Preplanned Studies

Antibiotics in Drinking Water and Health Risks — China, 2017

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Summary

What is already known about this topic?

Antibiotic contaminations in the environment are understood to pose human health risks including disturbing the microbiome in the human body and producing antibiotic-resistant bacteria, which pose serious public health risks. Antibiotics have been detected in aquatic environments and drinking water worldwide.

What is added by this report?

Contamination levels of antibiotics in raw, finished, and tap water were investigated systematically, to the best of our knowledge, in major Chinese water basins. Multiple antibiotic contaminations in raw water and their incomplete removal during water-treatment processes results in human exposure to antibiotics via drinking water. Human exposure to such antibiotics and its health risks were evaluated in this study.

What are the implications for public health practice?

This study highlights the need to strengthen management of antibiotic exposure from drinking water. A multisectoral action plan at the national level is required to curb the effects of environmental antibiotic pollution.

Antibiotic contamination in the environment has become a global issue attracting substantial attention from the general public. Intake of antibiotics from the environment by food and drinking water may disturb the microbiome, especially the gut microbiota in the human body (*1*). More importantly, antibiotic residues in the environment have the potential to produce antibiotic-resistant bacteria (ARB), which pose serious public health risks (*2*). Antibiotics in aquatic environments and drinking water have been detected in China (*3*), but studies measuring exposure to antibiotics in drinking water and associated health risks are limited. In this study, contamination levels of antibiotics in raw, finished, and tap water were investigated systematically for the first time in major Chinese water basins during the winter and summer of 2017. Human exposure and its health risks were also evaluated. Study results indicated that multiple antibiotics were generally detected in raw water from major Chinese water basins. Concentrations of detected antibiotics were at the nanogram per liter level, which were similar to those in other developed countries (*3*). Based on toxicity data or data on therapeutic approaches in the literature, health risk quotients (HRQs) for water basins from exposure to antibiotics via drinking water ranged from 5.1×10^{-7} to 2.2×10^{-3}, exhibiting spatial and seasonal variations. The HRQs quantified in this study were at an acceptable risk level (HRQs were much lower than 1), but the risks from antibiotic resistance are not well understood and should be researched further. Antibiotic contaminations in environments can induce environmental antibiotic-resistant bacteria (eARB) and horizontal gene transfer (HGT) between eARB and pathogens with antibiotic-resistance (pARB), which has been identified as a major threat to public health. A multisectoral action plan at the national level is required to curb the effects of environmental antibiotic pollution.

Contamination data on antibiotics were extracted from a project investigating emerging contaminants in drinking water in major Chinese river basins. In the project, the levels of contamination of 57 pharmaceuticals in raw, finished, and tap water from representative drinking water treatment plants (DWTPs) located in six large river basins, inland river areas, and key lake and reservoir areas of China during the winter and summer of 2017 were investigated. The water basins and areas investigated in the project included the Yangtze River, Yellow River, Pearl River, Songhua River, Huaihe River, Liaohe River, Northwest Rivers, Taihu Lake, Dianchi Lake, Chaohu Lake, Three Gorges Reservoir, and Danjiangkou Reservoir. Pharmaceuticals were analyzed by an ultra-performance liquid chromatography–tandem mass spectrometer (UPLC–MS/MS), as described in detail in a previous study (*3*). Based on a literature review and preliminary survey results, 21 antibiotics (Table 1) commonly used for human and animals were selected

TABLE 1. Detection rates and concentrations of antibiotics in raw water from major Chinese water basins during the winter and the summer of 2017.

