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Occurrence and Risk Assessment of Antibiotics in Urban River–Wetland–Lake Systems in Southwest China

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Abstract: Antibiotics in the aquatic environment are of great concern as novel contaminants. In this study, we investigated the occurrence, distribution, potential sources, and risk assessment of antibiotics in an interconnected river–wetland–lake system. Thirty-three target antibiotics, including sulfonamides (SAs), macrolides (MLs), fluoroquinolones (FQs), tetracyclines (TCs), and chloramphenicol (CLs) belong to five common groups of antibiotics, were tested from water samples collected in the Panlong River, Xinghai Wetland, and Lake Dian (or Dianchi). Mass spectrophotometry was used to detect the target antibiotics, and the water quality parameters were measured in situ. We found four antibiotics, lincomycin (LIN), trimethoprim (TMP), sulfamethoxazole (SMX), and ofloxacin (OFL), with relatively low concentrations at the ng/L level, and detection rates among sample sites ranged from 42.3% to 76.9%, with maximum concentrations of 0.71 ng/L~5.53 ng/L. TMP was not detected in the Panlong River but appeared in the wetlands and Lake Dian. Midstream urban areas of the Panlong River showed the highest pollution among sites. Antibiotic concentrations were positively correlated with total nitrogen (TN) ($p < 0.05$) and showed some negative correlation with pH, salinity, and DO. According to the risk assessment, antibiotics in water do not pose a threat to human health and aquatic ecosystems, but a potentially harmful combined effect cannot be excluded. Our research offers a geographical summary of the distribution of antibiotics in urban river, wetland, and lake ecosystems in the plateau (PWL), which is important for predicting the distribution characteristics of antibiotics in the plateau water environment and establishing a standardized antibiotic monitoring and management system for the government.

Keywords: antibiotics; risk assessment; freshwater ecosystem; water quality

Citation: Zeng, Y.; Duan, L.; Xu, T.; Hou, P.; Xu, J.; Li, H.; Zhang, H. Occurrence and Risk Assessment of Antibiotics in Urban River–Wetland–Lake Systems in Southwest China. *Water* **2024**, *16*, 1124. https://doi.org/10.3390/w16081124

Academic Editor: Abasiofiok Mark Ibekwe

Received: 21 March 2024
Revised: 6 April 2024
Accepted: 9 April 2024
Published: 15 April 2024

1. Introduction

Antibiotics are a type of antimicrobial drug produced by bacteria and fungi or synthesized artificially that have microbial inhibitory activity and are commonly used in human medicine and livestock farming [1,2], posing a higher ecological risk to water ecosystems and human health. The global antibiotic consumption was approximately 42 billion qualifying daily doses in 2015 and is estimated to increase by a further 200% by 2030 [3]. The heavy use of antibiotics has led to their entry into the aquatic environment (rivers and lakes) through a variety of pathways, including sewage discharge, agricultural activities, manure application, and runoff [4–6], making the aquatic environment a major sink for them and leading to many rivers already at high risk because of antibiotic concentrations [7,8].

The services of urban rivers include aquaculture, receiving surface runoff, sewage discharge and waterway transportation. It is greatly influenced by human activities. Urbanization discharges various pollutants into rivers [9], and some pollutants enter lakes via rivers and accumulate continuously, causing ecological risk problems in lakes [10]. Lake-entering rivers are important channels for land-based sources to enter lakes, constituting a tight terrestrial ecosystem of rivers and lakes and playing an important role in various ecological and economic services [11,12].

Lake Dian is the biggest freshwater lake located on the Yunnan–Guizhou Plateau in southwestern China. The Panlong River is the most important river entering Lake Dian and the main landscape river in Kunming. It originates from the Songhuaba Reservoir and runs through the whole main city of Kunming, and the watershed concentrates most of the developed economic zones of Kunming with a dense population and a high degree of human interactions with the river. The Panlong River is also the channel through which transregional water has been transferred from the Niulan River to Lake Dian and therefore plays an important role in the socioeconomic development of the Lake Dian basin in terms of flooding, pollution reduction, irrigation, urban beautification, humidity regulation, and water supply. With swift economic expansion and urban advancement, the consumption of antibiotics has increased significantly, and they may pose potential health risks to aquatic organisms in the Panlong biodiversity and even to humans. As a new pollutant, antibiotics are constantly detected in water bodies. When they cause water pollution, they can induce the generation and spread of resistant bacteria and resistant genes, which brings serious challenges to the protection of water ecology and environmental health management in river basins. Therefore, there is an urgent need to know the occurrence, amount, distribution, risks, and sources of antibiotics. Previous studies have focused on the occurrence and distribution of antibiotics in individual rivers, lakes, etc. [13,14]. Maghsodian et al. (2022) found that Lake Dian has very high levels of SMX (ranging from 17.6 to 499.2 ng/L) and OFL (ND—713.6 ng/L) [15]. However, as the most important river entering Lake Dian, antibiotic contamination in the Panlong River has rarely been reported, and none of the available literature data are sufficient for comparison with other urban rivers.

In this study, we selected a dense human activity area consisting of urban rivers, wetlands, and lakes and divided the watershed into urban river systems, wetland systems, and lake systems according to the functional distinction, aiming to (1) study the distribution characteristics of antibiotics and offer evidence to support the current distribution of antibiotics in the ecological environment of urban rivers, wetlands, and lakes in the plateau; (2) evaluate the pollution level and ecological threat posed by antibiotics in the water bodies of the Panlong River and explore the possible adverse effects to aquatic organisms at current concentrations; (3) study the pollution sources of antibiotics in the watershed; and (4) identify the antibiotics that need to be controlled as a priority and provide a scientific basis for decision-making regarding future development and integrated management of the watershed.

2. Materials and Methods

2.1. Study Area

The Panlong River (25°03′~25°27′ N, 102°40′~102°57′ E) belongs to the Jinsha River system and is located in Kunming, central Yunnan Province, China, running through the entire main city of Kunming. The basin concentrates most of the mature economic zone of Kunming, with a total length of 108 km, a runoff area of 847 km^2, an average flow of 7.17 m^3/s, a maximum flow of 126 m^3/s, with an annual runoff of 275 million m^3, and is the largest and longest river into Lake Dianchi. The Panlong River basin has a subtropical monsoon climate with an average annual temperature of 15 °C and an average annual precipitation of 1035 mm. Precipitation in the basin is unevenly distributed, with the rainy season (May–October) accounting for 85% to 90% of the annual precipitation. The vegetation cover is highly variable, and it is a typical urban-rural interlacing zone. Land use types include six categories: arable land, forestland, grassland, water, urban construction land, and bare land, of which arable land, forestland, and urban construction land account for more than 92% of the watershed area, and soil types consist of five categories: rice soil, red soil, subtropical mountain red soil, brown soil, and an urban impermeable layer.

