Seasonal variation, flux estimation, and source analysis of dissolved emerging organic contaminants in the Yangtze Estuary, China

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Abstract

The occurrence and seasonal variation of 24 dissolved emerging organic contaminants in the Yangtze Estuary were studied, including 12 non-antibiotic pharmaceuticals, seven sulfonamides, two macrolides and three chloramphenicols. Sulfadiazine, erythromycin, thiamphenicol and paracetamol were the primary contaminants in sulfonamides, macrolides, chloramphenicols and non-antibiotic pharmaceutical groups, respectively. Compared to the concentrations at Datong, chloramphenicols at Xuliujing were significantly higher in autumn and winter, while macrolides were lower in spring. Based on the flux estimation, approximately 37.1 tons of sulfonamides, 17.4 tons of macrolides, 79.2 tons of chloramphenicols and 14.1 tons of non-antibiotic pharmaceuticals were discharged into the Yangtze Estuary from June 2013 to May 2014. However, the total flux from the Huangpu River only represented 5% of the total. The pharmaceutical sources were speculated on by analyzing the seasonal variations in pharmaceutical concentrations and fluxes at various sites. Both environmental and social factors might affect the fluxes.

Keywords: Yangtze Estuary; Emerging organic contaminants; Seasonal variation; Flux estimation; Source analysis

1. Introduction

As a significant class of emerging organic contaminants (EOCs) in the aquatic environment, pharmaceuticals are becoming a growing concern. EOCs are broadly regarded as newly generated or detected chemicals that are not commonly monitored and do not have environmental protection laws and regulations (Ternes et al., 2015). EOCs and their transformation products have potential adverse effects on aquatic organisms and human health even at low concentrations via induction of resistance genes in harmful micro-organisms (Mohapatra et al., 2014; Cheng et al., 2016; Gabarrón et al., 2016; Hurtado et al., 2016; Zhou et al., 2016).

Generally, massive pollution load from land-based sources accu- mulates in the estuarine environment via river runoff. To date, a number of studies have focused on the environmental fate of pharma- ceuticals in estuarine systems and reported on pharmaceuticals released into coastal environments, and the environmental behavior of phar- maceuticals in estuarine and coast has become a research hotspot (Stewart et al., 2014; Birch et al., 2015; Boix et al., 2016; Zhao et al., 2016). These data are still limited, especially for seasonal variation and flux estimates of dissolved pharmaceuticals in the Yangtze River, which is the largest river in Asia and the fourth largest in the world in terms of both water and sediment discharge. The freshwater discharge of the Yangtze Estuary has annual and seasonal variations (Wang et al., 2010). The high water level period of the Yangtze River Basin is from July to September, while the low water level period is from December to February. The flow discharge into the East China Sea is recorded by the Datong Gauge Station located at the tidal limit, with an average annual flow discharge of 28,587 m^3/s from 1950 to 2002 (Yang et al., 2015). The Yangtze Basin covers one-fifth of the total land area of China, with a population of approximately 400 million. In the past several decades, the Yangtze River has received a high load of pharmaceutical contaminants from the discharge of municipal sewage, agricultural runoff, industrial wastewater and other human activities (Bu et al., 2013; Chen and Zhou, 2014; Yan et al., 2015). Moreover, a great deal of untreated municipal sewage is a primary source of pharmaceuticals (Nodler et al., 2014; Chen et al., 2015). Eventually, most of these pharmaceutical contaminants accumulate in the Yangtze estuarine system. Considering the mass production and use of pharmaceuticals with incomplete treatment in sewage treatment plants, some pharmaceuticals exhibit pseudopersistent when release rates are higher than transformation and removal rates (Zhou et al., 2009; Stuart et al., 2012).

Due to the large area and high discharge of the Yangtze Estuary, the transport process of pharmaceutical compounds to the Yangtze Estuary and East China Sea may have a potential impact on the aquatic eco- system even at low concentrations (Yang et al., 2011). However, information about seasonal variation and comprehensive flux data for pharmaceuticals discharged into the Yangtze Estuary is still lacking. Therefore, 24 pharmaceuticals that have been detected in the en- vironment were selected in this study, including three groups of anti- biotics (sulfonamides, macrolides and chloramphenicols) and 12 non- antibiotic pharmaceuticals. The objectives are the following: (1) to in- vestigate the seasonal variation of pharmaceuticals in two typical sec- tions of the main water channel of the Yangtze River, as well as Wu- songkou, where the Huangpu River meets the Yangtze River; (2) to study the transport process and sources of these pharmaceuticals; and (3) to estimate the annual fluxes discharged from the Yangtze Estuary to the coastal zone of the East China Sea.

