Occurrence, spatial and seasonal variation, and environmental risk of pharmaceutically active compounds in the Pearl River basin, South China

Frontiers of Environmental Science and Engineering

Lei, Haojun; Yao, Kaisheng; Yang, Bin; Xie, Lingtian; Ying, Guangguo

https://doi.org/10.1007/s11783-023-1646-8

Front. Environ. Sci. Eng. 2023, 17(4): 46
https://doi.org/10.1007/s11783-023-1646-8

RESEARCH ARTICLE

Occurrence, spatial and seasonal variation, and environmental risk of pharmaceutically active compounds in the Pearl River basin, South China

Haojun Lei[1,2], Kaisheng Yao[1,2,3], Bin Yang (✉)[1,2], Lingtian Xie[1,2], Guangguo Ying[1,2]

1 SCNU Environmental Research Institute, Guangdong Provincial Key Laboratory of Chemical Pollution and Environmental Safety & MOE Key Laboratory of Theoretical Chemistry of Environment, South China Normal University, Guangzhou 510006, China
2 School of Environment, South China Normal University, Guangzhou 510006, China
3 Aquatic Ecology and Water Quality Management Group, Wageningen University, 6700 AA Wageningen, Netherlands

HIGHLIGHTS

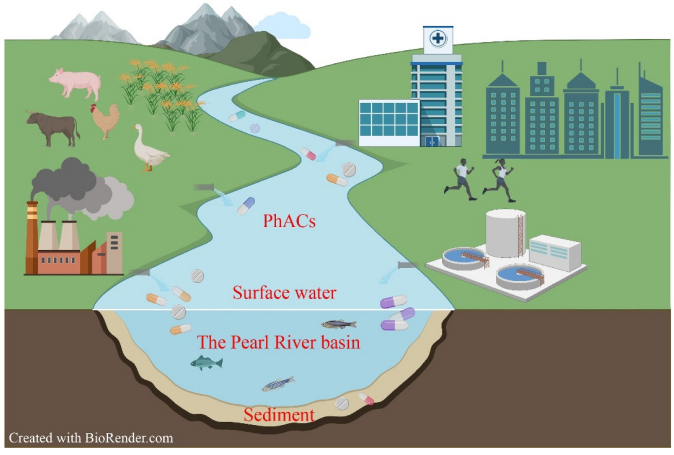
- 38 PhACs and 2 pesticides were detected in the three rivers of the Pearl River basin.
- Anti-inflammatory/analgesics drugs were the predominant PhACs.
- The concentrations of PhACs showed seasonal and spatial variation.
- Diazepam and ibuprofen were the two PhACs with a moderate environmental risk.

ARTICLE INFO

Article history:
Received 19 July 2022
Revised 18 August 2022
Accepted 20 September 2022
Available online 31 October 2022

Keywords:
Pharmaceutically active compounds
Occurrence
Spatiotemporal variations
Pearl River
Environmental risk assessment

GRAPHIC ABSTRACT



ABSTRACT

The occurrence, fate, and environmental risk of 40 pharmaceutically active compounds (PhACs) from surface waters and sediments were comprehensively investigated in the Beijiang River, Xijiang River, and Maozhou River of the Pearl River basin, South China. Salicylic acid and diclofenac (anti-inflammatory drugs), gemfibrozil (a lipid regulator), carbamazepine (an antiepileptic drug), diazepam (a psychoactive drug), and 2-methyl-4-chloro-phenoxyacetic acid (MCPA, a pesticide) were the most ubiquitous compounds in the studied region. The average concentrations of detected PhACs in surface waters and sediments ranged from 0.17 to 19.1 ng/L and 0.10 to 10.4 ng/g, respectively. Meanwhile, PhACs concentration in surface waters and sediments varied greatly among and within the Beijiang River, Xijiang River, and Maozhou River. The largest annual flux of PhACs of the Xijiang River and Beijiang River was more than 11 000 kg per annum, whereas only 25.7 kg/a in the Maozhou River. In addition, the estimated emissions of PhACs in the Beijiang River, Xijiang River, and Maozhou River ranged respectively from 0.28 to 4.22 kg/a, 0.12 to 6.72 kg/a, and 6.66 to 91.0 kg/a, and the back-estimated usage varied with a range from 12.0 to 293 kg/a, 6.79 to 944 kg/a, 368 to 17 459 kg/a. Moreover, the emissions of PhACs showed a close relationship with the gross domestic product (GDP) of each city along the Pearl River. The environmental risk assessment suggested that diazepam and ibuprofen had a moderate risk in this region.

1 Introduction

Pharmaceutically active compounds (PhACs) are widely

✉ Corresponding author
E-mail: bin.yang@m.scnu.edu.cn

used in humans and veterinaries to prevent, diagnose, and treat diseases. Major groups of the PhACs include non-steroidal anti-inflammatory drugs (NSAIDs), antidepressants, anxiolytics, and hypertension medicines. Most of these drugs have been regarded as emerging organic contaminants in aquatic ecosystems (Daughton and Ternes, 1999; Silva et al., 2015). The PhACs have attracted massive attention due to their large quantity of consumption, continuous discharge, and ecological risk to aquatic organisms in the receiving aquatic environments (Hu et al., 2019; Fatima et al., 2020; Szabelak and Bownik, 2021). The PhACs have been frequently detected in surface waters throughout the world at concentrations range of ng/L to μg/L over the past decades (Zhao et al., 2016; Valdez-Carrillo et al., 2020). The primary sources of PhACs to aquatic environments are effluents from the wastewater treatment plants (WWTPs), wastewaters from livestock and poultry industries, and sewage wastewater containing optionally disposal of expired or unused drugs (Subedi et al., 2017; Thiebault et al., 2017; Lei et al., 2021).

Among the PhACs, NSAIDs are one of the most frequently used pharmaceuticals globally, and listed among the top 10 persistent pollutants (Green et al., 2001). Widely detected NSAIDs in aquatic environments include ibuprofen, diclofenac, naproxen, ketoprofen, and salicylic acid (Świacka et al., 2020). For instance, the most prominent NSAIDs in African surface waters are ibuprofen, diclofenac, and naproxen, with maximum concentrations of μg/L (Madikizela and Chimuka, 2017; Madikizela et al., 2017; Sibeko et al., 2019). Meanwhile, psychotropic pharmaceuticals (PPhs) are widely consumed in the developed countries (Brauer et al., 2021). Antidepressants and anxiolytics are the most widely detected PPhs in aquatic environments (Mompelat et al., 2009; Schlüsener et al., 2015; Grabicová et al., 2020; Branchet et al., 2021). The presence of some PPhs in aquatic environments has been implicated a pollution source from the wastewater. For example, the presence of carbamazepine (an antiepileptic drug) has been deemed a ubiquitous indicator of wastewater pollution (Glassmeyer et al., 2005). Other PPhs, such as benzodiazepines (BZDs) and its various transformed products (i.e., diazepam and 6-chloro-4-phenyl-2(1H)-quinazolinone (6-CPQ), are frequently detected at a few ng/L to hundreds ng/L in different waters (Calamari et al., 2003; Calisto and Esteves, 2009; Hass et al., 2012; Lei et al., 2021).

Numerous studies have shown that many PhACs are toxic to aquatic organisms. For example, NSAIDs decrease the chlorophyll and carotenoid content for the green algae *Scenedesmus obliquus*, resulting in a reduced photosynthetic efficiency and growth (Wang et al., 2020). Psychoactive compounds such as diazepam at environmental concentrations can alter the transcriptional expression of genes and behavior of zebrafish (Oggier et al., 2010). In addition, exposure to sertraline disturbs the balance of microbial communities (Yang et al., 2019). Therefore, the environmental risk of PhACs cannot be simply ignored.

The Pearl River basin serves as an important source of drinking water for many cities in southern China. Previous research on the pollution of PhACs in the Pearl River basin has been conducted with one or two sampling campaigns along one main stream with recognized sources of PhACs contamination (Yang et al., 2017). This approach could not provide a complete understanding on variations in the frequency of occurrence and the environmental risk of PhACs. Moreover, data on PhACs for multiple rivers in the Pearl River basin by one sampling campaign in each of two seasons in a year are of relatively paucity. The main objective of this study was to evaluate the occurrence of PhACs in the Beijiang River, Xijiang River, and Maozhou River of the Pearl River basin. Major classes of PhACs in this study included NSAIDs, antidepressants, anxiolytics, and anti-hypertension drugs. In addition, the seasonal and temporal variations in the concentrations of these PhACs among and between different rivers, along with the environmental risk were evaluated. This study can provide important data on the fate and environmental assessment of the PhACs in the Pearl River basin.

