Journal of Hazardous Materials 354 (2018) 81–90

Contents lists available at ScienceDirect

Journal of Hazardous Materials

journal homepage: www.elsevier.com/locate/jhazmat

Monitoring, mass balance and fate of pharmaceuticals and personal care products in seven wastewater treatment plants in Xiamen City, China

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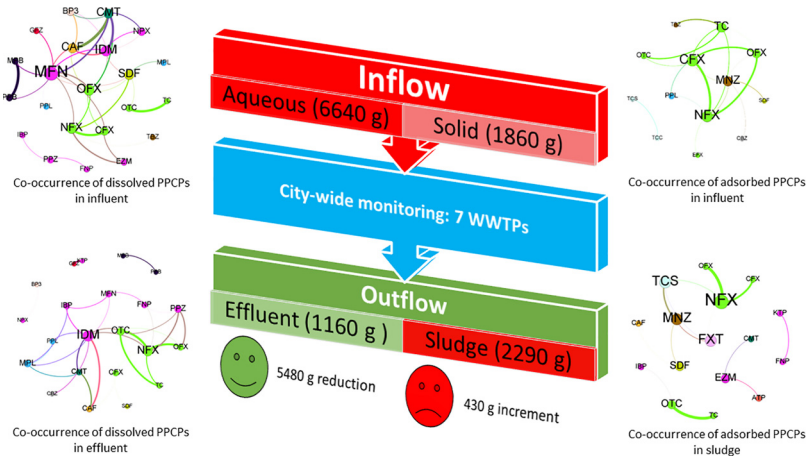
GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:
PPCPs
Co-occurrence
Mass balance
Temporal and spatial variations

ABSTRACT

The occurrence and fate of pharmaceuticals and personal care products (PPCPs) was investigated in seven wastewater treatment plants (WWTPs) in Xiamen City, China. Special emphasis was placed on their co-occurrence and the mass balances of both dissolved and adsorbed PPCPs in influent, effluent, and sludge samples. Results showed that PPCPs were widely detected and their co-occurrence was observed both in the wastewater and sludge that can be attributed to either their similar usage or similar physicochemical properties. These results further emphasize that some specific PPCPs have the potential as indicators or surrogate compounds to reduce the number of targeted PPCPs. The occurrence and distribution of PPCPs also showed strong spatial variations, as the PPCP mass loads per inhabitant were positively correlated with the urbanization levels. Both the removal efficiencies of dissolved PPCPs from the aqueous phase and mass loss proportion of the total PPCPs were evaluated and compared. Overall, a measured total amount of 8500 g PPCPs entered the seven WWTPs

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https://doi.org/10.1016/j.jhazmat.2018.04.064
Received 17 January 2018; Received in revised form 23 April 2018; Accepted 25 April 2018
Available online 26 April 2018
0304-3894/

daily via influent with 6640 g in the dissolved form, while 3450 g left the WWTPs. The large mass loads of antibiotics in the sludge and effluents indicated their potential adverse effects to the receiving environment.

1. Introduction

Pharmaceuticals and personal care products (PPCPs) have been an emerging concern since 1990s due to their continuous detection in the wastewater and the water bodies around wastewater treatment plants (WWTPs) [1]. Potential adverse effects of PPCPs on the biota and their habitat have been reported [2]. Consequently, great concerns have been raised on PPCP contamination since the PPCP usage and discharge tend to increase rapidly [2] with the population growth and evolving medical techniques. WWTPs are considered as the major unit for the removal of pollutants including PPCPs and to prevent their entry into the receiving water bodies [3]. Therefore, understanding of the PPCP occurrence and their fate during the wastewater treatment processes is of great importance.

Many previous studies have investigated the occurrence and distribution of PPCPs in the WWTPs and reported that the PPCPs were widely detected in the wastewater and sludge with the concentrations in ng/L-μg/L and μg/kg-mg/kg ranges, respectively [4]. However, the number of target PPCPs were limited [5] in some studies due to the limited availability of standards and the analytical method, hence, making it difficult to better understand their occurrence. In addition, the target PPCPs were different among the previous studies, which made it difficult to compare their pollution levels [6,7,8]. Recently, Hagemann noticed the site-specific co-occurrence of some endocrine disruptor compounds (EDCs) or PPCPs in the surface water, suggesting the potential of specific PPCPs as indicators or surrogates to predict the co-occurrence of related/associated PPCPs [9]. So far, limited studies have investigated the co-occurrence of PPCPs in WWTPs, which only focused on triclosan and triclocarban in the wastewater [10]. There is a knowledge gap on the co-occurrence of PPCPs, not only in wastewater but also in sludge and suspended solids.

Removal efficiencies of PPCPs from the aqueous phase, calculated as the difference between PPCPs concentrations in the influent and effluent, have often been used to investigate the fate of PPCP during the wastewater treatment processes [11]. Results have shown that the removal efficiencies ranging from negative values to 100%, which were mainly dependent upon the PPCP properties or treatment processes. In addition, the mass balance assessment of PPCPs, which is based on the dissolved concentrations in the aqueous phase and adsorbed concentration in the solid phase, provide better understanding of the fate and pathway of PPCPs dissipation, and their removal mechanism, namely adsorption or degradation/transformation [12]. However, limited number of studies have considered the PPCPs on the suspended solids during the mass balance assessment [13,14], which may lead to the overestimation or underestimation of the PPCP losses and bias for PPCP fate.

Previous studies have indicated that PPCPs levels increased with the urbanization levels [15,16]. Considering the rapid urbanization in China with subsequent environmental costs, especially in the megacities, it is necessary to perform a city-wide study to better understand the PPCP distribution in the wastewater treatment systems. In this study, we collected influent, effluent, and excess sludge samples from all the seven WWTPs in Xiamen, which is a major city in the southeast China. The occurrence and distribution of dissolved PPCPs in the aqueous phase along with the adsorbed PPCPs on the sludge as well as suspended solids were investigated with special emphasis on their co-occurrence. PPCP fate, based on the removal efficiencies from the aqueous phase and mass balance assessment during the wastewater treatment processes was evaluated. In addition, the city-wide mass loads were also estimated with special emphasis on their relationship with the urbanization levels.