2. Experimental Section

2.1. Chemicals

24 pharmaceuticals including three classes of antibiotics and ten non-antibiotic pharmaceuticals (sulfonamides: sulfadiazine, sulfapyridine, sulfamethoxazole, sulfathiazole, sulfamerazine, sulfamethazine and sulfaquinoxaline; macrolides: erythromycin and roxithromycin; chloramphenicols: chloramphenicol, thiamphenicol and florfenicol; non-antibiotic pharmaceuticals: paracetamol, carbamazepine, cimetidine, diazepam, omeprazole, indomethacin, fenofibrate, tamoxifen, simvastatin , paclitaxel, nimodipine, gemfibrozil) were selected in this study and their physicochemical properties were shown in Table S1 (Supporting Information). Stable isotope labeled compounds simvastatin-d_6, diclofenac-d_4, cimetidine-d_3, nifedipine-d_6 and carbamazepine-d_{10} were selected as the internal standards for non-antibiotics, while for sulfonamide, macrolide and chloramphenicol antibiotics, sulfamethoxazole-d_4, roxithromycin-d_7 and chloramphenicol-d_5 were used as the internal standards respectively. All these chemical standards were purchased from Dr. Ehrenstorfer (GmbH, Germany). Separate stock solutions of individual compounds and internal standards were prepared in methanol at

1000 mg/L. A mixture of working standards containing each compound was prepared by diluting the stock solution with methanol at 10 mg/L before use. The methanol (CNW, Germany) were of HPLC grade and purchased from ANPEL (Shanghai, China). All standard solutions were stored at -20°C.

2.2. Sampling

Water samples were collected from Datong (DT), Xuliujing (XLJ) and Wusongkou (WSK) (Fig. 1). Datong is the tidal limit of the Yangtze Estuary. Xuliujing as the bifurcation node of North and South Branch is influenced by tide but the salinity is 0 all year around, therefore, Xuliujing is considered suitable for observing the freshwater input of the Yangtze River to the sea [24]. Wusongkou is the confluence of the Huangpu River and the Yangtze River. From June 2013 to May 2014, sampling was conducted once a quarter at Datong section, twice a quarter during the ebb tide phase from Xuliujing section and Wusongkou. 5/10 L water samples were collected using amber glass bottles pre-cleaned by acetone, deionized water and Milli-Q water. The properties of water samples were also measured simultaneously. Once transported to the laboratory, the samples were stored in a cool condition before treatment.

2.3. Sample treatment and analyses

The water samples were filtered through 0.7 μm glass fiber filters (Whatman, USA). All filtration was done within 2 days. The filtered water samples divided in triplicate (1 L or 4 L). The internal standards (20 ng each) were spiked, the pH was adjusted to 4.0 with formic acid, and the addition of 0.2 g/L Na_2EDTA as the chelating agent followed. Then the samples were extracted by solid-phase extraction (SPE) via Oasis HLB cartridges (200 mg or 500 mg, 6 mL, Waters), which were preconditioned with 6 mL of methanol and 10 mL of ultrapure water following validated methods [19, 21]. The samples were extracted by SPE at a flow rate of approximately 5 mL/min. After loading, each cartridge was eluted with 10 mL methanol and evaporated to 0.5 mL under a gentle nitrogen stream. Each sample vial reached a final volume of 1.0 mL via the addition of 0.5 mL ultrapure water before the instrumental analysis.

The prepared samples were analyzed using a Waters Acquity™ UHPLC-MS/MS system. The target compounds were separated on a Waters HSS T3 column (100 mm × 2.1 mm, 1.8 μm) in multiple reactions monitoring (MRM) mode. The injection volume was set at 4 μL and the column temperature was kept at 40 °C. Mobile phase A was ultrapure water containing 0.1% formic acid and mobile phase B was acetonitrile containing 0.1% formic acid at 0.4 mL/min of the total flow rate. The gradient elution started with 95% A (0 min), then 0.5% A (6 min), finally to 95% A (8.1 min). The instrumental parameters and monitored MS/MS transitions can be found in our previous study [14].

