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Antibiotics in the aquatic environments: A review of lakes, China

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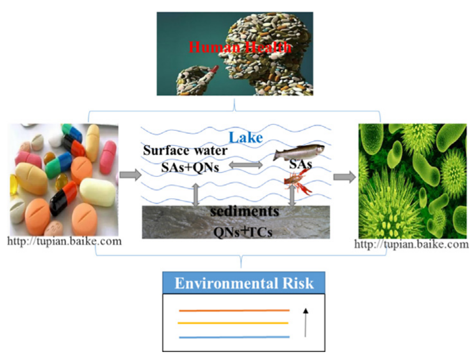
HIGHLIGHTS

- 39 antibiotics are detected in aquatic environment of lakes in China
- The quinolone antibiotics are predominant risk and pollution factors in aquatic environment of lakes.
- All Lakes experience ARGs pollution with high detection frequencies of sulfonamide and tetracycline resistance genes.

GRAPHICAL ABSTRACT



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ABSTRACT

The potential threat of antibiotics to the environment and human health has raised significant concerns in recent years. The consumption and production of antibiotics in China are the highest in the world due to its rapid economic development and huge population, possibly resulting in the high detection frequencies and concentrations of antibiotics in aquatic environments of China. As a water resource, lakes in China play an important role in sustainable economic and social development. Understanding the current state of antibiotics in lakes in China is important. Closed and semi-closed lakes provide an ideal medium for the accumulation of antibiotics and antibiotic resistance genes (ARGs). This review summarizes the current levels of antibiotic exposure in relevant environmental compartments in lakes. The ecological and health risks of antibiotics are also evaluated. This review concludes that 39 antibiotics have been detected in the aquatic environments of lakes in China. The levels of antibiotic contamination in lakes in China is relatively high on the global scale. Antibiotic contamination is higher in sediment than water and aquatic organisms. Quinolone antibiotics (QNs) pose the greatest risks. The contents of antibiotics in aquatic organisms are far lower than their maximum residual limits (MRLs), with the exception of the organisms in Honghu Lake. The lakes experience high levels of ARG contamination. A greater assessment of ARG presence and antibiotic exposure are urgent.

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Contents

1. Introduction

Antibiotics are routinely used in human and veterinary medicine for the therapeutic treatment of infectious diseases, as well as for animal growth promoters (Kümmerer, 2009a; Zhu et al., 2013). However, antibiotics are excreted as the parent compounds or metabolites due to poor gut absorption or incomplete metabolism (Q. Chen et al., 2017, Y. Chen et al., 2017), resulting in frequent detection in aquatic environment due to incomplete removal of antibiotics during wastewater treatment and their continued release into the environment (Hirsch et al., 1999; Kümmerer, 2009b; Ma et al., 2016). The consumption and production of antibiotics in China are the highest in the world (Xin, 2014). The prescriptions including antibiotics account for 70%, while the proportion is only about 30% in western countries, and annual per-capita consumption reaching 138 g are approximately 2 times those of the Europe and 10 times those of the United States (Richardson et al., 2005; Yang et al., 2012; Kan et al., 2015). The production of antibiotics in 2013 was up to 2.48×10^5 t which had almost tripled since 2009, and the usage of antibiotics in 2013 is up to 1.62×10^5t with antibiotics of 5.0 $\times$ 10^4t/yr into water and soil environment (Zhang et al., 2015). Therefore, the concentrations and detection frequencies of antibiotics in aquatic environment in China are higher than that of some western countries (Qiao et al., 2017). Antibiotics could lead to a selective pressure on the water bacteria and induce the formation of antibiotic resistant bacteria, reducing their therapeutic potential against human and animal pathogens (Carvalho and Santos, 2016; Qiao et al., 2017). Therefore, the antibiotic residues in aquatic environment could pose a potential threat to environment and human health.

Lakes, which are important freshwater resources and for flood regulation, are closely related to human production and life (Feng et al., 2012; Chen et al., 2014). China is a country with many lakes, and preliminary statistics show that China has approximately 2800 lakes with an area larger than 1 km^2 (Le et al., 2010, G. Yang et al., 2010, J.F. Yang et al., 2010). The freshwater resources amount to 2.3×10^{11} m^3 (Lu et al., 2017). Approximately 50% of urban drinking water sources, almost 1/3 of national grain output and over 30% of the total output value of industry and agriculture are from lake basins (Leng et al., 2003), However, rapid development has greatly expanded the industry, agriculture and aquaculture of lake basins, which inevitably causes a large number of antibiotics to be used. Zhang et al. (2015) found that the emissions of antibiotics (2190–3560 t yr^{-1}) in the Dongting Lake basin were the highest in China. However, the occurrence and environmental risk of antibiotics in the lakes of China are not clear.

To our knowledge, this study collected all published research of occurrence of antibiotics in water, sediment and aquatic organisms of typical Lakes by 2017 according to http://www.cnki.net/, https://xue.glgoo.net/, http://xueshu.baidu.com/, and http://www.sciencedirect.com/. Some information of Lakes are provided in Table S1. This review aims to summarize the contamination status of current antibiotics and antibiotic resistance genes in different environmental media of Lakes in China and assess their potential threats to environment and health risk. The results could provide reliable information regarding the exposure and risk levels of antibiotics of Lakes in China, which are important for establishment the supervision legal framework (market entry permitting system, drug advertising restrictions and strict and clear application process for antibiotic use) of the antibiotic misuse and the water quality criteria and discharging standard of antibiotics.

2. Occurrence

2.1. Surface water

The concentrations of antibiotics in the surface water of typical lakes in China are provided in Table 1. Thirty-seven antibiotics, including 14 sulfonamides (SAs), trimethoprim (TMP), 9 quinolones (QNs), 5 tetracyclines (TCs), 6 macrolides (MCs) and 2 lincosamides (LNs), have been detected in the surface water of typical lakes in China. Some information about antibiotics is provided in Table S2. The sulfonamides and quinolone antibiotics are the main contamination factors, which is similar to the case in other surface water bodies (Table 2). The concentrations of antibiotics in the surface water of lakes range from not detected (ND) (a concentration below the smallest value that the analytical methods measured) to 940 ng L^{-1}, which is below the μg L^{-1} grade.

The concentrations of SAs range from ND-940 ng L^{-1} (Table 1). The concentration of sulfamethoxazole (SMX) is higher than that of other SAs and includes the highest concentration, 940 ng L^{-1}. The highest concentration indicates that the exposure level to SMX is highest in Baiyangdian Lake, followed by Chaohu Lake and Taihu Lake. The production scale and the uses of SMX in China are among the highest in the world. In addition, detecting SMX, one of 14 sulfonamide antibiotics, needs to be prioritized according to the U.S. Food and Drug Administration (FDA) (Wang et al., 2016). SMX is among the most widely used prescribed antibiotics: the usage of SMX is sixth in Canada (Nasuhoglu et al., 2011), and the frequency of SMX detection in aquatic environments is high (Wang et al., 2014). The large scale of livestock and poultry farming and the high population density in lake basins result in high usage of SMX. The highest concentrations of sulfamethazine (SMT) and sulfadiazine (SDZ) are 654.0 ng L^{-1} (Taihu Lake) and 505 ng L^{-1} (Baiyangdian Lake), respectively, showing the high SA contamination levels; these levels may be related to the approval of SAs for use in aquaculture [http://www.fishfirst.cn/article-35467-1.html]. SMX, SMT and SDZ, as dominant SA contaminants, have similar levels in other surface water bodies (Table 2). The highest concentrations of SMZ and SMT

Table 1
Occurrence of antibiotics in surface water of Lakes in China (ng L^{-1}).

