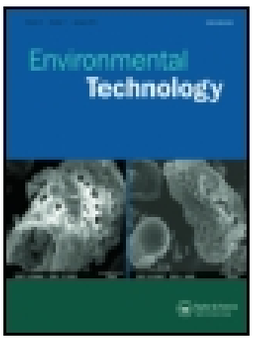

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Occurrence of antibiotics in rural drinking water and related human health risk assessment

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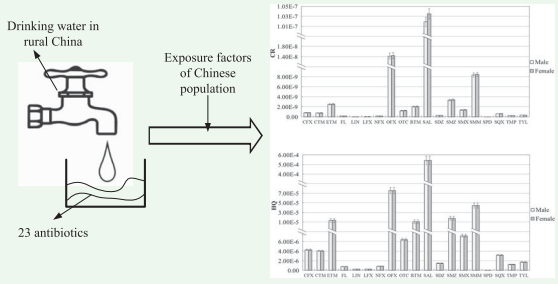
ABSTRACT

Antibiotic residues in drinking water can have a negative impact on both human and environmental health. However, drinking water purification processes employed in rural areas are often less complicated than those used in urban areas. The occurrence of antibiotic residues in rural drinking water and their potential effects on residents' health remains to be established. In this study, we measured antibiotic levels in rural drinking water using high-performance liquid chromatography–tandem mass spectrometry (HPLC–MS/MS), and evaluated the associated health risks based on Chinese population exposure parameters. Twenty-three antibiotics were detected in drinking water samples, of which fluoroquinolones and macrolides were the most common. The type and concentration of antibiotics in drinking water were affected both by the quality of the water source and by the water purification process used. The health risks associated with antibiotics in drinking water were within acceptable levels and likely to have little impact on human health. Of the antibiotics detected, salinomycin presented the greatest risk to human health. These findings can help to play a role in devising strategies to ensure drinking water safety.



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Rural drinking water; drinking water sources; antibiotic residues; water purification process; health risk assessment

1. Introduction

The adequate and safe supply of water important for social stability. However, problems associated with water availability and quality worldwide are exacerbated by the increasing size of the population and improvements in people's living standards [1]. China is a large agricultural country that had approximately 500 million people still living in rural areas in 2017 [2]. Therefore, ensuring the safety of drinking water and improving the living and working conditions of residents in China's rural areas is of great importance [3]. In 2007, China announced the 'Administrative Measures for Construction of a Rural Drinking Water Safety Project' to ensure the safety of drinking water in rural areas; this administrative measure was revised in 2013 [4]. To ensure the safety of the water supply system, the Water Safety Plan (WSP) requires comprehensive risk assessment and risk management to be conducted throughout all the processes carried out as part of the water supply systems [5].

A more recent problem affecting the quality of drinking water is the presence of emerging contaminants, which include pharmaceuticals, personal care products, endocrine disrupters and antibiotics [1,6]. However, conventional water purification processes do not involve the removal of such contaminants from drinking water supplies [1,6,7]. Thus, these contaminants can enter drinking water through the water supply system. A major concern with regard to emerging contaminants is the uncertainty surrounding

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their adverse ecological effects and the potential risk they pose to human health due to long-term exposure to trace levels of these substances [1,8]. Antibiotics, which are widely used to combat bacterial infections, and as growth promoters in aquaculture and agriculture, are viewed as a special class of emerging contaminants [9].

A large proportion of antibiotics used in humans and animals are not fully metabolized and are often excreted into the environment in the form of the original drug, although metabolites and other forms may also be released [10,11]. These antibiotics can remain in the environment and directly affect the ecological health of water and endanger the normal growth of water organisms, thus, destroying the balance of ecosystems while being passed along the food chain [9,12–14]. Although the aquatic environment is highly susceptible to such exposure to drugs, people are more concerned about the risk to human health associated with inadvertent exposure to antibiotics [1]. This can be especially a particular concern in areas that practice indirect water reuse, where antibiotics used by people are released to streams and rivers that are in turn, used as sources of drinking water for communities living downstream [15].

Although many studies have demonstrated the presence of antibiotics and assessed health risks associated with low levels of these drugs in drinking water [1,16–19], few studies have investigated on the risk to human health caused by antibiotics in rural areas. In this study, we investigated a typical rural area in southern China, where the drinking water of residents in the higher regions is obtained from mountain springs, while in the middle and lower reaches, drinking water is obtained from rivers. The study area is home to approximately 3 million rural inhabitants and has eight water purification plants employing three types of treatment processes. The rainy season runs from March to October and the dry season from November to March. The period with the highest incidence of disease in the region is from March to July. In this study, the presence and level of twenty-three antibiotic residues in rural drinking water were investigated and the potential risk to human health was evaluated.