2.4. Quality control

The quality control procedures were conducted similarly as described previously [14, 23]. The recoveries of the target compounds (500 ng/L) spiked to the filtered estuarine water (n = 3) were varied from 63.0% to 126.8% with the average standard deviations (SD) were lower than 5.5%. The linear calibration curves were obtained via analyzing standard solutions ranged from 0.05 to 500 ng/mL. The limit of detection (LOD) and the limit of quantification (LOQ) varied from 0.01-1.07 ng/L and 0.03-1.71 ng/L respectively, which were estimated using the lowest concentration detected in matrix matched standards with signal-to-noise (S/N) ratios of 3 and 10. Reagent blank experiment (n = 3) demonstrated that the analytical system and instrument were free of contamination.

2.5. Estimation of pharmaceutical fluxes into the Yangtze Estuary

Equation (1) is the second choice of the Oslo-Paris (OSPAR) Convention [25]. Mean daily flux is calculated and converted to the measuring period in this method. Only large variability of target concentration and river runoff over sampling period will bring substantial systematic errors. This method can lead to good estimation results when there is no correlative relation between concentration and runoff [26]. Pharmaceutical contaminants as man-made emissions, there was no significant correlation between concentration and instantaneous discharge, with more obvious characteristic of point source. Therefore, equation (1) is selected to estimate pharmaceutical fluxes at Datong and Xuliujing in this study.

$$F = K\frac{1}{N}\sum_{i=0}^{N} cQ \qquad (1)$$

where *F* is the flux (tons); *K* is factor to account for period of record; *c* is sample concentration (ng/L); *Q* is discharge at sample time (m^3/s); *N* is number of samples.

3. Results and discussion

3.1. Occurrence of pharmaceuticals in the Yangtze River and Wusongkou

The concentrations of selected pharmaceuticals in the water samples were provided in Table 1. Simvastatin and paclitaxel were not detected in any water samples from three sampling sites over four seasons (n = 69), while the average detection frequencies of omeprazole, nifedipine, nimodipine and sulfathiazole were lower than 50%. Five non-antibiotic pharmaceuticals (carbamazepine, cimetidine, diazepam, indomethacin and tamoxifen), five sulfonamides (except sulfathiazole and sulfamerazine), two chloramphenicols (thiamphenicol and florfenicol), and macrolides in this study were detected in each sample over four seasons. The concentrations of selected antibiotics were relatively high compared with non-antibiotic pharmaceuticals due to their extensive usage in humans, animal husbandry and aquaculture, which widely distributed within the Yangtze River basin. Thiamphenicol was detected with the highest medium concentration (216.6 ng/L) in the winter, while the maximum concentration was 535.2 ng/L of erythromycin in Wusongkou in the spring of 2014.

In the group of non-antibiotic pharmaceuticals, both the maximum concentration (99.8 ng/L) and the highest medium concentration (21.7 ng/L) were presented via detecting paracetamol, followed by diazepam, carbamazepine, cimetidine and indomethacin. These five pharmaceuticals were the dominating non-antibiotic pharmaceuticals, combined accounted for 64% to 100% of the total non-antibiotic pharmaceuticals. It was worth noting that paracetamol did not detected in any water samples in the summer, but in other seasons, its concentrations were significantly higher than other non-antibiotic pharmaceuticals. Paracetamol is not only a very common analgesic and antipyretic drug, but also an important material to manufacture azo dyes and photographic chemicals. Paracetamol as a kind of aromatic amines was highly sensitive towards light and temperature, and the oxidation would be caused by its continuous exposure to intense heat and light [27]. In addition, paracetamol was susceptible to degrade by microorganisms [28]. Due to the double effects of natural environment and microorganisms, degradation of paracetamol in the summer was accelerated. Among the sulfonamides, sulfadiazine, sulfamethoxazole and sulfamethazine were dominating. These three antibiotics combined accounted for 48% to 99% of the total sulfonamides. Of the chloramphenicols, the concentrations of thiamphenicol and florfenicol were far higher than the one of chloramphenicol, duo to chloramphenicol has been strictly prohibited for use in food-producing animals in many countries including China [29]. In the macrolides group, the concentrations of erythromycin (1.61-22.74 ng/L) were about one to two orders of magnitude higher than the ones of roxithromycin. Erythromycin mainly exists in dehydration form in aquatic environment [30]. In this study, the original erythromycin accounted for up to 32% of the total erythromycin. Consequently, the concentrations of erythromycin were expressed as the total concentrations. It could be speculated that the usage and stability of pharmaceuticals with high concentrations would be higher than others in the lower Yangtze River and based on the experimental data [31-33]. In comparison to pharmaceutical concentrations at river waters and coastline sites in the Yangtze estuary, the concentrations in this study were lower.[21, 22, 34, 35]

