Occurrence, source apportionment and risk assessment of antibiotics in water and sediment from the subtropical Beibu Gulf, South China

Qi Wu [a,b,c], Shao-Ke Xiao [a,b,c], Chang-Gui Pan [a,b,c,d,*], Chao Yin [a,b,c], Ying-Hui Wang [a,b,c,*], Ke-Fu Yu [a,b,c,d]

[a] Guangxi Laboratory on the Study of Coral Reefs in the South China Sea, Guangxi University, Nanning 530004, China
[b] Coral Reef Research Center of China, Guangxi University, Nanning 530004, China
[c] School of Marine Sciences, Guangxi University, Nanning 530004, China
[d] Southern Marine Science and Engineering Guangdong Laboratory (Zhuhai), Zhuhai, China

HIGHLIGHTS

- 19 and 17 antibiotics were detected in the seawater, sediment of the Beibu Gulf.
- $\sum$antibiotic levels were 1.74–23.83 ng/L for seawater and 1.33–8.55 ng/g for sediment.
- Livestock activities and aquaculture were major antibiotics sources in the Beibu Gulf.
- SMX, CIX may pose adverse ecotoxicological risks to algae.

GRAPHICAL ABSTRACT
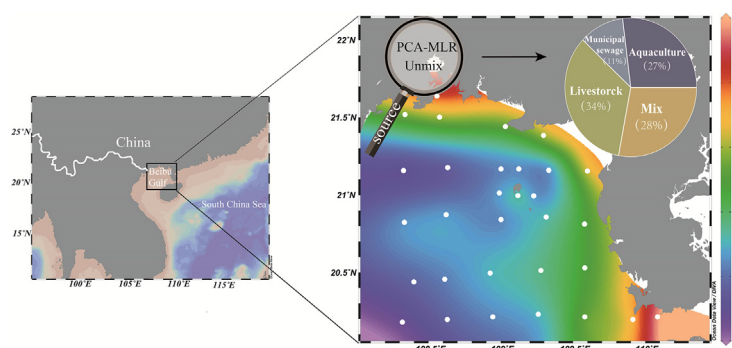
ARTICLE INFO

ABSTRACT

The widespread use of antibiotics has raised global concerns, but scarce information on antibiotics in the subtropical marine environment is available. In the present study, seawater and sediment samples were collected to investigate the occurrence, spatial distribution, source, and ecological risks of 22 antibiotics in the Beibu Gulf. The total concentrations of target antibiotics ($\sum$ antibiotics) were in the range of 1.74 ng/L to 23.83 ng/L for seawater and 1.33 ng/g to 8.55 ng/g dry weight (dw) for sediment. Spatially, a decreasing trend of antibiotic levels from coast to offshore area was observed, with relatively high levels at the sites close to the Qinzhou Bay and Qiongzhou Strait. Sulfamethoxazole (SMX), trimethoprim (TMP), and norfloxacin (NOX) were predominant in seawater, while NOX, enoxacin (ENX), and enrofloxacin (ENR) were the most abundant antibiotics in sediment. In general, the sediment-water partitioning coefficients (K_d) were positively correlated with log molecular weight (MW). Salinity, particle size, and pH of water were predicted to be vital factors influencing the partition of sulfadiazine (SDZ), CIX, and ENR ($p < 0.05$). Livestock and aquaculture were identified as dominant sources of antibiotics in the Beibu Gulf based on PCA-MLR and Unmix model. Risk assessment revealed that SMX, CIX could pose medium risks to algae in the Beibu Gulf. Overall, our results provided paramount insights into understanding the fate and transport behaviors of antibiotics in the subtropical marine environment.

© 2021 Elsevier B.V. All rights reserved.

1. Introduction

The advent of penicillin in 1928 began the era of antibiotics, which have been considered as one of the most significant milestones in science and medicine. During the last decades, hundreds of antibiotics

have been widely applied in disease prevention, disease treatment, and as prophylaxis and growth promoters in aquaculture and husbandry (Kummerer, 2009; Sarmah et al., 2006). The global antibiotic consumption increased by 65%, from 21.1 to 34.8 billion defined daily doses (DDDs) between 2000 and 2015 (Klein et al., 2018). In China, the total consumption of 36 commonly used antibiotics was up to 92,700 tons in 2013 (Zhang et al., 2015). Further, the consumption of veterinary antibiotics in China will be doubled by 2030 (Klein et al., 2018). It was reported that more than half of antibiotics had been released into various environmental matrices owing to their unreasonable use, incomplete metabolism, and limited wastewater treatment facilities (Carvalho and Santos, 2016). Antibiotics have been regarded as metastable pollutants and present a pseudo-persistent behavior, finally resulting in long-range transport (Klatte et al., 2016; Kummerer, 2009).

The ocean plays an vital role in the global transport of antibiotics and has been consequently served as a final sink and major reservoir for numerous pollutants (e.g., antibiotics) (Bayen et al., 2013; McEneff et al., 2014). Once entering into the (marine) environment, antibiotics might induce chronic effects on aquatic organisms (Brausch and Rand, 2011; Halling-Sorensen, 2000; Robinson et al., 2005). For example, antibiotics could decrease the plankton and algae population, affect the behavior of aquatic organisms, and alter the aquatic community structure (Kovalakova et al., 2020; Kummerer, 2009). Meanwhile, sulfamethoxazole (SMX) and enoxacin (ENX) can be biomagnified in marine organisms and may pose adverse effects on human health via food chain transfer (Lagesson et al., 2016; Liu et al., 2017). Also, antibiotics promote the rapid emergence and spread of resistant bacteria and genes, which have been confirmed as one of the three health threats by the World Health Organization (WHO, 2015). Therefore, it is imperative to understand the transport and fate of antibiotics in the marine environment.

Transportation and adsorption onto sediments are two crucial routes of antibiotics in the environment (Kummerer, 2009). Previous studies investigated the occurrence and distribution of antibiotics in seawater from different marine areas around the world, such as Bohai Bay (Liu et al., 2016), the Yellow Sea (Du et al., 2017), the East Sea of China (Li et al., 2020a), and South China Sea (Liu et al., 2020b; Zhang et al., 2018c), Cadiz Gulf of Spain (Biel-Maeso et al., 2018), San Francisco Bay of the United States (Nodler et al., 2014) and the southern Baltic Sea (Siedlewicz et al., 2018). However, most of these studies were conducted in estuaries and coastal waters close to highly urbanized or developed regions. Systematic knowledge on the transport behavior of antibiotics from nearshore area to offshore area in developing areas, particularly in the subtropical marine environment, is very limited (Celic et al., 2019; Kotke et al., 2019).

The partitioning of organic chemicals between sediment and seawater is very complicated (Huang et al., 2020; Moreno-González et al., 2015). It has been demonstrated that the partition of antibiotics can be affected by many factors, such as physicochemical properties (molecular structure of contaminant, octanol-water partition coefficient (K_{ow})), as well as environmental parameters (total organic content (TOC), particle size and pH) (Chen and Zhou, 2014; Saranjampour et al., 2017). Considering that antibiotics have different physicochemical properties, a comprehensive research is required to investigate the governing factors influencing their partitioning behaviors in the marine environment.

Source identification is the fundamental precondition for formulating strategies to prevent and control pollution. Until now, there are several literatures on source identification of antibiotics in the environment. However, most of them were based on the marker (Jia et al., 2011), ratio method (Zhang et al., 2018c), and principal component analysis (PCA) (Ali et al., 2017; Somma et al., 2021). The multivariate receptor models, including PCA with multiple linear regression (PCA-MLR) and Unmix, have been extensively used to trace the origins and source contributions of anthropogenic contaminants in the environment (Li et al., 2020b; Sofowote et al., 2008). PCA-MLR is the most used and traditional source receptor model by reducing the data

dimensionality (Cui et al., 2019; Zhang et al., 2020), while Unmix is a comparatively advanced receptor model based on the singular value decomposition (SVD) method (Larsen and Baker, 2003; Li et al., 2020b). In general, each model has its pros and cons and the conclusions drawn by different models could be inconsistent (Lang et al., 2015; Zhang et al., 2019). To obtain more reliable source contributions and interpretations, the source results generated by multiple receptor models should be compared and evaluated.

The primary objectives of the present study were to: (1) investigate the distribution and partitioning behavior of antibiotics between water and sediment in the Beibu Gulf. (2) identify the potential source of antibiotics by combing different source receptor models. (3) characterize the ecological risks of antibiotics in the Beibu Gulf. This is the first comprehensive field monitoring study of antibiotics covering approximately 27,000 km^2 of the Beibu Gulf and represents the first attempt to quantify the source contributions of antibiotics by various models.

2. Materials and methods

2.1. Study area and sampling campaign

Beibu Gulf (17–22°N, 105–110°E), a marginal sea, is located in the northern South China Sea (SCS). Since the establishment of the Beibu Gulf Economic Rim in 2006 and the launch of China-ASEAN Free Trade Area in 2010, the accelerating industrialization and increasing population have brought more and more pressure on the environmental quality of this area (Cui et al., 2019; Pan et al., 2021; Xiao et al., 2021). Further, the excellent geographical position makes Beibu Gulf an ideal area for the breeding industry. In 2017, the total farmed seafood production in this region was 1.3 million tons (Xue et al., 2020), which would inevitably result in contamination of antibiotics. Previous studies indicated that several antibiotics were detected in water, sediment, and organism from estuaries, nearshore and the vicinity of an aquaculture farm in the Beibu Gulf (Wu et al., 2021; Zhang et al., 2021). For example, Zhang et al. (2018b) found that the total concentrations of antibiotics in nearshore seawater were in the range of 22.70–24.50 ng/L. Leng et al. (2020) reported that the concentrations of antibiotics ranged from 51.04 to 137.64 ng/g in the coastal sediment of the Beibu Gulf.