Sub-category	Antibiotic	Usage*	Detection rate in winter(n=54)	Concentration in winter	Detection rate in summer(n=54)	Concentration in summer
			Percentage (%)	Median (P_{25}, P_{75}) (ng/L)	Percentage (%)	Median (P_{25}, P_{75}) (ng/L)
β-lactams (βLs)	Penicillin G	1	0 (0/54)	ND	0 (0/54)	ND
	Cloxacillin	1	1.9 (1/54)	11.0	1.9 (1/54)	1.2
	Cephalecxin	1	38.9 (21/54)	5.1 (2.1, 9.9)	9.3 (5/54)	0.6 (0.5, 0.8)
	Ceftiofur	2	0 (0/54)	ND	0 (0/54)	ND
Macrolides (MLs)	Clarithromycin	1	13.0 (7/54)	1.1 (1.0, 1.5)	68.5 (37/54)	0.3 (0.2, 0.6)
	Roxithromycin	1	77.8 (42/54)	1.0 (0.7,1.8)	83.3 (45/54)	0.8 (0.4, 1.7)
	Tylosin	2	3.7 (2/54)	2.8 (2.7, 2.9)	11.1 (6/54)	10.0 (2.7, 83.0)
Sulfonamides (SAs)	Sulfapyridine	2	33.3 (18/54)	0.8 (0.6, 1.1)	57.4 (31/54)	0.2 (0.1, 0.4)
	Sulfadiazine	1	50.0 (27/54)	2.5 (1.6, 3.2)	88.9 (48/54)	0.7 (0.2, 1.6)
	Sulfamethoxazole	1	88.9 (48/54)	9.1 (6.3, 14.0)	90.7 (49/54)	2.4 (1.5, 4.2)
	Sulfathiazole	1	1.9 (1/54)	98.0	37.0 (20/54)	0.1 (0.1, 0.4)
	Sulfamethazine	1	46.3 (25/54)	2.2 (1.8, 11.0)	53.7 (29/54)	1.0 (0.4, 2.6)
	Sulfaquinoxaline	2	7.4 (4/54)	1.1 (0.8, 1.3)	18.5 (10/54)	0.2 (0.1, 0.4)
	Sulfadoxin	2	0 (0/54)	ND	24.1 (13/54)	0.1 (0.1,0.2)
	Trimethoprim	1	27.8 (15/54)	2.5 (1.9, 2.7)	48.1 (26/54)	0.7 (0.4, 1.0)
Quinolones (QNs)	Norfloxacin	1	0 (0/54)	ND	0 (0/54)	ND
	Ciprofloxacin	1	0 (0/54)	ND	14.8 (8/54)	1.8 (0.8, 2.9)
	Enrofloxacin	2	0 (0/54)	ND	20.4 (11/54)	1.4 (0.9, 7.5)
	Ofloxacin	1	0 (0/54)	ND	5.6 (3/54)	1.3 (1.2, 29.0)
	Clinafloxacin	2	0 (0/54)	ND	0 (0/54)	ND
	Sarafloxacin	2	1.9 (1/54)	1.9	59.3 (32/54)	0.4 (0.2, 0.7)
The number of detected antibiotics			13		17	

* 1=Use for both human and animals; 2=Use for animals only.
Abbreviation: ND=not detected.

for analysis in this study. Removal rates (percent eliminated) of antibiotics in DWTPs were calculated by dividing the removal concentration by the concentration in raw water, and the removal concentration was obtained through subtracting finished water concentration from raw water concentration*.

The HRQ for each water basin was the sum of the HRQs for each antibiotic detected in tap water. An HRQ for each antibiotic was calculated by dividing its average daily potential dose (ADD) by the acceptable daily intake (ADI) or risk-specific dose (RSD)†. The ADI or RSD for each antibiotic was obtained from literature research. When there were more than one ADIs or RSDs for each antibiotic, HRQs were calculated using the most restrictive ADI or RSD (*4*). ADD was the antibiotic exposure dose ingested through drinking and dermal absorption during water consumption, calculated with exposure parameters according to *Chinese Exposure Factor Handbook* and the concentrations of antibiotics in tap water. HRQ above 1 is interpreted as indicating the potential for adverse effects, while HRQ below 1 is interpreted as indicating acceptable risk.

Multiple antibiotics were generally detected in raw water from major Chinese water basins (Table 1), and the detection of antibiotics exhibited seasonal variation. The composition of antibiotic contamination in raw water during the summer was more complex than that during the winter. A total of

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* The formula of removal rate of an antibiotic: Removal rate = $(C_{raw}-C_{finished})/C_{raw}\times100\%$, where C_{raw} is the concentration of the antibiotic in raw water (ng/L), $C_{finished}$ is the concentration of the antibiotic in finished water in the same DWTP (ng/L).

† HRQs for antibiotic exposure via drinking water were calculated using the concentration of antibiotics in tap water, exposure parameters, and the ADIs or RSDs from literatures. The formulae are presented in the Supplementary Materials available in http://weekly.chinacdc.cn/.

