Science of the Total Environment 704 (2020) 135288

Contents lists available at ScienceDirect

Science of the Total Environment

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

Antibiotics in coral reef fishes from the South China Sea: Occurrence, distribution, bioaccumulation, and dietary exposure risk to human

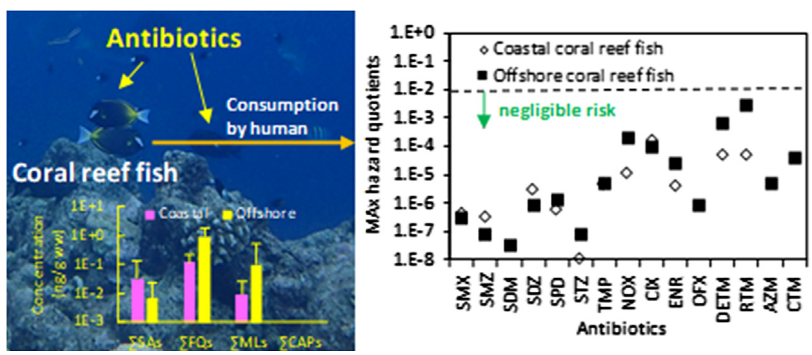
Ruijie Zhang [a,b], Kefu Yu [a,*], An Li [b], Yinghui Wang [a], Changgui Pan [a], Xueyong Huang [a]

[a] Guangxi Laboratory on the Study of Coral Reefs in the South China Sea, Coral Reef Research Center of China, School of Marine Sciences, Guangxi University, Nanning 530004, China
[b] Environmental and Occupational Health Sciences, School of Public Health, University of Illinois at Chicago, Chicago 60612, USA

HIGHLIGHTS

- 19 man-made antibiotics were firstly studied in coral reef fishes, South China Sea.
- 17 antibiotics were detected in the fishes at the level of 10^{-2}–10^{-1} ng/g ww.
- The concentrations were generally higher in offshore fishes than in coastal fishes.
- Consumption of coral reef fish might not pose a significant risk to human health.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 16 September 2019
Received in revised form 25 October 2019
Accepted 28 October 2019
Available online 23 November 2019

Editor: Adrian Covaci

Keywords:
Coral reef fish
Antibiotics
Bioaccumulation
Trophic transfer factor
South China Sea

ABSTRACT

Coral reef fishes are about 10% of commercial fishes worldwide. Their pollution is close to human's health. Antibiotics are one group of emerging organic pollutants in the marine environment. However, little data is available on the bioaccumulation and dietary risks of antibiotics in coral reef fish from the South China Sea (SCS) or any other parts of the global coral reef environment. In this study, we examined 19 antibiotics in 18 species of coral reef fish collected from coastal and offshore regions in the SCS. The results revealed that 17 antibiotics were detected in the fishes. Their average concentrations ranged from 1.3×10^{-5} to 7.9×10^{-1} ng/g ww, which were at the lower end of the global range about antibiotic levels in fish. The average total antibiotic concentrations ($\sum_{19}$ABs) were significantly higher in the offshore fish (1.2 ng/g ww) than in the coastal fish (0.16 ng/g ww). Different fish species or the protection of mucus produced by coastal fish at severe environmental stress may cause the differences. Fluoroquinolones (FQs) accounted for 89% and 74% of the average $\sum_{19}$ABs in the offshore and coastal fish, respectively. It may relate to their relative high aqueous solubility and adsorption ability to particles. The log BAFs (bioaccumulation factors) of the antibiotics ranged from −0.34 to 4.12. Norfloxacin, dehydrated erythromycin (DETM), and roxithromycin were bioaccumulative in some offshore fish samples with their log BAFs higher than 3.7. The results of trophic magnification factors (TMFs) demonstrated that DETM underwent significant trophic dilution while enoxacin underwent trophic magnification in the food web of coral reef fishes. The estimated daily intakes of antibiotics via fish consumption by China residents ranged from 2.0×10^{-4} to 2.7 ng/kg weight body/day, which was 3 to 8 orders of magnitude lower than the respective acceptable daily intakes.

* Corresponding author.
E-mail addresses: rjzhang@gxu.edu.cn (R. Zhang), kefuyu@gxu.edu.cn (K. Yu), anli@uic.edu (A. Li), wyh@gxu.edu.cn (Y. Wang), panchanggui@hotmail.com (C. Pan), huangxueyong@gxu.edu.cn (X. Huang).

https://doi.org/10.1016/j.scitotenv.2019.135288
0048-9697/

1. Introduction

Antibiotics are extensively used in human medical treatment, animal husbandry, and aquaculture as antibacterial drugs and animal growth promoter. Between 2000 and 2015, antibiotic consumption used as human medical treatment increased 65% [21.1–34.8 billion DDDs (defined daily doses)], and the antibiotic consumption rate increased 39% (11.3–15.7 DDDs per 1000 inhabitants per day) in 76 countries (Klein et al., 2018). More than half of the antibiotics has entered the environment due to their wasteful uses, incomplete metabolism in human and animals, and inefficient removal during wastewater treatment (Kim and Carlson, 2007; Lindberg et al., 2005; McArdell et al., 2003; Zhang et al., 2015). As a result, antibiotics have been widely detected in soils, sediments, and surface waters such as rivers, lakes, reservoirs, and seas (Luo et al., 2011; Martinez-Carballo et al., 2007; Stoob et al., 2007; Xu et al., 2013; Zhang et al., 2018a; Zhang et al., 2012; Zou et al., 2011). Because they can cause ecological harm in organisms and promote antibiotic resistance gene (ARG) (Eguchi et al., 2004; Kummerer, 2004), which is a significant cause of morbidity and mortality globally (Laxminarayan et al., 2013), antibiotics have been regarded as global emerging environmental pollutants. Many antibiotics in the aquatic environment can be accumulated in aquatic organisms at various trophic levels (Chen et al., 2015; Done and Halden, 2015; Li et al., 2012a; Li et al., 2012b; Liu et al., 2017; Zhao et al., 2015), and some are biomagnifying (Liu et al., 2017). Consumption of contaminated aquatic plants and animals may pose health risks to humans.

Coral reef fishes, which live amongst or in close relation to coral reefs, occupy 25 percent of all marine fish species (Wikipedia, 2019). A healthy coral reef system produces 35 tonnes of fish per square kilometer per year (Connell, 1978). The outputs of coral reef fish are about 10% of commercial fishes worldwide (Connell, 1978), and up to 25% in some developing countries from Indo-Pacific area (Cesar, 1996). They have provided plenty of protein to humans (Zhao et al., 2006). Therefore, their edible safety caused by contaminants is of great importance. Previous studies indicated that many organic pollutants, such as polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs), dichlorodiphenyltrichloroethane and its metabolites (DDTs) (Sun et al., 2014; Sun et al., 2017), perfluoroalkyl substances (PFAS) (Pan et al., 2018), organophosphorus flame retardants (OPFRs) (Kim et al., 2011), and so on, can be accumulated in coral fishes and the concentrations of some pollutants can pose dietary health risks to consumers. However, little is known about the occurrence, bioaccumulation character, and dietary exposure risks to humans of antibiotics in the coral reef fishes.

The South China Sea (SCS), one of the world's five most-productive fishing zones, is home to the most diverse and well-developed coral reefs and fishes in the world (Yu, 2012). The antibiotic contamination in the SCS has been aggravated by the input of contaminated river and marine aquaculture wastewater (Chen et al., 2015; Hoang Thi Thanh et al., 2011; Shimizu et al., 2013; Xu et al., 2013; Zhang et al., 2018a). However, there are no previous studies reporting the occurrence of antibiotics in coral fishes for the SCS or any other parts of the global marine environment.

