 0.16)	42,000	Not stated	Activated sludge
Spain (Santos et al. 2007)	Ibuprofen (94.1; 10.9) Carbamazepine (0.30; 0.50)	164,500	Not stated	Activated sludge

	Caffeine (2.17; 1.24)			
Switzerland (Tauxe-Wuersch et al. 2005)	Diclofenac (1.90; 1.90) Ibuprofen (2.80; 0.60)	9,300	23,000	Modified activated sludge ^g
Switzerland (Maurer et al. 2007)	Metoprolol (0.15; 0.10)	n.a.	36,000	Activated sludge + sand filter
Finland (Lindqvist et al. 2005)	Diclofenac (1.00; 0.35) Ibuprofen (13.3; 1.10) Bezafibrate (0.50; 0.33)	353,330	1,174,000	Modified activated sludge ^g
UK (Kasprzyk-Hordern et al. 2009)	Acetaminophen (211; 11.7) Diclofenac (0.07; 0.10) Ibuprofen (1.68; 0.26) Trimethoprim (2.19; 1.15) Erythromycin (1.61; 1.39) Sulfamethoxazole (0.03; 0.01) Metoprolol (0.08; 0.07) Bezafibrate (0.42; 0.23) Carbamazepine (1.69; 2.50)	36,160	111,000	Trickling filter beds
UK (Jones et al. 2007)	Acetaminophen (2.00; 0.10) Ibuprofen (4.00; 0.50)	Not stated	150,000	Activated sludge
UK (Zhou et al. 2009)	Diclofenac (0.98; 0.08) Sulfamethoxazole (0.18; 0.03) Carbamazepine (1.83; 0.84)	34,992	32,000	Activated sludge + sand filter
UK (Roberts & Thomas 2006)	Acetaminophen (27.3; 0.002) Diclofenac (0.98; 0.34) Ibuprofen (23.2; 12.8) Trimethoprim (0.26; 0.40) Erythromycin (0.11; 0.20)	230,000	Not stated	Activated sludge
Sweden (Zorita et al. 2009)	Diclofenac (0.23; 0.49) Ibuprofen (6.90; 0.09) Estrone (0.02; 0.07) 17 β -estradiol (0.003; 0.0025)	20,000	55,000	Activated sludge
Sweden (Lindberg et al. 2005)	Trimethoprim (0.25; 0.22) Sulfamethoxazole (0.41; 0.19)	1,400,000	644,000	Modified activated sludge ^g
Italy (Baronti et al. 2000)	Estrone (0.04; 0.03) 17 β -estradiol (0.01; 0.002)	734,000	1,200,000	Activated sludge
Australia (Watkinson et al. 2007)	Trimethoprim (0.34; 0.05) Sulfamethoxazole (0.36; 0.27)	140,000	700,000	Activated sludge

^a 3 lagoons, 8 conventional activated sludge plants and 2 activated sludge + media filtration plants.

^b 2 conventional activated sludge plants, 1 modified activated sludge plants and 2 other plants.

^c 5 activated sludge and 6 other plants.

^d 5 conventional activated sludge plants.

^e 10 conventional activated sludge plants.

^f 2 activated sludge plants and 5 other plants.

^g chemically enhanced.

^h 1 activated sludge with ultrafiltration and ozone plant, 1 activated sludge and sand filtration plant, 1 oxidation ditch plant and 1 activated sludge with microfiltration and reverse osmosis plant.

2.2. Estimation of influx of PPCPs into WWTPs and removal efficiencies

The estimations in this and the subsequent steps are predicated on the following assumptions:

- the amount of PPCPs in the WWTP influent is directly proportional to the per-capita consumption of PPCP, meaning that a plant serving a larger number of inhabitants will receive a proportionally higher amount of compounds in its influent;
- the consumption of the target compounds is assumed to be constant throughout the year due to a lack of data; although it is acknowledged that some compounds, such as analgesics, are expected to have higher consumption values and, therefore, influx in winter, the seasonal variations will even out over a year; and
- daily variations in the influent volume and any reactions of the compounds in urban effluents before reaching the WWTP are not considered, again due to a lack of data.

The annual per-capita influx of PPCP compounds into a WWTP is estimated as follows, using the relevant data in Table 1 for each WWTP:

$$IM_{inf,i} = 365 \times 10^{-3} \times \left[\frac{C_{inf,i} \times Q}{p} \right] \quad (\text{mg/inhab} \cdot \text{year}) \quad (1)$$

where:

$IM_{inf,i}$ annual per-capita influx of PPCP compound i into WWTP (mg/inhab·year)
 $C_{inf,i}$ concentration of PPCP compound i in the WWTP influent ($\mu\text{g/L}$)
 Q daily wastewater influent into WWTP (L/day)
 p population served by WWTP (number of inhabitants)

The removal efficiency is calculated based on the WWTP influent and effluent concentrations of PPCPs (see Table 1):

$$R_{efficiency,i} = \frac{C_{inf,i} - C_{eff,i}}{C_{inf,i}} \times 100 \quad (\%) \quad (2)$$

where:

$R_{efficiency,i}$ removal efficiency of PPCP compound i in a WWTP (%)
 $C_{eff,i}$ concentration of PPCP compound i in the effluent of a WWTP ($\mu\text{g/L}$).