2.2. Sample Collection and Pretreatment

On 10–12 April 2022, we collected water samples along the Panlong River to Lake Dianchi and at the Xinghai wetlands (Figure 1), with 8 sampling sites (P1, P2, P3, P4, P5, P6, P7, P8) in the Panlong River, 8 sampling sites (L1, L2, L3, L4, L5, L6, L7, L8) in the Lake Dianchi inlet, and 10 sampling sites (W1, W2, W3, W4, W5, W6, W7, W8, W9, W10) in the Xinghai wetlands. The sampling points were distributed in the main urban area of Kunming, wetlands, and shoreline where the Panlong River and Lake Dianchi meet. Each sampling site in the Panlong River consisted of 2 samples on the left and right. During the sampling process, we measured water temperature (WT), pH, dissolved oxygen (DO), conductivity, and turbidity with a YSI 6600 V multiparameter water quality monitor (Xylem, Inc., Rye Brook, NY, USA). In advance, a quantity of 150 mg antioxidant and 0.25 g of EDTA were introduced into the 1 L brown Nalgene sample bottle in which the water samples were stored. After collecting the water samples, the pH was adjusted to 2 by adding HCl immediately at the site, and the samples were stored under refrigeration and protected from light at 0 to 4 °C until they were processed.

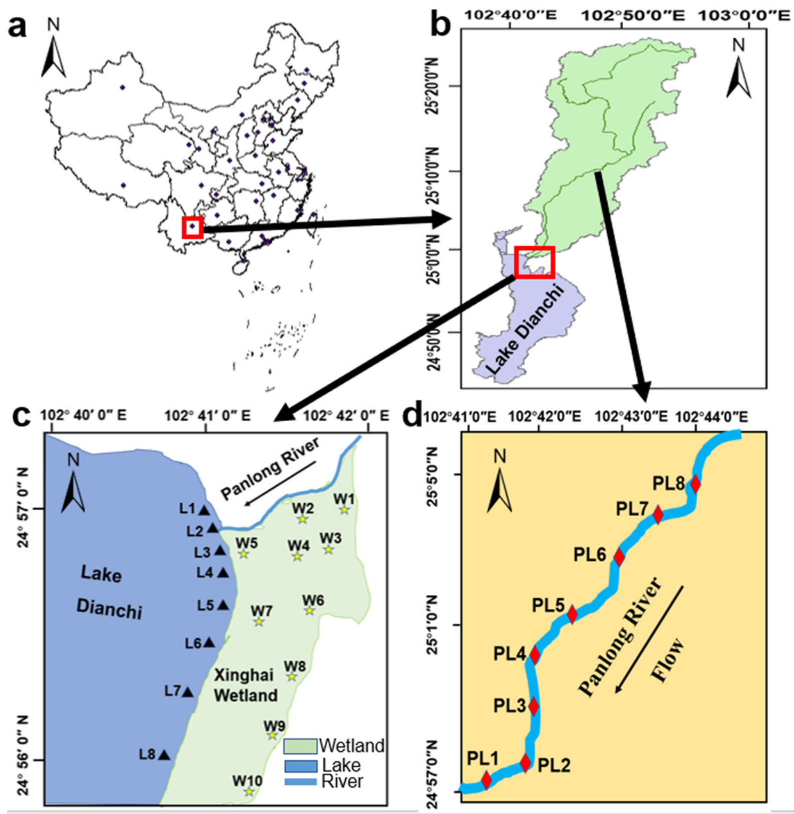

Figure 1. Locations of the sampling sites around the Panlong River, Xinghai Wetland and Lake Dianchi.

Water samples were filtered through a 0.45 µm pore size glass fiber membrane, 0.2 g Na_2EDTA was included to minimize the chelation of antibiotics with metal ions present in the water sample, 25 ng of antibiotic internal standard was included, followed by passing through an Oasis HLB (200 mg/6 cc) solid phase extraction column at a flow rate of 5 mL/min. The HLB column underwent activation sequentially with 10 mL methanol, 10 mL pure water, and 10 mL pure water (pH = 4) in turn. Then, the column was rinsed with 10 mL of distilled water, drained, dried under N_2 protection for a duration of 30 min, eluted with 6 mL methanol in 3 portions, blown with nitrogen to near dryness, and redissolved with the initial mobile phase (0.1% $CH_2O_2^-$ NH_4HCO_2/CH_3CN) to be measured. We also measured total nitrogen and total phosphorus according to the standard method [16,17].

2.3. Sample Treatment and Analysis

We conducted HPLC-MS/MS analysis utilizing an Agilent 6410B triple tandem quadrupole LC-MS/MS, Waters Xterra C18 separation column (100 mm × 2.1 mm, 3.5 µm) ESI ionization source. The mobile phase consisted of phase A, 0.1% $CH_2O_2^-$ NH_4HCO_2; B: CH_3CN. Linear gradient: 0 min, 5% B; 0.1~10 min, 10%~60% B; 10~12 min, 60%; 12.1~22 min 10% B. The rate of flow was 0.25 mL/min. The MS conditions included a gas temperature of 350 °C, gas flow rate of 8 mL/s, nebulizer pressure of 25 psi, and capillary voltage of 4000 V. Table 1 gives the ion, fragmentation voltage, and collision energies. The MDL is the standard deviation of these measured concentrations multiplied by the t value with n-1 degrees of freedom at the 99% confidence level. The detection limits and recoveries of individual compounds in water samples are shown in Table 2.

Table 1. LC-MS/MS parameters for the target antibiotics.