The objectives of this work are to characterize the exposure of coral reef fishes to antibiotics and estimate potential health risks to human fish consumers in the study region. Concentrations of 19 antibiotics were analyzed in the muscle of 80 coral reef fish samples (18 species) from coastal and offshore coral reef regions (CRRs) of the SCS. To our knowledge, this is the first report on the occurrence of antibiotics in coral reef fishes.

2. Materials and methods

2.1. Study areas and sample collection.

The study areas included one coastal and two offshore CRRs (Fig. 1). Table S1 in the Supplementary Material detailed the location and time of sampling as well as the primary water quality data. The coastal CRR Weizhou Island is a famous scenic spot and affected by intensive human activities with 17,000 residents and about 600,000 tourists/year in recent years (Wang et al., 2016). The offshore CRRs include eight islands or reefs from the Xisha and Zhongsha Islands (Fig. 1), which usually suffered from lighter human activity than the coastal regions.

A total of 18 species of coral reef fishes were sampled from the study areas. Eight species were collected in the offshore CRRs from May to July 2015, including *Myripristis murdjan* (M.M, n = 6), *Melichthys vidua* (M.V, n = 5), *Lethrinus olivaceus* (L.O, n = 6), *Gnathodentex aureolineatus* (G.A, n = 7), *Parupeneus trifasciatus* (P.T, n = 9), *Lutjanus kasmira* (L.K, n = 9), *Cephalopholis urodeta* (C.U, n = 8), *Caranx ignobilis* (C.I, n = 1). Ten species were collected in the Weizhou Island CRR in October 2015, including *Abudefduf septemfasciatus* (A.S, n = 10), *Cephalopholis boenak* (C.B, n = 10), *Chaetodon octofasciatus* (C.O, n = 12), *Chaetodon modestus* (CH., n = 10), *Cynoglossus macrolepidotus* (CY., n = 10), *Parajulis poecilepterus* (P.P, n = 12), *Siganus fuscescens* (S.F, n = 15), *Selaroides leptolepis* (S.L, n = 15), *Sargocentron melanospilos* (S.M, n = 15), *Rhabdosargus sarba* (R.S, n = 6). All the fishes were collected by fishing using fishhooks. They were placed in polyethylene bags, which was then put in a cooler with ice, immediately after being taken out the sea surface. The length and weight of each fish were measured in our laboratory before the fish was stored in a −20 °C freezer. Detailed information about the fish and their catch locations are presented in Tables S2 and S3.

2.2. Analytical procedures

This study selected nineteen antibiotics as targeted antibiotics (Table 1). They belonged to four types of antibiotics: fluoroquinolones (FQs), macrolides (MLs) chloramphenicols (CAPs), and sulfonamides (SAs). Trimethoprim, which is one synergist of SAs and has similar physicochemical properties to SAs, was also grouped into SAs in this study. Some important physicochemical properties and chemical structure of the target antibiotics were shown in our previous studies (Zhang et al., 2019; Zhang et al., 2018b) and also listed in Tables S4 and S5. We selected four isotope-labeled compounds ($^{13}C_6$-Sulfamethoxazole, D_5-Norfloxacin, ^{13}C,D3-Erythromycin, $^{13}C_3$-Caffeine) as analytical surrogates. We also summarized the providers and pre-treatment of all the chemicals and materials used in this study in Table S4 and Text S1.

The fish samples were thawed, and their skins removed before the muscle were collected and cut into small pieces. The muscle sample from each fish was individually wrapped in a piece of aluminum foil and put in a polyethylene bag. Then the muscle was freeze-dried, ground to a fine powder for homogenization, wrapped in aluminum foil, and stored at −20 °C until chemical analysis. The moisture content of muscle was determined gravimetrically in the process of freeze-drying and shown in Table S2.

Fish samples were analyzed using a method previously established (Zhang et al., 2018a). In brief, 1.0 g dried muscle was extracted by ultrasonic-assisted extraction following by solid-phase extraction as detailed in Text S2. The 19 target chemicals and four surrogates in all the concentrated extract were analyzed using ultra-high-performance liquid chromatography (Agilent

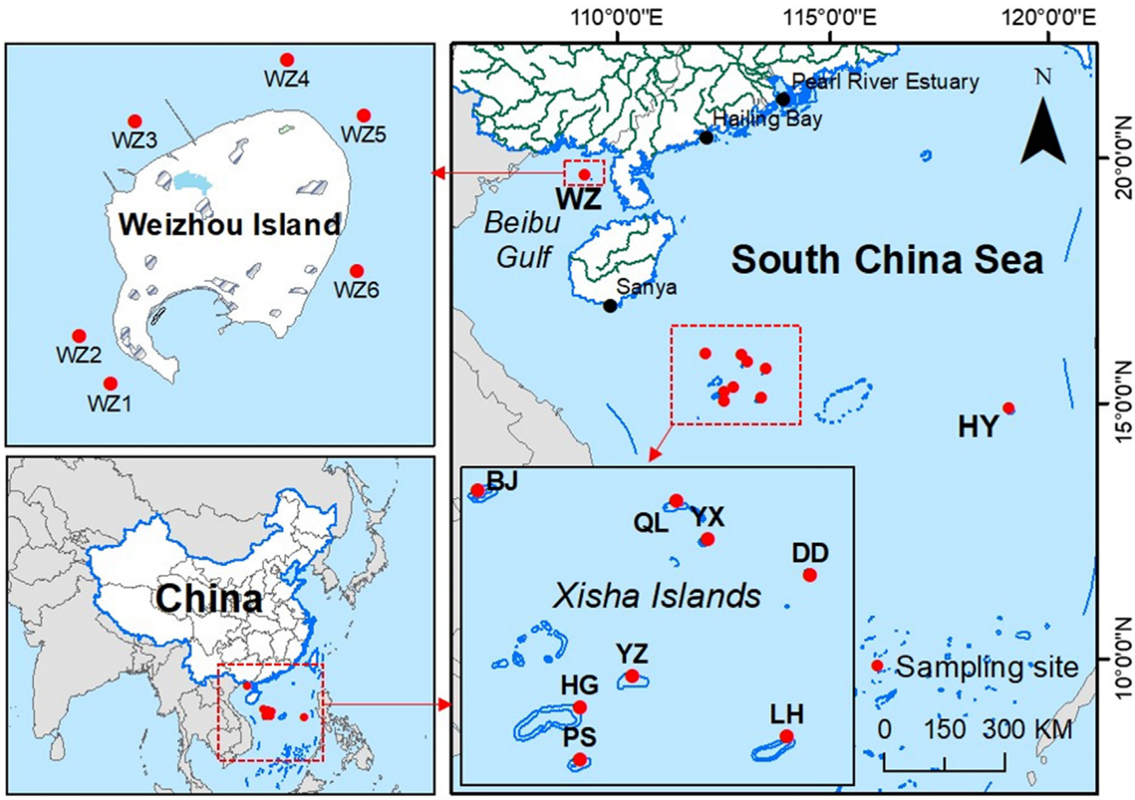


Fig. 1. Sampling location of coral reef fishes and ambient seawater samples in the South China Sea. The Weizhou Island (WZ) coral reef region (CRR) is a coastal region. The offshore sampling regions include Xisha Islands and Huangyan Island (HY) CRRs. The Xisha Islands sampling locations include Beijiao Reef (BJ), Qilian Islets (QL), Yongxing Island (YX), Dongdao Island (DD), Langhua Reef (LH), Panshi Islet (PS), Huaguang Reef (HG), and Yuzuo Reef (YZ).

1290 UHPLC) coupled with triple quadrupole mass spectrometry (Agilent 6460) (Zhang et al., 2018a; Zhang et al., 2018b). Text S2, Tables S6, and S7 detailed the methods and parameters of the instrument analysis.

