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Distribution patterns of antibiotic residues in an urban river catchment

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antibiotics; catchment; Ningbo; residual pattern; urbanization.

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Abstract

The residual patterns of 23 target antibiotics in five classes of compound in catchment sediments of a rapidly urbanizing city in east China were studied. A total of 14 antibiotics were detected in the catchment. The dominant classes were tetracyclines and fluoroquinolones and these occurred at substantial concentrations. High environmental risk at the sites sampled may be associated with antibiotics detected at high concentrations. For example, at one site chlortetracycline was found to occur at concentrations ≤ 4496 ng/g. Source traceability indicates that high intensity of urbanization (e.g. hospitals and livestock farms) had a high spatial relationship with sites of high antibiotic contaminations. Urban and suburban areas had some impacts on antibiotic residues in the catchment, especially on veterinary antibiotics such as chlortetracycline in suburban areas. Moreover, antibiotics detected at high concentrations in urban areas included fluoroquinolones associated with human medicine.

Introduction

Antibiotics are a large group of compounds used extensively in human and veterinary healthcare (Cromwell, 2002; Kümmerer, 2009). Antibiotics cannot be fully taken up by living organisms and this results in the release of a large proportion of these compounds or their metabolites into wastewater systems (Bound and Voulvoulis, 2004; Kümmerer, 2009). Wastewater treatment plants (WTPs) cannot remove antibiotics completely because antibiotics inhibit the biological activity of activated sludges. The target compounds for recent wastewater treatment technologies do not include antibiotics, resulting in the substantial release of antibiotics into the surrounding environment (Michael *et al.*, 2013). Additional potential sources include pharmaceutical and aquaculture facilities and agricultural land application of manures. Thus, antibiotics are ubiquitous contaminants and are subject to emerging concern because of their stimulatory effects on the emergence of antibiotic resistance genes.

Numerous studies have explored the residues and the fate of antibiotics in various environmental matrices (Bu *et al.*, 2013) such as WTPs (Jia *et al.*, 2012; Östman *et al.*, 2017), surface waters (Zuccato *et al.*, 2010; Yao *et al.*, 2017), groundwater (Balzer *et al.*, 2016; Burke *et al.*, 2016) and drinking water (Wang *et al.*, 2016; Li *et al.*, 2017). The levels of antibiotics present vary greatly at different sampling sites (Liu and Wong, 2013; Carvalho and Santos, 2016) but the concentrations detected are mostly of the magnitude of ng/g or ng/L. In addition, large amounts of antibiotics are entering the environment due a lack of investment and the mismanagement of wastewater treatment facilities. Very high concentrations are frequently found in aquatic environments in China at sites adjacent to pollution sources such as pig farms (Tong *et al.*, 2017). Levels of antibiotics in the environment near veterinary sources have been reported to be much higher (1–2 orders of magnitude) than in other environmental matrices (Luo *et al.*, 2011). The pollution point sources responsible for these high levels of antibiotic residues in a catchment or lake can be easily identified. However, in urban inland river systems the river water flows are more complex, depending on the location, direction and altitude of the effluent. In addition, with various coexisting sources such as sewage treatment plants, hospitals and pharmaceutical and veterinary facilities, the residual patterns of antibiotics in urban inland rivers represent a different scenario with an uncertain source traceability that may be more complicated. The current study therefore focused on commonly used antibiotics in a typical Chinese urban inland river system to elucidate the residual pattern and source traceability at spatial levels in urbanization gradients.

China is undergoing a rapid urbanization process following the accelerating economic development since 1978. Pollution is a consequence of the environmental challenge resulting from rapid urbanization. An understanding of the effects of urbanization on environmental pollution processes may facilitate pollution control and deliver a healthy urban environment to the population. However, in contrast to developed megacities with high population densities such as Beijing, Guangdong and Shanghai, smaller cities are only now starting the demographic transition which will lead to greater antibiotic pollution from different sources (Bu *et al*., 2013). Economic and population increases enhance antibiotic consumption in agricultural production and human healthcare. Urbanization processes can also affect the distribution of potential sources of antibiotics in one area through city planning. However, knowledge of antibiotic residues in developing urban areas in China is lacking (Liu and Wong, 2013; Sun *et al*., 2016), especially the source traceability of the residual compounds in inner cities. The aims of the present study were therefore to characterize the residual pattern of commonly used antibiotics such as tetracyclines, sulfonamides, fluoroquinolones, macrolides and trimethoprim in urban inland rivers of Ningbo city, to identify and map the potential sources of the antibiotics present at spatial level and to investigate the effects of urbanization on the levels of antibiotic residues.

