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RESEARCH ARTICLE

Acidic pharmaceuticals in domestic wastewater and receiving water from hyper-urbanization city of China (Shanghai): environmental release and ecological risk

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Abstract The occurrence, behavior, and release of five acidic pharmaceuticals, including ibuprofen (IBP), naproxen (NPX), ketoprofen (KEP), diclofenac (DFC), and clofibric acid (CA), have been investigated along the different units in a tertiary-level domestic wastewater treatment plant (WWTP) in hyper-urbanization city of China (Shanghai). IBP was the most abundant chemicals among the measured in raw wastewater. The loads of the acidic pharmaceuticals in the WWTP influent ranged from 7.5 to 414 mg/day/1,000 inh, which were lower than those reported in the developed countries suggesting a less per capita consumption of pharmaceuticals in Shanghai. IBP obtained by highest removal (87 %); NPX and KEP were also significantly removed (69–76 %). However, DFC and CA were only moderately removed by 37–53 %, respectively. Biodegradation seemed to play a key role in the elimination of the studied pharmaceuticals except for DFC and CA. An annual release of acidic pharmaceuticals was estimated at 1,499 and 61.7 kg/year through wastewater and sludge, respectively, from Shanghai. Highest pharmaceuticals concentrations were detected in the effluent discharge point of the WWTP, indicating that WWTP effluent is the main source of the acidic pharmaceuticals to its receiving river. Preliminary results indicated that only DFC in river had a high risk to aquatic organisms. Nevertheless, the joint toxicity effects of these chemicals are needed to further investigate.

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Keywords Acidic pharmaceuticals · Wastewater · Ecological risk · Shanghai

Introduction

Many studies have shown that urbanization has led to serious environmental and ecological problems, including air and water pollution, both in urban and surrounding areas. Rapid increase in urban population as a proportion of total population is resulting in high urbanization of China. As the largest and the most modern city in China, Shanghai has also experienced extensive urban expansion over the past three decades. Currently, Shanghai is one of the most urbanized cities in China, with a percentage of urban population of 88.6 % in 2009 (Peng 2011). Thus, more and more people in Shanghai can afford medical treatment and the usage of pharmaceuticals can be expected to increase rapidly. Nevertheless, most of the pharmaceuticals and their metabolites are excreted in human feces and urine after use and eventually enter sewage systems. As a result, wastewater treatment plants (WWTPs) receive wastewater containing various pharmaceuticals residues at concentrations from nanograms per liter (ng/L) to micrograms per liter (μg/L).

Current WWTPs are not designed to remove these emerging pollutants and their capability for removing pharmaceuticals is therefore not efficient (Heberer 2002; Ternes 1998). Carballa et al. (2007) reported that only 40–65 % of anti-inflammatory pharmaceuticals were completely removed from WWTPs. Together with treated wastewater, these pharmaceuticals are released to the aquatic environment and consequently found to contaminate the receiving water bodies (Heberer 2002; Lindqvist et al. 2005; Yang et al. 2011b) or even raw water sources of drinking water treatment plant (Ternes et al. 2002; Vieno et al. 2007b).

Once pharmaceuticals enter the environment, they have the potential to bio-accumulate which causes chronic effects on the environment and living organisms. Ibuprofen (IBP) and naproxen (NPX) have been found to have toxic effects on different species of bacteria and algae at high concentration (mg/L) (Brun et al. 2006; Cleuvers 2003). Furthermore, the widespread veterinary use of diclofenac (DFC) has indirectly caused the near extinction of vultures in South Asia (Oaks et al. 2004).

So far, occurrence of pharmaceuticals from various therapeutic classes in the WWTPs has been well documented in the North America, Europe, and Japan (Castiglioni et al. 2006; Jones et al. 2007; Lishman et al. 2006; Nakada et al. 2006; Santos et al. 2007; Ternes 1998; Thomas and Foster 2005; Vieno et al. 2007a). However, studies about pharmaceuticals in the WWTPs in China are limited, especially in developed cities such as Shanghai, the most urbanized and densely populated city in China. Also, there is lack of the data information of pharmaceuticals potential discharges through wastewater into the Yangtze River, the largest river and the important freshwater source in China. Therefore, knowledge of pharmaceuticals in the environment in China is necessary to gain a full scenario of pharmaceutical contamination around the world considering the large scale of the urbanization and population, and consequently potential high consumption of pharmaceuticals in the country.