Antibiotics	Baiyangdian Lake		Bosteng Lake	Ulungur Lake	Taihu Lake		
	Range (mean)	Range (mean)	Range	Range	Range (mean)	Range (mean)	Mean
SMM	ND-23.1(6.92)	–	–	–	–	–	–
SPD	ND-85(13)	–		–	–	–	–
SDZ	0.86–505(118)	–	2.88–37.27	1.03–3.68	–	–	–
STZ	ND-1.38(0.08)	–	–	–	ND-134.5(45.9)	–	–
SAAM	–	–	11.56–48.26	0.53–2.2	–	–	–
SIZ	–	–	3.34–10.36	1.45–5.38	–	–	–
SMT	ND-16.1(5.25)	–	1.12–13.28	ND-1.87	ND-654.0(252.7)	–	ND
SMX	ND-940(240)	–	–	–	ND-114.7(48.4)	7.4–53.7(24.01)	15.7
SMR	ND	–	–	–	ND-61.4(44.4)	–	–
SDX	ND	–	–	–	–	–	–
SCP	–	–	–	–	ND-43.3(11.9)	–	–
SIA	ND	–	–	–	ND-89.4(27.1)	–	–
TMP	–	–	–	–	ND-40.8(12.0)	–	12.6
FLE	ND-6.35(2.29)	–	–	–	–	–	–
NOR	ND-156(28.6)	3–97(31.6)	–	–	ND-6.5(4.3)	15.4–55.6(27.8)	–
OFL	0.38–32.6(9.23)	2.02–9.43(4.33)	1.3–32.4	ND-9.41	ND-82.8(32.2)	7.4–16.68(12.8)	–
CIP	ND-60.3(9.45)	–	17.33–112.3	2.56–28.65	ND-43.6(8.8)	–	–
ENR	ND-4.42(1.28)	–	ND-15.22	ND-0.58	ND	–	–
SFL	ND-28.2(9.3)	–	–	–	–	–	–
LOM	ND	–	ND	6.34–53.85	–	–	–
DIF	ND	–	–	–	–	–	–
OTC	–	4.64–90.3(27.17)	ND-6.6	<LOQ-9.89	ND-72.8(44.2)	–	–
TC	–	8.07–85.19(25.95)	ND-2.84	0.69–2.7	ND-87.9(43.2)	–	–
CTC	–	–	ND-3.11	ND-6.67	ND-142.5(67.9)	–	–
DC	–	–	ND-4.92	ND-2.06	–	–	–
ERM	ND-121(19.5)	–	ND-0.97	ND-1.24	ND-624.8(109.1)	–	6.7
ROM	ND-155(27.2)	–	0.68–5.94	ND-4.87	ND-218.3(50.7)	–	–
SPI	ND-2.92(0.24)	–	ND-3.99	ND-1.86	–	–	–
TYL	ND-1.88(0.1)	–	ND-0.66	ND	–	–	–
JOS	ND-0.9(0.07)	–	–	–	–	–	–
CLA	–	–	–	–	–	–	ND
LIN	–	–	–	–	–	–	357
CLD	–	–	–	–	–	–	503
Reference	Li et al., 2012	Cheng et al., 2014	Lei, 2014		Xu et al., 2014	Lu et al., 2013	Wu et al., 2014

Antibiotics	Poyang Lake		Chao lake			Dongting Lake			Dianchi Lake
	Mean	Range	Mean	Range (mean)	Range	Range	Mean	Range	Range
SCY	–	–	–	ND - 4. 6(2.6)	–	–	–	–	–
SPD	–	ND-17.2	–	–	–	–	–	–	–
SDZ	–	ND-56.2	–	ND-45.6(7)	ND-8.4	–		ND-61.28	–
STZ	–	ND-16.7	–	–	–	–	–	–	–
SMT	0.9	ND-22.2	3.0	ND-4.7(2.1)	ND-9.9	–	ND	ND-14.88	–
SMX	ND	ND-14.5	18.9	ND-137. 9(19.6)	ND-171.6	–	ND	ND-47.41	17.6–499.2
SCP	–	–	–	ND-8. 8(4.3)	ND-1.1	–	–	–	–
SIA	–	–	–	–	ND-3.7	–	–	–	–
TMP	ND	–	26.0	–	–	ND	10	ND-2.25	–
NOR	–	ND ≤ LOQ	–	ND-34.8(17.1)	ND-70.2	–	–	ND-1.65	–
OFL	–	ND ≤ LOQ	–	–	ND-50.6	–	–	ND-0.53	ND-713.6
CIP	–	ND-8.6	–	ND-13.6(10.4)	ND-23.2	–	–	ND-36.17	–
ENR	–	ND-5.5	–	ND-81.7(13.7)	ND-10.8	–	–	ND-4.61	–
SFL	–	<LOQ-3.4	–	–	–	–	–	ND-21.29	–
LOM	–	–	–	ND-2.6(1.3)	ND-5.5	–	–	–	–
ENX	–	ND ≤ LOQ	–	–	–	–	–	–	–
DIF	–	ND-5.3	–	ND-4.4(4.1)	ND-10.4	–	–	–	–
DOC	–		–	–	ND-5.7	–	–	–	–
OTC	–	ND-48.7	–	ND-4.9(4.2)	ND-2.5	–	–	ND	<20
TC	–	ND-10.8	–	ND-9.8(5.5)	ND-17.8	–	–	ND-21.51	
CTC	–	ND-18.1	–	ND-4.4(3.5)	ND-4	–	–	ND-6.5	
DC	–	ND-39.7	–	ND-42.3(42.3)	–	–	–	–	–
ERM	1.1	ND-10.7	20.7	–	–	–	8.4	–	–
ROM	–	ND-11.1		–	–	–	–	–	0.9–314.2
CLA	0.4	–	10.6	–	–	–	ND		–
LIN	50.2	ND-16.5	64.5	–	–	–	11.3		–
CLD	0.6	–	46.7	–	–	–	7.8		–
Reference	Wu et al., 2014	Ding et al., 2017	Wu et al., 2014	Tang et al., 2013, 2014	Tang et al., 2015	Ma et al., 2016	Wu et al., 2014	Our research	Wei et al., 2014

–: not studied, ND (not detected) is not a concentration or lower end of analytics.

are higher in lakes than other surface water bodies except for the Liao River and the Huangpujiang River, and the SDZ level is significantly higher in lakes than other surface water bodies. The concentrations of other SAs are lower than four antibiotics listed above. Trimethoprim (TMP), an antibacterial synergist, is commonly used in combination with sulfa drugs, especially SMX and SDZ, in a ratio of 1:5 (Ryan et al., 2011; Fu et al., 2016). The maximum concentrations of SAs are 3 ng L^{-1} in the Choptank River in the U.S.A., 77 ng L^{-1} in Lake Michigan

Table 2
Occurrence of antibiotics in other surface water bodies (ng L^{-1}).

Antibiotics	U.S.A (Choptank River)	U.S.A (Michigan Lake)	UK·(Taff River)	UK (Ely River)	Vietnam (the Mekong River and the canals)	France (Seine River)	Finland (Vantaa River)	France (small Mediterranean stream)	Beibu Gulf	Bohai Bay
	Range	Max	Range	Range	Range (mean)	Max	Range	Range	Range	Range (mean)
SCY	ND	<4.1	–	–	–	–	–	–	–	–
SDZ	–	ND-3.8	–	–	–	–	–	–	ND-3.41	ND-41(17)
STZ	ND	<2.6	–	–	–	–	–	–	ND	–
SAAM	–		–	–	–	–	–	–	ND	–
SMT	ND	<4.0			15–328(62)	<10	–	–	ND-3.39	ND-130 (37)
SMX	ND-2	ND-77	ND-8	ND-4	20–174(80)	544	–	ND	ND-10.4	ND-140 (19)
SMR	ND	ND-3.6	–	–	–	–	–	–	–	–
SDX	ND-3	<2.4	–	–	–	–	–	–	–	–
TMP	–	ND-13	ND-120	ND-183	7–44(20)	45	–		ND-3.77	ND-120 (54)
NOR	–	<5.1	–	–	–	163	<LOQ			ND-6800 (460)
OFL	–	21	–	–	–	–	<LOQ-5			ND-5100 (390)
CIP	–	<3.3	–	–	–	<10	<LOQ-36	ND-9660		ND-390 (110)
ENR	–		–	–	–	<10	–	–	–	–
SFL	–	<5.4	–	–	–	<10	–	–	–	–
LOM	–	<4.7	–	–	–	<10	–	–	–	–
OTC	ND-47		–	–	–	–	–	ND-680		ND-270 (93)
TC	ND-5		–	–	–	–	–	–	–	ND-30(16)
CTC	ND-34		–	–	–	–	–	–	–	–
DC	ND-20		–	–	–	–	–	–	–	–
ERM	–		ND-121	ND-72	9–41(32)	–	–	–	1.1–50.9	ND-150 (30)
ROM	–	ND-39	–	–	–	–	–	–	ND-0.53	ND-630 (113)
ATM	–	ND-22	–	–	–	–	–	ND	ND-0.64	–
LIN	–	<3.2	–	–	–	–	–	–	–	–
SPI	–	–	–	–	–	–	–	–	ND	–
CLA	–	<3.1	–	–	–	–	–	ND-2330	ND-0.72	–
	Arikan et al., 2008	Blair et al., 2013	Kasprzyk-Hordern et al., 2009	Managaki et al., 2007	Tamtam et al., 2008	Vieno et al., 2007	Feitosa-Felizzola and Chiron, 2009	Zheng et al., 2012	Zou et al., 2011	