Thirty-one seawater and twenty-six sediment samples were collected within the Beibu Gulf in April 2019 (Fig. 1). Seawater samples (depth = 3 m) were collected using a water sampler, which was pre-rinsed with ultra-pure water and water from the specific sampling site. Sediment samples were collected using a stainless-steel grab sampler and packed in polyethylene (PE) bags. Detailed information on sampling sites is listed in Table S1.

2.2. Chemicals and reagents

Based on usage volume and their detection rates in the environment, 22 antibiotics, including 9 sulfonamides (SAs), 5 fluoroquinolones (FQs), 4 macrolides (MLs), 2 chloramphenicols (CAPs), trimethoprim and lincomycin were selected as target compounds. Meanwhile, seven deuterium-labeled antibiotics were used as internal standards. HPLC grade methanol and acetonitrile were obtained from Merck (Darmstadt, Germany). Formic acid and ammonium acetate were supplied by CNW (Germany). Disodium edetate dihydrate (Na$_2$EDTA) was acquired from J&K® (Beijing, China). The detailed information on antibiotics, reagents, and solvents is described in Text S1 and Table S2.

2.3. Sample extraction and instrumental analysis

The extraction protocols of antibiotics from water and sediment samples were based on our previously published paper (Wu et al.,
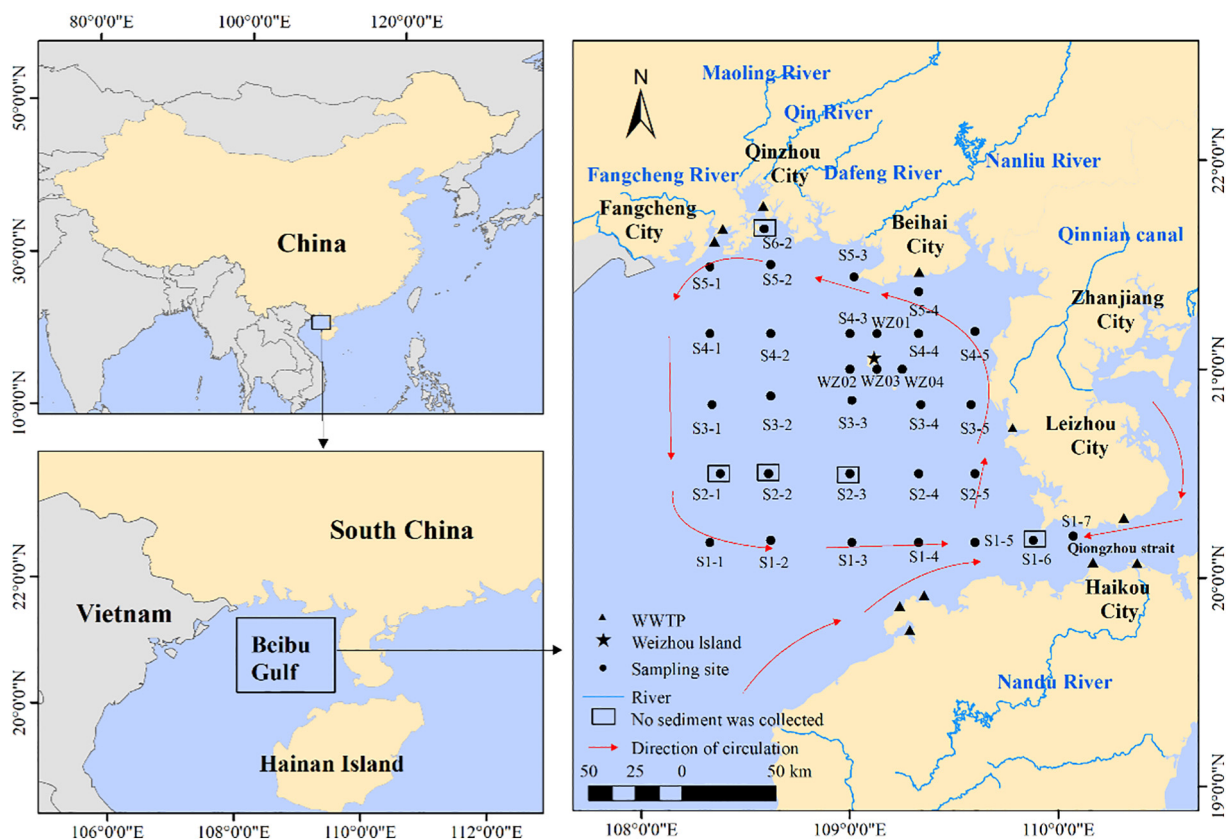
Fig. 1. Map showing the sampling sites in the Beibu Gulf, South China.

2021). Briefly, for water samples, 2.5 L of seawater was filtered using GF/F glass filters (Whatman) and pH was adjusted to 3 with 4 M H_2SO_4. 10 ng of internal standards and 0.2 g Na_2EDTA were added into individual samples, then the aqueous phase were loaded on HLB cartridges (6 mL, 500 mg). For sediment samples, 5 g of freeze-dried sediment was added with a mixture of acetonitrile and citric acid buffer of pH 3.0 (V:V = 1:1), then ultrasonicated for 15 min and centrifuged for 10 min. The extraction process was repeated twice. All the supernatant was combined, followed by purification with SAX-HLB cartridges in tandem (Details in Text S2).

Antibiotics were quantified by an Agilent 1290 ultra-performance liquid chromatography interfaced with a 6460 triple quadrupole mass spectrometer (UPLC-MS/MS, Agilent Technologies, Santa Clara, CA). The optimized instrumental parameters are provided in Text S3 and Tables S3, S4.

2.4. Quality assurance and quality control (QA/QC)

Sampling and experimental procedures were subject to strict QA/QC procedures. All glass containers were rinsed with Milli-Q water and methanol, then baked at 450 °C for 4 h in a muffle furnace. Quantification of antibiotics was conducted using an internal standard curve approach, with correlation coefficients of individual antibiotics greater than 0.995. Procedural blanks were included in each batch of ten samples to check the possible interference or background contamination. All the target antibiotics were not detected in the procedural blanks. The recoveries of target antibiotics ranged from 64 to 137% for water and 61–142% for sediments with relative standard deviations (RSD) lower than 20%. Limits of detection (LOD) and limits of quantification (LOQ) were assigned 3 and 10 of the signal-to-noise ratio (S/N) with the results being listed in Table S5.

2.5. Sediment-water distribution coefficient (K_d) and organic carbon partition coefficient (K_{oc}) calculation

Field-based partition coefficients of antibiotics between sediment and water were calculated by the following equation (Kim and Carlson, 2007):

$$K_d = C_s/C_w \times 1000$$

where C_s refers to the concentration of individual antibiotics (ng/g dw) in sediment, while C_w is the concentration in seawater (ng/L) at the same site.

Additionally, K_{oc} of antibiotic was derived from the K_d value using the following equation (Horsing et al., 2011):

$$K_{oc} = K_d \times 100/f_{oc}$$

where f_{oc} represents the percentage of organic carbon in the sediment (%) (Table S1).

2.6. Ecological risk assessment

The potential ecological risks associated with target antibiotics were evaluated by risk quotients (RQs), which were estimated using the following equation:

$$RQ = MEC/PNEC$$

$$PNEC = (LC_{50} \text{ or } EC_{50})/AF$$

where MEC and PNEC represent the measured environmental concentration and predicted no-effect concentration of individual antibiotics, respectively. EC_{50} or LC_{50} refers to the acute toxicity data from

previous literature or ECOSAR (Table S6). AF represents the assessment factor with 100 for chronic toxicity and 1000 for acute toxicity. The RQ values are classified into the following levels: insignificant risk (< 0.01), low risk (0.01–0.1), and medium risk (0.1–1), as well as high risk (> 1) (Rodriguez-Mozaz et al., 2020).

The classical concentration addition (CA) model was used to assess the mixture effect of detected antibiotics. The risk quotients of the mixtures (MRQ) were calculated by two methods, according to the equation as follows (Backhaus and Faust, 2012):

$$MRQ_{MEC/PNEC} = \Sigma_{i=1}^{n} \frac{MEC_i}{PNEC_i}$$
$$= \Sigma_{i=1}^{n} \frac{MEC_i}{\min{(EC_{50\,algae}, EC_{50\,invertebrate}, EC_{50\,fish})_i \times (1/AF)}}$$

$$MRQ_{STU} = \max{(STU_{algae}, STU_{invertebrate}, STU_{fish})} \times AF$$
$$= \max{\left(\Sigma_{i=1}^{n} \frac{MEC_i}{EC_{50i\,algae}}, \Sigma_{i=1}^{n} \frac{MEC_i}{EC_{50i\,invertebrate}}, \Sigma_{i=1}^{n} \frac{MEC_i}{EC_{50i\,fish}}\right)} \times AF$$

where $MRQ_{MEC/PNEC}$ is the sum of the highest RQs in three different trophic level organisms (algae, invertebrates, and fish), and MRQ_{STU} represents the sum of the toxic unit value for the most sensitive organism.