In this study, a detailed investigation of five acidic pharmaceuticals widely consumed in China, including four nonsteroidal anti-inflammatory drugs [ibuprofen (IBP), ketoprofen (KEP), naproxen (NPX), and diclofenac (DFC)] and one lipid regulator (clofibric acid, CA), was conducted in a typical tertiary-level WWTP of Shanghai to characterize the occurrence of pharmaceuticals in domestic wastewater and its receiving water, to explore their behavior and fate during typical wastewater treatment, and to estimate the potential releases of pharmaceuticals through wastewater from Shanghai into the Yangtze River, the most important water source of Shanghai. Moreover, potential risks of pharmaceuticals on the aquatic organisms in the WWTP receiving river were evaluated.

Materials and methods

Chemicals

IBP, KEP, NPX, DFC, and CA were obtained from Sigma-Aldrich (St. Louis, MO, USA). HPLC grade methanol, acetone as well as formic acid were purchased from Tedia Company, Inc. (USA), and ultra-pure water was produced by a Milli-Q water purification system (Millipore, Bedford, MA, USA). Standard stock solutions of individual pharmaceuticals (50 mg/L) were prepared in methanol and renewed every 3 months, respectively. Working solutions of mixture standards with different concentrations (1 μg/L, 5 μg/L, 10 μg/L, 50 μg/L, 100 μg/L, and 500 μg/L) were prepared by diluting the stock solutions before each analytical run. All the solutions were stored at 4 °C in the dark.

Description of the wastewater treatment plant and sampling

Wastewater and sludge samples were collected from a tertiary-level WWTP in Shanghai, China. The plant serves approximately 200,000 people and the daily average wastewater [mainly from domestic wastewater (93 %)] flow is 60,000 m^3/day. Daily treated sludge production is 32 tons. As shown in Fig. 1, the mechanical treatment includes a screen and an aerated grit chamber. The primary sludge was pumped into the dehydrating house, while the primary effluent was directed to the activated sludge system. For the secondary biological treatment processes, anaerobic/anoxic/oxic (A^2/O) activated sludge process was used. The hydraulic retention times (HRTs) in anaerobic tank, anoxic tank, and oxic tank were 1.5 h, 1.5 h, and 4.7 h, respectively. After settling in the secondary clarifier, part of the activated sludge was returned to the anaerobic tank, and the rest of the sludge was conveyed to be dehydrated. The total sludge retention time (SRT) was 8–10 days. The secondary effluent was introduced to the biological aerated filtrate (BAF) for advanced treatment. Finally, the effluent of BAF was subjected to UV disinfection prior to discharge. Three sampling campaigns were conducted on December 22, 2010, and January 4 and 8, 2011, respectively, and all sampling locations are depicted in Fig. 1. During the sampling campaigns, time-integrated sampling was collected each hour over an 8-h period in the WWTP to approximately compensate for the HRT of each treatment step. All of them were collected as grab samples in duplicate (4 L for each sample) in amber glass bottles prewashed with ultra-pure water, kept in the cooler, and transported to the laboratory. Immediately after delivery to the laboratory, wastewater samples of each treatment step were mixed as 8-h composite samples, respectively, for analysis. During sampling period, precipitation is low, so dilution of the sewage influent is minimal. Dehydrated sludge was collected in prewashed jars and kept in a cooler during transport to the laboratory. The primary and secondary sludge samples were not collected due to their inaccessibility.

In addition, surface water samples of a river receiving the WWTP effluent were taken from the upstream (50 m) and downstream (200 m) of the WWTP effluent discharge point to assess the impact of WWTP effluent on the receiving river.

Sample pretreatment and analysis

Immediately after delivery to the laboratory, wastewater samples and surface water samples were filtered through

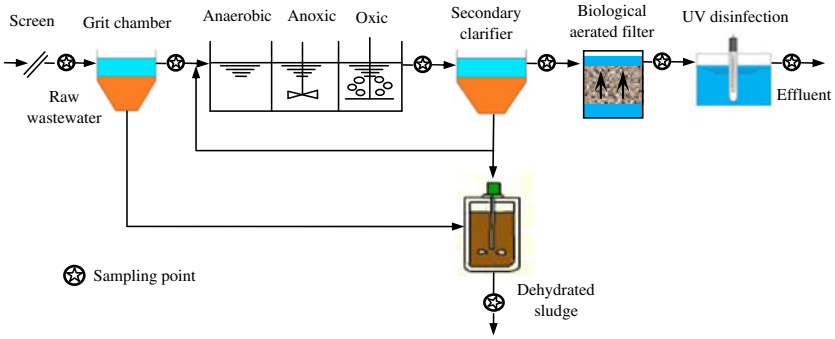

Fig. 1 The scheme of the studied tertiary-level WWTP in Shanghai, China and the sampling points