2. Materials and methods

2.1 *A antibiotics selected, sampling and analysis*

The twenty-three antibiotics investigated during this study belong to different families and have been detected in various aquatic environments [20–22]. They comprised fluoroquinolones [ciprofloxacin (CFX), danofloxacin (DAN), difloxacin (DIF), fleroxacin (FL), lomefloxacin (LFX), norfloxacin (NFX) ofloxacin (OFX) and sarafloxacin (SAR)]; macrolides [clarithromycin (CTM), erythromycin (ETM), roxithromycin (RTM) and tylosin (TYL)]; tetracyclines [oxytetracycline (OTC)]; sulfonamides [sulfadiazine (SDZ), sulfamethazine (SMZ), sulfachlorpyridazine (SCP), sulfamethoxazole (SMX), sulfamethoxine (SMM), sulfapyridine (SPD), sulfaquinoxaline (SQX) and trimethoprim (TMP)]; and others [lincomycin (LIN) and salinomycin (SAL)]. All antibiotics were obtained from Sigma–Aldrich (St. Louis, MO, USA).

The area under investigation is a typical southern rural area of China located along a river. The main sources of drinking water include mountain springs, groundwater and river water. Seven water treatment plants that implement conventional treatment processes (flocculation-precipitation-chlorination) and one that implements advanced treatment processes (nanofiltration) are located along the river. The selection of sampling points is shown in Table 1 and the layout of sampling points is shown in Figure S1. We collected seven household drinking water samples from taps on three occasions: October 2015 (first sampling), May 2016 (second sampling), and January 2017 (third sampling). We analysed a total of nineteen drinking water samples (three from mountain springs, three from groundwater and thirteen from river water).

For each water sample, we collected 5 L of water, added 500 mL of methanol and adjusted the pH to 3 with diluted sulfuric acid (4 mol/L). All drinking water samples were pretreated within two days of collection. The samples were filtered through glass fibre filters (0.45 μm) to remove suspended particles. After adding internal standard substances (100 ng/L), the water samples (5 L) were extracted by solid phase extraction using Oasis HLB columns (500 mg and 6 mL, Waters, Milford, MA, USA) optimized with methanol and ultra-

Table 1. Details of the drinking water survey and sampling point selection.

Sample number	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 7
Sample point marker	A1	A2	A3	A4	A5	A6	A7
Type of water source	Mountain spring	Groundwater	River	River	River	River	River

Note: The water treatment technology of A1 and A2 is flocculation-precipitation; the water treatment technology of A3-A6 is flocculation-precipitation-filtration-disinfection; the water treatment technology of A7 is flocculation-precipitation-ultrafiltration-disinfection.

pure water. Any antibiotics retained on the HLB columns were eluted with 12 mL methanol. The eluates were then dried under a gentle stream of nitrogen and redissolved in 1 mL methanol. After filtration through a 0.22 μm organic membrane to remove any particles, the final extract was transferred to a 2 mL brown glass vial and stored at −18°C prior to high-performance liquid chromatography-tandem mass spectrometry (HPLC–MS/MS) analysis [21].

Analysis of antibiotics was achieved using HPLC–MS/MS (an Agilent Liquid Chromatography 1200 series HPLC system coupled to an Agilent 6460 triple quadrupole MS) equipped with an electrospray ionization (ESI) source (Agilent, Palo Alto, CA, USA) in multiple-reaction monitoring (MRM) mode. The Agilent Eclipse Plus-C18 (100 × 2.1 mm, 1.8 μm) with its corresponding pre-column filter (2.1 mm, 0.2 μm) was set to 40°C with a flow rate of 0.3 mL/min. The mobile phase (A) was a mixture of 0.2% formic acid and 2 mmol/L ammonium acetate and the mobile phase (B) was acetonitrile. The gradient elution procedure was performed as follows: 0 min 90% A, 5 min 85% A, 7 min 80% A, 11 min 60% A, 15 min 40% A, 16 min 5% A, and 25 min 5% A [21]. A 5 μL sample was injected, and the analyses were performed in the positive mode. Nitrogen gas was used as the drying and collision gas. The MS parameters are listed in Table 2. Mass spectrometric conditions were optimized using Optimizer (Agilent, Palo Alto, USA) for collision energy (CE), fragmentor voltage, and multiple reaction monitoring mode (MRM) transitions for each compound [21].

For the target antibiotic compounds, the method quantification limit (MQL) was in the range of 0.63–4.43 ng/L, the repeatability varied from 0.63% to 9.67%, and the reproducibility ranged from 2.74% to 21.3% [21]. Standard addition (100 ng/L) of sulfonamides, quinolones, tetracyclines, macrolides and other antibiotics to the water samples resulted in recovery rates of 65–129%, 53–151%, 115.3%, 82–142% and 84–123%, respectively. This method is well established for the detection of antibiotics in environmental water samples [19,21,22].

2.2 *Human health risk analysis*

The main ways in which humans are exposed to antibiotics in tap water are through drinking and bathing [16]. Boursi reported that the cancer risk in some specific organ sites might be associated with recurrent exposure to certain antibiotics [23]. For the present study, the risk to humans of drinking-water mediated exposure to antibiotics was assesses using risk quotients (RQs) according to previously described methods [1,20]. The US Environmental Protection Agency (EPA) exposure calculation method was also used to conduct a human-health risk assessment based on antibiotics in drinking water, which includes both carcinogenic and non-carcinogenic risks [9,24,25]. The carcinogenic risk and non-carcinogenic risk associated with exposure to a single pollutant in drinking water were expressed as carcinogenic risk (CR) and hazard quotient (HQ), respectively [9,24,25]. Thus, RQ, CR and HQ were used to evaluate the health risks associated with antibiotics in drinking water.

