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The occurrence of quinolone and imidazole antibiotics in rivers in Central Taiwan

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ABSTRACT

The occurrence of antibiotics in aquatic environments has been of increasing concern around the world due to their ability to alter the structure of microbial communities and to promote the development of antimicrobial-resistant pathogens. Six major rivers in Central Taiwan were investigated for the occurrence of the eight most frequently prescribed quinolone and imidazole antibiotics using solid-phase extraction followed by high performance liquid chromatography–electrospray ionization–tandem mass spectrometry. Nalidixic acid, flumequine, ofloxacin, dimetridazole, and metronidazole were detected at 0.8–192 ng/L in the water samples. The three most frequently detected antibiotics at all sampling sites were metronidazole, nalidixic acid, and flumequine (detection frequency ($n = 24$) $\geqslant 19$ sites). The highest concentration of flumequine was detected at 192 ± 6.5 ng/L in the Old Zhuoshui River. Compared to the available predicted no-effect concentration data, the risk quotients of flumequine and ofloxacin were estimated to be close to one. The Old Zhuoshui and Beigang Rivers were shown to be the two most contaminated rivers with the nearby animal husbandries being the important source of contamination. The information provided here warrants future attention and is useful for the development of regulation and remediation strategies.

Keywords: HPLC–ESI–tandem MS; Solid-phase extraction; Quinolone antibiotics; Imidazole antibiotics

1. Introduction

In many European and North American countries, the adverse health effects and potential risks to ecosystems associated with the occurrence of emerging contaminants in aqueous environments have been an increasing concern among researchers, policy-makers, and industry personnel [1,2]. Emerging contaminants are a group of nonregulated contaminants that require evaluation by the US EPA. They include a variety of compounds such as pharmaceuticals, hormones, and surfactants. Quinolone and imidazole antibiotics are two groups of pharmaceuticals that are commonly used in human medications and veterinary drugs. Quinolones are used to treat serious bacterial infections, particularly hospital-acquired infections. However, adverse effects include toxicity to the central nervous system, convulsions, and hypoglycemia. Metronidazole is widely used to treat Giardia infections in dogs and cats. The US National Toxicology Program lists this antibiotic as an anticipated human

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carcinogen. Dimetridazole is often used in livestock feed, but this compound should not be detectable at the aquaculture drug residue tolerance level in Taiwan, Japan, and the European Union.

Previous studies have reported the half-maximum effective concentrations (EC_{50}) of ciprofloxacin and flumequine at 5–19 μg/L [3–5]. The no observed effect concentration (NOEC) of ofloxacin on *Synechococcus leopoliensis* was observed at a concentration of 5 μg/L [6]. The NOEC values of flumequine and nalidixic acid are 2.6 and 72 μg/L, respectively, which are determined using a 24-h *Vibrio fischeri* bioluminescence study.

Many studies have detected quinolones and imidazoles in wastewater treatment plants (WWTPs), sewage treatment plants, hospital effluents, and river waters [1,7–19]. Removing these contaminants by conventional treatment procedures were reported to be inefficient as these compounds are found in significant concentrations in hospital and WWTP effluents. In hospital effluents, Lindberg et al. [8] reported ciprofloxacin, ofloxacin, and metronidazole at concentrations of 0.1–101 μg/L.

The environmental occurrence of quinolones and imidazoles has never been investigated in Taiwan. Consequently, the objectives of this study were: (1) to develop a method for the simultaneous determination of six quinolone antibiotics (nalidixic acid, flumequine, pipemidic acid, norfloxacin, ciprofloxacin, and ofloxacin) and two imidazole antibiotics (dimetridazole and metronidazole) and (2) to investigate the occurrence of target antibiotics in six major rivers in Central Taiwan that are heavily impacted by waste streams from hospitals, agriculture, and animal husbandry activities.