2 Materials and methods

2.1 Chemicals

Standards (total number of 40) of 11 non-steroidal anti-inflammatory drugs (NSAIDs), 2 antiepileptic drugs (primidone and carbamazepine), 2 lipid regulators (gemfibrozil and clofibric acid), 1 antineoplastic drug (cyclophosphamide), 22 psychoactive drugs (fluoxetine, sertraline, 17 benzodiazepines and their 3 transformed products), 2 pesticides (bentazone and 2-methyl-4-chlorophenoxyacetic acid (MCPA)), and 13 internal standards were obtained from Sigma-Aldrich (USA), Cerilliant Corporation (USA), Dr. Ehrenstorfer GmbH (Germany), and Riedel-de Haen (Germany). Chemical information of these pharmaceutically active compounds (PhACs) is provided in Table S1, Supplementary Information. The HPLC-grade organic solvents used were all purchased from the Merck Corporation (Shanghai, China).

2.2 Sample collection

The Pearl River is a major river and main drinking water source in south China, which covers approximately 453,690 square kilometers. The Xijiang River, Beijiang River, and Maozhou River belong to the Pearl River basin. The Xijiang River and Beijiang River are the main tributaries of the Pearl River, crossing Guangxi and Guangdong in China, with a full-length of 2214 km and

573 km, respectively. The Maozhou River is a tributary crossing Shenzhen and Dongguan with a length of 41.6 km.

Twenty-two sampling sites in the Xijiang River, 13 in the Beijiang River, and 7 in the Maozhou River were respectively selected as representative sites. Table S2 provides detailed information about the sampling sites in this study. Sample collection of surface waters and sediments was conducted in July and December 2018 for the wet and dry seasons, respectively. Surface water samples were taken in 1 L amber bottles, followed by immediate field adjustment of the pH to 3.0 with 4 mol/L H_2SO_4, while sediment samples were collected in 200 mL glass bottles. Three replicate samples were collected for each sampling site. After collection, appropriate volume of methanol (final concentration: 5 % *v/v*) was immediately added to the surface water samples, and sodium azide (1 g/L each) was added to the sediment samples to suppress microbial activity. All the pre-treated samples were delivered to the lab in coolers. The surface water samples were kept at 4 °C and extracted within 24 h. Additionally, the sediment samples were freeze-dried, sieved by a standard 60-mesh sieve, and stored at –20 °C.

2.3 Sample preparation and chemical analysis

The extraction methods for the 40 PhACs in the surface water samples and sediment samples followed our previous study (Chen et al., 2010; Lei et al., 2021). Briefly, the solid-phase extraction (SPE) method was applied using Oasis HLB cartridges to extract the water samples. The sediment samples were extracted using SPE clean-up and ultrasonic-assisted extraction. Details of the extraction methods are provided in Text S1.

The target compounds were analyzed on an Agilent 1290 liquid chromatography with an Agilent 6495 triple quadrupole mass spectrometer (HPLC-MS/MS). The HPLC-MS/MS was conducted in both negative and positive ionization modes with an electrospray ionization (ESI) source. The operating conditions of LC and MS for analyzing the target compounds can be found in our recent papers (Yang et al., 2017; Lei et al., 2021).

2.4 Quality assurance and quality control

The internal standard method was used to determine the quality assurance and quality control (QA/QC) for chemical analysis. Table S3 shows the method quantitation limits (MQLs) for each target in the water and sediment samples. For the surface water and sediment samples, the MQLs ranged from 0.024 to 1.552 ng/L and 0.007 to 2.915 ng/g, respectively. The recoveries were between 80 % and 120 %, which were validated in our previous studies as well (Chen et al., 2010; Yang et al., 2017; Lei et al., 2021). Additionally, the mixture of standard samples, procedural blank samples, and instrumental blank samples were detected in each batch of ~ 10 samples. No target compounds were detected in the blank samples.

2.5 Calculation of contaminant flux, emission, and usage

Contaminant flux was used to evaluate the quantity, the rate, and the moving of a contaminant between two sites and calculated using Eq. (1). The estimated emission and the back-estimated usage of a detected compound in water samples were calculated using Eqs. (2)–(3).

$$\text{Contaminant flux (kg/a)} = C_{\text{water}} \times Q_{\text{wet/dry season flow}} \times 3600 \times 24 \times 365 \times 10^{-9} \quad (1)$$

$$\text{Emission (kg/a)} = C_{\text{water}} \times Q_{\text{capacity}} \times 10^{-5} \quad (2)$$

$$\text{Usage (kg/a)} = \frac{C_{\text{water}} \times Q_{\text{discharge}} \times 10^{-5}}{1 - \text{Removal rate}\%} \times \frac{100}{100 + \text{Stability}} \times \frac{100}{\text{Excretion}} \quad (3)$$

where C_{water} (ng/L) represented the concentration of each detected compound in waters in the wet or dry season; $Q_{\text{wet/dry season flow}}$ (m^3/s) referred to flow rate for the surface waters at each sampling time (shown in Table S2); Q_{capacity} and $Q_{\text{discharge}}$ (10000 t/a) respectively designated the wastewater treatment capacity and wastewater discharge at each sampling site (listed in Table S4); Removal rate (%) was the percentage of the detected compound removed after sewage treatment, and stability was a measure of stability change (%) of each PhACs after 12 h, and excretion was the percentage of PhACs from human body after the relevant forms of administration (listed in Table S5).

2.6 Environmental risk assessment

The environmental risk of the detected PhACs was evaluated using Eqs. (4) and (5) based on European Union Technical Guidance Document (EU TGD, 2003).

$$\text{RQ} = \text{MEC}/\text{PNEC} \quad (4)$$

$$\text{PNEC} = \text{EC}_{50}/\text{AF} \quad (5)$$

where RQ was the risk quotient; MEC was the measured concentration of each PhACs; PNEC was the predicted no-effect concentration; AF was the assessment factor and an AF of 1000 was used due to at least one short-term EC_{50} was available (Chen et al., 2015; Biel-Maeso et al., 2018).

2.7 Statistical analyses

Data were shown as mean with standard deviation. Spearman's correlation analysis was used to analyze the relationship between the concentrations of the detected

PhACs in the surface waters and sediments. To examine the variation in the concentrations of the target compounds among the sample sites and within each site, the data were analyzed using the principal coordinate analysis (PCoA) (Gower, 1966). Prior to PCoA analyses, Euclidean distance matrices were generated using the data on the standardized variables. The scatter of sites in the unconstrained ordination space was visualized since PCoA placed the sites onto Euclidean distance ordination axes using a matrix of inter-point dissimilarities (Anderson et al., 2008).

3 Results and discussion

A cross-basin and cross-season monitoring program was implemented to evaluate the usage and emissions of 40 PhACs and their environmental risk in Pearl River basin, South China. The detection concentrations and frequencies of PhACs determined in Beijiang River, Xijiang River, and Maozhou River are shown in Fig. 1 and summarized in Table 1. The PhACs were ubiquitously present in all samples at the 42 sampling sites. Out of the 40 compounds, 18 targets were detected in surface water samples and 7 in sediment samples.

3.1 Occurrence and seasonal distribution of PhACs in surface waters

The concentrations of the 40 PhACs ranged from ND to 289 ng/L (Table 1). Fourteen, 14, and 16 PhACs were found in the surface waters of the Beijiang River, Xijiang River, and Maozhou River, respectively. Among them, the detection frequency and concentrations of anti-inflammatory/analgesics drugs were higher than those of others. In the Beijiang River, salicylic acid (32.0 ng/L), diclofenac (15.0 ng/L), MCPA (13.2 ng/L), and gemfibrozil (9.04 ng/L) were the compound detected at the highest concentrations (Fig. S1(a)). Salicylic acid (160 ng/L), MCPA (86.7 ng/L), diclofenac (53.9 ng/L), and ibuprofen (48.1 ng/L) showed the largest concentrations in the Xijiang River (Fig S1(c)), whereas ibuprofen (289.0 ng/L), salicylic acid (60.3 ng/L), paracetamol (62.5 ng/L) and diclofenac (47.3 ng/L) were detected with maximum concentrations in the Maozhou river (Fig S1(e)). Compared with their concentrations in the wet and dry seasons, the summed detected concentrations of PhACs were higher in the wet season than in dry season at most sampling sites and maintained roughly the same among sites across each river. The concentrations of the PhACs observed at the estuarine sampling sites of NR13, WR22, and MZR6 were not the highest, possibly due to the high dilution effect by tidal intrusion (Mijangos et al., 2018).