2.2.1. *Risk quotients (RQ)*

RQ values were estimated for each antibiotic quantified in the drinking water samples according to Equation (1), where C_s is the maximum level of antibiotic present in the drinking water and DWEL is the corresponding Drinking Water Equivalent Level [1]. The maximum concentration was used to provide a conservative 'worst-case' scenario approach [1]. DWELs were estimated according to Equation (2) defined in the 'Wyoming Water Rules and Regulations' [26]. Equation (2) is cited by many antibiotic health risk studies in Asia [1,6,20,27,28]:

$$\mathrm{RQ} = C_s/\mathrm{DWEL} \tag{1}$$

$$\mathrm{DWEL} = \frac{\mathrm{ADI} \times \mathrm{BW} \times \mathrm{HI}}{\mathrm{DWI} \times \mathrm{AB} \times \mathrm{FOE}} \tag{2}$$

In Equation (2), ADI is acceptable daily intake (mg/kg day) (see below); BW is the 50th percentile value of body weight (kg); HI represents the hazard index (arbitrarily assigned a value of 1); DWI is recommended drinking water intake (L day^{-1}) the different sexes; AB is the gastrointestinal absorption rate (arbitrarily assigned a value of 1); and FOE is the frequency of exposure (350 days/365 days = 0.96). Values for BW and DWI were obtained from the Chinese Population Exposure Parameter Manual and are shown in Table 3 [29].

Table 2. MS parameters for the detection of antibiotics.

Gas temperature	325°C
Gas flow rate	6 L/min
Nebulizer	45 psi
Sheath gas temperature	350°C
Sheath gas flow rate	11 L/min
Capillary voltage	3500 V
Nozzle voltage	0 V

Table 3. Health risk-assessment of various parameter values [29].

Parameter	Male	Female
BW/(kg/person)	65	56.8
EF/(days/year)	350	350
ED/years	73.64	79.43
AT/days	26,879	28,992
DWI/(L/day)	2	1.775

The ADI represents a level of daily intake that is based on the chemical evaluation of pesticide residues by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) [30]. For compounds detected in this study, the ADI used was adopted either from provisional values established in the literature or reference limits of veterinary drugs in animal foods. The reference values of ADI used in some studies were also from animal food reference limits [6,27,28].

An increased risk to human health due to the consumption of drinking water is indicated by an RQ > 1. Antibiotics in drinking water with an RQ between 0.2 and 1 are considered to warrant further investigation, whereas an RQ ≤ 0.2 is presumed to present no appreciable concern for human health [30,31].

2.2.2. Carcinogenic risk (CR) and hazard quotient (HQ)

The CR used to evaluate the carcinogenic risk of antibiotics [16,32] is calculated as follows:

$$CR = CDI \times \beta_h \quad (3)$$

where CR is the carcinogenic risk of pollutants present in drinking water [unitless]; CDI is the chronic daily average exposure (dose) to pollutants per unit body weight [mg/(kg day)]; and β_h is the carcinogenic intensity coefficient of exposure for humans [kg day/mg], according to a model established by Zeise et al. [33]. β_h was calculated according to the following formulae:

$$\beta_h = \beta_a \times K_{ah} \quad (4)$$

$$\beta_a = \frac{D}{C \times LD_{50}} \quad (5)$$

where K_{ah} is an interspecies extrapolation factor, set to 4.7 based on Crouch [34]; β_a is the carcinogenic intensity coefficient of exposure for animals; C and D are parameters targeted at different experimental animals and reported by Zeise et al. [33]; and LD_{50} is the median lethal dose in animals [mg/kg]. The hazard quotient (HQ) used to evaluate the non-carcinogenic risks of antibiotics was calculated as follows [35]:

$$HQ = \frac{CDI}{RfD} \quad (6)$$

where HQ is the hazard quotient [unitless]; CDI is the daily average exposure (dose) to pollutants per unit body weight [mg/(kg day)]; and RfD is the non-carcinogenic reference dose of contaminants [mg/(kg day)].

The non-carcinogenic reference dose of contaminants is estimated as follows [32,36]:

$$RfD = LD_{50} \times 4 \times 10^{-5}$$

where 4×10^{-5} is the empirical conversion coefficient [1/day].

The quantitative estimation model for people consuming pollutants through their diet (mainly drinking water) is as follows [16,29]:

$$CDI = C_w \times DWI \times AB \times \frac{EF \times ED}{BW \times AT} \quad (5)$$

where CDI is the daily average exposure (dose) to pollutants per unit body weight [mg/(kg·day)]; C_w is the concentration of antibiotics in drinking water [mg/L]; DWI is the average daily consumption of drinking water [L/day]; AB is the gastrointestinal absorption rate (defined to 1) [unitless]; EF is the frequency of exposure [days/year], ED is the exposure period [years]; AT is the average exposure time [days]; and BW is the average body weight [kg] [29].

The total carcinogenic risk (TCR) is the sum of the CR values of the various antibiotics, in addition, the total hazard quotient (THQ) is the sum of the HQ values of the various antibiotics.

