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PAPER

Occurrence and behavior of non-steroidal anti-inflammatory drugs and lipid regulators in wastewater and urban river water of the Pearl River Delta, South China†

Qiuxin Huang,[ab] Yiyi Yu,[ab] Caiming Tang,[ab] Kun Zhang,[ab] Jianlan Cui[ab] and Xianzhi Peng*[a]

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Occurrence of five non-steroidal anti-inflammatory drugs (salicylic acid, ibuprofen, naproxen, indomethacin and diclofenac) and three lipid regulators (bezafibrate, clofibric acid and gemfibrozil) was investigated in wastewater, sewage sludge, and river water of the urban section of the Pearl River at Guangzhou in South China. Behavior and fate of the pharmaceuticals during treatment in two sewage treatment plants (STPs) were also studied in depth by determining concentrations in the influents and effluents at major treatment units and the sewage sludge. Concentrations of the pharmaceuticals in the raw wastewater were mostly at ng L^{-1} levels except salicylic acid whose concentrations ranged from 9.6 to 23.3 μg L^{-1}. No significant amount of the pharmaceuticals was detected in the suspended particulate matter of wastewater and sewage sludge. Salicylic acid, indomethacin, and naproxen were almost completely removed (≥99%); gemfibrozil, ibuprofen and bezafibrate were significantly removed (>75%), whereas diclofenac and clofibric acid were removed by 60–70% during treatment in the STPs. Generally, biodegradation was the governing process for elimination of the investigated pharmaceuticals. Anaerobic biodegradation was responsible for most of the removal of diclofenac whereas aerobic biodegradation also played an important role in elimination of the other pharmaceuticals except SA, which was nearly completely removed after the anoxic process. In the Pearl River, the pharmaceuticals were widely detected. Both the concentrations and detection frequency were higher in March 2008 than those in the other seasons, which may be ascribed mainly to less dilution caused by lower precipitation. Besides the STPs, urban canals directly connected with the Pearl River may also be important contributors to the pharmaceutical contamination in the river.

Introduction

As an important class of emerging contaminants, pharmaceuticals in the environment have attracted increasing concerns in recent decades.[1–5] Although most pharmaceuticals showed no significantly acute toxicity at environmentally relevant concentrations,[6,7] the potential effects on non-target organisms, the chronic toxicity, and the possible additive effects of a vast range of such chemicals co-occurring in the environment may still be an issue given the biological activity of the compounds.[8] For instance, diclofenac residue in carcasses of domestic ungulates was believed to be the cause of the catastrophic decline of vulture populations in Western Asia.[9] A mixture of drugs at ng L^{-1} levels was reported to be able to inhibit cell proliferation by affecting their physiology and morphology.[10] Recent research reported that sub-chronic exposure to diclofenac at μg L^{-1} levels can

[a]*State Key Laboratory of Organic Geochemistry, Guangzhou Institute of Geochemistry, Chinese Academy of Sciences, 510640 Guangzhou, China*
[b]*Graduate University of Chinese Academy of Sciences, 100049 Beijing, China*

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Environmental impact

Pharmaceuticals in the environment have become an increasing issue. In this work, occurrence of commonly consumed non-steroidal anti-inflammatory drugs and lipid regulating agents was investigated in river water, municipal wastewater, and sewage sludge in the Pearl River Delta. Behavior and fate of the pharmaceuticals were studied in depth by determining the concentrations in the effluents at major treatment units in typical sewage treatment plants in South China. To the best of our knowledge, occurrence, transport, and fate of most of these pharmaceuticals have been rarely reported in wastewater in Mainland China.

interfere with the biochemical functions and cause tissue damage in fish.[11]

Pharmaceuticals are continuously introduced into the environment unchanged and/or in metabolites through discharge of wastewater.[12] Some conjugates can transform back into parent compounds by cleavage in the environment and/or during treatment in sewage treatment plants (STPs).[1] STPs have therefore been considered as one of the most important point sources of pharmaceuticals in the environment.[13–18] Several pharmaceuticals have been detected in wastewater, surface water, groundwater, and even drinking water around the world.[13,16,19–24] Environmental behavior and fate of some pharmaceuticals have also been studied.[16,20,25–29] In contrast to intensive reports for European and North American countries, data about pharmaceuticals in the environment in China are still scarce.[23,30,31] It is recognized that occurrence of the pharmaceuticals may be closely related with the consumption patterns and volumes.[16,29,32] Furthermore, occurrence and fate of pharmaceuticals may be affected by climatic conditions and site-specific environmental factors.[27] Therefore, knowledge of pharmaceuticals in the environment in China is necessary to gain a full scenario of pharmaceutical contamination around the world given the large population and consequently potential high consumption of pharmaceuticals in the country.

The aims of this work include: (1) Developing a reliable and sensitive method for rapid determination of commonly consumed non-steroidal anti-inflammatory drugs and lipid regulators in water and sewage sludge using ultra-high performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS); (2) Investigating occurrence of these pharmaceuticals in river water, municipal wastewater, and sewage sludge in the Pearl River Delta, one of the most urbanized and densely populated regions in South China; (3) Studying in depth behaviors and fate of these pharmaceuticals in typical STPs in China. To the best of our knowledge, occurrence, transport, and fate of most of these pharmaceuticals in wastewater in Mainland China have not been reported previously.