2. Experimental

2.1. Sample collection

Xiamen is a subtropical monsoonal city located in the southeast of China. The resident population was 3.92 million in 2016 with urbanization rate of 89.0% [17]. Seven WWTPs (W1-W7) undertake over 92% of wastewater from the Xiamen city, with two additional small scale WWTPs under test run. Composite samples (0:00-24:00) of influent, effluent, and sludge were collected by automatic samplers (Hach, Sigma SD900) in W1-W7 from 28th February to 6th March, 2016. The treatment processes of each WWTP are shown in Fig. S1 in the supplementary information (SI).

2.2. Sample analysis

Wastewater, sludge, and suspended solid samples were prepared and analyzed under the guidance of EPA 1694 [18] with slight modifications. Details are provided in SI. The wastewater sample (500 mL for influent and 1000 mL for effluent) was filtered to get water and suspended solid samples for PPCPs extraction. For sludge analysis, 0.100 g freeze dried sludge was used. 42 PPCPs (Table S1 in SI) were detected using high performance liquid chromatography tandem mass spectrometry (HPLC-MS/MS, ABI 3200 QTRAP). Chromatographic separation was performed by using a Kinetex C18 column (100 mm × 4.6 mm, 2.6 μm, Phenomenex) from Shimadzu LC system (Shimadzu). A binary gradient was used as shown in SI Table S2. An ABI triple quadrupole (QqQ) MS were applied in both positive and negative modes for the mass spectrometric measurement. Multiple reaction monitoring (MRM) mode was applied with the monitored targets shown in Table S1 in SI.

2.3. Quality assurance and quality control (QA/QC)

QA/QC was implemented for the accuracy of the quantification of the target PPCPs. Two highest precursor ion/product ion transition pairs (SI Table S1) were used for the PPCPs identification. Method quantification limits (MQLs), which were evaluated based on the instrument quantification limits and analyte recoveries, were in the range of 0.0020–5.0 ng/L for wastewater and 0.070–5.4 μg/kg for sludge (SI Table S1). An instrument blank and a procedural blank were applied for each batch, and results showed the absence of target analytes in the blanks. In addition, the matrix spiked was conducted in each batch. The recoveries of 70% target PPCPs were in the range of 40–130% for the wastewater and sludge, which met the requirement for the simultaneous analysis of diverse targets in the challenging matrices [18]. Details are provided in SI Table S1.

2.4. Data processing

Mass load of each PPCP in the sludge, influent, and effluent was calculated according to Eqs. (1)–(3), respectively. We assumed that the load of influent was equal to the load from discharge source via effluent and sludge, and the losses via transit or volatility were considered negligible according to the steady state assumption [19]. Therefore, the mass balance was performed via Eq. (4) and mass loss portion was calculated via Eq. (5). In addition, the removal efficiency of each PPCP from the aqueous phase was calculated using Eq. (6) based on the

dissolved concentrations only.

$$M_{excess\ sludge} = C_{sludge} \times Q_{excess\ sludge} \quad (1)$$

$$M_{influent} = C_{influent} \times Q_{wastewater} + C_{influent\ (SS)} \times Q_{wastewater} \times C_{SS} \quad (2)$$

$$M_{effluent} = C_{effluent} \times Q_{wastewater} + C_{effluent\ (SS)} \times Q_{wastewater} \times C_{SS} \quad (3)$$

$$M_{loss} = M_{influent} - M_{effluent} - M_{excess\ sludge} \quad (4)$$

$$M_{loss}\% = \frac{\sum M_{influent} - \sum M_{effluent} - \sum M_{excess\ \ sludge}}{M_{influent}} \times 100 \quad (5)$$

$$Aqueous\ removal\ efficency\,(\%) = \frac{C_{influent} - C_{effluent}}{C_{influent}} \times 100 \quad (6)$$

Where M refers to the calculated mass load of each pollutant everyday (g/d); $C_{influent}$ and $C_{effluent}$ are the dissolved PPCPs concentration (10^{-9} g/L) in the influent and effluent, respectively; C_{sludge}, $C_{influent\ (SS)}$, and $C_{effluent(SS)}$ are the adsorbed PPCPs in the sludge, suspended solids in the influent and effluent, respectively (10^{-9} g/g); C_{SS} indicates the suspended solid concentration in the wastewater (g/L); $Q_{excess\ sludge}$ and $Q_{wastewater}$ mean the daily flux of excess sludge and wastewater (L/d). The daily values of $Q_{wastewater}$, $Q_{excess\ sludge}$, $C_{influent(ss)}$, $C_{effleunt(ss)}$ were provided in our previous study regarding the study of bisphenol analogues [20].

Friedman test (PAST v 2.17) was used to compare the temporal and spatial variations of PPCPs in the 7 WWTPs in 7 days, and principal component analysis (PAST v 2.17) was conducted to investigate spatial variations of PPCPs distribution in 7 WWTPs. Network analysis, which can reveal the co-occurrence relationship between entities or parameters, has been widely used in the area of mathematics, computer science, social science and biology [21,22]. For network analysis, pairwise Spearman's rank coefficients between all PPCPs with occurrence in more than 50% of analyzed samples were calculated using R package Hmisc [23]. The false discovery rate (Benjamini-Hochberg adjustment) was used for multiple testing corrections [24]. Subsequently, the highly significant associations (Spearman's correlation: $r \geq 0.6$, FDR-adjusted p-value < 0.01) between PPCPs were exported using R package igraph [25], and were visualized using Gephi [26]. The custom R scripts for network analysis were published in our previous work [27].

3. Results and discussion

3.1. General occurrence

Forty-two target PPCPs were detected at least once in the wastewater or sludge samples. The concentration ranges, median concentrations, and arithmetic mean concentrations, together with their detection frequencies of both dissolved PPCPs in the influent and effluent, and adsorbed PPCPs onto the suspended solids and sludge based on the 7-day sampling in all WWTPs are shown in Table S3 and S4, respectively.

3.1.1. PPCPs in influent

Forty-two PPCPs were detected at least once in the influent, and they are arranged in a high to low order according to their concentrations as shown in Fig. 1A. The most abundant categories included stimulant, non-steroidal anti-inflammatory drugs (NSAIDs), and antibiotics. For example, the median concentration of caffeine was 2160 ng/L with a peak value of 6220 ng/L observed on February 28th in W1. The median concentrations of acetaminophen, ibuprofen, norfloxacin, ofloxacin, ketoprofen reached 250–2500 ng/L. In addition, compounds with median concentrations in the range of 10–187 ng/L included methyl paraben, propyl paraben, oxytetracycline, tetracycline hydrochloride, ciprofloxacin, metoprolol, fenoprofen, naproxen, acetophenone, fluoxetine, (3-(4-methylbenzylidene)-camphor), triclocarban, triclosan, aspartame, and carbamazepine. These levels of PPCPs were similar to those detected in Guangzhou [28], Hong Kong [29], Beijing [30], Sweden [31], and Xiamen [16] with the exception of one study in Beijing, where nearly forty times higher concentration of caffeine was observed [32].