pre-baked (400 °C, >4 h) glass fiber filters (0.7 μm, GF/F; Whatman, Mainstone, UK). The filtrate was stored at 4 °C to avoid any degradation until extraction. The suspended particles collected on glass fiber filters and sludge were wrapped with pre-baked (450 °C) aluminum foil, sealed in Ziploc bags, and stored at −18 °C until further treatment. The method for the extraction and analysis of pharmaceuticals in water samples was described elsewhere (Kimura et al. 2007). Briefly, wastewater (200 mL for influent and 500 mL for other samples) were extracted using a solid-phase extraction (SPE) system. The pH of the samples was adjusted to 2.0 with 2 mol/L HCl. A known amount (200 ng) of fenoprop was added as surrogate standard. After the cartridges (ENVI-18, 500 mg, 3 mL) were conditioned by applying 2 mL of methanol and 2 mL of Milli-Q water (pH=2), the water samples were introduced to the cartridges by means of PTFE tubes at a flow rate of approximately 5–8 mL/min. After washing by 5 mL of 5.0 % methanol solution, the cartridges were dried under vacuum for 2 h and eluted with 3 mL of acetone. The extracts were then evaporated to approximately 500 μL under a gentle nitrogen stream and 500 μL of methanol was added. Evaporation continued until the final volume of the extracts was 500 μL. Suspended particles and sludge samples were extracted by the ultrasonic solvent extraction method reported by Ternes et al. (2005) with a slight modification here. Suspended particles and sludge were freeze-dried and were accurately weighed before being extracted. Then dried sludge or suspended particles was extracted with 6 mL and 2 mL of methanol in series and twice with 2 mL acetone. Two hundred nanograms of surrogate standard (fenoprop) was spiked into the slurry in the first extraction step. In all extraction steps, the slurry was ultrasonicated for 10 min and then centrifuged at 5,000 rpm for 5 min. Supernatants from all of the extraction steps were combined and evaporated to 1 mL under a stream of nitrogen. These concentrates were redissolved in 100 mL of distilled water (pH=2), and the SPE was carried out in the same manner as that described above. By using this method, recoveries with a range from 43 % to 72 % can be expected for acidic pharmaceuticals from sludge (Ternes et al. 2005).

All samples were analyzed by TSQ Quantum high performance liquid chromatography coupled with mass spectrometry (Thermo Fisher Scientific, San Jose, CA, USA). The separation was performed on an Agilent Eclipse XDB C18 reversed phase column (150 mm×2.1 mm, 5 μm), with a flow rate of 350 μL/min. Methanol and water with 0.1 % (v/v) acetic acid were used for separation. The injection volume was 10 μL, and the column temperature was 30 °C. The gradient was held at 75 % of methanol for 5 min, and increased to 90 % of methanol within 5 min and held for 5 min, and then reset to initial conditions of 75 % of methanol in 5 min and held for 5 min. The mass spectrometer detection of pharmaceuticals was operated in selected reaction monitoring (SRM) mode. Analyses were performed in the negative ion mode. Quantification of the target compounds was performed using an external standard method. The linear range was established between 1 and 500 μg/L with a correlation coefficient (R^2) of 0.9997. The limit of detection (LOD) were 1 pg for CA and 5 pg for the other tested compounds, respectively. The limit of quantitation (LOQ) was 50 pg for all target compounds. On the basis of the volume of the samples filtered, the volume-basis concentrations (ng/L) were calculated for particulate pharmaceuticals. The total pharmaceutical concentrations in wastewater were defined as the sum of targets in dissolved and particulate phases.

Quality assurance/quality control (QA/QC)

The precision of the analytical method was validated by observing the short-term and long-term relative standard deviation (RSD) under identical conditions. The RSD for intra- and inter-day precision were 2.4–7.4 % and 2.1–6.2 %. For each batch of six samples, a procedural blank, a spiked blank, a matrix spiking sample, and a matrix spiking duplicate were processed. No quantifiable analytes were detected in the blank samples. The recoveries of five acidic pharmaceuticals and surrogate compound were 81.7±8.2 % for water samples and 74.5±9.3 % for solid samples, respectively. The concentrations of targets were not recoveries corrected.