Experimental

Sampling

Two STPs, located in Guangzhou, the biggest city of the Pearl River Delta, and referred to as GZSTPA and GZSTPB were selected because they represent typical wastewater sources and treatment techniques in China. GZSTPA serves a population equivalent of about 370 000 and treats a mixture of domestic/industrial (~4/6) wastewater with a capacity of 30 000 $m^3\ d^{-1}$. It uses conventional activated sludge treatment consisting of only an aerobic process with a hydraulic retention time (HRT) of 12 h. Ultraviolet (~3 mW cm^{-2}, TROJAN UV3000™ PLUS, Canada) disinfection is employed before the final discharge of the treatment effluent. GZSTPB has three parallel treatment systems with a total capacity of 550 000 $m^3\ d^{-1}$ and serves a population of about 2 500 000. The first and second treatment systems treat predominantly domestic wastewater (~90%) and use identical treatment techniques composed of a grit chamber, a bioreactor (consisting successively of anaerobic, anoxic, and oxic processes) and a secondary clarifier. The third system (GZSTPB3) has a bioreactor that consists successively of anoxic, anaerobic, and oxic processes and treats also a certain amount of industrial wastewater and municipal landfill leachate. The HRT of GZSTPB is 11.5 h. Chlorination is employed before the final discharge of the treated effluent. Samplings were conducted in August 2007 (summer), March 2008 (late winter), May 2008 (spring) and November 2008 (autumn). The influent and effluents after primary sedimentation, secondary clarification and UV irradiation were collected in GZSTPA. In GZSTPB, the influent and effluents at the outlets of the anaerobic tank, secondary clarifier and chlorination tank were collected along the first treatment system (GZSTPB1) in all sampling campaigns. The effluent samples at the outlets of the anoxic tank were also collected in August 2007 and November 2008 in order to investigate in depth the fate of the pharmaceuticals. The influent and the final effluent were also sampled in GZSTPB3 in order to fully screen the pharmaceuticals in the wastewater. Samples were collected hourly from 8:00 to 12:00 am on a weekday to build a composite sample (10 L for the influents and 40 L for the effluents) into amber glass bottles without headspace. Sodium azide (NaN_3) was added (0.5 g L^{-1}) immediately after sampling to suppress potential biological activities. Untreated solid from the grit chambers and dewatered sludge were sampled in May and November 2008 in both STPs.

The Pearl River is the longest river in South China and the most important water source of the Pearl River Delta. The river runs through Guangzhou city from west to east and finally merges into the South China Sea at the Pearl River Estuary (Fig. 1). Thirteen sampling sites were set along the urban section of the river at Guangzhou. Three urban canals, namely Shijing River (C01), Shahe Canal (C02) and Liede Canal (C03) were also sampled for better explanation of sources of the pharmaceuticals in the Pearl River. The Shijin River links directly to the Pearl River while the other two canals connect to the river with sluice gates that are open only in big storms in order to release flood. Samplings were performed in August 2007, March and May 2008. Grab samples (10 L) were always collected during the ebb period to prevent dilution by intruding seawater.

Samples were placed on icepacks during transport to the laboratory, where water samples were stored at 4 °C in darkness until treatment within 48 h and sludge samples were stored at −20 °C.

Chemicals and reagents

Salicylic acid (SA), ibuprofen (IPF), naproxen (NPX), indomethacin (IDM), diclofenac (DCF), bezafibrate (BZF), clofibric acid (CFA) and gemfibrozil (GFZ) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Gemfibrozil-d_6 (GFZ-d_6) and ibuprofen-d_3 (IPF-d_3) were bought from C/D/N isotopes Inc. (Pointe-Claire, Quebec, Canada). Ibuprofen-$^{13}C_3$ (IPF-$^{13}C_3$) was from Cambridge Isotope Laboratories, Inc. (Andover Massachusetts, USA). The standards were obtained in solid form except IPF-$^{13}C_3$ (100 μg mL^{-1} in acetonitrile). Their key physicochemical parameters are summarized in Table 1. Individual stock standard solutions were prepared in methanol at 500 μg mL^{-1} for the pharmaceuticals and 100 μg mL^{-1} for the isotope-labeled standards. A standard mixture solution containing all the

