

Supplementary Materials

Impact of log(K_{ow}) value on the extraction of antibiotics from river sediments with pressurized liquid extraction

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Text S1 Chemicals and reagents

Erythromycin hydrat (96%), roxithromycin (95.3%), chlortetracycline•HCl (81.7%), oxytetracyclin•HCl (98.3%), meclocyclin sulfosalicylat (99%), ciprofloxacin (99.9%), sulfadimethoxine (98.5%), sulfachloropyridazine (pure) and sulfapyridine (99%) were bought at Sigma Aldrich (Germany).

Clarithromycin (98.4%), clindamycin•HCl (pure), tetracycline•HCl (99.1%), doxycycline hyclate, demeclocycline (93.2%), enrofloxacin (98%), ofloxacin (>98.5%), norfloxacin, sulfadiazine (99.8%), sulfamethazine (99.7%), sulfamethoxazole (98%) and trimethoprim (99.8%) were purchased at Alfa Aesar (Germany).

Erythromycin-d3 (pure), roxithromycin-d7 (pure), doxycycline-d3 hyclate (pure), ciprofloxacin-d8 (pure), enrofloxacin-d5 (pure), norfloxacin-d5 (pure), sulfadiazine-d4 (pure), sulfamethazine-d4 (pure), sulfamethoxazole-d4 (pure), sulfapyridine-d4 (pure), clindamycin-d3•HCl (pure) were purchased at TRC Canada.

Clarithromycin-d3 (10 µg/mL), oleandomycin-triacetat (100 µg/mL) were acquired from Neochema (Germany).

Ofloxacin-d3 (100 µg/mL), sulfadimethoxine-d6 (pure), trimethoprim-d3 (pure) and clinafloxacin•HCl (95%) were obtained from LGC Dr. Ehrenhofer (Germany) and Cayman Chemicals (USA), respectively.

Erythromycin-H₂O was produced in the study according to [61].

Acetonitrile (≥ 99.9%), methanol (≥ 99.9%), hydrochloric acid (37%), phosphoric acid (>85%), HPLC LC-MS grade water, sodium hydroxide (for analysis), formic acid (99%) and Ethylenediaminetetra-acetic acid disodium salt dihydrate (≥99%) were obtained from VWR (Germany). Acetone (≥ 99.8%), ethyl acetate (≥ 99.8%) and ammonium solution (>25%) were purchased from Merck (Darmstadt, Germany), (VWR), Citric acid (≥ 99.5%) was obtained from Carl Roth GmbH + Co. KG (Karlsruhe, Germany).

Ottawa sand (grain size 0.595-0.841 mm) of general-purpose grade was obtained from Fisher Scientific (United Kingdom) and sea sand from Supelco (grain size 0.1-0.315 mm) was purchased from Sigma Aldrich/Merck (Germany).

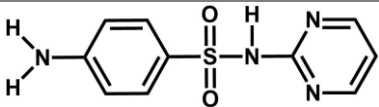
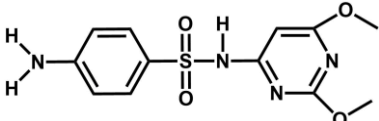
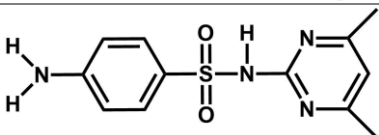
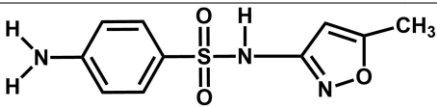
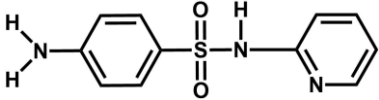
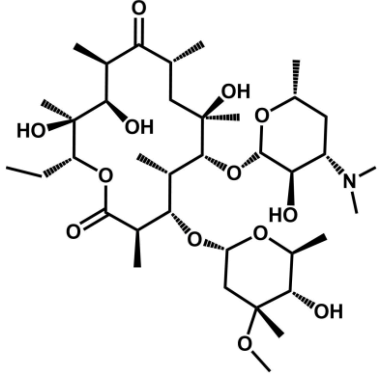
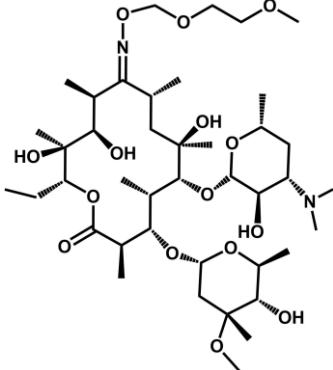
[61] Mc Ardell, C.S.; Molnar, E.; Suter, M.J.-F.; Giger, W. Occurrence and Fate of Macrolide Antibiotics in Wastewater Treatment Plants and in the Glatt Valley Watershed, Switzerland.