17 antibiotics were detected in raw water during the summer with median detected concentrations ranging from 0.1 ng/L to 10.0 ng/L. Among which, seven antibiotics had detection rates above 50%, with 2 of these used for animals only, and the others used for both humans and animals. A total of 13 antibiotics were detected in raw water during the winter, and only two antibiotics detected had detection rates above 50%.

The removal efficiency of each antibiotic from DWTPs was shown in Figure 1. A total of 17 antibiotics detected in raw water had average removal rates of above 50%. β-lactams had average removal rates above 98% and were rarely detected in finished and tap water. Although macrolides (MLs), sulfonamides (SAs), and quinolones (QNs) had average removal rates of 51%–97%, incomplete removal of these antibiotics by conventional technologies in drinking-water treatment plants leaves antibiotic residues in finished and tap water. A total of 16 antibiotics were detected in finished water, and similar results were observed in tap water.

HRQs for water basins ranged from 4.79×10^{-6} to 2.15×10^{-3} in the summer and from 5.10×10^{-7} to 1.69×10^{-3} in the winter (Table 2). HRQs of human exposure to antibiotics through drinking water exhibited spatial and seasonal variations. Huaihe River and Chaohu Lake basins had HRQs above 10^{-3} during the summer and the main antibiotic residues in drinking water in these areas were ciprofloxacin and sarafloxacin. Songhua River Basin had HRQs above 10^{-3} during the winter and the main antibiotic residues in drinking water were clarithromycin and roxithromycin. Additionally, among six large Chinese water basins investigated, the contamination risks in the Yangtze River and Yellow River basins were mainly from sarafloxacin and clarithromycin. The contamination risk in the Pearl River Basin was mainly attributable to tylosin.

DISCUSSION

Investigation of antibiotic contaminations in raw, finished, and tap water in major Chinese river basins indicated that the general population had been exposed to multiple antibiotics through drinking water. Concentrations of detected antibiotics were at the nanogram per liter level in raw, finished, and tap water samples. Contamination levels were similar to those in other developed countries (*3*). Among these antibiotics detected in tap water, seven were used for animals only including sarafloxacin and tylosin. Sarafloxacin was one of the main risk components of antibiotic contaminant exposure for people in the Huaihe River, Yellow River, and Yangtze River basins. Tylosin was the main risk component in the Pearl River Basin.

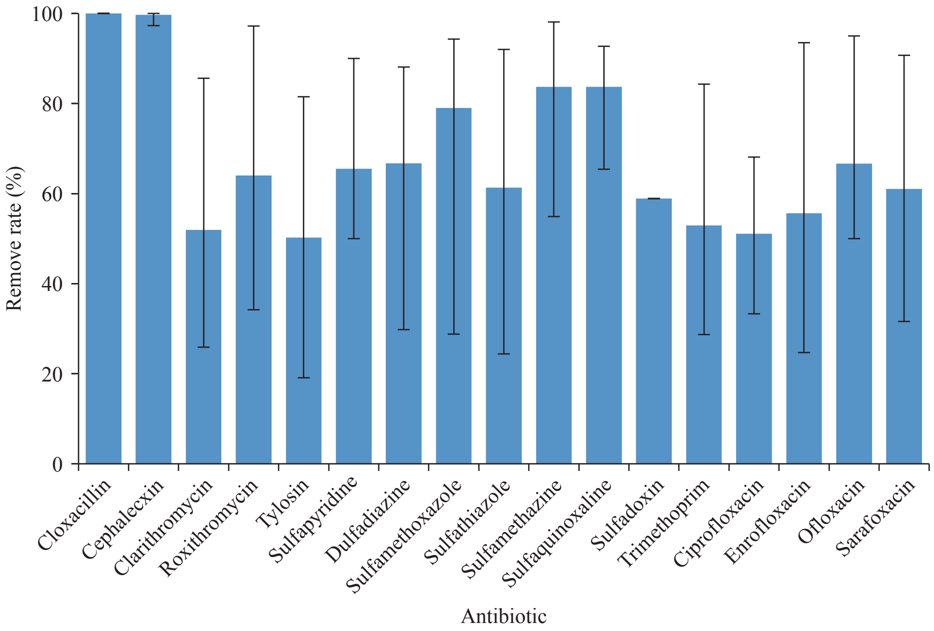

FIGURE 1. Removal efficiency of 17 antibiotics detected in raw water with positive removal rates in the DWTPs. Removal rates (% elimination) were calculated by dividing the removal concentration by the concentration in raw water, and the removal concentration was obtained through subtracting finished water concentration from raw water concentration.