2. Materials and methods

2.1. Chemicals and standards

All target antibiotic standards were of high purity grade (>96%). Nalidixic acid (99.4%), flumequine (99%), pipemidic acid (100%), metronidazole (100%), sodium hydroxide (⩾97%), and sulfuric acid (96.3%) were purchased from Sigma–Aldrich (St. Louis, MO, USA). Norfloxacin (99%), ciprofloxacin (99.1%), ofloxacin (99.3%), ciprofloxacin-d_8 hydrochloride monohydrate (99.1%), and metronidazole-$^{13}C_2$, $^{15}N_2$ (99.9%) were obtained from Fluka (Buchs, Switzerland). Dimetridazole (99.9%) and ACS-grade formic acid were purchased from Riedel-de Haën (Seelze, Germany). LC-grade methanol, ACS-grade ether, and disodium ethylenediaminetetraacetate (EDTA-2Na) were obtained from Mallinckrodt Baker (Phillipsburg, PA, USA). ACS-grade acetic acid and LC-grade acetonitrile were purchased from J.T. Baker (Phillipsburg, PA, USA).

The dimetridazole, metronidazole, ciprofloxacin-d_8, and metronidazole-$^{13}C_2$, $^{15}N_2$ standard stock solutions were prepared in methanol; the nalidixic acid and flumequine standard stock solutions were prepared in methanol–acetonitrile (50:50, v/v); and the pipemidic acid, norfloxacin, ciprofloxacin, and ofloxacin standard stock solutions were prepared in methanol–DI water (50:50, v/v) with 0.5% acetic acid. All solutions were refrigerated in amber glass bottles at −20°C. Prior to each analytical run, working solutions were prepared in methanol–DI water (25:75, v/v) by diluting stock solutions.

2.2. Site selection and sampling

Fig. 1 shows the six major streams in Central Taiwan (Wuchi, Old Zhuochui, Zhouchui, Beigang, Puzih, and Bajhang Rivers). Twenty-four sampling sites were chosen because they were likely to be impacted by the nearby agricultural and animal husbandry activities and by the discharge from the hospital and regional WWTP. The potential pollution sources contributing to these six rivers are shown in Table 1. Triplicate grab samples were collected from 24 selected sites in 1-L amber glass bottles during the same day and stored in ice-packed coolers. Eight mL of 0.125M EDTA–2Na was added to the sampling bottles prior to sample collection. All samples were collected in July 2010, and analyses were completed within two weeks of sample collection.

2.3. Sample preparation

All water samples were vacuum-filtered through 0.45 and 0.22 μm cellulose acetate membrane filters (Advantec; Toyo Roshi Kaisha. Ltd., Japan), acidified to pH 4.0 using 1 M sulfuric acid, and stored at 4°C until analysis. Oasis HLB cartridges (500 mg, 6 mL; Waters; Milford, MA, USA) were used for SPE and were preconditioned with 6 mL of methanol and 6 mL of deionized (DI) water. Aliquots of 400 mL water samples were spiked with 40 μL of 1 mg/L ciprofloxacin-d_8 and metronidazole-$^{12}C_2$, $^{15}N_2$ were used as internal standards for quinolones and imidazoles, respectively, and loaded into the cartridges with a flow rate of 3–6 mL/min. After passing the samples through the columns, the cartridges were rinsed with 6 mL of DI water and dried under an air stream for 5 min. Analytes were eluted with 3 mL of methanol