In addition to the influent concentrations, the removal efficiency is influenced by the design and operation of WWTPs, which in turn affect the concentration of the compounds in the effluent (Clara et al. 2005, Ratola et al. 2012). To account for the variation in different parameters, the expected concentration ranges for each PPCP compound in the WWTP influent and effluent are considered in step 3, as detailed in the next section.

2.3. Estimation of concentration ranges of PPCP compounds in WWTPs

The box plot method is used to determine the expected influent and effluent ranges for the PPCP compounds, due to its non-parametric nature. For these purposes, the values for $IM_{inf,i}$ and $R_{efficiency,i}$, estimated in the previous step for each compound and WWTP in Table 1, are grouped into two datasets (A and B), respectively. Each dataset is then divided into four equal quartiles, each containing a quarter of the data. Then, the first quartile is defined as the middle (median) value between the lowest and the median value of the data set, the second quartile as the median of the data set and the third quartile as the middle value between the highest and the median value of the data set. The interquartile range, defined as the difference between the third (upper) and first (lower) quartile, assumes that the values will be bundled around a central (or median) value, as per the box-plot method. As a result, the interquartile range is considered to be representative of the whole dataset for each PPCP compound if it contains more than 50% of values (Potter 2006). The interquartile range can also be used to define outliers, i.e. the values too far from the central value or the expected range. Here, the high and low outliers are defined, respectively, as those 1.5 times above the upper quartile value and 1.5 times below the lower quartile value, following the box-plot method. Accordingly, the daily influx range for each PPCP compound can be estimated as:

$$\alpha_{range,i} = \frac{\lambda_{range,i}}{365 \times 10^3} \times p \quad \lambda_{range,i} \subseteq A \quad (\text{g/day}) \quad (3)$$

where:

$\alpha_{range,i}$ estimated daily influx range for compound i in WWTP (g/day)
 $\lambda_{range,i}$ $IM_{inf,i}$ value for compound i within the interquartile range (mg/inhab·year)
 A dataset of $IM_{inf,i}$ values (mg/inhab·year).

The influent concentration range $\beta_{range,i}$ in a WWTP is calculated according to:

$$\beta_{range,i} = \frac{10^3}{365} \times \frac{\lambda_{range,i}}{q} \quad \lambda_{range,i} \subseteq A \quad (\mu\text{g/L}) \quad (4)$$

where:

$\beta_{range,i}$ estimated influent concentration range for PPCP compound i ($\mu\text{g/L}$)
 q average per-capita daily wastewater influent into WWTP ($\text{L/inhab}\cdot\text{day}$).

The expected range of removal efficiencies $R_{range,i}$ for each PPCP compound i is determined using dataset B, where $R_{range,i}$ represents the interquartile range of $R_{efficiency,i}$ values (%).

Therefore, the effluent concentration range for PPCP compound i can be estimated according to:

$$\gamma_{range,i} = \beta_{range,i} \times (R_{range,i} \times 10^{-2}) \quad R_{range,i} \subseteq B \quad (\mu\text{g/L}) \quad (5)$$

where

$\gamma_{range,i}$ estimated effluent concentration range for PPCP compound i ($\mu\text{g/L}$)
 B dataset of $R_{efficiency,i}$ values (%).

The concentration range of PPCP compounds retained by the sludge can be estimated using the solid-water distribution coefficient and the sludge solids content (Verlicchi & Zambello 2015):

$$S_{range,i} = \frac{\alpha_{range,i} \times 10^{-3}}{[p \times q]/K_{d,i} + [p \times s_{DM}]} \quad (\text{kg/kg}) \quad (6)$$

where:

$S_{range,i}$ concentration range of compound i in the sludge (kg/kg)
 $K_{d,i}$ solid–water distribution coefficient of compound i (L/kg)
 s_{DM} per-capita amount of dry matter in the sludge ($\text{kg/inhab}\cdot\text{day}$)
 10^{-3} conversion from g to kg.

2.4. Estimation of freshwater concentrations of PPCP compounds

Finally, using the values estimated in the previous steps, the predicted freshwater concentration of the target PPCP compounds after the release of the WWTP effluent can be estimated according to the following equation:

$$PEC_{range,i} = \gamma_{range,i} \left[\frac{p \times q}{F + (p \times q)} \right] \quad (\mu\text{g/L}) \quad (7)$$

where:

$PEC_{range,i}$ predicted environmental concentration range of compound i in freshwater after the release of WWTP effluent ($\mu\text{g/L}$)
 F daily flow of a freshwater body (L/day).

The estimate of PEC is based on the following assumptions: there is no previous PPCP contamination of a freshwater body; there is no prompt degradation of PPCP compounds after the effluent discharge; and spatial and time variations in the concentration of the target compounds are homogeneous.