Antibiotics	Hai River	Pearl River Estuary	Yellow River	Huangpu River		Jiulong River	Laizhou Bay	Liao River	Yangtze River
	Average	Average (max)		Range	Range (mean)	Range	Range (mean)	Range (mean)	Range (mean)
SCY	(2.1 ± 1.7) × 10^2	–	–	3.25–58.29	–	–	–	ND-13.52(0.98)	–
SMM	–	–	–	–	–	ND-46	–	–	–
SPD	–	–	–	1.14–57.39	ND-103.1(24.1)		–	ND-0.96	–
SDZ	(1.7 ± 0.8) × 10^2	18 (4.42)	–	1.39–40.55	4.9–112.5(53.6)	ND-60.5	ND-0.43(0.02)	–	–
SME	–	–	–	–	–	–	–	–	–
STZ	–	–	–	–	ND-121.1(34.1)	–	–	ND-7.5(0.8)	–
SAAM	–	–	–	–		–	–	ND-12.5(1.24)	–
SMT	–	28.9(218)	–	2.05–623.27	19.9–389.4(188.9)	ND-124.4	1.5–82(19)	ND-15.91(3.55)	4.4–20.9 (14.5)
SMX	(1.9 ± 0.1) × 10^2	37.6 (12.4)	<LOQ-56(25)	4.86–55.24	2.2–764.9(259.6)	ND-93.4	ND-1.5(0.13)	ND-1483.9(104.9)	ND-18.5(7.9)
SIA	–	–	–	–	–	–	–	–	–
SMR	–	–	–	ND	<LOQ	–	–	ND	–
SDX	–	–	–	–	–	–	–	ND-5.9(0.94)	–
TMP	(1.4 ± 0.8) × 10^2		–	2.23–62.39		–	1.3–330(53)	–	ND
FLE	–	–		ND	–	–		–	–
NOR	–	136 (67)	<LOQ-300 (152)	ND	ND-0.2		7.5–103(40)	ND-256.03(49.03)	–
OFL	(1.8 ± 1.2) × 10^2	15.8 (7.1)	LOQ-264 (114)	<LOQ	ND-28.5(6.5)	ND-46.2	ND-6.5(0.24)	ND-632.52(37.93)	–
CIP	(1.3 ± 0.5) × 10^2		–	<LOQ	ND-34.2(2.7)		Nd-66(31)	ND-185.14(11.6)	–
ENR	–	ND	–	<LOQ	ND-14.6(2.8)	ND-60.8	N-7.6(1.8)	ND-70.36(25.72)	–
SFL	–	–	–	ND	–	–	–	–	–
LOM	–	–	–	–	–	–	–	–	–

Table 2 (*continued*)

	Hai River	Pearl River Estuary	Yellow River	Huangpu River		Jiulong River	Laizhou Bay	Liao River	Yangtze River
	Average	Average (max)		Range	Range (mean)	Range	Range (mean)	Range (mean)	Range (mean)
ENX	–	–	–	–	–	–	ND-209(62)	–	–
DOC	–	–	–	<LOQ-46.93	ND-112.3(11.3)	–	–	–	–
OTC	$(4.0 \pm 0) \times 10$	–	–	11.49–84.54	ND-219.8(78.3)	–	–	ND-741.85(22.41)	–
TC	$(2.7 \pm 0.3) \times 10$	13.1 (7.37)	–	<LOQ-113.89	ND-54.3(4.2)	–	–	ND-28.65	–
CTC	–	–	–	<LOQ-16.8	ND-46.7(3.6)	–	–	ND-25.05(1.38)	–
DC	–	–	–			–	–	–	–
ERM-H_2O	$(3.8 \pm 0.6) \times 10$	121 (29.9)	<LOQ-102 (34)	0.13–9.93	0.4–6.9(3.9)	–	0.9–8.5(2.6)	ND-2834.36 (165.41)	ND-808(296)
ROM	$(3.7 \pm 0.8) \times 10$	ND	<LOQ-95(53)		0.2–2.2(0.9)	–	<LOQ-0.5(0.38)	ND-740.99(36.47)	–
ATM	–	–	–	–	–	–	ND-1.2(0.14)	–	–
SPI	–	–	–	–	–	–	–	–	–
TYL	–	–	–	0.06–0.61	–	–	–	–	–
JOS	–	–	–		–	–	–	–	–
LIN	–	–	–	–	–	–	–	–	ND-71.9 (13.3)
CLD	–	–	–	–	–	–	–	–	1.2–16.5(9.1)
CLA	–	–	–	–	–	–	ND-0.82(0.19)	–	ND-103(18)
	Luo et al., 2011	Liang et al., 2013	Xu et al., 2009	Jiang et al., 2011	Chen and Zhou, 2014	Zheng et al., 2011	Zhang et al., 2012	Bai et al., 2014	Wu et al., 2014

–: not studied, ND (not detected) is not a concentration or lower end of analytics.

in the U.S.A., 8 ng L^{-1} in the Taff River in the U.K., 4 ng L^{-1} in the Ely River in the U.K., 328 ng L^{-1} in the Mekong River and canals in Vietnam, and 544 ng L^{-1} in the Seine River in France. Based on these data, the maximum detected concentration of SAs in lakes in China is considerably higher than that in surface water in the U.S.A., the U.K., Vietnam and France. Most developed countries began controlling the release of antibiotics into water at an earlier date. The maximum detected concentration of SAs in lakes in China are higher than those in rivers or bays in China, except for that of the Liao River, which reflected a high quantity of antibiotic usage and waste discharge into the river. On the whole, the maximum concentration of SAs in Lakes in China are at high levels when compared to other surface water worldwide. The highest concentration of TMP is 40.8 ng L^{-1} (Taihu Lake), which is similar to its level in the Huangpujiang River and significantly lower than that in the Taff River, the Ely River, Bohai Bay, the Hai River and Laizhou Bay. Aquatic environments of lakes are contaminated with TMP at a lower level than other antibiotics.

Among the QNs, the concentration of ofloxacin (OFL) (713.6 ng L^{-1}, Dianchi Lake) is the highest (Table 1); its level at Dianchi Lake is lower than at Bohai Bay, similar to its level at the Liaohe River and significantly higher than its level at the surface of other rivers (Table 2). The concentration of norfloxacin (NOR) (156 ng L^{-1}, Baiyangdian Lake) is the second highest of the quinolone antibiotics in lakes after OFL, is lower than the NOR level in Bohai Bay, the Yellow River and the Liaohe River and is similar to the NOR level in the Seine River, the Pearl River Estuary and Laizhou Bay. The use of lomefloxacin (LOM) is low in most lakes in China. However, the highest concentration of LOM is 53.85 ng L^{-1}, which is higher than that found in other surface water bodies. In Ulungur Lake of north Xinjiang, the detection frequency of LOM is the highest of the detected antibiotics, which are closely related to developed livestock and poultry breeding (Lei, 2014). Because of potential safety hazards, LOM, OFL and NOR were prohibited from being produced and used in food animals after September 1, 2015, and these antibiotics were no longer circulated after December 1, 2015 (Ministry of Agriculture of the People's Republic of China, 2015). Future surveys should be enhanced to explore the occurrence of these 3 antibiotics in aquatic environments before and after the policy. In addition, the highest concentrations of ciprofloxacin (CIP) and enrofloxacin (ENR) are 112.3 ng L^{-1} (Bosten Lake) and 81.7 ng L^{-1} (Chaohu Lake), respectively, which are higher than their levels in other surface water bodies (Table 2) except for a small Mediterranean stream (Feitosa-Felizzola and Chiron, 2009), Bohai Bay (Zou et al., 2011) and the Liao River (Bai et al., 2014). The usage of CIP peaks in the medical field (Zhang and Liu, 2010), and ENR and CIP are permitted for use in aquaculture, which might result in their high concentrations in water. The concentrations of sarafloxacin (SFLO), enoxacin (ENX), fleroxacin (FLE) and difloxacin (DIF), ranging from ND-28.2 ng L^{-1}, are lower than those of other QNs. The maximum concentration of QNs is far higher in the surface water of China than in the surface water in other countries and regions (U.S.A., U.K., Finland and France). However, the maximum concentration of QNs in lakes is less than only that in the surface water of Bohai Bay and is similar to that of the Liao River. Bohai Bay, a typical semi-enclosed inner sea, receives wastewater and municipal sewage from not only many factories located in the vicinity but also from the city of Beijing (Zou et al., 2011), which results in high concentrations of antibiotics. The maximum concentration of QNs in lakes in China are high on the global scale.