Materials and methods

Chemical compounds and reagents

Antibiotic standards (Supporting Information Table S1) comprising tetracycline (TC), oxtetracycline (OTC), chlortetracycline (CTC), doxycycline (DOC), sulfadiazine (SDZ), sulfamethoxazole (SMX), sulfamethazine (SMT), sulfamonomethoxine sodium hydrate (SSH), sulfadimethoxine (SDM), sulfachinoxalin (SCX), sulfaclozine sodium monohydrate (SSM), sulfathiazole (STZ), sulfameter (SM), sulfamerazine (SMZ), trimethoprim (TMP), norfloxacin (NFC), ofloxacin (OFC), enrofloxacin (EFC), ciprofloxacin (CPC), difluoxacin (DFC), erythromycin (ETM), roxithromycin (RTM) and tylosin (TYL) were purchased from Sigma-Aldrich and Dr Ehrenstorfer GmbH (Augsburg, Germany). The internal standards (D4-sulfamethazine, D8-ofloxacin, C13, D4-erythromycin) and surrogate standards (C13-phenacetin, D5-atrazine, D7-DEET) were obtained from Dr Ehrenstorfer GmbH (Augsburg, Germany) and Toronto Research Chemicals Inc. (Toronto, Canada). HPLC grade methanol and acetonitrile were provided by Tedia (Fairfield, OH) and formic acid and ammonium acetate by CNW Technologies GmbH (Düsseldorf, Germany). Other reagents such as acid-monohydrate and sodium phosphate-dibasic anhydrous were purchased from Sinopharm Chemical Reagent Co. Ltd., Shanghai, China.

The experimental materials for cartridges (Oasis HLB, 6 mL per 500 mg) were obtained from Waters Corporation (Milford, MA), glass microfibre filters (GF/F) from Whatman Ltd. (Little Chalfont, Buckinghamshire, UK) and syringe-driven filters (0.2 µm, PTFE) from Millipore (Burlington, MA). All antibiotic standards were prepared in methanol solution and stored frozen at −18°C before analysis. The extracted solvents acetonitrile, EDTA-McIlvaine buffer (pH 4), 50% (v/v) Mg $(NO_3)_2$ and 2.5% (v/v) $NH_3 \cdot H_2O$ were prepared according to Huang *et al*. (2013).

Description of sites and sample collection

The sampling sites were located at urban inland river systems and the Yong River catchment in Ningbo city (Fig. 1). The city is located on the Yong River catchment and is divided into five districts, namely Haishu, Yinzhou, Jiangbei, Jiangdong and Zhenhai. Urban inland rivers from each district are well developed and connected with the Yong River catchment (Fig. 1). Twenty samples were collected from the Yong River to investigate the antibiotic residues in Ningbo city and 21 samples were collected from urban inland rivers to evaluate source traceability. Sediment samples (about 10–15 cm depth) were carefully grabbed from the aquatic environment with a Lenz collector (Hydro-Bios, Kiel, Germany). Each sample was obtained by mixing equal quantities of 3–5 discrete subsamples which were grabbed from individual sample sites. The samples collected were then transported to the laboratory at −20°C in a car freezer (CF-110DC, Waeco, Emsdetten, Germany) and deep frozen at −40°C prior to sample extraction. The deep frozen samples were freeze-dried in a freezer dryer (FD-1C-50, Boyikang, Beijing, China) and homogenized to pass a 0.30-mm sieve. Sediment properties were characterized in terms of total carbon (TC) content, total nitrogen (TN) content, total sulphur (TS) content, pH and electrical conductivity (EC). TC, TN, TS in sediments were determined using an Elementar Vario Max (Analysensysteme GmbH, Langenselbold, Germany). EC and pH were determined in a 1 : 2.5 (w/v) mixture of soil and water with a pH-EC meter (Excel Xl60, Fisher Scientific Inc., Hampton, NH). Sediment particle size distribution was determined using a particle sizing instrument (Mastersizer 2000, Malvern, UK).