3.1.2. PPCPs in effluent

In the effluent, forty-two PPCPs were detected at least once, and the median concentrations range from BDLs (below detection limits) to 175 ng/L as shown in Fig. 1B. Ketoprofen, ofloxacin, metoprolol, ibuprofen, norfloxacin, caffeine, oxytetracycline, triclocarban, and propyl paraben were among the most abundant PPCPs, with median concentrations ranging from 18 to 180 ng/L. PPCPs, including caffeine, ibuprofen, oxytetracycline, propyl paraben, and norfloxacin, which showed higher levels in the influent, were also detected in higher concentration levels in the effluent.

3.1.3. PPCPs in sludge

Forty-one PPCPs were detected in the sludge. As shown in Fig. 1C, antibiotics were abundant in the sludge with highest median concentration of 9140 μg/kg for norfloxacin, followed by ofloxacin (3080 μg/kg), oxytetracycline (887 μg/kg), tetracycline hydrochloride (542 μg/kg) and ciprofloxacin (405 μg/kg). Although, the antimicrobials were with relatively low concentrations in the influent, they accumulated in the sludge, with triclocarban and triclosan concentrations of 1090 μg/kg and 172 μg/kg, respectively. The levels of antimicrobials detected in this study were 2–3 orders of magnitude lower than those detected in USA (530–30,000 μg/kg [33] and 133,000 μg/kg [34] for triclosan). In sludge, miconazole, acetophenone, ketoprofen, methyl paraben, fluoxetine, ibuprofen and fenoprofen were detected in a considerable concentration range of 50–130 μg/kg, while the others were below 15.0 μg/kg.

3.1.4. PPCPs in the suspended solids

PPCPs adsorbed on the suspended solids were also investigated in this study, and thirty-nine of them were detected at least once. Range of the PPCPs concentrations on the suspended solids of the influent was from BDL to 24,000 μg/kg. Norfloxacin (9580 μg/kg), ofloxacin (2570 μg/kg), oxytetracycline (2180 μg/kg), tetracycline hydrochloride (1470 μg/kg), and triclocarban (616 μg/kg) were top five PPCPs adsorbed on the influent suspended solid (Fig. 1D). In the effluent, ofloxacin (2240 μg/kg), triclocarban (968 μg/kg), methyl paraben (882 μg/kg), oxytetracycline (776 μg/kg), and norfloxacin (691 μg/kg) had highest median concentration levels (Fig. 1E).

So far, limited information on the PPCP distribution on the suspended solids has been provided [6,14]. In the present study, marginal difference was observed between the median concentrations of PPCPs (above the method detection limits) in the sludge and suspended solids of the effluent (Kruskal-Wallis test, $p = 0.056$), while no significant difference was observed between sludge and suspended solids of the influent (Kruskal-Wallis test, $p = 0.732$), which suggested that the PPCP levels on the sludge may be applied to indicate the information about the suspended solids. However, some exceptions were also noticed. For instance, the median concentration of aspartame was 65 times higher in the suspended solids (199 μg/kg) than that in the sludge (3.05 μg/kg). In case of ofloxacin and triclocarban, the respective median concentrations on the sludge (3080 and 1090 μg/kg) were also higher than that on the suspended solids in the influent (484 and 510 μg/kg), respectively (Table S4).