TABLE 2. Health risk quotients of exposures to antibiotics via drinking water for people from major Chinese water basins during the winter and the summer of 2017.

Water Basins	Season	Health risk quotient		
		Minimum	Median	Maximum
Yangtze River (*n*=10)	Winter	8.62×10^{-6}	1.89×10^{-5}	2.57×10^{-5}
	Summer	3.71×10^{-5}	4.19×10^{-5}	1.04×10^{-4}
Yellow River (*n*=10)	Winter	2.33×10^{-5}	4.23×10^{-5}	4.40×10^{-5}
	Summer	7.17×10^{-5}	1.52×10^{-4}	9.67×10^{-4}
Pearl River (*n*=10)	Winter	5.10×10^{-7}	1.33×10^{-6}	1.73×10^{-6}
	Summer	3.33×10^{-4}	5.31×10^{-4}	7.67×10^{-4}
Songhua River (*n*=10)	Winter	9.63×10^{-5}	8.75×10^{-4}	1.69×10^{-3}
	Summer	3.67×10^{-5}	3.08×10^{-4}	3.64×10^{-4}
Huaihe River (*n*=10)	Winter	7.48×10^{-5}	2.83×10^{-4}	3.96×10^{-4}
	Summer	1.09×10^{-3}	1.81×10^{-3}	2.15×10^{-3}
Liaohe River (*n*=10)	Winter	2.83×10^{-5}	3.01×10^{-5}	6.35×10^{-5}
	Summer	1.16×10^{-4}	1.52×10^{-4}	1.80×10^{-4}
Northwest Rivers (*n*=2)	Winter	ND*	ND*	ND*
	Summer	4.79×10^{-6}	4.79×10^{-6}	4.79×10^{-6}
Taihu Lake (*n*=10)	Winter	1.51×10^{-5}	5.73×10^{-5}	1.23×10^{-4}
	Summer	4.40×10^{-5}	7.86×10^{-5}	8.22×10^{-5}
Dianchi Lake (*n*=10)	Winter	2.03×10^{-5}	2.86×10^{-5}	3.00×10^{-5}
	Summer	3.35×10^{-5}	7.16×10^{-5}	3.73×10^{-4}
Chaohu Lake (*n*=10)	Winter	3.74×10^{-5}	6.27×10^{-5}	8.02×10^{-5}
	Summer	2.95×10^{-4}	1.40×10^{-3}	1.44×10^{-3}
Three Gorges Reservoir (*n*=10)	winter	3.71×10^{-5}	9.59×10^{-5}	1.78×10^{-4}
	Summer	1.67×10^{-5}	3.07×10^{-5}	4.20×10^{-5}
Danjiangkou Reservoir (*n*=8)	Winter	3.92×10^{-5}	4.88×10^{-5}	4.92×10^{-5}
	Summer	2.32×10^{-5}	1.62×10^{-4}	2.98×10^{-4}

* No antibiotic was detected in drinking water samples from Northwest Rivers Basin area during the winter.

Antibiotic contaminations in the environment were mainly attributed to the extensive use and emission of antibiotics in livestock farming and aquaculture (*5–6*).

The removal rate of each antibiotic in DWTPs investigated in this study showed that conventional purification methods during water treatment cannot remove antibiotics from raw water completely. Similar removal effects of antibiotics were also seen in previous studies (*7*). Incomplete removal during water-treatment processes results in human exposure to antibiotics from contaminated environments via drinking water. Antibiotics can enter an aquatic environment through effluents from sewage treatment plants (STPs) because of the limited removal efficiency from such plants (*8*). In addition to emissions of antibiotics from livestock farming and aquaculture, industrial effluent from drug manufacturing is another major source of antibiotic contamination, contributing high-level contaminations by some antibiotics in surface water and thus in drinking water through water system.