3. Results and discussion

3.1. Selection of target PPCP compounds and data collection

As can be seen in Table 1, the data for the influent flow Q and the served population p range widely. For example, the smallest treatment facility has an average flow of $7,200 \text{ m}^3/\text{day}$ and the largest $2,785,000 \text{ m}^3/\text{day}$; the population served varies from 23,000 to 6.1 million. However, as indicated in Figure 1, the influent flow and the population served are well correlated linearly ($R^2 = 0.9225$). Based on these data, the average per-capita influent flow q is equivalent to 428

L/inhab.day. This value is used for the estimations of different parameters in the next steps. Using the average q , estimated based on multiple data points from small to large WWTPs, decreases the influence of the variations in daily and seasonal flows, in industrial and storm water contributions to the influent flow and, consequently, in PPCP concentrations. While the estimated value is greater than the average in Europe (150-200 L/inhab./day), it is within the range in the US, Canada and Australia (400-500 L/inhab./day). Since the data include these regions and Asian countries, combined with the fact that many of the considered WWTPs also treat storm water (Environmental Agency 2008; Sperling 2007), this value is arguably representative.

Figure 1 Correlation between daily water influent Q and population p served by WWTP based on the data in Table 1.

3.2. Estimation of influx of PPCPs into WWTPs and removal efficiency

The annual per-capita influx $IM_{inf,i}$ into WWTPs of the target PPCPs and their removal efficiencies $R_{efficiency,i}$, estimated using data in Table 1 and eqns. (1) and (2), are shown in Figure 2 and Figure 3, respectively. As can be seen in Figure 2, the great majority of the $IM_{inf,i}$ values fall between 1 and 100 mg/inhab/year, with only three being above 1,000 and three below 1 mg/inhab/year. Similarly, most of the removal efficiencies $R_{efficiency,i,s}$ in Figure 3 vary between 20% and 100%, with only a few falling below 20%. It can also be observed that removal efficiencies for some compounds have negative values – this is due either to their accumulation (Gao et al. 2012, Katsoyiannis & Samara 2005, Li & Zhang 2011, Quintana et al. 2005) or chemical reactions during the treatment process (Carballa et al. 2004, Esperanza et al. 2007, Schlüsener & Bester 2008, Xu et al. 2012) which can lead to higher concentrations in the effluent than in the influent.

The estimated $IM_{inf,i}$ and $R_{efficiency,i}$ values are then grouped respectively into the datasets A and B for each target compound (see Tables S1 and S2 in the Supplementary Information (SI)) to determine the interquartile values and the outliers. The latter, summarised in Table 2, are excluded from further consideration. It can be noticed in Table 2 that there are only four outliers for $IM_{inf,i}$, out of 85 data points in total. All of these are for the WWTPs based in the UK, with one being shared with Switzerland. Given that consumption of PPCPs in the UK is amongst the highest in the world

(WHO 2004), this would suggest that higher consumption leads to their higher influx into WWTPs (Lindqvist et al. 2005, Oosterhuis et al. 2013, Zhang & Geißen 2010).

Figure 2 Annual per-capita discharge $IM_{inf,i}$ of target PPCP compounds estimated using eqn. (1) and data from Table 1. Each point on the graph represents IM_{inf} for one target compound i .

Figure 3 Removal efficiencies $R_{efficiency,i}$ for target PPCP compounds estimated using eqn. (2) and data from Table 1. Each point in the graph represents $R_{efficiency}$ for one target compound i .

For the removal efficiencies (dataset B in Table 2), out of 142 data points, 10 are outliers, with the majority being for the WWTPs in the UK and Spain. However, no correlation is apparent between the number of outliers and the type of WWTP or operational parameters (for the latter two, see Table 1), despite a wide range covered by the data in the literature.

Table 2 Outliers for the influx of PPCP compounds (A dataset) and removal efficiencies (dataset B) in WWTPs

Compound i	WWTP location	Dataset A, $IM_{inf,i}$ (mg/inhab/year)	Total number of data points	Dataset B, $R_{efficiency,i}$ (%)	Total number of data points
Acetaminophen	UK	- ^a	4	94.45; 95.00	10
Diclofenac	UK	391.14	10	-	14
Ibuprofen	Spain; UK	-	10	44.83; 64.05	18
Trimethoprim	UK	260.40	8	-	13
Erythromycin	South Korea; UK	-	5	-81.82; 80.00	8
Sulfamethoxazole	UK	71.84	8	-	15
Metoprolol	US	-	3	90.48	6
Gemfibrozil	Spain	-	4	-133.33	7
Bezafibrate	-	-	4	-	5
Carbamazepine	UK	730.40	7	-	13
Estrone	-	-	7	-	10
17β-estradiol	Sweden	-	7	16.67	8
Triclosan	-	-	4	-	6
Caffeine	Spain	-	4	42.86	9

^a One of the values was much higher than the rest (see Table S1 in Supplementary information), but due to a small data sample, that value has not been considered as an outlier.

Figure 4 Minimum (a) and maximum (b) daily influx of target PPCPs estimated according to eqn. (3) for different size of the population served by WWTPs.

3.3. Estimation of concentration ranges of PPCP compounds in WWTPs

3.3.1. Daily influx ranges

The expected range of the daily influx of the target compounds into WWTPs, $\alpha_{range,i}$, estimated by eqn. (3) is given in Figure 5; for further details, see Table S3 in SI. The figure shows minimum (Figure 5a) and maximum (Figure 5b) values, taking into account the size of the population p served by WWTP. As can be seen, the expected daily influx of PPCP compounds is correlated linearly with the size of the population. This is in congruence with the assumption discussed in the previous section that a greater per-capita consumption of PPCPs leads to a higher influx of their compounds into WWTPs. For example, it can be inferred from Figure 4Figure 5 that a WWTP serving 200,000 inhabitants has an expected daily influx of acetaminophen in the range of 600 g/day to 10 kg/day while that serving twice as many people can expect double the influx.