USEPA regulations indicated that the carcinogenic risk is acceptable [18,24,37] when the CR of pollutants is $\leq 10^{-6}$. The HQ is classified as follows: if the risk index is greater than 1, the risk is high (unacceptable); if the risk index is between 0.1 and 1, the risk is moderate; and if the risk index is less than 0.1, the risk is low (acceptable) [16,38].

3. Results

3.1. Residues of antibiotics in drinking water

A total of 23 antibiotics were detected in 19 drinking water samples. A summary of all results obtained in the monitoring study of drinking water samples is shown in Table S1. In order to investigate the total concentration of each antibiotic in the study rural area, the same antibiotic concentrations of the 19 samples were summed. Table 4 shows the total concentration and detectable rate of each antibiotic detected in the 19 drinking water samples. OFX was detected at the highest rate (74%). ETM, SAL and CFX were also detected at high rates, reaching 47.4%, 42.1% and 36.8%, respectively. Among the 23 antibiotics detected, the total concentration of FLX, ETM, SMZ and SMM in all samplings exceeded 100 ng/L.

In order to investigate the concentration of antibiotic at each sampling points, the concentrations of antibiotics at each sampling point were summed (Table 5), Table 5 shows the total concentration of antibiotics at each drinking water sampling point. The largest number of different antibiotics (19) was detected at the A6 sampling

Table 4. Total antibiotics detected in all drinking water samples.

Types of antibiotics	Total concentration (ng/L)	Frequency	Detectable rate (%)
CFX	31.56	7	36.8
CTM	5.66	3	15.8
DAN	1.97	1	5.26
DIF	1.46	2	10.5
ETM	169.65	9	47.4
FL	1.61	2	10.5
LIN	1.46	1	5.26
LFX	1.47	1	5.26
NFX	16.32	5	26.3
OFX	453.86	14	73.7
OTC	27.54	2	10.5
RTM	11.84	3	15.8
SAL	89.64	8	42.1
SAR	1.3	1	5.26
SCP	4.74	1	5.26
SDZ	6.05	3	15.8
SMZ	181.29	3	15.8
SMX	52.56	4	21.0
SMM	146.08	3	15.8
SPD	3.37	4	21.0
SQX	4.09	2	10.5
TMP	24	5	26.3
TYL	2.54	2	10.5

point, followed by the A5 sampling point (16). A5 and A6 received drinking water from the same source – river water. The fewest different antibiotics of antibiotics were detected at the A2 sampling point (4). The source of drinking water at A2 was groundwater. There were 11 antibiotics detected in drinking water sourced from mountain spring water (A1). In drinking water treated by a nanofiltration process, which was highly effective for the removal of antibiotic residues, there were 5 different antibiotics detected.

All families of antibiotics were detected in the drinking water samples: fluoroquinolones (80% of samples), macrolides (50%), tetracyclines (10%), sulfonamides (30%), others antibiotics (35%) (Figure 1). Fluoroquinolones and macrolides were, therefore, the two main families of antibiotics detected in drinking water in this study area.

Figure 2 shows that the detectable frequency of five families of antibiotics at the three sampling times. Fluoroquinolones were the most ubiquitous antibiotics detected at different sampling times. At the first sampling (October 2015), the detection rate of fluoroquinolones and macrolides was 100% (Figure 2). Compared with other antibiotics (tetracyclines, sulfonamides and others), fluoroquinolone antibiotics were most prevalent in the study area. It can be speculated that this is because fluoroquinolones are the most frequently used antibiotics in the rural area under investigation. Compared with the detection frequency at the first and second sampling time-points, at the third time-point sulfonamides and 'other' antibiotics were detected with the highest frequency.

Table 5. The total concentration and type of antibiotics detected at each sampling point.

Drinking water sampling point	A1			A2			A3			A4			A5			A6			A7		
Sampling time-point	3rd	2nd	1st	3rd	2nd	1st	3rd	2nd	1st	3rd	2nd	1st	3rd	2nd	1st	3rd	2nd	1st	3rd	2nd	1st
Detected concentration[a] (ng/L)	27.07	40.85	24.22	2.53	Nd	6.2	0.14	5.48	36.94	8.02	Nd	9.17	2.31	530.57	257.7	234.23	42.72	– –	1.85	12.56	– –
Number of types of antibiotics	11			4			5			6			16			19			5		

Note: 1st, 2nd and 3rd indicates the first sampling (October 2015), the second sampling (May 2016) and the third sampling (January 2017), respectively.
[a]The total concentration of antibiotics detected in each sample.

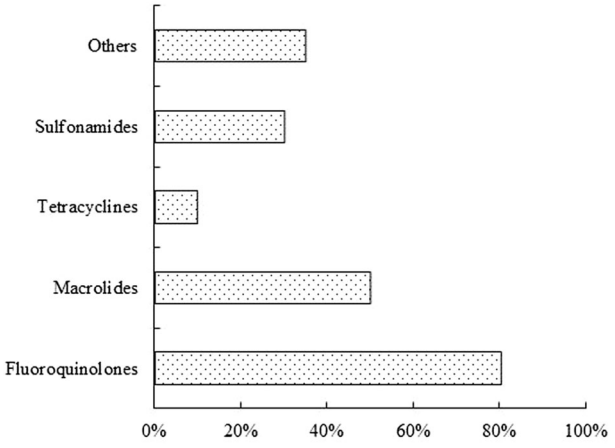

Figure 1. Percentage of antibiotic-positive drinking water samples.

