



## Trace level analysis and risk assessment of typical antibiotics in drinking water by liquid chromatography-tandem mass spectrometry (LC-MC/MS)

Feng Li<sup>a,c</sup>, Feng Lei<sup>b,d,†</sup>, Cheng Yanru<sup>a</sup>, Zhang Jun<sup>e</sup>, Zhang Sheng<sup>a,\*</sup>

<sup>a</sup>Chongqing Environmental Sciences Research Institute, Chongqing Collaborative Innovation Center of Big Data Application in Eco-Environmental Remote Sensing, Chongqing 401147, China, Tel. +86 13996226697; email: 254305323@qq.com (Z. Sheng)

<sup>b</sup>SUCEE, Chongqing University, Chongqing 400044, China

<sup>c</sup>College of Materials Science and Engineering, Chongqing University, Chongqing 400044, China

<sup>d</sup>Chongqing Institute of Green and Intelligent Technology, Chinese Academy of Sciences, Online Monitoring Center of Ecological and Environmental of the Three Gorges Project, Chongqing 400714, China

<sup>e</sup>Ecological and Environmental Monitoring Center of Chongqing, Chongqing 401147, China

Received 16 September 2018; Accepted 33 January 2019

### ABSTRACT

This research evaluated the occurrence and distribution of 28 antibiotics from the sulfonamides, tetracyclines, macrolides, fluoroquinolones,  $\beta$ -lactams and the others in drinking water in upper reach of Three Gorges Reservoir, China. With three types of eight kinds of antibiotics detected, the concentration in the range of 0.4–140.0 ng/L includes sulfa sulfamethoxazole (SMX), sulfamethazine (SMZ), macrolide erythromycin, roxithromycin (ERM), roxithromycin (ROM), tylosin (TYL), lincomycin (LIN), chloramphenicol amine benzene alcohol (CAP), florfenicol (FF). In addition to CAP, the remaining seven kinds of antibiotics are poultry drugs, and the usage rank of FF and LIN are the top five in the antibiotics list of China. According to the analysis of different water sources, ecological risk level ( $RQ_{sum}$ ) from high to low were T-R-CK > C-R-BB > T-L-JM > C-R-DY > T-R-GQ > T-L-ZJ > C-L-GSQ > C-R-LT > C-R-FSB, the  $RQ_{sum}$  of T-R-CK water source up to 1.981, indicating that the corresponding aquatic organisms in the water source exhibit higher toxicity risk. The detection of antibiotics in C-R-FSB and C-R-LT water source were at low risk, indicating that both were affected by human activities at minimal interference. According to the analysis of the detection of antibiotics, SMX, TYL, ERM and ROM showed moderate risk level, the potential impact on ecological should be paid more attention. In view of the risk of antibiotics are major livestock and poultry drugs, the Three Gorges Reservoir area should further regulate the use of antibiotics in livestock and poultry breeding.

**Keywords:** Trace analysis; Risk assessment; Antibiotics; Drinking water; LC-MC/MS; Environmental protection

### 1. Introduction

With the development of medical and diagnostic levels, as well as more attention to the human health, more and more antibiotics have been widely used for clinical, veterinary, agricultural, food, and industrial applications [1–4]. Most antibiotics used for humans and animals are excreted

in the form of drugs, metabolites, or other ways, which have been proved to perform high performances to treat various bacterial infections and inhibit the infection of pathogenic microorganisms [5,6]. However, most of the antibiotics were finally moved to the water systems including surface water, seawater, groundwater, and even drinking water through the discharge of domestic sewage, aquaculture wastewater,

\* Corresponding author.

† Contributed as first author.

agricultural manure, and irrigation runoff, revealing high risk for human living. The situation of the excessive use of antibiotics is extremely serious in China [7], and the antibiotic usage in 2013 was about 162,000 t. After the use by human beings and livestock, antibiotics were excreted from the body by the ways of primary or metabolic product, and finally about 53,800 t antibiotics entered into the natural environment [8].

Antibiotics may have some acute or chronic toxicity to aquatic organisms. While inhibiting or killing pathogens, they may also kill some beneficial microorganisms in the environment and disturb (or even destroy in some degree) the ecosystem cycles [9,10]. Therefore, it is highly necessary for precise determination and risk assessment of antibiotics in every water system. Previously, many studies have been performed to understand the distribution of antibiotics in the systems including surface water, groundwater, river water, and sea water [11–18]. For instance, Zin and Nail [11] and Richardson et al. [12] studied the distribution and ecological risk of antibiotics in the river of north China and Hongkong, respectively, with the liquid chromatography-tandem mass spectrometry (LC-MC/MS) technique; Zhang et al. [13] reported the profiling of antibiotic resistance genes in drinking water treatment plants with high-throughput quantitative PCR technique; and Sufiyan and Magaji [14] investigated the occurrences and regional distributions of 20 antibiotics in groundwater with LC-MC/MS. However, only less amount of studies have been done to know the distribution and risk of antibiotics in concentrated drinking water [19–21]. Therefore, there is still some space and significance for measuring trace level antibiotic in drinking water system and evaluating their risk to human living around.

As the largest strategic freshwater resource in China, the Three Gorges Reservoir (TGR, center of China) plays important roles in the Yangtze River Basin and strategic resource allocation. With the economic development, the increasing number of pollutants in the water environment poses a potential threat to the drinking water safety of urban residents in the TGR area [22,23]. In addition, it has been found that the detection of antibiotics in the water environment was significantly affected by the usage habits of antibiotics in various regions.

In this study, we focus on the trace level determination and risk assessment of various antibiotics in the drinking water of the upper reach of TGR by using LC-MC/MS technique. Based on the types and characteristics of various antibiotics that are used in China and the relevant information of antibiotics that is provided by the Food and Drug Administration and the Department of Health, six types of 28 categories of antibiotics were selected as the analysis objects [24–30]. The purpose of this study is to understand the distribution characteristics of antibiotics in nine centralized drinking water sources, to evaluate their potential ecological risks towards reservoir, and to explore the possibility by using large-scale urban sewage treatment plants for removing antibiotics from the drinking water system. It is expected that this study will be useful to supply the basic database of regional distribution of antibiotics in drinking water sources of China in one way, meanwhile to develop new treatment methods on reducing the pollution of antibiotics towards the drinking water sources.