NO.	Antibiotics	Parent Ion (m/z, Da)	Daughter Ion (m/z, Da)	Frag (V)	CE (eV)	RT (min)
1	Erythromycin	734	158	135	33	10.218
2	Roxithromycin	847	679.4	190	21	11.732
3	Lincomycin	407.5	126.1	150	33	5.502
4	Azithromycin	749.9	591.4	215	29	8.576
5	Tylosin	1042.4	814	135	27	13.495
6	Clindamycin	425	126.1	80	35	8.779
7	Sulfacetamide	215	156.3	110	10	2.948
8	Sulfachloropyridazine	285	155.9	110	13	8.087
9	Sulfadimoxine	311	155.9	125	17	9.854
10	Sulfapyridine	250.3	155.9	110	13	5.328
11	Sulfathiazole	256	155.9	92	13	5.043
12	Sulfamethizole	271.1	156.1	60	21	7.567
13	Sulfapyridine	251.2	156.1	102	13	3.729
14	Sulfamonomethoxine	281	156	160	18	7.149
15	Sulfamethoxazole	254	155.8	105	13	8.616
16	Sulfamethazine	279	156	112	17	6.941
17	Trimethoprim	291	230	165	21	6.406
18	Sulfaquinoxaline	301	156	118	16	10.120
19	Ofloxacin	362	318	180	15	6.848
20	Norfloxacin	320	302	128	21	6.882
21	Ciprofloxacin	332.1	314	100	18	6.938
22	Enrofloxacin	360	316	180	17	7.424
23	Sarafloxacin	386	268.1	180	29	8.541
24	Lomefloxacin	352	265	180	23	7.168
25	Fleroxacin	370	326	180	16	6.770
26	Difloxacin	400	356	180	23	8.122
27	Doxycycline Hydrochloride	445.2	427.9	115	15	8.914
28	Tetracycline	445.2	410	115	20	7.351
29	Oxytetracycline	461.2	442.9	130	10	6.987
30	Aureomycin	479.3	443.8	142	25	7.351
31	Chloramphenicol	321	152	110	9	9.260
32	Florfenicol	356	185	110	20	8.709
33	Thiamphenicol	354	184.7	140	13	6.521
34	Rifampicin	821	397	220	30	12.285

Notes: Daughter ion: quantification ion/confirmation ion; CE: collision energy; RT: retention time; Frag: fragment.

Table 2. The instrument limitations and recoveries of the target antibiotics.

NO.	Antibiotics	MDLs (ng/L)	Linearity (R^2)	Recoveries (Average ± RSD, %)
1	Erythromycin	1	0.9986	81.2 ± 3.8
2	Roxithromycin	1	0.9995	90.1 ± 4.2
3	Lincomycin	0.5	0.9945	85.6 ± 3.5
4	Azithromycin	1	0.9930	87.2 ± 3.4

Table 2. *Cont.*

NO.	Antibiotics	MDLs (ng/L)	Linearity (R^2)	Recoveries (Average ± RSD, %)
5	Tylosin	2	0.9901	76.9 ± 8.7
6	Clindamycin	1	0.9851	81.2 ± 6.7
7	Sulfacetamide	1	0.9971	61.23 ± 3.5
8	Sulfachloropyridazine	1	0.9976	89.1 ± 2.5
9	Sulfadimoxine	1	0.9974	85.1 ± 5.1
10	Sulfapyridine	1	0.9977	79.6 ± 4.6
11	Sulfathiazole	1	0.9975	83.7 ± 5.2
12	Sulfamethizole	1	0.9994	81.3 ± 6.3
13	Sulfapyridine	1	0.9987	98.3 ± 2.1
14	Sulfamonomethoxine	1	0.9975	100.1 ± 7.2
15	Sulfamethoxazole	1	0.9956	79.5 ± 6.1
16	Sulfamethazine	1	0.9980	87.6 ± 5.5
17	Trimethoprim	1	0.9997	86.4 ± 3.4
18	Sulfaquinoxaline	1	0.9938	75.6 ± 4.2
19	Ofloxacin	1	0.9971	76.8 ± 3.8
20	Norfloxacin	1	0.9999	89.5 ± 3.8
21	Ciprofloxacin	1	0.9998	71.2 ± 4.5
22	Enrofloxacin	1	0.9998	78.6 ± 3.4
23	Sarafloxacin	1	0.9999	78.9 ± 4.2
24	Lomefloxacin	1	0.9998	61.8 ± 8.2
25	Fleroxacin	1	0.9994	61.2 ± 7.9
26	Difloxacin	1	0.9999	61.45 ± 8.7
27	Doxycycline Hydrochloride	20	0.9961	76.1 ± 3.8
28	Tetracycline	20	0.9971	64.1 ± 8.9
29	Oxytetracycline	20	0.9912	74.1 ± 10.1
30	Aureomycin	20	0.9941	82.7 ± 6.9
31	Chloramphenicol	1	0.9984	88.2 ± 7.7
32	Florfenicol	1	0.9986	85.3 ± 7.8
33	Thiamphenicol	1	0.9981	78.9 ± 5.6
34	Rifampicin	1	0.9987	82.6 ± 8.9

Note: MDLs: Method detection limits.

2.4. Human Health Risk Assessment

The risk evaluation for human health was carried out using the recommended method [18]. The initial step in performing a health risk evaluation is to determine the type and toxicity of a pollutant. The carcinogenicity of various chemical compounds has been categorized and measured by several agencies or departments, such as the USEPA and the International Agency for Research on Cancer (IARC), and chemicals with varied carcinogenicity have been grouped into many groups.

As river water may be used in a variety of ways, individuals may meet contaminants in the water in a variety of ways, resulting in varying amounts of exposure. This research looked at 3 possible reuse scenarios: (1) urban greening, (2) recreational (such as swimming), and (3) agricultural usage. Individuals can be exposed to chemicals in water through one or multiple pathways in each scenario, orally, inhalationally, or dermally, and various categories of individuals experience exposure to the water at varied frequencies and quantities. Equations (1)–(4) may be utilized for calculating the life average daily dose (LADD) of pollutants consumed by people under different reuse situations and exposure pathways [19].

$$LADD_{Inhal} = (C_i \times IR \times ET \times EF \times F \times 0.63 \times ED)/(BW \times LT) \quad (1)$$

$$LADD_{Dermal} = (C_i \times SA \times PC \times EF \times ET \times 1000 \times ED)/(BW \times LT) \quad (2)$$

$$LADD_{oral} = (C_i \times IR \times ET \times EF \times F \times 0.63 \times ED)/(BW \times LT) \quad (3)$$

$$LADD_{Inhal} = (C_i \times ET \times EF \times F \times 0.63 \times ED)/(24 \times LT) \quad (4)$$

LADD denotes the mean daily dose of oral, exposure, and inhalation contaminants, mg/(kg·d), respectively, C_i represents the level of contaminant i, mg/L, IR is the inhalation rate (oral route in L/day), EF is the exposure frequency, day/year, BW represents body weight measured in kilograms, while LT denotes time expressed in days, SA is surface area, m^2, PC is the skin surface permeability constant for a specific of chemical pollutants, m/h, ET is the exposure time in a day, h/day, 0.63 is the rate of inhalation of pollutants from the air, and F is the water mist in the air, L/m^3. The values of other parameters refer to the Chinese exposure factors [20].

