Occurrence and Health Risk Assessment of Antibiotics in Drinking Water of a City in Southern China

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Abstract. In recent years, antibiotics have been widely used to treat some human and animal diseases, which due to their large production and usage. The antibiotic pollution in the environment has attracted more and more people's attention. As a large country in the production and use of antibiotics, antibiotics has been detected in various environmental media in China, even in drinking water. However, drinking water is closely related to the health of residents. It is very necessary to understand the occurrence of antibiotics in drinking water and assess the health risk. Therefore, in this study, taking a city in southern China as an example, it was detected that the concentration of antibiotics in the drinking water was 226.8~498.1 ng/L, and the main pollutants were tetracycline and quinolone antibiotics. The non-carcinogenic risk assessment shows that drinking tap water for residents in this area will not pose a risk to their health.

1. Introduction
As a kind of secondary metabolites, antibiotics can inhibit the growth and reproduction of bacteria, effectively treat some human and animal diseases, and can also be used as growth promoters to improve the efficiency of livestock feeding, are widely used worldwide. However, antibiotics cannot be completely absorbed in humans and animals. Nearly 90% of antibiotics are discharged into the environment in the form of mothers or metabolites through excrement [1]. Most of the antibiotics will be treated in sewage treatment plants and eventually discharged into the environment [2]. In China, antibiotics a detected in various environmental media such as rivers [3,4], lakes [4,5], reservoirs [6,7], sea water [8,9], sediments [10], and even drinking water [11,12]. Drinking water is closely related to human health. Therefore, this study assessed the health risks of residents exposed to antibiotics through drinking water by detecting the content of antibiotics in the drinking water of a city in southern China.

2. Materials and methods
2.1. Target antibiotics
This study detected 30 common antibiotics in the environment, including 9 quinolones: pipemidic acid (PIP), marbofloxacin (MAR), fleroxacin (FLE), ofloxacin (OFL), Enoxacin (ENO), Norfloxacin (NOR), Enrofloxacin (ENR), Ciprofloxacin (CIP), Oxolinic Acid (OXO); 15 kinds of sulfonamides: sulfacetamide (STD), Sulfamethizole (SMTZ), Sulfafoxazole (SXZ), Sulfadiazine (SDZ), Sulfamethoxazole (SMOZ), Sulfathiazole (STZ), sulfamonomethoxin e (SUL), Sulfamerazine (SM1), Sulfadoxine (SDMX), Sulfonylpyridine (SPD), Sulfamer (SMT), Sulfamethoxypyridazine (SMP),
Sulfamethazine (SMA), Sulfaphenazole (SPP), Sulfadimethoxine (SMMX); 6 kinds of tetracyclines: oxytetracycline (OTC), tetracycline (TC), demeclocycline (DEM), Chlortetracycline (CTC), Methacycline (MET), Doxycycline (DOX).

2.2. Sample preparation and test
Taking 6 water samples from the tap water in residents' homes to detect and analysis, which take 6 parallel samples from each sampling point. Add 0.5g/L Na2EDTA and 0.2g/L ascorbic acid to the water sample, and adjust the pH to 3-4 with dilute sulfuric acid. The HLB solid phase extraction cartridge was activated with 5ml methanol and 5ml ultrapure water in sequence before use. The samples are filtered through the HLB extraction column at a speed of 5ml/min, and then use 5 ml ultrapure water to rinse the extraction column to remove impurities, dried completely under vacuum. The target analyte was eluted twice with 6 mL methanol, and the eluate was collected. Blow the nitrogen to dryness at room temperature, transfer the sample to chromatographic bottles, wash the glass tube and dropper with methanol aqueous solution (V:V=1:1), and dilute the volume to 1ml to measure.

This study use Waters e2695 liquid chromatography with Waters TQ Detector tandem triple quadrupole mass spectrometry (LC-MS/MS) to detect antibiotics. Agilent eclipse XDB C18 column (4.6×150mm, 5μm) was used for liquid chromatography analysis, column temperature was 30℃, and flow rate was 0.3ml. min⁻¹, injection volume 10μL, mobile phase A is 0.1% formic acid aqueous solution, mobile phase B is acetonitrile, mobile phase elution procedure is: 0~2min, keep 10%B; 8min, 40%B; 24min, 90%B; 26min, 10%B; 26~30min, keep 10%. Mass spectrometry analysis adopts electrospray ionization source (ESI+), multiple reaction monitoring (MRM) mode, spray voltage 4000V, ion source temperature 120℃, carrier gas temperature 350℃, carrier gas flow rate 550L. h⁻¹.