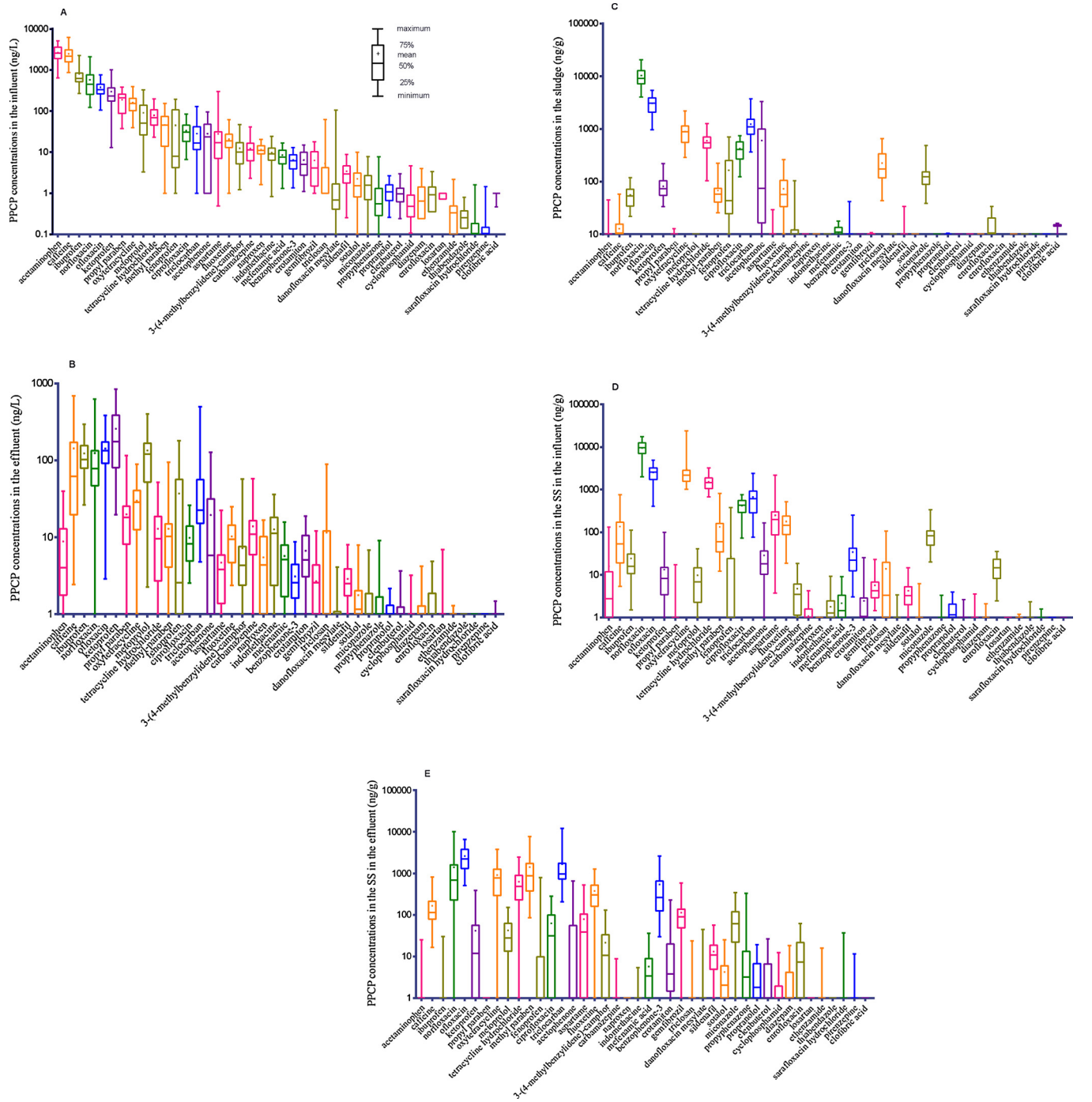

Fig. 1. PPCP concentrations: (A), dissolved PPCPs in influent (ng/L); (B), dissolved PPCPs in effluent (ng/L); (C), PPCPs in sludge (ng/g); (D), adsorbed PPCPs in suspended solids of influent (ng/g); (E), adsorbed PPCPs in suspended solids of effluent (ng/g).

3.1.5. PPCP co-occurrence

Due to the similar usage, properties, disposal and environmental behavior, the co-occurrence of PPCPs was reported earlier [10]. In this study, network analysis was conducted to investigate the co-occurrence of PPCPs visualized using Gephi as shown in Fig. 2. The node indicates each PPCP, where the bigger node size indicates more relations of one PPCP with the others. The solid lines indicate the positive correlations between PPCPs with stronger correlations in thick lines than fine lines. In the influent, PPCPs with similar usage showed co-occurrence (Fig. 2A). For example, strong correlation was observed in the preservatives (propyl paraben and methyl paraben, r = 0.89), tetracycline antibiotics (tetracycline hydrochloride and oxytetracycline, r = 0.86), quinolone antibiotics (norfloxacin, ciprofloxacin, and ofloxacin, r > 0.65), and NSAIDs (fenoprofen, propyphenazone, and ibuprofen, r > 0.63). In the effluent, the relationship among PPCPs was complicated as shown in the Fig. 2B. Co-occurrence of PPCPs in the effluent might be due to PPCP concentrations in the influent, together with their degradation or transformation during wastewater treatment process, and their translocation between liquid and solid phase. In the sludge, PPCPs with similar physico-chemical properties showed co-occurrence (Fig. 2C). For example, strong correlation was observed among ciprofloxacin, norfloxacin, and ofloxacin (r > 0.78), between oxytetracycline and tetracycline hydrochloride (r = 0.86), and between miconazole and triclosan (r = 0.75). Their similarity in environmental

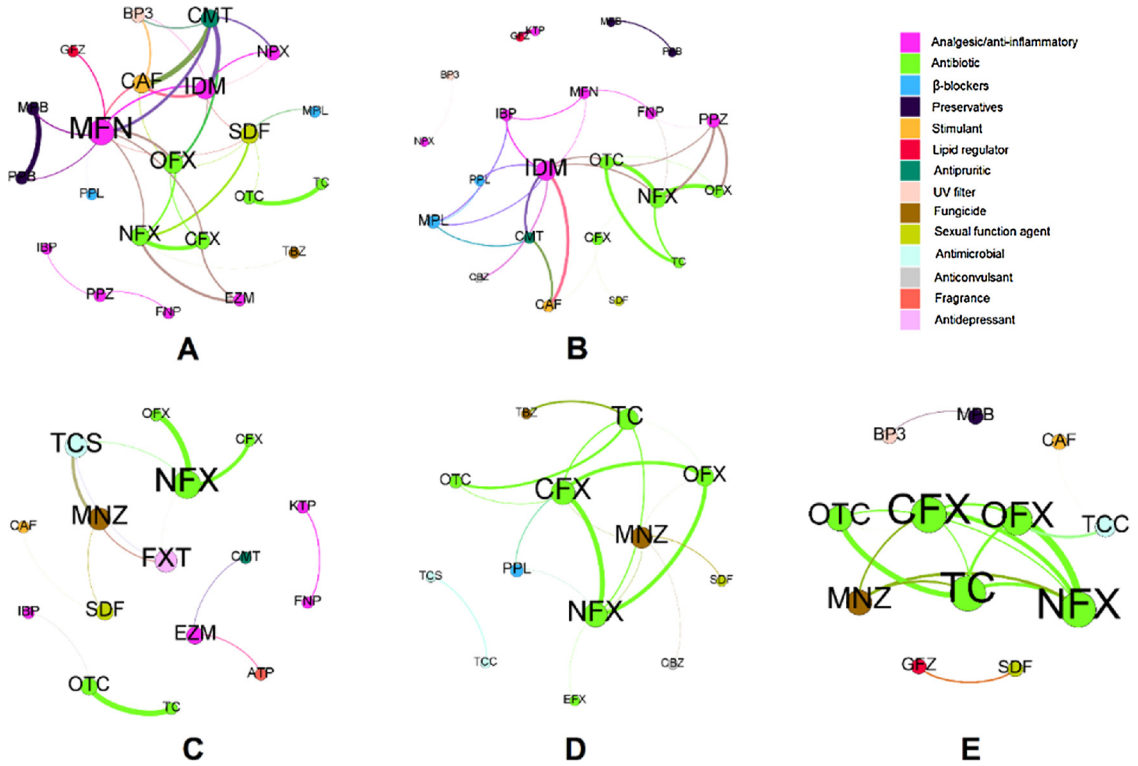

Fig. 2. PPCP co-occurrence: (A), dissolved PPCPs in influent; (B), dissolved PPCPs in effluent; (C), adsorbed PPCPs in excessive sludge; (D), adsorbed PPCPs in the suspended solid of influent; (E), adsorbed PPCPs in the suspended solid of effluent. Abbreviations: ATP, acetophenone; BP3, benzophenone-3; CAF, caffeine; CBZ, carbamazepine; CFX, ciprofloxacin; CMT, crotamiton; EFX, enrofloxacin; EZM, ethenzamide; FNP, fenoprofen; FXT, fluoxetine; GFZ, gemfibrozil; IBP, ibuprofen; IDM, indomethacin; KTP, ketoprofen; MFN, mefenamic acid; MNZ, miconazole; MPB, methyl paraben; MPL, metoprolol; NFX, norfloxacin; NPX, naproxen; OFX, ofloxacin; OTC, oxytetracycline; PPB, propyl paraben; PPL, propranolol; PPZ, propyphenazone; SDF, sidenafil; TBZ, thiabendazole; TC, tetracycline hydochloride; TCC, triclocarban; TCS, triclosan.

behavior and co-occurrence on sludge might be due to the similar physicochemical properties, including the adsorption onto the sludge and degradation during the wastewater treatment processes. In the suspended solids of influent and effluent (Fig. 2D and E), the antibiotics showed strong correlations ($r > 0.61$) owing to their similar physicochemical properties, molecular structures, and adsorption potential.