## 2. Materials and methods

### 2.1. Chemicals and materials

28 standard antibiotics were purchased from Dr. Ehrenstorfer GmbH (Germany). 1,000 mg/L standard stock solution were prepared by using methanol as solvent. Then the standard stock solution was used to prepare the mixed standard solution of 1,000 µg/L with methanol. Water is used as solvent to dilute the mixed standard liquid, and six series of standard solutions of mass concentration are prepared. The concentrations were 0.8, 4, 10, 20, 100 and 200 g/L, respectively [31–38]. 28 kinds of target components are in the range of 0.9975–0.9996. 10, 50 and 200 ng antibiotic standards were added into 1 L of water. The antibiotic content of the blank component was determined and the classification rate of recovery rate was calculated. Three parallel samples were set in each group; the result shows that the recovery rate of antibiotics range from 89.2% to 105.8%, the relative standard deviation is less than 5%.

### 2.2. Sample collection

In May and October of 2016, nine typical centralized drinking water samples were collected in the reservoir area. Six river-type water sources were set up monitoring section by water intake location. Each section set three horizontal sampling points in the left, middle and right [39–45]. The collection and preservation of water samples shall be carried out in accordance with the general provisions of GB/T 12999-1999 “Technical Regulations for the Storage and Management of Samples for Water Sampling Samples” [46]. After the water samples are collected, the pH is adjusted to 3 and the samples are kept in a brown glass sampling bottle, and are treated by solid-phase extraction enrichment as soon as possible. As shown in Fig. 1, C-R is urban river-type water source, C-L is city lake-type water source, T-R is town river-type water source, T-L is town lake-type water source.

### 2.3. Sample extraction

One-liter sample was filtered by 0.7 µm pore diameter glass fiber membrane, and then 0.5 g ethylene diamine tetra acetic acid disodium and 8.7 g dipotassium phosphate were added into the sample, then stirring and using ultrasonic dissolved. The HLB solid-phase extraction column was activated in 10 mL of methanol and 10 mL of ultrapure water before use. The water samples were passed through an HLB solid-phase extraction column at a flow rate of 3 to 5 mL/min [47–49]. After extraction of the water sample, the extraction column was dried under vacuum for 30 min, eluted with 10 mL of water, and finally eluted with 5 mL of pure methanol, 10 mL of 5% (by volume) of aqueous ammonia. The eluate was collected at 40°C water bath, slowly with nitrogen blowing to near dryness to 1 mL 20% (by volume) aqueous. The residual acetonitrile was dissolved and filtered through a 0.22 µm filter.

### 2.4. Quantitative determination

Liquid chromatography-mass spectrometry/mass spectrometry (LC-MC/MS) model Shimadzu LC-20A+ AB Sciex;

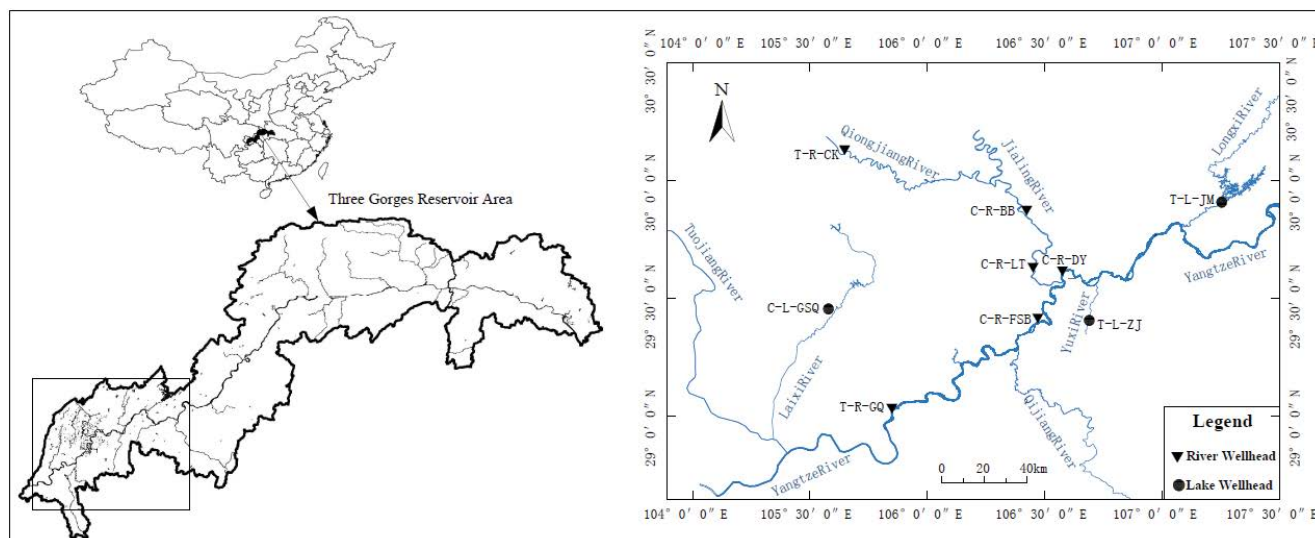


Fig. 1. Distribution of sampling sites in drinking water sources of the Three Gorges Reservoir upper area.

automatic solid-phase extraction apparatus model Reeko FOTECTOR; HLB solid phase extraction column models 6 mL, 1,000 mg, waters Oasis HLB WXH; micro vortex mixer; ultrasonic cleaner; DC-12 nitrogen concentration; 0.7 m glass fiber filter; 0.22 m syringe filters.