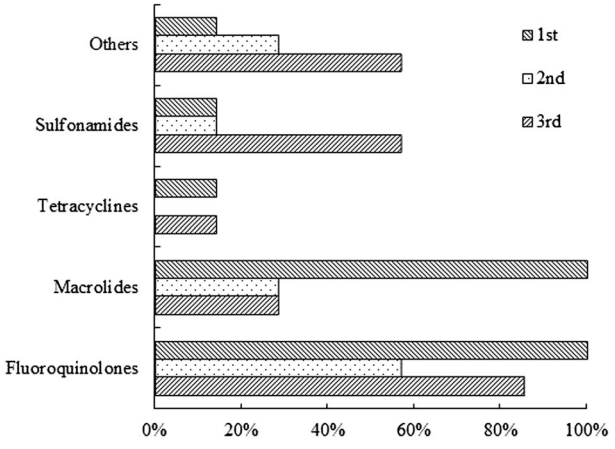

Figure 2. Detectable frequency of five families antibiotics at different sampling times. (1st, 2nd and 3rd indicates the first sampling (October 2015), the second sampling (May 2016) and the third sampling (January 2017), respectively).

3.2. *Relationship between drinking water quality and water source*

Figure 3 shows the average concentration of antibiotics over the three sampling times. Samples from sites A1 and A2 were obtained from mountain spring water and groundwater, respectively (Table 1). The antibiotic concentrations (average values of three samples) for sites A1 and A2 were 30.71 and 2.94 ng/L, respectively. Samples A5 and A6 were derived from river water sources and had high concentrations of antibiotic. So, the concentration of antibiotics in drinking water was greatly affected by the water sources the drinking water was derived forms, with lower concentrations detected in drinking water sourced from groundwater and mountain spring water.

As can be seen in Figure 3, the antibiotic concentration in drinking water in the upper and middle reaches of the river (A3) was 14.49 ng/L and was 142.9 ng/L downstream (A6). The concentration of antibiotics in drinking water sourced from river water (A3, A4 and A6; A5 was not included due to changes in the sampling point) was also related to whether the sample was taken upstream or downstream.

The distance between the two sampling points, A6and A7, was approximately 150 km in the lower reaches of the river. However, far fewer types and lower concentrations of antibiotics were detected in drinking water samples from A7 than in samples from A6 (5 vs. 19, respectively) (Table 5). Compared with the conventional treatment process (flocculation-precipitation-filtration-disinfection) used for drinking water obtained from A6, drinking water sampled from A7 had undergone an advanced treatment process (flocculation-precipitation-ultrafiltration-disinfection). Therefore, the type of water purification process used clearly influenced the concentration of antibiotics in drinking water.

3.3. *Health risk analysis of antibiotics in drinking water*

Previous studies [39,40] have shown that the bacteria can be changed at the genetic level when the concentration of antibiotics reaches a critical level in the water, leading to bacterial genetic mutations or death. Although antibiotics have been reported to pose a potential health risk to humans [16,17,41], information relating to this issue in rural areas was still very limited. In addition, some studies have shown that the risk of carcinogenic caused by exposure to antibiotics in drinking water is much higher than that associated with skin contact [41]. Thus, the health risks in terms of the RQ, CR and HQ were carefully analysed.

3.3.1. Health risk quotient

The health risk quotients (RQ) of antibiotics in drinking water are shown in Table 6.

The health risk quotients were calculated using the maximum concentration of antibiotics detected at each sampling point. The health risk quotient of antibiotics in drinking water was between 10^{-2} and 10^{-6}, which represents a negligible health-risk level and indicates that the current level of antibiotics in drinking water in this river basin would not cause harm to human health. This level was similar to that detected in effluent from a drinking-water plant in Shanghai, China [9]. Of the various antibiotics detected in the present study, OFX and ETM levels in drinking water presented the highest risk to human health, reaching the level of 10^{-3} (shown in bold in Table 6).