Noncarcinogenic Risk Assessment

We refer to Lin et al. [18], and the following formula is used for the assessment of noncarcinogenic risk.

$$\mathrm{NCRi} = \frac{\mathrm{LADD_i}}{\mathrm{RfD_i \text{ or } RfC_i}} \tag{5}$$

where $\mathrm{LADD_i}$ is as above, $\mathrm{NCR_i}$ indicates the noncarcinogenic posed by pollutant i to humans, mg/(kg·day), mg/(m^3·day), and $\mathrm{RfD_i}$ represents the reference dose, mg/(kg·d) or mg/(m^3·day).

The RfD of the pollutant was found in the USEPA IRIS database [21]. Or it can be calculated using the following formula [22].

$$\mathrm{RfD} = \frac{\mathrm{NOAEL}}{\mathrm{MF} \times \mathrm{UF}} \tag{6}$$

where NOAEL is the no observed adverse effect level dose, MF represents the modification factor, and UF represents the uncertainty factor.

The acceptable noncarcinogenic risk limit is set at 1 [23].

2.5. Ecological Risk Assessment

The potential aquatic ecological risk of antibiotics was assessed based on the risk quotient (RQ) approach [24], calculated as follows:

$$\mathrm{RQ} = \frac{\mathrm{MEC}}{\mathrm{PNEC}} \tag{7}$$

$$\mathrm{PNEC} = (\mathrm{LOEC \text{ or } L(E)C_{50}})/\mathrm{AF} \tag{8}$$

where MEC and PNEC represent the environmental detection concentration and predicted no effect concentration of antibiotics, respectively. The above parameters were obtained from the US EPA Ecotoxicology Knowledge Base [25] and some of the referenced literature data [24].

RQ > 1 represents a high ecological risk, $0.1 \leq R \leq 1$ indicates a medium ecological risk, and RQ < 0.1 signifies a low ecological risk [18,26].

2.6. Source Identification Analysis

The potential sources of antibiotics in PWD were analyzed using a positive matrix factorization model (EPA 5.0). (PMF), which was solved using a bilinear model with a residual matrix and a user-supplied uncertainty matrix to estimate the minimum Q value.

$$\mathrm{X_{ij}} = \sum_{k=1}^{p} \mathrm{g_{ik} f_{kj}} + \mathrm{e_{ij}} \tag{9}$$

where p denotes the number of factors, f is the species profile of each source, g is the mass contribution of each factor to each sample, e_{ij} is the residual of each sample/species, and x_{ij} is the concentration of each sample/species.

$$Q = \sum_{i}^{m} \sum_{j}^{n} (\frac{e_{ij}}{\mu_{ij}})^{2} \tag{10}$$

where u_{ij} is the uncertainty of each measured value.

3. Results

3.1. Occurrence of Target Antibiotics

We chose 34 antibiotics as targets, and 4 antibiotics were detected, including LIN, SMX, TMP and OFL, belonging to the three classes of Sas (SMX, TMP), MLs (LIN), and FQs (OFL), indicating the presence of target antibiotic residues in the PWL. The frequency and mean concentrations of sulfonamides were higher than those of macrolides and quinolones, and the levels and occurrence rates of each antibiotic class in PWL are shown in Table 1. Although tetracycline (TC) antibiotics are the most widely used antibiotics for both human and veterinary treatments in China [27,28], they were not detected at concentrations above 20 ng/L. This is because tetracyclines are photodegraded in shallow lakes [29], and tetracyclines also have complexing properties; they readily combine with calcium and similar ions to form stable complexes that bind to suspended matter and sediments [30], they may not exist as free molecules, and tetracyclines have large K values and are more distributed in sediments [31]. In addition, the detection of a limited number of tetracycline species and the detection limit of 20 ng/L for tetracycline may be incomplete and not sensitive enough.

The average detection rate of antibiotics at 26 sampling points was 92.3%. Among them, the detection rate of LIN was 57.7%, SMX was 76.9%, TMP was 38.5%, and OFL was 42.3%. For sampling sites where those four antibiotics were detected in the water, approximately 96.4% had concentrations below 5.0 ng/L (Figure 2). TMP 2.07~4.66 ng/L (mean 3.27 ng/L) and OFL (1.8~5.47 ng/L, mean 3.21 ng/L) were the top two contributors to the antibiotic concentration in water, followed by LIN 0.71~1.51 ng/L (mean 1.1 ng/L) and SMX 0.78~5.53 ng/L, with an average of 2.96 ng/L. OFL (1.8~5.47 ng/L, mean 3.21 ng/L) was the major antibiotic detected in this study. LIN is one of the five most commonly used antibiotics (amoxicillin, florfenicol, LIN, penicillin, and norfloxacin) in China [27]. In addition, LIN exhibited higher hydrophilicity and lower solubility in water collected from saltwater pools, rendering it more enduring in seawater ($t_{1/2}$ = 809 days) [32]. Sulfonamides are very common antibiotics that have been detected in many Chinese rivers [33,34], and some have been detected at high concentrations. Through monitoring 1052 rivers worldwide, SMX was detected in 140 (13%) of them at concentrations exceeding their predicted no-effect concentrations for aquatic organisms. Similarly, TMP was detected in some rivers in Africa and South America at concentrations exceeding the safety target for biological resistance [35]. The high detection rate of sulfonamides (76.9%) could be attributed to the use of SMX and TMP as feed additives in livestock and aquaculture and their synergistic effect in combination with other drugs [36]. In addition, prior research indicates that sulfonamides are difficult to degrade in water, so their concentrations in the aquatic environment are relatively high [37]. QNs are frequently detected in rivers and lakes as major aquaculture inputs [38]. Previous studies have shown that QNs are the major antibiotics in sediments, accounting for 80.9% of total antibiotics [39]. This is because the chemical structure of QNs makes it extremely easy to form complexes with mineral cations or solid particulate organics, so they are more likely to be deposited in sediments [40]. Because the sediment was not tested for antibiotic content in this study, the actual QN content may be higher. Although the type of antibiotics in the sediment was not detected at this time, there is also a possibility of antibiotic contamination in the sediment because the diffusion of antibiotics in water is greater than that in sediment, and antibiotics can migrate from water to sediment [41].