### 2.5. Risk assessment

The method of pollutants risk assessment based on the EU environmental risk assessment method, using RQS (risk quotient) to assess its ecological risk:

$$RQS = PEC/PNEC \quad (1)$$

Or

$$RQS = MEC/PNEC \quad (2)$$

In this formula: PEC is pollutant prediction environmental concentration, ng/L; MEC is pollutant monitoring environmental concentration, ng/L; PNEC is a predicted no-effect concentration that can be obtained by collecting antibiotics data for acute and chronic toxicology of some species in literature, ng/L.

## 3. Results and discussion

Table 1 have shown that after 28 kinds of six categories of antibiotics in nine typical centralized drinking water sources were analyzed, eight kinds of three categories of antibiotics were detected, and the mass concentration range is 0.4–140.0 ng/L. Detection of antibiotics including sulfamethoxazole (SMX), sulfamethazine (SMZ), erythromycin (ERM), roxithromycin (ROM), tylosin (TYL), lincomycin (LIN); chloramphenicol (CAP), florfenicol (FF).

Research shows that tetracycline antibiotic is a strong chelating agent, which has an excellent adsorption ability on the surface of the solid particles. More tetracycline

antibiotic was detected in the sediment and fewer in water. Fluoroquinolones have some adsorption ability, and it has higher removal rate in the sewage treatment plant. For four lake-type centralized drinking water sources, the water is relatively closed and has longer residence time which facilitates the deposition of fluoroquinolones and tetracycline antibiotics in suspended matter;  $\beta$ -lactam is easily degraded in environment, usage is high, but less detected in the water body.

As shown in Fig. 2, the detection rate of LIN and FF was the highest among the eight detected antibiotics, and the detection rate reaches to 100%; the detection rates of ERM, ROM and CAP were above 60%; the detection rate of SMZ was lowest only 10%. The detection rate of LIN, FF, ERM, ROM and CAP is higher, which means that these antibiotics are main residual in the centralized drinking source water.

Antibiotics in the environment are mainly from the use of medicine, livestock, poultry farming, aquaculture, pharmaceutical industry and wastewater discharge. Among the eight antibiotics detected, seven antibiotics were the main livestock and poultry drugs (that is SMX, SMZ, ERM, ROM, TYL, LIN and FF). In 2016, there were about 5,600 livestock and poultry farms in the studied area, which included 3,556 pig farms (55% intensive farms), 248 cattle farms (15% intensive farms) and 920 chicken farms (broilers, hens, 31% intensive farms). The above three types of farming basically cover more than 90% of the total amount of aquaculture, the amount of manure produced also covers more than 90% (estimated by the amount of perennial stock). Antibiotics in animals cannot be completely metabolized and are excreted directly into the water through animal feces and urine, or into the soil by utilization of sewage irrigation and fertilizer manure, with surface runoff and other ways entering the water environment. The usage of LIN and FF ranks top five in the antibiotic drugs of China. LIN has a strong antibacterial capacity and inhibition on anaerobic bacteria and Gram-positive bacteria. Conventional sewage treatment process is difficult to degrade it. Attention should be paid

Table 1  
Concentrations of antibiotics in the drinking water sources of Three Gorges Reservoir upper area (unit: ng/L)

Antibiotics		Name of water source								
Category	Name	T-R-GQ	C-R-FSB	C-R-DY	C-R-BB	C-R-LT	C-L-GSQ	T-L-ZJ	T-R-CK	T-L-JM
Sulfonamides	SMX	nd	nd	nd	nd	nd	nd	nd	nd~25.5	nd~13
	SMZ	nd	nd	nd	nd	nd	nd	nd	nd	nd~14.7
	ERM	nd~3	nd	nd~2.5	nd~2.8	nd	nd	nd~2.1	nd~9.2	nd~5.1
Macrolides	ROM	nd~11.1	nd	nd~31.4	nd~32	nd	nd	nd~1.2	nd~8.7	nd~2.2
	TYL	nd~8.2	nd	nd~13.4	nd~19.5	nd	nd	nd	nd~3.0	nd
	LIN	nd~4.1	nd~5.4	nd~6.3	nd~8.7	nd~3.7	nd~34.6	nd~13.9	nd~140.0	nd~68.2
Aniline alcohols	CAP	nd~0.8	nd~0.8	nd~3.4	nd~2.2	nd~10.1	nd~0.4	nd	nd~0.6	nd~0.6
	FF	nd~7	nd~7.7	nd~8	nd~11.4	nd~25.3	nd~2.5	nd~3.4	nd~1.1	nd~7.1

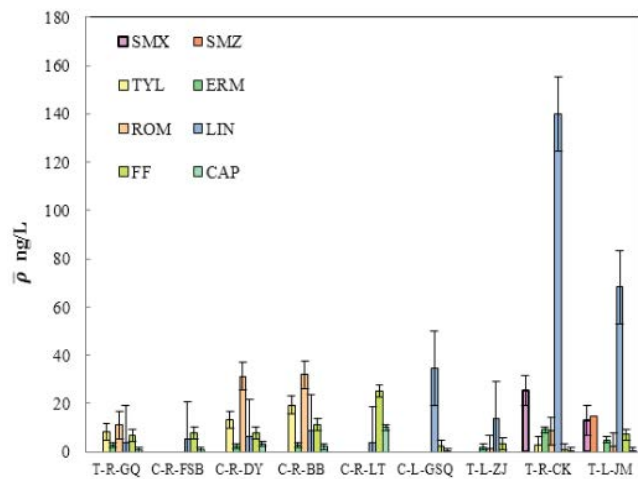


Fig. 2. Concentration level of antibiotics in drinking water sources of the Three Gorges Reservoir upper area.

to the high level of concentration and detection rate of LIN and FF in nine typical centralized drinking water sources; Sulfa drugs are the earliest synthetic antibacterial drugs. Although the detection rate of SMX and SMZ is not high, but the quality and concentration of them are both high. Studies show that sulfonamide antibiotics are the dominant component in swine manure supernatant. Macrolides are easy to be hydrolyzed or adsorbed in soil and destroy soil ecological balance, which affect soil nitrification and plant nutrient intake. The highest concentration of ERM (max = 9.2 ng/L), ROM (max = 32 ng/L), TYL (max = 19.5 ng/L) was low, but the detection rate was above 40%. The detection rate of CAP (amine alcohol) in the study area reaches 88.9%, which widely used in the diseases prevention and treatment of human, livestock and aquaculture, but due to the serious side effects on the human body, China has banned the use of CAP in livestock, aquaculture or as raw materials for the product.