2.3. Quality control

Procedural blanks using silica sand without antibiotic contamination were included with each batch of 12 samples to check for possible contamination during the analytical procedure. All the target compounds in the blanks were lower than Instrumental quantitative limits (IQLs). Before ultrasonic-assisted extraction, each fish sample was spiked with 50 ng surrogates. The four surrogates presented the recoveries of ranging from 65% to 82%. The final concentrations of each antibiotic were not adjusted by the recoveries of the surrogates. IQLs were determined to be the lowest concentration resulting in a signal-to-noise ratio (S/N) $\geq$ 10 (Luo et al., 2011). The method quantitative limits (MQLs) were calculated using IQLs, the reconstitution volume, and weight of samples. The MQLs of the antibiotics ranged from 1.4×10^{-3} to 2.7×10^{-1} ng/g dw (dry weight) (Table S7). The concentration of antibiotics in the fish was reported as wet-weight-based concentrations (ng/g ww), which was calculated using dry-weight-based concentration (ng/g dw) and the moisture content of each sample.

2.4. Calculation of bioaccumulation factors (BAFs)

To gain insights into the bioaccumulation ability of antibiotics in coral reef fish from seawater, BAFs (in L/kg) were calculated using the following equation:

$$BAFs = \frac{C_{fish}}{C_{water}} \times 1000 \quad (1)$$

where C_{fish} and C_{water} is the antibiotic concentrations in fish (ng/g ww) and in the ambient seawater (ng/L), respectively. We used the average antibiotic concentrations in coastal seawater and offshore seawater for the calculation of BAFs in the coastal and offshore fish, respectively. The MQLs of the seawater were used if the concentrations in the water were lower than the MQLs while BAFs were not calculated if the concentrations in fish were below the MQLs. According to European Chemicals Agency, a chemical is "bioaccumulative" if its BAF $\geq$ 5000 L/kg (log BAF $\geq$ 3.7) and as "potentially bioaccumulative" if 2000 $\leq$ BAF < 5000 L/kg (3.3 $\leq$ log BAF < 3.7) in biota sample (European Chemicals Agency, 2012).

2.5. Statistical analysis

The Shapiro–Wilk test was used to test the normality of one group data. When the data show normal distribution, independent sample *t*-test (IBM SPSS Statistics 24.0) was applied to various variables to examine the statistical significance of the differences between sub-groups; otherwise, a non-parametric test was used. The one-way analysis of variance (ANOVA) was used to test the differences in $\sum_{19}$ABs among multiple fish species. The *p*-value of lower than 0.05 was regarded as significant, whereas $p < 0.01$ was considered highly significant.

3. Results and discussion

3.1. Occurrence of antibiotics in coral reef fish

This study detected 17 of the 19 target antibiotics in the offshore fish, while 13 in the coastal fish (Table 1 and Table S8). The total concentrations of the target antibiotics ($\sum_{19}$ABs) in the offshore and coastal fish averaged 1.2 ± 1.1 ng/g ww and 0.16 ± 0.

Table 1
Antibiotic concentrations in seawater and coral reef fish samples from the South China Sea.

Antibiotics		Coastal seawater (ng/L) (n = 6)		Offshore seawater (ng/L) (n = 7)		Coastal fish (ng/g ww) (n = 29)		Offshore fish (ng/g ww) (n = 51)		Log BAFs[d]	
Name	Abbrev	D.F. [a]	Mean ± SD[b]	D.R.	Mean ± SD	D.F.	Mean ± SD	D.F.	Mean ± SD	Coastal fish Range	Offshore fish Range
Sulfamethoxazole	SMX	100%	1.07 ± 0.19	0%	nd [c]	45%	(6.4 ± 13) × 10^{-3}	55%	(2.1 ± 5.5) × 10^{-3}	0.81 ± 0.59	1.28 ± 0.54
Sulfamethazine	SMZ	50%	0.11 ± 0.15	43%	0.12 ± 0.20	28%	(3.6 ± 7.7) × 10^{-3}	5.90%	(1.9 ± 11) × 10^{-4}	1.95 ± 0.34	1.49 ± 0.59
Sulfadimethoxine	SDM	50%	0.051 ± 0.068	0%	nd	nd	nd	2.00%	(1.3 ± 9.1) × 10^{-5}	/	1.44
Sulfadiazine	SDZ	67%	0.10 ± 0.14	0%	nd	66%	(9.1 ± 27) × 10^{-3}	78%	(2.2 ± 5.0) × 10^{-3}	1.13 ± 0.82	1.39 ± 0.57
Sulfacetamide	SAAM	0%	nd	0%	nd	6.90%	(9.1 ± 48) × 10^{-3}	2.00%	(6.8 ± 48) × 10^{-5}	2.75 ± 1.35	1.83
Sulfapyridine	SPD	100%	0.13 ± 0.11	0%	nd	38%	(4.9 ± 9.1) × 10^{-4}	29%	(3.7 ± 12) × 10^{-4}	0.83 ± 0.38	1.3 ± 0.38
Sulfathiazole	STZ	0%	nd	0%	nd	21%	(1.4 ± 2.9) × 10^{-4}	7.80%	(1.6 ± 10) × 10^{-4}	1.61 ± 0.14	1.37 ± 0.87
Trimethoprim	TMP	100%	0.43 ± 0.29	0%	nd	17%	(3.1 ± 9.4) × 10^{-3}	29%	(1.7 ± 6.0) × 10^{-3}	1.29 ± 0.71	1.79 ± 0.52
Sulfonamides and synergist	**∑SAs**	**100%**	**1.90 ± 0.82**	**43%**	**0.12 ± 0.20**	**86%**	**(3.2 ± 9.4) × 10^{-2}**	**86%**	**(6.8 ± 16) × 10^{-3}**	**0.39 ± 0.87**	**0.87 ± 0.57**
Norfloxacin	NOX	0%	nd	0%	nd	100%	(8.9 ± 5.3) × 10^{-2}	100%	(7.9 ± 8.5) × 10^{-1}	2.22 ± 0.31	3.01 ± 0.49
Ciprofloxacin	CIX	0%	nd	0%	nd	28%	(1.9 ± 8.5) × 10^{-2}	29%	(1.1 ± 4.1) × 10^{-2}	1.77 ± 0.65	1.77 ± 0.51
Enoxacin	ENX	0%	nd	0%	nd	76%	(7.4 ± 6.6) × 10^{-3}	94%	(9.4 ± 10) × 10^{-2}	1.39 ± 0.25	2.24 ± 0.48
Enrofloxacin	ENR	0%	nd	0%	nd	17%	(1.3 ± 3.6) × 10^{-3}	7.80%	(2.3 ± 13) × 10^{-3}	1.89 ± 0.29	2.23 ± 0.58
Ofloxacin	OFX	0%	nd	0%	nd	0%	nd	2.00%	(1.9 ± 14) × 10^{-4}	/	1.66
Fluoroquinolones	**∑FQs**	**0%**	**nd**	0%	**nd**	**100%**	**(12 ± 9.3) × 10^{-2}**	**100%**	**(9.0 ± 9.6) × 10^{-1}**	**1.84 ± 0.30**	**2.59 ± 0.5**
Dehydrated erythromycin	DETM	100%	0.49 ± 0.28	100%	0.072 ± 0.014	100%	(7.1 ± 11) × 10^{-3}	98%	(4.1 ± 15) × 10^{-2}	0.97 ± 0.35	2.01 ± 0.67
Roxithromycin	RTM	100%	0.23 ± 0.08	100%	0.17 ± 0.008	14%	(1.8 ± 7.2) × 10^{-3}	82%	(5.7 ± 31) × 10^{-2}	1.36 ± 0.75	1.73 ± 0.71
Azithromycin	AZM	33%	0.12 ± 0.22	0%	nd	0%	nd	2.00%	(3.2 ± 22) × 10^{-4}	/	2.76
Clarithromycin	CTM	100%	0.29 ± 0.22	71%	0.025 ± 0.017	0%	nd	3.90%	(3.1 ± 21) × 10^{-4}	/	1.93 ± 0.99
Macrolides	**∑MLs**	**100%**	**1.13 ± 0.75**	**100%**	**0.27 ± 0.03**	**100%**	**(9.0 ± 18) × 10^{-3}**	**100%**	**(9.9 ± 44) × 10^{-2}**	**0.63 ± 0.39**	**1.65 ± 0.71**
Florfenicol	FF	100%	1.10 ± 0.72	29%	0.12 ± 0.21	0%	nd	0%	nd	/	/
Chloramphenicol	CAP	17%	0.042 ± 0.10	0%	nd	0%	nd	0%	nd	/	/
Chloramphenicols	**∑CAPs**	**100%**	**1.14 ± 0.78**	**29%**	**0.12 ± 0.21**	**0%**	**nd**	**0%**	**nd**	/	/
All target antibiotics	**$\sum_{19}$ABs**	**100%**	**4.17 ± 1.93**	**100%**	**0.50 ± 0.35**	**100%**	**(1.6 ± 1.4) × 10^{-1}**	**100%**	**1.2 ± 1.1**	**1.32 ± 0.34**	**2.38 ± 0.45**