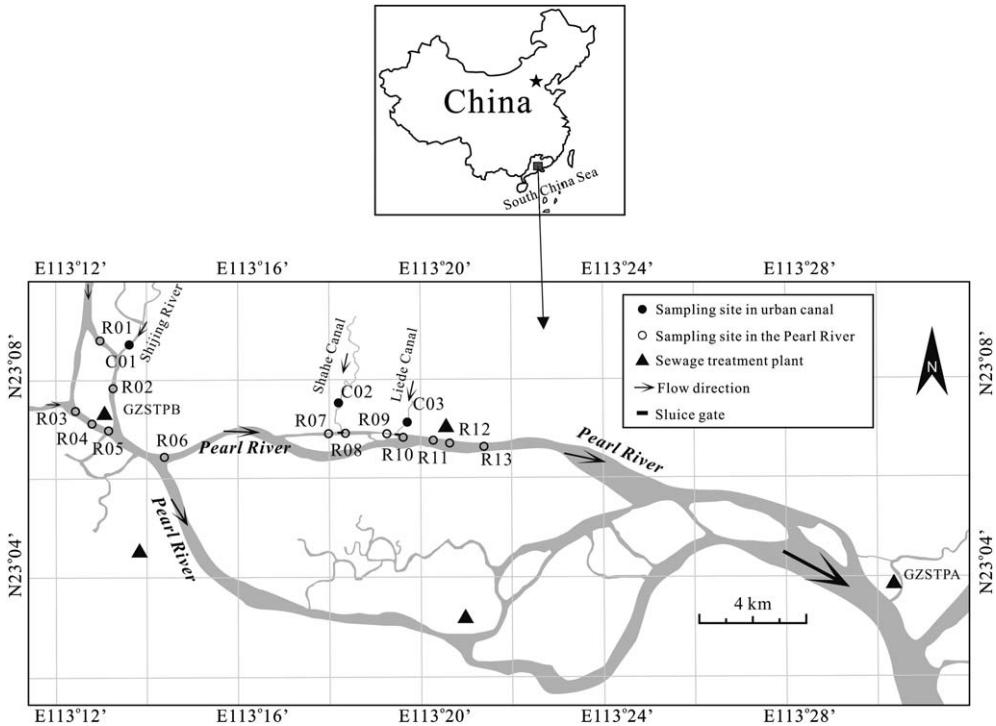

Fig. 1 Sketch of the study area and sampling sites.

acidic pharmaceuticals was then prepared in methanol at 10 μg mL^{-1}. Working standard solutions were obtained by further diluting the standard mixture solution. All the standard solutions were stored in amber glass vials and kept at −20 °C in a freezer. HPLC grade methanol, acetonitrile, formic acid, and ammonium acetate were purchased from Merck (Darmstadt, Germany). Ultra-pure water (UPW) was generated by a Milli-Q ultra-pure water system (Millipore, Billerica, MA, USA). Analytical grade sodium chloride (NaCl) and NaN_3 were obtained from Bodi Chemical (Tianjin, China), and were washed with methanol prior to use. Hydrochloric acid (HCl) was also from Bodi and was used as received.

Analytical methods

Water samples were filtered with 0.7 μm glass fiber filters (GFF, Whatman, Maidstone, England). The filtrate and suspended particulate matter (SPM) retained on the GFFs were analyzed

Table 1 Properties of investigated acidic pharmaceuticals and their optimal UHPLC-MS/MS conditions

Compounds (abbreviation)	CAS. No.	pK_a	Log K_{ow}	Log D_{ow} (pH 7.0)[c]	Water solubility (mg L^{-1})	H[d]	Retention time (min)	MRM transitions (m/z[e])	Fragmentor (eV)	Collision energy (eV)
Salicylic acid (SA)	69-72-7	2.97[a]	2.4[a]	–1.63	11 300[a]	7.34E-009	1.61	**137.0 → 93.0**	90	15
Ibuprofen (IPF)	15687-27-1	4.91[a]	3.6[a]	1.51	68.4[a]	1.5E-007	6.50	**205.1 → 161.2**	80	1
Naproxen (NPX)	22204-53-1	4.15[a]	2.8[a]	−0.05	51[a]	3.39E-010	5.96	**229.0 → 170.1**	70	10
								229.0 → 184.8	70	5
Indomethacin (IDM)	53-86-1	4.5[a]	3.4[a]	0.9	2.4[a]	3.13E-014	6.36	**356.1 → 282.1**	90	25
								356.1 → 255.1	90	20
Diclofenac (DCF)	15307-86-5	4.15[a]	3.9[a]	1.05	4.47[a]	4.73E-012	6.32	**294.0 → 250.0**	80	5
								294.0 → 214.0	80	15
Bezafibrate (BZF)	41859-67-0	3.61[b]	3.97[a]	0.58	1.55[a]	2.12E-015	6.04	**360.1 → 274.1**	110	10
								360.1 → 154.1	110	20
Clofibric acid (CFA)	882-09-7	2.95[b]	2.57[e]	−1.48	29[a]	2.19E-008	5.43	**213.0 → 127.0**	80	10
								213.0 → 85.0	80	5
Gemfibrozil (GFZ)	25812-30-0	4.7[b]	3.4[a]	1.1	27.8	1.19E-008	7.27	**249.2 → 121.1**	90	10
								249.2 → 127.1	90	5
Ibuprofen-d_3 (IPF-d_3)							6.50	**208.2 → 164.0**	80	1
Ibuprofen-$^{13}C_3$ (IPF-$^{13}C_3$)							6.50	**208.2 → 163.1**	80	1
Gemfibrozil-d_6 (GFZ-d_6)							7.27	**255.2 → 121.1**	90	10

[a] Available at http://www.drugbank.ca/. [b] Available at http://www.druginfosys.com/index.aspx. [c] Octanol–water distribution coefficient. $D_{ow} = K_{ow}/(1 + 10^{pH-pK_a})$. [d] Henry's Law Constant in atm m^3 mol^{-1} (25 °C), available from Syracuse Research Corporation (SRC). [e] Mass-to-charge ratio. Quantification transitions are in bold.

separately. An aliquot of filtrates (100–200 mL) was spiked with GFZ-d_6 (50 ng L^{-1}) and IPF-$^{13}C_3$ (100 ng L^{-1}), adjusted to pH 4.0 with diluted HCl, and NaCl added at 0.1 mol L^{-1} prior to being loaded onto an HLB cartridge (Waters, Milliford, MA, USA) at about 5 mL min^{-1}. The cartridge had been preconditioned successively with 5 mL of methanol and 5 mL of UPW (pH 4.0). After sample passage, the cartridge was rinsed with 5 mL of 5% methanol solution and vacuum dried for 10 min. The analytes were then eluted with 3 × 1.5 mL methanol. The eluent was added with 50 ng IPF-d_3, concentrated to 0.2 mL under a gentle flow of high purity nitrogen, and filtered through a 0.22 μm syringe filter (ANPEL, Shanghai, China) prior to UHPLC-MS/MS analysis.