TCs constitute one of the most extensively used antibiotic classes due to their low cost, ease of use and relatively minor side effects (Li et al., 2016; Ahmed et al., 2017). In Kenya, 14.6 t of antibiotics are used in livestock and poultry farming each year; TCs account for 56% of these (Sarmah et al., 2006). TCs are also the most widely used veterinary drugs and feed additives in aquaculture and livestock industries of China. The concentrations of TC and oxytetracycline (OTC) in lakes are higher than those of other TC antibiotics (Table 1), which is similar to what is found in rivers (Table 2). In China, TCs are produced and consumed in large scale. In 2008, the exports of TCs were 1.34×10^7 t (He et al., 2011). TC and OTC are also added at the subtherapeutic level to animal feed to prevent infection and act as growth promoters. In 1999, the usage of tetracycline reached 9413 t (Hu et al., 2008). The production of OTC in China has increased to 10^4 t, which accounts for 65% of the world's total OTC production (Sarmah et al., 2006). In addition, the highest concentration of chlortetracycline (CTC) is 142.5 ng L^{-1} (Taihu Lake), which is higher than the highest concentrations of TC and OTC. In 2010, the CTC usage reached approximately 7.19×10^4 t, which is 22 times the annual usage of TCs in America (Sarmah et al., 2006; Kim et al., 2011). However, the concentrations of TCs are lower than those of other antibiotic classes. TCs have high distribution coefficients (Kd) (e.g., OTC 420–1030 L kg^{-1}, TC 1140–1620 L kg^{-1} and CTC 401 L kg^{-1}) and are susceptible to being preferentially adsorbed on solid environmental matrices (Beausse, 2004; Xu et al., 2014). In addition, the degradation of TCs, in contrast to that of other antibiotics, is greatly affected by the pH and temperatures of surface water (Doi and Stoskopf, 2000). The maximum concentration of TCs in lakes in China is higher than that in the Choptank River in the U.S.A., the Haihe River, the Pearl River Estuary and the Yellow River; however, that concentration is lower than that in a small Mediterranean stream in France, the Beibu Gulf, Bohai Bay, Laizhou Bay, the Huangpu River, the Jiulong River and the Liao River. Exposure to TCs is at moderate levels or below.

The concentrations of erythromycin (ERM) and roxithromycin (ROM) are relatively high among those of the six MCs, with maximum concentrations of 624.8 ng L^{-1} and 218.3 ng L^{-1} (Taihu Lake) (Table 1), respectively. These concentrations are higher than those of other surface water bodies except for those of the Yangtze River, the Liaohe River and Bohai Bay (Table 2). Exposure to MCs in aquatic environments of China is similar to that of other surface water bodies. MCs are widely used in concentrated animal feeding operations to treat bacterial infection diseases of animal and human, such as respiratory diseases, intestinal infections and mastitis (Sevilla-Sánchez et al., 2010). The MCs ERM and ROM are mainly used in clinics and are stable in sewage during treatment (Xu et al., 2007). Tylosin (TYL), clarithromycin (CLA) and azithromycin (AZM) are used to a great degree. The usage of TYL in China is 15 times of that of the U.S.A. (Sarmah et al., 2006; Kim et al., 2011). However, the concentrations of TYL and CLA are relatively low among the MCs; a limited number of studies concentrate on exposure to AZM in lakes, so subsequent studies should be strengthened. The maximum concentration of MCs in lakes in China is higher than that in Lake Michigan in the U.S.A., the Taff River in the U.K., the Ely River in the U.K., the Mekong River and canals in Vietnam, the Beibu Gulf, Laizhou Bay, the Haihe River, the Pearl River Estuary, the Yellow River, the Huangpu River and the Jiulong River but is lower than that in the Liao River, the Yangtze River and Bohai Bay. The maximum concentration of MCs in lakes in China are high on the global scale.

LNs are useful against gram-positive bacteria and usually used for the treatment of aerobic and anaerobic mixed infections (Kadlcik et al., 2017). In addition, LNs are widely used in the treatment of respiratory diseases and intestinal bacterial infections of livestock and poultry but are also used in feed additives to improve feed conversion rates and to promote livestock and poultry growth [http://www.moa.gov.cn/zwllm/zcfg/qtbmgz/200601/t20060123_540610.htm]. Relatively high concentrations of lincomycin (LIN) (357 ng L^{-1}) and clindamycin (CLD) (503 ng L^{-1}) are detected in Tai Lake (Table 1). The thriving animal and aquaculture operations near the lakes may be important sources of LIN and CLD (Wu et al., 2014). The levels of exposure to LIN and CLD are relatively higher in lakes than in other surface water bodies (Table 2).

At present, most studies of antibiotics in the lakes of China concentrate on the lakes of the middle and lower reaches of the Yangtze River. The levels of exposure to SAs are the highest, followed by those of QNs > MCs > LINs > TCs > TMP according to their highest concentrations. SAs exhibit high solubility and chemical stability in water, resulting in their high accumulation (Huang et al., 2011). The contamination of SAs is most prominent in Taihu Lake and Baiyangdian Lake, while QN contamination is highest in Dianchi Lake and Baiyangdian Lake, Chaohu Lake for TMP, Taihu Lake and Baiyangdian Lake for TCs, Taihu Lake, Baiyangdian Lake and Dianchi Lake for MCs and Taihu Lake and Chaohu Lake for LINs. The exposure to antibiotics is greater in Taihu Lake and Baiyangdian Lake than the other lakes due to a higher emission density of antibiotics. Insight into why these concentrations differed is limited at the regional scale. The occurrence of antibiotics in aquatic environments could be affected by photolysis, temperature, pH, dilution factors, the populations being served, and hydraulic residence times (Yoshizaki and Tomida, 2000; Loftin et al., 2008, Kümmerer, 2009a, b). However, most studies concentrated on bench-scale experiments (Luo et al., 2011), which do not reflect actual environments at the regional scale of lakes or rivers. The differences in the occurrence of antibiotics in different lakes and rivers should therefore receive further exploration. The reasons that the concentrations differ are poorly understood and include dilution factors, wastewater treatment plant (WWTP) discharge, the populations that are served, and the hydraulic residence time. The contamination level is relatively high on a global scale. Most of the lakes are half-closed or enclosed water bodies, which results in insufficient water mobility and a high pollution load.

2.2. Sediment

The contents of antibiotics in the sediment of typical lakes in China are shown in Table 3. Twenty-nine antibiotics, including 13 SAs, TMP, 7 QNs, 4 TCs and 4 MCs, are detected in the sediment of typical lakes in China. The contents of antibiotics in the sediment of lakes range from ND to 1140 ng g^{-1}. The QNs and TCs are the main contamination factors, which is similar to the case in other surface water bodies (Table 4). QNs are easily adsorbed in sediment, and TCs have a high affinity for soil organic matter through cation bridging and cation exchange (Figueroa et al., 2004; Zhang and Dong, 2008).

The contents of SAs in the sediment of lakes range from ND to 118.76 ng g^{-1} (Table 3). The concentration of SMX in sediment is higher than that of other SAs, and its highest concentration is 118.76 ng g^{-1} (Honghu Lake). The second highest SA concentration is that of sulfameter (SME) (114.24 ng g^{-1}, Honghu Lake). The SA content is higher in Honghu Lake than other lakes. In 2015, the aquaculture area in Honghu Lake reached 5.79×10^4 ha, with a total output of aquatic organisms of 4.85×10^5 t, which was at the top of Hubei province and country rankings [http://www.hppc.gov.cn/2016/0708/18825.html]. The use of a large number of SAs may therefore be inevitable. Sediment, the source and point of convergence of various pollutants, could record the contamination of antibiotics, and antibiotics could accumulate as contamination in sediment. In addition, the SA contents in East Dongting Lake are relatively high. The population around East Dongting Lake is 1.78 × 106, the population density is high, and the two WWTPs of Yueyang City are very close to East Dongting Lake (Yang et al., 2016). The maximum concentration of SAs in other surface water bodies (Table 4) are below 11 ng g^{-1}, which is far lower than that in lakes in China. The SA contents in the sediment of lakes in China are therefore at high levels. However, the contents of SAs are relatively lower than those of other antibiotic classes, which may be related to their low Kds (e.g., SMT 1–3.1 L kg^{-1}, SMX 0.22 L kg^{-1}, and STZ 4.9 L kg^{-1}) (Beausse, 2004). The highest content of TMP in the lakes of China is 39.3 ng g^{-1}, which is similar to the level found in the Wangyang River (Jiang et al., 2014).