2.7. Data processing and statistical analysis

Levels of individual antibiotics below their corresponding LOD were reported as zero, concentrations between LOD and LOQ were treated as LOQ/2. Shapiro-Wilk test and Levene's test were used to evaluate the normality and homogeneity of data, respectively. Spearman's test was utilized to analyze the bivariate relations between antibiotics (detection frequencies (DF) > 30%) and environmental parameters. Also, multiple regression analysis was performed to explore the relationship between K_d of antibiotics and different environmental factors. All descriptive statistics were carried out in SPSS 24.0, while PCA-MLR and hierarchical cluster analysis (HCA) were performed by Origin 2018. To prevent high-

concentration variables from decomposition analysis, Z-transform was performed to center and scale the data before conducting PCA and HCA. The significance level was defined as $p \leq 0.05$.

3. Results and discussion

3.1. Occurrence and distribution of antibiotics in seawater from the Beibu Gulf

19 out of the 22 target antibiotics except sulfapyridine (SPD), sulfapyridine (SMR) and azithromycin (ATM) were detected in surface seawater. Trimethoprim (TMP), SMX, and norfloxacin (NOX) were quantified in all the seawater samples, and the detection frequencies (DF) of dehydrated erythromycin (ETM-H$_2$O), ENX, sulfamethazine (SMZ), enrofloxacin (ENR), florfenicol (FF), ciprofloxacin (CIX), sulfadimethoxine (SDM), sulfadiazine (SDZ) were 97%, 94%, 90%, 87%, 77%, 71%, 68%, and 65%, respectively (Table 1). These results demonstrated the widespread occurrence of the target antibiotics in the Beibu Gulf. The total concentrations of all detected antibiotics ($\sum_{19}$ antibiotics) varied from 1.74 ng/L to 23.83 ng/L, with the mean and median values of 9.51 and 7.53 ng/L, respectively (Fig. 2). The distribution pattern of the $\sum_{19}$ antibiotics was characterized by high concentrations in the nearshore area and decreasing gradually toward the offshore area (Fig. 3). On average, SAs (0.36–9.23 ng/L) and FQs (1.27–13.41 ng/L) occupied nearly 40% and 45% of the total antibiotics, which was consistent with those reported in the coastal area of the Yellow Sea, the Bohai Sea (Yang et al., 2020) and Pearl River Delta (Li et al., 2018). In general, the levels of different categories of antibiotics (SAs, MLs, and FQs) displayed great variations from different sampling sites (Fig. S1). For instance, the relatively high concentrations of SAs and FQs were found around the Qinzhou Bay at the northern Beibu Gulf (sampling sites of 6–2 and 5–2). Qinzhou Bay, China's largest oyster seedling base, has been gradually contaminated by antibiotics due to the growth of coastal aquaculture year by year (Cui et al., 2019; Meng et al., 2017). It has been illustrated that riverine inputs had an important impact on the occurrence of antibiotics in estuaries and bays (Liu et al., 2020a; Zou et al., 2011). For instance, our previous study found that the

Table 1
Detection frequencies (DF, %) and concentrations of 22 antibiotics in water (ng/L) and sediment (ng/g dw) from the Beibu Gulf.

Compounds	Water				Sediment			
	DF	Mean	Median	Range	DF	Mean	Median	Range
Sulfonamides								
SAAM	23	0.04	< LOD	< LOD-0.36	0	< LOD	< LOD	< LOD
SPD	0	< LOD	< LOD	< LOD	24	0.01	< LOD	< LOD-0.14
SMR	0	< LOD	< LOD	< LOD	24	0.08	< LOD	< LOD-0.35
STZ	19	0.01	< LOD	< LOD-0.10	0	< LOD	< LOD	< LOD
SDZ	65	0.10	0.03	< LOD-0.87	72	0.05	0.06	< LOD-0.09
SMZ	90	0.13	0.09	< LOD -0.56	0	< LOD	< LOD	< LOD
SMM	16	0.06	< LOD	< LOD-0.53	0	< LOD	< LOD	< LOD
SMX	100	2.98	2.43	0.090–7.43	28	0.01	< LOD	< LOD-0.02
SDM	68	0.08	0.07	< LOD-0.24	28	0.01	< LOD	< LOD-0.09
TMP	100	0.46	0.39	0.023–1.13	88	0.01	0.01	< LOD-0.02
Macrolides								
ETM-H$_2$O	97	0.68	0.42	< LOD-3.43	8	0.03	< LOD	< LOD-0.57
ATM	0	< LOD	< LOD	< LOD	16	0.03	0.01	< LOD-0.11
CTM	13	0.02	< LOD	< LOD-0.27	48	0.02	0.01	< LOD-0.07
RTM	6	0.02	< LOD	< LOD-0.58	48	0.01	< LOD	< LOD-0.10
Fluoroquinolones								
ENR	87	0.25	0.19	< LOD-1.10	88	0.49	0.46	< LOD-1.11
CIX	71	0.57	0.46	< LOD-2.76	28	0.11	< LOD	< LOD-0.78
OFX	58	0.07	0.02	< LOD-0.46	12	0.02	< LOD	< LOD-0.40
NOX	100	2.10	1.83	0.43–6.17	96	2.02	1.90	< LOD-4.06
ENX	94	1.24	0.85	< LOD -2.95	92	1.15	1.08	< LOD -2.76
Others								
FF	77	0.42	0.26	< LOD-2.40	12	0.01	< LOD	< LOD-0.10
CAP	48	0.08	< LOD	< LOD-0.24	0	0.01	< LOD	< LOD-0.04
LIN	38	0.18	< LOD	< LOD-0.76	30	0.05	< LOD	< LOD
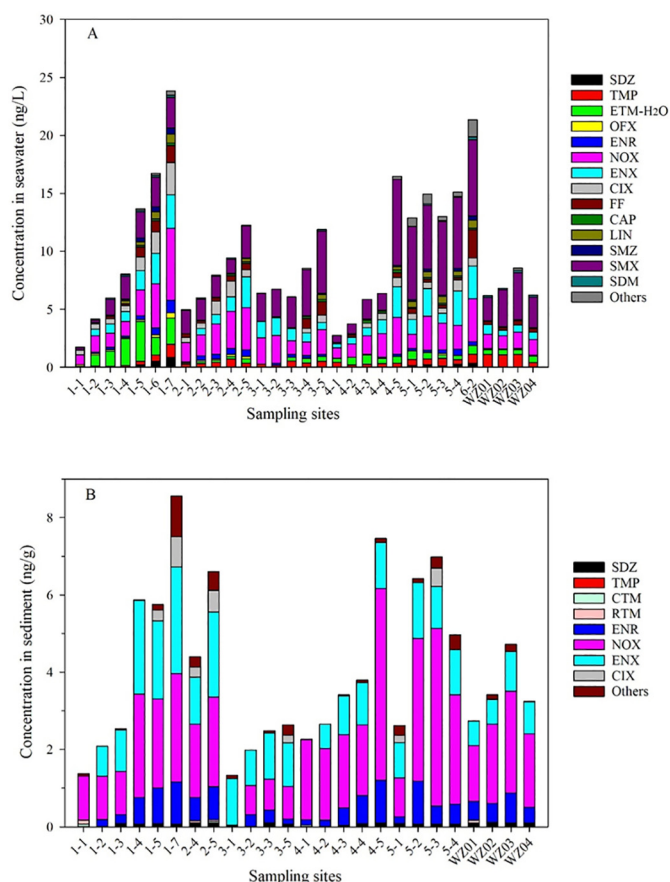
Fig. 2. Concentrations of individual antibiotics in surface seawater (A) and sediment (B) from the Beibu Gulf. Note: others included remaining antibiotics.

mean concentration of SAs in the Qin River (flow into the Qinzhou Bay) was up to 10 ng/L (Xue et al., 2013).

Regarding individual antibiotics, the highest mean concentration was observed for SMX (2.98 ng/L), and decreased in the following order: NOX (2.10 ng/L) > ENX (1.24 ng/L) > ETM-H$_2$O (0.68 ng/L) > CIX (0.57 ng/L) > TMP (0.47 ng/L) > FF (0.42 ng/L). SMX (0.09–7.43 ng/L) was the predominant antibiotic with an average contribution of 31%, probably because SMX is frequently used in the therapy of infections (e.g., *Enterococcus*, *Lactococcus*, and *Staphylococcus* diseases) in human and animals (Borecka et al., 2015; Shimizu et al., 2013). Moreover, previous studies also demonstrated that SMX had high water solubility and fast mobility, which may cause their extensive presence in the water of the Beibu Gulf (Shimizu et al., 2013; Stewart et al., 2014). The concentrations of SMX in the studied region were comparable to those reported in the surface water of Singapore mangrove (0.06–6.26 ng/L) (Bayen et al., 2016), Yangtze Estuary (1.00–8.40 ng/L) (Guo et al., 2019) and Pearl River Delta (nd-4.50 ng/L) (Fisch et al., 2021), but lower than those found from Victoria Harbour of Hong Kong (mean value of 13 ng/L) (Minh et al., 2009) (Table S7). NOX (0.43–6.17 ng/L), ENX (<LOD-2.95 ng/L) and ETM-H$_2$O (<LOD-3.43 ng/L) were other dominant antibiotics, which accounted for 22.1%, 13.0%, 7.2% of the total antibiotics, respectively. It was reported that NOX was one of the main antibiotics used in the mariculture ponds of the Beibu Gulf (Zhang et al., 2021), although it has been forbidden as a veterinary drug in China since 2015 (Ministry of Agriculture the PRC, 2015).