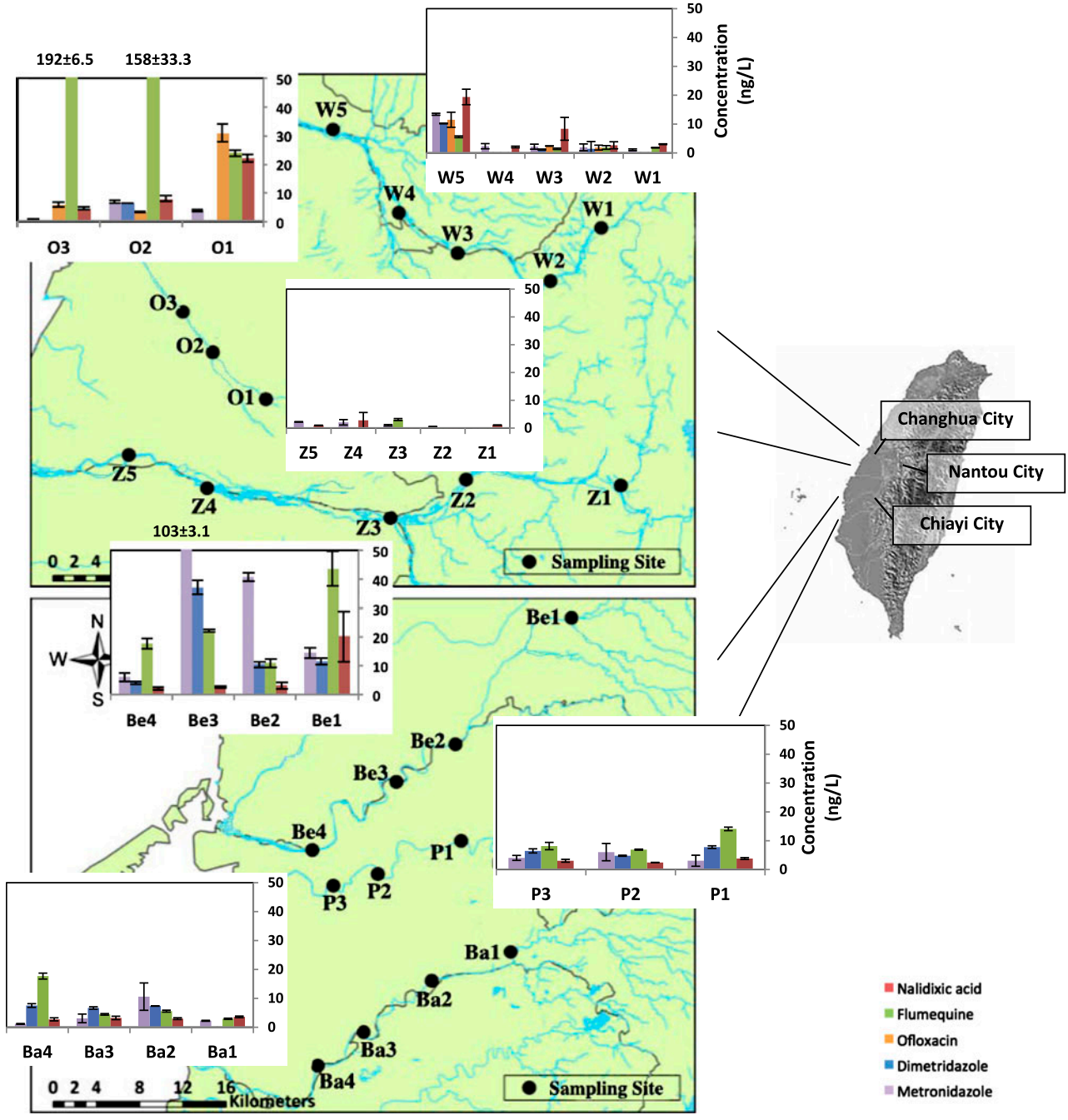

Fig. 1. The sampling sites and the occurrence of antibiotics in six rivers in central Taiwan: Wuchi River (W1–W5), Old Zhuoshui River (O1–O3), Zhoushui River (Z1–Z5), Beigang River (Be1–Be4), Puzih River (P1–P3), and Bajhang River (Ba1–Ba4).

and 3 mL of ether–methanol (50:50, v/v). The eluates were collected and evaporated to dryness under a nitrogen stream and then reconstituted in 0.4 mL 25% aqueous methanol (v/v). Final solutions were filtered through a 0.45 μm PVDF membrane filter before LC–MS/MS analysis.

2.4. LC–ESI–MS/MS analysis

The concentration of analytes was determined using an Agilent 1200 liquid chromatography system (Agilent Technologies, Palo Alto, CA, USA) equipped with a ZORBAX Eclipse XDB-C_{18} column (19 × 4.6 mm, 5 μm). The mobile phases A and B contained 0.1% formic acid

Table 1
Pollution sources of six rivers in central Taiwan

	Hospitals, medical institutions	Pharmacies	Animal husbandries (a)	Animal husbandries (b)
Wuchi River	23	1	44	4
Zhuoshui River	5	–	191	16
Old Zhuoshui River	3	6	122	12
Beigang River	9	–	180	25
Puzih River	12	2	87	6
Bajhang River	1	–	94	6

Notes: Animal husbandries (a): Nonherbivores, e.g. Pigs, chickens, ducks, and geese.
Animal husbandries (b): Herbivores, e.g. Cattle, horses, sheep, deer, and rabbit.