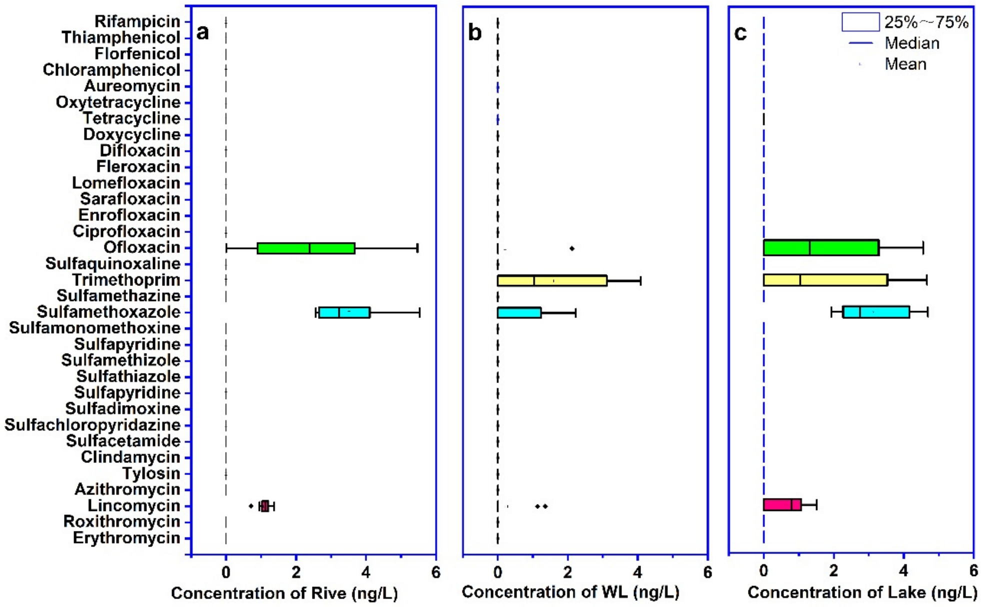

Figure 2. Box-and-whisker plots of the levels and occurrence rates of antibiotics in the water, (**a**) Panlong river; (**b**) Xinghai Wetland; (**c**) Lake Dianchi.

3.2. Antibiotic Compositions in Different Areas and Comparison with Other Regions

The total antibiotic concentration in the Panlong River was 7.85 ng/L. Both LIN and SMX were found in every sample (Figure 3), and the highest concentrations were at site 5, at 1.37 and 5.53 ng/L, respectively (Table 3). The average concentration of LIN in each sample was approximately 1 ng/L, with little difference in concentration among the sampling sites, further confirming the stability of LIN in water. The concentration of SMX ranged from 2.56 to 5.53 ng/L (mean 3.51 ng/L), continued to increase from upstream to midstream, and began to decrease from midstream to downstream; however, at the inlet of Lake Dianchi, the concentration suddenly increased. OFL was detected in samples 1 to 6 with an average detection frequency of 75% and concentrations from 1.80 to 5.47 ng/L (mean 3.24 ng/L). At sampling 2, there was a sudden increase in concentration, reaching 5.47 ng/L. TMP was not detected. The high concentrations of target antibiotics at the inlet of Lake Dianchi suggest that the Panlong River has an important role in the source of antibiotics to Lake Dianchi. In the XingHai wetland, the detection rate of LIN was 20%, SMX was 40%, TMP was 50%, and OFL was 10%. The concentration of LIN ranged from 1.14 to 1.35 ng/L (mean 1.25 ng/L), the concentration of SMX ranged from 0.78 to 2.23 ng/L (mean 1.56 ng/L), and the concentration of TMP ranged from 2.07 to 4.09 ng/L (mean 3.12 ng/L), while OFL was not detected. The collective antibiotic concentration in the XingHai wetland measured 8.05 ng/L. In the inlet of Lake Dianchi, all four kinds of antibiotics were detected, and SMX was detected in all water samples, with the highest detection rate, followed by LIN, with a detection rate of 62.5%, TMP and OFL, both with a detection rate of 50%. The concentration range of LIN was 0.75 to 1.51 ng/L (mean 1.05 ng/L), SMX was 1.93 to 4.69 ng/L (mean 3.12 ng/L), TMP was 2.08 to 4.66 ng/L (mean 3.45 ng/L), and OFL was 2.63 to 4.55 ng/L (mean 3.44 ng/L). The total antibiotic concentration in the inlet of Lake Dian was 11.06 ng/L. The highest total antibiotic concentration was found in the inlet of Lake Dian at 11.06 ng/L, with TMP and OFL accounting for 31.2% and 31.1%, respectively. As shown in Figure 4, in the water samples, the primary antibiotics identified in the Panlong River (P) were SMX and OFL. The main antibiotic species detected in Lake Dianchi (L) were SMX, OFL, and TMP, with SMX predominating. This indicates that the same source of SMX may exist in the Panlong River and Lake Dianchi. SMX is one of the most common sulfonamides in natural waters, and the main source putatively is aquaculture, and it was detected in high concentrations in aquatic environments [42]. In contrast, the dominant antibiotic species in the Xinghai wetland (W) was TMP.

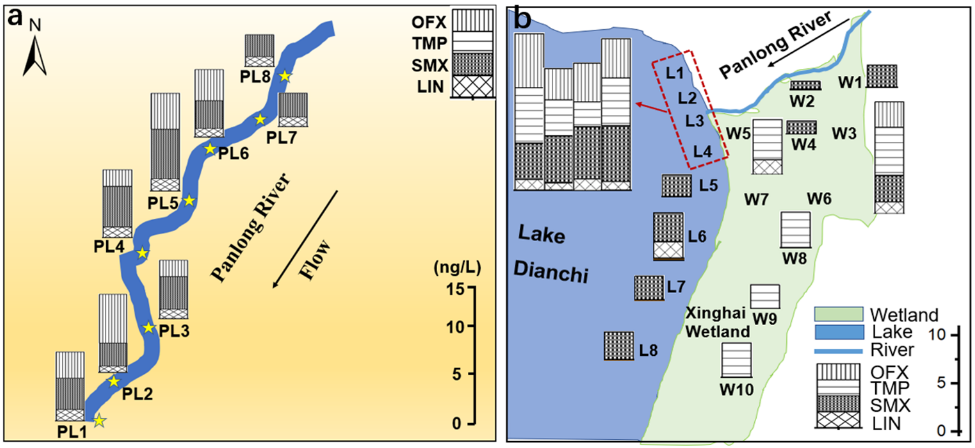

Figure 3. Spatial distribution of antibiotic concentrations in water, (**a**) Panlong River; (**b**) Xinghai Wetland and Lake Dianchi.