3.2. Spatial and seasonal variability of pharmaceutical concentrations

The seasonal distribution pattern of pharmaceuticals at three sampling sites was shown in Fig. 2. It was obvious that the concentrations were relatively close between Datong and Xuliujing, while, the concentrations at the site of Wusongkou were generally higher than at Xuliujing and Datong sites during the same period, due to dilution of great runoff in the Yangtze River. Both Datong and Xuliujing are in the downstream of the Yangtze River, with a distance of about 500 km. Water need 4-6 d to transport from Datong to Xuliujing [36]. The Huangpu River system is in the downstream of the Tai Lake basin, flows through Shanghai City and joins the Yangtze River at Wusongkou. Discharge of treated and untreated municipal and industrial wastewater from the urban area and input of agricultural runoff along the Huangpu River and the Tai Lake acted as potential sources introducing a high load of pharmaceuticals into the river. The annual mean runoff of the Huangpu River outlet over years was about 1.09×10^{10} m^3 [37], which was far lower than the one of the Yangtze River.

In the non-antibiotic pharmaceutical group, the trend of concentrations at Datong and Xuliujing during the year was very close on the whole. The concentrations in the winter and spring (dry seasons) were significantly higher than those in summer, with the middle ones in the autumn. For the major compounds, it was notable that paracetamol could not detected in the summer, but its concentration rose from the autumn and peaked in the second year spring (Datong 32.3 ng/L, Xuliujing 29.6 ng/L), when it accounted for more than 75% of total concentrations of the non-antibiotic pharmaceuticals. The concentration of carbamazepine was little changed in different seasons (0.77-1.6 ng/L). The fluctuating ranges of cimetidine and diazepam were slightly greater than carbamazepine (0.70-2.62 ng/L for cimetidine and 1.7-6.2 ng/L for diazepam, respectively). However, cimetidine peaked in the autumn at Xuliujing (1.58ng/L), while in the spring at Datong (2.26ng/L). Concentration difference of indomethacin existed during four seasons at Datong and Xuliujing (0.27-5.53 ng/L). Indomethacin peaked in the autumn at Xuliujing, while it peaked in the spring at Datong. In addition, the concentrations of indomethacin at Xuliujing were significantly higher than those at Datong in the summer and autumn, but the opposite in the spring.

For antibiotics, the concentration of sulfadiazine at Datong was higher than the one at Xuliujing in the summer, and its concentration changed in trend in other seasons with the maximum in the spring (53.5ng/L). The concentrations of sulfapyridine at both Datong and Xuliujing were very low (0.60-1.28 ng/L). The concentrations of sulfamethoxazole increased from the summer to the second spring at Xuliiujing, but its concentrations remained stable at Datong during a year. The highest concentration of sulfamerazine appeared in the autumn, while an obvious higher value arose in the spring at Datong (31.0ng/L) than Xuliujing (6.94ng/L). Erythromycin showed a increasing trend from the summer to the nest spring, but the concentrations at Datong were higher than the ones at Xuliujing over the same period. Thiamphenicol and florfenicol had a similar seasonal variation trend with higher concentrations in the autumn and winter but lower in the spring and summer. Unlike erythromycin, the concentrations of thiamphenicol and florfenicol were higher at Xuliujing than those at Datong over the same period.