[a] Detection frequencies.
[b] All the "nd" values were regarded as zero in the calculation of mean and standard deviation (SD).
[c] Not detected.
[d] All the "nd" values in the fish were not included in the calculation of Log BAF.

14 ng/g ww, respectively. The two averages are significantly different (*t*-test, p < 0.001).

Despite the significant differences between fishes from the coastal and offshore CRRs, the relative abundances of different antibiotics were similar (Figs. 2 and 4). The antibiotics that were detected in >70% of the offshore fish included two FQs (norfloxacin and enoxacin), two MLs (dehydrated erythromycin and roxithromycin), and one SA (sulfadiazine). In coastal fish, two FQs (norfloxacin and enoxacin) and one ML (dehydrated erythromycin) were found with detection rate >70%. Among the four antibiotic groups, ∑FQs was significantly higher than the other three groups. It accounted for 89% and 74% of the average $\sum_{19}$ABs in the offshore and coastal fish, respectively (Fig. 2). Among the individual antibiotics, norfloxacin (NOX) showed the highest average concentration. It averaged 0.79 ± 0.85 ng/g ww and accounted 79% of the average $\sum_{19}$ABs in the offshore fish while averaged 0.089 ± 0.053 ng/g ww, which contributed 56% of the $\sum_{19}$ABs in the coastal fish. ENX showed the second and third highest average concentration in the offshore and coastal fish, respectively. Moreover, a significant positive correlation was observed between the concentrations of NOX and ENX (p < 0.01) (Fig. S1), indicating a similar source and accumulation ability of the two contaminants.

For all the SA and FQ antibiotics excluding those with detection rates lower than 20%, the logarithm of average concentrations of

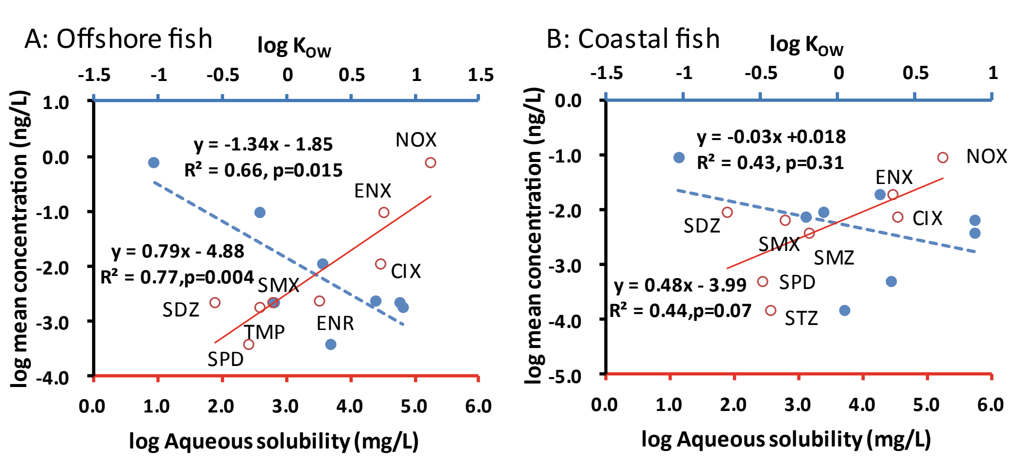


Fig. 2. Relationships of concentrations of antibiotics in the coral fish with their aqueous solubilities and K_{OW}.

each antibiotic in the offshore fishes significantly positively correlated to logarithm of their aqueous solubility (R^2 = 0.77, $p < 0.01$) and negatively correlated to their K_{OW} (R^2 = 0.66, $p < 0.05$) (Fig. 3A). The aqueous solubility and K_{OW} were the main controlling factors influencing the levels of SA and FQ antibiotics in the offshore coral reef fish. The logarithm of average concentrations of each antibiotic in the coastal fishes also positively correlated to the logarithm of their aqueous solubility (R^2 = 0.44, p = 0.07) and negatively correlated to their K_{OW} (R^2 = 0.43, p = 0.31) (Fig. 2B) although their relationship was not significant. Therefore, relative higher concentrations were detected in the fish for the FQs rather than SAs because of FQs' high solubility and low K_{OW}. Similar observations have been reported for invertebrates and mollusks from the Bohai Sea, China (Li et al., 2012b; Liu et al., 2017). For the predominant ML antibiotics DETM and RTM, their relatively high concentrations in the coral reef fish may relate to their relative high K_{OW}.

We also collected ambient seawater when sampled the fish samples. Tables S1 and S2 summarized the seawater samples' information and measured water quality. Our previous study reported the occurrence and level of antibiotics in the seawater (Zhang et al., 2018b). In order to compare with the occurrence of antibiotics in the fish, Table 1 and Fig. 3 also included the summary results of seawater related to the fish sampling sites. The detailed results were shown in Table S9. In brief, we detected fewer kinds of antibiotics in the seawater (12 and 5 antibiotics in coastal and offshore seawater, respectively) than in the fish (13 and 17 antibiotics in coastal and offshore fishes, respectively). Notably, five FQs were not detected in the waters but found in the fishes with higher concentrations than other antibiotic groups despite high aqueous solubility of FQs. That may relate to FQs' higher tendency of sorption on the particle surface due to the FQs' planar quinolone core structure. Previous studies have demonstrated the sorption of FQs onto suspended particles and sediments (Kim and Carlson, 2007; Tolls, 2001; Yang et al., 2010). The $\sum_{19}$ABs was significantly higher (t-test, p = 0.004) in the coastal water (mean: 4.17 ± 1.93 ng/L) than in the offshore water (mean: 0.50 ± 0.35 ng/L). The $\sum$SAs, $\sum$MLs, and $\sum$CAPs were all also higher in the coastal seawater than in the offshore seawater (t-test, p = 0.003, 0.038, and 0.023, respectively).

A composition with earlier studies revealed that the antibiotic levels in the coral reef fish collected from the SCS were generally lower than those in fish from other natural waters (Table S10).