HRQs of antibiotic contaminations in drinking water were less than or equal to 10^{-3} level, which were much lower than 1, indicating an acceptable level of risk from exposure to antibiotics via drinking water. However, these risks from exposure to antibiotics via drinking water varied across water basins and seasons. HRQs above 1×10^{-3} were observed in Huaihe River and Chaohu Lake Basins during the summer and in Songhua River Basin during the winter.

There are three limitations in our analysis. First, contamination data used in this study were collected from representative DWTPs in major river basins, which did not cover all river basins and regions in

China. Hence, study results only represented the population in water-supply areas of these DWTPs. Second, ADIs used in this study to calculate HRQs of antibiotics were derived from the data based on the toxicity of experimental animal or microbiological effects in the literature. There is a lack of study on the adverse effects induced by antibiotics exposure from environments among all age groups and sensitive groups such as children and pregnant women. Finally, antibiotic contaminations in environments can induce eARB (*9*). Previous studies have highlighted the potential for environmental HGT between eARB and pARB, which has been identified as a major threat to public health (*10*). However, the risk of antibiotic resistance is not quantified in this study because of the limited research data. A study on the health risks of environmental antibiotic pollution is crucially needed to provide data to support for risk management in China.

From both human and environmental health perspectives, it is a significant task to establish a systematic project for curbing the effects of environmental antibiotic pollution. A multisectoral action plan at the national level is required: (a) to strengthen the control of antibiotic use in livestock farming and aquaculture, taking steps to reduce usage and emissions of antibiotics at national levels; (b) to improve a standard wastewater discharge system for antibiotic industries and to establish an emission standard for antibiotics to strengthen discharge management; (c) to conduct further research on removal mechanisms of antibiotics by water-treatment technology, exploring the applicability of upgrading treatment processes in STPs and DWTPs; (d) to carry out systematic research on environmental antibiotic pollution and antibiotic resistance; and (e) to conduct research on and investigate antibiotic contamination exposure and health risk assessment among all age groups and sensitive groups.

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Supplementary Material

Health risk quotient (HRQ) calculation

$$HRQ_{an} = \frac{ADD}{ADI\ or\ RSD} \tag{1}$$

HRQ_{an} is the health risk quotient of an antibiotic, ADD is the average daily potential dose of this antibiotic through drinking and dermal absorption during drinking water consumption [μg/(kg·day)], ADI is the acceptable daily intake [μg/(kg·day)] for noncarcinogenic effects, RSD is the risk-specific dose for carcinogenic effects.

HRQ for each water basin was the sum of the HRQs for each detected antibiotic in tap water from this water basin.

ADI or RSD selection

Acceptable daily intake (ADI) or risk-specific dose (RSD) were found via literature search. ADIs or RSDs of antibiotics were adopted from provisional values established in the literature or derived using previously applied toxicological, microbiological, or therapeutic approaches. When there are more than one ADIs or RSDs for each antibiotic, the most restrictive ADIs or RSDs were selected. The ADIs used for HRQ calculation of each antibiotic are described in Supplementary Table S1.

Evaluation of average daily potential dose (ADD) of each antibiotic

Drinking and dermal absorption are the main intake and uptake routes for human exposure to antibiotics through drinking water consumption.

ADD through intake water (ADD_{dw}) was calculated using Equation S2:

$$ADD_{dw} = \frac{C_{dw} \times IngR \times EF \times ED}{BW \times AT \times 1,000} \tag{2}$$

SUPPLEMENTARY TABLE S1. Acceptable daily intakes (ADIs) or risk-specific dose (RSD) used for Health risk quotient (HRQ) calculation of each antibiotic were selected from literature search.