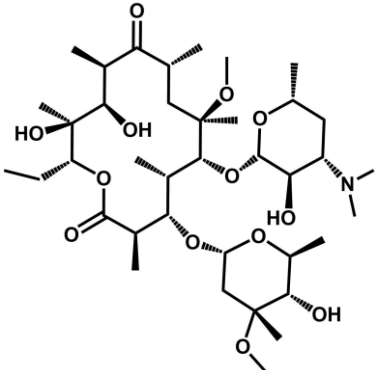
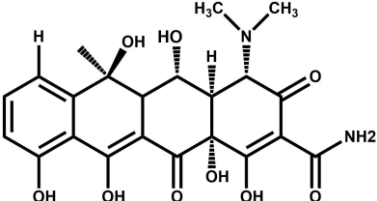
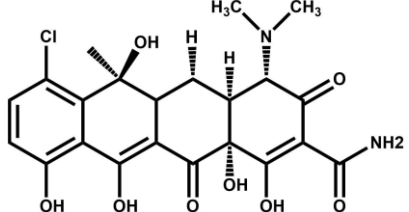
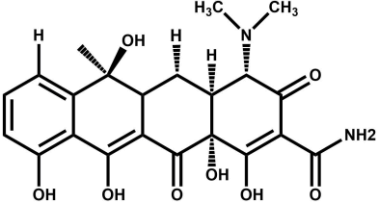
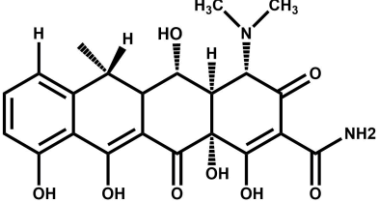
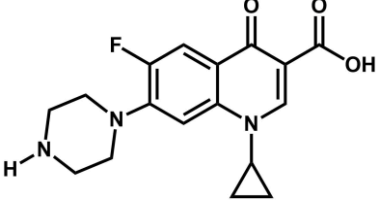
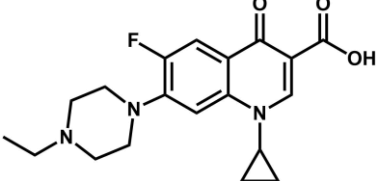
Environ. Sci. Technol. **2003**, *37*, 5479–5486, doi:10.1021/es034368i.

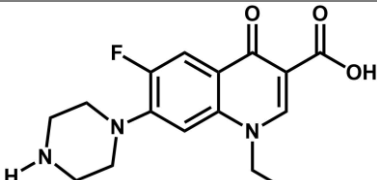
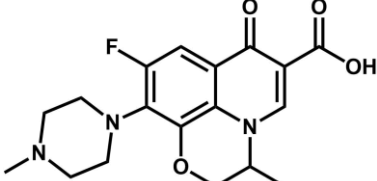
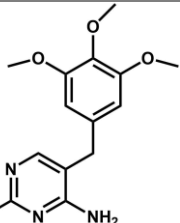
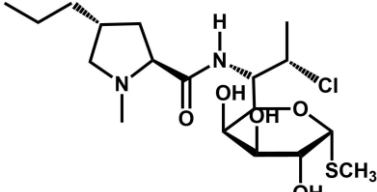
Text S2: Characterization of sediment samples

Soil pH and electrical conductivity was measured in water (ratio 1:2.5). Particle-size distribution of the fine-earth fraction (< 2mm) was determined by a combined wet-sieving and pipette method after oxidation of organic matter with H₂O₂ and dispersion with 0.1 M sodium pyrophosphate. Total C and N measurements were performed with milled aliquots by elemental analysis via thermal combustion and thermal conductivity detection of CO₂ and N₂ in a He flow (Thermo Scientific, Flash 2000 HT Plus, Bremen, Germany). Total organic carbon (TOC) was calculated as the difference between total C and total inorganic carbon (TIC) determined by acid treatment and measurement of evolved CO₂ in a Scheibler device. Effective cationic exchange capacity and exchangeable cations were determined by extraction with 1 M NH₄NO₃ and measured by ICP-OES (5100 VDV ICP-OES, Agilent, Waldbronn, Germany). For total element concentrations, we digested the samples with a mix of HNO₃, HF and H₂O₂ (4:2:1) in a microwave oven (Mars 6, CEM, Kamp-Lintfort, Germany), complexed excess HF with H₃BO₃. Macroelements (Al, Ca, Fe, K, Mg, Na, and P) concentrations were subsequently measured by ICP-OES (5100 VDV ICP-OES, Agilent, Waldbronn, Germany), while microelements (Cd, Cu, Mo, Mn, Pb and Zn) were measured by ICP-MS (7900 MS, Agilent, Waldbronn, Germany). Complete element recovery of total digestions was confirmed with certified reference material (BCR2, Columbia river basalt). All analyses were performed in the Laboratory for Soil Biogeochemistry of the Institute of Geography and Geoecology at the Karlsruhe Institute of Technology, Germany.