Most of the PhACs were detected at concentration levels similar to the previously reported concentrations in the Chinese streams (Bu et al., 2013). For instance, the concentrations of diclofenac acid, gemfibrozil, carbamazepine, and ibuprofen are close to those reported in the Liuxi, Zhujiang, and Dongjiang River, which are also part of the Pearl River basin (Peng et al., 2008; Yang et al., 2017; Yang et al., 2018). In contrast, in this study, naproxen, clofibric acid, and salicylic acid had relatively low concentrations (with a range from < MQL–28.5, 0.43–2.74, and 6.04–160 ng/L, respectively). Interestingly, diazepam, nordiazepam, and 6-CPQ (the transformed product of oxazepam) were found in the surface water samples, with a detection frequency of up to 91.7 %. It is known that diazepam is poorly removed by the WWTPs in Guangdong Province, China (Lei et al., 2021), which could account for its high detection frequency in this region. Meanwhile, the highest detected concentration of diclofenac (53.9 ng/L) was comparable with that in the Yangtze River in Jiangsu Province (58 ng/L) (Duan et al., 2021), Xiangjiang River in Hunan Province (32 ng/L) (Lin et al., 2018), and Jiulong River in Fujian Province (11 ng/L) (Sun et al., 2016), but approximately half of that in the Beiyun River in Beijing city (121.6 ng/L) (Ma et al., 2017). Similarly, the concentrations of gemfibrozil and carbamazepine were similar to those in the above-mentioned rivers, with a high detection frequency of 96.4 % and 97.6 %, respectively.

However, the concentrations of the detected PhACs in this study were different from those reported in other countries, especially in Europe and South Africa. For example, the highest detected concentration of diclofenac acid (53.9 ng/L in this study) is up to 18740 ng/L in Spain (Muñoz et al., 2009; Osorio et al., 2012; 2016; Mijangos et al., 2018), 568 ng/L in UK (Ashton et al., 2004; Kasprzyk-Hordern et al., 2008a; 2008b; 2009), 675 ng/L in Italy (Mandaric et al., 2017), and 11400 ng/L in South Africa (Madikizela and Chimuka, 2016). Similarly, the concentrations of ibuprofen, naproxen, carbamazepine, and mefenamic acid are relatively low compared with those from those rivers. Moreover, clozapine is detected in concentrations of 2180–8890 ng/L in the KwaZulu-Natal River, South Africa (Matongo et al., 2015), which is much larger than the concentrations of clozapine (< MQL–5.83 ng/L) in this study. The differences in these detected PhACs concentrations in the rivers are possibly due to the usages of these PhACs in different countries (Waleng and Nomngongo, 2022).

3.2 Occurrence and distribution of PhACs in the sediments

For the sediment samples, 7 PhACs were detected, with concentrations in the range of MQL–63.2 ng/g, MQL–31.3 ng/g, and MQL–28.3 ng/g for the Beijiang River, Xijiang River, and Maozhou River, respectively (Figs. S1(b), S1(d), S1(f)). Similar to the water samples, the predominant PhACs was the analgesics/anti-inflammatory, with salicylic acid being found in all the sediment

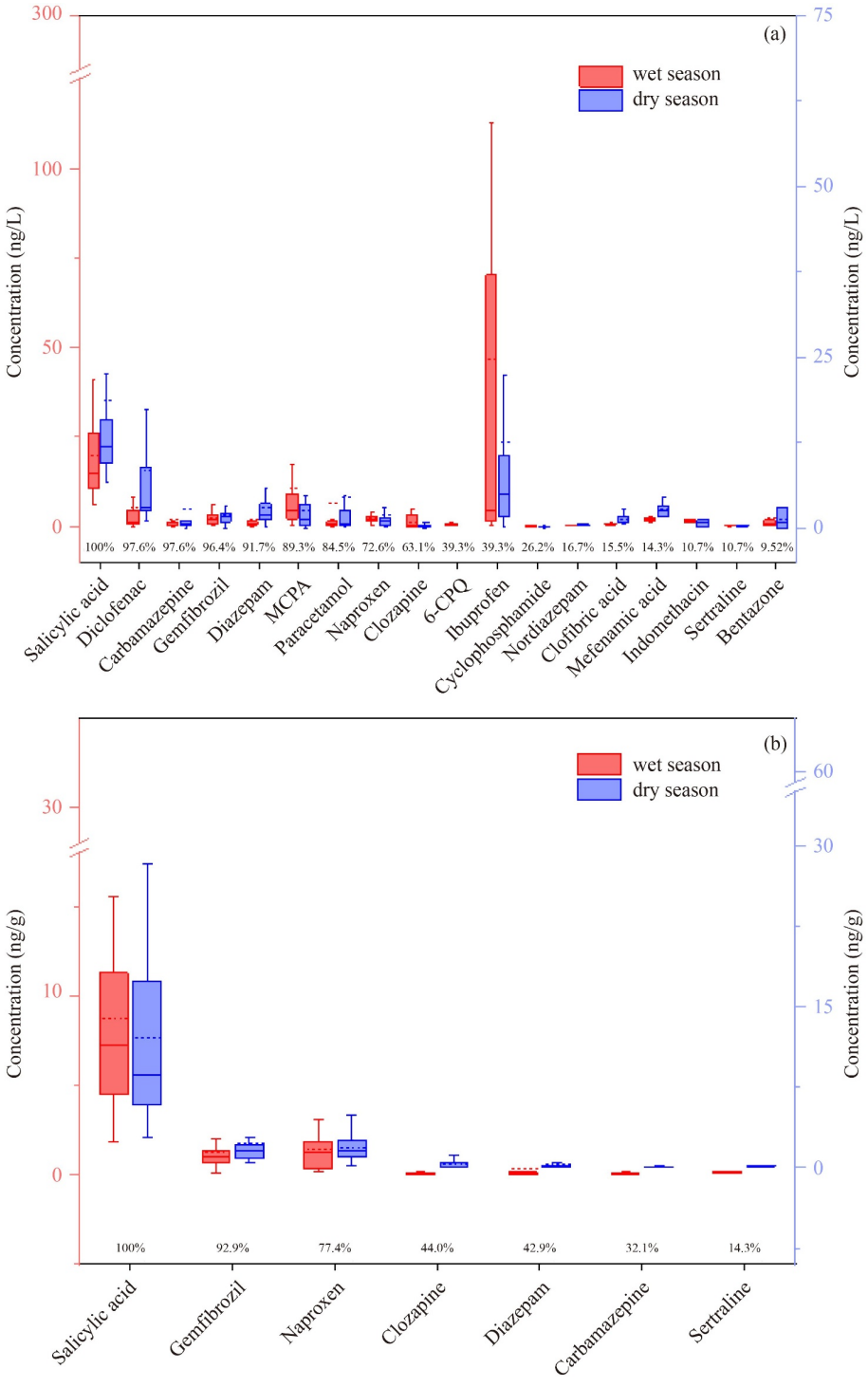


Fig. 1 Box-and-whisker plots showing the concentrations of the detected PhACs compounds in surface waters (Panel a) and sediments (Panel b) of the Beijiang River, Xijiang River, and Maozhou River in the wet and dry seasons. The whiskers indicate the maximum and minimum concentrations. The boxes stretch from 25th to 75th percentiles. The solid and dotted horizontal lines in the boxes respectively indicate the median and average concentrations. The number at the bottom of each box is the detection frequency of the corresponding compound.

samples. In the three rivers, among the 7 detected PhACs, salicylic acid and gemfibrozil showed the highest detection frequencies (100 % and 92.9 %), followed by naproxen (77.4 %), clozapine (44.0 %), and diazepam (42.9 %). On the other hand, diclofenac, ibuprofen, MCPA, and paracetamol were not detected in any

Table 1 Detected PhACs and their concentration ranges (ng/L for surface water, ng/g for sediments) and detection frequencies (Freq., %) in surface waters and sediments of the Beijiang River, Xijiang River, and Maozhou River