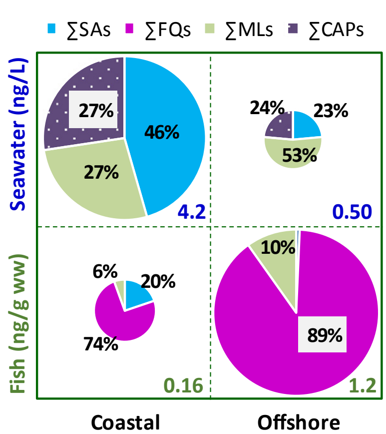


Fig. 3. Comparison in the relative abundance of antibiotic groups between coastal and offshore regions as well as between seawater and coral reef fish. The size of the pies and data under the pies represents average concentration of total antibiotics. $\sum$SAs is the sum of eight sulfonamides and synergists, $\sum$FQs is the sum of five fluoroquinolones, $\sum$MLs is the sum of four macrolides, and $\sum$CAPs is the sum of two chloramphenicols.

The concentrations of $\sum$SAs, $\sum$FQs, and $\sum$MLs were the lowest among those reported from China, such as marine fish and other organisms from Hailing Bay (coastal area of the South China Sea) (Chen et al., 2015) and Laizhou Bay (coastal area of Bohai Sea, North China) (Zhong et al., 2017), freshwater field fish from rivers of Pearl River Delta (Zhao et al., 2015), Haihe River (Gao et al., 2012) and Baiyangdian Lake (Li et al., 2012a). The antibiotic levels in the coral reef fish samples of this work were also lower than those in the fish imported to the United States from 11 countries (Done and Halden, 2015) and fish from rivers of United States (Ramirez et al., 2009).

3.2. Species-specific profiles of antibiotics in coral reef fishes

Among the eight offshore coral reef fish species, the mean concentrations of $\sum_{19}$ABs were ranked in the order: *Gnathodentex aureolineatus* (G.A, 1.7 ng/g ww) > *Melichthys vidua* (M.V) > *Myripristis murdjan* (M.M) > *Cephalopholis urodeta* (C.U) > *Lutjanus kasmira* (L.K) > *Parupeneus trifasciatus* (P.T) > *Lethrinus olivaceus* (L.O) > *Caranx ignobilis* (C.I, 0.18 ng/g ww) (Fig. 4 and Table S11). ANOVA showed significant differences in $\sum_{19}$ABs among some fish species ($p < 0.05$) (Table S12). For the $\sum$FQs, *Gnathodentex aureolineatus* (G.A) was obviously higher than *Parupeneus trifasciatus* (P.T) and *Lethrinus olivaceus* (L.O) (Table S11). *Melichthys vidua* (M.V) and *Myripristis murdjan* (M.M) had higher $\sum$MLs than the other fishes. No significant differences were found between the fish species for $\sum$SAs. Among the ten coastal coral reef fish species, significant differences in $\sum_{19}$ABs, $\sum$SAs, $\sum$FQs, and $\sum$MLs were observed for some fish species ($p < 0.05$) (Table S12). For example, *Selaroides leptolepis* (S.L) had higher $\sum_{19}$ABs (0.37 ng/g ww) and $\sum$SAs (0.37 ng/g ww) than the other fish species except for *Cephalopholis boenak* (C.B). *Cephalopholis boenak* (C.B) had significantly higher $\sum$FQs (0.33 ng/g ww) than the other six fish species. For $\sum$MLs, significantly higher levels were found in *Siganus fuscescens* (S.F) (0.062 ng/g ww) than in the other nine fish species. Previous studies indicated that taxon, size, life cycle, reproductive strategy, and habitat preference could affect contaminants in organisms (Baird and Van den Brink, 2007; Rubach et al., 2010a; Rubach et al., 2010b; Usseglio-Polatera et al., 2000).

As described above, the antibiotic concentrations in the coastal fishes were generally lower than those in the offshore fishes (Table 1) although the antibiotic concentrations in the coastal seawater were higher than in the offshore seawater while the lipid contents were higher in the coastal fish than in the offshore fish (Table S2 and Table 1). Besides the concentration of pollutants in water and the fish lipid contents, many other factors, such as the fish species, growth stage, gender, weight, size, could affect the concentration of pollutants in fish tissues. It is a pity that neither same fish species were collected in the two different regions, so it reduces the significance of the comparison between different species of fish in different regions, and it is also difficult to evaluate which factor played a key role in the differences of antibiotic concentration between the coast fish and offshore fish. However, this interesting differences could cause our thinking. Besides the above factors, surface mucus of fish may play an important role in this study because we noticed that coastal fish produce an excess amount of surface mucus, which is likely in response to poorer water quality near the coast (Shephard, 1994). The increased mucus may defend against the uptake of antibiotics by fish muscle because of the physical and chemical barrier function of mucus (Shephard, 1994). As Shephard (1994) reviewed, fish mucus is on all epidermal surfaces, such as the general skin surface, gills, and the gut lining, that mark the interface between the fish and external world. A similar phenomenon also occurred in the coral tissues between the coastal and offshore CRRs because of the impacts of coral mucus (Zhang et al., 2019), i.e., lower concentrations of

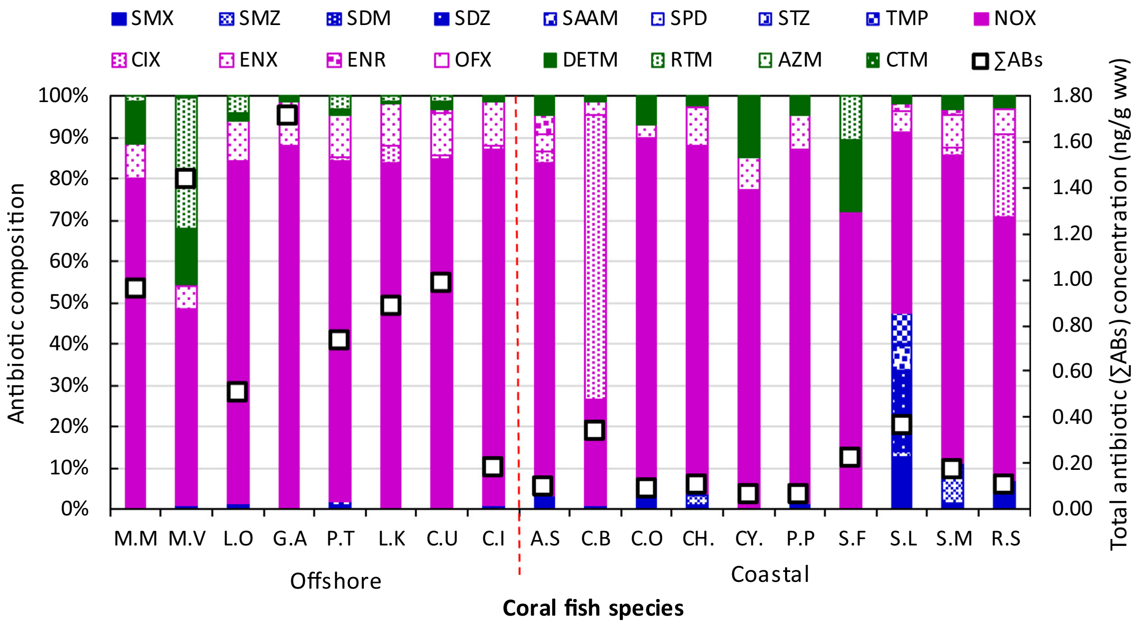


Fig. 4. Comparison in antibiotic concentrations and compositions among the fish species.

antibiotics occurred in the coastal coral tissues while higher concentrations occurred in the coastal coral mucus compared to the offshore corals although the concentrations were higher in the coastal seawater than in the offshore seawater.