Table S1 Properties of ABs used in the study

AB-Class	AB (abbreviation)	Structure	M _w [g/mol]	pK _a	log(K _{ow})
SULFONAMIDES (SAs)	Sulfadiazine (SDZ)		250.3	6.36 ^[b]	-0.09 ^[b]
	Sulfadimethoxine (SDM)		310.33	2.5 ^[c] 5.94 ^[c]	1.63 ^[b]
	Sulfamethazine (SMZ)		278.33	2.65 ^[c] 7.24 ^[c]	0.89 ^[b]
	Sulfa- methoxazole (SMX)		252.2	1.6 ^[b] 5.7 ^[b]	0.89 ^[b]
	Sulfapyridine (SPD)		249.3	8.43 ^[b]	0.35 ^[b]
MACROLIDES (MLs)	Erythromycin (ETM)		734	8.88 ^[b]	3.06 ^[d]
	Roxythromycin (RTM)		837	9.17 ^[d]	1.7 ^[b]

TETRACYCLINES (TCs)	Clarithromycin (CTM)		748	8.99 ^[b]	3.16 ^[b]
	Oxytetracyclin (OTC)		460.4	3.27 7.32 9.11 ^[a]	-0.90 ^[a]
	Chlortetracyclin (CTC)		478.9	3.3 7.44 9.27 ^[a]	-0.62 ^[a]
	Tetracyclin (TCT)		444.4	3.3 7.68 9.30 ^[a]	-1.37 ^[b]
	Doxycyclin (DXC)		444.4	3.50 7.70 9.70 ^[a]	-0.02 ^[a]
	Ciprofloxacin (CFC)		331.3	6.09 8.74 ^[b]	0.28 ^[b]
FLUOROQUINOLONES (FCs)	Enrofloxacin (EFC)		359.4	6.27 8.30 ^[a]	0.70 ^[a]

OTHERS	Norfloxacin (NFC)		319.3	6.23 8.55 ^[a]	-1.03 ^[b]
	Ofloxacin (OFC)		347.3	5.97 8.28 ^[a]	-0.39 ^[b]
	Trimethoprim (TMP)		290.3	7.12 ^[c]	0.91 ^[b]
	Clindamycin•HCl (CDC)		425	7.79 ^[b]	2.16 ^[b]

[a]: Salvia et al., 2015; [17]; [b]: PubChem [62] ; [c]: ChemicalBook, 2021., [63]; [d] MacLeo, 2007 [64]

[17] Salvia, M.-V.; Fieu, M.; Vulliet, E. Determination of Tetracycline and Fluoroquinolone Antibiotics at Trace Levels in Sludge and Soil. *Applied and Environmental Soil Science* **2015**, *2015*, 1–10, doi:10.1155/2015/435741.

[62] PubChem PubChem Available online: <https://pubchem.ncbi.nlm.nih.gov/> (accessed on 18 May 2022).

[63] ChemicalBook---Chemical Search Engine Available online: https://www.chemicalbook.com/ProductIndex_DE.aspx (accessed on 18 May 2022).

[64] MacLeod, S.L.; McClure, E.L.; Wong, C.S. Laboratory Calibration and Field Deployment of the Polar Organic Chemical Integrative Sampler for Pharmaceuticals and Personal Care Products in Wastewater and Surface Water. *Environmental Toxicology and Chemistry* **2007**, *26*, 2517–2529, doi:10.1897/07-238.1.

