Supplementary Material

Health risk quotient (HRQ) calculation

$$HRQ_{an} = \frac{ADD}{ADI\ or\ RSD} \quad (1)$$

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:

$$\mathrm{ADD_{dw}} = \frac{\mathrm{C_{dw} \times IngR \times EF \times ED}}{\mathrm{BW \times AT \times 1,000}} \quad (2)$$

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 (ADD_{dermal}) was calculated using Equation S3:

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

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. $DA_{event-i}$ refers to the absorbed dose from one event [μg/cm^2·day)], as calculated using Equation S4 below. SA_i refers to the skin surface area available for contact (cm^2), according to the *Chinese Exposure Factor Handbook* (China EPA 2009; values summarized in Supplementary Table S3. EF_i refers to the exposure frequency (days/year), ED_i to the exposure duration (years), BW to body weight (kg), and AT_i to averaging time (days). $DA_{event-i}$ was calculated as follows:

$$DA_{event-i} = K_p \times C \times T \times 10^{-6} \quad (4)$$

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*):

$$\log Kp = 2.80 + 0.66 \log Kow 0.0056 MW \quad (5)$$

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 (SA_i) were obtained according to the Chinese Exposure Factor Handbook

SA_i (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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