3.3. Bioaccumulation and trophic magnification factors of antibiotics in coral reef fishes

The calculated BAFs were shown in Table 1 and Fig. 5. The log BAFs of the SAs, FQs, and MLs in the coral reef fish range from −0.34 to 3.70, 0.79 to 4.02, and 0.33 to 4.12, respectively. Most of them were lower than 3.3, so according to the criteria from European Chemicals Agency, most antibiotics involved in this work are not bioaccumulative. However, norfloxacin (NOX), dehydrated erythromycin (DETM), duoy and roxithromycin (RTM) are bioaccumulative in some offshore fish samples. Compared to the coastal

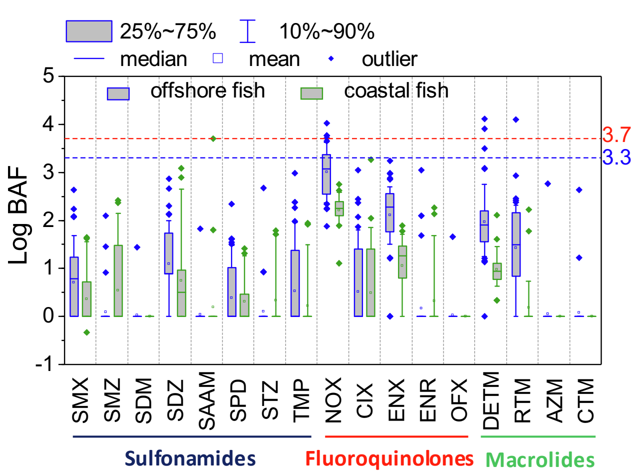


Fig. 5. Bioaccumulation factors (BAFs) of antibiotics in coral reef fish from the South China Sea. The full names of individual antibiotics are given in Table 1. A chemical is "bioaccumulative" if its log BAF is greater than 3.7 (red dotted line), and "potentially bioaccumulative" if log BAF is between 3.3 (blue dotted line) to 3.7. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

fish, offshore fish presented stronger bioaccumulative to most antibiotics, in particular to FQs and MLs. Compared to the cultured fish in the coastal mariculture farms of the Hailing Bay in the South China Sea (log BAFs: 2.27–3.81), the freshwater fish in the Baiyangdian Lake (log BAFs < 4.22) and the Haihe River of North China (2.45–3.65) (Chen et al., 2018; Gao et al., 2012; Li et al., 2012a), the coral reef fish of this study generally present lower BAFs. The calculation of BAFs assumes the steady-state of antibiotics in the portioning between the coral reef fish and the surrounding water environment (Tsui et al., 2017). The unknown conditions regarding steady states could introduce uncertainties to the BAF values reported here.

The coral fish collected in this work included detritivores (dt), herbivores (hb), planktivores (pk), omnivores (om), invertebrate feeders (iv), invertebrate feeder & piscivores (ip), piscivores (pi), etc. (Table S2). Their trophic levels (*TLs*) were ranged from 3.4 ± 0.1 to 4.2 ± 0.4 for the offshore coral reef fish and from 2.0 ± 0.1 to 4.1 ± 0.6 for the coastal coral reef fish (Table S2). Among the detected antibiotics, log-transformed wet-weight-based concentrations of dehydrated erythromycin (DETM) in both offshore and coastal fishes were decreased significantly with increasing *TLs* ($p < 0.05$), while enoxacin (ENO) in the coastal fishes showed the significantly opposite tendency ($p < 0.05$) (Fig. 6). These results demonstrated that dehydrated erythromycin undergoes trophic dilution while enoxacin undergoes trophic magnification in the food web of coral reef fishes.

The trophic magnification factors (TMFs) were determined from the slope of the regression between log-transformed antibiotic concentrations (ww) in biota and the trophic levels (*TLs*) of the sampled biota (Text S3), with value >1 indicating biomagnifying. The TMFs of dehydrated erythromycin in the offshore fishes and coastal fishes were 0.02 and 0.45, respectively (Fig. 6), which were lower than that in the marine food web (0.6) of the Laizhou Bay, North China (Liu et al., 2017). The TMF value of enoxacin in the coastal fish was 2.75, which is higher than that (0.5) in the marine food web of the Laizhou Bay (Liu et al., 2017). On the contrary, the enoxacin in the offshore fishes undergo trophic dilution with the TMF value 0.15 although no significant correlation ($p > 0.05$) was observed between tropic level values and their log-transformed concentrations. For other antibiotics, no significant correlations

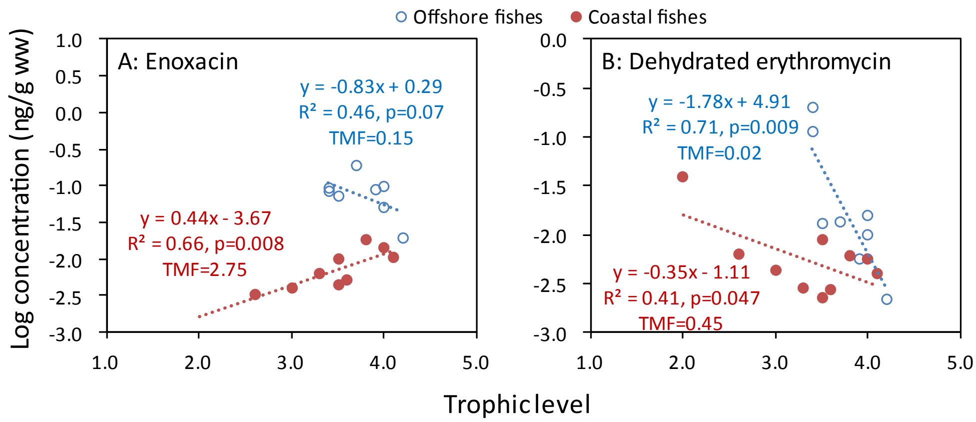


Fig. 6. Relationship between trophic levels and log-transformed wet weight (ww) normalized concentrations for (A) enoxacin and (B) dehydrated erythromycin in the coral reef fishes from the South China Sea. Trophic magnification factors (TMFs) were calculated using the method of Liu et al. (2017).

(p > 0.05) were observed between tropic level values and their log-transformed wet-weight-based concentrations.

3.4. Assessment of human dietary exposure risks

Coral reef fishes investigated in this study are suitable for human consumption except for the two aquarium fish (*Chaetodon octofasciatus* and *Chaetodon modestus*) from the coastal CRR. Based on a previously published assessment method (Zhong et al., 2017), we estimated daily intakes (EDI, Table S13) for each following antibiotic consumption of seafood, assuming a worst-case scenario for urban and rural residents in China by using the highest measured concentrations in the calculation. The EDIs for urban residents were two times higher than those for rural residents because of the higher fish consumption of urban residents than rural residents (Whittemore et al., 1994). Among all the antibiotics, norfloxacin (NOX) in offshore fish showed the highest EDI: 2.7 ng/kg body weight per day (bw/d) for urban residents and 1.4 ng/kg bw/d for the rural resident. All EDI values were 3 to 8 orders of magnitude lower than the respective acceptable daily intakes (ADI, Table S13).

Defined as the ratio of EDI to respective ADIs (Text S5), hazard quotients (HQ) of each antibiotic (Table S13) were calculated and used to assess potential human health risks from dietary exposure to antibiotics. Vragovic et al. (2011) suggested that an HQ lower than 0.01, from 0.01 to 0.05, and higher than 0.05 indicates a negligible risk, a considerable risk, and a distinct risk, respectively. The highest HQ is roxithromycin (RTM) for urban residents (HQ = 0.0032, that is, 0.32% of ADI). It is still much lower than 0.01.

Hazard index values ($HI = \Sigma HQ_i$) were also calculated assuming a similar toxicological mode of action for substances belonging to the same group to assess if consumption of the coral reef fish represents a human health risk. The HI values of $\sum$SAs, $\sum$FQs, and $\sum$MLs ranged from 4.7×10^{-6} to 4.0×10^{-3}. These values are much lower than 0.01. Therefore, there is a negligible human health risk associated with the exposure to antibiotics due to the consumption of coral reef fish from the South China Sea.