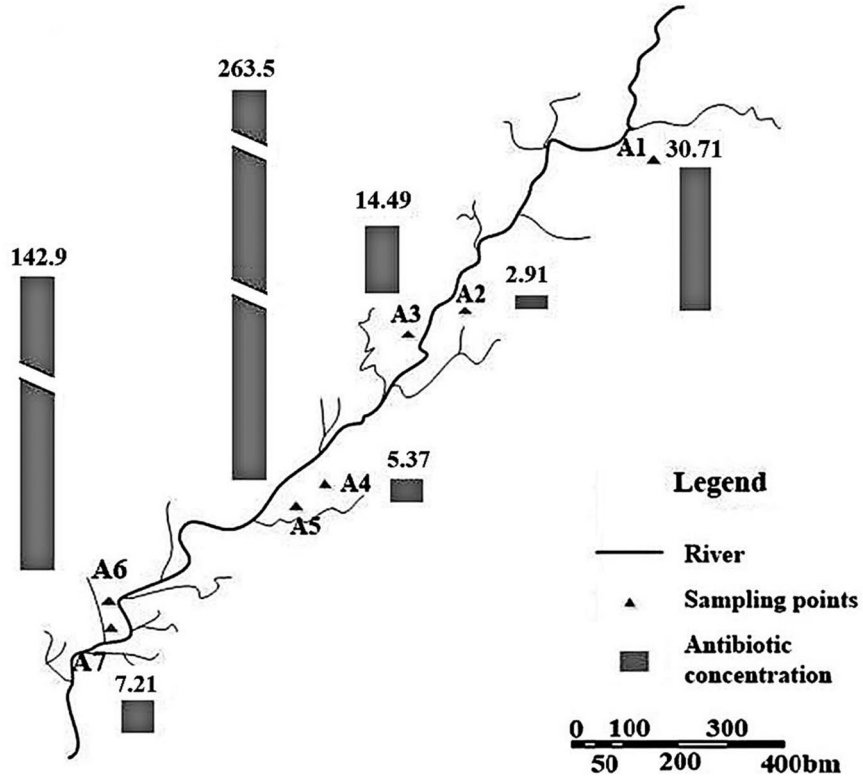

Figure 3. The distribution of antibiotics in rural drinking water (ng/L): average concentration of three sampling times.

Table 6. Maximum concentration and ADI of each antibiotic, and risk quotients (RQ) for males and females.

	Pollutant concentration (ng/L)	ADI (mg/(d kg))	RQ	
			Male (CN)	Female (CN)
CFX	11.65	0.0031 [20]	1.11E − 04	1.13E − 04
DAN	1.965	0.01 [20]	5.80E − 06	5.90E − 06
DIF	0.845	0.005 [20]	4.99E − 06	5.07E − 06
LFX	1.465	0.0031[a]	1.40E − 05	1.42E − 05
NFX	4.79	0.0031[a]	4.56E − 05	4.64E − 05
OFX	368.21	0.0031[a]	**3.51E − 03**	**3.56E − 03**
SAR	1.295	0.00015 [20]	2.55E − 04	2.59E − 04
CTM	3.68	0.05 [42]	2.17E − 06	2.21E − 06
ETM	82.52	0.00035 [20]	**6.96E − 03**	**7.07E − 03**
RTM	9.65	0.0145 [43]	1.97E − 05	2.00E − 05
LIN	1.455	0.003 [40]	1.43E − 05	1.46E − 05
SAL	36.74	0.0025 [20]	4.34E − 04	4.41E − 04
TYL	1.89	0.003 [20]	1.86E − 05	1.89E − 05
OTC	17.38	0.003 [42]	1.71E − 04	1.74E − 04
SCP	4.735	0.0025 [20]	5.59E − 05	5.68E − 05
SDZ	2.98	0.02 [42]	4.40E − 06	4.47E − 06
SMZ	120.03	0.02 [42]	1.77E − 04	1.80E − 04
SMX	22.47	0.0025 [20]	2.65E − 04	2.70E − 04
SMM	60.11	0.006 [42]	2.96E − 04	3.01E − 04
SPD	1.65	0.0025 [20]	1.95E − 05	1.98E − 05
SQX	2.63	0.01 [20]	7.77E − 06	7.89E − 06
TMP	8.83	0.0021 [20]	1.24E − 04	1.26E − 04

[a] Refers to the Chinese Ministry of Agriculture's announcement, 'Maximum Residue Limits of Veterinary Drugs in Animal Foods (2017)', for daily allowances of quinolones, ADI = 0–6.2 μg/L. The ADI values of LFX, NFX and OFX were 3.1 μg/L (shown in this table).

3.3.2. Carcinogenic risk and hazard quotient

Figures 4 and 5 show the carcinogenic risks (CR) and hazard quotients (HQ), respectively, presented by the main antibiotics detected in this study. The LD_{50} used in the calculation of CR and HQ refers to values obtained from earlier studies [44,45]. Carcinogenic risks and hazard quotients were calculated using the maximum concentration of antibiotics detected. The CR (1.45×10^{-11}–1.03×10^{-7}) and HQ (7.70×10^{-8}–5.42×10^{-4}) associated with antibiotics in drinking water were within acceptable ranges (CR < 10^{-6}; HQ < 10^{-1}).

SAL had the highest CR and HQ, with values of approximately 10^{-7} (<10^{-6}) (Figure 4) and 10^{-4} (<10^{-1}) (Figure 5), respectively. SPD had the lowest CR (10^{-11}) and HQ (10^{-8}). The CR and HQ values associated with antibiotics in drinking water were higher in females than in males.

The total carcinogenic risk (TCR) and total hazard quotient (THQ) of the main antibiotics at each sampling point are shown in Figures 6 and 7, respectively. The health risks from antibiotics at different sample points were similar for both men and women. Antibiotics in the A1, A5 and A6 samples showed higher TCR and THQ values, while, the TCR and THQ of antibiotics in A2, A3, A4 and A7 samples were lower.