Extraction and determination of antibiotics

The exaction procedure followed Huang *et al*. (2013). In brief, freeze-dried and homogenized sediment samples (~ 5.00 g) were transferred to 50-mL glass centrifuge tubes with 25-mL exaction solvent overnight. The tubes were then ultrasonically extracted for 30 min and the slurries were separated by centrifugation to collect the supernatants. The residues were re-suspended in 20 mL of the extraction solvent followed by ultrasonic extraction and centrifugation and then the supernatants were collected again. This procedure was repeated twice. The three supernatants from each sample were combined and diluted to 500 mL with ultrapure water. Solid phase extraction (SPE) with Oasis HLB cartridges was then used for clean-up and extraction of antibiotics. The HLB cartridges were pre-conditioned sequentially with methanol and ultrapure water before passing through the diluted sample. After extraction, the HLB cartridges were rinsed with 10 mL ultrapure water and dried under vacuum for 1 h. The dried cartridges were then eluted twice with 10 mL of methanol. The eluents were collected in 15-mL brown glass vials and concentrated down to 0.10 mL under nitrogen.

Antibiotic residues were separated and quantified by HPLC-ESI-MS/MS (LC20A, Shimadzu Corp., Kyoto, Japan integrated with ABI320, AB Sciex, Framingham, MA). The gradient separation in HPLC was performed with a Kromasil C18 column (5 μm × 4.6 mm × 150 mm, Akzo Nobel, Göteborg, Sweden) at 35°C. The mobile phases were treated with ultra-pure water (containing 0.10% formic acid) and methanol. Multiple reaction monitoring (MRM) mode was used for the detection of fragment ions from each target compound. The two most intense and specific fragment ions (one for qualitative and the other for quantitative determination) were selected and used in the MS/MS determination. Optimized parameters of ESI for each compound are shown in Supporting Information Table S2.

Quality assurance and quality control

The internal standard method was used to quantify the antibiotic concentrations with high correlation coefficients ($r^2 > 0.99$, $n = 5$) of the linear calibration (range 10.00–200.00 μg/L). A laboratory blank was tested using dried quartz sand and was processed in exactly the same way as the sediment samples. The concentrations of the target compounds in laboratory blank testing were below the detection limits. Spiking experiments using 25 ng/g standards in sediment samples with overnight equilibration were included for quality assurance of the protocol. Recovery rates of 46.7–124.8% were obtained. Three surrogates for each sample (C13-phenacetin, D5-atrazine and D7-DEET) were spiked and aged overnight before extraction processing to confirm the high quality of the exaction procedure. Detailed information on method quality and

