Marine Pollution Bulletin 109 (2016) 597–602

Contents lists available at ScienceDirect

Marine Pollution Bulletin

journal homepage: www.elsevier.com/locate/marpolbul

Baseline

Levels, distributions and sources of veterinary antibiotics in the sediments of the Bohai Sea in China and surrounding estuaries

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ARTICLE INFO

Article history:
Received 8 October 2015
Received in revised form 13 May 2016
Accepted 16 May 2016
Available online 28 May 2016

Keywords:
Emerging contaminants
Estuaries
Marine sediment
Risk assessment
Spatial distribution
Source apportionment

ABSTRACT

Veterinary antibiotics are emerging contaminants of concern. A total of 139 samples comprising 104 marine sediments and 35 estuarine sediments were collected from the Bohai Sea area and analyzed for seventeen antibiotics. The results reveal that the presence and concentration of antibiotics were generally higher in the estuaries than in the sea. The highest antibiotic concentration, 4695 μg kg^{-1} of oxytetracycline, occurred in the estuarine sediment from Ziya New River. Bohai Bay and Laizhou Bay and the surrounding estuaries had higher concentrations of antibiotics. However, low levels of antibiotics detected were detected in Liaodong Bay in contrast to the high concentrations present in the surrounding estuaries. Spatial heterogeneity and principal component analysis suggest a large impact of terrestrial sources of the antibiotics contaminating the Bohai Sea. Risk quotients indicate that current levels of norfloxacin and oxytetracycline might be potentially hazardous to sensitive biota both in the Bohai Sea and in its surrounding estuaries.

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Veterinary antibiotics are emerging contaminants in both terrestrial and marine environments of increasing concern in recent years. Antibiotic residues in the environment are mainly derived from the extensive and long-term use of both human and veterinary medicines (Kümmerer, 2009). China leads the world in volume of antibiotic production and usage. Although some antibiotics have been regulated in animal feeds since 1989, the amount used was up to 92,700 tonnes in 2013 (Zhang et al., 2015b). Antibiotics are poorly adsorbed in the gut of the animals and as much as 90% of each dose is excreted in urine and 75% remains unchanged in the feces (Halling-Sørensen, 2000; Sarmah et al., 2006). Thus, a substantial proportion of administered antibiotics enters the environment through wastewater discharge and the land application of manures and sludges, eventually entering the marine environment by riverine input (Jia et al., 2011; Zhang et al., 2012; Zou et al., 2011) and sewage discharge (Gulkowska et al., 2007; Minh et al., 2009). It was reported that over thirty-five main rivers surrounding the Bohai Sea were severely polluted (Jun, 2007; Mao et al., 2009) and transported 36% of wastewaters and 47% of the solid pollutants to the Bohai Sea (Wang and Wang, 2007). Increasing use of antibiotics in aquaculture is another important source for the marine environment (Jia et al., 2011; Kümmerer, 2009; Martins et al., 2008; Minh et al., 2009; Wille et al., 2010; Xu et al., 2007; Zou et al., 2011). The Bohai Sea is the only continental sea in China and has a low exchange rate of seawater, resulting in the long-term residence of pollutants in the sea (Li et al., 2014). Several studies have indicated the presence of high antibiotic contamination in the surface waters of the Bohai Sea (Zhang et al., 2013; Zhang et al., 2012). More than ten antibiotics were found at high detectable frequencies in the surface waters with maximum concentrations of roxithromycin (RTM), trimethoprim (TMP) and sulfamethoxazole (SMX) of 0.63, 0.33 and 0.077 μg L^{-1}, respectively (Zhang et al., 2012; Zou et al., 2011). Many antibiotics have a high K_d value and are liable to be adsorbed by solid particles such as sediments (Wang and Wang, 2015).

Antibiotic residues in the marine sediments are also very important in terms of the fate of antibiotics in the marine environment and their ecological risks (Bu et al., 2013; Eguchi et al., 2004; Kümmerer, 2004). However, until now to our knowledge no available data have been reported regarding the antibiotic contamination in the sediments of the Bohai Sea. The purposes of the present study were therefore to fill the knowledge gap regarding the occurrence of antibiotics in the marine and estuarine sediments and to identify the potential sources of the antibiotics in this area.