Tables S2a to d Characterization of sediment used in the study

Table S2a General parameters

pH (in H ₂ O)	Carbonate as CaCO ₃ [%]	TIC [%]	TC [%]	TOC [%]	TN [%]
7.20	4.38	0.53	8.58	8.06	0.61

Table S2b Particle size analysis

Sand [%]				Silt [%]				Clay [%]	Error [%]
2000-630 μm	630-200 μm	200-63 μm	Sum	63-20 μm	20-6.3 μm	6.3-2 μm	Sum	< 2 μm	
0.42	0.89	28.31	29.6 2	25.47	13.64	9.78	48.8 9	21.49	-1.54

Table S2c Exchangeable cations, cation exchange capacity and base saturation

Al mmolc/ kg	Ba mmolc/ kg	Ca mmolc/ kg	Cu mmolc/ kg	Fe mmolc/ kg	K mmolc/ kg	Mg mmol c/kg	Mn mmolc/k g	Na mmolc/ kg	Zn mmolc/ kg
0.31	0.87	396.91	0.01	0.06	2.63	19.92	0.27	2.48	0.02

Cation exchange capacity CEC [mmolc/kg]: 423.48

Base saturation [%]: 99.64

Table S2d Total element content

Al mg/k g	Ca mg/k g	Fe mg/k g	K mg/k g	Mg mg/k g	Na mg/k g	P mg/ kg	Cd mg/k g	Cu mg/k g	Mo mg/k g	Mn mg/k g	Pb mg/k g	Zn mg/k g
5209 3	2727 8	2123 3	1801 6	7526	6819	122 9	1.4	99	0.7	557	79	551

Table S3 Conditions used for tandem SPE method

	HLB	MCX
Conditioning	5 mL Methanol	2.5 mL Methanol
	5 mL Acetonitrile	2.5 mL Acetonitrile
	5 mL Ultrapure water	2.5 mL 5 % NH ₄ OH in methanol
	2 x 5 mL ultrapure water at pH 2	2.5 mL Ultrapure water
		2.5 mL 0.1 mol/L HCl
		2 x 2.5 mL ultrapure water at pH 2
Washing	5 mL Ultrapure water	2.5 mL 0.1 M HCl
Elution	5 mL Methanol	2.5 mL Methanol
	5 mL Acetonitrile	5 mL Acetonitrile
		2.5 mL Methanol with 5 % NH ₄ OH

Table S4 Chromatographic conditions used for quantification of selected antibiotics

Eluent A:	0.05 % Formic acid in HPLC water	
Eluent B:	0.05 % Formic acid in acetonitrile	
Flow:	300 µL/min	
Injection volume:	50 µL	
Post-time	2.0 min	
Time [min]	A [%]	B [%]
0	95	5
0.2	95	5
4.2	5	95
6.0	5	95

Table S5 Setting of mass spectrometer used for quantification of ABs

AB class	AB	Retention time (min)	Precursor ion (m/z)	Quantifier (m/z)	Qualifier (m/z)	Fragmentor (V)	Collision energie (V)
Sulfonamides	Sulfadiazine	2.50	251.1	155.9	108.0	110	12
	<i>Sulfadiazine-d4</i>	2.50	255.1	159.9	112.0	120	16
	Sulfamethoxazole	3.33	254.1	155.9	92.0	105	16
	<i>Sulfamethoxazole-d4</i>	3.32	258.1	159.9	96.0	90	12
	Sulfapyridine	2.70	250.1	155.9	108.0	120	16
	<i>Sulfapyridine-d4</i>	2.70	254.1	159.9	112.0	115	16
	Sulfadimethoxine	3.60	311.1	155.9	92.0	145	20
	<i>Sulfadimethoxine-d6</i>	3.64	317.1	162	65	145	24
	Sulfamethazine	3.01	279.1	185.9	148.9	120	16
	<i>Sulfamethazine-d4</i>	3.01	283.1	185.9	124	125	16
	Sulfachloropyridazine	3.23	285.0	155.9	92.0	105	12
Fluoroquinolones	Ciprofloxacin	2.75	332.1	314.1	288.1	120	20
	<i>Ciprofloxacin-d8</i>	2.75	340.2	322.2	296.3	130	20
	Ofloxacin	2.76	362.2	344.1	318.1	150	20
	<i>Ofloxacin-d3</i>	2.76	365.2	321.1	261.0	150	20
	Norfloxacin	2.82	320.1	302.1	276.0	145	20
	<i>Norfloxacin-d5</i>	2.85	325.2	307.1	281.1	145	20
	Enrofloxacin	2.91	360.2	342.1	316.1	155	20
	<i>Enrofloxacin-d5</i>	2.82	365.2	321.2	245	145	20
	<i>Clinafloxacin</i>	2.97	366.1	348.1	305.1	135	20
Tetracyclines	Tetracyclin	2.86	445.2	410.1	153.9	125	20
	Oxytetracyclin	2.76	461.2	426.1	200.9	130	20
	Chlortetracyclin	2.96	479.1	462.0	444.0	140	20
	Doxycyclin	3.19	445.2	428.1	267.0	130	16
	<i>Doxycyclin-d3</i>	3.20	448.2	431.1	154.9	145	20
	<i>Meclocycline</i>	3.37	477.1	460	234.9	140	16
	Demeclocycline	3.00	465.1	448	430	145	16