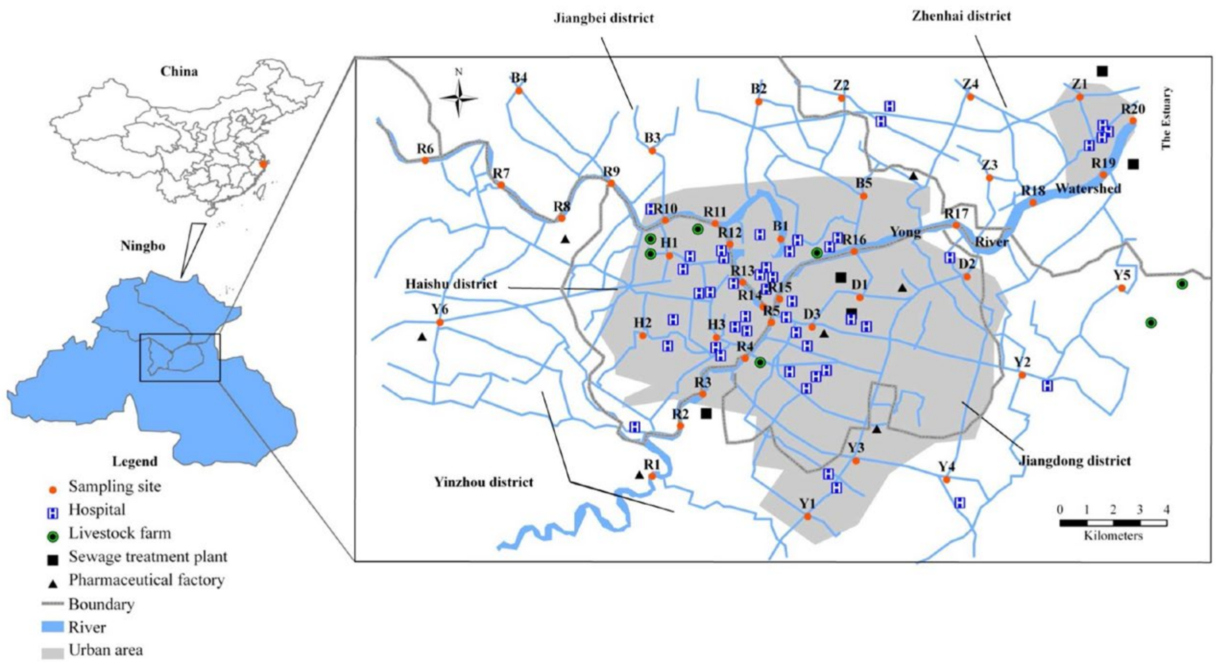

Fig. 1. Sampling sites in Ningbo City (eastern China). Site R1–R20 are located Yong River watershed. Site H1–H3 are located in Haishu District; site Y1–Y6 are located in Yinzhou District; Site B1–B5 are located in Jiangbei District; Site D1–D3 are located in Jiangdong district, while Z1–Z4 are located in Zhenhai District. The information of hospital, livestock farm, sewage treatment plant and pharmaceutical factory was from Baidu map.

assurance is provided by Huang *et al*. (2013) and is briefly listed in Supporting Information Table S3.

Results and discussion

Occurrence of antibiotics in the urban catchment

A total of 14 out of 23 target antibiotics were found in sediments at Ningbo city with concentrations ranging from not detected or < LOQ (limit of quantification) to 4496.0 ng/g (Fig. 2), magnitudes similar to those commonly found in Chinese freshwater and marine sediments (Liu *et al*., 2016; Yang *et al*., 2016). The residual patterns of the antibiotics were generally related to medicine prescription and environmental stability. Compounds such as tetracyclines and fluroquinolones tend to be absorbed by suspended matter because of their hydrophobicity and interaction with clay or organic particles (Tolls, 2001; Carrasquillo *et al*., 2008), leading to significant detection in sediments. Four tetracyclines (tetracycline, oxytetracycline, chlortetracycline and doxycycline) were found in sediment samples from urban inland rivers from Ningbo city. Maximum concentrations were much higher than those found in catchment systems such as the Pearl River (Yang *et al*., 2010), the Huangpu River (Chen and Zhou, 2014) and the Yellow River (Zhou *et al*., 2011). However, they were lower than reported in the Jiulong River (Zhang

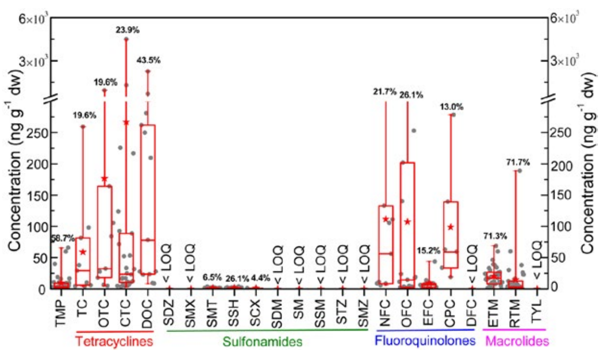

Fig. 2. Occurrence of target antibiotics in sediment form Ningbo watersheds, eastern China. Each box plot described the concentration distribution of each antibiotic from all sampled sites. Mean and median concentrations are depicted as pentagram and solid horizontal lines in the box, respectively. Circle dot around the boxes represented the detected data of each compound (TC= tetracycline, OTC= oxtetracycline, CTC= chlortetracycline, DOC= doxycycline, SDZ= sulfadiazine, SMX= sulfamethoxazole, SMT= sulfamethazine, SSH= sulfamonomethoxine sodium hydrate, SCX= sulfachinoxalin, SDM= sulfadimethoxine, SM= sulfameter, SSM= sulfaclozine sodium monohydrate, STZ= sulfathiazole, SMZ= sulfamerazine, NFC= norfloxacin, OFC= ofloxacin, EFC= enrofloxacin, CPC= ciprofloxacin, DFC= difluoxacin, ETM= erythromycin, RTM= roxithromycin, TYL= tylosin). Detection frequency of each antibiotic was listed above the box. < LOQ means value below the limit of quantification.