Due to more direct impact by human activity, pharmaceutical concentrations changed more complex in Huangpu River during a year. Sometimes, twice sampling in the same quarter had a greater difference for the same pharmaceutical. For the non-antibiotic pharmaceuticals, the highest concentration of paracetamol in Wusongkou appeared in the autumn (99.8ng/L) and higher than that in Yangtze River, followed by the spring and winter, but its concentrations in these two quarters were lower than those during the same period of the Yangtze River, not detected in the summer. Variation at Datong and Xuliujing had a similar trend for carbamazepine and diazepam, but the concentrations of carbamazepine and diazepam were 10-23 times and 3-6 times those in Yangtze River, respectively. The concentration of cimetidine was the highest in the summer (12.0ng/L), and then decreased over the autumn and winter, raised again in the spring at Wusongkou. Indomethacin peaked in the winter (25.2ng/L), followed by summer, autumn and spring. For antibiotic pharmaceuticals at Wusongkou, sulfadiazine was at a lower level of concentration in the summer and autumn, and when heading into winter, its concentration had a dramatic increase, but it gradually decreased as the spring coming. The concentration difference of sulfapyridine was larger between twice sampling in the summer. The concentration of sulfamethoxazole was a little higher in the winter. The concentration of sulfamethazine was higher in the summer than that in the autumn and winter, in which was higher than that in the spring again. An extreme fluctuation of erythromycin was that both high and low values appeared over the same sampling period in the spring. The lowest concentration of thiamphenicol in the summer (4.33ng/L), reached the highest in the winter (145.9ng/L). The concentrations of florfenicol had a smaller fluctuation over a year, with a little higher in the autumn and winter but lower in the spring.

Even though the pharmaceutical contaminants presented different concentration trends at the three sampling sites over a year, the actual pharmaceutical fluxes would show different trends from concentrations due to the fluctuation of river runoff in a year. This trend may herald the difference of usage and the diversity of pollutant sources over four seasons.

3.3. Pharmaceutical fluxes and source analysis from the Yangtze estuary into coastal water

As the runoff of the Yangtze River changes a lot over a year, the pharmaceutical concentrations cannot response actual pollution load, It is necessary to estimating the pharmaceutical fluxes in order to understand the pollution load of these pharmaceuticals from the Yangtze River estuary into coastal water more clearly. In addition, the sources and usage of the pharmaceuticals can be speculated by comparing the flux change in the different monitoring sections. Pharmaceutical fluxes in the monitoring sections displayed seasonal and spatial variations during the study period (Fig. 3).

For the non-antibiotic pharmaceutical, the seasonal flux of paracetamol continued to rise after the summer, rapidly rising from the autumn (0.23-0.35 ton) to the winter (2.02-2.29 ton), then to the top in the spring (2.88-6.15 ton). This study assumed that this trend had a close relationship with the chemical properties and usage of paracetamol. Paracetamol is a very common over-the-counter (can sell without prescription) analgesic and antipyretic drug. Cold entered a frequent period in winter and spring, which made usage of paracetamol more than other seasons. Sun et al. found that the concentration of paracetamol was significantly higher in February, May, and November in Auguest in the influent of sewage treatment plants in Xiamen, China [38]. Yu et al. also found that the concentration of paracetamol was higher in winter than in summer in both influent and effluent of sewage treatment plants [39]. There would be two reasons to lead large quantity of paracetamol discharge by sewage treatment plant at low temperature; on the one hand, its input was increased in cold weather. Even if paracetamol removal efficiencies reached up to more than 91% in sewage treatment plants [38-40], there was still a lot of this drug discharging into aquatic environment. The other hand is environmental factors, biological degradation works with a lower efficiency at a lower water temperature in the sewage treatment process or natural aquatic environment [41] and weaken photodegradation in low levels of sunlight in cold seasons because paracetamol can be removed by photodegradation [40, 42, 43].