Macrolides	Erythromycin	3.05	734.5	576.3	158.0	175	20
	Erythromycin-H ₂ O	3.69	716.5	558.3	158.0	165	12
	<i>Erythromycin-d3</i>	3.49	737.5	579.4	161.0	170	20
	Roxithromycin	3.70	837.5	679.4	158.0	175	20
	<i>Roxithromycin-d7</i>	3.69	844.6	686.5	158.0	185	20
	Clarithromycin	3.77	748.5	590.3	158.0	175	16
	Clarithromycin-d3	3.76	751.5	593.3	161.0	175	20
	<i>Oleandomycin-triacetat</i>	3.88	814.5	200	98.1	185	24
Others	Trimethoprim	2.74	291.2	261.0	230.0	150	28
	<i>Trimethoprim-d3</i>						
	Clindamycin	3.17	425.2	126.0	69.7	155	28
	<i>Clindamycin-d3</i>	3.10	428.2	129	45.1	160	32

Table S6 Source parameters used for ABs quantification

Source parameter	Value	Unit
Gas temperature	230	⁰ C
Gas flow	8	L/min
Nebulizer	40	psi
Sheath gas temperature	400	⁰ C
Capillary voltage	Positive: 3500	v
	Negative: 3500	v

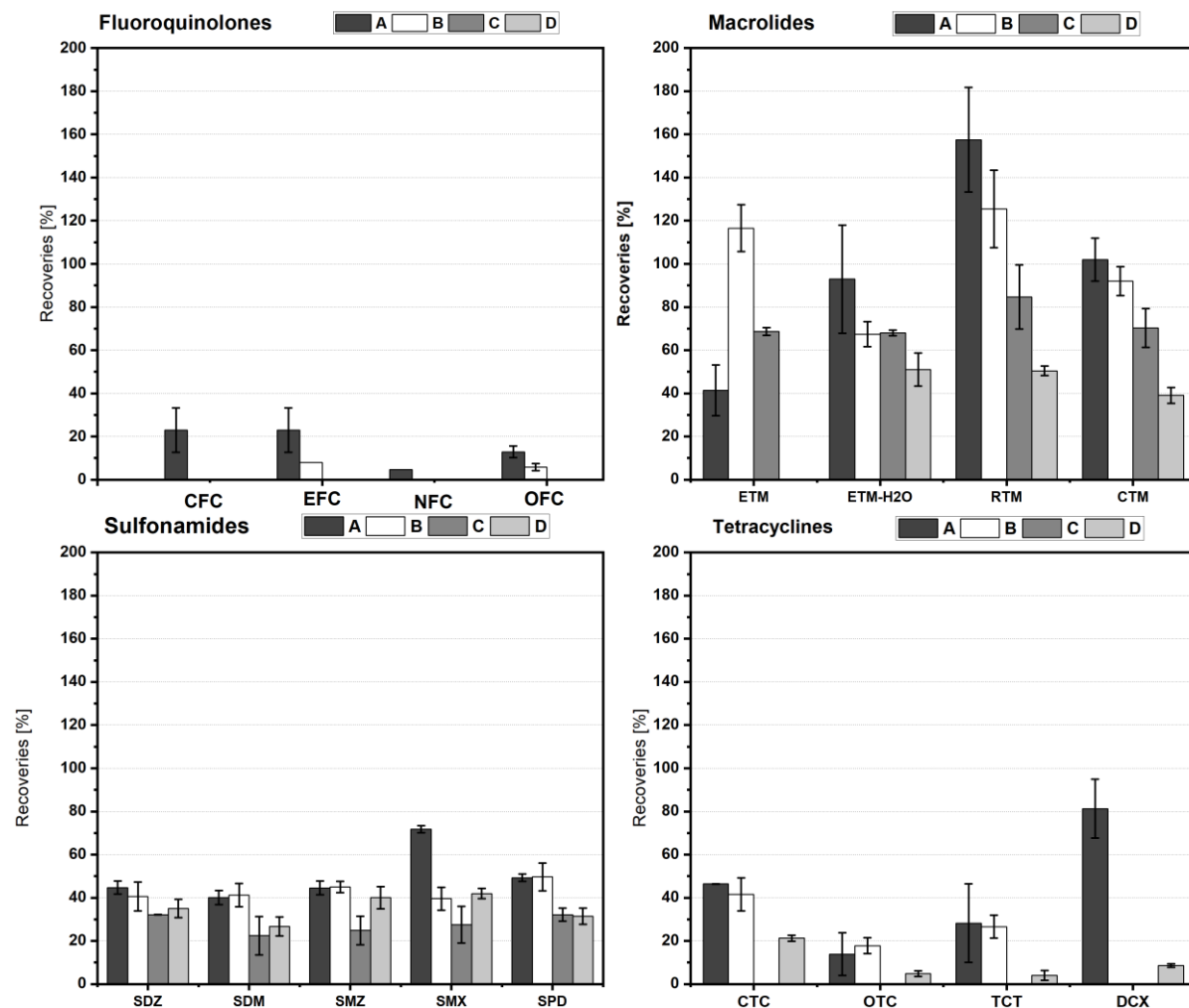
Table S7 Surrogates and Internal standards for protocol A to G