et al., 2011). Fluoroquinolones (ofloxacin, norfloxacin, ciprofloxacin and enrofloxacin) were the second commonest class of antibiotics. Maximum concentrations of these compounds were also higher than found in the Yellow River and the Liao River, but lower than in the Hai River (Zhou *et al*., 2011). Sulfonamides are weakly absorbed by sediments and are therefore readily transferred to the aquatic environment and washed out from the sediment environment. This may be the main explanation for the low concentrations and detection frequencies of sulfonamides (10 compounds in this study) in sediments. Similar results were found in the Hai River and the Liao River (Zhou *et al*., 2011), Baiyang Lake (Li *et al*., 2012) and Yangtze Estuary (Yan *et al*., 2013). Trimethoprim is commonly used in combination with other antibiotics as a synergist, resulting in significant detection frequency and levels which were higher than found in the Hai River, the Yellow River and the Liao River (Zhou *et al*., 2011) but lower than reported in the Dagu Sewage Discharge Channel (Hu *et al*., 2012).

Of the macrolides, erythromycin and roxithromycin showed the highest frequency of detection (71.3 and 71.7%, respectively, Fig. 2) among the target compounds. The maximum levels of erythromycin and roxithromycin were higher than those detected in the Huangpu River (Chen and Zhou, 2014) and the Baiyang Lake (Li *et al*., 2014) but lower than in the Hai River (Luo *et al*., 2011). Medical prescription for human healthcare of these two drugs is the likely explanation for their frequent detection in urban catchments (Murata *et al*., 2011). Tylosin, which is mainly used in veterinary medicine, was not observed at all sampling sites. Compared with the occurrence of chlortetracycline (which is considered a semi-quantitative marker of antibiotic pollution from livestock units) the absence of tylosin in all samples was likely due to local patterns of usage of drugs.

Spatial relationship between antibiotics distribution and urbanization intensity

The variables of residual antibiotics at spatial level can be correlated with two principal components which explained 59.40% of the total variance in the data (Fig. 3 and Supporting Information Table S4 and in Supporting Information). The clustering pattern of residual antibiotics in the sampled sites suggests that they are strongly correlated, while deviating sites such as Y5 and Y6 infer a poor relationship. This significant deviation of sites Y5 and Y6 might be explained by the large contributions from source to samples sites, as these two sites are surrounded by important sources such as animal breeding farms and pharmaceutical factories (see sampling sites in Fig. 1 and antibiotic concentrations in Fig. 4). All the potential sources of the target antibiotics in Ningbo city were showed on Fig. 4, coupled with the total concentrations at each site. Sampling sites close to these potential sources were always found to be high in antibiotic residues. For example, site H1 located near the hospitals and livestock farms was found to have higher antibiotic levels than sites H2 and H3 (see sampling sites in Fig. 1 and antibiotic concentrations in Fig. 4). Similar results were found at sites D3, Y3 and D1. High concentrations of target compounds were found in sites located in the vicinity of pharmaceuticals factories (PFs) also, such as site Y6 with a total concentration of detected antibiotics of up to 2338.8 ng/g (13 of 14 antibiotics detected). In addition, the source properties had great effects on sites near to them in the antibiotics present. Sites located near to hospitals such as H1, D3, Y3 and D1 showed significant presence of the fluoroquinolone group, while sites close to livestock farms such as site Y5 had very high detection levels of tetracyclines. Sewage treatment plants (STPs) are important sources of antibiotics in the aquatic environment (Kaplan, 2013). However, no special contributions were found at sites (except D1) near STPs. Dilution can reduce the source contributions since the sites at the Yong River had low concentrations of residual antibiotics, although the sites may receive the effects of dense distribution of potential sources. In contrast, high levels of antibiotics (Fig. 4) were detected at some sites (B2, B4 and R7) without potential sources surrounding them as shown in Fig. 1, indicating the presence of other unrecognized potential sources. The discharges of antibiotics from small health stations with disposal of unused medicines and untreated effluents, agricultural land amended with human and animal wastes as fertilizers and intensive pig breeding might be the explanation for these sites located in suburban areas (Bu *et al*., 2013).