Results and discussion

Occurrence and load of pharmaceuticals in the influent and sludge

All of the five pharmaceuticals were found in the WWTP wastewater and sludge samples (Table S1). Concentrations of the pharmaceuticals in WWTP influents were multiplied by the flow rate to obtain pharmaceutical loads for the WWTP and normalized for the population equivalent of the WWTP. Table 1 shows the load of each pharmaceutical in the influent [expressed in milligrams per day per 1,000 inhabitants (inh)] of the WWTP. Clearly, IBP had the highest load with the mean of 414 mg/day/1,000 inh. The second most abundant pharmaceutical in the influent is DFC with the load of 95.4 mg/day/1,000 inh. Loads of KEP, CA, and NPX were 7.5, 17.4, and 24.3 mg/day/1,000 inh, respectively. This reflects the wide range of the consumption of these pharmaceuticals in Shanghai. IBP has been listed as one of the four most often-used anti-inflammatory pharmaceuticals (the other three are paracetamol, aspirin, and DFC) in China, with an annual production more than 1,000 tons. On the other hand, KEP is relatively less produced (about 92 tons per year) and used (http://www.chinaccm.com/).

In addition, we compared the pharmaceuticals load via wastewater discharge in the globe using the data reported in the previous studies, as shown in Table 1. Overall, the loads of the acidic pharmaceuticals in the WWTP influent in this study were lower than those in the developed countries including Europe, USA, and Japan, while were slightly higher than those in Guangzhou, China. This suggests a higher consumption of pharmaceuticals in the developed countries or regions. For example, the load of IBP (414 mg/day/1,000 inh) was lower than those in WWTP influent reported in European countries, Japan, and USA (Lindqvist et al. 2005; Ternes 1998; Nakada et al. 2006; Thomas and Foster 2005). While the IBP load in this study was higher than that (12–129 mg/day/1,000 inh) in Guangzhou, China (Huang et al. 2011), probably due to the less usage of this pharmaceutical in Guangzhou. KEP has also been ubiquitously detected in raw waters of Europe, North America, and Japan. The load of KEP in the WWTP influents were reported to be 16–808 mg/day/1,000 inh in Finland, Spain, Switzerland, USA, and Japan (Lindqvist et al. 2005; Nakada et al. 2006; Santos et al. 2007; Tauxe-Wuersch et al. 2005; Thomas and Foster 2005). As for NPX, the load in this study was 17.4 mg/day/1,000 inh, which was much lower than its levels in Finland and USA (Lindqvist et al. 2005; Thomas and Foster 2005). A possible explanation for the lower NPX load is less usage of this pharmaceutical in China. The per capita consumption rate of NPX was estimated at 0.5 g/person/day (CMEIN 2005), which was one order of magnitude lower than that calculated for Europe (Lindqvist et al. 2005). DFC load in this work (95.4 mg/day/1,000 inh) was in the same range of or slightly higher than those in Finland , UK, Sweden, and USA (Lindqvist et al. 2005; Roberts and Thomas 2006; Thomas and Foster 2005; Zorita et al. 2009), while it was much lower than those reported in Switzerland, Germany, and Spain (Jelic et al. 2011; Tauxe-Wuersch et al. 2005; Ternes 1998). The load of CA in the influent in this study was much lower than those in Germany and Switzerland (Tauxe-Wuersch et al. 2005; Ternes 1998), while it was comparable with those reported in Japan and Guangzhou (Huang et al. 2011; Nakada et al. 2006). CA has been reported to be fairly persistent in the environment (Vieno et al. 2005). Its frequent detection in the Shanghai raw wastewater may reflect the usage of this drug and/or its parent lipid regulators.

Overall, the loads of the acidic pharmaceuticals were at the lower level compared with Europe and USA. The most possible explanation was probably due to their lower use in China than in the countries with higher socioeconomic statuses, where medical care is more prevalent (Thomas and Foster 2005).

All of the investigated pharmaceuticals were also found in dehydrated sludge samples but at relatively low concentrations (Table S1). The concentration of DFC (80±21.9 ng/g) was higher than those of IBP (68.6±12.6 ng/g), KEP (7.6±3 ng/g), NPX (14.9±9.2 ng/g), and CA (20.4±12.8 ng/g). These acidic pharmaceuticals generally present as anionic species at pH 6–7 and have low logK_{ow} values. Therefore, sorption to the sludge is expected to be weak due to electrostatic

Table 1 Global comparison of pharmaceutical loads in influent of WWTPs [mg/day/1,000 inhabitants (inh)] (Huang et al. 2011; Lindqvist et al. 2005; Nakada et al. 2006; Roberts and Thomas 2006; Santos et al. 2007; Tauxe-Wuersch et al. 2005; Ternes 1998; Thomas and Foster 2005; Vieno et al. 2005; Zorita et al. 2009)