(v/v) in water and in methanol, respectively, and were used in a binary gradient with a flow rate of 1.0 mL/min. Twenty microliters of sample was injected and eluted out of the column within 15 min. The gradient elution program started with 0% mobile phase B for 0.5 min, increased to 40% from 0.5 to 3.0 min, increased to 70% from 3.0 to 7.5 min, increased to 95% from 7.5 to 9 min, remained at 95% until 11 min, decreased to 0% from 11 to 12 min, and remained at 0% until 15 min. The autosampler was operated at room temperature.

The mass spectrometric measurements were carried out on a Sciex API 4000 instrument (Applied Biosystems, Foster City, CA, USA) equipped with an ESI interface. Analyses were performed in the positive mode for all compounds. Ions were acquired in the multiple reaction monitoring (MRM) mode with a dwell time of 10 msec. The mass spectrometer conditions were as follows: ion spray voltage, 5.5 kV; curtain gas, 10 L/h; nebulizer gas, 50 L/h; turbo gas, 60 L/h; and heated capillary temperature, 500˚C.

After selecting the precursor ions, product ions were obtained and optimized using four key parameters: declustering potential, entrance potential, collision energy, and collision cell exit potential by the direct infusion of the pure analytes into the MS–MS compartment.

2.5. Detection, quantification, and quality control

Using LC–MS/MS in the MRM mode, quantification of quinolones and imidazoles used the two highest characteristic precursor-ion/product-ion transition pairs. Compounds were identified using the LC retention time ±30% of the retention time of the standard.

Recovery experiments were performed in DI water and river water spiked with 5, 50, and 250 ng/L of the target analyte. Absolute recoveries were determined by comparing the concentrations of the spiked DI and river water before and after the SPE. Relative recoveries were determined with ciprofloxacin-d_8 and metronidazole-$^{13}C_2$, $^{15}N_2$ internal standards, which were spiked into DI and river water along with the target analytes before the SPE procedure. Pipemidic acid, norfloxacin, ciprofloxacin, ofloxacin, and dimetridazole were quantified by ciprofloxacin-d_8, and metronidazole was quantified by metronidazole-$^{13}C_2$, $^{15}N_2$.

Standard calibration curves were constructed by spiking target pharmaceutical standard solutions (0.25–250 μg/L) into 25% methanol (v/v), and the linearity of the calibration curves was estimated by fitting a linear mode, least-squares regression analysis ($y = a + bx$). The method detection limits (MDLs) for the entire method (including SPE) were determined by spiking diluted antibiotic solutions into DI and river water, and the MDLs were the minimum concentration of analyte in the linear range with a signal-to-noise ratio of at least 10:1.

3. Results and discussion

3.1. Analytical method validation

All eight target antibiotics were detected by LC–MS/MS, and the detailed MS–MS parameters of the target compounds and internal standards are listed in Table 2. After selecting the precursor ions for the target compounds, product ions were selected by their higher signals. Two MRM pairs were used to identify the target antibiotics.

The relative and absolute recoveries of the standards from DI water and river water with different spiked concentrations (5, 50, and 250 ng/L) are presented in Table 3. Absolute recoveries for all target antibiotics at all concentrations were 37.9–109.8% in DI water and 34.2–105.4% in river water. The relative recoveries of the target antibiotics were 98.5–139.7% (DI water) and 81.1–147.2% (river water). The results showed that pipemidic acid, norfloxacin, ciprofloxacin, ofloxacin, dimetridazole, and metronidazole had good relative recoveries and should be quantified with the

Table 2
The MS–MS parameters for target compounds and internal standards for the MRM mode with positive ionization

Compounds	Retention time (min)	Precursor ion (m/z)	Product ions (m/z)	MS/MS parameters			
				DP (V)	EP (V)	CE (V)	CXP (V)
Quinolones							
Nalidixic acid	9.83	233	187	37	10	35.3	10.6
			215			18.9	11.2
Flumequine	10.09	262	202	44	10	44.6	15.1
			244			24.2	19.9
Pipemidic acid	5.91	304	217	48	10	28.9	17.9
			286			24.2	7.1
Norfloxacin	6.38	320	276	40	10	23.4	7.0
			302			28.7	17.1
Ciprofloxacin	6.48	332	288	45	10	24.5	7.5
			314			26.2	8.6
Ofloxacin	6.20	362	261	55	10	36.9	14.8
			318			27.8	8.5
Ciprofloxacin-d_8	6.45	340.2	296.2	50	10	24.5	24.0
			322.2			31.0	24.0
Imidazoles							
Dimetridazole	6.02	142	81	32	10	35.8	3.9
			96			23.8	7.5
Metronidazole	5.68	172	82	30	10	31.3	6.7
			128			20.8	9.0
Metronidazole-$^{13}C_2$,$^{15}N_2$	5.67	176	86	50	10	36.0	14.0
			132			27.0	24.0

Note: DP: declustering potential; EP: entrance potential; CE: collision energy potential; and CXP: collision cell exit potential.