Ultrasonic solvent extraction (USE) has been used to extract the pharmaceuticals from sediment and sludge previously.[33,34] Lyophilized and homogenized SPM and sludge samples were accurately weighed (0.1 g for each sludge sample) into 10-mL Kimax heavy duty glass centrifugal tubes (Kimble, Vineland, NJ, USA) and spiked with GFZ-d_6 at 50 ng g^{-1} dry weight (dw). Four millilitres of methanol containing 0.1% formic acid was added. The slurry was successively vortexed (XW-80A Mixer, Shanghai, China) for 2 min, ultrasonicated (YJ-5200D Ultrasonic Cleaner, 40 kHz, 300 W, Ningbo, China) for 10 min, and centrifuged (Avanti^{TM30} centrifuge, Beckman, California, USA) at 4000 rpm for 5 min at 4 °C. The supernatant was collected into an amber glass bottle. The extraction procedure was repeated twice. The supernatants were combined and diluted with UPW to bring the methanol content to <2% prior to being treated by the SPE procedure as described above.

The pharmaceuticals were determined on an Agilent Liquid Chromatography 1200 system coupled with an Agilent 6410 triple quadrupole mass spectrometer with electrospray ionization in negative mode (Agilent, Palo Alto, CA, USA). An Agilent ZORBAX Eclipse XDB C18 rapid resolution high throughput narrow column (2.1 mm × 50 mm, 1.8 μm particle size) was used for separation of the pharmaceuticals at 25 °C pre-connected with a guard column (2.0 mm × 4.0 mm, Phenomenex, Torrance, CA, USA) containing the same sorbent. The injection volume was 2 μL. The mobile phases consisted of UPW with 5 mM ammonium acetate (pH 6.8, mobile phase A) and acetonitrile (mobile phase B) with a flow rate of 0.2 mL min^{-1}. Separation of the pharmaceuticals was achieved with a gradient elution as follows: 10% B at 0 min, increased to 40% in 0.5 min and held for 1.5 min, ramped to 60% in 0.1 min and held for 0.9 min, then ramped to 100% in 0.1 min and held for 4.9 min. A post-time of 7 min was set for column equilibration prior to the next injection. Data acquisition was performed in multiple reaction monitoring (MRM) mode. The MS source temperature was set at 100 °C. Nitrogen was used as the drying gas at 350 °C and 10 L min^{-1}. The capillary voltage was 3.0 kV. The nebulizer (nitrogen) pressure was 40 psi. Dwell time for each ion transition was 50 ms. The optimized MS parameters and qualification/quantification ion transitions for each compound are presented in Table 1. A nine-point calibration curve was established using IPF-d_3 as the internal standard for each analyte and surrogate standard with good linearity ($r^2 > 0.999$).

Contents of dissolved organic carbon (DOC) of the water samples were measured using a Shimadzu TOC-V analyzer (Shimadzu Scientific Instruments, Kyoto, Japan).

Quality assurance and quality control

Recovery tests were performed by spiking the analytes into water samples at 50, 200 and 500 ng L^{-1} and sludge samples at 100 and 500 ng g^{-1} dw. The method quantification limits (MQLs) were estimated based on instrumental quantification limits (S/N > 10), recoveries and sample volumes. Procedural blanks (UPW for water and clean quartz sand for sludge samples) and instrumental blanks were set to monitor laboratory contamination and instrumental performance. Other procedures of quality assurance and quality control, such as breakthrough during SPE, exhausted extraction, and matrix effect, have been detailed elsewhere.[35]

Results and discussion

Method performance

The HLB cartridge has been widely used to extract various pharmaceuticals in water samples.[36,37] Optimization of pH conditions for the SPE procedure was accomplished by spiking the analytes into UPW (100 ng mL^{-1}) at pH 2.0, 4.0, 6.0 and 7.0 considering the acidic properties of the pharmaceuticals with pK_a of 2.95–4.7 (Table 1). SA got satisfactory recoveries (85.0–119.3%) at pH ≤ 4.0. IDM had an acceptable recovery (70.2%) only at pH 4.0. On the other hand, recoveries of DCF, IPF and GFZ decreased with the decrease in pH. However, pH did not show any significant impact on the recoveries of CFA, BZF, and NPX. Therefore, SPE of water samples was finally performed at pH 4.0 to ensure an acceptable recovery for each analyte.

Recoveries ranged from 78% to 138% in river water and from 56% to 133% in wastewater at various spiking levels, with relative standard deviations (RSDs) within 20% (Table 2).

For sewage sludge samples, recoveries ranged from 64% to 143% for most pharmaceuticals except for SA (Table 2). The poor recovery of SA (21%) may be associated with its hydrophilicity and high water solubility (Table 1). However, further work is needed to improve the extraction efficiency of SA from solid matrices. Data of SA in sewage sludge will therefore be used only for reference and will not be included in the following detailed discussion.

Recoveries of 95% to 103% were obtained from USE of clean quartz sand fortified with the pharmaceuticals for 45 min, showing no evidence of significant decomposition of these compounds during the USE procedure.