As shown in Fig. 3, the average concentration of antibiotics in the Three Gorges Reservoir upstream drinking water sources from high to low is the  $\bar{p}(T-R-CK) > \bar{p}(T-L-JM) > \bar{p}(C-R-BB) > \bar{p}(C-R-DY) > \bar{p}(C-R-LT) > \bar{p}(C-L-GSQ) > \bar{p}(T-R-GQ) > \bar{p}(T-L-ZJ) > \bar{p}(C-R-FSB)$ . The concentration of

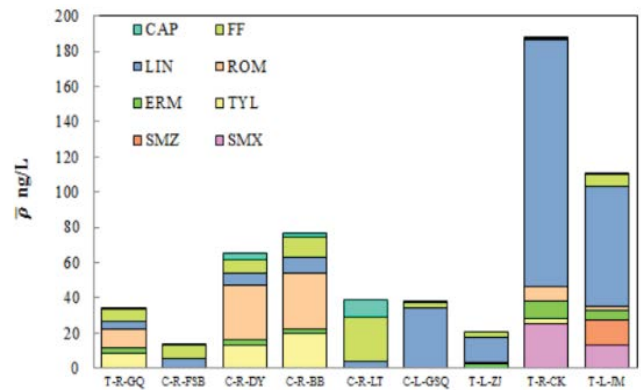


Fig. 3. Contamination of antibiotics in drinking water sources of the Three Gorges Reservoir upper area.

antibiotics in six river-type drinking water sources ranges from 13.9 to 188.1 ng/L, and the concentration of antibiotics in the three lake-type drinking water sources ranges from 20.6 to 110.9 ng/L. The average concentration of antibiotics in only two water sources (T-R-CK and T-L-JM) was higher than 100 ng/L. The water intake of T-R-CK is located in the downstream 200 m of the confluence of the Yaoshi River and Qiongjiang River, which eastward flow through Anyue County, Yuanda, Chengbei, Changhe, Yaoshi and others, and the Yaoshi River flows into Qiongjiang River in the Chongkan (Tongnan District of Chongqing). The construction of domestic sewage treatment facilities in Sichuan is lagging behind. Livestock and poultry breeding is developed, and the water intake is effected by the downstream reservoir series Qiong Jiang. Water flow is slow, causing the concentration of antibiotic residues being the highest water in the study area ( $P$  is = 188.1 ng/L). Seven kinds of antibiotics are detected. In addition to CAP, the rest of them are for livestock and poultry medicine. The content of LIN is up to 140 ng/L. T-L-JM reservoir is located in Changshou District of Chongqing. It is the controlling reservoir of Longxi River downstream basin. The Longxi River originates from Liangping County, flows through Dianjiang county and Changshou district, and then flows into the Yangtze River. The annual average flow rate of 31.7 m<sup>3</sup>/s and the watershed area is 3,302 km<sup>2</sup>, involving 17 villages, towns and streets.

Table 2  
Comparison of drinking water sources quality and concentration in different regions

p/(ng/L)	Shanghai	Shenzhen		Guangdong Province		Jiangsu Province			This paper	
	Water source of a reservoir	Water source of Xili Reservoir	Water source of Tiegang Reservoir	Water source of Dongjiang River	Three urban water sources	Three water sources in Nanjing	Water source of the Gonghu Bay	Water source in Jiaying Lake		Water source in Taihu Lake
Sulfadiazine (SDI)	nd~5.97	-	-	nd~12.0	nd~52.7	nd~8.5	-	nd~2.61	nd~25.5	nd
Sulfamerazine (SMA)	nd~4.72	-	-	-	-	-	-	-	nd~3.4	nd
Sulfamethoxazole (SMX)	8.71~107.0	3.9~6.3	2.5~10.0	-	nd~8.6	nd~12.5	nd~7	0.69~10.6	31.7~48.0	nd~25.5
Sulfamethazine (SMZ)	nd~14.5	6.7~9.3	nd~12.0	-	nd~1.29	nd~0.87	-	-	-	nd~14.7
Sulfamer (SMID)	nd~5.09	-	-	-	-	-	nd	-	-	nd
Sulfamonomethoxine (SMM)	nd~4.18	-	-	8.0~16.0	-	-	nd	-	-	nd
Sulfamethoxine (SD)	-	-	-	-	-	-	-	-	63.1~883	-
Sulfonamide (SAM)	1.81~43.1	-	-	-	-	-	-	-	-	-
Sulfamide (SG)	nd~8.32	-	-	-	-	-	-	-	-	-
Sulfathiazole (STZ)	nd~5.10	-	-	-	-	-	-	-	-	nd
Trimethoprim (TMP)	nd~22.0	-	-	-	-	-	64~208	nd~8.14	-	-
Tetracycline (TC)	-	-	-	nd~49.0	nd~2.3	nd~14.9	nd~1850	-	-	nd
Oxytetracycline (OTC)	-	-	-	nd~23.0	nd~15.4	nd~9.2	-	-	-	nd
Chlortetracycline (CTC)	-	-	-	-	nd~6.0	nd~3.3	nd~4720	-	-	-
Doxycycline (DOX)	-	-	-	-	nd~8.5	nd~4.7	-	-	-	-
Norfloxacin (NFX)	-	-	-	18.0~39.0	nd~4.4	nd~4.2	59~271	nd~162	-	nd
Ofloxacin (OFX)	-	-	-	2.0~4.0	nd~13.2	nd~5.5	14~474	21.4~68.9	-	nd
Erythromycin (ERM)	-	8.5~13.0	2.5~12.5	-	nd~4.0	nd~5.4	-	-	-	nd~9.2
Roxithromycin (ROM)	-	nd	nd	-	nd	nd	14~23	-	-	nd~31.4
Tylosin (TYL)	-	-	-	nd~16.0	-	-	-	-	-	nd~19.5
Cephalexin (CPX)	-	nd~1.6	nd	4.5~11.0	-	-	-	-	-	-
Cefuroxime (URO)	-	nd	nd	-	-	-	-	-	-	-
Chloramphenicol (CAP)	-	nd	-	-	nd~1.7	nd	-	-	-	nd~10.1
Florfenicol (FF)	-	-	-	-	nd	nd~2.3	-	121~259	-	1.1~25.3
Lincomycin (LIN)	-	8.0~19.0	2.5~12.5	nd~3.0	-	-	-	-	-	3.7~140