Class	Name	Abb.	LOD (ng/L)	LOQ (ng/L)	Internal standards		Surrogates
Fluoroquinolones	Ciprofloxacin	CFC	5	10	Ciprofloxacin-d8	CFC-d8	Cilnafloxacin
	<i>Clinafloxacin</i>	CLF	100	250	Enrofloxacin-d5		
	Enrofloxacin	EFC	25	50	Enrofloxacin-d5	EFC-d5	
	Norfloxacin	NFC	100	250	Norfloxacin-d5	NFC-d5	
	Ofloxacin	OFC	50	75	Ofloxacin-d3	OFC-d3	
Macrolides	Clarithromycin	CTM	10	25	Clarithromycin-d3	CTM-d3	Oleandomycin-triacetat
	Erythromycin	ETM	10	25	Erythromycin-d3	ETM-d3	
	Erythromycin-H ₂ O	ETM-H ₂ O	10	25	Erythromycin-d3	ETM-d3	
	Roxithromycin	RTM	10	25	Roxithromycin-d7	RTM-d7	
	Oleandomycin-triacetat	ODL	10	25	Clarithromycin-d3		
Sulfonamides	Sulfadiazine	SDZ	2.5	5	Sulfadiazined-4	SDZ-d4	Sulfachloropyridazine
	Sulfadimethoxine	SDM	2-5	5	Sulfadimethoxine-d6	SDM-d6	
	Sulfamethazine	SMZ	5	7.5	Sulfamethazine-d4	SMZ-d4	
	Sulfamethoxazole	SMX	5	7.5	Sulfamethoxazole-d4	SMX-d4	
	Sulfapyridine	SPD	2.5	5	Sulfapyridine-d4	SPD-d4	
	Sulfachloropyridazine	SCP	5	7.5	Sulfadiazine-d4		
Tetracyclines	Chlortetracycline	CTC	50	75	Demeclocycline	DMC	Meclocycline
	Doxycycline	DCX	50	75	Doxycycline-d3	DCX-d3	
	Oxytetracycline	OTC	50	75	Demeclocycline	DMC	
	Meclocycline	MCC	10	50	Demeclocycline		
	Tetracycline	TCT	50	75	Demeclocycline	DMC	
Others	Clindamycin	CDC	2.5	5	Clindamycin-d3	CDC-d3	Sulfachloropyridazine
	Trimethoprim	TMP	5	7.5	Trimethoprim-d3	TMP-d3	Sulfachloropyridazine

Table S8 Classification of ABs related to their $\log(K_{ow})$ values

	AB name	$\log(K_{ow})$
Group1: $\log(K_{ow}) \leq -1$	Norfloxacin	-1.03
	Tetracycline	-1.37
Group 2 $-1 < \log(K_{ow}) \leq 0$	Doxycycline	-0.02
	Sulfadiazine	-0.09
	Ofloxacin	-0.39
	Chlortetracycline	-0.62
	Oxytetracycline	-0.90
	Trimethoprim	0.91
Group 3 $0 < \log(K_{ow}) \leq 1$	Sulfamethoxazole	0.89
	Sulfamethazine	0.89
	Enrofloxacin	0.70
	Sulfapyridine	0.35
	Ciprofloxacin	0.28
	Demeclocycline	0.20
Group 4 $\log(K_{ow}) > 1$	Sulfadimethoxine	1.63
	Roxithromycin	1.7
	Clindamycin	2.16
	Erythromycin	3.06
	Clarithromycin	3.16