Results demonstrated that the distance from the sampling sites to the coastline was negatively correlated with the log $\sum_{19}$ antibiotics in seawater ($p < 0.01$; Fig. S2), revealing that the dilution effect of seawater can play a non-negligible role. Similarly, a significant

relationship was observed between salinity and the levels of log $\sum_{19}$ antibiotics in water ($p < 0.01$), which was consistent with the result observed in the Gulf of Cadiz (SW Spain) and Long Island Sound (NY, USA) (Biel-Maeso et al., 2018; Xie et al., 2019). The inverse correlation may be caused by the dilution of antibiotics in marine waters and/or riverine inputs (Siedlewicz et al., 2016). pH in water was also negatively correlated with the concentrations of SDZ, SDM, ETM-H$_2$O, OFX, and MLs (Fig. S3), which was consistent with the relationships reported in Jiaozhou Bay and the East China Sea of China (Li et al., 2020a; Xie et al., 2019).

3.2. Occurrence and distribution of antibiotics in sediment from the Beibu Gulf

Seventeen antibiotics were detected in sediment, with NOX, ENR, TMP, and ENX showing detection frequencies greater than 80% (Table 1). However, none of the antibiotics analyzed were detected in all the sediment samples. The total concentrations of these antibiotics ($\sum_{17}$ antibiotics) ranged from 1.33 ng/g dw to 8.55 ng/g dw with a mean value of 4.01 ng/g dw. Not surprisingly, levels of $\sum_{17}$ antibiotics from the offshore area were generally lower than the coast, and the similar spatial distributions were observed in the Yellow Sea (Du et al., 2017), the Pearl River Estuary of China (Fisch et al., 2021), and Cadiz Gulf in the Spain (Biel-Maeso et al., 2018). FQ was the most abundant antibiotic with a contribution more than 90% of the total antibiotics, which was in line with numerous previous surveys reported in the Yangtze Estuary (Guo et al., 2019) and Persian Gulf (Kafaei et al., 2018). It was found that FQ had a high capacity to chelate with cations and bind with particulate matter (Cheng et al., 2014; Liang et al., 2013). The concentrations of $\sum$FQs were in the range of 1.14–7.83 ng/g dw with a mean value of 3.78 ng/g dw, which was parallel to the levels observed in the Jiaozhou Bay (0.28 to 5.23 ng/g) and the East China Sea of China (mean, 7.3 ng/g) (Li et al., 2020a; Liu et al., 2018). On the contrary, much lower values were reported in Bohai Bay (<LOQ-24.30 ng/g) (Cheng et al., 2014). In general, the levels of $\sum$SAs were lower than 0.20 ng/g dw in most sampling sites. The contributions of SAs and FQs in the water phase were around 40% and 45%, respectively. However, their contributions were approximately 5% and 90% in sediment, which could be related to the relatively weak interaction of SAs with the binding sites of sediments (Liu et al., 2016).

NOX exhibited relatively high average concentrations of 2.02 ng/g dw, followed by ENX (1.15 ng/g dw), ENR (0.49 ng/g dw), CIX (0.11 ng/g dw), sulfamerazine (SMR) (0.08 ng/g dw). NOX was the predominant antibiotic, which contributed nearly 50% to the total antibiotic burden. However, the overall concentrations of NOX (<LOD-4.96 ng/g, dw) in the present study were lower than the values reported in the Bohai Sea (<LOD-20.86 ng/g) (Cheng et al., 2014), East China Sea (<LOD-32.16 ng/g) (Li et al., 2020a) and the Persian Gulf, Iran (mean, 24.98 ng/g) (Kafaei et al., 2018) (Table S8).

There was a significantly positive correlation between SDZ concentrations and TOC of sediment (Fig. S2). A previous research found that organic matter would enhance the cation-exchange capacity, which contributed to react with antibiotics on charged sites (Richter et al., 2009). Zhou et al. (2011) found relatively high antibiotic concentrations at the sampling sites with high TOC content.

3.3. Partitioning of antibiotics between water and sediment in the Beibu Gulf

Based on available data, the average K_d and K_{oc} values for 7 antibiotics (SDZ, SMX, TMP, ENR, CIX, NOX, and ENX) were calculated and the values ranged from 3 to 2818 L/kg and 4 to 8089 L/kg, respectively (Tables S2, S9). The K_d values were highly variable with 3–2622 L/kg for SAs and 192–2818 L/kg for FQs. FQs presented higher K_d values, which could be explained by the ionic functional group in the molecules of FQs and their strong hydrophobicity (Tang et al., 2019). Generally, the K_d values for SDZ, SMX, NOX, ENR, and TMP
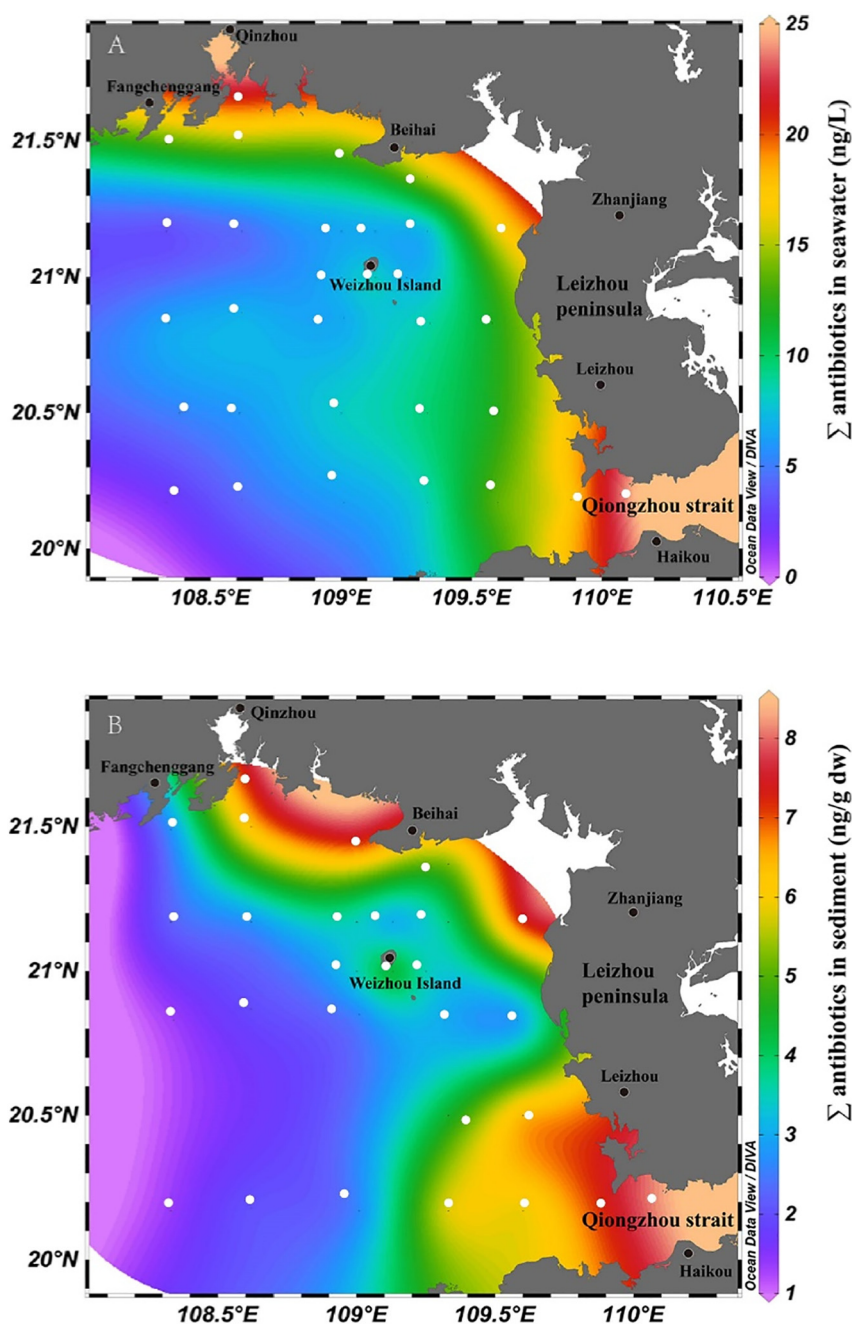
Fig. 3. The concentration and distribution of total antibiotics in seawater (A) and sediment (B) in the Beibu Gulf, China.

were comparable to those determined from Bohai Bay (Cheng et al., 2014), Hailing Bay (Chen et al., 2015), and the southern Baltic (Siedlewicz et al., 2018), while K_d values of CIX were lower than the values reported in the Hailing Bay and Yellow River Delta (Table S9) (Chen et al., 2015; Zhao et al., 2016).

A significantly positive correlation was observed between log K_d values and log molecular weight (MW) ($p < 0.05$, Fig. S4), which indicated that the heavy and large molecules of antibiotics were more easily absorbed onto sediment (Chen and Zhou, 2014). There was no significant correlation between Log K_d and log K_{ow} of the target antibiotics ($p > 0.05$, Fig. S4), suggesting that hydrophobic interaction maybe not the main factor controlling the partition between water and sediment. Multiple regression analysis showed a negative correlation

between salinity and the log K_d values of SDZ, CIX, and ENR ($p < 0.05$, Table S10). The significant negative correlation between K_d values of SDZ and the Dv$_{50}$ values (median size of the particle) demonstrated that SDZ tended to be adsorbed more easily by fine sediments. These results illustrated the partition of antibiotics between seawater-sediment is very complicated and the exact dynamic mechanisms require further investigation.