Antibiotic	ADI or RSD [μg/(kg·day)]	Toxicity endpoint	References
Cephalecxin	10	Microbiological	(*2*)
Clarithromycin	0.2	MIC_{50} on Peptostreptococcus spp.	(*1*)
Roxithromycin	0.4	MIC_{50} on Eubacterum spp.	(*1*)
Tylosin	0.85	MIC_{50} on Bifidobacterium spp. and Clostridium spp.	(*1*)
Sulfapyridine	10	Microbiological	(*3*)
Sulfadiazine	20	reduced fetal bodyweight and C-R length at the next higher dose	(*4*)
Sulfamethoxazole	130	Thyroid tumors in rats	(*1*)
Sulfathiazole	50	Changes in thyroid tissue. a NOEL of 5 mg/kg for the thyroid effects in animal studies	(*1*)
Sulfamethazine	1.6	Thyroid gland follicular adenoma in rats with tumor incidence data	(*1*)
Sulfaquinoxaline	10	Increased thyroid weights at the next higher dose	(*2*)
Sulfadoxin	50	Increased liver weights at the next higher dose	(*2*)
Norfloxacin	14.2	Microbiological	(*4*)
Ciprofloxacin	0.15	Microbiological	(*4*)
Enrofloxacin	6.2	Microbiological	(*3*)
Ofloxacin	3.2	Microbiological	(*4*)
Sarafloxacin	0.3	Microbiological	(*4*)
Trimethoprim	4.2	MIC of the most sensitive species in human gut flora	(*3*)

ADD_{dw} is the average daily potential dose from intake of water [μg/(kg·day)], C_{dw} is the concentration of antibiotics in drinking water (ng/L), IngR is the ingestion rate (L/day), including both direct and indirect ingestion, EF is the exposure frequency (days/year), ED is the exposure duration (years), BW is body weight (kg), and AT is averaging time (days). To reduce uncertainties in exposure variation between different geographical areas, across seasons, and between men and women, the IngR values were used corresponding to area, season, and sex as well as the sex-specific BW value in China according to the *Chinese Exposure Factor Handbook* (China EPA 2009; area, season and sex-specific values are shown in Supplementary Table S2).

SUPPLEMENTARY TABLE S2. IngR values corresponding to area, season and sex in China were selected to calculate ADD_{dw}.

Area	Season	Gender	IngR (L/day)
Liaoning	Winter	Male	1,742
Heilongjiang	Winter	Male	1,881
Jiangsu	Winter	Male	2,267
Anhui	Winter	Male	2,944
Hubei	Winter	Male	1,500
Guangdong	Winter	Male	1,695
Chongqing	Winter	Male	1,215
Sichuan	Winter	Male	1,862
Yunnan	Winter	Male	1,895
Gansu	Winter	Male	2,587
Xinjiang	Winter	Male	2,974
Liaoning	Summer	Male	2,090
Heilongjiang	Summer	Male	2,196
Jiangsu	Summer	Male	3,204
Anhui	Summer	Male	4,063
Hubei	Summer	Male	2,570
Guangdong	Summer	Male	2,411
Chongqing	Summer	Male	2,053
Sichuan	Summer	Male	3,184
Yunnan	Summer	Male	2,719
Gansu	Summer	Male	3,990
Xinjiang	Summer	Male	3,716
Liaoning	Winter	Female	1,425
Heilongjiang	Winter	Female	2,180
Jiangsu	Winter	Female	1,817
Anhui	Winter	Female	2,432
Hubei	Winter	Female	1,366
Guangdong	Winter	Female	1,663
Chongqing	Winter	Female	1,293
Sichuan	Winter	Female	1,691
Yunnan	Winter	Female	1,492
Gansu	Winter	Female	2,050
Xinjiang	Winter	Female	2,086
Liaoning	Summer	Female	1,706

TABLE S2. (Continued)

Area	Season	Gender	IngR (L/day)
Heilongjiang	Summer	Female	1,826
Jiangsu	Summer	Female	2,558
Anhui	Summer	Female	3,423
Hubei	Summer	Female	2,376
Guangdong	Summer	Female	2,347
Chongqing	Summer	Female	2,164
Sichuan	Summer	Female	3,062
Yunnan	Summer	Female	2,203
Gansu	Summer	Female	3,133
Xinjiang	Summer	Female	2,703

ADD through dermal absorption with water use ($\mathrm{ADD_{dermal}}$) was calculated using Equation S3:

$$\mathrm{ADD_{dermal}} = \sum_{i=1}^{9} \frac{\mathrm{DA_{event-i}} \times \mathrm{SA_i} \times \mathrm{EF_i} \times \mathrm{ED_i}}{\mathrm{BW} \times \mathrm{AT_i}} \tag{3}$$