Compounds	Surface water				Sediment			
	Range	Mean	Median	Freq.	Range	Mean	Median	Freq.
Salicylic acid	6.04–160	19.1	12.3	100	1.87–63.2	10.43	7.93	100
Diclofenac	< MQL–53.9	6.78	2.82	97.6	ND			0
Gemfibrozil	< MQL–12.4	2.07	1.63	96.4	< MQL–19.2	1.80	1.19	92.9
Naproxen	< MQL–28.5	2.21	1.34	71.4	< MQL–8.58	1.70	1.55	77.4
Ibuprofen	< MQL–289	25.1	4.65	39.3	ND			0
Clofibric acid	0.43–2.74	1.03	0.82	15.5	ND			0
Mefenamic acid	1.02–4.56	2.26	2.08	14.3	ND			0
Indomethacin	< MQL–4.68	1.37	1.24	10.7	ND			0
MCPA	< MQL–86.7	6.89	2.53	89.3	ND			0
Bentazone	< MQL–8.65	1.93	0.74	9.52	ND			0
Carbamazepine	< MQL–19.6	2.43	0.49	97.6	< MQL–0.61	0.10	0.05	32.1
Sertraline	< MQL–0.71	0.29	0.28	10.7	0.08–0.23	0.16	0.17	14.3
Paracetamol	< MQL–62.5	5.34	0.64	84.5	ND			0
Cyclophosphamide	< MQL–0.37	0.17	0.18	26.2	ND			0
Diazepam	0.03–25.0	2.35	1.25	91.7	< MQL–2.46	0.34	0.07	42.9
Clozapine	< MQL–5.83	0.94	0.11	63.1	< MQL–3.28	0.28	0.04	44.0
Nordiazepam	0.24–0.98	0.48	0.38	16.7	ND			0
6-CPQ	< MQL–4.57	0.56	0.21	39.3	ND			0

ND: not detected.

sediments though they had relatively elevated concentrations in the surface waters samples. This could be due to the physicochemical properties of these four compounds. These compounds are not readily distributed into the sediments since they have relatively Log K_{ow} values (0.70, 3.97, 2.53 and 0.46). Nonetheless, diclofenac, ibuprofen, and paracetamol are detected in the Spanish sediments at levels up to 11.0 ng/g, 24.9 ng/g and 222 ng/g, respectively (Biel-Maeso et al., 2017; Silva et al., 2011). Meanwhile, in South Africa, the concentration of ibuprofen in the sediments is up to 659 ng/g (Matongo et al., 2015).

There were large differences in the concentrations of PhACs in the sediments between the dry and wet seasons in most sampling sites. The concentrations of PhACs in the wet season were generally lower than those in the dry season, especially in the Maozhou River. The summed concentrations of determined PhACs in the Maozhou River ranged from 11.6 to 36.8 ng/g in the dry season, and from 3.68 to 7.46 ng/g in the wet season. Similar to these results, the detected PPCPs concentrations in the summer (wet season) are lower than in the winter (dry season) period for the Alpine River sediments (Mandaric et al., 2017). The differences of PhACs in the sediments between the dry and wet seasons could be due to the elevated water flow in wet season and small adsorption of these compounds on sediments. Overall, the concentrations of some detected PhACs in surface waters and sediments were highly correlated, including clozapine ($p < 0.01$), diazepam ($p < 0.01$), carbamazepine ($p < 0.01$), and salicylic acid ($p < 0.05$) (Table S9).

3.3 Seasonal variation in concentrations of PhACs

The relationship among different PhACs in waters and sediments in the dry and wet seasons was revealed by the heatmap - hierarchical cluster analysis (HM-HCA) (Fig. 2 and Fig. S2). Among these PhACs, salicylic acid was classified as a unique class, while the rests were grouped into a class, regardless of the wet or dry season, because salicylic acid maintained a high concentration in surface waters from most sites with high detection frequency. Meanwhile, the sampling sites of the Maozhou River differed from those of the Beijiang River and Xijiang River in the concentrations of PhACs, except for the MZR0 site in the wet season (Fig. 2). The Maozhou River could be more polluted than the other rivers since it flows through Shenzhen and Dongguan city. These two cities have more than 4.17 million residents and highly developed industry, therefore potentially contributing more PhACs into this river. However, the concentrations of PhACs in the sediments did not show much differences among the sites from different rivers in this study (Fig. S2).

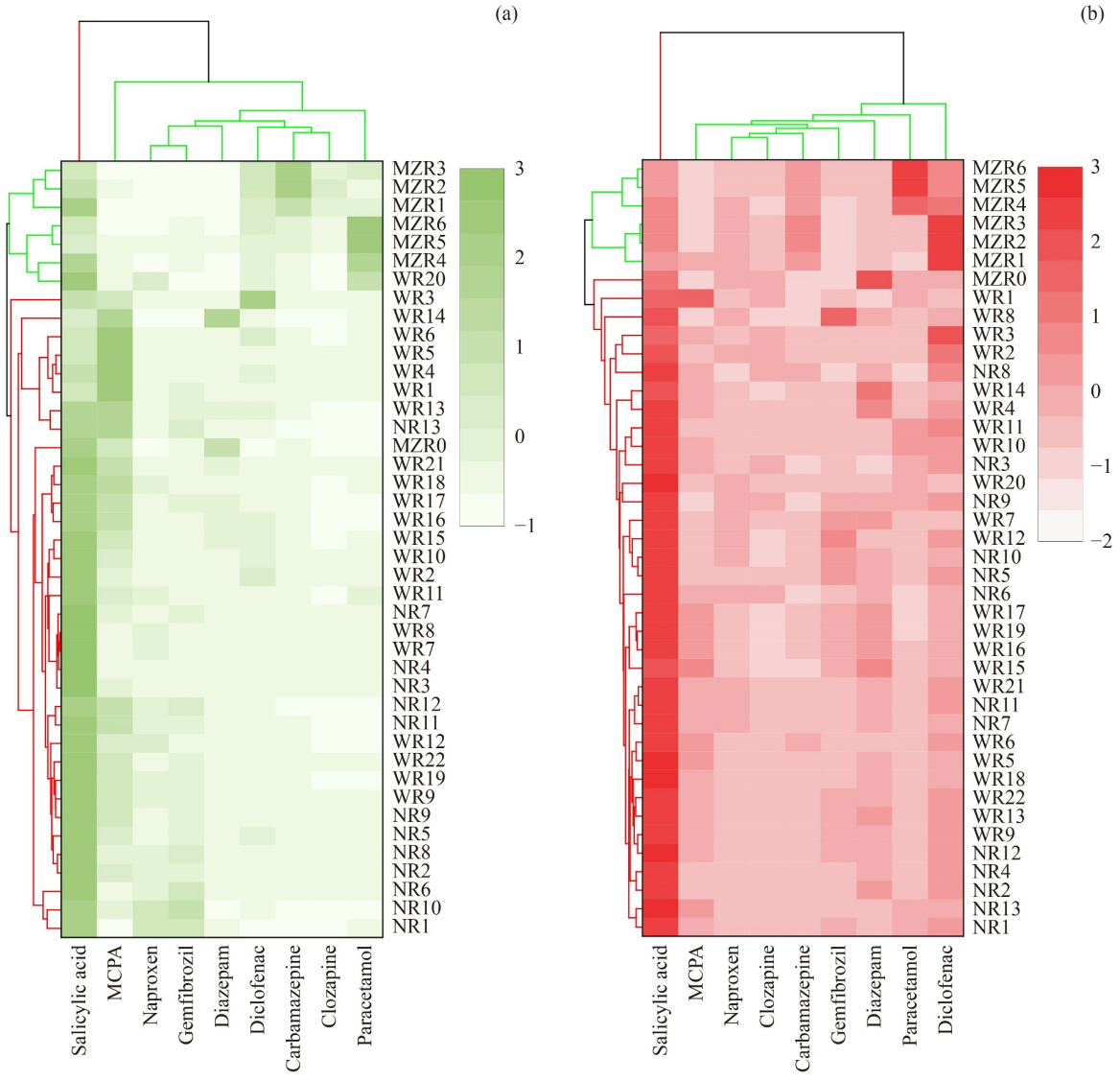


Fig. 2 The heatmap-hierarchical cluster analysis for detected PhACs in surface waters in the wet (Panel a) and dry (Panel b) seasons.

The concentrations of PhACs in surface waters and sediments varied among and within the sampling sites of the Beijiang River, Xijiang River, and Maozhou River (Fig. 3). A significant difference can be found in concentrations of PhACs in both the surface waters (PERMANOVA; pseudo–F = 23.874, $p < 0.001$) and sediments (PERMANOVA; pseudo–F = 7.489, $p < 0.001$) among the Beijiang River, Xijiang River, and Maozhou River (Fig. 3a). In the PCoAs, 3 principal components (PCOs) could account for up to 69.0 % of the variance, with 45.2 % of the variance by the first PCO (PCO1), 14.5 % by PCO2, and 9.25 % by the PCO3. Similarly, these 3 PCOs could explain 66.8 % of the variance of the PhACs concentrations in sediments among the Beijiang River, Xijiang River, and Maozhou River, with 28.6 % by PCO1, 22.8 % by PCO2, and 15.3 % by PCO3 (Fig. 3b).