4. Conclusions

This study detected most of the target antibiotics (17/19) in the coral reef fish species collected from the coastal CRR Weizhou Island and offshore CRRs Xisha Islands & Huangyan Island, the South China Sea, with the summed concentrations ($\sum_{19}$ABs) ranging from 1.3×10^{-5} to 7.9×10^{-1} ng/g ww. The concentrations were at the lower end of the global range. The average $\sum_{19}$ABs was significantly higher in the fishes from the offshore CRRs (1.2 ± 1.1 ng/g ww) than from the coastal CRR (0.16 ± 0.14 ng/g ww), despite the opposite trend in the seawaters between the two CRRs. FQs were the dominating contaminants in all fishes, accounting for 89% and 74% of $\sum_{19}$ABs in the offshore and coastal fish, respectively, on average. Significant differences in the average $\sum_{19}$ABs were observed among some fish species. *Gnathodentex aureolineatus* presented the highest level of $\sum_{19}$ABs among the 17 fish species. BAFs for antibiotics NOX, DETM and RTM were higher than 5000 L/kg in some offshore fish sample, suggesting that they are bioaccumulative. The TMFs results demonstrate that DETM undergoes significant trophic dilution while ENO undergoes trophic magnification in the food web of coral reef fishes. The calculated EDIs of antibiotics suggested that consumption of coral reef fish in the South China Sea may not pose a significant health risk to China residents. However, because other antibiotics not targeted in this study might accumulate in the fish and greater compounded effects of different antibiotics might occur, the risks of antibiotics in the coral reef fish cannot be ignored.

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.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (91428203, 41463011 and 41673105), the Guangxi scientific projects (NOs. AD17129063, AA17204074, and 2016GXNSFAA380011), the BaGui Fellowship from Guangxi Province of China (2014BGXZGX03), China Postdoctoral Science Foundation (2016M602614) and the Guangxi Postdoctoral Special Fund. We would also like to thank Yang Ding, Ruiling Zhang, Minwei Han and Weibin Zeng for assistance with sample collecting, treatment, and analysis.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2019.135288.

References

Baird, D.J., Van den Brink, P.J., 2007. Using biological traits to predict species sensitivity to toxic substances. Ecotoxicol. Environ. Saf. 67, 296–301. https://doi.org/10.1016/j.ecoenv.2006.07.001.

Cesar, H. Economican alysisofIndonesian Coral Reefs. The World Bank 1996.

Chen, H., Liu, S., Xu, X.R., Diao, Z.H., Sun, K.F., Hao, Q.W., et al., 2018. Tissue distribution, bioaccumulation characteristics and health risk of antibiotics in cultured fish from a typical aquaculture area. J. Hazard. Mater. 343, 140–148. https://doi.org/10.1016/j.jhazmat.2017.09.017.

Chen, H., Liu, S., Xu, X.R., Liu, S.S., Zhou, G.J., Sun, K.Y., et al., 2015. Antibiotics in typical marine aquaculture farms surrounding Hailing Island, South China: Occurrence, bioaccumulation and human dietary exposure. Mar. Pollut. Bull. 90, 181–187. https://doi.org/10.1016/j.marpolbul.2014.10.053.

Connell, J.H. Diversity in tropical rain forests and coral reefs. Science (New York, N. Y.) 1978; 199: 1302–1310. doi: 10.1126/science.199.4335.1302.

Done, H.Y., Halden, R.U., 2015. Reconnaissance of 47 antibiotics and associated microbial risks in seafood sold in the United States. J. Hazard. Mater. 282, 10–17. https://doi.org/10.1016/j.jhazmat.2014.08.075.

Eguchi, K., Nagase, H., Ozawa, M., Endoh, Y.S., Goto, K., Hirata, K., et al., 2004. Evaluation of antimicrobial agents for veterinary use in the ecotoxicity test using microalgae. Chemosphere 57, 1733–1738. https://doi.org/10.1016/j.chemosphere.2004.07.017.

European Chemicals Agency. Guidance on information requirements and chemical safety assessment: Chapter R.11: PBT Assessment (Version 1.1), 2012.

Gao, L., Shi, Y., Li, W., Liu, J., Cai, Y., 2012. Occurrence, distribution and bioaccumulation of antibiotics in the Haihe River in China. J. Environ. Monit. 14, 1248–1255. https://doi.org/10.1039/c2em10916f.

Hoang Thi Thanh, T., Le Phi, N., Tu Thi Cam, L., 2011. Antibiotic contaminants in coastal wetlands from Vietnamese shrimp farming. Environ. Sci. Pollut. Res. 18, 835–841. https://doi.org/10.1007/s11356-011-0475-7.

Kim, J.W., Isobe, T., Chang, K.H., Amano, A., Maneja, R.H., Zamora, P.B., et al., 2011. Levels and distribution of organophosphorus flame retardants and plasticizers in fishes from Manila Bay, the Philippines. Environ. Pollut. 159, 3653–3659. https://doi.org/10.1016/j.envpol.2011.07.020.

Kim, S.C., 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. https://doi.org/10.1021/es060737+.

Klein, E.Y., Van Boeckel, T.P., Martinez, E.M., Pant, S., Gandra, S., Levin, S.A., et al., 2018. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc. Natl. Acad. Sci. 115, E3463–E3470. https://doi.org/10.1073/pnas.1717295115.

Kummerer, K., 2004. Resistance in the environment. J. Antimicrob. Chemother. 54, 311–320. https://doi.org/10.1093/jac/dkh325.

Laxminarayan, R., Duse, A., Wattal, C., Zaidi, A.K.M., Wertheim, H.F.L., Sumpradit, N., et al., 2013. Antibiotic resistance—the need for global solutions. Lancet. Infect. Dis 13, 1057–1098. https://doi.org/10.1016/S1473-3099(13)70318-9.

Li, W., Shi, Y., Gao, L., Liu, J., Cai, Y., 2012a. Occurrence of antibiotics in water, sediments, aquatic plants, and animals from Baiyangdian Lake in North China. Chemosphere 89, 1307–1315. https://doi.org/10.1016/j.chemosphere.2012.05.079.

Li, W.H., Shi, Y.L., Gao, L.H., Liu, J.M., Cai, Y.Q., 2012b. Investigation of antibiotics in mollusks from coastal waters in the Bohai Sea of China. Environ. Pollut. 162, 56–62. https://doi.org/10.1016/j.envpol.2011.10.022.

Lindberg, R.H., Wennberg, P., Johansson, M.I., Tysklind, M., Andersson, B.A.V., 2005. Screening of human antibiotic substances and determination of weekly mass flows in five sewage treatment plants in Sweden. Environ. Sci. Technol. 39, 3421–3429. https://doi.org/10.1021/es048143z.

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. https://doi.org/10.1021/acs.est.6b04556.

Luo, Y., Xu, L., Rysz, M., Wang, Y., Zhang, H., Alvarez, P.J.J., 2011. Occurrence and transport of tetracycline, sulfonamide, quinolone, and macrolide antibiotics in the Haihe River Basin, China. Environ. Sci. Technol. 45, 1827–1833. https://doi.org/10.1021/es104009s.

Martinez-Carballo, E., Gonzalez-Barreiro, C., Scharf, S., Gans, O., 2007. Environmental monitoring study of selected veterinary antibiotics in animal manure and soils in Austria. Environ. Pollut. 148, 570–579. https://doi.org/10.1016/j.envpol.2006.11.035.

McArdell, C.S., Molnar, E., Suter, M.J.F., Giger, W., 2003. Occurrence and fate of macrolide antibiotics in wastewater treatment plants and in the Glatt Valley Watershed, Switzerland. Environ. Sci. Technol. 37, 5479–5486. https://doi.org/10.1021/es034368i.