$\mathrm{ADD_{dermal}}$ is the average daily potential dose through dermal absorption [μg/(kg·day)]. Dermal exposure was calculated from nine daily activities, including washing hands, face, hair, feet; washing vegetables, dishes, and clothes; and bathing and swimming. $\mathrm{DA_{event\text{-}i}}$ refers to the absorbed dose from one event [μg/$\mathrm{cm^2}$·day)], as calculated using Equation S4 below. $\mathrm{SA_i}$ refers to the skin surface area available for contact ($\mathrm{cm^2}$), according to the *Chinese Exposure Factor Handbook* (China EPA 2009; values summarized in Supplementary Table S3. $\mathrm{EF_i}$ refers to the exposure frequency (days/year), $\mathrm{ED_i}$ to the exposure duration (years), BW to body weight (kg), and $\mathrm{AT_i}$ to averaging time (days). $\mathrm{DA_{event\text{-}i}}$ was calculated as follows:

$$\mathrm{DA_{event\text{-}i}} = \mathrm{K_p} \times \mathrm{C} \times \mathrm{T} \times 10^{-6} \tag{4}$$

Kp is the permeability coefficient (cm/hr), C is the chemical concentration in water that is in contact with the skin (ng/L), and T is the time of contact (hours/day), which was determined from references on water usage habits in northern and southern China, as summarized in Supplementary Table S4 (*5*–*6*).

It is difficult to obtain permeability coefficients of antibiotics directly from references. Accordingly, we used a model developed by ten Berge (2010) and recommended by Brown et al. (2016) in a study of eight models for calculating Kp, as follows (*7*):

$$\log \mathrm{Kp} = 2.80 + 0.66 \log \mathrm{Kow} 0.0056 \mathrm{MW} \tag{5}$$

where Kow is the octanol/water partition coefficient of the target antibiotic and MW is the molecular weight

SUPPLEMENTARY TABLE S3. The skin surface area available for contact ($\mathrm{SA_i}$) were obtained according to the Chinese Exposure Factor Handbook

$\mathrm{SA_i}$ ($\mathrm{cm^2}$)	Hand cleaning	Face and hair cleaning	Foot cleaning	Dish washing	Vegetable washing	Clothes washing	Bathing	Swimming
Male	800	1,300	1,100	800	800	800	17,000	6,300
Female	700	1,200	1,000	700	700	700	15,000	5,700

SUPPLEMENTARY TABLE S4. The time of contact (T, hours/day) was determined from references on water usage habits in northern and southern China.

Time of contact (hours/day)	Hand cleaning	Face and hair cleaning	Foot cleaning	Dishes washing	Vegetable washing	Clothes washing	Bathing	Swimming
Male in South China	0.0500	0.0783	0.0167	0.0000	0.0000	0.0000	0.1750	0.086
Female in South China	0.0667	0.1117	0.0117	0.0850	0.0717	0.0467	0.2083	0.088
Male in Nouth China	0.0627	0.1012	0.0146	0.0115	0.0091	0.0462	0.2553	0.086
Female in Nouth China	0.0614	0.1168	0.0165	0.1606	0.1364	0.3050	0.2424	0.088

SUPPLEMENTARY TABLE S5. Kow and MW of target antibiotics were used to calculate the permeability coefficient (Kp, cm/hr)

Antibiotic	**log Kow**	**MW(g/mol)**
Penicillin G	1.83	334.38
Cloxacillin	2.44	435.88
Cephalecxin	0.65	347.39
Ceftiofur	1.60	523.57
Clarithromycin	3.16	747.95
Roxithromycin	2.21	837.05
Tylosin	1.63	916.11
Sulfapyridine	0.35	249.29
Sulfadiazine	2.59	250.27
Sulfamethoxazole	0.89	253.28
Sulfathiazole	0.05	255.32
Sulfamethazine	0.14	278.33
Sulfaquinoxaline	1.68	300.34
Sulfadoxin	0.43	310.33
Norfloxacin	0.46	319.33
Ciprofloxacin	0.28	331.34
Enrofloxacin	0.64	359.40
Ofloxacin	-0.39	371.37
Sarafloxacin	0.57	385.36
Trimethoprim	0.91	290.32

Abbreviation: Kow=octanol water partition coefficient, MW = molecular weight.

(g/mole). Kow and MW of target antibiotics are summarized in Supplementary Table S5.

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