	Finland	UK	Switzerland	Sweden	Germany	Spain	USA	Japan	Guangzhou	This study
IBP	2,571–3,900	32–2,475	586–1,548	1,907	770	NA	397–1,502	0.52–1,231	12–129	414
NPX	750–2,379	16–43	NA	2,693	224	225–2,432	406–1,772	7.6–173	1.8–11	17.4
DFC	21–140	1.0–159	263–768	93	324	184–338	12–61	157	0.2–19.8	95.4
KEP	428–808	0.4–0.5	70–137	NA	NA	63–372	16–24	16–661	NA	7.5
CA	NA	0.03–57	9.6–64	3.3	224	NA	NA	17.5	2.4–19.1	24.3

KEP ketoprofen, *NPX* naproxen, *CA* clofibric acid, *DFC* diclofenac, *IBP* ibuprofen, *NA* not available

repulsion from the negatively charged functional groups in the sludge.

Removal of acidic pharmaceuticals in the WWTP

Figure 2 shows the concentration profiles of the acidic pharmaceuticals in the wastewater along treatment in the WWTP. It can be seen that the acidic pharmaceuticals concentrations decreased along the treatment in the WWTP. Using the concentrations of the acidic pharmaceuticals in the influent and the corresponding treatment unit effluents, we calculated their removal efficiencies after major treatment units (Table 2). No obvious variation of removal for each pharmaceuticals was observed during the three sampling campaign. Thus, we used the mean removal efficiencies of the three sampling campaigns in the following discussion. As shown in Fig. 2 and Table 2, only 10–21 % of removal for the pharmaceuticals was observed in the aerated grit chamber. This is mainly due to their acidic structures, with very low solid–liquid partition coefficients (Ra et al. 2008), and also consistent with their no significant amount detected in suspended particles (unpublished data). After anaerobic/anoxic/oxic biological treatment and secondary clarification, significant removal was observed for IBP, NPX, and KEP (59–65 %) whereas about 80 % of CA and 60 % of DFC still remained in wastewater (Fig. 2 and Table 2). Thus, the high removal rate of IBP and NPX in biological treatment stage led to their high total removal compared with DFC and CA. High decrease of the amount of IBP and NPX found during the biological treatment in consistent with the previous study (Jones et al. 2007). Tauxe-Wuersch et al. (2005) defined a critical value for the SRT to remove IBP from the influent as about 5 days. Higher removal efficiency of IBP in the WWTP in this study is probably due to longer SRT (8 days) and hydraulic retention time (~10 h). Complete removal of IBP has been found in activated sludge system with longer SRT (>50 days) (Andreozzi et al. 2003). Lower removal efficiency of NPX was reported from WWTPs in Spain (40–55 %) (Carballa et al. 2004), although higher removal (~98 %) was reported from WWTPs in Finland (Lindqvist et al. 2005). It should be noted that despite DFC belongs to the same pharmaceutical family as IBP, it behaves somewhat differently. A hypothesis for this difference is that compounds such as DFC and CA owe their persistence to the presence of chlorine groups in the molecule (Cirja et al. 2008). CA seems to be removed more efficiently in MBR (72–86 %) compared to in activated sludge (26–51 %) (Radjenović et al. 2007). The tertiary treatment, including a BAF step, did not seem to largely affect any of the pharmaceuticals loads except for IBP. A small decrease in concentration was seen for KEP after the BAF, as well as a decrease for NPX. And no obvious removal was found for CA and DFC. Different levels of removal efficiencies were shown for the acidic pharmaceuticals after UV treatment (Fig. 2 and Table 2). This is consistent with previous reported results which demonstrated that simple UV treatment can help to decompose organic compounds including pharmaceuticals as a consequence of light absorption (Gagnon et al. 2008). However, the treatment efficiency was not obvious after UV disinfection, which may be due to a short contact time (15 s) or insufficient UV dose (not available) as well as the competitive reactions of other organic contaminants.