3.4. Potential sources of antibiotics in the Beibu Gulf

PCA-MLR, HCA, and Unmix models were utilized to identify the potential sources of antibiotics and their specific contributions in the Beibu Gulf. The principal component 1, 2, and 3 of the PCA explained 33%, 28%, and

Fig. 4. Score plot and loading plot for antibiotics in water from the Beibu Gulf (A). Source profiles and contribution of antibiotics predicted by Unmix model (B). The percentage contributions of different sources in each sample estimated by Unmix model (C).
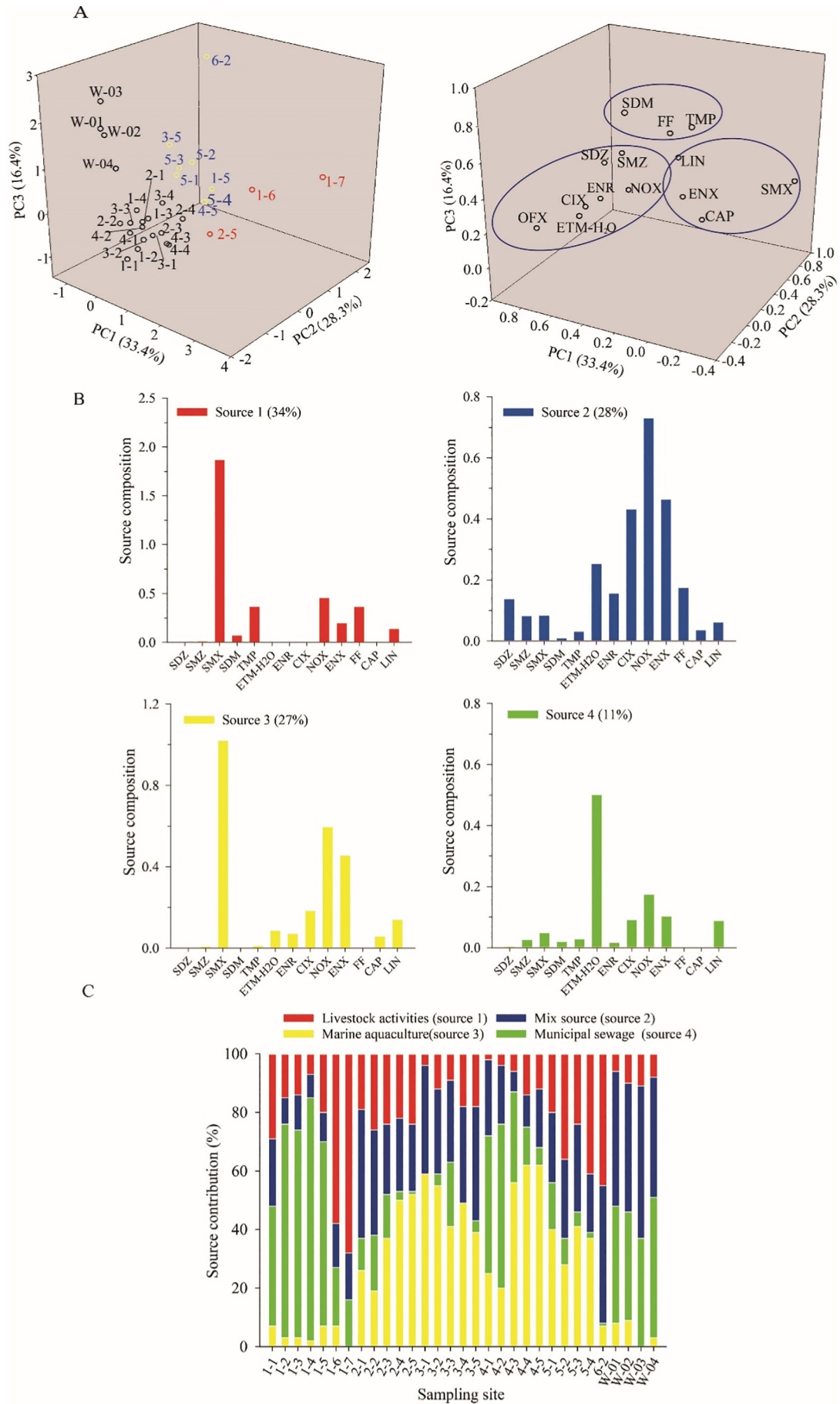
16% of the total variance, respectively (Fig. 4A). As shown in Table S11, factor 1 was dominated by SMX, CAP, ENX, LIN, NOX, accounting for 50% of the total variation. SMX is a typical antibiotic used for both humans and animals, but more than 90% was widely applied to animals (Zheng et al., 2012; Zhou et al., 2013). A previous study demonstrated that CAP and LIN were frequently added in animal feed to prevent and treat diseases in livestock and aquaculture (Zhou et al., 2013). Also, QN concentration in the coastal water was positively correlated with the production of marine aquaculture and animal husbandry (Lyu et al., 2020). Hence, factor 1 was considered to represent the source from marine aquaculture and livestock industries. Factor 2 was heavily weighted by OFX, CIX, ETM-H$_2$O, and SDZ, which accounted for 26% of the total source contribution. These antibiotics have been frequently detected in wastewater treatment plants (Behera et al., 2011; Xu et al., 2015). Besides, ETM-H$_2$O and OFX were reported to be too recalcitrant to remove in conventional sewage treatments with removal rates lower than 20% (Behera et al., 2011; Leung et al., 2012; Xu et al., 2007). Lyu et al. (2020) found that significantly positive correlations were observed between the levels of MLs (ETM-H$_2$O, clarithromycin (CTM), roxithromycin (RTM)) and human healthcare costs or the number of the antibiotic production plants. Therefore, factor 2 can be used as chemical marker for wastewater, including domestic and industrial sewage. SDM, TMP, and FF were grouped together (group 3) and occupied 24% of the total contribution. SDM and FF are veterinary antimicrobial drugs with high detection rates and concentrations in the wastewater from pig farms and culture ponds (Zhang et al., 2018a; Zhang et al., 2018b; Zhou et al., 2013), while TMP was generally regarded as a potentiator of sulfonamide and extensively applied to human and animal (Zhang et al., 2015; Zhang et al., 2018b). Thus, factor 3 was considered to be the mixed source of domestic sewage and aquaculture wastewater.

All seawater sampling sites were distinctly divided into three groups (Fig. 4A, Fig. S5). In the first group, three sampling sites (sampling sites of 1–7, 1–6, and 2–5) located at the southeast of the Beibu Gulf were clustered together, in which almost all target antibiotics were detected. Sampling sites of 5–1, 5–2, 5–3, 5–4, 4–5, 3–5, and 6–2 were grouped together. Most of these sampling points were located at the northern Beibu Gulf with more proportions of SMX, NOX, and FF. The remaining sampling sites were almost located in the offshore area, which constituted the third group. The total concentrations of antibiotics at these sites were much lower than those quantified at other nearshore sampling sites.

Unmix model was further used to explore the specific contributions and four sources were extracted (Fig. 4B). SMX, FF, and SDM were the dominating components of source 1. It was reported that these antibiotics were commonly used in animal husbandry, including the chicken, cow, swine, and duck industries (Zhang et al., 2021; Zhou et al., 2013). Thus, source 1 was interpreted as stock farming, which accounted for 34% of the variance. Source 2 occupied 28% of the total variance and included almost all target antibiotics derived from a mixed source. Source 3 had high loading of SMX, NOX, ENX, and CIX, explaining 27% of the total variance. A previous research reported that these antibiotics were found widespread in the aquaculture of the Beibu Gulf (Zheng et al., 2012). Hence, source 3 was considered from aquaculture. Source 4 was characterized by the high percentage of ETM-H$_2$O and accounted for 11% of the source contribution, which was in line with the factor 1 of PCA-MLR and was regarded as wastewater emissions.

Fig. 4C illustrated the source contributions of antibiotics in each sample predicted by Unmix model. The result revealed that municipal wastewater (source 1) was recognized as the main source of antibiotics at the sampling sites of 1–1, 1–2, 1–3, 1–4, and 1–5. There are several wastewater treatment plants located on the eastern part of Hainan
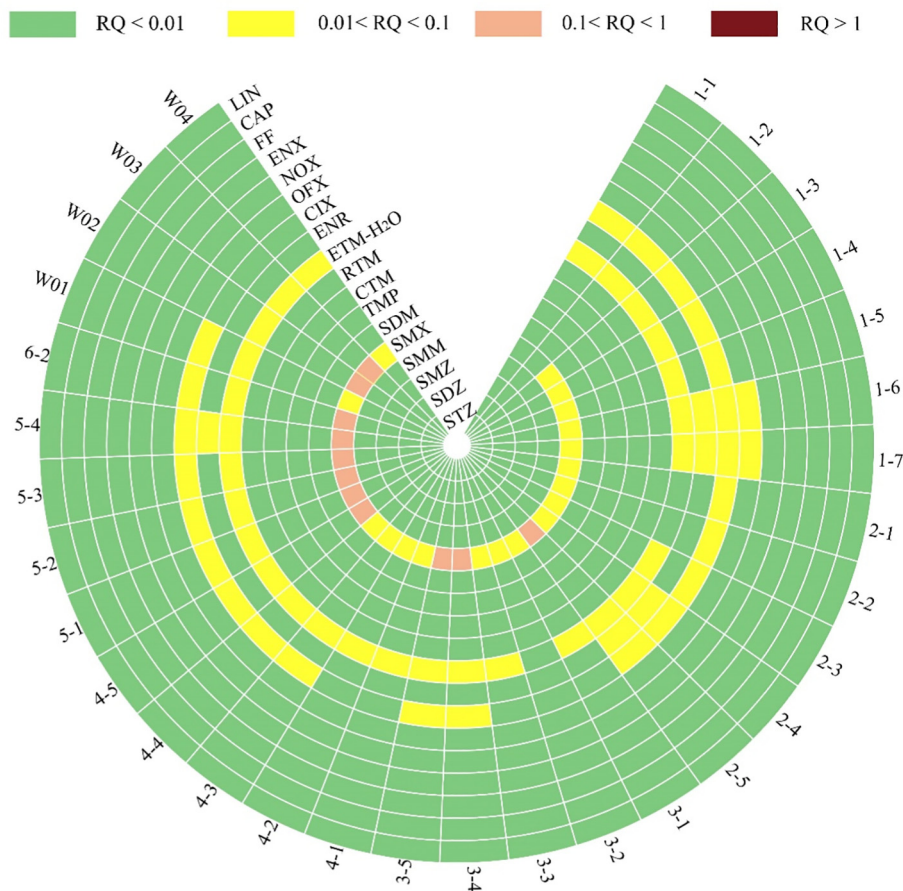

Fig. 5. Risk quotients (RQs) of the detected antibiotics toward algae in the seawater of the Beibu Gulf.