For each river, the PCoA analysis showed that the PhACs concentrations in the waters and sediments varied between the wet and dry seasons, which was obvious in the two-dimensional ordination plots (Figs. 3(c)–3(h)). In surface waters, approximately 59.2 %, 69.5 % and 80.1 % of the variance in the PhACs concentrations in the waters between wet and dry season in the Beijiang River, Xijiang River, and Maozhou River was respectively explained by 3 PCOs (PERMANOVA; pseudo–F = 6.663, $p < 0.001$; pseudo–F = 3.5502, $p < 0.001$; pseudo–F = 1.3523, $p = 0.2667$, respectively). Similarly, 70.0 %, 63.3 % and 90.4 % of the variance in those of the sediments of the Beijiang River, Xijiang River, and Maozhou River was accounted by the 3 PCOs, respectively (PERMANOVA; pseudo–F = 1.3099, $p = 0.2482$; pseudo–F = 0.98594, $p = 0.4353$; pseudo–F = 6.1122, $p < 0.001$, respectively).

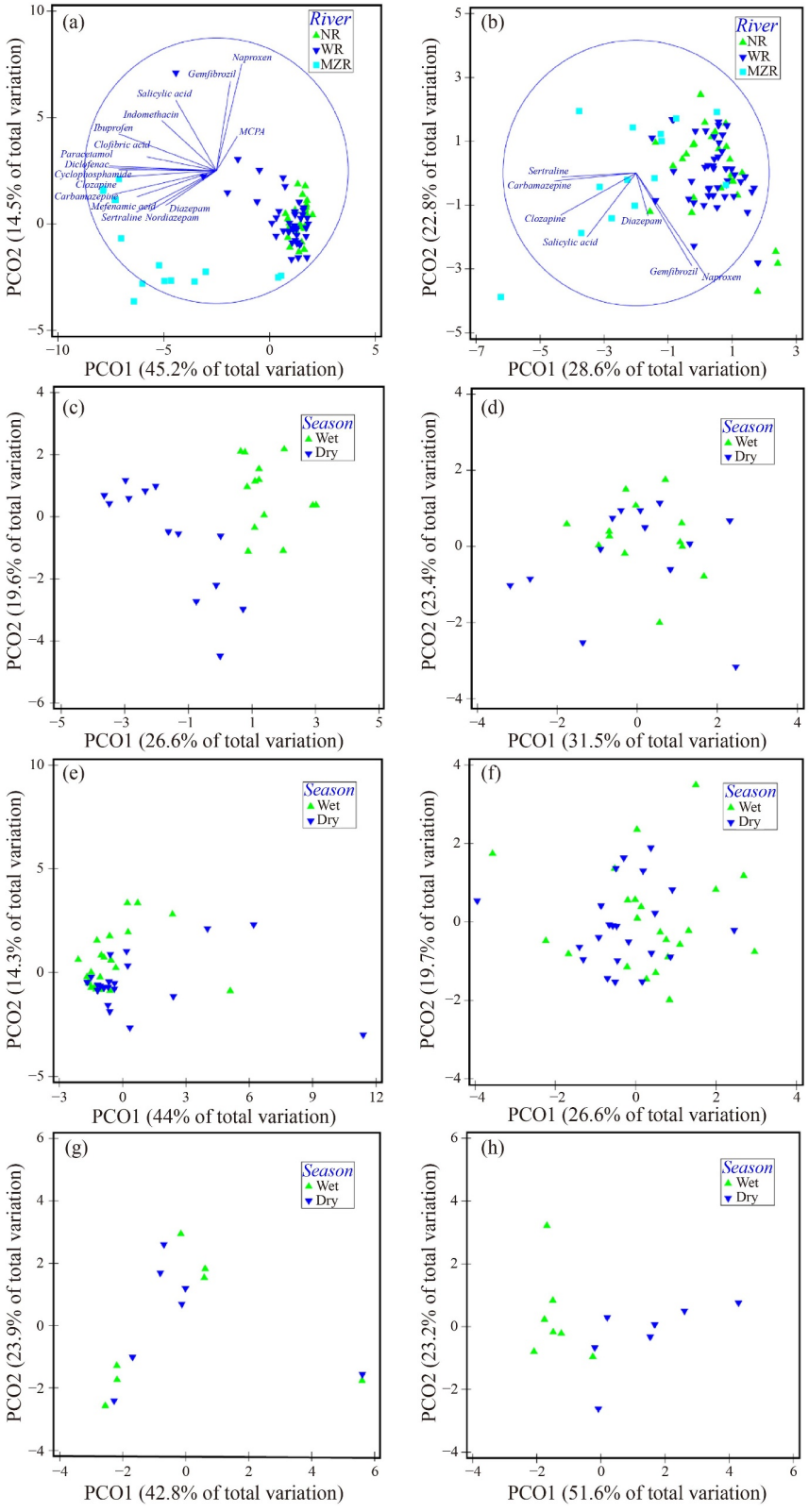


Fig. 3 PCoA analysis of the detected PhACs concentrations between and within the Beijiang River, Xijiang River, and Maozhou River basins. Panel a and Panel b display the PCoA analysis of the detected PhACs concentrations in surface waters and sediments. Panel c, Panel e, and Panel g display the PCoA analysis of the detected PhACs concentrations in surface waters between the wet and dry season. Panel d, Panel f, and Panel h displays the PCoA analysis of the detected PhACs concentrations in sediment between the wet and dry season.

3.4 Contaminant flux, estimated emission, and usage

The contaminant flux of each site in the wet and dry seasons for different rivers was estimated (Fig. 4). The contaminant flux of the detected PhACs compounds in the dry season was significantly lower than that in the wet