The PPCP compound with the highest estimated influx is acetaminophen, followed by ibuprofen and caffeine. This is not surprising since all three products are available over the counter and used widely. The lowest influx is found for the hormones 17 β -estradiol and estrone.

3.3.2. Influent concentration ranges

The influent concentration range of PPCP compounds in a WWTP, $\beta_{range,i}$, calculated according to eqn. (4) for the average per-capita influent of 428 L/inhab/day, is given in Table 3. As can be seen, the expected mean concentration for most compounds ranges between 0.02 μ g/L for 17 β -estradiol to 66.9 μ g/L for acetaminophen. In the worst case, the latter can reach 127 μ g/L; the next worst are ibuprofen with 6.1 μ g/L and caffeine at 5.7 μ g/L. The lowest minimum concentrations can be expected for metoprolol and 17 β -estradiol (0 μ g/L or below detection levels).

Table 3 Estimated influent concentration ranges for the target PPCP compounds^a

Compound i	$\beta_{range,i}$ (μ g/L)			Variation ($\beta_{max,i} - \beta_{min,i}$) (μ g/L)
	$\beta_{min,i}$	$\beta_{mean,i}$	$\beta_{max,i}$	
Acetaminophen	6.87	66.9	127	120
Diclofenac	0.06	0.52	0.97	0.91
Ibuprofen	1.04	3.57	6.10	5.06
Trimethoprim	0.08	0.16	0.24	0.16
Erythromycin	0.57	0.84	1.11	0.54
Sulfamethoxazole	0.03	0.11	0.20	0.17
Metoprolol	0.00	0.04	0.08	0.08
Gemfibrozil	0.02	0.09	0.17	0.15
Bezafibrate	0.03	0.19	0.35	0.31
Carbamazepine	0.10	0.69	1.29	1.19
Estrone	0.03	0.05	0.06	0.03
17 β -estradiol	0.00	0.02	0.04	0.03
Triclosan	0.42	0.59	0.76	0.33
Caffeine	3.06	4.40	5.74	2.68

^a $q=428$ L/inhab day.

3.3.3. Expected removal ranges

To estimate the expected concentration range $\gamma_{range,i}$ of PPCPs in the WWTP effluent (eqn. (5)), it was first necessary to determine the expected range of removal efficiencies $R_{range,i}$ for each compound using dataset B (see Table S2 in SI). As shown in Figure 5 and Table S4, the expected removal efficiencies vary greatly with the lowest removal ($\leq 25\%$) expected for erythromycin, metoprolol, carbamazepine and estrone and the highest ($>90\%$) for acetaminophen, ibuprofen and caffeine. For some compounds (gemfibrozil, carbamazepine and estrone), negative removal efficiencies can be expected resulting in a higher concentration in the effluent than in the influent into WWTP. As mentioned earlier, this is due to possible transformation, recombination and/or accumulation of the compounds during the secondary treatment (Gao et al. 2012, Kagle et al. 2009, Verlicchi et al. 2012). For instance, among the PPCPs, carbamazepine has the lowest sorption and

biodegradability in wastewater treatments (Clara et al. 2004, Onesios et al. 2009, Ying et al. 2009). Estrone also has an unpredictable behaviour owing to an irregular sorption potential, dependence on the oxidation conditions and microbial activity in biological treatment (Atkinson et al. 2012, Esperanza et al. 2007, Evgenidou et al. 2014, Koh et al. 2008). By contrast, the lowest variation in the removal efficiencies ($\leq 1\%$) was found for caffeine and acetaminophen, suggesting that their removal is not dependent on the type of treatment or operating conditions of the plant.

However, the variation in the removal efficiencies could also be attributed to a wide variation in their physicochemical properties which can impair their removal by conventional wastewater treatment methods (Daughton & Ternes 1999, Jelic et al. 2011, Onesios et al. 2009, Ying et al. 2009). To examine the possible effects of this, some physicochemical properties of the target compounds were considered in relation to their removal efficiencies estimated here. As shown in Table 4 and Figures S2 and S3 in the SI, the acidic compounds were found to have moderate removal efficiencies (30%-62.5%) and removal variations (35-80%), with ibuprofen being the only exception. The basic compounds exhibited more extreme mean removal efficiencies (lower than 22.5% or higher than 80%) and the removal variation ($<30\%$ and $>80\%$). These observations are in agreement with the findings by other authors related to the behaviour of acidic PPCPs during biological treatment and their presence in the environment (Metcalf et al. 2003, Quintana et al. 2005, Thomas & Foster 2005, Wang et al. 2010).

Figure 5 – Estimated range of WWTP removal efficiencies ($R_{\text{range},i}$) for the target compounds.