The intra-day and inter-day precisions of the instrumental analysis were 3.3–6.2% and 3.6–5.8% respectively for the analytes calculated by replicate injections of standard solutions at 10, 50 and 200 μg L^{-1} (Table 2). MQLs were 1–56 ng L^{-1}, 3–61 ng L^{-1}, and 5–113 ng g^{-1} dw for river water, wastewater, and dewatered sludge, respectively (Table 2). No quantifiable amounts of the analytes were detected in procedural and instrumental blanks.

Recoveries of the surrogate standards IPF-$^{13}C_3$ and GFZ-d_6 were 98 ± 12% (mean ± standard deviation) and 101 ± 14%, 100 ± 14% and 88 ± 10% in river water samples (n = 43) and wastewater samples (n = 11), respectively. Recoveries of GFZ-d_6 were 89 ± 14% in sewage sludge (n = 8). These results further confirmed the good performance of the methods. The reported

Table 2 Method quantification limit (MQL, ng L^{-1} for water and ng g^{-1} for sewage sludge) and recovery (%) of the pharmaceuticals[a]

	MQL			Recovery (mean ± standard deviation)			
	RW	WW	SS	UPW	RW	WW	SS
SA	20	NC	NC	144 ± 1	103 ± 21	—[b]	21 ± 3
CFA	2	3	7	99 ± 3	138 ± 12	133 ± 5	143 ± 20
BZF	2	6	11	90 ± 3	94 ± 5	72 ± 1	92 ± 6
NPX	2	6	12	86 ± 3	93 ± 10	71 ± 7	85 ± 6
DCF	6	18	39	112 ± 7	85 ± 14	56 ± 4	64 ± 8
IDM	6	12	37	85 ± 10	89 ± 17	83 ± 2	67 ± 10
IPF	56	61	113	90 ± 2	85 ± 12	66 ± 6	89 ± 14
GFZ	1	3	5	93 ± 2	79 ± 8	69 ± 5	104 ± 24
GFZ-d_6				93 ± 4	84 ± 4	NA	103 ± 14
IPF-$^{13}C_3$				78 ± 3	85 ± 7	NA	NA

[a] UPW = ultra-pure water spiked at 20 ng L^{-1}. RW = river water spiked at 50 and 500 ng L^{-1}. WW = wastewater spiked at 200 ng L^{-1}. SS = sewage sludge spiked at 100 and 500 ng g^{-1}. NC = not calculated. NA = not analyzed. See Table 1 for full names of the compounds. [b] Reliable recoveries cannot be calculated because the spiking level was within the analytical precision (<10% of the background concentration).

results of the environmental samples were therefore not corrected with recoveries of the surrogate standards.

Occurrence of the pharmaceuticals in wastewater and sewage sludge

Distribution of the pharmaceuticals in the wastewater is shown in Fig. 2. In GZSTPA, SA, CFA, NPX, IPF and GFZ were detected in the influent, ranging from 3 ng L^{-1} to 23.3 μg L^{-1}. Concentrations of the pharmaceuticals decreased significantly after treatment. Only CFA and SA were detected at 21–128 ng L^{-1} in the final effluent samples. In GZSTPB, the investigated pharmaceuticals were omnipresent in the influent samples. Likewise, SA had the highest concentration, ranging from 9.6 to 16.0 μg L^{-1} and 10.2 to 18.6 μg L^{-1} in the influents from GZSTPB1 and GZSTPB3, respectively. The second most abundant pharmaceutical was IPF, with concentrations of 264–588 ng L^{-1} and 396–997 ng L^{-1} in the influents from GZSTPB1 and GZSTPB3, respectively. Concentrations of the other pharmaceuticals varied from 10 (BZF) to 119 ng L^{-1} (DCF) in the influent samples from both GZSTPB1 and GZSTPB3 except for IDM which was only quantifiable in August 2007 and March 2008 in GZSTPB1 and in March 2008 in GZSTPB3. Concentrations of the pharmaceuticals decreased by varying degrees, ranging from non-detectable to 223 ng L^{-1} in the final effluent samples from both treatment lines. These results fell into the range reported previously in countries in Europe, Asia and North America.[13,38,39] The high concentrations of SA in both STPs are not surprising because SA is also a widely used additive in cosmetics and foodstuff and occurs naturally in the environment.[40] Without taking SA into consideration due to its various origins, the sum of concentrations of the non-steroidal anti-inflammatory drugs (*i.e.*, DCF, IPF, IDM and NPX) were 374–864 ng L^{-1} and 521–1119 ng L^{-1} in the influents from GZSTPB1 and GZSTPB3, respectively. The total concentrations of the lipid regulators (*i.e.*, BZF, CFA and GFZ) were 136–195 ng L^{-1} in the influents from GZSTPB1 and 96–183 ng L^{-1} in the influents from GZSTPB3. These concentrations were slightly higher than those in the influent samples from GZSTPA (non-quantifiable to 322 ng L^{-1} and non-quantifiable to 100 ng L^{-1}, respectively), probably associated with the predominance of domestic wastewater in GZSTPB. In addition, the larger potential consumption because of the bigger served population of GZSTPB (2.5 million) may also contribute to the higher pharmaceutical concentrations in the wastewater.