Surface sediment (0–10 cm depth) samples were collected using a stainless steel sediment sampler from 139 sites comprising 104 marine sites and 35 estuarine sites on one research cruise covering the whole Bohai Sea from August 11 to September 5, 2014 (Fig. 1). All the samples

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http://dx.doi.org/10.1016/j.marpolbul.2016.05.033
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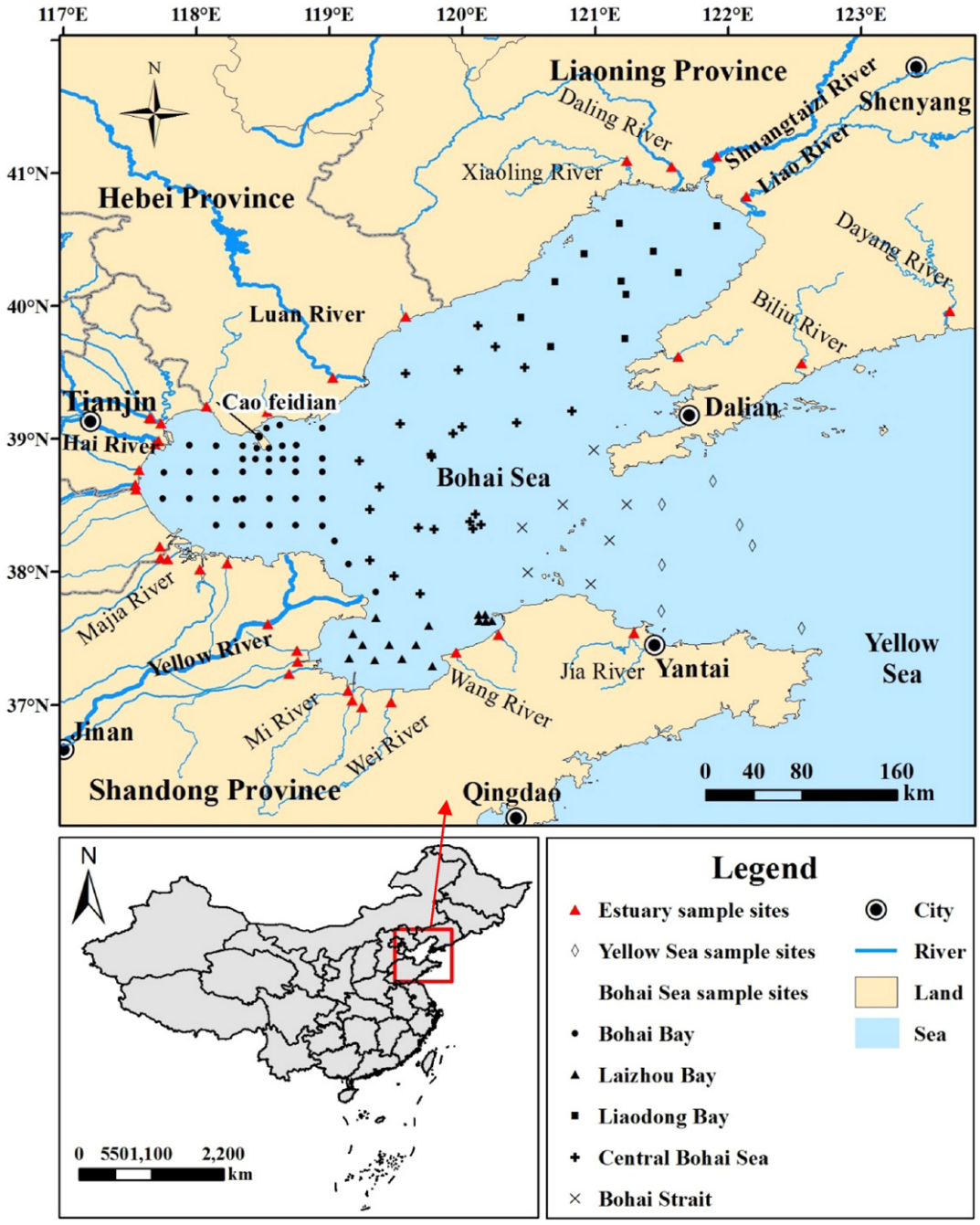

Fig. 1. Map of the Bohai Sea showing the surrounding estuaries and sampling sites.

were immediately transferred to clean plastic closure pockets, chilled to near freezing, transported to the laboratory, and stored at −20 °C in the dark. Before extraction, the samples were freeze-dried, large calcareous debris and rocks and plant fragments were removed, and the samples were ground with an agate mortar and homogenized by sieving through a 0.15-mm mesh.