Service population are 2,067,000.839 scale livestock and poultry farms are within the river basin, mainly feeding pig, cattle and chicken. At the end of 2016, 170 thousand pigs, 3 million 10 thousand poultry and 13 thousand large livestock were slaughtered. The level of antibiotic concentration in this watershed is up to 110.9 ng/L, and seven antibiotics were detected. Except for CAP, the rest are livestock and poultry drugs, LIN content of up to 68.2 ng/L. The above two water sources significantly affected by livestock and poultry breeding should be valued.

There were significant regional differences in the detection of antibiotics in the study area. SMZ ( $\rho_{\max} = 14.7$  ng/L) only detected in T-L-JM. SMX only detected from T-R-CK and T-L-JM showed the maximum ( $\rho_{\max} = 25.5$  ng/L) only appear in T-R-CK. LIN and FF have been detected from nine water sources, and the maximum concentration ( $\rho_{\max} = 25.3$  ng/L) of FF appears in C-R-LT. CAP was detected in the remaining eight water sources except T-L-ZJ, and the maximum ( $\rho_{\max} = 10.1$  ng/L) appeared in C-R-LT.

At present, more than 30 kinds of antibiotics have been found in China's drinking water sources. The differences in the concentration of antibiotics in the water environment reflect the differences of antibiotic use in different areas. It can be seen from Table 2 that the concentration of antibiotics detected in the drinking water source of the Three Gorges Reservoir Upper Area is comparable with Shanghai, Shenzhen and Guangdong Province, just with  $\rho(\text{LIN})$  significantly higher. Jiangsu Province has been detected 20 kinds of antibiotics, and this area has the most kinds of antibiotics and high concentrations. Especially the Gonghu Bay, Except  $\rho(\text{SMX})$ ,  $\rho(\text{ROM})$ , the rest of the antibiotic concentration was higher than past research data, The maximum of  $\rho(\text{TMP})$ ,  $\rho(\text{TC})$ ,  $\rho(\text{CTC})$ ,  $\rho(\text{NFX})$ ,  $\rho(\text{OFX})$ ,  $\rho(\text{CFX})$  more than 200 ng/L. In general, the type and quality of antibiotics in drinking water sources in China are significantly lower than those in other water bodies, and the detected concentrations are mostly in the range of several to several tens of ng/L. The main detection of antibiotics in the Three Gorges Reservoir Upper Area is macrolide (including LIN), followed by sulfonamides and amines. Compared with the lower reaches of the Yangtze River (Shanghai, Jiangsu), the rest has same concentration level

while TYL and LIN are not detected in the literature. With the detection of antibiotics maintained in high concentration, antibiotic pollution in Jiangsu Gonghu Bay water is more serious, especially the maximum of  $\rho(\text{TC})$  and  $\rho(\text{CTC})$  is around 1,850 and 4,720 ng/L. Therefore, the antibiotic residues in the water environment in China should be paid attention to.

For the worst-case, the calculation of RQS should use PNEC method to screen the most sensitive species and use the maximum mass concentration of the antibiotic to calculate the value. The result is shown in Table 3.

$\text{RQS} < 0.1$  is low risk,  $0.1 \leq \text{RQS} < 1$  is moderate risk,  $\text{RQS} \geq 1$  is high risk, according to the RQS classification method proposed by Hernando. The current studies have shown that water toxicity can be exacerbated by the coexistence of multiple drugs in the water environment. According to references, the simple additive model can be used to calculate toxicity risk entropy ( $\text{RQ}_{\text{sum}}$ ):

$$\text{RQ}_{\text{sum}} = \sum_{i=1}^n \text{RQ}_i \tag{3}$$

In formula  $\text{RQ}_i$  is the RQ value of compound  $i$  and  $n$  is the number of species of the target compound.

According to the analysis of water sources, Fig. 4 and Table 4 show that the  $\text{RQ}_{\text{sum}}$  of nine water sources from high to low is T-R-CK > C-R-BB > T-L-JM > C-R-DY > T-R-GQ > T-L-ZJ > C-L-GSQ > C-R-LT > C-R-FSB. Among them, the  $\text{RQ}_{\text{sum}}$  of T-R-CK is up to 1.981, SMX, ERM and LIN are in moderate risk. SMX ( $\text{RQS} = 0.944$ ) is near the high risk, indicating that aquatic organisms in this water show very high risk of toxicity. Followed by C-R-BB water source,  $\text{RQ}_{\text{sum}}$  is 1.077, showing a high ecological risk. But single RQS is less than 1 and in a low risk level. The  $\text{RQ}_{\text{sum}}$  of five water sources (T-L-JM, C-R-DY, T-R-GQ, T-L-ZJ, C-L-GSQ) ranged from 0.1 to 1 and are at moderate risk, but the values of RQS of antibiotics SMZ, FF, CAP, FF were all less than 0.1. The values of  $\text{RQ}_{\text{sum}}$  of the C-R-LT and C-R-FSB sources are 0.055 and 0.028, respectively, and the antibiotics are at low risk, indicating the water source is minimally disturbed by human activities.

Table 3  
Toxicity data for the most sensitive species of antibiotics

Antibiotics	Toxicity types	Evaluation factors	Toxicity data (mg/L)		PNEC (ng/L)
			EC50	NOEC	
SMX	Acute	1,000	0.027	—	27
SMZ	Acute	1,000	19.5	—	19,500
TYL	Chronic	100	—	0.0034	34
ERM	Chronic	100	—	0.002	20
ROM	Chronic	100	—	0.01	100
LIN	Acute	1,000	0.35	—	350
FF	Acute	1,000	0.649	—	649
CAP	Acute	1,000	1.6	—	1,600

EC50 is the half maximum concentration; NOEC is the maximum no effect concentration.