In GZSTPB, the concentrations of the non-steroidal anti-inflammatory drugs (excluding SA) in the influents were observed to be higher in late winter (895 ng L^{-1}) and spring (743 ng L^{-1}) than those in summer (455 ng L^{-1}) and autumn (528 ng L^{-1}), whereas no statistical seasonal difference was found for the lipid regulators. By contrast, in GZSTPA, the concentrations of all the pharmaceuticals (excluding SA) in the influent were relatively higher in spring than those in summer and autumn (late winter data were missing due to analytical problems). Seasonal effects on the occurrence of pharmaceuticals have been reported in wastewater in Europe, North America and South Korea, which were ascribed to different consumption.[19,29,41,42]

No significant amount of the pharmaceuticals was detected in SPM and the sewage sludge, indicating that sorption is of little importance in the fate of the pharmaceuticals in wastewater. The octanol–water distribution coefficient (log D_{ow}) is preferred to predict the potential of absorption onto organic matter for ionizable chemicals.[43] The investigated pharmaceuticals are all ionizable and have low log D_{ow} values at neutral pH conditions (Table 1), suggesting that they are not likely to absorb significantly onto either particles of wastewater or sewage sludge that are abundant in organic matter. Besides, the pH values of the wastewater were 6.7–7.2 throughout treatment in the STPs, under which these pharmaceuticals were negatively charged and therefore would not adsorb onto sludge.[44] Weak sorption of these pharmaceuticals has been reported previously.[38,45,46]

Behaviors and fate of the pharmaceuticals during wastewater treatment

The fate of chemicals in STPs includes volatilization, sorption to solids, biodegradation and chemical transformation.[44] However, volatilization appears negligible for the investigated pharmaceuticals due to their poor volatility as indicated by the Henry's Law Constants (Table 1).

Fig. 2 also shows the behavior of the pharmaceuticals during treatment in the STPs in the four sampling campaigns. Table 3 shows the different behaviors of the pharmaceuticals among anaerobic, anoxic and aerobic treatments in GZSTPB1 in

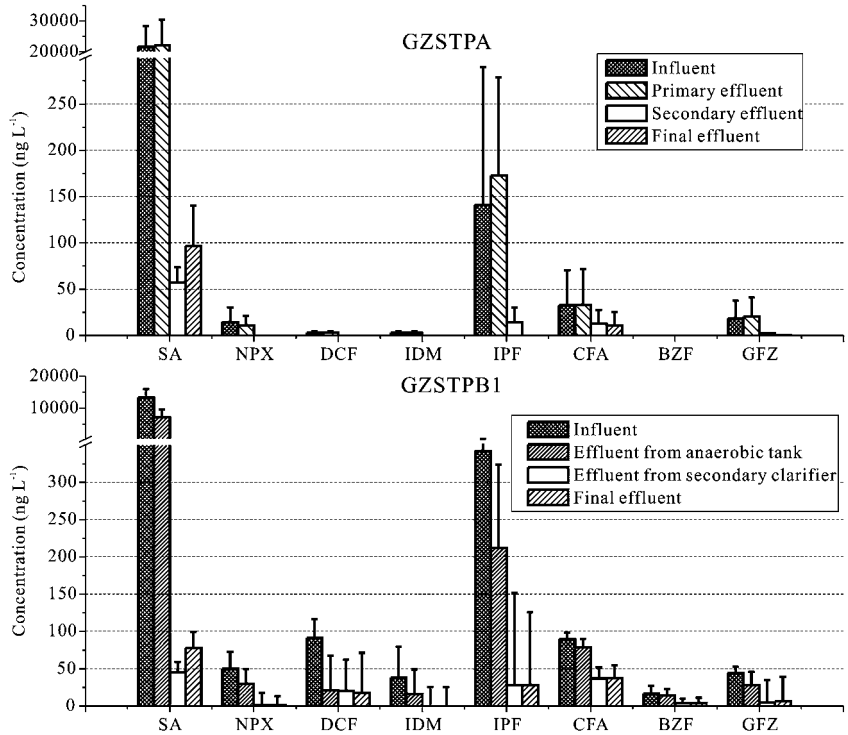

Fig. 2 Median concentrations of the pharmaceuticals in the wastewater along treatment in the sewage treatment plants at Guangzhou. Error bars represent standard deviations in the four sampling campaigns. Results of non-detectable were replaced with zero and non-quantifiable were replaced with half of the method quantification limits. See Table 1 for full names of the abbreviated compounds.

August 2007 and November 2008. Mechanical sedimentation led to no difference in the concentrations of the pharmaceuticals, which is reasonable given weak sorption of the pharmaceuticals as discussed above. After anaerobically activated sludge treatment, DCF, IDM and NPX were significantly eliminated whereas a significant amount of the other pharmaceuticals remained in the wastewater (Fig. 2, Table 3). Anaerobic degradation of DCF has been reported previously.[47] The anoxic process resulted in no further significant losses of the pharmaceuticals except for SA for which only less than 10% remained (Table 3). After aerobically activated sludge treatment and secondary clarification, SA, IDM and NPX were almost completely removed (≥99%), GFZ, IPF and BZF were largely eliminated (>75%), whereas a median of 30–40% of DCF and CFA remained in the wastewater (Fig. 2). DCF and CFA were reported to be refractory to biodegradation previously.[19,48] Previous research has also revealed that some of the pharmaceuticals (*e.g.*, DCF, NPX, IPF and GFZ) could be efficiently removed by chlorination after a 24-h contact time.[49] However, no further removal of the pharmaceuticals was observed after chlorinated disinfection (Fig. 2 and Table 3), which may be due to either a short contact time (0.5 h) or insufficient Cl_2 dose (not available) or both. IPF, NPX, IDM and DCF were reported to be liable to phototransformation.[26,29,50–53] Nevertheless, they were not detected above the quantification limit before UV irradiation in wastewater at GZSTPA and therefore no further discussion can be presented here.