Seasonal flux variations of carbamazepine and cimetidine had a similar tendency, which was in synchrony with the runoff, higher flux with more runoff in the summer and spring. Carbamazepine as psychiatric drug seemed to be persistent in natural degradation processes [44] with strong resistance to biodegradation [45], photodegradation [46, 47] and adsorption [48]. Although removal of carbamazepine in sewage treatment plant was limited, the efficiencies in spring with higher temperature were still slightly higher than those in winter [49, 50]. Some study showed that, carbamazepine concentration was highest in summer, followed by autumn, with minimum in spring in both influent and effluent of sewage treatment plant [38]. Yu et al. found that carbamazepine concentration of effluent in summer was about 1 times higher than that in winter [39]. Carbamazepine was mainly used to treat epilepsy, and the symptoms of epilepsy were more significant in high temperature [51, 52], result in the increase of carbamazepine in summer. Cimetidine as an antacid, is similar to carbamazepine, with low biodegradation and low photodegradation of long wavelength ultraviolet light [53]. The removal efficiency of cimetidine in sewage treatment plant was still not high [54]. There was some solid evidence to conclude that peptic ulcer disease was lower during the summer than the other seasons [55], but in the present study, the seasonal flux of cimetidine did not show a consistent trend with the morbidity.

The seasonal characteristics of diazepam flux was not significant. High fluxes appeared in the autumn and spring at Datong, while fluxes were slightly higher in the summer and spring at Xuliujing. Diazepam as another anxiolytic and anti-epileptic drug except carbamazepine is highly stable in waters, soils and during sewage treatment [48, 56]. Vystavna et al. studied pharmaceuticals of the Lopan River in Ukraine in different seasons, and the results showed that the concentration of diazepam in summer was higher than in winter [57], while Mendoza's study of a river in central Spain showed the concentration of diazepam did not differ significantly between summer and winter [58]. Given that much of the precipitation in Ukraine occurred during summer, so actual pollution load of diazepam in summer was higher than in winter. And yet the rainy season in Spain was winter with a higher pollution load. Some study of the disease also showed that, the severity of depressive and anxiety symptoms did not show a seasonal pattern [59].

The seasonal fluxes of indomethacin was different from other non-antibiotic pharmaceuticals, with the fluxes at Datong lower than at Xuliujing in the summer, autumn and winter and the maximum flux appeared at Xuliujing in autumn. Indomethacin concentrations in effluent from different sewage treatment plants might behave very differently from one another. After different sewage treatment process, the removal efficiency of indomethacin ranged from 11% to 100% [11, 60-62]. The concentrations of effluent from a sewage treatment plant in Kumamoto, Japan were about 164-268 ng/L [62], and in effluent of two sewage treatment plant in Guangzhou, China, the concentration was zero [60]. A large part of indomethacin may discharged into aquatic environment. The reason that indomethacin flux at Datong section was generally lower than that at Xuliujing section may be the cities in the downstream of Datong with more densely population, such as Nanjing, Suzhou, discharged effluent with a much higher concentration of indomethacin into the Yangtze River.

In the group of antibiotics, the seasonal flux trends of three main sulfonamides, sulfadiazine, sulfamethoxazole and sulfamethazine varied. The sulfadiazine flux was the largest in the spring with almost zero flux in the summer and autumn at Xuliujing, and yet the second high flux in the summer at Datong. The sulfamethoxazole flux showed high in the spring and summer, while the lowest in the winter. The difference of sulfamethoxazole flux between Datong and Xuliujing was which season a high value presented. The sulfamethazine flux was the lowest in the winter, with a peak in the autumn at Xuliujing, and a peak in the spring at Datong. Sulfonamides are widely used in livestock. They can be used alone or with other antibiotics for prevention and treatment of infections [63], and they are one kind of the largest veterinary antimicrobial drugs [64]. Wei et al. studied antibiotics in wastewater from livestock breeding field in Jiangsu, China and suggested that the concentration of sulfadiazine in poultry wastewater (median: 0.37 μg/L) was significantly higher than that of sulfamethoxazole (0.09 μg/L) and sulfamethazine (0.09 μg/L). The concentration of sulfadiazine in wastewater from dairy farms (0.89 μg/L) was the highest, followed by sulfamethazine (0.36 μg/L), sulfamethoxazole in last place (median: 0.04 μg/L). In wastewater from swine farms, sulfamethazine concentration (4.66 μg/L) was much higher than sulfadiazine (0.42 μg/L) and sulfamethoxazole (0.27 μg/L) [65]. The weather in Yangtze River Basin with much precipitation, high humidity, and a dramatic change in spring, was easy to make livestock disease, which led to the fluxes of sulfonamides appearing generally high values in the spring. Due to the earlier sampling time in the summer, the sulfadiazine flux exhibited a high value of continuity. Winter as a sale season of swine, pig breeding stock showed a cyclical change with decreasing in winter, then gradually rising, resulting in the lowest usage of sulfamethazine in the winter. According to China's National Bureau of statistics data in 2013, the number of swine was the largest in Hubei Province located above Datong in the middle and lower reaches of Yangtze River [66]. That temperature fluctuation in spring led to swine disease might raise sulfamethazine flux at Datong.