Figure S1: Recoveries of four different AB classes for four different protocols A, B, C and D (see Table 1)

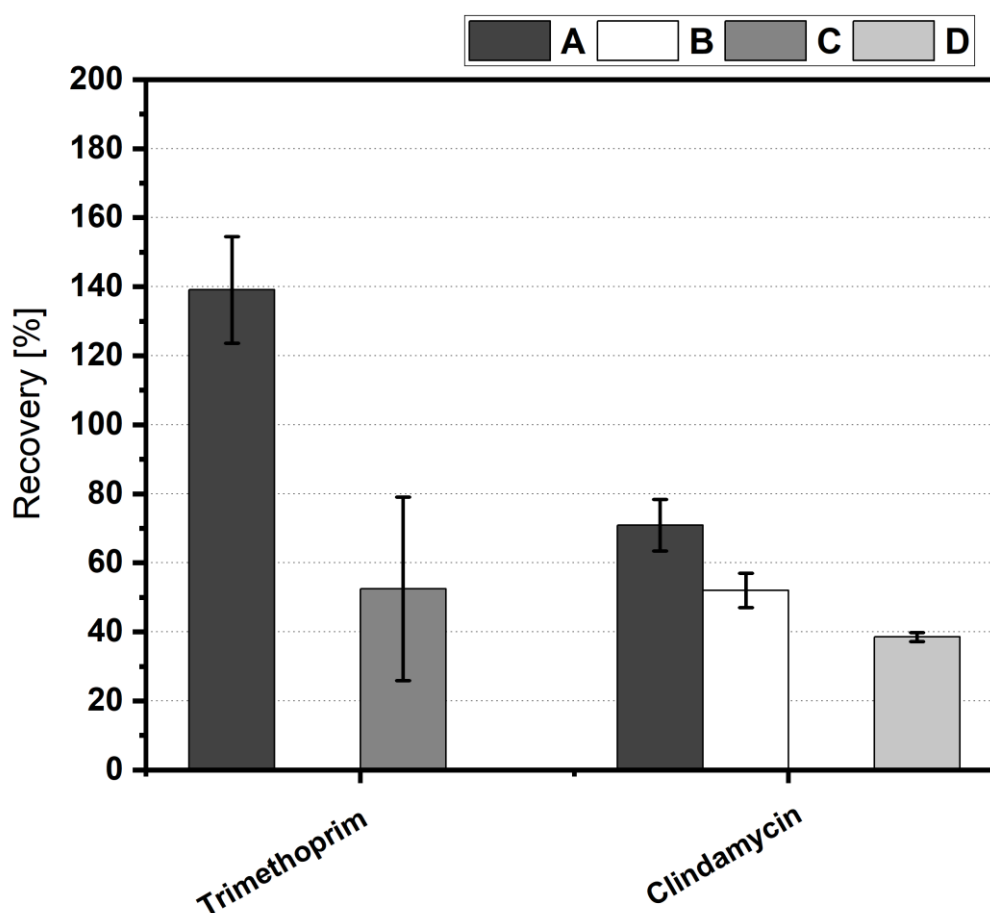


Methods modified after: Golet et al. (A) [37], Salvia et al. (B) [17], Kerrigan et al. (C) [35] and Senta et al. (D) [36]. Ciprofloxacin (CFC), Enrofloxacin (EFC), Norfloxacin (NFC), Ofloxacin (OFC), Erythromycin (ETM), Erythromycin-H₂O (ETM-H₂O), Roxithromycin (RTM), Clarithromycin (CTM), Sulfadiazine (SDZ), Sulfadimethoxine (SDM), Sulfamethazine (SMZ), Sulfamethoxazole (SMX), Sulfapyridine (SPD), Chlortetracyclin (CTC), Oxytetracyclin (OTC), Tetracyclin (TCT), Doxycycline (DCX) for which in protocol B and C signal to noise ratio was below 10, which made the quantification impossible

[17] Salvia, M.-V.; Fieu, M.; Vulliet, E. Determination of Tetracycline and Fluoroquinolone Antibiotics at Trace Levels in Sludge and Soil. *Applied and Environmental Soil Science* **2015**, *2015*, 1–10, doi:10.1155/2015/435741.