The co-occurrence of PPCPs in the wastewater, sludge, and suspended solids in our study confirmed the findings of Hagemann and associates, which indicated that the specific co-occurring PPCPs can potentially serve as indicator or surrogate compounds to reduce the number of target compounds [9]. For example, due to the co-occurrence of quinolone antibiotics in influent, effluent and sludge, one of quinolones (norfloxacin, ofloxacin or ciprofloxacin) can be used as indicator for the long-term monitoring to indicate the quinolone levels. Consequently, the cost could be decreased in terms of chemicals, labor and analysis time by reducing sample preparation, detection, and data processing.

3.2. Mass loads of PPCPs

Mass loads of dissolved and adsorbed forms of the PPCPs in influent, effluent, and excess sludge were calculated via Eqs. (1)–(3), and are presented in Table 1 and Table S5 to understand the city-wide pollution inventory of PPCPs. Overall, 8500 g of the investigated PPCPs entered the seven WWTPs via influent with 6640 g in the dissolved form, and 1160 g and 2290 g left the WWTPs via effluent and excess sludge on daily basis, respectively. The PPCP mass loads in the excess sludge indicated the potential risk of PPCPs via sludge disposal, as 83% of the sludge in China is disposed-off improperly [35]. Among the different therapeutic groups, NSAIDs, stimulant, and antibiotics showed high mass loads in the influent, with the values of 2980 g, 2200 g, and 2810 g, respectively. The antibiotics showed higher mass loads in the effluent with the values of 304 g. Where, both the antibiotics and antimicrobial agents showed high mass loads (1937 g and 178 g, respectively) in the sludge. The large amount of antibiotics in the effluent and sludge can potentially induce antibiotic resistance in the receiving biotic component of the ecosystem [36]. In addition, PPCP mass loads per inhabitant based on the served population were also calculated and are presented in Table 2. Generally, the mass load per inhabitant (μg/d·inhabitant) of the total PPCPs in each WWTP were 662–3090, 72-449 and 87-1040 in the influent, effluent, and excess sludge, respectively.

3.3. Temporal and spatial variations

3.3.1. Daily variation

Fluctuations in the PPCPs concentrations were observed in influent, effluent, and sludge among seven continuous days, although, composite samples were collected. The daily variations indicated that the study over extended periods is necessary to better understand the PPCP occurrence. A nonparametric Mann-Whitney test was conducted to examine the differences between weekdays and weekend. Overall, no significant difference ($p > 0.05$) was observed among the arithmetic mean concentrations of all the detected PPCPs from seven WWTPs with the exceptions for diazepam (higher concentrations in the weekend $p = 0.031$), and thiabendazole (marginal higher concentrations in the weekend $p = 0.090$). Their higher usage might have led to their higher concentrations in the influent during the weekend.

3.3.2. Spatial variation

Spatial variations of PPCP concentrations among the seven WWTPs were investigated. As shown in Fig. S2 in SI, PCA revealed that the dissolved PPCP concentrations in the influent could be clustered into

Table 1
Daily mass load (g/d), removal efficiencies and mass loss proportion of PPCPs in seven WWTPs.

PPCPs	Influent (dissolved)	Effluent (dissolved)	Influent (adsorbed)	Effluent (adsorbed)	Excess sludge	Removal efficiency (%)	Mass loss proportion (%)
3-(4-methylbenzylidene)-camphor	7.90	4.37	0.560	0.0800	1.60	43.8	28.5
acetaminophen	1970	9.00	1.38	0.00690	0.520	99.7	99.5
acetophenone	19.3	12.5	2.97	0.260	60	19.1	−227
aspartame	19.4	3.36	22.7	0.370	0.720	80.5	89.4
benzophenone-3	5.30	2.48	3.04	2.24	0.750	49.5	34.4
caffeine	2160	167	13.2	0.560	1.39	95.4	92.2
carbamazepine	10.7	13.1	0.120	0.00670	0.130	−14.7	−22.3
ciprofloxacin	27.4	8.46	46.0	0.590	42.0	66.1	30.4
clenbuterol	0.740	0.720	0.0740	0.0190	0.130	0.313	−6.76
clofibric acid	0.0120	0.0380	0	0	1.50	−30.8	−13000
crotamiton	6.30	6.79	0.200	0.094	0.240	−6.80	−9.6
cyclophosphamid	1.00	0.650	0.0710	0.0068	0.0640	22.0	32.7
danofloxacin mesylate	2.30	0.670	0.0390	0.0050	0.160	24.8	64.3
diazepam	0.640	0.760	0.0310	0.00740	0.0720	−16.8	−25.1
enrofloxacin	0.640	0.880	1.88	0.0710	1.60	−50.2	−1.23
ethenzamide	0.290	0.230	0.0210	0.00290	0.170	16.2	−29.5
fenoprofen	40.6	35.7	2.74	0.0760	24.0	17.5	−37.9
fluoxetine	15.8	7.42	20.1	1.70	10.0	49.7	46.7
gemfibrozil	5.78	2.39	0.470	0.350	1.00	49.0	40.1
ibuprofen	673	100	2.06	0.0270	6.20	83.2	84.2
indomethacine	8.93	13.6	0.220	0.00290	0.410	−13.3	−53.14
ketoprofen	218	220	1.43	0.200	9.30	10.7	−4.59
losartan	0.660	1.06	0.00	0.00	0.00	35.4	−60.6
mefenamic acid	7.58	5.38	0.190	0.0310	1.10	32.6	16.2
methyl paraben	42.5	8.10	9.71	4.50	8.80	36.2	59.0
metoprolol	91.4	126	0.980	0.470	0.120	−64.9	−37.0
miconazole	1.76	0.870	9.33	0.580	15.0	10.6	−48.3
naproxen	9.52	5.79	0.00	0.00	0.55	57.2	33.4
norfloxacin	515	112	1050	15.9	1210	77.0	14.5
ofloxacin	317	116	253	16.6	360	58.1	13.6
oxytetracycline	132	25.4	263	6.81	99.0	81.3	66.8
pirenzepine	0.120	0.0830	0.00810	0.000810	0.0170	3.81	21.3
propranolol	0.920	0.780	0.170	0.0130	0.200	17.7	8.89
propyl paraben	157	12.0	0.00950	0	0.490	87.7	92.0
propyphenazone	1.43	1.46	0.0390	0.0280	0.0440	11.4	−4.29
sarafloxacin hydrochloride	0.110	0.0760	0.0250	0.00330	0.0250	18.8	22.7
sildenafil	2.98	2.51	0.550	0.0540	0.730	8.57	−6.69
sotalol	1.98	1.29	0.0650	0.0150	0.0990	1.15	31.3
tetracycline hydrochloride	64.1	10.9	150	4.71	69.0	84.2	60.5
thiabendazole	0.210	0.280	0.0410	0	0.0950	−23.2	−49.4
triclocarban	26.4	47.0	74.0	9.64	140	−193	−95.9
triclosan	7.16	9.21	2.13	0.0150	29.0	−36.9	−311.5
Total PPCPs	**6570**	**1100**	**1930**	**66.0**	**2100**		
NSAIDs	**980**	**395**	**9.67**	**0.628**	**102**		
Antibiotics	**1060**	**274**	**1760**	**44.7**	**1780**		
Stimulant	**2160**	**167**	**13.2**	**0.560**	**1.39**		
Other PPCPs	**2380**	**260**	**146**	**20.2**	**211**		