Table 4  
Antibiotic risk assessment in drinking water sources of the Three Gorges Reservoir upper area

Sampling site	Sulfonamides		Macrolides				Aniline alcohols		RQ <sub>sum</sub>
	SMX	SMZ	TYL	ERM	ROM	LIN	FF	CAP	
T-R-GQ	–	–	0.241	0.15	0.111	0.012	0.011	0.0005	0.525
C-R-FSB	–	–	–	–	–	0.015	0.012	0.0005	0.028
C-R-DY	–	–	0.394	0.125	0.314	0.018	0.012	0.002	0.866
C-R-BB	–	–	0.574	0.14	0.32	0.025	0.018	0.001	1.077
C-R-LT	–	–	–	–	–	0.011	0.039	0.0059	0.055
C-L-GSQ	–	–	–	–	–	0.099	0.004	0.0003	0.103
T-L-ZJ	–	–	–	0.105	0.012	0.04	0.005	–	0.162
T-R-CK	0.944	–	0.088	0.46	0.087	0.400	0.002	0.0004	1.981
T-L-JM	0.481	0.001	–	0.255	0.022	0.195	0.011	0.0004	0.965

4. Conclusions

According to the antibiotic species, the study result can be seen from Fig. 5 that the values of RQS of SMZ, FF and CAP were all less than 0.1, except that the TL-ZJ water source was not detected with CAP and the rest of them have been

detected with FF and CAP already. It is indicating that these two antibiotics are widely used in the reservoir area, but the ecological risk is not significant. SMX, TYL, ERM and ROM are at moderate risk levels. In addition to CL-GSQ, CR-LT, CR-FSB water sources, the remaining water sources are both detected with ERM and ROM. It means the potential effects of these four antibiotics on ecology should be taken into account. From the study of antibiotics limit values in poultry manure, we know that the main risk of antibiotics from livestock and poultry drugs. The government should control the usage of livestock and poultry antibiotics in Three Gorges Reservoir Area. The specification for antibiotics straw-return techniques in livestock and poultry manure should be established by government.

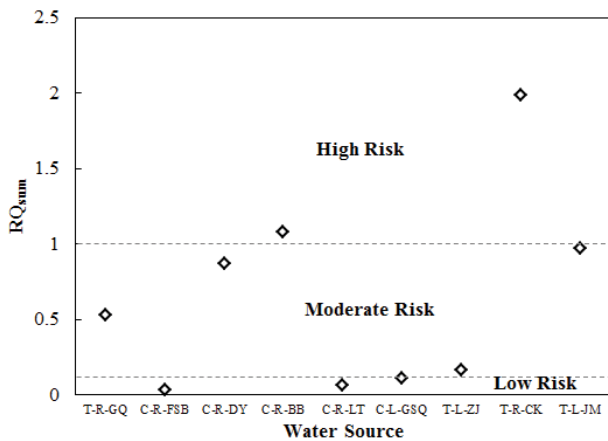


Fig. 4. Combined ecological risk of antibiotics in drinking water sources of the Three Gorges Reservoir upper area.

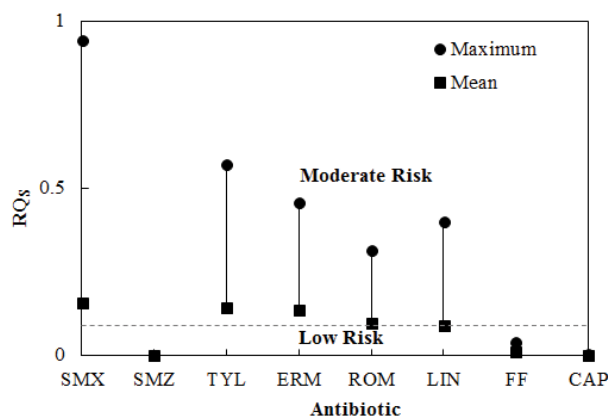


Fig. 5. Risk quotient of antibiotics in drinking water sources of the Three Gorges Reservoir upper area.

Acknowledgments

The authors thank Liu Yiqi and Liu Xing for helpful discussions. The authors acknowledge the support through the instruments and equipment for experimental analysis services at the Chongqing Academy of Environmental Sciences. The authors also thank the computing facilities of the Department of Big data analysis center at the Chinese academy of sciences Chongqing institute. The authors acknowledge the support of the Entrepreneurial Innovative Talents Program of Personnel & Labour Security Department of Chongqing.

References

- [1] K. Oberlé, M.J. Capdeville, T. Berthe, H. Budzinski, F. Petit, Evidence for a complex relationship between antibiotics and antibiotic-resistant escherichia coli: from medical center patients to a receiving environment, *Environ. Sci. Technol.*, 46 (2012) 1859–1868.
- [2] J. Wang, T. Gu, J. Wang, Y. Xu, P. Chen, M.A. Ashraf, Environmental geological features of the red clay surrounding rock deformation under the influence of rock-fracture water, *Sains Malaysiana*, 46 (2017) 2049–2059.
- [3] M.A. Ashraf, M.M. Hanfiah, Recent advances in assessment on clear water, soil and air, *Environ. Sci. Pollut. Res.*, 24 (2017) 22753–22754.
- [4] L.Y. He, G.G. Ying, Y.S. Liu, H.C. Su, J. Chen, S.S. Liu, J.L. Zhao, Discharge of swine wastes risks water quality and food safety: antibiotics and antibiotic resistance genes from swine sources