Sample preparation and antibiotics analysis were based on previously developed methods (Huang et al., 2013). The 17 target veterinary antibiotics belong to four different classes of compound: (1) four tetracyclines comprising tetracycline (TC), oxytetracycline (OTC), chlortetracycline (CTC), and doxycycline (DOC); (2) eight sulfonamides comprising sulfadiazine (SDZ), sulfamethoxazole (SMX), sulfamethazine (SMZ), sulfamonomethoxine (SMM), sulfachinoxalin (SCX), sulfadimethoxine (SDM), sulfameter (SM), and sulfaclozine (SCZ); (3) the four fluoroquinolones norfloxacin (NFC), ofloxacin (OFC), ciprofloxacin (CFC), and enrofloxacin (EFC), and (4) the one macrolide roxithromycin (RTM). Four isotope-labelled antibiotics consisting of tetracycline-D6, enrofloxacin-D5, sulfamethazine-D4, and sulfadimethoxine-D6 and demeclocycline were selected as internal standards. All target compounds were simultaneously extracted with $Mg(NO_3)_2$-$NH_3 \cdot H_2O$ solution coupled with ethylenediaminetetraacetic acid-sodium perborate (EDTA-SPB) at 3:1 (v/v). The $Mg(NO_3)_2$-$NH_3 \cdot H_2O$ solution was prepared by mixing the 50% $Mg(NO_3)_2$ and 2.5% $NH_3 \cdot H_2O$ at 96:4 (v/v). The SPB solution was prepared by dissolving 10.56 g of NaH_2PO_4 and 0.82 mL of H_3PO_4 to 1 L with ultrapure water. The EDTA-SPB (pH 4) mixture was obtained by dissolving 80.0 g of Na_2EDTA to 1 L in SPB. The 2.5000 (±0.0005) g aliquots of sediment sample spiked with internal standards (100.0 μg kg^{-1}) were extracted ultrasonically three times using 20 mL extraction solvent for the first extraction and 10 mL for each of the remaining two. All the 40 mL extracts were purified and

concentrated through an oasis hydrophilic-lipophilic balance (HLB) cartridge. Methanol (10 mL, containing 0.1% formic acid) was used to elute the target compounds from the HLB cartridge. The target antibiotics were analyzed by liquid chromatography-electrospray ionization tandem mass spectrometry (LC-ESI-MS/MS) with a Shimadzu LC-20AD and triple quadrupole mass spectrometer (API 3200, AB Sciex, Framingham, MA). Separations were performed on a Kromasil C18 column (5 μm, 250 × 4.6 mm, Akzo Nobel, Sweden) at a constant temperature of 35 °C. The details of the gradient elution program and the optimized MS operating parameters of the antibiotics are described by Huang et al. (2013). Quantification was performed by internal standard calibration. The recoveries of the target compounds were checked by spiking with standards of 50.0, 100.0, and 200.0 μg kg^{-1} with three replicates (n = 3) of each. The mean recoveries and relative standard deviation of all the target antibiotics in the sediments ranged from 73.2% to 127.2% and 2.0% to 11.0% on average, respectively (Table 1). Method blanks showed no detectable amounts of the analytes. The calculations of the limit of detection (LOD), limit of quantification (LOQ), and method detection limit (MDL) are described by Zhang et al. (2015a). The LOD and LOQ ranged from 0.09 to 3.16 μg L^{-1} and 0.49 to 10.5 μg L^{-1}, respectively (Table 1). A total of 9 out of the 17 antibiotics were detected at least once in the sediment samples. None of the eight sulfonamides was detected at any of the sampling sites. In contrast, all four FQs were detected in the sediment samples (Table 2). OFC had the highest detection frequency both in marine and estuarine sediments among the four FQs, followed by NFC, EFC and CFC. However, the detection frequencies of the TCs were different between the marine and estuarine sediments. OTC and CTC were the only two detectable TCs in the marine sediments and both had a detection frequency of <10%. All four TCs were detected in the estuarine sediments and OTC had the highest detection frequency of 54.2%. RTM was detected only in the estuarine sediment as with TC and DOC. The concentrations of all the detectable antibiotics ranged from 0.2 to 4695 μg kg^{-1}. The average concentrations of the detectable antibiotics were higher in the estuarine sediments than in the marine sediments. The highest concentration of antibiotics (OTC) was detected in estuarine sediment from the Ziya New River. TCs had higher average and maximum concentrations than the other three types of antibiotic in general. Particularly, the concentration of DOC was high in all the detected samples although the detection frequency was much lower than that of most other antibiotics. The concentrations of the veterinary antibiotics in the estuarine sediments of the Bohai Sea are comparable to results reported from other study areas (Lalumera et al., 2004; Le and Munekage, 2004) as shown in Table 3. The average concentrations of OTC, TC and EFC were generally higher in the present study area than most other study areas. This implies a large impact of antibiotics consumption in the aquaculture industry in this area (Jia et al., 2011; Xu et al., 2007). In contrast, the average concentrations of CFC and RTM were lower than reported from other studies.