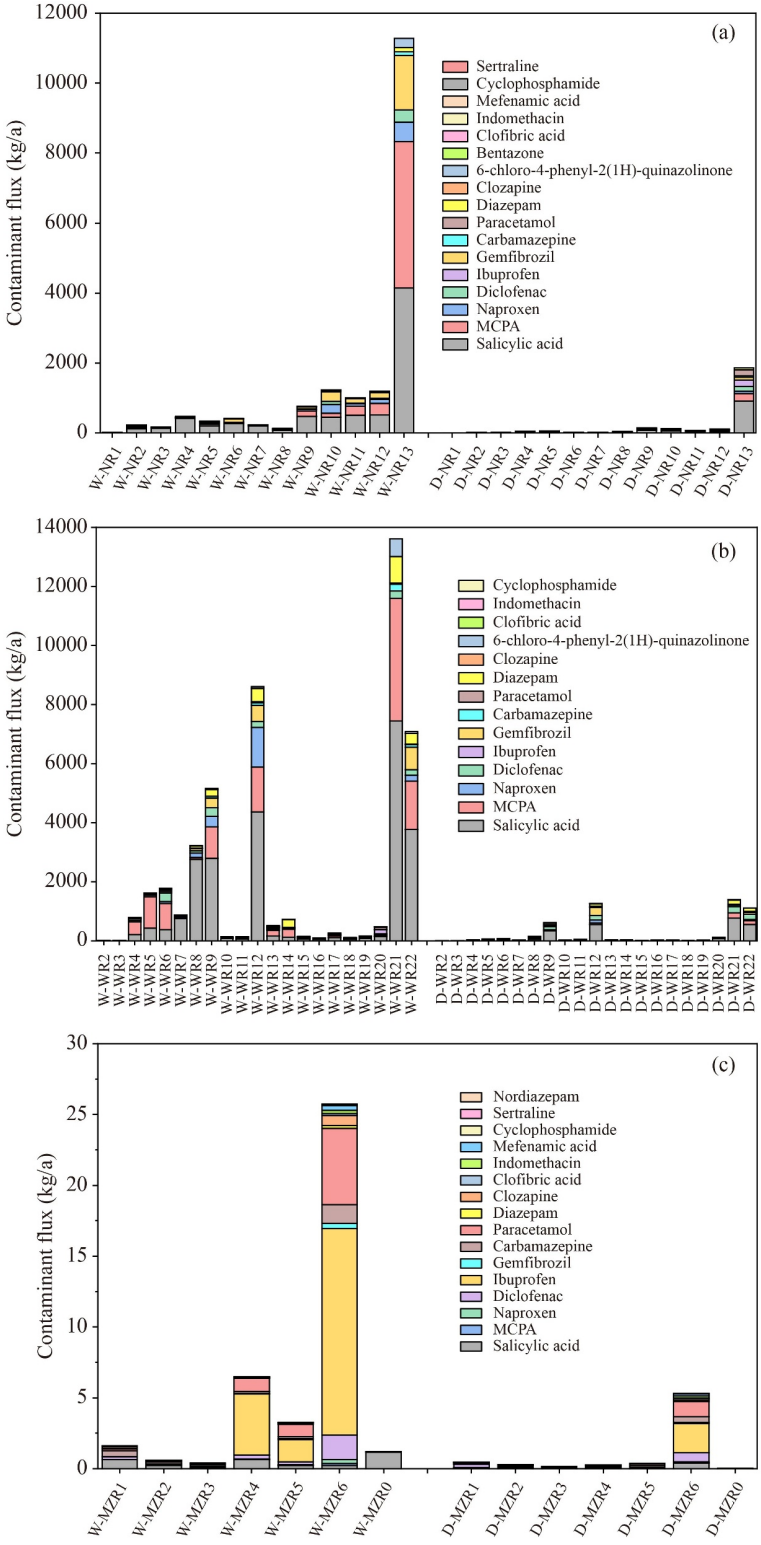


Fig. 4 Contaminant flux (kg/a) of the detected PhACs in the Beijiang River (Panel a), Xijiang River (Panel b), and Maozhou River (Panel c).

season, probably due to the higher surface water flow in the wet season. 81.3 % (Fig. S3(b)), 76.6 % (Fig. S3(c)), and 93.7 % (Fig. S3(d)) of the variance of contaminant flux between the wet and dry season within the Beijiang River, Xijiang River, and Maozhou River was accounted for by the 3 PCOs in the PCoAs analysis. In addition, the contaminant flux at the sites near the estuaries was relatively higher than that of other sites. The Xijiang River and Beijiang River had the highest contaminant flux in both seasons, approximating more than 11 000 kg/a, whereas only 25.7 kg/a in the Maozhou River. The spatial variation of contaminant flux varied significantly (Fig. S3a, PERMANOVA; Pseudo–F = 6.7305, $p < 0.001$) among the Beijiang River, Xijiang River, and Maozhou River, with 38.0 % of the variance explained by PCO1, 16.6 % by PCO2, and 13.1 % by PCO3.

The estimated emission and back-estimated usage of detected PhACs compounds for each sampling site were calculated (Fig. S4). According to volume of the sewage discharge (Table S4) and the concentrations of the detected compounds (Fig. 1), the PhACs emission at each sampling site was estimated. The estimated emission of the Maozhou River (6.66–91.0 kg/a) was higher than that of the Beijiang River (0.28–4.22 kg/a) and the Xijiang River (0.12–6.72 kg/a). The higher emission of Maozhou River is most likely due to that Maozhou River flows through Shenzhen city, which produces larger volume of municipal sewage from its larger population. In addition, the estimated emission of Maozhou River was mainly contributed by commonly used painkillers, such as ibuprofen (37.9 %), paracetamol (16.4 %), salicylic acid (13.5 %), and diclofenac (13.2 %), while the emission of Beijiang River and Xijiang River was mainly contributed by salicylic acid (51.1 % and 41.7 %), MCPA (14.1 % and 19.6 %) and diclofenac (7.0 % and 12.3 %). It should be noted that the dilution factor of the river was ignored in the estimation, which may lead to the underestimated emission.

The usage was back-estimated using Eq. (3) and the removal rate of each compound obtained from our early study (Yang et al., 2017, 2018; Lei et al., 2021) (Figs. S4(b), S4(d), S4(f)). Salicylic acid and paracetamol were the main compounds in the Beijiang River and Xijiang River by back estimation. The highest back-estimated usage of salicylic acid and paracetamol was respectively 161 and 754 kg/a for the WR20 site of the Xijiang River. In the Maozhou River, the back-estimated usage of paracetamol was the largest. The usage of paracetamol at the MZR5 site was estimated to be 16 584 kg/a.

The widespread distribution of PhACs in the Pearl River basin is mainly due to anthropogenic activities. In order to explore the relationship between the emission of PhACs and gross domestic product (GDP), the correlation between PhACs-related data and the GDP of the city was determined by linear regression analysis (Table S4). The correlation coefficient (R^2) between the estimated emission and GDP was 0.895 (Fig. S5), implying a close relationship between the PhACs emissions and GDP of each city. However, the R^2 between the average concentrations of PhACs in the surface waters in the dry and wet seasons and GDP was 0.137.

3.5 Environmental risk assessment

For each individual compound, the MEC and PNEC were used to calculate risk quotients (RQs) for aquatic organisms (algae, daphnia, and fish) (Table 2). The criteria for the RQs were as follows in order to define different levels of environmental risk: RQ < 0.01 (insignificant risk), 0.01 < RQ < 0.1 (low risk), 0.1 < RQ < 1 (moderate risk), and RQ > 1 (high risk) (Ågerstrand and Rudén, 2010; Hernando et al., 2006; Bu et al., 2020). Among all the detected compounds, diazepam and ibuprofen were shown to have a moderate risk, which is also supported by other studies (Cunha et al., 2019; Ashfaq et al., 2017). While diclofenac, naproxen, carbamazepine, and gemfibrozil were considered to have a relatively low risk. In addition, the maximum concentrations of other detected PhACs compounds were lower than their PNECs, implying their relatively low environmental risk.

4 Conclusions

This study has revealed that PhACs are ubiquitous in the surface waters and sediments of the three major rivers of the Pearl River basin. The concentrations of commonly detected PhACs are comparable to those detected in many other river basins in China, and lower than in other countries. Meanwhile, there is a distinctive spatial and seasonal variation in PhACs occurrence profiles within and among the three river basins. In addition, the estimated emissions and back-estimated usage of PhACs in the Beijiang River and Xijiang River are lower than the Maozhou River, a river running through Shenzhen and Dongguan cities with large volume of municipal sewage due to the large population size. Diazepam and ibuprofen are considered to have a moderate risk among these PhACs in the Pearl River basin. This study suggests that a multiple-year monitoring the pollution of PhACs is necessary for a complete understanding of the risk of PhACs in the Pearl River basin.

Acknowledgements This work was financially supported by the National Natural Science Foundation of China (Nos. 41877358 and U1701242), the Pearl River Talent Plan of Guangdong Province (No. 2017GC010244) and the Key R&D projects of Guangxi (No. 2018AB36018).

Electronic Supplementary Material Supplementary material is available in the online version of this article at https://doi.org/10.1007/s11783-023-1646-8 and is accessible for authorized users.

Table 2 Risk Quotients (RQs) of the target compounds

Compounds	Therapeutic class	MEC (ng/L)	PNEC (μg/L)			RQ			RQ_{max}	Risk
			Algae	Daphnia	Fish	Algae	Daphnia	Fish		
Diazepam	Psycholeptics	25.0	–	4.20[b]	0.10/7.00[c]		0.01	0.25	0.25	moderate
Ibuprofen	Anti-inflammatory drugs	289	2.60[a]	25.4[a]	3.20[a]	0.11	0.01	0.09	0.11	moderate
Diclofenac	Anti-inflammatory and antirheumatic products	53.9	1.94[a]	11.3[a]	0.70[a]	0.028	0.01	0.08	0.08	low
Naproxen	Anti-inflammatory and antirheumatic products	28.5	2.31[a]	10.4[a]	1.10[a]	0.01	0.003	0.03	0.03	low
Carbamazepine	Antiepileptics	19.6	2.13[a]	5.57[a]	1.10[a]	0.009	0.004	0.018	0.018	low
Gemfibrozil	Lipid modifying agents	12.4	6.43[a]	25.0[a]	1.10[a]	0.002	0.000	0.011	0.011	low
Paracetamol	Analgesics and antipyretics	62.5	17.0[a]	28.7[a]	47.0[a]	0.004	0.002	0.001	0.004	/
Mefenamic acid	Anti-inflammatory and antirheumaticproducts	4.56	1.25a	8.53a	1.40a	0.004	0.001	0.003	0.004	/
Clozapine	Psycholeptics	5.83	2.23[a]	6.09[a]	1.70[a]	0.003	0.001	0.003	0.003	/
Salicylic acid	Anti-inflammatory drugs	160	60[d]	6.16[e]	–	0.003			0.003	/
Clofibric acid	Lipid-lowering drugs	2.74	4.2			0.001			0.001	/
Cyclophosphamide	Antineoplastic agents	0.37	1.38[a]	166[a]	140[a]	0.000	0.000	0.000	0.000	/
Sertraline	Psychoanaleptics	0.71								
MCPA	Herbicides	86.7	304[f]	334[f]	562[f]					
6-CPQ	Psycholeptics	4.57	/	/	/	/	/	/	/	
Bentazone	Herbicides	8.65	141[f]	215[f]	390[f]					
Indomethacin	Nonsteroidal anti-inflammatory drugs	4.68	3.57[f]	2.05[f]	2.94[f]					
Nordiazepam	Psycholeptics	0.98	23.4[f]	22.5[f]	36.6[f]					