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Figure S2 Recoveries for Trimethoprim and Clindamycin for four different methods



Methods modified after: Golet et al. (A) [37], Salvia et al. (B) [17], Kerrigan et al. (C) [35] and Senta et al. (D) [36]. When no column showed quantification wasn't possible because out side calibration range.

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Table S9 Parameters of the method validation

Class	Name	Accuracy [%] (50 µg/kg)	Accuracy [%] (100 µg/kg)	Repeatability (50 µg/kg)	Repeatability (100 µg/kg)	Coefficient of variation [%] (50 µg/kg)	Coefficient of variation [%] (100 µg/kg)	Method detection limit (µg/kg)	Method quantification limit (µg/kg)	Matrix effect
Fluoroquinolones	Ciprofloxacin	1.9	0.8	1.1	0.1	61	15	0.2	0.4	0.25
	Clinafloxacin	-	-	-	-	-	-	58	144.9	0.01
	Enrofloxacin	1.8	1.4	0.2	0.3	11	20	2.9	5.7	0.08
	Norfloxacin	1.1	1.1	-	0.2	-	16	3.4	8.5	0.42
	Ofloxacin	0.2	0.3	0.1	0.3	55	80	4.9	7.3	0.08
Macrolides	Clarithromycin	25.9	14	8.9	5.2	34	38	0.2	0.5	0.40
	Erythromycin	14.3	11	2.6	-	18	-	0.1	0.3	0.95
	Erythromycin-H ₂ O	30.9	31	8.8	5.3	29	17	0.6	1.5	0.20
	Olendomycin- triacetat	3.8	3.3	2.1	1.3	56	38	0.2	0.4	0.49
	Roxithromycin	29.2	15	8.0	7.0	27	48	0.1	0.3	0.66
Sulfonamides	Sulfachloropyridazine	8.7	18.8	2.3	3.4	27	18	0.7	1.1	0.07
	Sulfadiazine	21.3	22	3.7	0.9	17	4	0.3	0.6	0.09
	Sulfadimethoxine	13.5	19	2.4	2.5	18	14	0.6	1.1	0.03
	Sulfamethazine	28.2	33	4.8	2.4	17	7	0.5	0.8	0.07
	Sulfamethoxazole	16.1	21	2.8	2.2	17	11	0.6	0.9	0.04
	Sulfapyridine	22.3	27	3.2	2.1	14	8	0.3	0.5	0.07
Tetracyclines	Chlortetracycline	-	-	-	-	-	-	0.6	1.0	0.77
	Doxycycline	26.3	-	5.1	-	19	-	1.6	2.4	0.26
	Meclocycline	4.3	5	1.4	1.7	32	35	13.6	27.1	0.12
	Oxytetracycline	7.2	5	1.8	2.4	25	44	0.7	1.0	0.83
	Tetracycline	10.6	4	3.3	1.3	32	32	0.7	1.0	0.83
Others	Clindamycin	48.8	45	10.4	8.1	21	-	0.1	0.1	0.38
	Trimethoprim	64.8	59	12.8	9.6	20	16	0.1	0.2	0.29

Table S10 Recoveries for the SPE protocol

PLE matrix blanks extracts were spiked with AB stock solution cartridges order were HLB on top of MCX for loading and elution of the sample, replicates is two.

			HLB-MCX	
			average	Standard derivation
Sulfonamides	Sulfadiazine	SDZ	4.47	0.14
	Sulfadimethoxine	SDM	39.41	0.88
	Sulfamethazine	SMZ	25.85	5.38
	Sulfamethoxazole	SMX	24.66	0.64
	Sulfapyridine	SPD	48.12	6.42
	Sulfachloropyridazine		28.50	4.48
Macrolides	Erythromycin	ETM	7.47	
	Erythromycin-H2O	ETM-H2O	33.18	7.66
	Roxithromycin	RTM	52.01	1.55
	Clarithromycin	CTM	48.56	2.83
	Olendomycin-triacetat		2.54	0.06
Fluoroquinolones	Ciprofloxacin	CFC	1.05	0.05
	Enrofloxacin	EFC	4.23	0.80
	Norfloxacin	NFC	0.69	0.22
	Ofloxacin	OFC	2.76	0.56
Tetracyclines	Chlortetracycline	CTC	5.12	0.67
	Oxytetracycline	OTC	29.56	9.43
	Tetracycline	TCT	36.63	4.40
	Doxycycline	DCX	32.34	1.68
	Meclocycline		S/N < 10	-
Others	Trimethoprim	TMP	69.15	0.40
	Clindamycin	CDC	62.12	1.50