Table 4 - Estimated removal efficiencies of the target PPCPs based on their physicochemical properties

Compound <i>i</i>	MW ^a (g/mol)	Log K _{ow} ^a	pK _a ^a	K _d (L/kg)	Mean removal efficiency, <i>R</i> _{mean,<i>i</i>} (%)	Removal efficiency variation (%)
Carbamazepine	236.27	2.45	13.90	135.0 ^c	-5.00	90.0
Bezafibrate	361.83 ^b	4.30 ^b	3.60 ^b	-	55.00	40.0
Diclofenac	296.15	0.70	4.20	118.0 ^c	40.00	80.0
Ibuprofen	206.23	3.97	4.90	227.51 ^d	93.50	11.0
Gemfibrozil	250.34	4.77	4.70	19.30 ^c	30.00	70.0
Sulfamethoxazole	253.28	0.89	5.70	77.00 ^c	62.50	35.0
Trimethoprim	290.30	0.91	6.80	253.00 ^c	42.50	65.0
Triclosan	289.55	4.76	7.80	8,600.0 ^e	89.50	15.0
Erythromycin	733.95 ^b	3.10 ^b	8.90 ^b	74.00 ^c	12.50	25.0
Acetaminophen	151.17	0.46	9.40	0.42 ^d	99.49	1.00
Metoprolol	267.30	2.15	9.60	-	22.50	25.0
17 β -estradiol	272.20	4.01	10.34	354.81 ^f	80.00	30.0
Caffeine	194.19	-0.07	10.40	19.00 ^g	99.45	0.90
Estrone	270.40	3.13	10.46	293.00 ^f	-25.00	150

MW: molecular weight. K_{ow}: octanol-water partition coefficients. pK_a: acid dissociation constant. K_d: solid–water distribution coefficient.

^a Behera et al. (2011)

^b Muñoz et al. (2008)

^c Radjenović et al. (2009)

^d StuerLauridsen et al. (2000)

^e Stasinakis et al. (2010)

^f Carballa et al. (2008)

^g Karnjanapiboonwong et al. (2011).

Table 5 Estimated effluent concentration ranges for the target PPCP compounds^a

Compound <i>i</i>	$\gamma_{range,i}$ ($\mu\text{g/L}$)			Variation ($\gamma_{max,i} - \gamma_{min,i}$) ($\mu\text{g/L}$)
	$\gamma_{min,i}$	$\gamma_{mean,i}$	$\gamma_{max,i}$	
Acetaminophen	0.00	0.64	1.28	1.28
Diclofenac	0.01	0.49	0.97	0.96
Ibuprofen	0.01	0.37	0.73	0.72
Trimethoprim	0.02	0.12	0.21	0.19
Erythromycin	0.43	0.77	1.11	0.68
Sulfamethoxazole	0.01	0.06	0.11	0.10
Metoprolol	0.00	0.04	0.07	0.07
Gemfibrozil	0.01	0.09	0.17	0.17
Bezafibrate	0.01	0.12	0.22	0.22
Carbamazepine	0.06	0.99	1.93	1.87
Estrone	0.02	0.07	0.13	0.11
17 β -estradiol	0.002	0.008	0.013	0.011
Triclosan	0.01	0.07	0.14	0.12
Caffeine	0.00	0.03	0.06	0.05

^a q=428 L/inhab.day.

3.3.4. Effluent concentration ranges

The expected concentration range $\gamma_{range,i}$ of PPCPs in the WWTP effluent, estimated by using the influent concentration and the removal efficiency ranges (eqn. (5)), are summarised in Table 5. The results suggest that, similar to the influent concentrations, the minimum mean effluent concentration is expected for 17 β -estradiol (0.008 $\mu\text{g/L}$). However, unlike the influent concentrations, the highest mean effluent value was found for carbamazepine (0.99 $\mu\text{g/L}$); this is due to its accumulation and inefficient removal in WWTPs.

3.3.5. Sludge concentration ranges

The concentration ranges $S_{range,i}$ of the target PPCP compounds in the sludge from WWTPs, calculated according to eqn. (6), are given in Figure 6 and Table S5 in the SI. Following the trend for the influent concentrations, the highest mean concentrations in the sludge are expected for triclosan and ibuprofen (2,526.38 and 791.62 $\mu\text{g/kg}$, respectively) and the lowest for sulfamethoxazole, 17 β -estradiol, and gemfibrozil (all below a mean concentration of 9 $\mu\text{g/kg}$).

These results are in broad agreement with previous estimates. For instance, according to the findings by McClellan & Halden (2010), triclosan, erythromycin, caffeine and ibuprofen were found at the highest concentration in 94 wastewater treatment plants in the district of Columbia, US. This is in accordance with the present work, where these three compounds have the highest mean concentrations. Although triclosan in McClellan & Halden (2010) had a much higher mean concentration (10,000 $\mu\text{g/kg}$), caffeine, ibuprofen, erythromycin, trimethoprim and sulfamethoxazole were in the same range as calculated here. The results for these and the other compounds obtained in this work are also in agreement with the ranges obtained in the literature (Petrovic et al. 2009, Verlicchi & Zambello 2015). The only exception was found to be gemfibrozil which appears to be underestimated in the current work. This is possibly due to its recalcitrant behaviour, as noted by some other authors who reported its variable sorption in sewage sludge (Radjenović et al. 2009, Ying et al. 2009).

Figure 6 Estimated sludge concentration ranges ($S_{\text{range},i}$) for the target PPCP compounds. (Values calculated from eq. (6) and K_d values from Table 4; $q=428$ L/inhab.day and $s_{\text{DM}}=50$ g/inhab.day)

Figure 7 – Predicted environmental concentration (PEC) of target PPCP compounds in freshwaters for the mean expected effluent concentration ($\gamma_{\text{mean},i}$) and for different freshwater flows: F1 = 5bn L/day; F2 = 500 ML/day; F3 = 100 ML/day; F4 = 50 ML/day.