Four levels of risk were considered: RQ < 0.01, insignificant risk; 0.01 < RQ < 0.1, low risk; 0.1 < RQ < 1, moderate risk; RQ > 1, high risk (Ågerstrand and Rudén, 2010; Bu et al., 2013). a) (Bu et al., 2020), b) (Stuer-Lauridsen et al., 2000), c) (Cunha et al., 2019), d) (You et al., 2015), e) (Szabelak and Bownik, 2021). f) EC50 values (mg/L) for Daphnia magna (48 h), algae (96 h) and fish (96 h) used to calculate PNEC based on QSAR models (The Ecological Structure Activity Relationships, ECOSAR Version 1.11).

References

Ågerstrand M, Rudén C (2010). Evaluation of the accuracy and consistency of the Swedish environmental classification and information system for pharmaceuticals. Science of the Total Environment, 408(11): 2327–2339

Anderson M J, Gorley R N, Clarke K R (2008). PERMANOVA+ for PRIMER. Guide to Software and Statistical Methods. PRIMER-E Ltd., Plymouth

Ashfaq M, Nawaz Khan K, Saif Ur Rehman M, Mustafa G, Faizan Nazar M, Sun Q, Iqbal J, Mulla S I, Yu C P (2017). Ecological risk assessment of pharmaceuticals in the receiving environment of pharmaceutical wastewater in Pakistan. Ecotoxicology and Environmental Safety, 136: 31–39

Ashton D, Hilton M, Thomas K V (2004). Investigating the environmental transport of human pharmaceuticals to streams in the United Kingdom. Science of the Total Environment, 333(1–3): 167–184

Biel-Maeso M, Baena-Nogueras R M, Corada-Fernández C, Lara-Martín P A (2018). Occurrence, distribution and environmental risk of pharmaceutically active compounds (PhACs) in coastal and ocean waters from the Gulf of Cadiz (SW Spain). Science of the Total Environment, 612: 649–659

Biel-Maeso M, Corada-Fernández C, Lara-Martín P A (2017). Determining the distribution of pharmaceutically active compounds (PhACs) in soils and sediments by pressurized hot water extraction (PHWE). Chemosphere, 185: 1001–1010

Branchet P, Arpin-Pont L, Piram A, Boissery P, Wong-Wah-Chung P, Doumenq P (2021). Pharmaceuticals in the marine environment: what are the present challenges in their monitoring? Science of the Total Environment, 766: 142644

Brauer R, Alfageh B, Blais J E, Chan E W, Chui C S L, Hayes J F, Man K K C, Lau W C Y, Yan V K C, Beykloo M Y, Wang Z, Wei L, Wong I C K (2021). Psychotropic medicine consumption in 65 countries and regions, 2008–2019: a longitudinal study. Lancet Psychiatry, 8(12): 1071–1082

Bu Q, Cao Y, Yu G, He X, Zhang H, Sun J, Yun M, Cao Z (2020). Identifying targets of potential concern by a screening level ecological risk assessment of human use pharmaceuticals in China. Chemosphere, 246: 125818

Bu Q, Wang B, Huang J, Deng S, Yu G (2013). Pharmaceuticals and personal care products in the aquatic environment in China: a review. Journal of Hazardous Materials, 262: 189–211

Calamari D, Zuccato E, Castiglioni S, Bagnati R, Fanelli R (2003). Strategic survey of therapeutic drugs in the rivers Po and Lambro in northern Italy. Environmental Science & Technology, 37(7): 1241–1248

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

Chen F, Ying G G, Yang J F, Zhao J L, Wang L (2010). Rapid resolution liquid chromatography-tandem mass spectrometry method for the determination of endocrine disrupting chemicals

(EDCs), pharmaceuticals and personal care products (PPCPs) in wastewater irrigated soils. Journal of Environmental Science and Health. Part B, Pesticides, Food Contaminants, and Agricultural Wastes, 45(7): 682–693

Chen Y S, Xi X P, Yu G, Cao Q M, Wang B, Vince F, Hong Y W (2015). Pharmaceutical compounds in aquatic environment in China: locally screening and environmental risk assessment. Frontiers of Environmental Science & Engineering, 9(3): 394–401

Cunha D L, Mendes M P, Marques M (2019). Environmental risk assessment of psychoactive drugs in the aquatic environment. Environmental Science and Pollution Research International, 26(1): 78–90

Daughton C G, Ternes T A (1999). Pharmaceuticals and personal care products in the environment: agents of subtle change? Environmental Health Perspectives, 107(Suppl 6): 907–938

Duan L, Zhang Y, Wang B, Zhou Y, Wang F, Sui Q, Xu D, Yu G (2021). Seasonal occurrence and source analysis of pharmaceutically active compounds (PhACs) in aquatic environment in a small and medium-sized city, China. Science of the Total Environment, 769: 144272

EU TGD (2003). Technical Guidance Document on Risk Assessment in Support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances, Commission Regulation (EC) 1488/94 on Risk Assessment for Existing Substances and Directive 98/8/EC of the European

Fatima S, Asif N, Ahmad R, Fatma T (2020). Toxicity of NSAID drug (paracetamol) to nontarget organism-*Nostoc muscorum*. Environmental Science and Pollution Research International, 27(28): 35208–35216

Glassmeyer S T, Furlong E T, Kolpin D W, Cahill J D, Zaugg S D, Werner S L, Meyer M T, Kryak D D (2005). Transport of chemical and microbial compounds from known wastewater discharges: potential for use as indicators of human fecal contamination. Environmental Science & Technology, 39(14): 5157–5169

Gower J C (1966). Some distance properties of latent root and vector methods used in multivariate analysis. Biometrika, 53(3–4): 325–338

Grabicová K, Grabic R, Fedorova G, Kolářová J, Turek J, Brooks B W, Randák T (2020). Psychoactive pharmaceuticals in aquatic systems: a comparative assessment of environmental monitoring approaches for water and fish. Environmental Pollution, 261: 114150

Green S, Buchbinder R, Barnsley L, Hall S, White M, Smidt N, Assendelft W J (2001). Non‐steroidal anti‐inflammatory drugs (NSAIDs) for treating lateral elbow pain in adults. Cochrane Database of Systematic Reviews, 2: CD003686

Hass U, Duennbier U, Massmann G (2012). Occurrence and distribution of psychoactive compounds and their metabolites in the urban water cycle of Berlin (Germany). Water Research, 46(18): 6013–6022

Hernando M D, Mezcua M, Fernández-Alba A R, Barceló D (2006). Environmental risk assessment of pharmaceutical residues in wastewater effluents, surface waters and sediments. Talanta, 69(2): 334–342

Hu P, Guo C S, Zhang Y, Lv J P, Zhang Y, Xu J (2019). Occurrence, distribution and risk assessment of abused drugs and their metabolites in a typical urban river in north China. Frontiers of Environmental Science & Engineering, 13(4): 56

Kasprzyk-Hordern B, Dinsdale R M, Guwy A J (2008a). Multiresidue methods for the analysis of pharmaceuticals, personal care products and illicit drugs in surface water and wastewater by solid-phase extraction and ultra performance liquid chromatography-electrospray tandem mass spectrometry. Analytical and Bioanalytical Chemistry, 391(4): 1293–1308

Kasprzyk-Hordern B, Dinsdale R M, Guwy A J (2008b). The occurrence of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs in surface water in South Wales, UK. Water Research, 42(13): 3498–3518

Kasprzyk-Hordern B, Dinsdale R M, Guwy A J (2009). The removal of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs during wastewater treatment and its impact on the quality of receiving waters. Water Research, 43(2): 363–380

Lei H J, Yang B, Ye P, Yang Y Y, Zhao J L, Liu Y S, Xie L, Ying G G (2021). Occurrence, fate and mass loading of benzodiazepines and their transformation products in eleven wastewater treatment plants in Guangdong Province, China. Science of the Total Environment, 755(Pt 2): 142648