Table 2
Summary of the antibiotics concentrations and detection frequencies in the surface sediments of the Bohai Sea and surrounding estuaries (μg kg^{-1}).

	Marine sediments (n = 104)				Estuarine sediments (n = 35)			
	Mean	Min.	Max.	DF (%)	Mean	Min.	Max.	DF (%)
NFC	2.5	1.2	6.4	14.5	15.1	1.8	66.6	45.7
OFC	1.5	0.2	6.0	22.3	7.6	0.6	42.1	71.4
CFC	4.4	2.4	9.8	6.8	12.9	2.7	47.9	28.6
EFC	2.0	0.9	5.7	14.5	19.9	0.9	252.4	51.4
TC	–	–	–	0	25.3	1.9	126.1	11.4
OTC	9.4	1.6	48.4	9.7	268.8	2.2	4695	54.2
CTC	9.1	9.1	9.1	1.0	11.2	11.2	11.2	2.9
DOC	–	–	–	0	110.8	106.4	115.2	5.7
RTM	–	–	–	0	2.5	1.9	3.5	8.5

Note: Min., Max. and DF denote minimum concentration, maximum concentration and detectable frequency, respectively; n denotes sample numbers.

High spatial heterogeneity of the antibiotics was observed in both marine and estuarine sediments (Fig. 2). A relatively high detection frequency and concentration of FQs occurred in the sediments of Bohai Bay and Laizhou Bay and its surrounding estuaries. However, almost no antibiotics were detected in the marine sediments from Liaodong Bay, in contrast to the high antibiotic concentrations found in the surrounding estuaries. Sediment samples with high concentrations of EFC and CFC in Laizhou Bay were found adjacent to the estuaries of the Wanghe River and the Yellow River. This spatial distribution implies a contribution of terrestrial sources to the antibiotics contamination of the marine sediments. A similar spatial distribution was also found in Bohai Bay and the antibiotics sources were likely associated with the discharge of domestic and agricultural wastewaters (Jiang et al., 2011). A high impact of terrestrial sources was also found in the Bohai Strait and outside the Bohai Sea where higher antibiotics concentrations occurred close to the coastal land. In contrast, the sediments located in the central part of the Bohai Sea were generally characterized by lower concentrations of antibiotics. Similar spatial distributions of FQs have been observed in the surface water of the Bohai Sea (Jia et al., 2011; Zhang et al., 2012; Zou et al., 2011) and the Yellow Sea (Zhang et al., 2013).

All the antibiotics detected together with sediment properties (total organic carbon content (TOC), clay content (CLAY), C/N ratio (C:N)) and the pH and salt content of the marine water were incorporated into the principal component analysis (PCA). The TCs and FQs were separated

Table 1
Relative recoveries, limits of detection (LOD), limits of quantification (LOQ) and method detection limits (MDL) of the analysis of antibiotics in sediments.