Daily total PPCPs were calculated via $\overline{M} = \frac{\sum_{i=1}^{7}\sum_{j=1}^{7} C_{ij} \times V_{ij}}{7}$, where i indicates each day of seven sampling days and j indicates each WWTP of seven WWTPs.

Table 2
Mass load per inhabitant (μg/d•inhabitant) of PPCPs in seven WWTPs.

	Influent					Effluent					Sludge				
	Total PPCPs	NSAIDs	Antibiotics	Stimulant	Other PPCPs	Total PPCPs	NSAIDs	Antibiotics	Stimulant	Other PPCPs	Total PPCPs	NSAIDs	Antibiotics	Stimulant	Other PPCPs
W1	3090	968	807	1084	228	394	106	69.4	123	96.0	276	8.00	234	0.692	33.7
W2	2330	806	900	450	172	449	174	155	23.3	96.2	1010	20.8	843	0.530	141
W3	2530	1050	854	498	128	268	96.0	68.0	9.62	93.9	1040	8.1	919	0.436	113
W4	1950	621	826	386	114	179	68.0	29.3	34.3	47.6	908	13.3	784	0.403	110
W5	2220	920	642	539	121	136	51.0	29.2	2.95	52.4	523	5.78	438	0.373	78.6
W6	1230	415	486	249	78.0	190	58.0	80.7	9.41	42.3	311	17.1	250	0.330	43.7
W7	662	252	261	109	39.4	72.0	25.0	26.5	0.871	19.7	87.0	1.27	74.8	0.0384	10.5

Calculation is done by $\overline{M} = \frac{\sum_{i=1}^{7}\sum_{j=1}^{7} C_{ij} \times V_{ij}}{7}$, where i indicates each day of seven sampling days and j indicates each WWTP of seven WWTPs; both aqueous and solid compartments have been taken into account in the influent and effluent.

separate groups among seven WWTPs, indicating the different discharge pattern of the PPCPs in each WWTP. According to Friedman test, significantly high concentrations of PPCPs ($p < 0.01$, Wilcoxon pairwise comparison) in the influent was observed in W1 and W2 compared to the other WWTPs, while low concentrations ($p < 0.05$) were observed in W7. Generally, PPCPs are released via domestic wastewater after usage. The higher ratio of the domestic wastewater in the influent of W1 (100%) and W2 (> 90%) might be the reason of more PPCPs, whereas, in the other five WWTPs, the ratio of industrial wastewater (20–55%) was higher to dilute the PPCPs.

The mass loads of PPCPs (Table S5) and mass loads per inhabitant (Table 2) were also higher in W1 and W2 compared to the other WWTPs. Since the mass loads per inhabitant in the influent provided the information of PPCPs discharged per inhabitant; therefore, the results suggest that the PPCP mass loads per inhabitant increased with the rapid urbanization rate (Pearson correlation analysis, linear fitting, Table S6-7, and Fig. S3 in SI). Actually, the served area of W1 and W2 is in the city core, with per capita disposable income of 45850–55840 RMB in 2016 [17], while the served area of the other WWTPs is in the suburban zone with per capita disposable income of 32988–42146 RMB [17] (Table S6 in SI). A positive correlation between the PPCP mass loads per inhabitant and the per capita disposable income was also observed as shown in Table S8 and Fig. S4 in SI. The results suggest that the higher disposable income together with more awareness of health and hygiene might be the reasons for higher consumption or use, consequently, the higher release of the PPCPs.

Spatial variations were also observed in the effluent and sludge. Generally, WWTPs with higher levels of PPCPs in the influent showed higher levels in the effluent. However, in sludge, levels of PPCPs did not reciprocate the PPCP levels of the influent. PPCP levels in the influent of W1 and W2 were higher than those in W3-7 but only W2 was detected with higher PPCP deposits in the sludge compared to other WWTPs. The other WWTPs had almost similar levels of PPCPs in the sludge irrespective of the influent concentration. This might be due to the variations in the processes of different WWTPs [37].