The contents of QNs are relatively higher than those of other antibiotic classes, ranging from ND-1140 ng g^{-1} (Table 3). NOR content is the highest of the QNs, 1140 ng g^{-1} in Baiyangdian Lake, which is significantly higher than that in other surface water bodies (Table 4). According to the maximum concentrations, OFL (362 ng g^{-1}) and CIP (364.39 ng g^{-1}) are the second most abundant QNs after NOR, and their concentrations are higher in lakes in China than in other surface water bodies (Table 4) except for the Hai River (Zhou et al., 2011) and the Wangyang River (Jiang et al., 2014). NOR, CIP and OFL are the most used QNs, with over 5000 tons of each being used in 2013 (Zhang, 2015), resulting in antibiotic residue in sediment. The level of CIP exposure in Ulungur Lake and Bosten Lake of Xinjiang (Lei, 2014) is higher than that in other lakes. Animal husbandry is developed in Xinjiang, which has 18 counties in grazing areas, including 130 ranches that collectively account for an area of over 5.33×10^7 ha (Li, 2016). Most farms in Xinjiang are far from the city or in the suburbs of the city, and no sewage treatment facilities are essentially present, which results in large quantities of antibiotics being discharged into the environment. The usage of ENR in the breeding industry is large, similar to that of NOR, CIP and OFL (Zhang, 2015). However, the content of ENR in the sediment of lakes is relatively low, ranging from ND-

Table 3
Occurrence of antibiotics in sediments of Lakes (ng g^{-1}).

Antibiotics	Baiyangdian Lake		Dianchi Lake	Dongting Lake	East Dongting Lake	Hong Lake
	Range (mean)	Range (mean)	Range	Range	Range (mean)	Range (mean)
SDZ	ND-2.07(0.41)	–	–	ND-5.56	1.54–38.69(8.65)	0.81–77.26(37.74)
STZ	ND-5.94(0.64)	–	–	–	–	
SME	–	–	–	–	ND-105.29(32.27)	ND-114.24(49.65)
SMM	ND-0.5(0.06)	–	–	–	–	–
SMR	ND-2.47(0.05)	–	–	–	–	
SPD	ND-1.4(0.16)	–	–	–	–	–
SMZ	ND-6.92(1.47)	–	–	ND-1.63	ND-15.43(6.24)	ND-29.47(7.24)
SMX	ND-7.86(0.28)	–	–	ND-1.38	ND-115.35(30.57)	ND-118.765(7.32)
SIA	ND-1.71(0.71)	–	–	–	–	–
SDX	ND-0.2(0.04)	–	–	–	–	–
TMP	–	–	–	ND-0.6	–	–
FLE	ND-6.69(0.15)	–	–		–	–
NOR	49.4–1140(267)	103.97–550(274.76)	ND-55.2	ND	–	–
OFL	ND-362(21)	18.62–71.51(39.73)	ND-108.9	ND	–	–
CIP	ND-46(2.49)	–	ND-75.8	ND-1.89	–	–
ENR	ND-13(0.46)	–	–	ND-4.34	–	–
SFLO	ND	–	–	ND-1.84	–	–
LOM	ND-29(0.98)	–	–	–	–	–
DIF	ND	–	–	–	–	–
OTC	–	4.28–35.4(15.66)	ND-64.8	ND-1.34	0.26–42.77(18.4)	0.72–74.73(37.96)
TC	–	4.78–93.36(25.71)	ND-50.2	ND-3.76	3.07–84.35(39.85)	5.46–114.36(48.02)
CTC	–	–	ND-92.1	ND-3.01	ND-83.48(15.87)	ND-55.57(6.27)
DC	–	–	–	–	7.48–98.5(43.84)	ND-74.63(34.02)
ERY	ND-3.04(0.59)	–	–	–	–	–
ROM	ND-302(64.9)	–	–	–	–	–
SPI	ND	–	–	–	–	–
TYL	ND	–	–	–	–	–
JOS	ND	–	–	–	–	–
References	Li et al., 2012	Cheng et al., 2014	Wei et al., 2014	Our research	Yang et al., 2016	

Antibiotics	Hongze Lake	Taihu Lake	Ulungur Lake	Bosten Lake
	Range	Range (mean)	Range	Range
SDZ	–	–	ND-1.52	<LOQ-4.46
STZ	–	ND-51.7(17.8)	–	–
SAAM	–	–	ND- < LOQ	<LOQ-1.25
SIZ	–	–	ND- < LOQ	ND- < LOQ
SMZ	–	ND-99.8(39.8)	ND	ND
SMX	–	ND-49.3(16.1)	–	–
SIA	–	ND-22.6(11)	–	–
SDX	–	ND-15.7(6.9)	–	–
SCP	–	ND-15.8(7.3)	–	–
TMP	–	ND-39.3(9.3)	–	–
NOR	–	ND-28.4(9.9)	–	–
OFL	–	ND-52.8(16.5)	0.65–6.47	18.39–94.1
CIP	–	ND-25.3(9.8)	27.35–364.39	21.18–213.38
ENR	–	ND	ND-1.16	3.42–19.96
SFLO	–	–	8.27–66.5	–
LOM	–	–	–	ND
OTC	1.35–25.43	ND-196.7(52.8)	<LOQ-14.86	4.61–20.67
TC		ND-112.2(47.9)	3.65–16.31	2.65–11.65
CTC	–	ND-48.5(19)	2.79–42.83	4.62–17.28
DC	–	–	ND-3.69	<LOQ-9.96
ERY	–	ND-120.3(27.7)	0.82–3.51	2.18–6.01
ROM	–	ND-45.2(16.9)	3.21–9.06	4.10–14.74
SPI	–	–	ND-2.62	2.02–7.80
TYL	–	–	ND	ND-1.21
References	Luo et al., 2017	Xu et al., 2014	Lei, 2014	

–: not studied. ND (not detected) is not a concentration or lower end of analytics.

19.96 ng g^{-1} (Table 3), which is similar to that in other surface water bodies (Table 4). The nature of ENR and different doses in which it is applied could be the main reason for this behavior. The contents of other QNs except SFLO (66.5 ng g^{-1}) are in the range from ND-29 ng g^{-1}. SFLO is becoming increasingly widespread in clinical animal applications (Pulgarín et al., 2013). However, a limited number of studies concentrate on the level of exposure to SFLO in lakes. SFLO has a low PNEC (Lützhøft et al., 1999), which can pose a great potential threat to environments and humans, should be not ignored. On the whole, the contents of QNs are higher in lakes than other surface water bodies (Table 4) except for the Haihe River (Zhou et al., 2011) and the Wangyang River (Jiang et al., 2014). The contents of QNs are particularly high in the Yangyang River due to the sewage discharges it receives (Jiang et al., 2014), supporting that the occurrence of antibiotics are closely related to their sources.

The TC contents in the sediment of lakes are in range from ND-196.7 ng g^{-1} (Table 3). OTC content is the highest (196.7 ng g^{-1}, Taihu Lake), followed by TC (114.36 ng g^{-1}, Honghu Lake), and the contents of both antibiotics are higher in lakes than other surface water bodies (Table 4) except for the Liaohe River and the Wangyang River. In addition, the content of CTC is higher in some lakes than that of TC or OTC; this relation is found in Dianchi Lake (Wei et al., 2014)

Table 4
Occurrence of antibiotics in sediments of other surface water bodies (ng g^{-1}).