2.3. Methods of health risk assessment
This study use the Hazard quotient (HQ) model proposed by the EPA to calculate the non-carcinogenic risk. the formula is HQ=DI/RfD, where HQ is the hazard quotient, dimensionless; DI is daily intake of antibiotics through drinking water (mg/kg/d); RfD is the reference dose (mg/kg/d). Because the RfD value is difficult to obtain, according to the model RfD=LD50×4×10⁻⁵ proposed in the reference [13], RfD is calculated by the LD50 value. The DI value is calculated by the following formula:

\[
DI = \frac{c \times IR \times EF \times ED}{BW \times AT} \quad (1)
\]

Where c is the concentration of the target antibiotic in the drinking water (mg/L); IR is the daily water consumption (L/d); EF is the exposure frequency (d/a), and the EF value is 365; ED is the exposure time (A); BW is body weight (kg); AT is life expectancy (d). The above parameters are calculated with reference to the data of Zhejiang Province in the "Chinese Population Exposure Parameters Manual".

3. Results and discussion
3.1. Concentrations of antibiotics in drinking water
The total concentrations of antibiotics in tap water samples are 226.8~498.1ng/L, which is lower than the result of Ben et al. [14]. The concentrations of tetracyclines and quinolones are relatively high: the tetracyclines account for 25.8~64.3%, and the quinolones account for 35.4~73.6%. The main antibiotics are NOR, CIP, DAN, MIN, OTC. The types of antibiotics in drinking water in this area are the same as those in source water, indicating that antibiotics in drinking water are mainly affected by regional pollution. Therefore, to reduce the content of antibiotics in drinking water, reducing the environmental pollution of antibiotics from the source is the key.
3.2. Health assessment of antibiotics in drinking water

Health risk assessments were carried out for people of different genders and different ages (children, adolescents, and adults). The results are shown in Table 1. According to the hazard quotient model, when HQ<1, it is considered that there is no non-carcinogenic risk; when HQ>1, it is considered that there is a non-carcinogenic risk. A risk assessment was conducted on 30 antibiotics in tap water samples. To calculate the maximum risk, the concentration of each antibiotic was selected from the maximum of 6 sampling points. The results show that the HQ value is between 1.29×10⁻⁹ to 2.69×10⁻³, which is far less than 1, so there is no non-carcinogenic risk for residents to drink the water. Among them, the non-carcinogenic risk of different groups of people from high to low is: adults>adolescents>children; among adults and adolescents, the risk of women is higher than that of men; while in children, the risk of boys is higher than that of girls.

Table 1. HQs of antibiotics in drinking water for different people.