These antibiotics were detected in other aquatics [43], and the SMX and OFL concentrations in the PWD system were lower than those in the Lake Fuxian and Erhai basins, which are in Yunnan Province. In the Lake Fuxian basin, seven antibiotics at concentrations ranging from 0 to 150 ng/L were detected, with sulfonamides and OFL accounting for 100% and 82% of the total content, respectively. Sulfonamide concentrations ranged from 0.98 to 14.32 ng/L (mean 6.52 ng/L), and OFL concentrations ranged from 0.77 to 7.3 ng/L (mean 3.40 ng/L) [14]. Sulfonamides and OFL were detected in the Erhai watershed by Zhi et al. [44]. They also found sulfonamides at significantly higher concentrations and frequencies in water than in other environmental media. In comparison with other urban rivers outside Yunnan Province, SMX and OFL concentrations were lower than those of the Bohai Rim, Yangtze River, Huangshui River (Xining City, China, concentrations of OFL exceeded those found in the Huangshui River), and urban rivers in Vietnam [45]. The maximum values detected for SMX, TMP, and OFL were significantly lower than those reported for the Nanming River (Guiyang City, China), Hanjiang River (Wuhan City, China), Wangyang River (Shijiazhuang City, China), and Ter River (Girona, Spain) [46–49]. SMX and TMP concentrations were significantly lower than those of the Chaobai River (Beijing, China) [50] and the Umgeni River (Durban, South Africa) [51]. The maximum detected concentrations of SMX and TMP in African rivers are 3320 and 38.9 μg/L [52,53], respectively. Lower concentrations of SMX and TMP were detected in rivers of developed countries. Significant differences in SMX and TMP concentrations in rivers of different countries were correlated with national income levels. Developed countries have better wastewater treatment facilities and strict antibiotic stewardship systems, despite their higher antibiotic consumption rates (DDDs per 1000 inhabitants per day) [3,54]. In comparison, the detected concentrations in OFL were higher than those in the Nera River (Tuscany, Italy) [55] and Han River (Seoul, Republic of Korea) [56].

Table 3. Concentrations and detection frequencies of antibiotics in water.

Classes	Abbreviations	Panlong River (ng/L)					XH Wetland (ng/L)					Lake Dianchi (ng/L)				
		Min	Max	Mean	Median	Freq	Min	Max	Mean	Median	Freq	Min	Max	Mean	Median	Freq
LNs	LIN	0.71	1.37	1.10	1.13	100	ND	1.35	1.25	0	20	ND	1.51	0.66	0.80	62.5
SAs	SMX	2.56	5.53	3.51	3.24	100	ND	2.23	0.63	0	40	1.93	4.69	3.12	2.75	100
	TMP	ND	2.02	1.01	0	12.5	ND	4.09	1.56	1.04	50	ND	4.66	1.73	1.04	50
QNs	OFL	ND	5.47	2.43	3.68	75	ND	2.12	0.21	0	10	ND	4.55	1.72	1.32	50

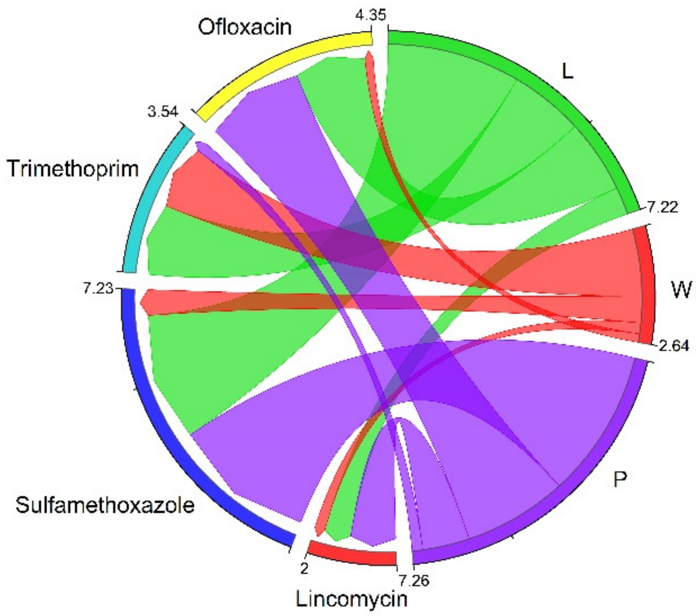

Figure 4. Composition of antibiotics at different sampling sites in water.

Human activity, population density, hydraulic properties of rivers and lakes, and land use type play an important role in the distribution of antibiotic concentrations. There were differences in the types of antibiotics detected between the Panlong River and Lake Dianchi. TMP were detected at the inlet of the lake, while they were not detected in the Panlong River, which indicates that there are other input sources around the river in addition to those evaluated in this study. The presence of TMP was detected at sampling sites W8, W9, and W10 in the Xinghai wetland, indicating the presence of nearby sources of contamination. The river eventually flows into Lake Dianchi, and the SMX and OFL concentrations in the inlet are higher than those in the Panlong River. Studies on Lake Dianchi have shown that the SMX and OFL concentrations in Lake Dianchi are 17.6–499.2 and ND—713.6 ng/L, respectively [57], suggesting that there are other sources in Lake Dianchi. Antibiotics carried by rivers entering the lake can affect the ecological risk and increase the uncertainty of microbial resistance risk [58–60]. In addition, due to the long residence time of the lake, the accumulated concentration of pollutants will increase. SMX was detected along the shoreline of Lake Dianchi by the wetland (sampling points L1 to L8), and OFL was detected at sampling points L1 to L4. Both antibiotics were also widely detected in the Panlong River, but SMX and OFL were not detected at most of the sampling points in the wetland, suggesting that there may be adsorption degradation of SMX and OFL by plants in the wetland, especially for SMX.

3.3. Correlation between Antibiotic Concentrations and Water Properties

The correlation between antibiotics and water quality parameters was evaluated (Figure 5), and the antibiotic concentrations showed some negative correlations with pH, salinity, DO, and CHl. The possible reason for the negative correlation between antibiotics and salinity is that the salinity of Dianchi (0.24) is higher than the salinity of Panlong River (0.22), and as the water flows into the lake, the salinity rises and pollutants are diluted. The salinity at the mouth of the lake was 0.225, and the injection of river water lowered the salinity at this confluence, which also indicates that the Panlong River imports antibiotics into Dianchi. This is consistent with previous reports that antibiotic concentrations exhibited a negative correlation with salinity in both the Bohai Sea and the Yellow Sea [61,62]. It has been shown that DO can affect the concentration of antibiotics because DO can directly affect the biodegradation activity of microorganisms [63], and the rate of antibiotics degradation is greater under aerobic conditions compared to anaerobic conditions [64], so antibiotics show a negative correlation with DO. Antibiotics showed a positive correlation with TN ($p < 0.05$), which is a similar pattern found in other water bodies. For example, a study of the Yangtze River, Pearl River, and Yellow Sea found that TN was positively correlated with antibiotics [6,65,66]. TN can reflect the degree of antibiotic pollution to some extent, and they probably have similar sources, such as human domestic sewage and aquaculture [67].