Sediment	U.S.A (Choptank River)	France (small Mediterranean stream)	U.S.A (Michigan Lake)	Northern (Colorado Cache La Poudre River)	Pearl River Estuary	Yellow River	Hai River	Liao River		Huangpu River	Wangyang River
	Max	Range	Mean		Max (mean)	Max		Max	Range	Range (mean)	Max
SCY	ND	–	–	–	–	–	–	–	ND	–	–
SPD	–	–		–	–	ND	ND	ND	ND-0.68	ND-6.6(1.7)	
SDZ	–	–	–	–	ND	22	1.18	11	–	0.07–0.71(0.4)	5.6
SME	–	–	–	–	–	–	–	–	–	–	–
STZ	ND	–			–	–	–	–	ND	ND-0.6(0.2)	1.7
SAAM	–	–	–	–	–	–	–	–	ND	–	–
SMT	0.816	–		13.7	3.24 (1.58)	ND	5.67	ND	ND-1.03	0.2–2.7(1.2)	2.2
SMX	0.145	–		1.9	ND	ND	ND	ND	ND-2.63	0.05–0.6(0.2)	2.4
SIA		–	–	–	–	–	–	–	–	–	–
SMR	ND	–		–	–	–	–	–	ND	0.03–0.8(0.2)	5.7
SDX	ND	–	–		–	–	–	–	ND-0.97	–	–
TMP		–	–	–	–	ND	5.63	9.84	–	–	38.4
NOR		–	36	–	20.5 (8.08)	141	5770	176	ND-52.48	–	801.3
OFL		–	7.7	–	12.6 (3.50)	123	653	50.5	ND-51.36	ND-12.4(4.1)	370.6
CIP		–	52	–	–	32.8	1290	28.7	ND-13.15	–	2118.9
ENR		–	6.6		1.43 (1.24)	ND	2.34	ND	ND-25.67	ND-8.9(3.2)	82.1
SFL	–	–	9.9	–	–	–	–	–	–	–	–
LOM		–	–	–		ND	298	5.82	–	–	–
DOC	–	–	–	–	–	–	–	–	–	ND-21.3(7)	–
OTC	ND	–	–	56.1	–	184	422	652	ND-384.59	0.6–18.6(6.9)	162,673
TC	ND	–	–	102.7	7.13 (2.64)	18	135	4.82	ND-7.97	ND-21.7(3.5)	16,799.1
CTC	10	–	–	30.8	–	ND	10.9	32.5	ND-12.26	ND-6.3(2.4)	698.3
DC	ND	–	–	38.9	–	ND	7	2.8	–	–	–
ERM-H_2O	–	–	25	25.6	14 (2.74)	49.8	67.7	40.3	ND-175.38	1.5–24.6(10.2)	26.7
ROM	–	–	71	5.9	13.5 (13.5)	6.8	11.7	29.6	ND-229.31	0.3–4.1(1.9)	2581.8
TYL	–	–	20	–	–	–	–	–	–	–	11.2
CLA	–	LOQ-3.82	130	–	–	–	–	–	–	–	–
	Arikan et al., 2008	Feitosa-Felizzola and Chiron, 2009	Blair et al., 2013	Kim and Carlson, 2007	Liang et al., 2013	Zhou et al., 2011			Bai et al., 2014	Chen and Zhou, 2014	Jiang et al., 2014

–: not studied, ND (not detected) is not a concentration or lower end of analytics.

and Ulungur Lake (Lei, 2014), whose levels of CTC, TC, and OTC are similar to those in the Liaohe River (Zhou et al., 2011; Bai et al., 2014). If the emission of CTC is similar to that of TC and OTC, the content of CTC in sediment could be higher due to a higher value of log Kow (the octanol/water partition coefficient) (Halling-Sørensen et al., 2003; Wollenberger et al., 2000). The content of doxycycline (DC, 98.5 ng g^{-1}) in sediment is higher in Honghu Lake (Yang et al., 2016) than in other lakes (Table 4), whose levels are higher than those in other surface water bodies (Table 4). The maximum TC contents descend in the following order: the Wangyang River (16,799.1 ng g^{-1}) > the Liao River (652 ng g^{-1}) > the Hai River (422 ng g^{-1}) > lakes in China (196.7 ng g^{-1}) > the Yellow River (184 ng g^{-1}) > the Colorado Cache la Poudre River (102.7 ng g^{-1}) > the Choptank River (10 ng g^{-1}) > the Pearl River Estuary (7.13 ng g^{-1}). The difference in TCs concentration is highly significant. The maximum TC content in the Wangyang River is 2–4 orders of magnitude higher than those in other surface water bodies, while this content is at a moderate level in lakes in China.

Compared with the contents of other antibiotics, the contents of MCs in the sediment of lakes are relatively low. ROM and ERM in MCs are dominant pollutants in the sediment of lakes (Table 3), which is similar to the case of surface water in rivers or bays (Table 2). The content of ROM is the highest (302 ng g^{-1}, Baiyangdian Lake) of the MC contents in sediment, followed by that of ERM (120.3 ng g^{-1}, Taihu Lake) (Xu et al., 2014). The contents of other MCs in sediment are below 20 ng g^{-1} at the low exposure level. The maximum contents of detected MCs descend in the following order: the Wangyang River (2581.8 ng g^{-1}) > lakes in China (302 ng g^{-1}) > the Liao River (229.31 ng g^{-1}) > Lake Michigan in the U.S.A. (71 ng g^{-1}) > the Hai River (67.7 ng g^{-1}) > the Yellow River (49.8 ng g^{-1}) > the Colorado Cache La Poudre River (25.6 ng g^{-1}) > the Huangpu River (24.6 ng g^{-1}) > the Pearl River Estuary (14 ng g^{-1}) (Table 4). The maximum contents of TCs in the Wangyang River is 1–2 order of magnitude higher than those in other surface water bodies, and TC contents in lakes in China are at a high level.

On the whole, the exposure levels of QNs are the highest, and those of the other antibiotics follow in the order of MCs > TCs > SAs > TMP according to their highest concentrations in lakes, which differ with the concentrations found in rivers. QN contamination in Dianchi Lake and Baiyangdian Lake is more prominent than in the other lakes, while Taihu Lake and Baiyangdian Lake are dominated by MCs, Taihu Lake and Honghu Lake by TCs, East Dongting Lake and Honghu Lake by SAs and Taihu Lake is dominated by TMP. The antibiotic contamination in the sediment of Taihu Lake and Baiyangdian Lake is higher than in the other lakes, which is similar to the trend in the surface water of lakes. The exposure levels of antibiotics in sediment are generally higher than that in water, which may be related to its strong adsorption capacity (Kim and Carlson, 2006, G. Yang et al., 2010, J.F. Yang et al., 2010). The concentration of antibiotics is more easily affected in surface water than sediment by external environmental factors, so the concentration of antibiotics in water varies greatly due to dilution effects (Ding et al., 2017), the adsorption effects of particulate matter (Q. Chen et al., 2017, Y. Chen et al., 2017), photodegradation (Mangalgiri and Blaney, 2017), etc. The adsorbed antibiotics are more stable due to the complex components of sediment, and antibiotics can accumulate in sediment, which results in higher content (G. Yang et al., 2010, J.F. Yang et al., 2010). The apparent partition coefficients in different lakes differ greatly due to the different hydrological environments that resulted in the sediments having different adsorption properties (Kim and Carlson, 2007). However, the occurrence of antibiotics is influenced by external environmental factors. For example, the concentrations of antibiotics in the sediment of Dongting Lake are significantly higher in the dry season than the wet season, which is related to the disturbance action of water flows. The average water level of Dongting Lake increased greatly from December 2015 (5.43 m) to August 2016 (14.29 m) (http://www.yymsa.gov.cn/yymsa/xxgk/xxgkml/aqxx/swgg/). In addition, antibiotics may be released into water under the large effects of water scouring and cause secondary pollution (Kim and Carlson, 2007; Radke et al., 2009).

2.3. Aquatic organisms

The contents of antibiotics in aquatic organisms of typical lakes in China are provided in Table 5. Having the most direct contact with antibiotics in aquatic environments, fish and shrimp can enrich antibiotics through the food chain. The residues of antibiotics in animal foods and their health risks have attracted much attention. The Codex Alimentarius Commission of the United Nations, China, the European Union and the United States have formulated relevant standards for antibiotic residues in food and feed.

According to published research, 24 antibiotics, including 7 SAs, TMP, 7 QNs and 2 TCs, are detected in the aquatic products of typical lakes in China. The contents of antibiotics in aquatic products are in range of ND-105 ng g^{-1} (Table 5). SD content is the highest (105 ng g^{-1}), followed by TC (101 ng g^{-1}). The contents of other antibiotics except NOR (38.5 ng g^{-1}) are below 10 ng g^{-1}, which is significantly lower than those of the Liao River (Bai et al., 2014), the Haihe River (L. Gao et al., 2012, P. Gao et al., 2012) and a drinking water protection area of Guangdong Province (Ren et al., 2016). The antibiotic contents in aquatic products of typical lakes in China are at low levels except for those of Honghu Lake (Wang and Sun, 2011; Lu et al., 2009). The contents of antibiotics in aquatic products are related to their living habits, their rank in the food chain and features of the aquatic product. Antibiotic concentrations in fish and shrimp from different water layers differ with location, with concentrations in benthos and middle-lower species being greater than those in middle-upper species. The level of antibiotic exposure decreases from carnivorous to omnivorous to phytophagous species. In addition, the bioaccumulation factors of different antibiotics have clear differences (Zhao et al., 2015). For example, SAs, as hydrophilic lipophilic compounds, have larger bioconcentration factor (*BCF*) values (SMX 2.80, SMT 2.30, and SDZ 0.50) (Liu et al., 2017) than other antibiotics, facilitating their enrichment in fish and shrimp.