Island ([Fig. 1](#)). It is very likely that the municipal wastewater flowed into the Beibu Gulf then transported by oceanic circulation (Gao et al., 2017). Marine aquaculture (source 3) was considered as the primary emission source of antibiotics at the sites located on the north the Beibu Gulf (sampling sites of 5–1, 5–2, 5–3, 5–4, 6–2). Previous investigations suggested that 20% of the population was engaged in capturing fisheries and/or mariculture in the northern Beibu Gulf and the fishery gross product in 2019 reached 4.4 billion US dollars (Xue et al., 2020; The Oceanic Administration of Guangxi, 2019).The results of Unmix analysis indicated that the estimated average contributions of antibiotics were in the order of livestock activities (34%) > mixed source (28%) > marine aquaculture (27%) > municipal sewage (11%). The overall results of Unmix model were in line with the results of PCA-MLR. It should be noted that the compositions of antibiotics in seawater were very complex and individual antibiotics may have different applications, which would bring difficulties to the source identification.

3.5. Risk assessment and environmental implications

The ecological risks of fourteen detected antibiotics were evaluated. Three trophic level aquatic organisms, including algae, fish, and invertebrate were selected to calculate the risk quotient (RQ) of antibiotics based on acute toxicity data (Table S9). Results suggested that antibiotics were not likely to pose risks on invertebrates and fish due to the low RQ values (<0.01). Algae was the most sensitive species to some antibiotics ([Fig. 5](#)), such as SMX, CIX, $ETM-H_2O$, and ENR. SMX and CIX presented medium risks to algae at 36%, 39% of the sampling sites of the Beibu Gulf. A few studies reported that $ETM-H_2O$ posed relatively high ecological risks in the Yellow Sea (Yang et al., 2020), Hai River (Lei et al., 2019), and the Pearl River Estuary (Li et al., 2018), while $ETM-H_2O$ posed low risks at most sampling sites (almost 70%) of the Beibu Gulf. Besides, SMX, CIX, ENR, and OFX also posed low risks to algae at 58%, 32%, 16%, and 7.0% of the sampling sites, respectively. Accordingly, more attention should be given to the use of SMX, CIX, and $ETM-H_2O$ in the Beibu Gulf due to their potential ecological risks.

Although ATM, FF, SDZ did not show high ecological risk, the degradation rates of these antibiotics were relatively low (10^{-6}–10^{-5}/min), resulting in their long-term existence in the aquatic environment (Lei et al., 2019). Furthermore, it should be noted that the risk of antibiotics never occurs individually and the mixture risk of multiple antibiotics can increase via synergistic effect (Liu and Wong, 2013). The calculated MRQs of antibiotic mixtures varied from 0.10–0.86 (Fig. S6), demonstrating that the target antibiotics might pose medium ecological risks in the Beibu Gulf. Additionally, there is a high possibility that antibiotics would cause the rapid emergence of antibiotic resistance genes (ARGs), which are relatively stable and can transfer globally in the marine environment (Leng et al., 2020). Therefore, long-term monitoring and scientific management of antibiotics are still essential due to their ubiquitousness in the Beibu Gulf.

4. Conclusions

This study investigated the spatial distribution, source identification, and ecological risks of commonly used antibiotics in the subtropical marine environment from the Beibu Gulf. 19 and 17 antibiotics were detected in seawater and sediment, respectively. The levels of antibiotics were higher in the coastal area than in the offshore area. In general, SMX, TMP, and NOX were the dominant antibiotics in seawaters, while NOX, ENX, and ENR were prevalent in sediment. Salinity, particle size, and pH of water were the dominant factors governing the sediment-water partition of SDZ, CIX, and ENR. Receptor models revealed that livestock and aquaculture were significant potential sources of antibiotics in the Beibu Gulf. Based on the risk assessment, SMX, CIX, and $ETM-H_2O$ could pose risks to algae in the Beibu Gulf. Overall, the Beibu Gulf was relatively less polluted by antibiotics compared with other coastal regions across the world.

CRediT authorship contribution statement

Qi Wu: Investigation, Writing – original draft. **Shao-Ke Xiao:** Investigation. **Chang-Gui Pan:** Conceptualization, Writing - review & editing. **Chao Yin:** Investigation. **Ying-Hui Wang:** Validation, Funding acquisition. **Ke-Fu Yu:** Conceptualization, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2021.150439.

References

Ali, A.M., Ronning, H.T., Alarif, W., Kallenborn, R., Al-Lihaibi, S.S., 2017. Occurrence of pharmaceuticals and personal care products in effluent-dominated saudi arabian coastal waters of the Red Sea. Chemosphere 175, 505–513.

Backhaus, T., Faust, M., 2012. Predictive environmental risk assessment of chemical mixtures: a conceptual framework. Environ. Sci. Technol. 46, 2564–2573.

Bayen, S., Zhang, H., Desai, M.M., Ooi, S.K., Kelly, B.C., 2013. Occurrence and distribution of pharmaceutically active and endocrine disrupting compounds in Singapore's marine environment: influence of hydrodynamics and physical-chemical properties. Environ. Pollut. 182, 1–8.

Bayen, S., Estrada, E.S., Juhel, G., Kit, L.W., Kelly, B.C., 2016. Pharmaceutically active compounds and endocrine disrupting chemicals in water, sediments and mollusks in mangrove ecosystems from Singapore. Mar. Pollut. Bull. 109, 716–722.

Behera, S.K., Kim, H.W., Oh, J.E., Park, H.S., 2011. Occurrence and removal of antibiotics, hormones and several other pharmaceuticals in wastewater treatment plants of the largest industrial city of Korea. Sci. Total Environ. 409, 4351–4360.

Biel-Maeso, M., Baena-Nogueras, R.M., Corada-Fernandez, C., Lara-Martin, 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). Sci. Total Environ. 612, 649–659.

Borecka, M., Siedlewicz, G., Halinski, L.P., Sikora, K., Pazdro, K., Stepnowski, P., Bialk-Bielinska, A., 2015. Contamination of the southern Baltic Sea waters by the residues of selected pharmaceuticals: method development and field studies. Mar. Pollut. Bull. 94, 62–71.

Brausch, J.M., Rand, G.M., 2011. A review of personal care products in the aquatic environment: environmental concentrations and toxicity. Chemosphere 82, 1518–1532.

Carvalho, I.T., Santos, L., 2016. Antibiotics in the aquatic environments: a review of the european scenario. Environ. Int. 94, 736–757.

Celic, M., Gros, M., Farre, M., Barcelo, D., Petrovic, M., 2019. Pharmaceuticals as chemical markers of wastewater contamination in the vulnerable area of the Ebro Delta (Spain). Sci. Total Environ. 652, 952–963.

Chen, K., Zhou, J.L., 2014. Occurrence and behavior of antibiotics in water and sediments from the Huangpu River, Shanghai, China. Chemosphere 95, 604–612.

Chen, H., Liu, S., Xu, X.R., Zhou, G.J., Liu, S.S., Yue, W.Z., Sun, K.F., Ying, G.G., 2015. Antibiotics in the coastal environment of the Hailing Bay region, South China Sea: spatial distribution, source analysis and ecological risks. Mar. Pollut. Bull. 95, 365–373.

Cheng, D., Xie, Y., Yu, Y., Liu, X., Zhao, S., Cui, B., Bai, J., 2014. Occurrence and partitioning of antibiotics in the water column and bottom sediments from the intertidal zone in the Bohai Bay, China. Wetlands 36, 167–179.

Cui, Y., Wang, Y., Pan, C., Li, R., Xue, R., Guo, J., Zhang, R., 2019. Spatiotemporal distributions, source apportionment and potential risks of 15 pharmaceuticals and personal care products (PPCPs) in Qinzhou Bay, South China. Mar. Pollut. Bull. 141, 104–111.

Du, J., Zhao, H., Liu, S., Xie, H., Wang, Y., Chen, J., 2017. Antibiotics in the coastal water of the South Yellow Sea in China: occurrence, distribution and ecological risks. Sci. Total Environ. 595, 521–527.

Fisch, K., Zhang, R., Zhou, M., Schulz-BullaJoanna, D.E., Waniek, J., 2021. PPCPs - a human and veterinary fingerprint in the Pearl River delta and northern South China Sea. Emerg. Contam. 7, 10–21.

Gao, J., Wu, G., Ya, H., 2017. Review of the circulation in the beibu gulf, South China Sea. Cont. Shelf Res. 138, 106–119.

Guo, X., Feng, C., Gu, E., Tian, C., Shen, Z., 2019. Spatial distribution, source apportionment and risk assessment of antibiotics in the surface water and sediments of the Yangtze estuary. Sci. Total Environ. 671, 548–557.

Halling-Sorensen, B., 2000. Algal toxicity of antibacterial agents used in intensive farming. Chemosphere 40, 731–739.