3.4. Aqueous removal efficiency and mass loss proportion of PPCPs

3.4.1. Aqueous removal efficiencies

The aqueous removal efficiency of each PPCP was evaluated based on the dissolved PPCP via Eq. (6) (Table 1 and Fig. 3). Higher aqueous removal efficiencies were observed for acetaminophen, caffeine, propyl paraben, tetracycline, ibuprofen, oxytetracycline, and norfloxacin, with the median values were higher than 80% based on the average PPCP concentration over 7 sampling days. Moderate aqueous removal was observed for aspartame, naproxen, methyl paraben, ciprofloxacin, ofloxacin, fluoxetine, and gemfibrozil, with the median removal efficiencies in the range of 50–80%. In addition, minor aqueous removal efficiencies (20-50%) were observed for benzophenone-3, 3-(4-methylbenzylidene)-camphor, miconazole, acetophenone, mefenamic acid, danofloxacin mesylate, sarafloxacin hydrochloride, cyclophosphamid, and sildenafil. However, aqueous removal efficiencies of the other PPCPs were lower than 20% with some negative values. The biological treatment processes in W1-W7 included biological aerated filters, oxidation ditches, and anaerobic-anoxic-oxic process. Although, the treatment processes was different among the seven WWTPs (Fig. S1), consistent aqueous removal efficiencies were observed from some PPCPs. Consistently higher aqueous removal efficiencies were observed for acetaminophen, caffeine, propyl paraben, ibuprofen, aspartame, tetracycline and oxytetracycline, while consistently lower aqueous removal efficiencies were observed for metoprolol, enrofloxacin, and triclocarban, which were in accordance with the previous studies [38]. Fluctuations in the aqueous removal efficiencies for some PPCPs in different WWTPs were also observed. For example, the removal efficiencies of ketoprofen were −72.9% in W2 and 62.0% in W5, while the aqueous removal efficiencies of sarafloxacin were −82.1% in W7 and 76.7% in W4. Luo and associates attributed these variations in the aqueous removal efficiencies of PPCPs to the microbes, hydraulic retention time, sludge retention time, and other operational parameters of WWTPs [38].

3.4.2. Mass loss proportion

The aqueous removal efficiency (Eq. (6)) is usually based on the dissolved PPCP concentrations that only provide information on the PPCP removal from the aqueous phase via degradation, transformation or adsorption. The additional information for the adsorbed PPCPs on suspended solids and sludge makes the mass loss proportion approach more realistic by giving the actual removal (Eq. (5)) of PPCPs via degradation or transformation during the entire wastewater treatment processes [39]. The mass loss proportion of acetaminophen, caffeine, ibuprofen, and propyl paraben (Table 1 and Fig. 4) was similar probably due to their high bio-degradation or bio-transformation, together with their higher mass loads in the dissolved phase than in the adsorbed phase. However, significant differences between mass loss proportion and the aqueous removal efficiencies existed in other PPCPs. The mass loss proportion of quinolone and tetracycline antibiotics, including sarafloxacin hydrochloride, danofloxacin mesylate, norfloxacin, ciprofloxacin, ofloxacin, tetracycline and oxytetracycline, were lower than

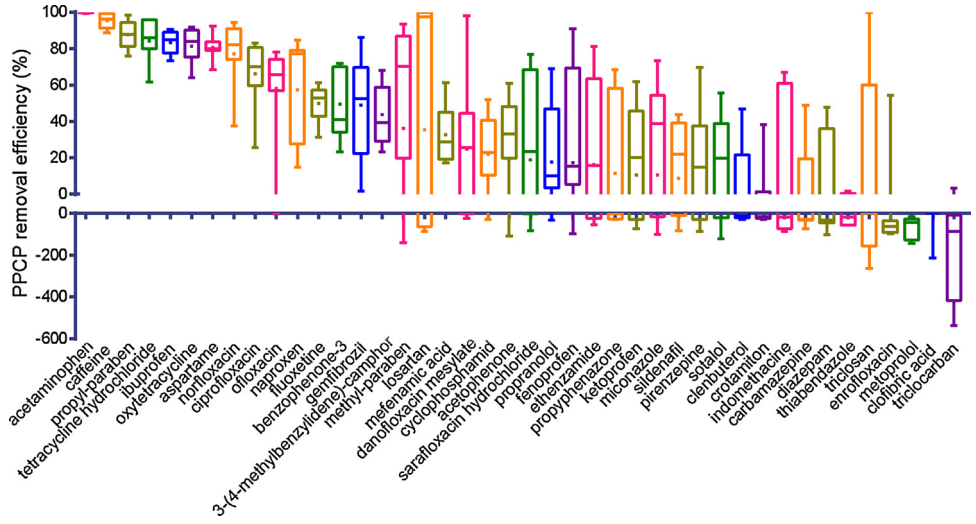

Fig. 3. Removal efficiencies of dissolved PPCPs from the aqueous phase.

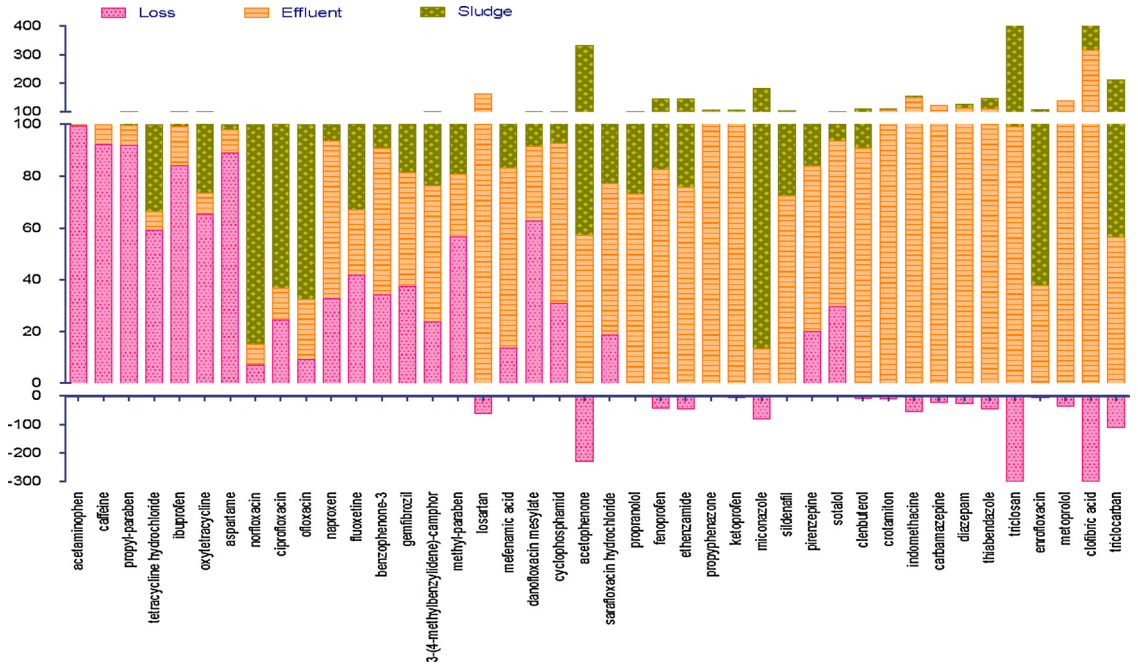

Fig. 4. Mass portion of the detected PPCPs in effluent, sludge and the mass loss during the wastewater treatment processes.