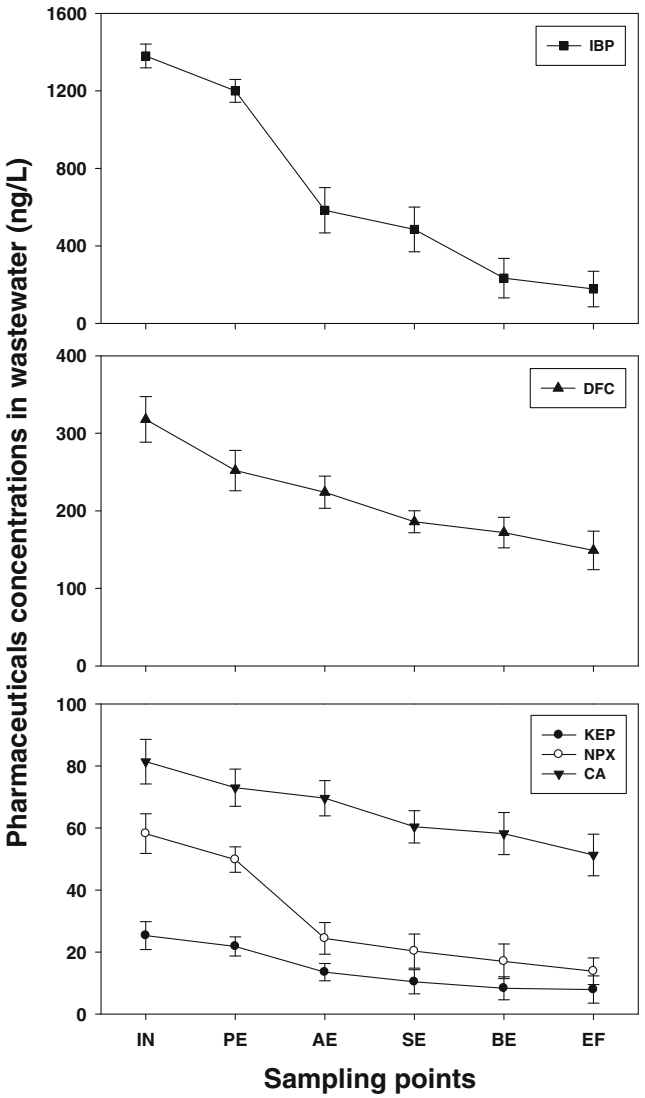

Fig. 2 Concentrations of the pharmaceuticals in wastewater along treatment in the WWTP. *IN* influent, *PE* primary effluent, *AE* A^2/O tank effluent, *SE* secondary clarifier effluent, *BE* BAF effluent, *EF* final effluent (UV disinfection), *KEP* ketoprofen, *NPX* naproxen, *CA* clofibric acid, *DFC* diclofenac, *IBP* ibuprofen

In summary, the behavior of the investigated pharmaceuticals in wastewater varied by compound during treatment in the WWTP. IBP was obtained by highest removal (87 %); NPX and KEP were also significantly removed (69–76 %). However, DFC and CA were only moderately removed by 37–53 %, respectively. The pharmaceuticals were not

Table 2 Removal (%) of the acidic pharmaceuticals after major treatment units

Units	1st sampling					2nd sampling					3rd sampling					Mean removal				
	KEP	NPX	CA	DFC	IBP	KEP	NPX	CA	DFC	IBP	KEP	NPX	CA	DFC	IBP	KEP	NPX	CA	DFC	IBP
Grit chamber	15	15	12	21	13	9	16	9	20	13	17	11	10	23	14	14	14	10	21	13
A^2/O tank	56	63	14	28	51	44	56	14	32	64	33	55	15	28	59	47	58	15	30	58
Secondary clarifier	69	69	26	40	58	51	65	25	43	70	50	62	26	42	67	59	65	26	42	65
BAF	77	74	29	43	76	59	68	27	47	86	58	71	29	48	88	67	71	29	46	83
Final effluent	78	79	39	49	80	63	75	34	54	90	60	76	37	57	91	69	76	37	53	87

A^2/O tank anaerobic/anoxic/oxic (A^2/O) activated sludge process unit, *BAF* biological aerated filtrate unit

subjected to sorption/sedimentation probably due to their acid structure, which can resist the sorption onto the suspended particles by interacting with water molecules (Ra et al. 2008). Biodegradation seemed to play a key role in the elimination of the tested pharmaceuticals in this study except for DFC and CA. BAF did not seem to largely affect the pharmaceuticals loads except for IBP. In addition, UV irradiation caused negligible losses of the pharmaceuticals, probably due to a short contact time and/or insufficient dose. Variation in the removal efficiencies has been reported in the literature and was also noticed in this study. The main reasons for variation may be the different treatment processes and the variation in the functioning of the process (Tixier et al. 2003). Further investigation for different types of WWTPs is necessary to confirm the results mentioned above.