Relatively poorer elimination was observed for the pharmaceuticals in March 2008 in GZSTPB except for SA whose elimination rate was always high (>99%). Previous research ascribed the lower elimination of pharmaceuticals in winter to weaker biological activities due to cold weather.[19,27] However, the mild

Table 3 Elimination rate (%) of the investigated pharmaceuticals leaving major treatment units in GZSTPB1[a]

	Anaerobic tank	Anoxic tank	Secondary clarifier	Final effluent
SA	43 (30–56)	93 (88–98)	99	99
NPX	73 (50–96)	71 (47–96)	99 (98–100)	99 (98–100)
DCF	67 (37–96)	62 (27–96)	67 (38–96)	72 (48–96)
IDM	79 (58–100)	76 (52–100)	100	100
IPF	28 (14–43)	45 (41–48)	91 (89–92)	91 (89–92)
CFA	14 (3–30)	17 (5–38)	58 (52–65)	57 (57–58)
BZF	34 (20–89)	42 (6–89)	81 (63–100)	79 (58–100)
GFZ	53 (37–69)	56 (49–64)	88 (80–96)	84 (80–88)

[a] Mean (range) data of two sampling campaigns in August 2007 and November 2008.

temperature in Guangzhou throughout the year is not likely to cause obvious differences in biological activities (Table 4). It was possible that the STP was not functioning well during our sampling. However, no more speculation can be made based on the limited data presented in this work and further work is needed to clarify the seasonal effects on the behavior of the pharmaceuticals in wastewater. In the other seasons, IDM, NPX, IPF, BZF, and GFZ were largely eliminated, whereas DCF was removed poorly (<50%) in August 2007 and CFA did not show good removal in all seasons. Reported removal of DCF in the literature varies significantly and appears associated with treatment technologies as well as operational parameters.[54]

No significant correlations were found between the pharmaceutical concentrations and DOC contents, suggesting that the dissolved organic matter is not of significance in the elimination of the pharmaceuticals in wastewater.

In summary, the behavior and fate of the investigated pharmaceuticals in wastewater varied by compound during treatment in the STPs. SA, IDM and NPX were almost completely removed (≥99%); GFZ, IPF and BZF were significantly removed (>75%). However, DCF and CFA were only moderately removed by 60–70%, respectively. The pharmaceuticals were not subjected to sorption/sedimentation due to their low affinity for solids. Biodegradation was the governing mechanism for elimination of the investigated pharmaceuticals. Anaerobic degradation was responsible for most of the removal of DCF whereas aerobic biodegradation also played an important role in elimination of the other pharmaceuticals. On the other hand, the anoxic bioprocess had little significance on the fate of most of the pharmaceuticals except for SA which was nearly completely removed after the anoxic process. In addition, chlorination caused negligible losses of the pharmaceuticals, probably due to a short contact time and/or insufficient dose. However, the water "package" of the influent did not correspond to that of the effluent due to the hydraulic retention time in the STPs. Previous research revealed diurnal variations in mass loads of pharmaceuticals, with generally 10–40% higher inflows at 8:00–16:00 than the daily average.[55] Therefore, the elimination rates obtained in this work may be overestimated due to the possible overestimation of the inflows resulted from sampling at 8:00–12:00. However, the obtained results illustrate the occurrence and behavior of the pharmaceuticals in wastewater in South China. Composite sampling, especially over a 24-h period, should be considered in future work in order to more accurately investigate the behavior and fate of the pharmaceuticals in wastewater.

Table 4 Precipitation, sunshine duration and monthly average temperature during the sampling months[a]

	Precipitation (mm)	T (°C)	Sunshine duration (h)
August 2007	309.5	29	155.8
March 2008	70.9	20.1	100.9
May 2008	285.2	25.6	69.1
November 2008	61.9	19.9	191.2

[a] http://www.stats.gov.cn/.

Occurrence and seasonal variations of the pharmaceuticals in the Pearl River

All the pharmaceuticals were detected at least once in the Pearl River (Fig. 3a). SA had the highest maximum concentration (6.7 μg L^{-1}) and median concentration (109 ng L^{-1}), most likely due to its several origins as discussed above. The second most abundant pharmaceutical was IPF with maximum and median concentrations of 288 and 78 ng L^{-1} respectively. Median concentrations of the other compounds ranged from non-detectable to 13 ng L^{-1}. These results agreed well with previous research about the Pearl River[30,31] and fell into the range reported worldwide.[20,25,56,57]

Distribution of the pharmaceuticals in the Pearl River at in the Guangzhou section showed obvious seasonal variations (Fig. 3b). Both the median concentrations (except SA) and detection frequency were in the order of late winter > spring > summer. Only CFA, GFZ, IPF, and SA were occasionally detected at relatively low levels in summer. This is fairly different from the distribution pattern in wastewater, especially for the lipid regulators that did not vary significantly by season. Seasonal variations of the pharmaceutical contaminants in surface water have been reported in the literature.[16,20,27,41,58] Vieno *et al.* (2005) attributed the higher pharmaceutical concentrations in winter in a treated wastewater receiving river of Finland to lower degradation due to cold weather. However, the temperature variations during our sampling (20–29 °C, Table 4) are not likely to cause obvious differences in microbial activities as discussed above. Therefore, the dilution effect by precipitation is likely to be the governing factor for seasonal differences in the distribution of pharmaceuticals in the Pearl River. The dilution effect of water flow on the occurrence of pharmaceuticals and personal care products has been reported for surface water in the U.S. and South Korea.[41,58] While, no obvious seasonal variations were observed in surface water of South Wales due to the mild climate and moderate variation in the flow rates.[20] Similar concentrations as well as detection frequency of DCF were observed in March and May 2008 (Fig. 3b) despite the much higher precipitation in May, which may be explained by stronger photodegradation by sunlight in March as indicated by the longer sunshine time (Table 4) because DCF is readily phototransformed.[26,29]