Horsing, M., Ledin, A., Grabic, R., Fick, J., Tysklind, M., la Cour Jansen, J., Andersen, H.R., 2011. Determination of sorption of seventy-five pharmaceuticals in sewage sludge. Water Res. 45, 4470–4482.

Huang, Y., Wang, Y., Huang, Y., Zhang, L., Ye, F., Wang, J., Shang, J., Liao, Q., 2020. Impact of sediment characteristics on adsorption behavior of typical antibiotics in Lake Taihu, China. Sci. Total Environ. 718, 137329.

Jia, A., Hu, J., Wu, X., Peng, H., Wu, S., Dong, Z., 2011. Occurrence and source apportionment of sulfonamides and their metabolites in Liaodong Bay and the adjacent Liao River basin, North China. Environ. Toxicol. Chem. 30, 1252–1260.

Kafaei, R., Papari, F., Seyedabadi, M., Sahebi, S., Tahmasebi, R., Ahmadi, M., Sorial, G.A., Asgari, G., Ramavandi, B., 2018. Occurrence, distribution, and potential sources of antibiotics pollution in the water-sediment of the northern coastline of the Persian Gulf, Iran. Sci. Total Environ. 627, 703–712.

Kim, S.Ch., Carlson, K., 2007. Temporal and spatial trends in the occurrence of human and veterinary antibiotics in aqueous and river sediment matrices. Environ. Sci. Technol. 41, 50–57.

Klatte, S., Schaefer, H.-Ch., Hempel, M., 2016. Pharmaceuticals in the environment - a short review on options to minimize the exposure of humans, animals and ecosystems. Sustain. Chem. Pharm. 5, 61–66.

Klein, E.Y., Van Boeckel, T.P., Martinez, E.M., Pant, S., Gandra, S., Levin, S.A., Goossens, H., Laxminarayan, R., 2018. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc. Natl Acad. Sci. USA 115, E3463–E3470.

Kotke, D., Gandrass, J., Xie, Z., Ebinghaus, R., 2019. Prioritised pharmaceuticals in german estuaries and coastal waters: occurrence and environmental risk assessment. Environ. Pollut. 255, 113161.

Kovalakova, P., Cizmas, L., McDonald, T.J., Marsalek, B., Feng, M., Sharma, V.K., 2020. Occurrence and toxicity of antibiotics in the aquatic environment: a review. Chemosphere 251, 126351.

Kummerer, K., 2009. Antibiotics in the aquatic environment - a review - part I. Chemosphere 75, 417–434.

Lagesson, A., Fahlman, J., Brodin, T., Fick, J., Jonsson, M., Bystrom, P., Klaminder, J., 2016. Bioaccumulation of five pharmaceuticals at multiple trophic levels in an aquatic food web - insights from a field experiment. Sci. Total Environ. 568, 208–215.

Lang, Y.H., Li, G.L., Wang, X.M., Peng, P., 2015. Combination of unmix and PMF receptor model to apportion the potential sources and contributions of PAHs in wetland soils from Jiaozhou Bay, China. Mar. Pollut. Bull. 90, 129–134.

Larsen, R.K., Baker, J.E., 2003. Source apportionment of polycyclic aromatic hydrocarbons in the urban atmosphere: a comparison of three methods. Environ. Sci. Technol. 37, 1873–1881.

Lei, K., Zhu, Y., Chen, W., Pan, H.Y., Cao, Y.X., Zhang, X., Guo, B.B., Sweetman, A., Lin, C.Y., Ouyang, W., He, M.C., Liu, X.T., 2019. Spatial and seasonal variations of antibiotics in river waters in the Haihe River catchment in China and ecotoxicological risk assessment. Environ. Int. 130, 104919.

Leng, Y., Xiao, H., Li, Z., Wang, J., 2020. Tetracyclines, sulfonamides and quinolones and their corresponding resistance genes in coastal areas of Beibu Gulf, China. Sci. Total Environ. 714, 136899.

Leung, H.W., Minh, T.B., Murphy, M.B., Lam, J.C., So, M.K., Martin, M., Lam, P.K., Richardson, B.J., 2012. Distribution, fate and risk assessment of antibiotics in sewage treatment plants in Hong Kong, South China. Environ. Int. 42, 1–9.

Li, S., Shi, W., Li, H., Xu, N., Zhang, R., Chen, X., Sun, W., Wen, D., He, S., Pan, J., He, Z., Fan, Y., 2018. Antibiotics in water and sediments of rivers and coastal area of Zhuhai City, Pearl River estuary, South China. Sci. Total Environ. 636, 1009–1019.

Li, F., Chen, L., Chen, W., Bao, Y., Zheng, Y., Huang, B., Mu, Q., Wen, D., Feng, C., 2020a. Antibiotics in coastal water and sediments of the East China Sea: distribution, ecological risk assessment and indicators screening. Mar. Pollut. Bull. 151, 110810.

Li, Y., Feng, X., Zhou, J., Zhu, L., 2020b. Occurrence and source apportionment of novel and legacy poly/perfluoroalkyl substances in Hai River basin in China using receptor models and isomeric fingerprints. Water Res. 168, 115145.

Liang, X., Chen, B., Nie, X., Shi, Z., Huang, X., Li, X., 2013. The distribution and partitioning of common antibiotics in water and sediment of the Pearl River estuary, South China. Chemosphere 92, 1410–1416.

Liu, J.L., Wong, M.H., 2013. Pharmaceuticals and personal care products (PPCPs): a review on environmental contamination in China. Environ. Int. 59, 208–224.

Liu, X., Zhang, H., Li, L., Fu, C., Tu, C., Huang, Y., Wu, L., Tang, J., Luo, Y., Christie, P., 2016. Levels, distributions and sources of veterinary antibiotics in the sediments of the Bohai Sea in China and surrounding estuaries. Mar. Pollut. Bull. 109, 597–602.

Liu, K., Zhang, D., Xiao, X., Cui, L., Zhang, H., 2020a. Occurrence of quinolone antibiotics and their impacts on aquatic environment in typical river-estuary system of Jiaozhou Bay, China. Ecotoxicol. Environ. Saf. 190, 109993.

Liu, S., Zhao, H., Lehmler, H.J., Cai, X., Chen, J., 2017. Antibiotic pollution in marine food webs in Laizhou Bay, North China: trophodynamics and human exposure implication. Environ. Sci. Technol. 51, 2392–2400.

Liu, K., Yin, X., Zhang, D., Yan, D., Cui, L., Zhu, Z., Wen, L., 2018. Distribution, sources, and ecological risk assessment of quinolone antibiotics in the surface sediments from Jiaozhou Bay wetland, China. Mar. Pollut. Bull. 129, 859–865.

Liu, S., Su, H., Pan, Y.F., Xu, X.R., 2020b. Spatial and seasonal variations of antibiotics and antibiotic resistance genes and ecological risks in the coral reef regions adjacent to two typical islands in South China Sea. Mar. Pollut. Bull. 158, 111424.

Lyu, J., Yang, L., Zhang, L., Ye, B., Wang, L., 2020. Antibiotics in soil and water in China-a systematic review and source analysis. Environ. Pollut. 266, 115147.

McEneff, G., Barron, L., Kelleher, B., Paull, B., Quinn, B., 2014. A year-long study of the spatial occurrence and relative distribution of pharmaceutical residues in sewage effluent, receiving marine waters and marine bivalves. Sci. Total Environ. 476–477, 317–326.

Meng, J., Hua, C., Zhang, J.B., Lu, Y., 2017. Analyses on spatial-temporal evolution pattern of coastal aquaculture in Guangxi coastal zone in the in the 1995–2015 years. Guangxu Sci. 24, 135–143.

Minh, T.B., Leung, H.W., Loi, I.H., Chan, W.H., So, M.K., Mao, J.Q., Choi, D., Lam, J.C.W., Zheng, G., Martin, M., Lee, J.H.W., Lam, P.K.S., Richardson, B.J., 2009. Antibiotics in the Hong Kong metropolitan area: ubiquitous distribution and fate in Victoria harbour. Mar. Pollut. Bull. 58, 1052–1062.

Ministry of Agriculture the PRC, 2015. Bulletin (NO. 2292): stop use of lomefloxacin, pefloxacin, ofloxacin and norfloxacin in food-producing animals. http://www.yc6318.cn/sycv/aritcle5008.html.

Moreno-González, R., Rodriguez-Mozaz, S., Gros, M., Barceló, D., León, V.M., 2015. Seasonal distribution of pharmaceuticals in marine water and sediment from a mediterranean coastal lagoon (SE Spain). Environ. Res. 138, 326–344.

Nodler, K., Voutsa, D., Licha, T., 2014. Polar organic micropollutants in the coastal environment of different marine systems. Mar. Pollut. Bull. 85, 50–59.

Pan, C.G., Xiao, S.K., Yu, K.F., Wu, Q., Wang, Y.H., 2021. Legacy and alternative per- and polyfluoroalkyl substances in a subtropical marine food web from the beibu gulf, South China: fate, trophic transfer and health risk assessment. J. Hazard. Mater. 403, 123618.

Richter, M.K., Sander, M., Krauss, M., Christl, I., Dahinden, M.G., Schneider, M.K., Schwarzenbach, R.P., 2009. Cation binding of antimicrobial sulfathiazole to leonardite humic acid. Environ. Sci. Technol. 43, 6632–6638.

Robinson, A.A., Belden, J.B., Lydy, M.J., 2005. Toxicity of fluoroquinolone antibiotics to aquatic organisms. Environ. Toxicol. Chem. 24, 423–430.