Mass balance and releases of the selected acidic pharmaceuticals

The transformation or lost mass of pharmaceuticals and their mass in water and sludge are estimated in order to further evaluate the operative removal process in the WWTP. The mass balance was examined for the pharmaceuticals and the results are shown in Fig. 3. As shown in Fig. 3, all the pharmaceuticals demonstrated a relatively low percentage of retention in the dewatered sludge. The distribution fractions in the final effluent ranged from 13 % (IBP) to 63 % (CA), and the lost fractions ranged from 24 % (CA) to 84 % (IBP). It was noted that mass loss of IBP accounted for 84 % of initial loading. There was only 3 % of IBP in the dewatered sludge. These results indicated that the conventional wastewater treatment processes could effectively remove IBP in the influent, and the contribution of sorption process to the removal can be negligible. In contrast, the treatment

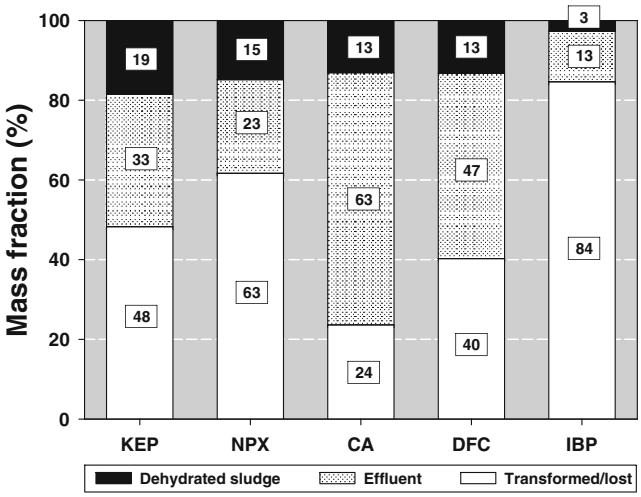

Fig. 3 Mass fractions (%) of KEP, NPX, CA, DFC, and IBP in dehydrated sludge, effluent, and transformed/lost in the WWTP. *KEP* ketoprofen, *NPX* naproxen, *CA* clofibric acid, *DFC* diclofenac, *IBP* ibuprofen

processes cannot eliminate the other target pharmaceuticals, especially DFC and CA.

The total mass loadings in the treated effluent and the treated sludge are believed to be representative of the acidic pharmaceuticals releases from WWTPs. The estimated acidic pharmaceuticals release was 24 g/day through the treated effluent of the WWTP. The dewatered sludge production is 32 tons/day in the WWTP. The acidic pharmaceuticals released through the dewatered sludge were estimated to be 6.1 g/day from the WWTP. In 2010, about 2.1 and 0.4 billion tons of domestic and industrial wastewaters, respectively, were generated in Shanghai, in which approximately 84 % of the domestic and 98 % of the industrial wastewaters were treated prior to discharge into the Yangtze River (http://www.sepb.gov.cn/). Therefore, a total of about 1,499 kg of acidic pharmaceuticals per year might be released into the Yangtze River with wastewater from Shanghai. This result revealed that wastewater from the Shanghai is a significant contributor of the acidic pharmaceuticals to the Yangtze River and then the Yangtze River Estuary and the coastal East China Sea. It should be noted that some error might be brought in due to variations in plant scale, treatment process, influent composition, and seasonal variation. A long-term study at this location may accentuate differences due to changes in pharmaceuticals usage before entrance into the wastewater treatment process. Seasonal variations of both occurrence and removal of the pharmaceuticals in various processes of WWTPs should also be considered in the future.

Furthermore, the use of treated sludge to agricultural land will increase the acidic pharmaceuticals burden in soil. The sewage sludge production was estimated to be 322,000 tons in Shanghai in 2010 (Yang et al. 2011a). Thus, the mass loading of the acidic pharmaceuticals in treated sludge was 61.7 kg from WWTPs in Shanghai. Significant quantities of the acidic pharmaceuticals may enter soils through land application of dewatered sludge and pretreatment solids from WWTP. Therefore, further studies of the fate, transport, and potential environmental impact of the selected acidic pharmaceuticals in treated sludge from WWTP are necessary.