Compound	Abbr.	Internal standard	Recovery %	LOD (μg L^{-1})	LOQ (μg L^{-1})	MDL (μg kg^{-1})
Tetracycline	TC	Tetracycline-D6	101.0 ± 6.1	0.52	1.74	2.1
Oxytetracycline	OTC	Tetracycline-D6	115.6 ± 11.0	0.44	1.48	5.3
Chlortetracycline	CTC	Tetracycline-D6	127.2 ± 9.0	2.29	7.62	4.2
Doxycycline	DOC	Tetracycline-D6	102.8 ± 4.0	3.16	10.5	8.5
Sulfadiazine	SDZ	Sulfamethazine-D4	103.7 ± 4.3	0.29	0.95	2.1
Sulfamethoxazole	SMX	Sulfamethazine-D4	115.4 ± 4.2	0.35	1.18	3.0
Sulfamethazine	SMZ	Sulfamethazine-D4	99.7 ± 4.3	0.77	2.58	2.8
Sulfamonomethoxine	SMM	Sulfamethazine-D4	113.3 ± 2.4	0.22	0.74	1.8
Sulfachinoxalin	SCX	Sulfadimethoxine-D6	90.7 ± 2.9	0.15	0.49	1.5
Sulfadimethoxine	SDM	Sulfadimethoxine-D6	101.9 ± 2.6	0.15	0.49	0.5
Sulfameter	SM	Sulfadimethoxine-D6	98.8 ± 2.0	0.22	0.74	1.4
Sulfaclozine	SCZ	Sulfadimethoxine-D6	103.5 ± 3.0	0.39	1.31	1.8
Norfloxacin	NFC	Enrofloxacin-D5	101.1 ± 9.7	0.41	1.38	4.2
Ofloxacin	OFC	Enrofloxacin-D5	73.2 ± 9.3	0.16	0.54	5.8
Ciprofloxacin	CFC	Enrofloxacin-D5	115.7 ± 9.3	0.73	2.42	14.1
Enrofloxacin	EFC	Enrofloxacin-D5	91.6 ± 5.7	0.26	0.87	7.9
Roxithromycin	RTM	Enrofloxacin-D5	76.2 ± 6.7	0.09	1.53	7.0

Table 3
Comparison of the antibiotics levels in the riverine sediments among the different study areas (μg kg^{-1}).

Study area	OTC	TC	NFC	OFC	CFC	EFC	RTM	Reference
Estuaries of the Bohai Sea, China[b]	268.8 (4695)	25.3 (126.1)	15.1 (66.6)	7.6 (42.1)	12.9 (47.9)	19.9 (252)	2.5 (3.5)	This study
Yellow River, China[b]	na (184)	na (18)	8.34 (141)	3.07 (123)	na (32.8)		na (6.8)	Zhou et al. (2011)
Haihe River, China[a]	2.52 (422)	2.0 (135)	32.0 (5770)	10.3 (653)	16.0 (1290)	1.6 (298)	2.29 (11.7)	Zhou et al. (2011)
Haihe River, China[c]	14.47	17.7			41.99		21.05	Xu et al. (2010)
Liaohe River, China[a]	2.34 (652)	na (4.82)	3.32 (176)	3.56 (50.5)	na (28.7)	na (5.82)	5.51 (29.6)	Zhou et al. (2011)
Pearl River, China[a]	7.15 (196)	4.0 (72.6)	88.0 (1120)	156 (1560)	21.8 (197)		nd	Yang et al. (2010)
Pearl River Estuary, China[c]		15.52	85.25	1.79	10.05	15.52		Liang et al. (2013)
Nanming River, China[c]	335	312						Liu et al. (2009)
Jiulongjiang River, China[b]	na (10,364)	na (7614)					na (5622)	Zhang et al. (2011)
Wangyang River, China[a]	604 (162,673)	40 (16,799)	29.8 (801.3)	23.2 (370.6)	13.1 (2118)	6.2 (82.1)		Jiang et al. (2014)
Oglio River, Italy[b]	56.28 (246.3)		0.6 (1.1)					Lalumera et al. (2004)
Ticino River, Switzerland[b]	0.69 (4.2)		30.16 (578.8)				37.7 (2581)	Lalumera et al. (2004)
Cache La Poudre River, USA[b]	56.28 (na)	17.9 (102)						Kim and Carlson (2007)
Cache La Poudre River, USA[a]	7.6 (56.1)	8.55 (102)					1.9 (5.9)	Pei et al. (2006)

nd: not detected, na: not available.
[a] Data presented are median concentrations (maximum concentrations), μg kg^{-1}.
[b] Data presented are mean concentrations (maximum concentrations), μg kg^{-1}.
[c] Data presented are mean concentrations, μg kg^{-1}.