Lin H, Chen L, Li H, Luo Z, Lu J, Yang Z (2018). Pharmaceutically active compounds in the Xiangjiang River, China: distribution pattern, source apportionment, and risk assessment. Science of the Total Environment, 636: 975–984

Ma R, Wang B, Yin L, Zhang Y, Deng S, Huang J, Wang Y, Yu G (2017). Characterization of pharmaceutically active compounds in Beijing, China: occurrence pattern, spatiotemporal distribution and its environmental implication. Journal of Hazardous Materials, 323(Pt A): 147–155

Madikizela L M, Chimuka L (2016). Determination of ibuprofen, naproxen and diclofenac in aqueous samples using a multi-template molecularly imprinted polymer as selective adsorbent for solid-phase extraction. Journal of Pharmaceutical and Biomedical Analysis, 128: 210–215

Madikizela L M, Chimuka L (2017). Occurrence of naproxen, ibuprofen, and diclofenac residues in wastewater and river water of KwaZulu-Natal Province in South Africa. Environmental Monitoring and Assessment, 189(7): 348

Madikizela L M, Mdluli P S, Chimuka L (2017). An initial assessment of naproxen, ibuprofen and diclofenac in ladysmith water resources in South Africa using molecularly imprinted solid-phase extraction followed by high performance liquid chromatography-photodiode array detection. South African Journal of Chemistry, 70: 145–153

Mandaric L, Diamantini E, Stella E, Cano-Paoli K, Valle-Sistac J, Molins-Delgado D, Bellin A, Chiogna G, Majone B, Diaz-Cruz M S, et al. (2017). Contamination sources and distribution patterns of pharmaceuticals and personal care products in Alpine rivers strongly affected by tourism. Science of the Total Environment, 590–591: 484–494

Matongo S, Birungi G, Moodley B, Ndungu P (2015). Pharmaceutical residues in water and sediment of Msunduzi River, KwaZulu-Natal, South Africa. Chemosphere, 134: 133–140

Mijangos L, Ziarrusta H, Ros O, Kortazar L, Fernández L A, Olivares M, Zuloaga O, Prieto A, Etxebarria N (2018). Occurrence of emerging pollutants in estuaries of the Basque Country: Analysis of sources and distribution, and assessment of the environmental risk.

Water Research, 147: 152–163

Mompelat S, Le Bot B, Thomas O (2009). Occurrence and fate of pharmaceutical products and by-products, from resource to drinking water. Environment International, 35(5): 803–814

Muñoz I, López-Doval J C, Ricart M, Villagrasa M, Brix R, Geiszinger A, Ginebreda A, Guasch H, Alda M J L, Romaní A M, et al. (2009). Bridging levels of pharmaceuticals in river water with biological community structure in the Llobregat River basin (northeast Spain). Environmental Toxicology and Chemistry, 28(12): 2706–2714

Oggier D M, Weisbrod C J, Stoller A M, Zenker A K, Fent K (2010). Effects of diazepam on gene expression and link to physiological effects in different life stages in zebrafish *Danio rerio*. Environmental Science & Technology, 44(19): 7685–7691

Osorio V, Larrañaga A, Aceña J, Pérez S, Barceló D (2016). Concentration and risk of pharmaceuticals in freshwater systems are related to the population density and the livestock units in Iberian Rivers. Science of the Total Environment, 540: 267–277

Osorio V, Marcé R, Pérez S, Ginebreda A, Cortina J L, Barceló D (2012). Occurrence and modeling of pharmaceuticals on a sewage-impacted Mediterranean river and their dynamics under different hydrological conditions. Science of the Total Environment, 440: 3–13

Peng X, Yu Y, Tang C, Tan J, Huang Q, Wang Z (2008). Occurrence of steroid estrogens, endocrine-disrupting phenols, and acid pharmaceutical residues in urban riverine water of the Pearl River Delta, South China. Science of the Total Environment, 397(1–3): 158–166

Schlüsener M P, Hardenbicker P, Nilson E, Schulz M, Viergutz C, Ternes T A (2015). Occurrence of venlafaxine, other antidepressants and selected metabolites in the Rhine catchment in the face of climate change. Environmental Pollution, 196: 247–256

Sibeko P A, Naicker D, Mdluli P S, Madikizela L M (2019). Naproxen, ibuprofen, and diclofenac residues in river water, sediments and Eichhornia crassipes of Mbokodweni river in South Africa: an initial screening. Environmental Forensics, 20(2): 129–138

Silva B F, Jelic A, López-Serna R, Mozeto A A, Petrovic M, Barceló D (2011). Occurrence and distribution of pharmaceuticals in surface water, suspended solids and sediments of the Ebro river basin, Spain. Chemosphere, 85(8): 1331–1339

Silva B, Costa F, Neves I, Tavares T (2015). Psychiatric Pharmaceuticals as Emerging Contaminants in Wastewater. Berlin: Springer

Stuer-Lauridsen F, Birkved M, Hansen L P, Holten Lützhøft H C, Halling-Sørensen B (2000). Environmental risk assessment of human pharmaceuticals in Denmark after normal therapeutic use. Chemosphere, 40(7): 783–793

Subedi B, Balakrishna K, Joshua D I, Kannan K (2017). Mass loading and removal of pharmaceuticals and personal care products including psychoactives, antihypertensives, and antibiotics in two sewage treatment plants in southern India. Chemosphere, 167: 429–437

Sun Q, Li Y, Li M, Ashfaq M, Lv M, Wang H, Hu A, Yu C P (2016). PPCPs in Jiulong River estuary (China): Spatiotemporal distributions, fate, and their use as chemical markers of wastewater. Chemosphere, 150: 596–604

Świacka K, Michnowska A, Maculewicz J, Caban M, Smolarz K (2021). Toxic effects of NSAIDs in non-target species: a review from the perspective of the aquatic environment. Environmental Pollution, 273(4): 115891

Szabelak A and Bownik A (2021). Behavioral and physiological responses of *Daphnia magna* to salicylic acid. Chemosphere, 270: 128660

Thiebault T, Boussafir M, Le Milbeau C (2017). Occurrence and removal efficiency of pharmaceuticals in an urban wastewater treatment plant: mass balance, fate and consumption assessment. Journal of Environmental Chemical Engineering, 5(3): 2894–2902

Valdez-Carrillo M, Abrell L, Ramírez-Hernández J, Reyes-López J A, Carreón-Diazconti C (2020). Pharmaceuticals as emerging contaminants in the aquatic environment of Latin America: a review. Environmental Science and Pollution Research International, 27(36): 44863–44891

Waleng N J, Nomngongo P N (2022). Occurrence of pharmaceuticals in the environmental waters: African and Asian perspectives. Environmental Chemistry and Ecotoxicology, 4: 50–66

Wang H, Jin M, Mao W, Chen C, Fu L, Li Z, Du S, Liu H (2020). Photosynthetic toxicity of non-steroidal anti-inflammatory drugs (NSAIDs) on green algae *Scenedesmus obliquus*. Science of the Total Environment, 707: 136176

Yang Y Y, Liu W R, Liu Y S, Zhao J L, Zhang Q Q, Zhang M, Zhang J N, Jiang Y X, Zhang L J, Ying G G (2017). Suitability of pharmaceuticals and personal care products (PPCPs) and artificial sweeteners (ASs) as wastewater indicators in the Pearl River Delta, South China. Science of the Total Environment, 590–591: 611–619

Yang Y Y, Zhao J L, Liu Y S, Liu W R, Zhang Q Q, Yao L, Hu L X, Zhang J N, Jiang Y X, Ying G G (2018). Pharmaceuticals and personal care products (PPCPs) and artificial sweeteners (ASs) in surface and ground waters and their application as indication of wastewater contamination. Science of the Total Environment, 616–617: 816–823

Yang Z, Lu T, Zhu Y, Zhang Q, Zhou Z, Pan X, Qian H (2019). Aquatic ecotoxicity of an antidepressant, sertraline hydrochloride, on microbial communities. Science of the Total Environment, 654: 129–134

You L, Nguyen V T, Pal A, Chen H, He Y, Reinhard M, Gin K Y (2015). Investigation of pharmaceuticals, personal care products and endocrine disrupting chemicals in a tropical urban catchment and the influence of environmental factors. Science of the Total Environment, 536: 955–963

Zhao W T, Guo Y, Lu S G, Yan P P, Sui Q (2016). Recent advances in pharmaceuticals and personal care products in the surface water and sediments in China. Frontiers of Environmental Science & Engineering, 10(6): 2