| HQ       | Children (0-5 years old) | Adolescents (6-17 years old) | Adults |
|----------|--------------------------|-------------------------------|--------|
|          | male         | female   | male         | female   | male         | female   |
| PIP      | 1.01E-07     | 9.38E-08 | 1.39E-07     | 1.48E-07 | 9.73E-07     | 1.03E-06 |
| MAR      | 9.30E-08     | 8.62E-08 | 1.27E-07     | 1.36E-07 | 8.94E-07     | 9.43E-07 |
| FLE      | 7.41E-08     | 6.87E-08 | 1.01E-07     | 1.09E-07 | 7.12E-07     | 7.51E-07 |
| OFL      | 4.83E-08     | 4.48E-08 | 6.62E-08     | 7.09E-08 | 4.65E-07     | 4.90E-07 |
| ENO      | 1.46E-07     | 1.35E-07 | 2.00E-07     | 2.14E-07 | 1.40E-06     | 1.48E-06 |
| NOR      | 1.40E-06     | 1.30E-06 | 1.92E-06     | 2.05E-06 | 1.35E-05     | 1.42E-05 |
| ENR      | 2.82E-07     | 2.61E-07 | 3.86E-07     | 4.13E-07 | 2.71E-06     | 2.86E-06 |
| CIP      | 2.65E-04     | 2.46E-04 | 3.63E-04     | 3.89E-04 | 2.55E-03     | 2.69E-03 |
| OXO      | 1.78E-06     | 1.65E-06 | 2.43E-06     | 2.60E-06 | 1.71E-05     | 1.80E-05 |
| STD      | 3.16E-09     | 2.93E-09 | 4.33E-09     | 4.64E-09 | 3.04E-08     | 3.20E-08 |
| SMTZ     | 1.24E-08     | 1.15E-08 | 1.70E-08     | 1.82E-08 | 1.19E-07     | 1.26E-07 |
| SXZ      | 8.67E-09     | 8.04E-09 | 1.19E-08     | 1.27E-08 | 8.34E-08     | 8.79E-08 |
| SDZ      | 4.77E-08     | 4.42E-08 | 6.53E-08     | 7.00E-08 | 4.59E-07     | 4.83E-07 |
| SMZ      | 2.56E-08     | 2.38E-08 | 3.51E-08     | 3.76E-08 | 2.47E-07     | 2.60E-07 |
| STZ      | 7.97E-08     | 7.39E-08 | 1.09E-07     | 1.17E-07 | 7.67E-07     | 8.08E-07 |
| SM1      | 2.31E-06     | 2.14E-06 | 3.17E-06     | 3.39E-06 | 2.22E-05     | 2.34E-05 |
| SDMX     | 1.39E-09     | 1.29E-09 | 1.90E-09     | 2.04E-09 | 1.34E-08     | 1.41E-08 |
| SPD      | 2.74E-09     | 2.54E-09 | 3.76E-09     | 4.03E-09 | 2.64E-08     | 2.78E-08 |
| SUL      | 5.78E-09     | 5.36E-09 | 7.92E-09     | 8.48E-09 | 5.56E-08     | 5.86E-08 |
| SMT      | 6.02E-09     | 5.58E-09 | 8.25E-09     | 8.83E-09 | 5.79E-08     | 6.10E-08 |
| SMP      | 1.85E-08     | 1.71E-08 | 2.53E-08     | 2.71E-08 | 1.78E-07     | 1.87E-07 |
| SMA      | 5.45E-08     | 5.06E-08 | 7.47E-08     | 8.00E-08 | 5.25E-07     | 5.53E-07 |
| SPP      | 3.83E-08     | 3.55E-08 | 5.25E-08     | 5.62E-08 | 3.69E-07     | 3.89E-07 |
| SMMX     | 4.52E-09     | 4.19E-09 | 6.19E-09     | 6.63E-09 | 4.34E-08     | 4.58E-08 |
| OTC      | 1.42E-05     | 1.32E-05 | 1.95E-05     | 2.08E-05 | 1.37E-04     | 1.44E-04 |
| TC       | 9.67E-07     | 8.97E-07 | 1.32E-06     | 1.42E-06 | 9.30E-06     | 9.80E-06 |
| DEM      | 2.04E-07     | 1.89E-07 | 2.80E-07     | 2.99E-07 | 1.96E-06     | 2.07E-06 |
| CTC      | 2.26E-07     | 2.10E-07 | 3.10E-07     | 3.32E-07 | 2.18E-06     | 2.30E-06 |
| MET      | 3.73E-06     | 3.46E-06 | 5.11E-06     | 5.47E-06 | 3.59E-05     | 3.78E-05 |
| DOX      | 3.23E-06     | 2.99E-06 | 4.42E-06     | 4.73E-06 | 3.10E-05     | 3.27E-05 |
4. Conclusion
This study detected the concentration of 30 antibiotics in the drinking water of a southern city in China, and assessed the non-carcinogenic risk of antibiotics exposed to residents through drinking tap water. The results show that the main antibiotics in the tap water in this area are tetracyclines and quinolones; drinking tap water in this area will not pose a non-carcinogenic risk to the health of residents. However, antibiotics have been detected in the source water. Drinking water is closely related to the health of residents, so it is significant to reduce the environmental pollution of antibiotics from the source.

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