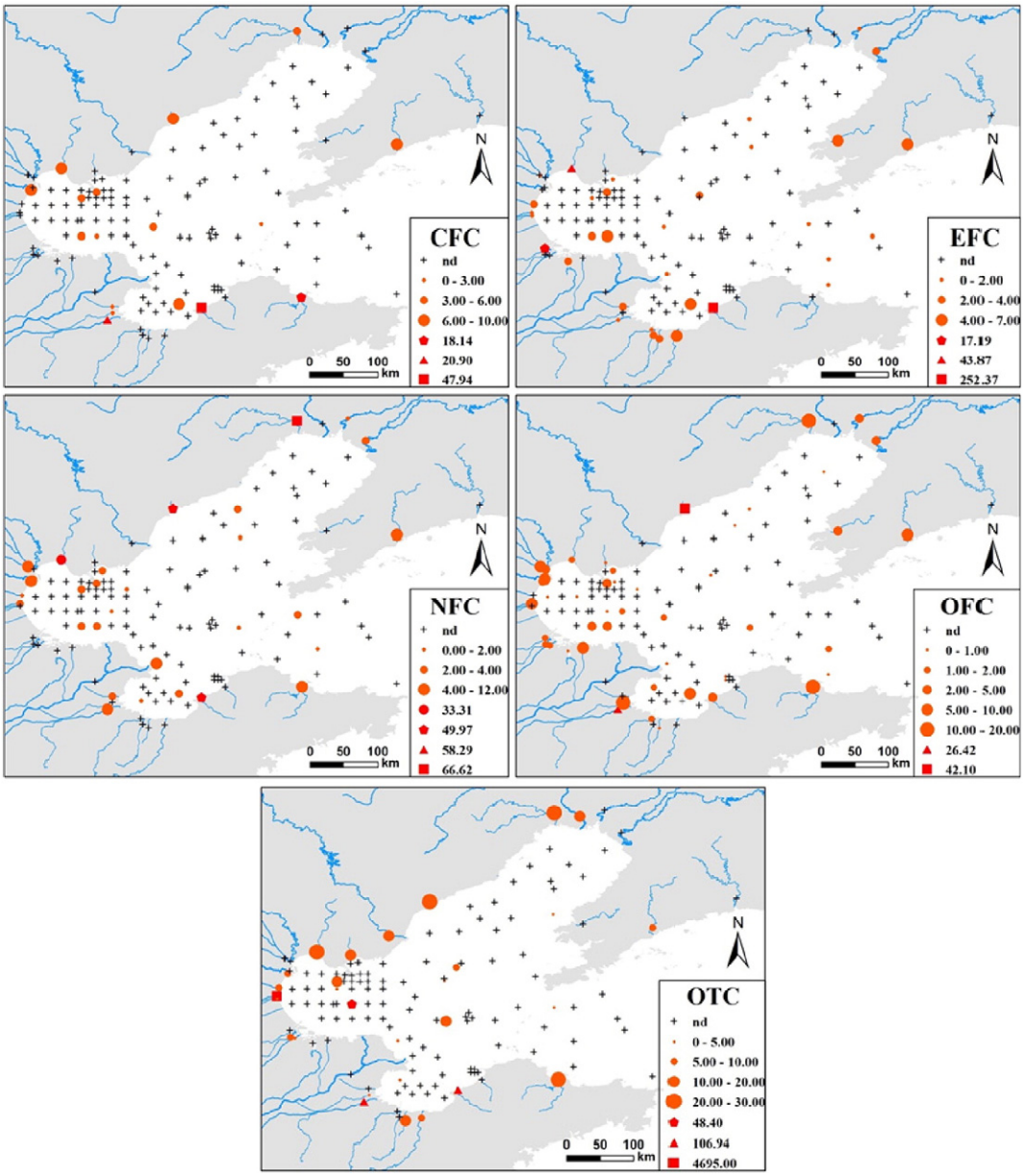

Fig. 2. Spatial distribution of the antibiotics detected in the sediments of the Bohai Sea and surrounding estuaries.