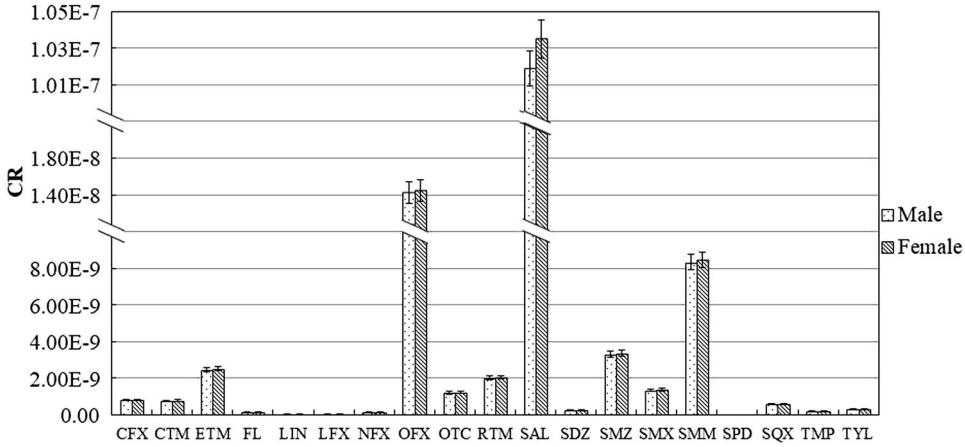

Figure 4. CR of antibiotics (based on maximum antibiotic concentrations).

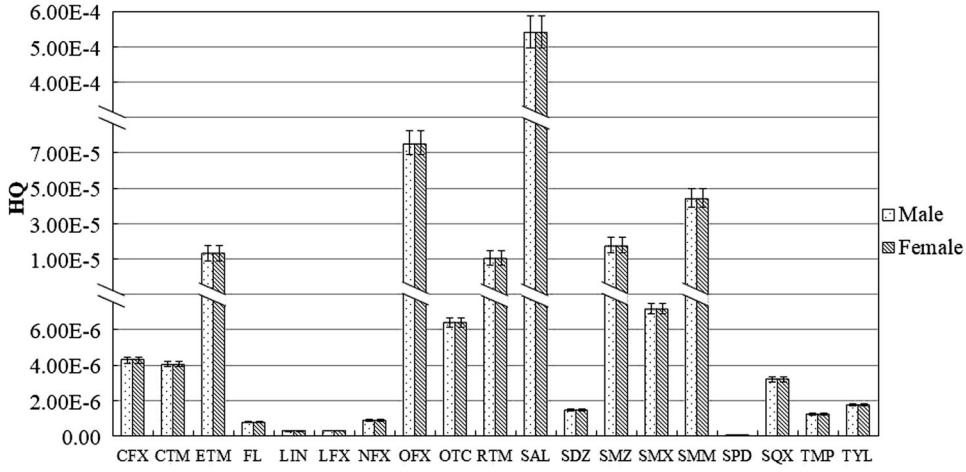

Figure 5. HQ of antibiotics (based on maximum antibiotic concentrations).

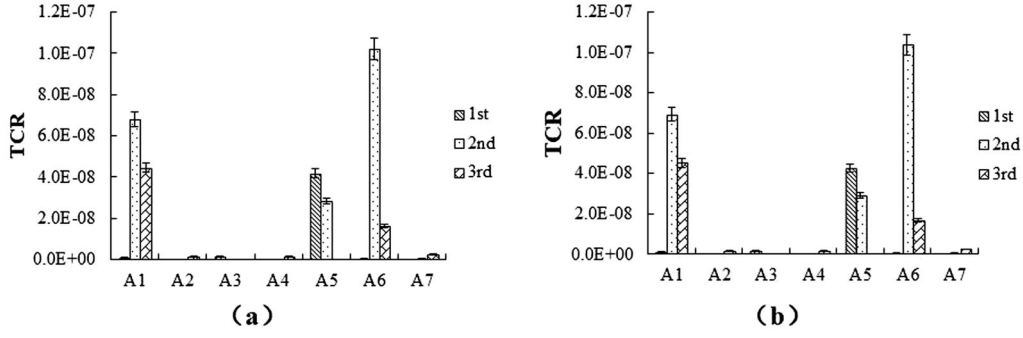

Figure 6. The TCR of antibiotics at each sampling points. (a) TCR of antibiotics for males; (2) TCR of antibiotics for females.

The TCR and THQ associated with antibiotics in drinking water during the rainy season (May 2016) were larger compared with the dry season (Oct 2015 and Jan 2017), except for the A5 sampling point. Drinking water from A5 had lower health risks at its second sampling time-point due to a technological transformation that had taken place at the water plant responsible for its purification.

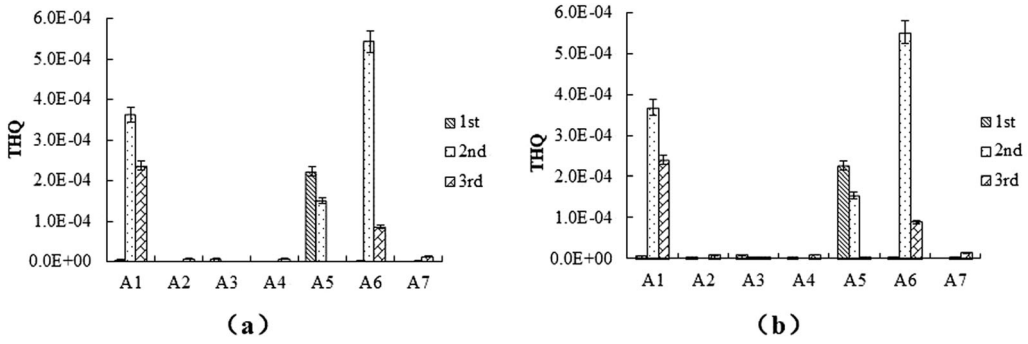

Figure 7. The THQ of antibiotics at each sampling points. (a) THQ of antibiotics for males; (2) THQ of antibiotics for females.