However, compared with studies in surface water and sediment, a limited number of studies concentrate on exposure of the aquatic products of lakes to antibiotics. The level to which the aquatic products of lakes are exposed to antibiotics is not well known. Lake basins are an important aquatic product base in China (Tao et al., 2012), which is closely related to human health. Studies on the contents of antibiotics in the aquatic organisms of lake basins in China should be strengthened in order to accurately evaluate the risks of antibiotics and provide references for the relevant departments in the management and control of fishery drugs.

3. Risk

3.1. Risk assessment

3.1.1. Surface water

Guidelines for the environmental risk assessment (ERA) of pharmaceuticals were introduced by the U.S. Food and Drug Administration (U.S. FDA) (2001) and the European Agency for the Evaluation of Medicinal Products (EMEA) (2006). Risk assessment studies of pharmaceuticals have been reported according to these guidelines (Vryzas et al., 2011; Ma et al., 2016; Hernando et al., 2006). The preliminary environmental risks of the antibiotics are based on the risk quotient (RQ) method. RQ values were calculated using the formula below:

$$RQ = \frac{MEC}{PNEC} \quad (1)$$

where MEC is the measured maximum environmental concentration in

Table 5
Occurrence of antibiotics in aquatic products of Lakes and other surface water bodies (ng g^{-1}).

	Dianchi Lake	Dongting Lake	Hongze Lake		Chao lake	Liao River	Hai River	A drinking water protection area of Guangdong Province	Maximum residue limits
	Range	Range	Range	Range	Range	Range	Range	Range	
SCY					0.27–0.42	ND		–	100
SDZ	–	ND-0.68	ND-47	10–105	0.21–0.27	–		–	100
STZ	ND-6.1		–	–	–	ND-1.61	ND-3.2	–	100
SMT		ND-0.57	–	–	ND	ND		–	100
SMX	ND-3.4	ND-1.06	–	–	ND	ND-2.85	ND-68	–	100
SDX	ND-5.3	–	–	–	–	ND		–	100
SDX	–	–	–	–	ND	–		–	100
TMP	–	ND-0.39	–	–	–	–		–	50
NOR	ND-38.5	ND	–	–	ND	ND-3.2	ND-63.5	46.53–103.18	NG
OFL	ND-4.5	ND	–	–	ND-1.29	ND-5.62	ND-10.5	–	NG
CIP	ND-3.9	ND	ND-24	–	ND	ND-12.54	ND-12.5	26.97–164.80	50(CIP +
ENR	–	ND-1.05	–	–	ND-1.94	280.95–1653.17	ND-50.8	ND-34.3	ENR)
SFL	–	ND-0.6	–	–	–	–	ND-3.5	–	30
LOM	–	–	–	–	ND-1.21	–	ND-2.3	–	
DIF	–	–	–	–	ND-1.47	–	ND-8.2	–	–
OTC	ND-2.8	ND	ND-74	12–101	ND	ND-2.24	–	–	100
TC	ND-4.2	ND	ND-11	11–15	ND	ND	–	–	100
CTC	–	ND- < LOQ	ND	ND	ND	ND-2.84	–	–	100
DC	–				ND	–	–	–	
ERM	ND-0.7	–	–	–	–	ND-6.59	ND-45.1	–	200
ROM	ND-0.4	–	–	–	–	ND-17.65		–	NG
FZD	–	–	ND	ND	–	–		–	NP
CMP	–	–	ND		–	–		–	NP
References	Wei et al., 2014	Liu et al., 2017	Wang and Sun, 2011	Lu et al., 2009	Wang et al., 2015	Bai et al., 2014	L. Gao et al., 2012, P. Gao et al., 2012	Ren et al., 2016	

NG: not given. NP: no prohibiting. –: not studied. ND (not detected) is not a concentration or lower end of analytics.

ng L^{-1} and PNEC is the predicted no effect concentration in water in ng L^{-1}. PNECs were based on reported acute or chronic toxicity data. The environmental risks were classified into 4 levels according to the calculated RQ values: no risk (RQ < 0.01), low risk (0.01–0.1), medium risk (0.1–1), and high risk (>1) (Hernando et al., 2006).

The results of the risk assessment are shown in Table 6. OFL had the highest RQ (up to 63.15), due to its low PNEC, followed by SMX (RQ = 34.81), CIP (RQ = 34.81), and ERM (RQ = 31.24), whose RQ values indicate they are a serious environmental risk to the aquatic environments of lakes. The RQs of NOR, SDZ, ENR, LOM, ROM, CLA and LIN are also over 1, which indicates they carry a significant environmental risk. The remaining antibiotics except for DC (medium risk) exhibit low or no environment risk. On the whole, quinolones are major health risk factors in the water of lakes, which explains why some quinolones are prohibited from being produced or used in food animals. The risk of LNs is also prominent, and all LNs are in the high risk category. However, studies on the concentrations of LNs are not abundant, requiring a reinforcement in subsequent studies. TCs exhibit low or no environmental risk. Of course, antibiotics often exist as mixtures in the actual environment, which can enhance their effects on the environment (Cleuvers, 2004). The antibiotic risk to the environment and human health should therefore not be ignored.

3.1.2. Sediment - a case study of Dongting Lake

Few studies on the risk assessment of antibiotics in sediments exist (Shi, 2014) due to a lack of data relating antibiotic levels in sediment to aquatic organisms. Antibiotics in the pore water of sediment directly contacts aquatic organisms and water (Xue et al., 2013). This study therefore calculates the risks of antibiotics in sediment by converting the concentration of antibiotics in sediment into that of pore water (Zhao et al., 2010; Xue et al., 2013). The RQ values were calculated using the formula below:

$$C_{PE,porewater} = \frac{C_{PE,Sediment}}{K_{OC} \times F_{OC,Sediment}} \quad (2)$$

$$LogK_{OW} = 0.623LogK_{OC} + 0.873 \quad (3)$$

where $C_{PE,\ porewater}$ is the concentration of antibiotics in pore water in mg L^{-1}, $C_{PE,\ Sediment}$ is the measured maximum environmental concentration in mg kg^{-1}, $F_{OC,\ sediment}$ is the total organic carbon (TOC) in sediment, and K_{OC} is the organic carbon-water distribution coefficient, which can calculated using the (K_{OW}) in L kg^{-1} (Piao et al., 1999).

In view of the lack of data concerning the TOC in sediment, Dongting Lake was taken as an example to evaluate the environmental risks of antibiotics to provide a basis for the further study of the risks of antibiotics in lake sediment. Detailed information about the contents of antibiotics in surface sediment from Dongting Lake is provided in Table S3. The RQ was estimated based on the reported PNECs. A worst case scenario for ERA was examined using the maximum MEC, and the results are shown in Fig. 1. The RQs of antibiotics in the sediment of Dongting Lake are in the range of 2.07×10^{-4}–29.87. The RQ of CIP is the highest, at 29.87, which poses adverse ecological effects. SFLO shows high risks with an RQ of 6.72(>1), and the acceptable daily intake (ADI) value of SFLO (0.3 μg (kg d)$^{-1}$) is low. The risk of SFLO must therefore be taken seriously. The RQs of SDZ and ENR are close to 1, indicating their high medium risk. The low concentration of SDZ has adverse impacts on hatching, heart rates and spontaneous movement (Marburger et al., 2002). The RQs of SMX, TC and OTC are in range of 0.1–1, indicating medium risk. Considering the high levels of SMX, TC and OTC consumption, their environmental risks cannot be ignored. TMP, SMT and CTC exhibit low or no environment risk. On the whole, the risks of antibiotics in sediment are high. K_{OC} was calculated in this study using K_{OW}, which may cause K_{OC} to be small and the RQs of antibiotics to be large. However, a worst case scenario for ERA was conducted in this study using the maximum MEC, which basically reflects the risk level of antibiotics. The secondary release of antibiotics from sediment should therefore not be ignored.

Table 6
RQs for the antibiotics in surface water from the lake in China.