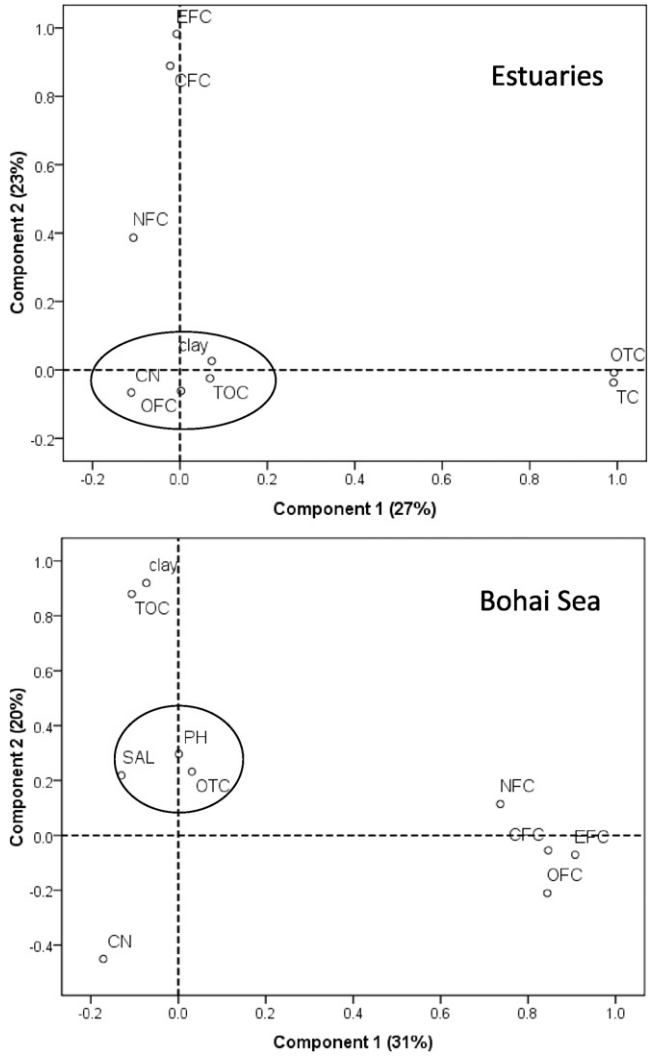

Fig. 3. Principal component analysis of the antibiotic concentrations and physicochemical properties of the sediments in the Bohai Sea and the surrounding estuaries (TOC: total organic carbon, SAL: salt content, CN: C/N ratio).