4. Discussion

This study examined the presence of five families of antibiotics, comprising twenty-three antibiotics in total, in nineteen drinking water samples (three sourced from mountain springs waters, three from groundwater and thirteen from river water). Fluoroquinolones and macrolides are the two main classes of antibiotics used to treat human diseases [46]; therefore, these two antibiotics are widely present in the environment, resulting in them being the most frequently detected antibiotics in drinking water. Overall, the average levels of antibiotics detected in drinking water from taps in the study area ranged from 0 to 368.21 ng/L, which were higher than the levels of antibiotics detected in a drinking water plant in Shanghai City (0.05–20.38 ng/L) [9] and Anhui Province (0–20.56 ng/L) in China [47]. However, the values reported here were lower than those detected in a pipe network in Tianjin, also in China (542.53–1683.17 ng/L) [16].

The antibiotics detected in drinking water samples in this study were influenced by the drinking water's source, with fewer antibiotics found in drinking water from groundwater and spring water sources and more antibiotics detected in drinking water from river water sources. The reason for reduced antibiotics in groundwater and mountain spring water might be adsorption by the soil and degradation by various microorganisms in the soil [48,49]. At the same time, river water is used as a drinking water source, especially in downstream areas, which are densely populated [12,20]. The more concentrated the population and industrial and agricultural activities, the more antibiotics are discharged into the environment [12,50].

Antibiotics detected in drinking water were also affected by the type of water purification technology used. We verified that the use of advanced treatment technology (flocculation-precipitation-ultrafiltration-disinfection) resulted in more effective water purification than conventional treatment technology (flocculation-precipitation-filtration-disinfection). Some studies have shown that advanced treatment processes (ozone pre-oxidation-enhanced filtration-ultraviolet disinfection or post-ozonation-biological activated carbon) remove antibiotics from the water supply system with greater than 30% more efficiency than conventional treatment process [9,16].

This study found the health risks related to antibiotics in drinking water to be within the range of negligible to acceptable risk. The ranges of RQ, CR and HQ values were 10^{-6}–10^{-3}, 10^{-11}–10^{-7} and 10^{-8}–10^{-4}, respectively. The health risks associated with drinking water were slightly higher for females than for males. ETM and OFX had high RQ values (Table 5), while SAL has the maximum CR (Figure 4) and HQ values (Figure 5). We hypothesized that a daily average exposure to some antibiotics (e.g. SAL) from tap water (taking only the drinking of water into account) reaching 10^{-5} mg/(kg d), representing a concentration of approximately 1.8 µg/L, would have a negative impact on human health. Thus, the concentrations of antibiotics in rural drinking water require further investigation.

The antibiotics detected in the A1, A5 and A6 samples showed higher TCR and THQ compared with the other sites. A1, A5 and A6 all contained SAL, which was responsible for the higher risk associated with the drinking water obtained from these sources. The sampling points A5 and A6 also drinking water samples sourced from river water, which contained many types of antibiotics. However, when the TCR and THQ of A6 and A7 (both sourced from river water, the distance of 150 km apart) were compared, it was seen that A7 had a lower health risk. Drinking water from sampling point A7 had undergone advanced treatment processes; this shows that advanced water purification technology can reduce the health risks linked to antibiotics in drinking water [16,51].

The CR and HQ value of A1 and A6 showed that health risks linked to antibiotics in drinking water during the

rainy season were relatively high (Figures 6 and 7). This finding was consistent with previously reported seasonal changes in antibiotic levels in water sources [47]. May is not only the rainy season but also a period of the high incidence of diseases, such as influenza. During the influenza season, antibiotics are frequently misused as a medical treatment [20]. In addition, many antibiotics are prescribed, especially the antimicrobials such as ofloxacin and erythromycin, and the concentrations of the drugs that are not absorbed by the patient increase in the water system.

Rural drinking water can be divided into centralized water supplied and non-centralized water supplies. This study focused on treated centralized drinking water supplies; untreated decentralized drinking water supplies were not considered. This could result in most of the collected samples having low concentrations of antibiotics and leading to an underestimation of the risk. The overall risk from antibiotics in drinking water is also affected by the interactions between antibiotics (e.g. antagonism, stress, etc.), which will be investigated in future studies.

5. Conclusion

In this study, we investigated and analysed the antibiotics present in typical rural drinking water in southern China. OFX and ETM were frequently detected at high concentrations and had large RQ values. Although SAL was not the most frequently detected antibiotic, it had the highest CR and HQ values. The concentration of antibiotics in drinking water and the associated health risks are closely related to drinking water sources and water purification processes. Therefore, to further improve the quality of drinking water in rural areas, it is necessary to strengthen the control of water sources and improve water purification processes.

Disclosure statement

No potential conflict of interest was reported by the authors.

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