3.4. Estimation of freshwater concentrations of PPCPs

The expected mean concentrations in freshwater bodies ($PEC_{mean,i}$), estimated according to eqn. (7) and based on the mean concentrations $\gamma_{mean,i}$ of PPCPs in WWTP effluents, are given in Figure 7. The figure shows the $PEC_{mean,i}$ values for different freshwater flows, ranging from 50 ML/day to 5 bn L/day and for effluent flows from WWTP varying from 31.5–442 ML/day. The latter corresponds to a WWTP serving 1 million inhabitants. For example, if a WWTP discharges 442 ML/day to a freshwater body with a 50 ML/day average flow, the mean expected concentration of acetaminophen is around 580 ng/L. If a WWTP discharges 150 ML/day to a body with a flow of 500 ML/day, the mean PEC of acetaminophen is expected to be around 150 ng/L. The best-fit curves given in Figure 7 can be used to estimate the values of $PEC_{mean,i}$ for each target PPCP over the flow ranges considered here. It can be noted from the figure that the best-fit relationship between the PEC and the volume of WWTP effluent changes with the freshwater flow: it is logarithmic for the lower flow range (50–100 ML/day), polynomial for the mid-range (500 ML/day) and linear for the highest flow (5 bn L/day).

4. **Conclusions**

This paper has proposed a new methodology for estimating expected concentrations of PPCPs in influents, effluents and sludge of conventional WWTPs, as well as their expected concentrations in freshwaters. Application of the methodology has been illustrated for 14 PPCPs for which the data were available; however, the methodology is generic and can be applied to other PPCPs or further emerging pollutants if and when the data become available. One of the advantages of this methodology is that enables more accurate and yet relatively simple estimates of the concentrations of PPCPs, reducing the need for direct measurements. Another advantage is that the database can be continuously updated, adding other compounds and types of WWTP.

The methodology could also assist in environmental risk assessments (ERA) by linking consumption of PPCPs with environmental concentrations, taking into account the actual measured data rather than relying solely on production or consumption data for PPCPs. Moreover, the outputs could be used for development of policy and regulations. For example, regulation could impose limits on the concentrations of these compounds in WWTPs effluents, also determining the necessity for monitoring the effluents for the presence of PPCP compounds. This is important not only because of the environmental pollution but also due to the increasing pressure on traditional water resources associated with pollution, urbanisation and climate change, which is necessitating reuse of wastewater in many regions worldwide. As a result, legislation to limit the presence of PPCP compounds in wastewaters intended for reuse as potable water has been considered in some regions. For example, California has recently introduced regulations for monitoring of some PPCPs in wastewaters intended for reuse (EPA 2012, NRC 2012).

Depending on the intended wastewater reuse, the adoption of advanced treatment techniques in WWTPs may be necessary in future to aid the removal of PPCPs. Thus, the methodology proposed in this work could also be applied to estimate the concentrations that such plants should expect in their influents from conventional treatment and the removal efficiencies that they should achieve to render the reused water safe for human health and aquatic organisms. This in turn could aid the selection and design of most effective advanced treatment plants to enable wastewater reuse.

Furthermore, environmental legislation for the traditional sewage sludge handling routes, such as agricultural spreading, is becoming increasingly more stringent, with some PPCP compounds already monitored in some European countries (Ellis 2006, Moran & Dann 2008, Roig 2010). Therefore, the results of this research could also be helpful for these purposes, helping to determine the expected concentrations in the sludge and to set the appropriate legislative limits.

Nomenclature

A	dataset of $IM_{inf,i}$ values (mg/inhab·year)
B	dataset of $R_{efficiency,s}$ values (%)
$C_{eff,i}$	concentration of PPCP compound i in the effluent of a WWTP ($\mu\text{g/L}$)
$C_{inf,i}$	concentration of PPCP compound i in the WWTP influent ($\mu\text{g/L}$)
F	daily flow of a freshwater body (L/day)
$IM_{inf,i}$	annual per-capita influx of PPCP compound i into WWTP (mg/inhab·year)
$K_{d,i}$	solid–water distribution coefficient of compound i (L/kg)
p	population served by WWTP (number of inhabitants)
$PEC_{range,i}$	predicted environmental concentration range of compound i in freshwater after the release of WWTP effluent ($\mu\text{g/L}$)
q	average per-capita daily wastewater influent into WWTP (L/inhab·day)
Q	daily wastewater influent into WWTP (L/day)
$R_{efficiency,i}$	removal efficiency of PPCP compound i in a WWTP (%)
S_{DM}	per-capita amount of dry matter in the sludge (kg/inhab·day)
$S_{range,i}$	concentration range of compound i in the sludge (kg/kg)

Greek symbols:

$\alpha_{range,i}$	estimated daily influx range for compound i in WWTP (g/day)
$\beta_{range,i}$	estimated influent concentration range for PPCP compound i ($\mu\text{g/L}$)
$\gamma_{range,i}$	estimated effluent concentration range for PPCP compound i ($\mu\text{g/L}$)
$\lambda_{range,i}$	$IM_{inf,i}$ value for compound i within the interquartile range (mg/inhab·year)

Acknowledgements

The authors would like to acknowledge CAPES/CNPq for the financial support.