Concentrations of pharmaceuticals in receiving river water and risk to the aquatic environment

To study the impact of WWTP effluent discharge into the environment, we analyzed samples of surface water of a river receiving the WWTP effluent. River water samples were taken from upstream (50 m) and downstream (200 m) of the WWTP effluent discharge point. All of the five acidic pharmaceuticals were detected in water samples from the receiving river (Fig. 4). Lower concentrations of the acidic pharmaceuticals were found in the upstream samples. This may be due to

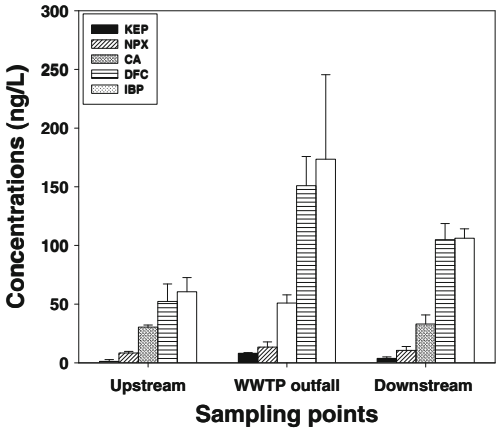

Fig. 4 Concentrations of acidic pharmaceuticals in the WWTP receiving river. *KEP* ketoprofen, *NPX* naproxen, *CA* clofibric acid, *DFC* diclofenac, *IBP* ibuprofen

effluent discharges of WWTPs further upstream. Highest pharmaceuticals concentrations were detected in the effluent discharge point of the WWTP, indicating that WWTP effluent is the main source of the acidic pharmaceuticals in river water.

Due to low pharmaceutical concentrations found in natural water, their risk of causing chronic toxicity to aquatic organisms is of more importance. To demonstrate their potential impact, we conducted a screening level risk assessment of the five acidic pharmaceuticals to aquatic organisms in river water. The environmental risk quotient (RQ) can be calculated by dividing the measured environmental concentration (MEC) by the Predicted No-Effect Concentrations (PNEC) of the compound. If RQ is higher or equal to 1, there is a risk for adverse effects in the aquatic environment (Tauxe-Wuersch et al. 2005). The PNECs for the acidic pharmaceuticals were adopted from the literatures (Tauxe-Wuersch et al. 2005; Wang et al. 2010; Zhao et al. 2010). Based on the worst-case scenario, only the RQ value for DFC in river water was higher than 1 (Table 3), indicating it poses a potential risk to aquatic organisms. Similar results for these pharmaceuticals with high risks were also found in surface waters of other regions. Hernando et al. (2006) reported high risk based on the RQ of DFC in

Table 3 Risk quotients (RQs) of each pharmaceutical in the wastewater treatment plant receiving river

Pharmaceuticals	PNEC (ng/L)	Maximum MEC (ng/L)	RQ (maximum MEC/PNEC)
KEP	15,600	8.1	0.000519
NPX	20,000	13.35	0.0006675
CA	1,000	50.94	0.05094
DFC	100	150.99	1.5099
IBP	2,000	173.5	0.08675

KEP ketoprofen, *NPX* naproxen, *CA* clofibric acid, *DFC* diclofenac, *IBP* ibuprofen, *PNEC* predicted no-effect concentrations, *MEC* measured environmental concentration

surface water. The RQ with values more than 1 have also been reported for DFC in a Norwegian river (Grung et al. 2008) and in the Pearl River (Zhao et al. 2010). Nevertheless, as this evaluation is only focused on the risk that individual compounds may cause to aquatic organisms, it must be noted that the impact of a mixture of these chemicals could prove more toxic than the individual compounds alone. For example, Flaherty and Dodson (2005) found that pharmaceutical mixtures behaved unpredictably and caused serious side effects such as deformities. The RQs were far less than 1 for IBP, NPX, CA, and KEP. This does not mean, however, that they pose no potential risk to long-term ecologic sustainability resulting from their continuous release to river water. Therefore, risk reduction could be achieved through application of proper wastewater treatment technologies in Shanghai.

Conclusions

Five acidic pharmaceuticals were investigated in a municipal WWTP that represents the typical municipal wastewater treatment techniques in Shanghai, China. The occurrence, behavior, and fate of the selected acidic pharmaceuticals during wastewater treatment in the WWTP were characterized. Pharmaceuticals were found to vary in mass loadings in the influent, with IBP being the most abundant. During wastewater treatment, all compounds were found to show concentration decline from influent to effluent, with removal efficiency from 37 % to 87 %. These pharmaceuticals were also found in both the upstream and downstream of the effluent outfall. A total of 1,440 kg of acidic pharmaceuticals per year was estimated to be released into the Yangtze River via wastewaters from Shanghai. The results revealed that acidic pharmaceuticals have not been sufficiently eliminated by biological and chemical treatments in the WWTP, and wastewater from Shanghai is a significant contributor of pharmaceuticals to the Yangtze River and thus the Yangtze River Estuary and the coastal East China Sea. Further research is needed to assess potential bioaccumulation of pharmaceuticals in aquatic organisms and resulting chronic toxic effects.

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