Erythromycin flux peaked in the spring, with much higher flux at Datong than at Xuliujing. Erythromycin is mainly used to treat upper respiratory infections for human and animal. The lower removal efficiencies of sewage treatment plants were measured for erythromycin (0-45%) [67, 68]. In addition, the breeding livestock would produce large amounts of wastewater containing erythromycin. Chen et al. studied prevalence of antibiotic resistance genes of wastewater and surface water in livestock farms of Jiangsu Province, China. The results indicated that the macrolide antibiotic resistance genes widely existed in wastewater of almost all swine farms and poultry farms, and in part of cattle farms [69]. The reason for erythromycin flux increasing in the spring at Datong might be related to numerous pig breeding industries along the Yangtze River above Datong.

For chloramphenicols, there were different trends for the seasonal fluxes of thiamphenicol and florfenicol at Datong and Xuliujing. The thiamphenicol represented the highest flux in the winter, slightly higher than in the autumn, and much higher than in the spring and summer at Xuliujing. The thiamphenicol flux at Datong accounted for 9% to 60% of the flux at Xuliujing over the same period. The florfenicol flux at Datong was close to that at Xuliujing in the summer, while in other seasons, the fluxes at Datong were lower. Chloramphenicols as main antibiotics were widely used in aquaculture around the Yangtze River delta [70]. Moreover, thiamphenicol and florfenicol were detected from municipal sewage. The average concentrations of thiamphenicol and florfenicol were 15.5 ng/L and 10.5 ng/L in the effluent of a typical sewage treatment plant in Shanghai, with average removal efficiencies 87% and 39%, respectively [71]. Thus, the main source of thiamphenicol and florfenicol in aquatic environment with higher stability may be aquaculture wastewater. The production of artificial cultured freshwater products in Jiangsu province in 2013 significantly exceeded those in the neighboring upstream provinces of Jiangxi and Anhui [66]. Therefore, the widespread use of chloramphenicols in aquaculture in the lower Yangtze River may be the reason for the rising fluxes at Xuliujing.

Due to the lack of real-time runoff data of the Huangpu River, only the annual mean runoff can be used to estimate the annual flux of pharmaceutical pollution discharged into the Yangtze River. The annual fluxes at Datong, Xuliujing and Wusongkou are shown in table 2. Compared with the fluxes at Datong and Xuliujing, total pharmaceutical flux at Wusongkou only was about 5% of the flux at Xuliujing. However, it was noteworthy that the fluxes of sulfapyridine and sulfathiazole at Wusongkou exceeded the fluxes at Xuliujing, which showed that these two sulfonamide antibiotics had a more widespread application in Huangpu River Basin compared with other regions.

In conclusion, such contrasting seasonal variations of pharmaceutical fluxes may depend upon both environmental factors (temperature, photodegradation, biodegradation, adsorption and precipitation, etc.) and societal factors (production, consumption, excretion).

4. Conclusions

Seasonal variations in pharmaceutical concentrations in different regions were obtained by setting monitoring sites in featured positions in the Yangtze Estuary and the estuary of the Huangpu River. The variation in seasonal concentration of most pharmaceuticals was consistent between the Xuliujing and Datong sections, while some anti- biotics differed greatly in concentration. Due to dilution, concentrations in the Yangtze River were generally lower than in the Huangpu River. Combined with the discharge data, the fluxes of pharmaceuticals in the Yangtze River and Huangpu River could be estimated. The flux differ- ence between the Xuliujing and Datong sections may be attributed to the various usage and emissions of these pharmaceuticals in different regions, as well as their fate under various environmental factors (such as temperature, photodegradation, biodegradation, adsorption and precipitation). To obtain a more accurate and comprehensive analysis of pharmaceutical sources in the Yangtze River basin, more monitoring sites will be needed in future studies, and the production, usage and emission process of pharmaceuticals should be investigated more fully.

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