Table 3
Relative and absolute recoveries of antibiotics in DI and river water with different spiked concentrations (5, 50, and 250 ng/L)

Compounds	Relative recovery ±SD (%) ($n=3$)						Absolute recovery ±SD (%) ($n=3$)					
	DI water			River water			DI water			River water		
	5 ng/L	50 ng/L	250 ng/L	5 ng/L	50 ng/L	250 ng/L	5 ng/L	50 ng/L	250 ng/L	5 ng/L	50 ng/L	250 ng/L
Nalidixic acid	–	–	–	–	–	–	93.6 ± 1.1	92.5 ± 3.3	86.9 ± 1.2	84.4 ± 0.7	92.5 ± 5.7	88.3 ± 2.0
Flumequine	–	–	–	–	–	–	90.2 ± 3.9	96.3 ± 1.7	90.3 ± 1.0	105.4 ± 4.7	100.9 ± 3.0	96.8 ± 4.1
Pipemidic acid	111.1 ± 9.8	101.5 ± 4.6	108.0 ± 3.4	101.7 ± 15.5	112.6 ± 5.2	104.3 ± 0.8	47.3 ± 4.6	61.7 ± 5.3	63.6 ± 3.6	54.4 ± 2.3	60.1 ± 2.7	66.9 ± 1.6
Norfloxacin	105.2 ± 10.4	101.7 ± 3.4	106.7 ± 3.7	105.9 ± 9.0	101.1 ± 0.8	100.0 ± 1.6	43.9 ± 3.2	68.5 ± 2.9	60.7 ± 2.2	52.2 ± 4.7	54.7 ± 0.5	61.2 ± 2.1
Ciprofloxacin	98.5 ± 13.3	98.7 ± 3.2	99.5 ± 2.0	97.5 ± 7.2	98.1 ± 2.5	98.4 ± 1.1	65.0 ± 3.9	56.9 ± 4.1	56.0 ± 2.1	69.7 ± 3.3	52.0 ± 0.7	58.0 ± 1.7
Ofloxacin	109.0 ± 5.4	104.1 ± 7.7	101.7 ± 1.5	92.3 ± 4.6	87.8 ± 1.6	81.1 ± 0.6	37.9 ± 1.0	50.3 ± 2.1	55.5 ± 1.7	34.2 ± 3.9	42.2 ± 0.5	48.0 ± 0.7
Dimetridazole	139.7 ± 36.3	104.3 ± 3.6	114.1 ± 8.6	147.2 ± 8.3	118.9 ± 2.3	118.1 ± 3.1	57.9 ± 13.7	68.3 ± 57.7	63.7 ± 5.4	73.9 ± 1.9	71.7 ± 1.1	72.8 ± 0.2
Metronidazole	104.5 ± 2.0	107.7 ± 3.5	101.9 ± 1.2	101.1 ± 1.3	102.2 ± 2.1	99.3 ± 1.6	109.3 ± 2.3	109.8 ± 4.3	100.5 ± 2.2	105.2 ± 1.7	100.5 ± 1.4	91.7 ± 2.5
Ciprofloxacin-d_8								56.2 ± 5.9			60.2 ± 2.0	
Metronidazole-$^{13}C_2$, $^{15}N_2$								90.9 ± 0.5			83.6 ± 1.0	

Table 4
The MDLs in both DI water and river water and the linearity (correlation coefficient) for target antibiotics

Compounds	MDLs DI water ng/L	MDLs River water ng/L	Linear range μg/L	Linearity *r*
Nalidixic acid	1.0	1.0	0.25–10	0.9998
			10–250	0.9973
Flumequine	0.5	0.5	0.5–10	0.9970
			10–250	0.9985
Pipemidic acid	1.0	1.0	0.5–5	0.9984
			5–250	0.9994
Norfloxacin	1.0	1.0	0.5–5	0.9996
			5–250	0.9994
Ciprofloxacin	0.5	1.0	0.5–5	0.9990
			5–250	0.9992
Ofloxacin	0.5	0.5	0.5–5	0.9974
			5–250	0.9978
Dimetridazole	0.5	0.5	0.25–5	0.9999
			5–250	0.9971
Metronidazole	0.5	0.5	0.25–10	0.9998
			10–250	0.9979

internal standards. Matrix interferences were observed in river waters; ofloxacin, ciprofloxacin, and metronidazole in river water showed a lower relative recovery than in DI water.