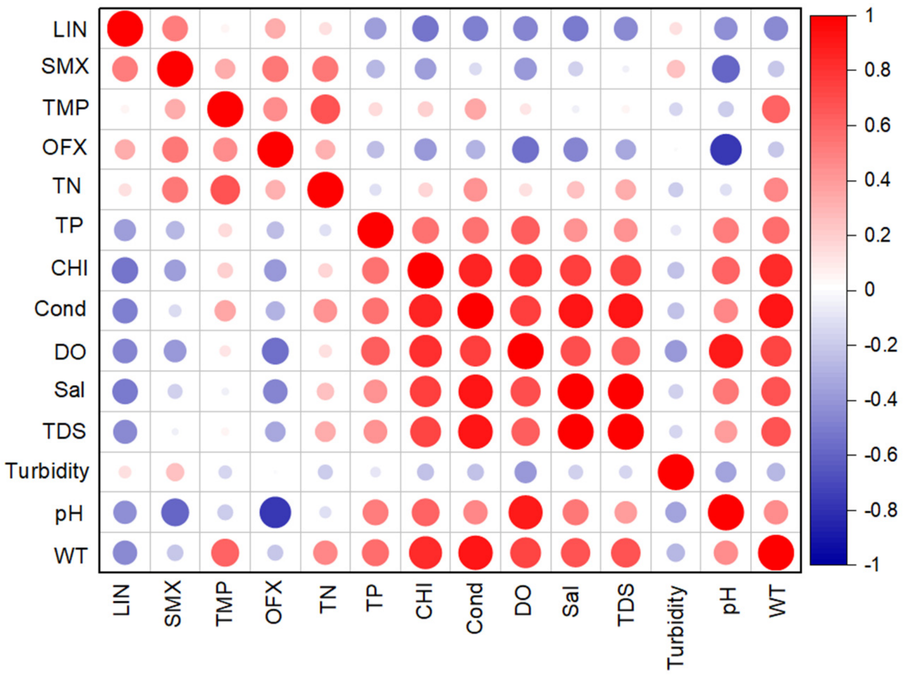

Figure 5. The correlation between antibiotics and water quality parameters.

3.4. Human Health Risk Assessment

These antibiotics were subjected to human health risk evaluations. Human health hazards of several pollutants reported in the Panlong River were analyzed using reference doses from the USEPA IRIS database and peer-reviewed literature. The maximum concentrations of these pollutants discovered in the Panlong River were utilized to estimate their maximum possible risks of carcinogenic and noncarcinogenic, and the maximum exposure of various groups was chosen to calculate the worst-case scenario. Their noncarcinogenic properties were computed using detected concentrations to forecast their greatest probable health risk during water reuse. Figure 6 illustrates the estimated human noncarcinogenic hazards. The analysis contaminant's noncarcinogenic hazard to humans was below the relevant tolerable risk level. The human health risk from various contaminants for water reuse, such as swimming, is generally higher than that in the other two scenarios, which may be due to the consideration of greater exposure methods and intake volume V than in the other two scenarios. The highest potential noncarcinogenic risk for OFL was 1.37×10^{-7} when swimming in water.

We evaluated the noncarcinogenic risk of pollutants to different populations under various scenarios examined in the human health risk assessment. Our data showed that the human health risk is low but should be monitored and controlled. Various precise human health risk evaluations should be undertaken in the future, considering variances in further features of exposure to different populations, as well as more studies on exposure parameters under diverse reuse situations.

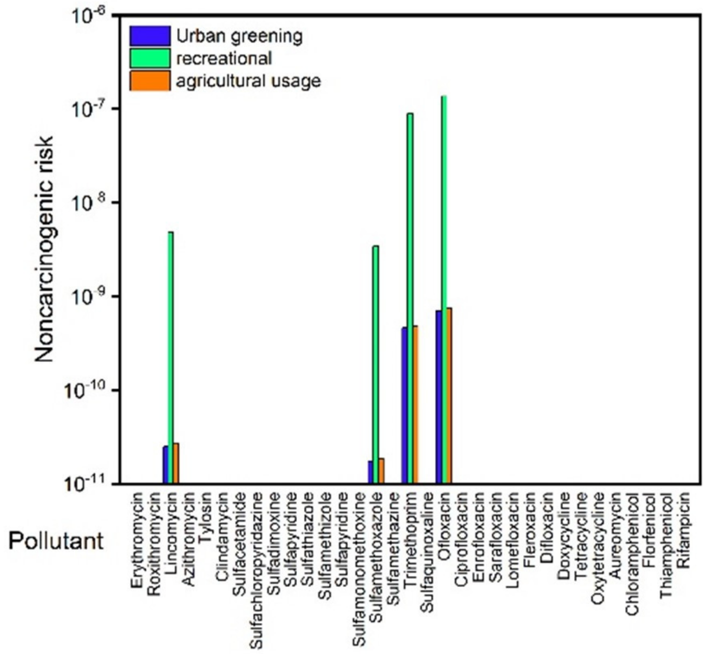

Figure 6. Noncarcinogenic risk of the Panlong River.

3.5. Ecological Risk Assessment

LIN, SMX, TMP, and OFL in water samples from the Panlong River were assessed based on acute and chronic toxicity RQs with three typical freshwater organisms (fish, daphnia, and algae) in the river (Figure 7). The acute and chronic toxicity of all antibiotics to fish, daphnia, and algae were not significant. The ecological risks of SMX, TMP, OFX, and LIN were generally higher for Daphnia than for algae and fish, probably due to the lower acute and chronic toxicity of PNECs in both daphnia than in fish and algae. Most SMX, TMP, OFX, and LIN showed higher ecological risks to algae than to fish. However, SMX and TMP showed higher chronic toxicity to fish than to algae.