Appendix A. Supplementary data

The Supplementary information includes data on datasets A and B, physicochemical properties, removal efficiency of the target PPCPs in WWTPs and concentrations of PPCPs in the sludge.

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A methodology for estimating concentrations of compounds from pharmaceuticals and personal care products in wastewater treatment plants and in freshwaters

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Supplementary information

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S3. Concentrations of PPCPs in the sludge

S1. Datasets A and B**Table S1.** Estimated annual per-capita influx into WWTPs of target PPCPs (dataset A)^a

Source ^b	Annual per-capita discharge of target PPCP compounds, $IM_{inf,i}$ (mg/inhab·year) ^a													
	Acetami- nophen	Diclo- fenac	Ibu- profen	Trimet- hoprim	Eryth- romycin	Sulfame- thoxazole	Meto- prolol	Gem- fibrozil	Beza- fibrate	Carbama- zepine	Estrone	17β- estradiol	Triclosan	Caffeine
Thomas & Foster (2004)		9.99	201.97										63.78	931.20
Atkinson et al. (2012)											9.80	9.80		
Behera et al. (2011)	1,122.38	22.45	329.23	29.93		13.47	0.75	29.93		14.97	7.48	0.60	82.31	374.13
Sim et al. (2010)	1,056.15	1.32	132.02		99.01			2.64		39.61				792.11
Nakada et al. (2006)			173.47							17.35	8.67	4.34	130.10	
Nakada et al. (2007)			53.96							10.79	5.40	2.70	74.19	
Leung et al. (2012)				28.23	141.13	14.11								
Xu et al. (2012)					154.71	8.99								
Gulkowska et al. (2008)				30.16	78.98									
Zhou et al. (2012)											12.17	6.08		
Sui et al. (2010)		46.01		39.43			13.14	5.26	5.26	19.72				788.67
Gracia-Lor et al. (2012)	4,022.30	38.69	1065.80	7.30		32.85		15.33	5.84					
Tauxe-Wuerersh et al. (2005)		280.42	413.24											
Lindqvist et al. (2005)		109.85	1461.02						54.93					
Kasprzyk-Hordern et al. (2009)	25,088.85	8.32	199.76	260.40	191.44	3.57	9.51		49.94	200.95				
Zhou et al. (2009)		391.14				71.84				730.40				
Zorita et al. (2009)		30.53	915.82								2.65	0.40		
Lindberg et al. (2005)				1.98		3.25								
Baronti et al. (2000)											8.93	2.23		
Watkinson et al. (2007)				24.82		26.28								

^a Estimated according to eqn. (1) and data in Table 1 in the paper.^b For the list of references, see the paper.

Table S2. Estimated removal efficiencies for the target PPCP compounds (dataset B)^a.

Source ^b	Removal rate, R _{rate,i} (%)													
	Acetami- nophen	Diclo- fenac	Ibu- profen	Trime- thoprim	Eryth- romycin	Sulfame- thoxazole	Meto- prolol	Gemfi- brozil	Beza- fibrate	Carbama- zepine	Estrone	17β- estradiol	Triclosan	Caffeine
Gao et al. (2012)						90.91				-100.00				98.33
Conkle et al. (2008)	99.95		99.19			92.42	90.48	-10.30		-50.00				99.88
Thomas & Foster (2004)		99.98	99.79										97.33	99.91
Batt et al. (2007)				96.71		77.50								
Yang et al. (2011)	99.94	95.45	99.45	54.10	20.59	83.85				-8.70			95.74	99.91
Lishman (2006)		5.00	95.50					44.44			66.67		100.00	
Atkinson et al. (2012)											-100.00	94.00		
Behera et al. (2011)	99.87	86.67	93.18	80.00		0.00	20.00	90.00		20.00	60.00	99.75	81.82	99.20
Sim et al. (2010)	100.00	0.00	99.99		80.00			99.50		33.33				99.67
Choi et al. (2008)	99.97			77.27		69.23				60.87				98.83
Nakada et al. (2006)			98.75							37.50	-25.00	50.00	83.33	
Nakada et al. (2007)			97.50							62.50	50.00	90.00	78.18	
Hashimoto (2007)											-33.33	83.33		
Leung et al. (2012)				5.00	0.00	30.00								
Xu et al. (2012)					13.95	40.00								
Gulkowska et al. (2008)				-9.52	7.27									
Zhou et al. (2012)											85.00	95.00		
Sui et al. (2010)		42.86		66.67			10.00	25.00	75.00	20.00				99.83
Gracia-Lor et al. (2012)	100.00	35.85	100.00	10.00		88.89		-133.33	25.00					
Carballa et al. (2004)			64.05			56.90					-100.00			
Radjenovic et al. (2009)	98.89	20.45	98.11	40.00	34.15	77.78	25.00	0.00	79.80	0.00				
Santos et al. (2006)			88.42							-66.67				42.86
Tauxe-Wuerersh et al. (2005)		0.00	78.57											
Maurer et al. (2007)							33.33							
Lindqvist et al. (2005)		65.00	91.73						34.00					
Kasprzyk-Hordern et al. (2009)	94.45	-42.86	84.52	47.49	13.66	66.67	12.50		45.24	-47.93				
Jones et al. (2007)	95.00		87.50											
Zhou et al. (2009)		91.84				83.33				54.10				
Roberts & Thomas (2006)	99.99	65.31	44.83	-53.85	-81.82									
Zorita et al. (2009)		-113.04	98.70								-250.00	16.67		
Lindberg et al. (2005)				12.00		53.66								
Baronti et al. (2000)											25.00	80.00		
Watkinson et al. (2007)				85.29		25.00								

^a Estimated according to eqn. (2) and data in Table 1 in the paper.^b For the list of references, see the paper.