No internal standards were used for nalidixic acid and flumequine. The absolute recoveries of nalidixic acid and flumequine from DI water were 86.9–93.6% and 90.2–96.36%, respectively, and were 84.4–92.5% and 96.8–105.4% in river water, respectively. Previous studies [20–24] have showed that nalidixic acid and flumequine have an absolute recovery of 70–130% and can be quantified without internal standards.

Table 4 shows the overall MDLs in DI and river water (0.5–1.0 ng/L) and the linear range of the eight antibiotics. The linear ranges were 0.25–250 μg/L with a linearity of greater than 0.9970. Our results are comparable to those of many previous studies, which reported a range of MDLs (1–20 ng/L) for quinolones and imidazoles in river waters [7,10,12,16,18] (Table 5).

3.2. Occurrence of target pharmaceuticals

Samples were collected from six major rivers in Central Taiwan (Fig. 1) to assess the impact of human activities on the contamination of receiving waters and the occurrence of target antibiotics. Except for the Zhuoshui River, significant concentrations of quinolones and imidazoles were detected in all rivers investigated. The Old Zhuoshui and Beigang Rivers were found to be the most contaminated rivers in the region.

Fig. 1 and Table 6 provide detailed results for the occurrence of eight target antibiotics. Pipemidic acid, norfloxacin, and ciprofloxacin were not detected in any of the river samples. Nalidixic acid, flumequine, and metronidazole were the most frequently detected compounds and were also found with higher concentrations in all rivers. The concentration range of nalidixic acid, flumequine, and metronidazole were 2.1–22.0, 2.9–192, and 0.8–103 ng/L, respectively. The highest concentrations of nalidixic acid (22 ± 1.3 ng/L) and flumequine (192 ± 6.5 ng/L) were detected in the Old Zhuoshui River while the highest concentration of metronidazole (103 ± 3.1 ng/L) was found in the Beigang River. Ofloxacin and dimetridazole were detected less frequently (25 and 58%, respectively) and generally detected at lower concentrations (3.3–30.9 ng/L and 4.1–37.1 ng/L, respectively). The concentrations found in this study for nalidixic acid, flumequine, and metronidazole were higher than in many other reported works. Tamtam et al. [10] reported trace concentrations of nalidixic acid (<10 ng/L) and flumequine (up to 32 ng/L) in river waters in France. Another study by Vulliet et al. [12] showed that metronidazole was detected at a trace level (n.d. – 0.1 ng/L) in surface waters.

The Zhuoshui and Beigang Rivers have a greater number of animal husbandries than the other rivers (Table 1). The antibiotics most frequently found in these two rivers were mostly used in animal medications for treating pigs (nalidixic acid and dimetridazole) and chickens (flumequine, ofloxacin and

Table 5
Previously reported MDLs and maximum detected concentrations of target antibiotics in different water matrices

Class	Compound	Matrix	MDL (ng/L)	Maximum concentration (ng/L)	Refs.
Quinolones	Nalidixic acid	River water	10	<10	[10]
	Flumequine			32	
	Pipemidic acid			<10	
	Norfloxacin			163	
	Ciprofloxacin			<10	
	Ofloxacin			55	
Quinolones	Ciprofloxacin	WWTP effluent	1–8	400	[16]
	Ofloxacin			506	
	Pipemidic acid			ND	
	Norfloxacin			112	
Quinolones	Ciprofloxacin	River water, hospital, WWTP	10–20	2,000	[7]
	Ofloxacin			35,500	
	Norfloxacin			ND	
Quinolones	Ciprofloxacin	Wastewater	50–100	310	[17]
	Norfloxacin			330	
Quinolones	Ciprofloxacin	Hospital sewage water	30–130	101,000	[8]
Imidazoles	Ofloxacin			7,600	
	Metronidazole			90,200	
Imidazoles	Metronidazole	River water, lake water, drinking water	1–5	0.1	[12]
Quinolones	Pipemidic acid	Wastewater	0.5–37	86	[19]
	Ofloxacin			1,575	
	Norfloxacin			831	
	Ciprofloxacin			105	
Quinolones	Ofloxacin	Groundwater, artificial seawater, river water	1.5–10	108	[18]
	Norfloxacin			251	