Pan, C.G., Yu, K.F., Wang, Y.H., Zhang, R.J., Huang, X.Y., Wei, C.S., et al., 2018. Species-specific profiles and risk assessment of perfluoroalkyl substances in coral reef fishes from the South China Sea. Chemosphere 191, 450–457. https://doi.org/10.1016/j.chemosphere.2017.10.071.

Ramirez, A.J., Brain, R.A., Usenko, S., Mottaleb, M.A., O'Donnell, J.G., Stahl, L.L., et al. Occurrence of Pharmaceuticals and Personal Care Products in Fish: Results of a National Pilot Study in the United States. Environ. Toxicol. Chem. 2009; 28: 2587–2597. Doi 10.1897/08-561.1

Rubach, M.N., Ashauer, R., Maund, S.J., Baird, D.J., Van den Brink, P.J., 2010a. Toxicokinetic variation in 15 freshwater arthropod species exposed to the insecticide chlorpyrifos. Environ. Toxicol. Chem. 29, 2225–2234. https://doi.org/10.1002/etc.273.

Rubach, M.N., Baird, D.J., Van den Brink, P.J., 2010b. A new method for ranking mode-specific sensitivity of freshwater arthropods to insecticides and its relationship to biological traits. Environ. Toxicol. Chem. 29, 476–487. https://doi.org/10.1002/etc.55.

Shephard, K.L. Functions for fish mucus. Reviews in Fish Biology and Fisheries 1994; 4: 401–429.

Shimizu, A., Takada, H., Koike, T., Takeshita, A., Saha, M., Rinawati, et al., 2013. Ubiquitous occurrence of sulfonamides in tropical Asian waters. Sci. Total Environ. 452, 108–115. https://doi.org/10.1016/j.scitotenv.2013.02.027.

Stoob, K., Singer, H.P., Mueller, S.R., Schwarzenbach, R.P., Stamm, C.H., 2007. Dissipation and transport of veterinary sulfonamide antibiotics after manure application to grassland in a small catchment. Environ. Sci. Technol. 41, 7349–7355. https://doi.org/10.1021/es070840e.

Sun, Y.X., Hao, Q., Xu, X.R., Luo, X.J., Wang, S.L., Zhang, Z.W., et al., 2014. Persistent organic pollutants in marine fish from Yongxing Island, South China Sea: levels, composition profiles and human dietary exposure assessment. Chemosphere 98, 84–90. https://doi.org/10.1016/j.chemosphere.2013.10.008.

Sun, Y.X., Hu, Y.X., Zhang, Z.W., Xu, X.R., Li, H.X., Zuo, L.Z., et al., 2017. Halogenated organic pollutants in marine biota from the Xuande Atoll, South China Sea: levels, biomagnification and dietary exposure. Mar. Pollut. Bull. 118, 413–419. https://doi.org/10.1016/j.marpolbul.2017.03.009.

Tolls, J., 2001. Sorption of veterinary pharmaceuticals in soils: a review. Environ. Sci. Technol. 35, 3397–3406. https://doi.org/10.1021/es0003021.

Tsui, M.M.P., Lam, J.C.W., Ng, T.Y., Ang, P.O., Murphy, M.B., Lam, P.K.S., 2017. Occurrence, distribution, and fate of organic UV filters in coral communities. Environ. Sci. Technol. 51, 4182–4190. https://doi.org/10.1021/acs.est.6b05211.

Usseglio-Polatera, P., Bournaud, M., Richoux, P., Tachet, H., 2000. Biological and ecological traits of benthic freshwater macroinvertebrates: relationships and definition of groups with similar traits. Freshw. Biol. 43, 175–205. https://doi.org/10.1046/j.1365-2427.2000.00535.x.

Vragovic, N., Bazulic, D., Njari, B., 2011. Risk assessment of streptomycin and tetracycline residues in meat and milk on Croatian market. Food Chem. Toxicol. 49, 352–355. https://doi.org/10.1016/j.fct.2010.11.006.

Wang, W., Yu, K., Wang, Y. A review on the research of coral reefs in the Weizhou Island, Beibu Gulf (in Chinese). Trop. Geogr. 2016; 36: 72–79. doi: Not Applicable.

Whittemore, A.S., Jung, D., Lee, M.M., Paffenbarger Jr, R.S., Wu-Williams, A., Ling, C., et al., 1994. Comparison of dietary habits, physical activity and body size among Chinese in North America and China. Int. J. Epidemiol. 23, 984–990. https://doi.org/10.1093/ije/23.5.984.

Wikipedia. Coral reef fish. 2019, 2019.

Xu, W.H., Yan, W., Li, X.D., Zou, Y.D., Chen, X.X., Huang, W.X., et al., 2013. Antibiotics in riverine runoff of the Pearl River Delta and Pearl River Estuary, China: concentrations, mass loading and ecological risks. Environ. Pollut. 182, 402–407. https://doi.org/10.1016/j.envpol.2013.08.004.

Yang, J.-F., Ying, G.-G., Zhao, J.-L., Tao, R., Su, H.-C., Chen, F., 2010. Simultaneous determination of four classes of antibiotics in sediments of the Pearl Rivers using RRLC-MS/MS. Sci. Total Environ. 408, 3424–3432. https://doi.org/10.1016/j.scitotenv.2010.03.049.

Yu, K., 2012. Coral reefs in the South China Sea: their response to and records on past environmental changes. Sci. China-Earth Sci. 55, 1217–1229. https://doi.org/10.1007/s11430-012-4449-5.

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. https://doi.org/10.1021/acs.est.5b00729.

Zhang, R., Pei, J., Zhang, R., Wang, S., Zeng, W., Huang, D., et al., 2018a. 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. https://doi.org/10.1016/j.ecoenv.2018.02.006.

Zhang, R., Tang, J., Li, J., Zheng, Q., Liu, D., Chen, Y., et al., 2012. Antibiotics in the offshore waters of the Bohai Sea and the Yellow Sea in China: occurrence, distribution and ecological risks. Environ. Pollut. 174, 71–77. https://doi.org/10.1016/j.envpol.2012.11.008.

Zhang, R., Yu, K., Li, A., Wang, Y., Huang, X., 2019. Antibiotics in corals of the South China Sea: occurrence, distribution, bioaccumulation, and considerable role of coral mucus. Environ. Pollut. 250, 503–510. https://doi.org/10.1016/j.envpol.2019.04.036.

Zhang, R., Zhang, R., Yu, K., Wang, Y., Huang, X., Pei, J., et al., 2018b. 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. https://doi.org/10.1016/j.envpol.2017.09.064.

Zhao, J.-L., Liu, Y.-S., Liu, W.-R., Jiang, Y.-X., Su, H.-C., Zhang, Q.-Q., et al., 2015. Tissue-specific bioaccumulation of human and veterinary antibiotics in bile, plasma, liver and muscle tissues of wild fish from a highly urbanized region. Environ. Pollut. 198, 15–24. https://doi.org/10.1016/j.envpol.2014.12.026.

Zhao, M., Yu, K., Zhang, Q. Review on coral reefs biodiversity and ecological function (in Chinese). Acta Ecol. Sin. 2006; 26: 186–194. doi: Not Applicable.

Zhong, M., Tang, J., Mi, L., Li, F., Wang, R., Huang, G., et al., 2017. Occurrence and spatial distribution of organophosphorus flame retardants and plasticizers in the Bohai and Yellow Seas, China. Marine Pollut. Bull. 121, 331–338. https://doi.org/10.1016/j.marpolbul.2017.06.034.

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. https://doi.org/10.1016/j.envpol.2011.04.037.