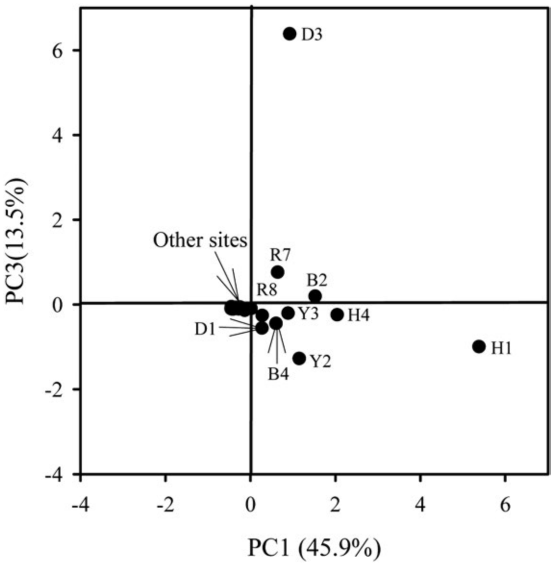

Fig. 3. PCA scores of the investigated sample sites: PC1 versus PC3. Other sites represented the sampling sites which got together including the sites of R1–R6, R9–R20, Z1–Z4 and H2, H3, Y1, Y4, B1, B3, B5, D2, D4 in Fig. 1.

Statistical analysis (Table 1) shows that concentrations of tetracyclines (TCs) and fluoroquinolones (FQs) detected in this urban inland river systems were found to be

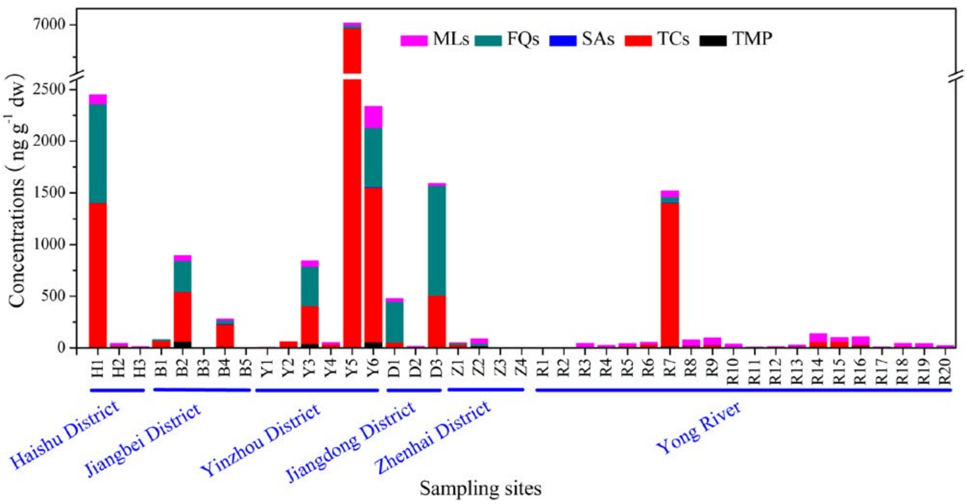

Fig. 4. Total concentrations of each sampled site in Ningbo city. MLs represented macrolide group comprising erythromycin, roxithromycin and tylosin in this study; FQs represented fluoroquinolone group comprising norfloxacin, ofloxacin, enrofloxacin, ciprofloxacin and difluoxacin; SAs represented sulfonamide group comprising sulfadiazine, sulfamethoxazole, sulfamethazine, sulfamonomethoxine sodium hydrate, sulfachinoxalin, sulfadimethoxine, sulfameter, sulfaclozine sodium monohydrate, sulfathiazole and sulfamerazine; TCs represented tetracycline group comprising tetracycline, oxtetracycline, chlortetracycline and doxycycline; TMP represented trimethoprim.