dimetridazole); this coincided with the types of animal husbandries neighboring the Zhuoshui and Beigang Rivers. Consequently, animal husbandries (especially pig and chicken husbandries) represent an important contamination source of quinolone and imidazole antibiotics in the rivers of Central Taiwan. The results also showed that sampling sites downstream were more contaminated than upstream, indicating the potential of the environmental accumulation of these antibiotics, which persist and travel with the flow of the river.

3.3. Health risk assessment

Limited studies have reported the health risk of these pharmaceuticals in the environment. A preliminary aquatic environmental risk assessment was performed by calculating the risk quotient (RQ) as a ratio of the measured environmental concentration to the predicted no-effect concentration (PNEC). The PNEC is normally estimated by dividing the lowest NOEC for the most sensitive species by a safety factor. When the NOEC data are not available, values such as the minimal inhibitory concentration can be used to estimate the PNECs. The lowest PNEC data are reported in Table 6 [25,26]. The highest detected concentrations were used to estimate the RQ, which represents the worst case scenario. The PNEC data were only available for three detected antibiotics and the resultant RQs were 0.6, 0.77, and 0.08 for flumequine, ofloxacin, and metronidazole, respectively. The RQ values of flumequine and ofloxacin were very close to the one which warrants future attention and continuing investigation.

4. Conclusion

This is the first study to investigate the occurrence and distribution of quinolone and imidazole antibiotics in six major rivers in Central Taiwan. Animal husbandries near surface waters represent an important contamination source. The most frequently detected compounds were metronidazole, nalidixic acid, and flumequine, which were found in more than 50% of the water samples ($n = 24$). Flumequine was found at

Table 6
Detection frequency, concentration range, median value, reported PNEC, and RQ value of target antibiotics in six rivers in central Taiwan

Compounds	River water samples ($n = 24$) Number of sites >MDL	Concentration range (median value) (ng/L)						Lowest PNEC reported ng/L	Highest RQ
		Wuchi River	Old Zhuoshui River	Zhuoshui River	Beigang River	Puzih River	Bajhang River		
Nalidixic acid	22	2.1–19.4 (3.0)	4.6–22.0 (7.9)	ND-2.8 (1.0)	2.1–20.2 (2.8)	2.4–3.8 (3.1)	2.7–3.6 (3.1)		
Flumequine	19	ND-5.6 (1.8)	24.0–192 (158)	ND-3.1 (ND)	10.9–43.5 (19.9)	6.9–14.1 (8.2)	2.9–17.7 (5.1)	320 [25]	0.6
Pipemidic acid	0	ND	ND	ND	ND	ND	ND		
Norfloxacin	0	ND	ND	ND	ND	ND	ND	150 [26]	–
Ciprofloxacin	0	ND	ND	ND	ND	ND	ND	20 [26]	–
Ofloxacin	6	ND-11.5 (1.8)	3.3–30.9 (5.8)	ND	ND	ND	ND	40 [26]	0.77
Dimetridazole	14	ND-10.2 (1.2)	ND-6.2 (ND)	ND	4.1–37.1 (11.0)	4.8–7.8 (6.5)	ND-7.5 (7.1)		
Metronidazole	23	1.1–13.4 (2.2)	0.8–6.8 (3.8)	ND-2.2 (1.0)	6.0–103 (27.6)	3.1–6.1 (4.0)	1.2–10.6 (2.7)	1,300 [26]	0.08

Note: ND = not detected

relatively high concentrations (up to 192 ± 6.5 ng/L) in the Old Zhuoshui River compared with the other rivers investigated. Metronidazole was also found at up to 103 ± 3.1 ng/L in the Beigang River. A preliminary risk assessment showed the potential risk of ofloxacin and flumequine, which warrants further attention and investigation.

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