their aqueous removal efficiencies. The difference was mainly due to their high mass loads in the sludge and suspended solids due to their transmission from the aqueous to solid phase via complexation [40]. In addition, for the compounds with high logK_{ow} values (Table S1 in SI), including fenoprofen, mefenamic acid, benzophenone-3, 3-(4-methylbenzylidene)-camphor, and gemfibrozil, lower value of mass loss proportion were observed compared to their aqueous removal efficiencies, which was probably due to their higher adsorption on the sludge. In contrast, the mass loss proportion of aspartame was higher than the aqueous removal efficiencies, which was probably due to the high mass loads in the suspended solids in the influent together with its fast removal [41]. Therefore, an overestimation or underestimation of PPCP removal is possible in the absence of information on adsorbed PPCPs on sludge and suspended solids, especially for the quinolone and tetracycline antibiotics, and PPCPs with higher logK_{ow} (> 4) thus higher sorption potential [42]. Thus, the mass balance analysis based on Eq. 4 and 5 can be a better way to describe the true fate of PPCPs in terms of degradation/transformation or adsorption during the wastewater treatment processes. Moreover, as shown in Fig. 4, some PPCPs (i.e. antibiotics) with large proportions in the effluent and excess sludge could be directly recognized, which indicated their potential risk for the receiving environment.

3.4.3. Reasons for negative removal values

Negative values of removal efficiencies and mass loss proportions were observed for several PPCPs, where higher concentrations were observed in the effluent than the influent, or larger mass loads in the effluent and sludge than in the influent. Such PPCPs included ketoprofen, metoprolol, triclocarban, carbamazepine, indomethacine, crotamiton, triclosan, propyphenazone, diazepam, enrofloxacin, losartan, and thiabendazole. The proposed explanations for the negative values included: (1) measurement uncertainty [43], (2) concentration fluctuations caused by the sample collection and hydraulic retention time (HRT), (3) PPCPs released from the adsorbed phase, (4) lack of the degrading bacteria in the activated sludge, and (5) analytes transformed from the conjugated forms [44]. In the present study, the composite sampling strategy and the average concentrations based on seven continuous days' data were applied for the evaluation of removal efficiencies, which minimized the uncertainty and concentration fluctuations due to HRT. Since the sampling period (seven days) did not cover the complete sludge retention time in WWTPs, therefore, fluctuations of sludge deposits might be responsible for uncertainty in the mass loss proportions [45]. In addition, the PPCPs adsorbed on the suspended solids and sludge were detected and used to evaluate the mass loss proportion, which should cover the contribution of PPCP released from the adsorbed phase in the case of mass loss proportion, consequently, excluding the 3rd reason. Generally, the low removal efficiencies or low mass loss proportions of ketoprofen, metoprolol, carbamazepinie, diazepam, triclocarban, and norfloxacin were in accordance with the previous studies [46]. The prevalent low removal of those PPCPs indicated their robust structure and recalcitrance to the degradation or transformation. In addition, PPCPs discharged into WWTPs could undergo several reactions with other chemicals or transformations by human/microbial enzymes. Therefore, the prime probable explanation might be the transformation/deconjugation of undetected PPCP metabolites/conjugates into the parent (target) compounds during wastewater treatment processes to cause higher concentration of some PPCPs in the effluent or sludge, hence, leading to negative values in both removal efficiencies and mass loss proportion [44]. Release of some PPCPs from human system and eventually in the influent in conjugated or conjugated metabolite forms has been reported in the earlier studies [47,48]. PPCPs in such forms are not biologically active and may not be essentially available for detection during the analysis of the influent. However, de-conjugation or back transformation during the wastewater treatment processing may increase the availability of PPCPs in the effluent, leading to a negative mass balance [47–49]. Therefore, it can be concluded that the estimation of the conjugated analytes is essential for the correct closure of the mass balance sheet.

4. Conclusion

This study investigated the occurrence and fate of 42 PPCPs in WWTPs of Xiamen City and closed the mass balance by analyzing the dissolved and adsorbed PPCPs in the influent, effluent, and sludge. PPCPs were widely detected. Strong spatial variation of PPCPs distribution was observed. The positive correlation between PPCP mass loads per inhabitant and urbanization levels indicated a serious and

rising trend of these emerging contaminants owing to rapid urbanization. Both the removal efficiencies from the aqueous phase and mass loss proportion were evaluated and compared. It was observed that the wastewater treatment processes could partially remove some PPCPs. However, an overestimation or underestimation of PPCP removal may occur without the information about PPCP on the sludge and suspended solids, especially, where the PPCPs may have large loads on the solid phase.

City-wide mass loads estimation suggested that 8500 g of the investigated PPCPs entered seven WWTPs daily via influent, where 6640 g were in the dissolved form, while, 1160 g left WWTPs via aqueous effluent and 2290 g via excess sludge. Among different therapeutic groups, NSAIDs, stimulant, and antibiotics showed higher mass loads in the influent, with the values of 2980 g, 2200 g, and 2810 g, respectively. The antibiotics showed relatively higher mass loads in the effluent with the values of 304 g, while both antibiotics and antimicrobial agents showed higher mass loads in the sludge (1940 g and 178 g).

The co-occurrence of some PPCPs was observed, which was mainly due to their similar usage or similar physicochemical properties. The co-occurrence indicated that the specific PPCPs could be used as indicators or surrogate compounds to reduce the number of target PPCPs in the long term monitoring to reduce the chemical, labor and time cost.

Competing financial interests

The authors declare that they have no competing interests.

Acknowledgments

We appreciated Mr. Lifeng Lin for his help for the maintenance of HPLC-MSMS and the staffs from General Water of Xiamen Sewage Co. Ltd. for the sampling assistance. This work was supported by the National Science Foundation of China (41573102, 41673099), Distinguished Young Scholars of Fujian Province (2017J06013), Youth Innovation Promotion Association CAS (2016280), and PIFI CAS (2017VEB0008)

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jhazmat.2018.04.064.

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