Rodriguez-Mozaz, S., Vaz-Moreira, I., Varela Della Giustina, S., Llorca, M., Barcelo, D., Schubert, S., Berendonk, T.U., Michael-Kordatou, I., Fatta-Kassinos, D., Martinez, J.L., Elpers, C., Henriques, I., Jaeger, T., Schwartz, T., Paulshus, E., O'Sullivan, C., Parnanen, K.M.M., Virta, M., Do, T.T., Walsh, F., Manaia, C.M., 2020. Antibiotic residues in final effluents of European wastewater treatment plants and their impact on the aquatic environment. Environ. Int. 140, 105733.

Saranjampour, P., Vebrosky, E.N., Armbrust, K.L., 2017. Salinity impacts on water solubility and n-octanol/water partition coefficients of selected pesticides and oil constituents. Environ. Toxicol. Chem. 36, 2274–2280.

Sarmah, A.K., Meyer, M.T., Boxall, A.B., 2006. A global perspective on the use, sales, exposure pathways, occurrence, fate and effects of veterinary antibiotics (VAs) in the environment. Chemosphere 65, 725–759.

Shimizu, A., Takada, H., Koike, T., Takeshita, A., Saha, M., Rinawati, Nakada, N., Murata, A., Suzuki, T., Suzuki, S., Chiem, N.H., Tuyen, B.C., Viet, P.H., Siringan, M.A., Kwan, C., Zakaria, M.P., Reungsang, A., 2013. Ubiquitous occurrence of sulfonamides in tropical Asian waters. Sci. Total Environ. 452-453, 108–115.

Siedlewicz, G., Borecka, M., Białk-Bielińska, A., Sikora, K., Stepnowski, P., Pazdro, K., 2016. Determination of antibiotic residues in southern Baltic Sea sediments using tandem solid-phase extraction and liquid chromatography coupled with tandem mass spectrometry. Oceanologia 58, 221–234.

Siedlewicz, G., Bialk-Bielinska, A., Borecka, M., Winogradow, A., Stepnowski, P., Pazdro, K., 2018. Presence, concentrations and risk assessment of selected antibiotic residues in sediments and near-bottom waters collected from the polish coastal zone in the southern Baltic Sea - summary of 3 years of studies. Mar. Pollut. Bull. 129, 787–801.

Sofowote, U.M., McCarry, B.E., Marvin, C.H., 2008. Source apportionment of PAH in Hamilton harbour suspended sediments: comparison of two factor analysis methods. Environ. Sci. Technol. 42, 6007–6014.

Somma, R., Ebrahimi, P., Troise, C., De Natale, G., Guarino, A., Cicchella, D., Albanese, S., 2021. The first application of compositional data analysis (CoDA) in a multivariate perspective for detection of pollution source in sea sediments: the Pozzuoli Bay (Italy) case study. Chemosphere 274, 129955.

Stewart, M., Olsen, G., Hickey, C.W., Ferreira, B., Jelic, A., Petrovic, M., Barcelo, D., 2014. A survey of emerging contaminants in the estuarine receiving environment around Auckland, New Zealand. Sci. Total Environ. 468–469, 202–210.

Tang, J., Wang, S., Fan, J., Long, S., Wang, L., Tang, C., Tam, N.F., Yang, Y., 2019. Predicting distribution coefficients for antibiotics in a river water-sediment using quantitative models based on their spatiotemporal variations. Sci. Total Environ. 655, 1301–1310.

The Oceanic Administration of Guangxi, 2019. Statistical Bulletin of Marine Economy. http://hyj.gxzf.gov.cn/zwgk_66846/hyjj_66894/t5430603.shtml.

WHO, 2015. Global Action Plan on Antimicrobial Resistance.

Wu, Q., Pan, C.G., Wang, Y.H., Xiao, S.K., Yu, K.F., 2021. Antibiotics in a subtropical food web from the beibu gulf, South China: occurrence, bioaccumulation and trophic transfer. Sci. Total Environ. 751, 141718.

Xiao, S.K., Wu, Q., Pan, C.G., Yin, C., Wang, Y.H., Yu, K.F., 2021. Distribution, partitioning behavior and potential source of legacy and alternative per- and polyfluoroalkyl substances (PFASs) in water and sediments from a subtropical Gulf, South China Sea. Environ. Res. 201, 111485.

Xie, H., Wang, X., Chen, J., Li, X., Jia, G., Zou, Y., Zhang, Y., Cui, Y., 2019. Occurrence, distribution and ecological risks of antibiotics and pesticides in coastal waters around liaodong peninsula, China. Sci. Total Environ. 656, 946–951.

Xu, W., Zhang, G., Li, X., Zou, S., Li, P., Hu, Z., Li, J., 2007. Occurrence and elimination of antibiotics at four sewage treatment plants in the Pearl River Delta (PRD), South China. Water Res. 41, 4526–4534.

Xu, J., Xu, Y., Wang, H., Guo, C., Qiu, H., He, Y., Zhang, Y., Li, X., Meng, W., 2015. Occurrence of antibiotics and antibiotic resistance genes in a sewage treatment plant and its effluent-receiving river. Chemosphere 119, 1379–1385.

Xue, B.M., Yang, W.W., Wang, Y.H., Huang, W.Y., Li, P.Y., Zhang, R.J., Huang, K., 2013. Occurrence, distribution and ecological risks of sulfonamides in the Qinzhou Bay, South China. China Environ. Sci. 33, 1664–1669.

Xue, B.M., Zhang, L.L., Li, R.L., Wang, Y.H., Guo, J., Yu, K.F., Wang, S.P., 2020. Underestimated microplastic pollution derived from fishery activities and "hidden" in deep sediment. Environ. Sci. Technol. 54, 2210–2217.

Yang, L., Zhou, Y., Shi, B., Meng, J., He, B., Yang, H., Yoon, S.J., Kim, T., Kwon, B.O., Khim, J.S., Wang, T., 2020. Anthropogenic impacts on the contamination of pharmaceuticals and personal care products (PPCPs) in the coastal environments of the yellow and bohai seas. Environ. Int. 135, 105306.

Zhang, Q.Q., Ying, G.G., Pan, C.G., Liu, Y.S., Zhao, J.L., 2015. Comprehensive evaluation of antibiotics emission and fate in the river basins of China: source analysis, multimedia modeling, and linkage to bacterial resistance. Environ. Sci. Technol. 49, 6772–6782.

Zhang, M., Liu, Y.S., Zhao, J.L., Liu, W.R., He, L.Y., Zhang, J.N., Chen, J., He, L.K., Zhang, Q.Q., Ying, G.G., 2018a. Occurrence, fate and mass loadings of antibiotics in two swine wastewater treatment systems. Sci. Total Environ. 639, 1421–1431.

Zhang, R., Pei, J., Zhang, R., Wang, S., Zeng, W., Huang, D., Wang, Y., Zhang, Y., Wang, Y., Yu, K., 2018b. Occurrence and distribution of antibiotics in mariculture farms, estuaries and the coast of the Beibu gulf, China: bioconcentration and diet safety of seafood. Ecotoxicol. Environ. Saf. 154, 27–35.

Zhang, R., Zhang, R., Yu, K., Wang, Y., Huang, X., Pei, J., Wei, C., Pan, Z., Qin, Z., Zhang, G., 2018c. Occurrence, sources and transport of antibiotics in the surface water of coral reef regions in the South China Sea: potential risk to coral growth. Environ. Pollut. 232, 450–457.

Zhang, J., Li, R., Zhang, X., Bai, Y., Cao, P., Hua, P., 2019. Vehicular contribution of PAHs in size dependent road dust: a source apportionment by PCA-MLR, PMF, and unmix receptor models. Sci. Total Environ. 649, 1314–1322.

Zhang, G., Liu, X., Lu, S., Zhang, J., Wang, W., 2020. Occurrence of typical antibiotics in nansi Lake's inflowing rivers and antibiotic source contribution to nansi Lake based on principal component analysis-multiple linear regression model. Chemosphere 242, 125269.

Zhang, R., Kang, Y., Zhang, R., Han, M., Zeng, W., Wang, Y., Yu, K., Yang, Y., 2021. Occurrence, source, and the fate of antibiotics in mariculture ponds near the Maowei Sea, South China: storm caused the increase of antibiotics usage. Sci. Total Environ. 752, 141882.

Zhao, S., Liu, X., Cheng, D., Liu, G., Liang, B., Cui, B., Bai, J., 2016. Temporal-spatial variation and partitioning prediction of antibiotics in surface water and sediments from the intertidal zones of the Yellow River Delta, China. Sci. Total Environ. 569–570, 1350–1358.

Zheng, Q., Zhang, R., Wang, Y., Pan, X., Tang, J., Zhang, G., 2012. Occurrence and distribution of antibiotics in the beibu gulf, China: impacts of river discharge and aquaculture activities. Mar. Environ. Res. 78, 26–33.

Zhou, L.J., Ying, G.G., Zhao, J.L., Yang, J.F., Wang, L., Yang, B., Liu, S., 2011. Trends in the occurrence of human and veterinary antibiotics in the sediments of the Yellow River, Hai River and Liao River in northern China. Environ. Pollut. 159, 1877–1885.

Zhou, L.J., Ying, G.G., Liu, S., Zhang, R.Q., Lai, H.J., Chen, Z.F., Pan, C.G., 2013. Excretion masses and environmental occurrence of antibiotics in typical swine and dairy cattle farms in China. Sci. Total Environ. 444, 183–195.

Zou, S., Xu, W., Zhang, R., Tang, J., Chen, Y., Zhang, G., 2011. Occurrence and distribution of antibiotics in coastal water of the Bohai Bay, China: impacts of river discharge and aquaculture activities. Environ. Pollut. 159, 2913–2920.