Figure S1. Box plots for the dataset A

Table S3. Estimated influx ranges of PPCP compounds according to a served population p

Compound	$\alpha_{range,i}$ (g/day)		
	α_{min}	α_{mean}	α_{max}
Acetaminophen	2.9397E-03 x p	2.8623E-02 x p	5.4307E-02 x p
Diclofenac	2.7397E-05 x p	2.2192E-04 x p	4.1644E-04 x p
Ibuprofen	4.4658E-04 x p	1.5288E-03 x p	2.6110E-03 x p
Trimethoprim	3.2877E-05 x p	6.7123E-05 x p	1.0137E-04 x p
Erythromycin	2.4384E-04 x p	3.5890E-04 x p	4.7397E-04 x p
Sulfamethoxazole	1.3425E-05 x p	4.9178E-05 x p	8.4932E-05 x p
Metoprolol	2.0548E-06 x p	1.8836E-05 x p	3.5616E-05 x p
Gemfibrozil	8.2192E-06 x p	3.9726E-05 x p	7.1233E-05 x p
Bezafibrate	1.4247E-05 x p	8.1096E-05 x p	1.4795E-04 x p
Carbamazepine	4.1096E-05 x p	2.9589E-04 x p	5.5068E-04 x p
Estrone	1.3699E-05 x p	2.0548E-05 x p	2.7397E-05 x p
17 β -Estradiol	1.6438E-06 x p	9.0411E-06 x p	1.6438E-05 x p
Triclosan	1.8082E-04 x p	2.5205E-04 x p	3.2329E-04 x p
Caffeine	1.3096E-03 x p	1.8822E-03 x p	2.4548E-03 x p

Table S4. Estimated ranges for the removal of the target PPCP compounds in WWTPs

Compound i	Removal efficiency range $R_{range,i}$ (%)		
	R_{min}	R_{mean}	R_{max}
Acetaminophen	98.99	99.49	99.99
Diclofenac	0	40	80
Ibuprofen	88	93.5	99
Trimethoprim	10	42.5	75
Erythromycin	0	12.5	25
Sulfamethoxazole	45	62.5	80
Metoprolol	10	22.5	35
Gemfibrozil	-5	30	65
Bezafibrate	35	55	75
Carbamazepine	-50	-5	40
Estrone	-100	-25	50
17 β -estradiol	65	80	95
Triclosan	82	89.5	97
Caffeine	99	99.45	99.9

S2. Physicochemical properties and removal efficiency of target PPCPs in WWTPs

Figure S2. Mean removal efficiency of the target PPCPs in WWTPs for different molecular weights (a); octanol-water partition coefficients, K_{ow} (b); solid–water distribution coefficient K_d (c) and the acid dissociation constant, pK_a (d)

Figure S3. Variation in the removal efficiency of the target PPCPs in WWTPs for different molecular weights (a); octanol-water partition coefficients K_{ow} (b); solid–water distribution coefficient K_d (c) and the acidity index pK_a (d).

S3. Concentrations of PPCPs in the sludge**Table S5.** Estimated range of concentrations of the target PPCPs in the sludge ($S_{\text{range},i}$) based on the solid–water distribution coefficient ($K_{d,i}$)

Compound <i>i</i>	$K_{d,i}$ (L/kg)	$S_{\text{range},i}$ (µg/kg)			Variation ($S_{\text{max},i} - S_{\text{min},i}$) (µg/kg)
		$S_{\text{min},i}$	$S_{\text{mean},i}$	$S_{\text{max},i}$	
Acetaminophen	0.42	2.88	28.09	53.29	50.40
Diclofenac	118.00	7.45	60.35	113.25	105.80
Ibuprofen	227.51	231.24	791.62	1,351.98	1,120.74
Trimethoprim	253.00	18.88	38.54	58.20	39.33
Erythromycin	74.00	41.80	61.52	81.25	39.45
Sulfamethoxazole	77.00	2.39	8.77	15.14	12.75
Metoprolol	-	-	-	-	-
Gemfibrozil	19.30	0.37	1.79	3.20	2.84
Bezafibrate	-	-	-	-	-
Carbamazepine	135.00	12.76	91.88	171.00	158.24
Estrone	293.00	9.07	13.60	18.13	9.07
17β-estradiol	354.81	1.31	7.20	13.08	11.78
Triclosan	8,600.00	1,812.41	2,526.38	3,240.44	1,428.02
Caffeine	19.00	58.01	83.37	108.73	50.73

^a For $q=428$ L/inhab.day and $s_{\text{DM}}=50$ g/inhab.day.