Table 1 Multiple linear regression analysis (SPSS) for the properties (total nitrogen content, total sulphur content, EC, pH, D (4, 3), d (0.9)) of sediments and concentrations of detected antibiotics in sediments from Ningbo city

		Total nitrogen content (TN)		Total sulphur content (TS)		pH		D (4,3)		d (0.9)	
Antibiotics	*N*	β[a]	*P*[b]	β[a]	*P*[b]	β[a]	*P*[b]	β[a]	*P*[b]	β[a]	*P*[b]
TMP	41	1.16	0.00	−0.65	0.02	–	–	–	–	–	–
TC	41	0.56	0.00	–	–	–	–	–	–	–	–
OTC	41	0.58	0.00	–	–	–	–	–	–	–	–
SMT	41	1.07	0.001	−0.83	0.01	–	–	–	–	–	–
SSH	41	1.61	0.00	−1.10	0.00	–	–	−0.59	0.03	−0.77	0.01
SCX	41	1.19	0.00	−0.87	0.004	–	–	–	–	–	–
NFC	41	–	–	0.67	0.00	–	–	–	–	–	–
OFC	41	0.78	0.00	–	–	–	–	–	–	–	–
EFC	41	0.46	0.002	–	–	–	–	–	–	–	–
CPC	41	–	–	0.57	0.00	–	–	–	–	–	–
ETM	41	–	–	−0.37	0.007	—0.601	0.00	−0.328	0.014	–	
RTM	41	−1.19	0.00	−0.624	0.019	–	–	–	–	–	–

TMP = trimethoprim, TC = tetracycline, OTC = oxytetracycline, SMT= sulfamethazine, SSH= sulfamonomethoxine sodium hydrate, SCX= sulfachinoxalin, NFC= norfloxacin, EFC= enrofloxacin, CPC= ciprofloxacin, ETM= erythromycin, RTM= roxithromycin.

[a]The standardized coefficient which was used to estimate the effect of properties of sediments on concentrations of targeted antibiotics.

[b]Significance of the effect of properties of sediments on levels of detected antibiotics was assessed at the 95% confidence level ($P < 0.05$). Values below the limit of quantification were analysed as half of the limit of quantification. D (4, 3) and d (0.9) is the parameters of sediment particle size distribution determined by the Mastersizer 2000 laser diffractometer, where D (4, 3) is the Volume Weighted Mean and d (0.9) is the size of particle below which 90% of the sample lies.

correlated with sediment properties such as total nitrogen (TN) content and total sulphur (TS) content. A positive relation was observed between TN and the two classes of antibiotic. This was likely due to this fact that organic matter discharged from potential sources such as hospitals and aquaculture have many functional groups containing nitrogen and sulphur which can absorb tetracyclines (TCs) and fluoroquinolones (FQs) by their hydrophobic interactions (Tolls, 2001). Similar correlations were found in a previous study on the Liao River (Zhou *et al*., 2011). Other sediment properties such as pH and particle size can also influence the residues of antibiotics in the aquatic environment (Tolls, 2001; Luo *et al*., 2011; Chen and Zhou, 2014). However, poor relationships were found between these and residual antibiotics, except for erythromycin with a negative correlation with pH. Source effects and water turbulence may explain these uncertain relationships.

Effects of urbanization levels on residual pattern of antibiotics

The sampling area was divided into two urbanizing sections, namely the urban and suburban areas according to the city planning diagram (Fig. 1). The comparison of detected antibiotics in the two areas is shown in Table 2. The presented median concentration of total target antibiotics (16.2 ng/g) in the suburban area was higher than that (11.6 ng/g) in the urban area. The macrolides (roxithromycin and erythromycin) and trimethoprim were frequently found (Table 2) in both suburban and urban areas, but there were higher detection frequencies of the three compounds in the urban area and this may be explained by the high population density in the urban area leading to the frequent detection of these compounds in the environment. In addition, chlortetracycline was present at higher detection frequency (61.1%) in the suburban area (see Table 2). The maximum concentrations of all target tetracyclines were found in the suburban area as well as detection frequencies of tetracyclines (except oxytetracycline). In contrast, the maximum levels of target fluoroquinolones (except enrofloxacin) were detected in the urban area (see Table 2). Prescription patterns may be the main explanation for these large differences. Tetracycline compounds such as tetracycline, chlortetracycline, oxytetracycline in this work were the first generation antibiotics and are used mainly in veterinary rather than human healthcare nowadays (Kim and Carlson, 2007; Zou *et al*., 2011), while fluoroquinolones (ofloxacin, norfloxacin and ciprofloxacin) are widely prescribed for human urinary and respiratory infections, and enrofloxacin is mainly used in veterinary medicine. The suburban area has more agricultural activities than the urban area, resulting in higher consumption of veterinary antibiotics as found in other parts of the world (Kim and Carlson, 2007). Personal income can also