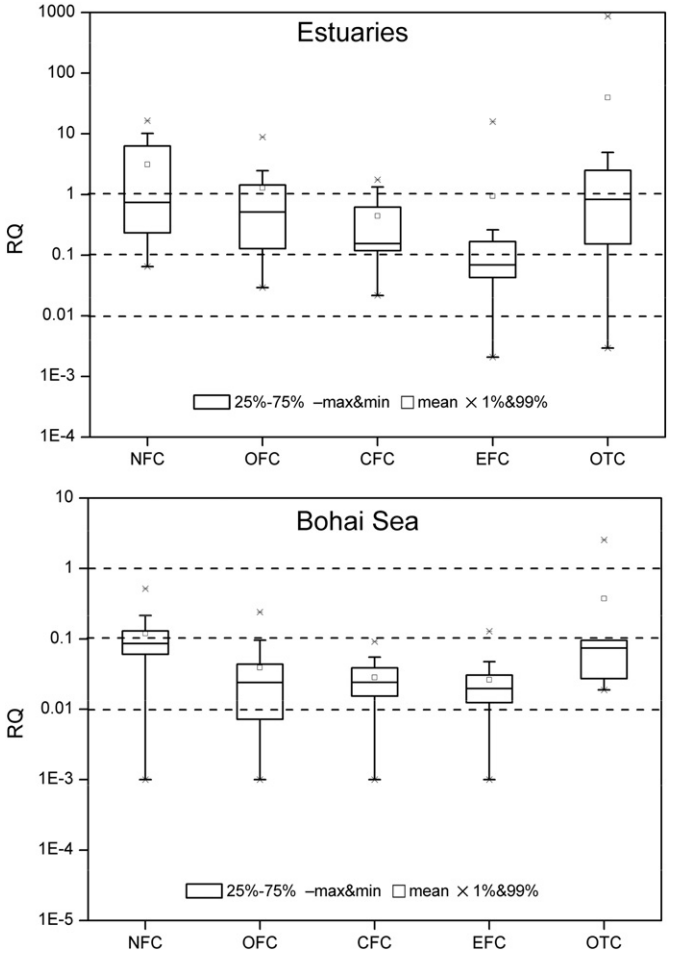

Fig. 4. Boxplots of the calculated risk quotients (RQs) of the antibiotics detected in the Bohai Sea and surrounding estuaries.

clearly on the score plots of both estuarine and marine sediments. Differences were observed in the groups of antibiotics in relation to sediment properties. In the case of estuarine sediments, OFC was grouped with TOC, and clay content with C/N ratio (Fig. 3), which implies effects of the sediment properties on the retention of OFC (Peng et al., 2015). In the case of the marine sediments, OTC was grouped with ocean water properties (pH and salt content) (Gothwal and Shashidhar, 2015) rather than sediment properties (Fig. 3).

The risk quotient (RQ) values were calculated using the following equation (Bodar et al., 2003):

$$RQ = MEC/PNEC \quad (1)$$

where MEC and PNEC denote the measured environmental concentration and predicted no-effect concentration, respectively. Most of the PNEC values are available for the antibiotics in water. The calculation was therefore performed by converting the measured antibiotics concentrations in the sediments into their corresponding pore water concentrations ($C_{pore\ water}$) using following equation (Zhao et al., 2010):

$$C_{pore\ water} = \frac{1000 \times C_S}{K_{OC}} \times \%\ \text{total organic carbon} \quad (2)$$

where K_{OC} is the organic carbon normalized partitioning coefficient and C_S ($\mu g\ kg^{-1}$) is the measured antibiotics concentrations in the sediment. The subsequent calculation of RQs in the sediments was as same as Eq. (1). The PNEC values were calculated based on the method recommended by the European Technical Guidance Document (TGD) in which PNEC was obtained from toxicity data of EC_{50} or LC_{50} divided by a fixed assessment factor (from 1000 to 10 depending on the ecotoxicological tests conducted) (Bodar et al., 2003). The aquatic toxicity data for the target antibiotics was obtained from the literature in order to calculate the PNEC (Boxall et al., 2004; Halling-Sørensen, 2000; Isidori et al., 2005; Kolar et al., 2014; Park and Choi, 2008; Robinson et al., 2005).

The risk was classified into three levels based on the RQ values, namely low risk at RQs ranging from 0.01 to 0.1, medium risk at RQs of 0.1–1 and high risk at RQs >1 (Hernando et al., 2006). The box plot of RQs indicates that the estuarine sediments presented a higher potential ecological antibiotics risk than the marine sediments in general (Fig. 4). Similar results have also been reported from surface waters of Laizhou Bay (Zhang et al., 2012), Germany (Kümmerer and Henninger, 2003), Wanghe River (Jiang et al., 2014), the Pearl River system (Yang et al., 2010) and Korea (Lee et al., 2008). Antibiotics such as NFC, OTC and OFC may show high risk to sensitive aquatic organisms (*Daphnia magna*) in some estuarine sediment samples and the highest RQ of OTC was 863.4, a high value which should be of great concern. In the case of marine sediments, NFC and OTC should be of concern mainly in the Bohai Sea because the average values of the RQs of NFC and OTC were at the medium and high risk levels, respectively.

Acknowledgements

This research was supported financially by the National Natural Science Foundation of China (41371313 and 41230858) and WPOS Project (no. XDA11020402).

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