The pharmaceuticals in the urban canals showed similar patterns to those in the Pearl River but the concentrations were much higher, probably due to random direct discharge of wastewater into the canals. The highest concentration was also found for SA (0.1–65.1 μg L^{-1}, median of 7.3 μg L^{-1}), followed by IPF (79–609 ng L^{-1}, median of 204 ng L^{-1}). The concentrations of CFA and GFZ ranged from non-detectable to 148 ng L^{-1} (median of 29 ng L^{-1}) and from 4 to 33 ng L^{-1} (median of 7 ng L^{-1}), respectively. The other pharmaceuticals were occasionally detected, with the highest concentrations of 10, 74, 94 and 94 ng L^{-1} for BZF, NPX, DCF and IDM, respectively.

Higher pharmaceutical concentrations were generally observed at sites immediately downstream of STP outfalls (R5 and R12, Fig. 1), indicating that the STPs are significant contributors to the pharmaceutical contamination in the Pearl River. In addition, the sampling site close to the outlet of the Shijing River (R02, Fig. 1) also showed relatively higher

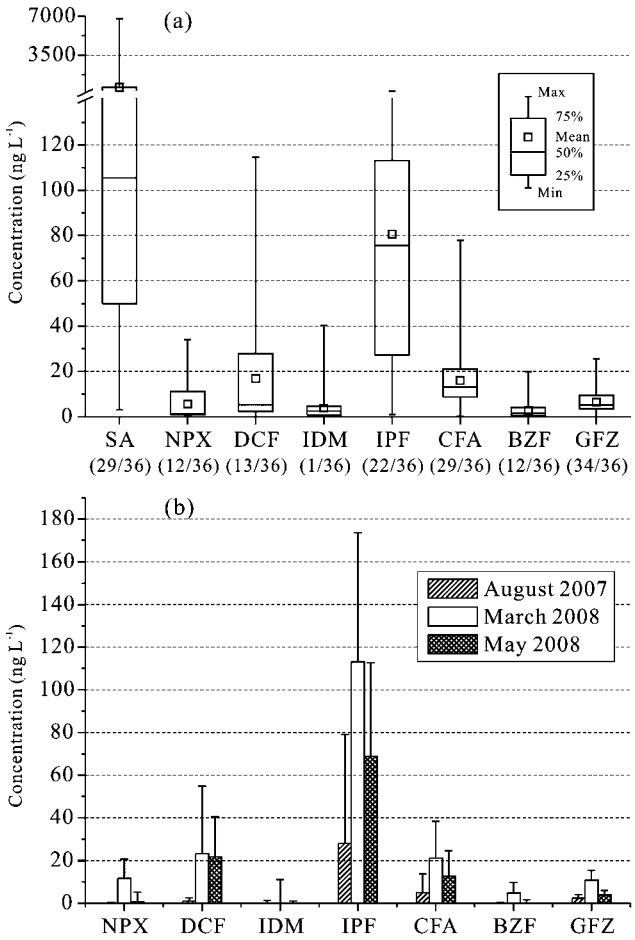

Fig. 3 Distribution (a) and seasonal variation (b) of the pharmaceuticals in the Pearl River. The detection frequency is given in parentheses as number of quantifiable samples/number of analyzed samples. Error bars in (B) represent the standard deviation of the sampling sites. Results of non-detectable were replaced with zero and non-quantifiable were replaced with half of method quantification limits. See Table 1 for full names of the abbreviated compounds.

pharmaceutical concentrations, whereas at sites close to the Shahe and Liede canals, the pharmaceutical distributions were not statistically different from those at ambient sites, which suggests that urban canals directly connected to the Pearl River are also point sources of the pharmaceuticals to the river.

Conclusions

(1) Five non-steroidal anti-inflammatory drugs (*i.e.*, SA, DCF, IPF, IDM and NPX) and three lipid regulators (*i.e.*, BZF, CFA and GFZ) were omnipresent in the wastewater of the Pearl River Delta, China. Generally, biodegradation was the governing process for elimination of the investigated pharmaceuticals. Anaerobic degradation was responsible for most of the removal of DCF whereas aerobic biodegradation also played an important role in elimination of the other pharmaceuticals except for SA which showed a substantial decrease after the anoxic process. SA, IDM and NPX were almost completely removed (≥99%), BZF, IPF and GFZ were largely removed (>75%) and DCF and CFA were removed by 60–70% during treatment in the STPs.

(2) The pharmaceuticals were widely detected in the urban section of the Pearl River at Guangzhou. Both detection frequency and concentrations in the river were higher in late winter than those in spring and summer, which may be mainly ascribed to the lower dilution by lower precipitation. Besides municipal STPs, urban canals directly connected with the Pearl River are also important point sources of the pharmaceutical contamination in the river.

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