- to the receiving environments, *Environ. Int.*, 92–93 (2016) 210–219.
- [5] O.S. Onwuka, C.K. Ezugwu, S.I. Ifediegwu, Assessment of the impact of onsite sanitary sewage system and agricultural wastes on groundwater quality in Ikem and its environs, south-eastern Nigeria, *Geol. Ecol. Landscapes*, 3 (2019) 65–81.
- [6] A. Boonyasiri, T. Tangkosul, C. Seenama, J. Saiyarin, S. Tiengrim, V. Thamlikitkul, Prevalence of antibiotic resistant bacteria in healthy adults, foods, food animals, and the environment in selected areas in Thailand, *Pathog. Global Health*, 108 (2014) 235–245.
- [7] A. Zouiten, A. Beltifa, J. Van Loco, H.B. Mansour, T. Reyns, Ecotoxicological potential of antibiotic pollution-industrial wastewater: bioavailability, biomarkers, and occurrence in *mytilus galloprovincialis*, *Environ. Sci. Pollut. Res.*, 23 (2016) 15343–15350.
- [8] Z. Zainuddin, A.M. Kamil, In-vitro regeneration of *Orthosiphon stamineus* (Misai Kucing) using axillary bud, *Sci. Heritage J.*, 3 (2019) 8–10.
- [9] A.R. Hauser, D.T. Moir, J. Mecsas, B. Berube, K. Murphy, N.O. Bowlin, J.D. Williams, T.L. Bowlin, Beyond antibiotics: new therapeutic approaches for bacterial infections, *Int. J. Antimicrob. Agents*, 50 (2017) S19–S20.
- [10] L. Ye, Y.-b. Liu, A.-I. Geng, H.-Y. Fu, Microbiological examination to investigate the differences in microorganisms and antibiotic sensitivity of head and neck space infections, *Biomed Res.*, 28 (2017) 290–294.
- [11] N.H.M. Zin, A.M.M. Nail, Anti-diabetic potential of peptide from *P. Niruri* reveals through carbohydrate hydrolyzing enzyme inhibition assay, *Sci. Heritage J.*, 3 (2019) 17–19.
- [12] B.J. Richardson, P.K.S. Larn, M. Martin, Emerging chemicals of concern: pharmaceuticals and personal care products (PPCPs) in Asia, with particular reference to Southern China, *Mar. Pollut. Bull.*, 50 (2005) 913–920.
- [13] Q.Q. Zhang, G.G. Ying, C.G. Pan, Y.S. Liu, J.L. Zhao, 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 (2015) 6772–6782.
- [14] I. Sufiyan, J.I. Magaji, Modeling flood hazard using swat and 3D analysis in Terengganu watershed, *J. Clean WAS*, 2 (2018) 19–24.
- [15] Y.-G. Zhu, T.A. Johnson, J.-Q. Su, M. Qiao, G.-X. Guo, R.D. Stedtfeld, S.A. Hashsham, J.M. Tiedje, Diverse and abundant antibiotic resistance genes in Chinese swine farms, *Proc. Natl. Acad. Sci. U.S.A.*, 110 (2013) 3435–3440.
- [16] O.A. Naik, R. Shashidhar, D. Rath, J.R. Bandekar, A. Rath, Metagenomic analysis of total microbial diversity and antibiotic resistance of culturable microorganisms in raw chicken meat and mung sprouts (*Phaseolus aureus*) sold in retail markets of Mumbai, India, *Curr. Sci.*, 113 (2017) 71–79.
- [17] K. Kadharsa, S.A. Khan, S. Lyla, P. Mohanchander, A. John, Checklist for commercially important food fishes of Parangipettai Southeast coast of India, *J. Clean WAS*, 2 (2018) 16–19.
- [18] Y.H. Jiang, M.X. Li, C.S. Guo, D. An, J. Xu, Y. Zhang, B.D. Xi, Distribution and ecological risk of antibiotics in a typical effluent-receiving river (Wangyang River) in North China, *Chemosphere*, 112 (2014) 267–274.
- [19] W.J. Deng, N. Li, H.L. Zheng, H.Y. Lin, Occurrence and risk assessment of antibiotics in river water in Hong Kong, *Ecotoxicol. Environ. Saf.*, 125 (2016) 121–127.
- [20] D. Baharuddin, M. Dinie, Effect of pH and moisture content on current density of impressed current cathodic protection: response surface methodology study, *Environ. Ecosyst. Sci.*, 2 (2018) 15–19.
- [21] L.K. Xu, W.Y. Ouyang, Y.Y. Qian, C. Su, J.Q. Su, H. Chen, High-throughput profiling of antibiotic resistance genes in drinking water treatment plants and distribution systems, *Environ. Pollut.*, 213 (2016) 119–126.
- [22] Y.P. Ma, M. Li, M.M. Wu, Z. Li, X. Liu, Occurrences and regional distributions of 20 antibiotics in water bodies during groundwater recharge, *Sci. Total Environ.*, 518 (2015) 498–506.
- [23] M. Afzal, K. Fatima, P. Khalid, Ejaz-ul-Haq, A. Abbas, S. Durrani, A. Sajid, M. Zaheer, Internet of things its environmental applications and challenges, *Environ. Contam. Rev.*, 1 (2018) 1–3.
- [24] J. Du, H. Zhao, S. Liu, H. Xie, Y. Wang, J. Chen, Antibiotics in the coastal water of the south yellow sea in China: occurrence, distribution and ecological risks, *Sci. Total Environ.*, 595 (2017) 521–527.
- [25] A. Hossain, S. Nakamichi, M. Habibullah-Al-Mamun, K. Tani, S. Masunaga, H. Matsuda, Occurrence, distribution, ecological and resistance risks of antibiotics in surface water of finfish and shellfish aquaculture in Bangladesh, *Chemosphere*, 188 (2017) 329–336.
- [26] K.A. Halim, E.L. Yong, Integrating two-stage up-flow anaerobic sludge blanket with a single-stage aerobic packed-bed reactor for raw palm oil mill effluent treatment, *Water Conserv. Manage.*, 2 (2018) 1–4.
- [27] F.H. Wang, M. Qiao, J.Q. Su, Z. Chen, X. Zhou, Y.G. Zhu, High throughput profiling of antibiotic resistance genes in urban park soils with reclaimed water irrigation, *Environ. Sci. Technol.*, 48 (2014) 9079–9085.
- [28] H. Ju, J. Zhang, C. Sun, Occurrence, spatial distribution and risk and hazard assessments of antibiotics in drinking water sources of a polluted large river basin in China, *Aquat. Ecosyst. Health Manage.*, 21 (2018) 107–117.
- [29] M.H. Mahtab, M. Ohara, M. Rasmy, The impact of rainfall variations on flash flooding in Haor Areas in Bangladesh, *Water Conserv. Manage.*, 2 (2018) 6–10.
- [30] J.P. Zhang, W.Y. Li, J.P. Chen, W.Q. Qi, F. Wang, Y.Y. Zhou, Impact of biofilm formation and detachment on the transmission of bacterial antibiotic resistance in drinking water distribution systems, *Chemosphere*, 203 (2018) 368–380.
- [31] C.W. Xi, Y.L. Zhang, C.F. Marrs, W. Ye, C. Simon, B. Foxman, J. Nriagu, Prevalence of antibiotic resistance in drinking water treatment and distribution systems, *Appl. Environ. Microbiol.*, 75 (2009) 5714–5718.
- [32] A.L. Li, L.J. Chen, Y. Zhang, Y.L. Tao, H. Xie, S. Li, W.L. Sun, J.G. Pan, Z.D. He, C.A. Mai, Y.Y. Fan, H.C. Xian, Z.B. Zhang, D.H. Wen, Occurrence and distribution of antibiotic resistance genes in the sediments of drinking water sources, urban rivers, and coastal areas in Zhuhai, China, *Environ. Sci. Pollut. Res.*, 25 (2018) 26209–26217.
- [33] X.S. Chang, M.T. Meyer, X.Y. Liu, Q. Zhao, H. Chen, J.-a. Chen, Z.Q. Qiu, L. Yang, J. Cao, W.Q. Shu, Determination of antibiotics in sewage from hospitals, nursery and slaughter house, wastewater treatment plant and source water in Chongqing region of Three Gorge Reservoir in China, *Environ. Pollut.*, 158 (2010) 1444–1450.
- [34] L.H. Lu, J. Liu, Z. Li, Z.P. Liu, J.S. Guo, Y. Xiao, J.X. Yang, Occurrence and distribution of tetracycline antibiotics and resistance genes in longshore sediments of the Three Gorges Reservoir, China, *Front. Microbiol.*, 9 (2018) 1911.
- [35] W. Yanhui, Beyond regular semigroups, *Semigroup Forum*, 92 (2016) 414–448.
- [36] J. Zhang, X. Wu, L. Xing, C. Zhang, H. Iu, T. Fernando, Bifurcation analysis of five-level cascaded H-bridge inverter using proportional-resonant plus time-delayed feedback, *Int. J. Bifurcation Chaos*, 26 (2016) 11.
- [37] Z. Wencai, L. Juan, M. Xinzhu, Dynamical analysis of sir epidemic model with nonlinear pulse vaccination and lifelong immunity, *Discrete Dyn. Nat. Soc.*, 2015 (2015) 10 p. Available at: <http://dx.doi.org/10.1155/2015/848623>.
- [38] Y. Zhang, D. Shen, Estimation of semi-parametric varying-coefficient spatial panel data models with random-effects, *J. Stat. Plann. Inference*, 159 (2015) 64–80.
- [39] D. Huanhe, Z. Kun, Y. Hongwei, L. Yuqing, Generalised (2+1)-dimensional super MKDV hierarchy for integrable systems in soliton theory, *East Asian J. Appl. Math.*, 5 (2015) 256–272.
- [40] Z. Tongqian, M. Xinzhu, Z. Tonghua, Global dynamics of a virus dynamical model with cell-to-cell transmission and cure rate, *Comput. Math. Methods Med.*, 2015 (2015), doi: 10.1155/2015/758362.