Antibiotics	MEC (ng L^{-1})	PNEC (ng L^{-1})	RQ
SCY	4.6	2330 (Pro et al., 2003)	0.002
SMM	23.1	1.72×10^6 (Zhao et al., 2016)	1.34×10^{-5}
SPD	85	5280 (Pro et al., 2003)	0.016
SDZ	505	135 (Zhao et al., 2016)	3.74
STZ	134.5	200 (Park and Kwak, 2012)	0.67
SAAM	48.26	83,594 (Zhang et al., 2017)	0.00058
SIZ	10.36	–	–
SMT	654	1277 (Brain et al., 2004)	0.51
SMX	940	27 (Ferrari et al., 2004)	34.81
SIA	89.4	–	–
SMR	61.4	2.5210^{-5} (Fang, 2016)	0.0024
SDX	ND	1247.04 (Brain et al., 2004)	0
SCP	43.3	2330 (Pro et al., 2003)	0.019
TMP	40.8	16,000 (Lützhøft et al., 1999)	0.0026
FLE	6.35	–	–
NOR	156	16 (Zhao et al., 2016)	9.75
OFL	713.6	11.3 (Backhaus et al., 2000)	63.15
CIP	112.3	5 (Isidori et al., 2005)	22.46
ENR	81.7	28.8 (Backhaus et al., 2000)	2.84
SFL	28.2	15 (Lützhøft et al., 1999)	1.88
LOM	53.85	19.9 (Backhaus et al., 2000)	2.71
ENX	0	28.8 (Backhaus et al., 2000)	0
DIF	10.4	–	–
DOC	5.7	–	–
OTC	90.3	1040 (Kolar et al., 2014)	0.087
TC	87.9	3310 (González-Pleiter et al., 2013)	0.027
CTC	142.5	9310 (Xu et al., 2013)	0.015
DC	42.3	131 (Zhao et al., 2016)	0.32
ERM	624.8	20 (Isidori et al., 2005)	31.24
ROM	314.2	100 (Yang et al., 2008)	3.14
SPI	3.99	–	–
TYL	1.88	24 (Zhao et al., 2016)	0.078
JOS	0.9	–	–
CLA	10.6	2 (Isidori et al., 2005)	5.3
LIN	357	50 (Zhao et al., 2016)	7.14
CLD	503	–	–

–: no enough data currently to evaluate.

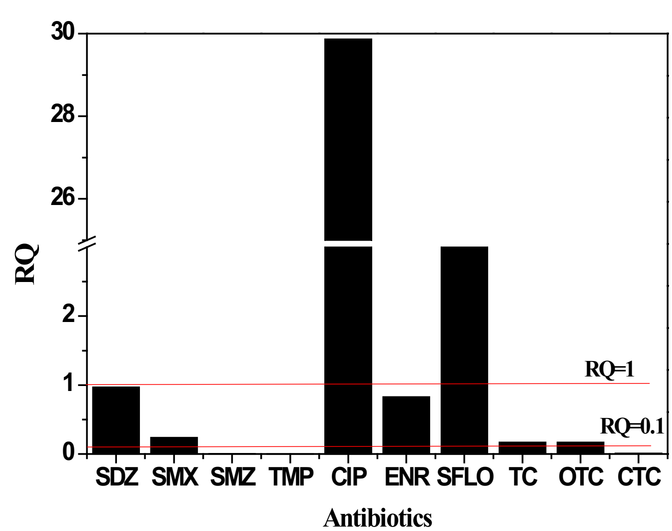

Fig. 1. RQs for the antibiotics in sediment from the Dongting Lake. Samples were collected in August 2016.

3.1.3. Excessive occurrence of antibiotic residues in aquatic organisms

The residues of antibiotics in animal-derived foods have raised significant concerns. The highest residue standards of some antibiotics are held in the United States, the European Union and China.

According to "The Residue Limits of Aquaculture Drugs in the Green Aquatic Organisms" (NY5070-2002), the residual contents of SDZ and OTC may be as high as 105 and 101 ng g^{-1}, respectively, which slightly exceeds their MRL values and threatens human health. The levels of other antibiotics in aquatic organisms are lower, far lower than their MRLs and meet dietary safety standards. According to previous research, levels of antibiotic residues are higher in the aquatic organisms of Honghu Lake than in those of other lakes. The management and monitoring of antibiotics in aquatic organisms of Honghu Lake should therefore be strengthened. In addition, fish and shrimp might contain other toxic pollutants (such as pesticides (Islam et al., 2016), heavy metals (Islam et al., 2016) and polycyclic aromatic hydrocarbons (Shi et al., 2016)), which could produce synergistic effects with antibiotics. The occurrence of antibiotics in aquatic organisms should therefore not be ignored.

3.2. Antibiotic resistance genes

The occurrence of antibiotic resistance genes (ARGs), as environmental contaminants, in aquatic environments is an emerging concern (Pruden et al., 2006). ARGs are transferred between non-pathogens, pathogens, and even distantly related organisms through horizontal gene transfer and are considered a potential threat to human health through the food chain (Pruden et al., 2006). Lakes provide an ideal medium for the accumulation and propagation of ARGs because they are susceptible to anthropogenic impact (Rodriguez-Mozaz et al., 2015).

In China, antibiotic-resistant bacteria and ARGs are abundant in aquatic environments. The detection frequencies of antibiotic-resistant bacteria and ARGs in Bosten Lake, Jinsha Lake and Taihu Lake are high. In Bosten Lake, the relative abundance of sulfonamide resistance genes are higher than that of tetracycline resistance genes, with 100% detection frequencies of genes conferring resistance to sulfonamide (*sul1*and *sul2*) and tetracycline (*tetM* and *tetW*) (Zhou et al., 2014). The highest rates of resistance to sulfamethoxazole/trimethoprim are 85% (Jinsha Lake), and sulfonamide- and tetracycline-resistant bacteria are widely distributed (Wang et al., 2013). In Taihu Lake, the resistance rates against streptomycin and ampicillin are over 60% (Han et al., 2013). The results of a study indicated that 80.8% of all tested strains can transfer antibiotic resistance through conjugation (Yin et al., 2013; Han et al., 2013). The studies on antibiotic resistance in the sediment of lakes are more abundant than similar studies on water. The lakes in the middle and lower reaches of the Yangtze River (Yang et al., 2016; Yang et al., 2017; Luo et al., 2017) (Honghu Lake, Dongting Lake, Datong Lake, Bajiao Lake, Dongting Lake, Xiliang Lake, Hongzehu Lake, Wanghu Lake, Futou Lake, Saihu Lake, Junshan Lake, Nanyi Lake, Shijiu Lake, Gehu Lake, Changdang Lake, Taihu Lake, Duyang Lake and Yangcheng Lake), Plateau Lake (Dianchi Lake) (Yao, 2016), lakes in a cold alpine region (Basongco Lake, Qinghai Lake, Namco Lake and Cake Salt Lake) and high latitude alpine lakes (Xingkai Lake) (Yao, 2016) experience ARG contamination.

Sulfonamide and tetracycline resistance genes are the ARGs most frequently detected in aquatic environments (Zhou et al., 2014, Zhang et al., 2009, Wang et al., 2013). Sulfonamide and tetracycline resistance genes have a broad host range and can be carried by strains in different environments, which results in their high detection frequencies (Zhang et al., 2009, Luo et al., 2017, L. Gao et al., 2012, P. Gao et al., 2012). The relative abundances of ARGs have clear regional differences. Regions with developed economies and high population densities such as the Yangtze River and the Yellow River have higher levels of ARG exposure. In addition, the differences in the composition of multidrug resistance patterns may be ascribed to the sources of these isolates, which receive different doses, frequencies, and species of antibiotics.

4. Conclusions and suggestions

Antibiotics are ubiquitous in different environmental media in the aquatic environments of lakes in China. The levels of antibiotic contamination in surface water range from ng L^{-1} to μg L^{-1}, while its levels in sediment and aquatic organisms range from ng g^{-1} to μg g^{-1} (dw). The exposure level of antibiotics in water and sediment is relatively high on the global scale. In addition, the differences in levels of different media and lakes are clear and are related to the population density, antibiotic doses, source scales, etc. However, studies on the antibiotic contamination in aquatic environments of lakes are only the tip of the iceberg. A limited number of studies concentrate on eastern and southern lakes. In addition, studies on the residues of antibiotics and ARGs in the aquatic organisms of lakes are lacking. The usage and emission of typical antibiotics in lake basins and the rates with which they are contributed from different sources are not clear.

Therefore, the occurrence of antibiotics in aquatic environment of Lakes in China should be carried out a comprehensive survey in order to make clear exposure level of antibiotics in aquatic environment of Lakes and draw a map of exposure of antibiotics in Lake. Lakes should be studied as a whole for exploring the migration and transformation of the antibiotics in the lake system. In addition, the evaluation system of antibiotics to environment and human health is imperfect. The permissible limits of antibiotics in lakes of China should be established, and the ecological effect and human health need to be explored at trace level of concentration of antibiotics.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2018.01.271.

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