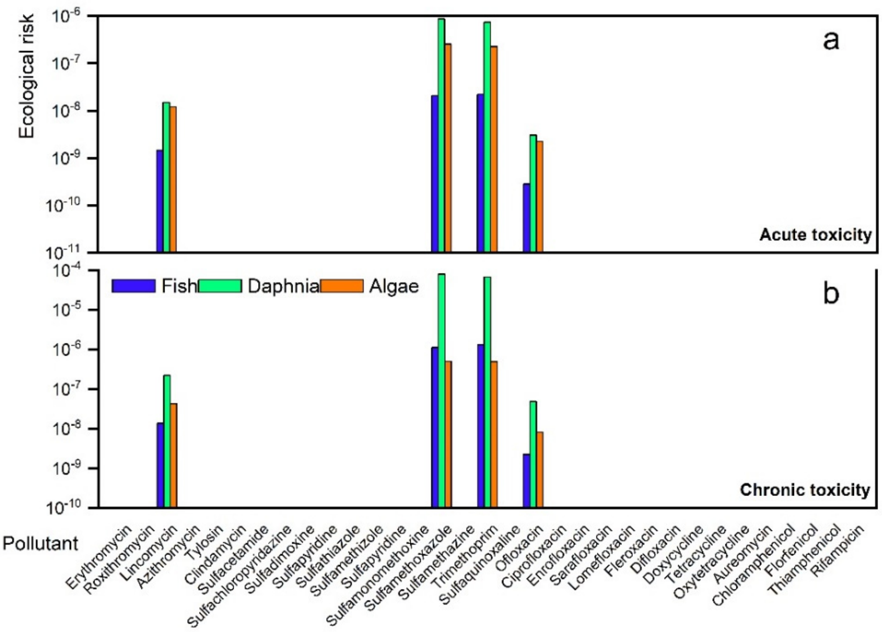

Figure 7. The ecological risk posed by antibiotics in Panlong River to three typical organisms (fish, daphnia, and algae), (**a**) Acute toxicity; (**b**) chronic toxicity.

3.6. Pollution Source Analysis

The results of the PMF model analysis (Figure 8) showed that there were three influencing factors in the PXD region. Factor 1 contributed the most, accounting for approximately 43.7% of the total contamination contribution and mainly consisted of LIN, SMX, and OFX. These antibiotics are mainly veterinary antibiotics in China, among which SMX has been approved for veterinary use and is generally used as a sulfonamide synergist in livestock farming and aquaculture, thus enhancing antimicrobial efficacy [68]. It has been reported that most of the veterinary antibiotics in livestock farming in China are directly discharged into the environment, such as water or soil with animal manure and urine [69]; therefore, factor 1 may originate from livestock farming and aquaculture wastewater. Factor 2 accounted for 34.7% of the total pollution contribution, and its contributions to TN, DTN, and NO_3^--N were 59.4%, 51.9%, and 55.2%, respectively. Since fertilizers may be discharged into the lake with surface runoff, considered one of the main sources of nitrogen in the lake [70], agricultural activities may account for the high nitrogen index, and factor 2 may represent agricultural surface source pollution. Factor 3 accounted for 22.4% of the total contamination, and its contributions to TP, PO_4^{3-}-P, SMX, OFX, and TMP were 43.7%, 40%, 23.7%, 25.8%, and 31.5%, respectively. It is well known that SMX and OFX are commonly used antibiotics in humans, usually for the treatment of bacterial infections [71]. The Panlong River runs through the city of Kunming, which is densely populated, and factor 3 may come from the discharge of human antibiotics, representing the impact of domestic wastewater.

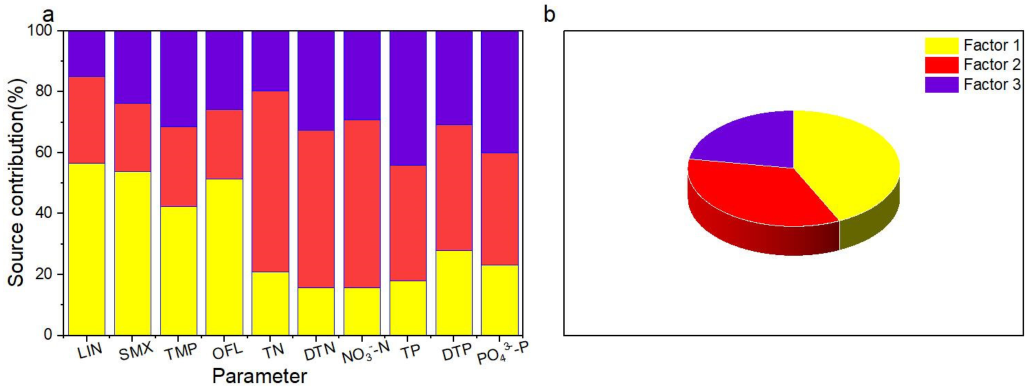

Figure 8. Source compositions (**a**) and mean contributions (**b**) of water quality variables in the PWD area according to the PMF analysis.

4. Conclusions

In this study, we targeted 34 antibiotics, including SAs, MLs, FQs, TCs, and CLs, in the PWL. The study results indicated that sulfonamides were the most widely distributed compounds in the area. Spatially, high concentrations of antibiotics were detected at sampling sites near the city center, which may accurately represent anthropogenic pollutants in urban rivers. TMP was the predominant antibiotic in the Xinghai wetland, accounting for nearly 60% of the total antibiotic concentrations. TMP was not detected in the Panlong River but was widely present in wetlands and the lake Dianchi inlet. Our findings demonstrated that antibiotic concentrations were positively correlated with TN and showed some negative correlation with pH, salinity, and DO as water quality parameters. In addition, the risk evaluate results showed that none of the sampling sites posed a risk to human health or aquatic ecosystems. Currently, our research is limited to antibiotics in surface waters, and the next step should be to explore sediments and other environmental media. In addition, there is a need to model the sources and transport of antibiotics at the watershed scale to better understand the fate of antibiotics in shallow lakes. This study helps to deepen the understanding of the current water quality of urban river–wetland–lake systems and provides guidance for the improvement of ecological services of urban water.

Author Contributions: Conceptualization, methodology, supervision, resources, foundation acquisition, writing—review and editing, H.Z.; formal analysis, writing—original draft preparation, Y.Z.; investigation and data curation, Y.Z., L.D., T.X., P.H., J.X. and H.L. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the NSFC (Grant No. U2202207) and the Special Project for Social Development of Yunnan Province (Grant No. 202103AC100001).

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Acknowledgments: We thank all the students who participated in the fieldwork and laboratory analyses.

Conflicts of Interest: The authors declare no conflicts of interest.

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