- [41] L. Fei, W. Zhiyu, W. Fang, Hamiltonian systems with positive topological entropy and conjugate points, *J. Appl. Anal. Comput.*, 5 (2015) 527–533.
- [42] L. Gang, C. Ming, Infinite horizon linear quadratic optimal control for stochastic difference time-delay systems, *Adv. Differ. Equations*, 2015 (2015) 14.
- [43] L. Feng, M. Suzhen,  $L^p$  bounds for nonisotropic Marcinkiewicz integrals associated to surfaces, *J. Aust. Math. Soc.*, 99 (2015) 380–398.
- [44] T. Fabio, A.A. Elsadany, X. Baogui, H.N. Agiza, Local stability of the cournot solution with increasing heterogeneous competitors, *Nonlinear Anal. Real World Appl.*, 26 (2015) 150–160.
- [45] G. Pascual-Córdova, Indicadores de calidad del suelo en el agroecosistema caña de azúcar (*Saccharum spp.*), *Revista de la Facultad de Agronomía de la Universidad del Zulia*, 35 (2018) 130–140.
- [46] J. HongMei, W. HuaShan, G. RuiHua, H. HongYing, Removal characteristics of nitrogen and phosphorus and their land application rates during a multi-level treatment process for manure and waste water: an example from intensive swine farm in water network region of southern Jiangsu province, China, *J. Agric. Resour. Environ.*, 35 (2018) 237.
- [47] E. Charani, The competitive ability of maize (*Zea mays L.*)-common bean (*Phaseolus vulgaris L.*) intercrops against weeds, *Revista de la Facultad de Agronomía de la Universidad del Zulia*, 35 (2018) 35–45.
- [48] S.F. Marashi, The life cycle assessment of sugarcane: a case study of Amir Kabir cultivation and industry, *Revista de la Facultad de Agronomía de la Universidad del Zulia*, 35 (2018) 102–130.
- [49] V. Barbosa-Brandão, F. Pérez Rodríguez, A. Rojo-Alboreca, Selección de criterios sociales y ambientales para la delimitación de núcleos rurales en Galicia, España, *Revista de la Facultad de Agronomía de la Universidad del Zulia*, 35 (2018) 80–90.