Table 2 Comparison of targeted antibiotics in suburban area and urban area from Ningbo city, eastern China

	Suburban area				Urban area			
	Concentrations (ng/g dw)			Detection	Concentrations (ng/g dw)			Detection
Antibiotics[a]	min	median	max	frequency (%)	min	median	max	frequency (%)
Chlortetracycline	10.6	31.9	4496	61.1	11.8	53	225.6	39.1
Oxytetracycline	32.6	94.8	928	22.2	5.3	23.1	396	26.1
Tetracycline	6.1	54.2	259.2	22.2	4.4	29.2	81.6	21.7
Doxycycline	22.7	170	2248	33.3	23.9	209.6	695.2	21.7
Ciprofloxacin	19.3	39.3	59.4	11.1	33.7	101.1	278.4	17.4
Norfloxacin	8.6	11.4	132.8	27.8	6.3	111.2	363.2	21.7
Enrofloxacin	6.4	12.3	44	22.2	7.7	8.6	8.8	13
Ofloxacin	14.4	21.7	426.4	33.3	5.2	227.2	494.4	26.1
Roxithromycin	0.6	12.6	188.8	72.2	0.7	3.4	59.8	87
Erythromycin	1.2	15.8	46.4	66.7	1.2	18.6	68.9	78.3
Trimethoprim	1.8	9.6	65.8	61.1	1.4	3.6	39.8	69.6
Sulfamonomethoxine	1.2	2.1	3.7	44.4	1.2	1.3	1.5	17.4
Sulfachinoxalin	1.4	1.5	1.6	11.1	–	–	–	–
Sulfamethazine	2.2	2.4	3.3	16.7	–	–	–	–

[a]Antibiotics detected were listed.

impact medicine usage and cheaper drugs are the first choice in low-income communities (Chen *et al*., 2013). In addition, low investment and poor management of wastewater treatment programmes may also lead to different levels of residual antibiotics in suburban and urban areas (Tijani *et al*., 2013). For example, the Zhangzhou city with a lower urbanization level was found to have more pharmaceutical residues in its catchment than Fuzhou and Wenzhou cities with higher urbanization levels (Chen *et al*., 2013). High densities of hospitals in urban areas (Fig. 1) may lead to the discharge of more antibiotics derived from human healthcare into the surrounding environment. Similar results have been reported in other developed regions of China such as the urban areas of Hangzhou and Nanning cities, where high concentrations have been detected derived from human healthcare antibiotics (Chen *et al*., 2012; Xue *et al*., 2013).

Conclusions

A total of 14 antibiotics from 23 target compounds were detected in the urban inland river system of Ningbo city, with the dominant antibiotics comprising the tetracycline and fluoroquinolone groups according to the maximum concentrations. Veterinary medicine makes a large contribution to the high detection levels and frequencies of antibiotics in this river system, followed by hospitals and pharmaceutical factories, based on the source traceability at spatial levels. The distribution of sewage treatment plants had a negligible spatial relationship with the antibiotic residues, likely due to water dilution in large rivers. The sampling sites located in the suburban area had higher concentrations and detection frequencies of tetracyclines (veterinary antibiotics) such as chlortetracycline compared with the urban area, while the urban area showed highest levels of fluoroquinolones (except enrofloxacin) such as ofloxacin derived from human healthcare. This indicates that the changeable patterns of medical prescriptions during the urbanization process leads to some differences in antibiotics residues in the urban inland river system.

Additional Supporting Information may be found in the online version of this article at the publisher's website.

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Conflicts of interest

There are no conflicts to declare.

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