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Antibiotics residues in inland and transitional sediments

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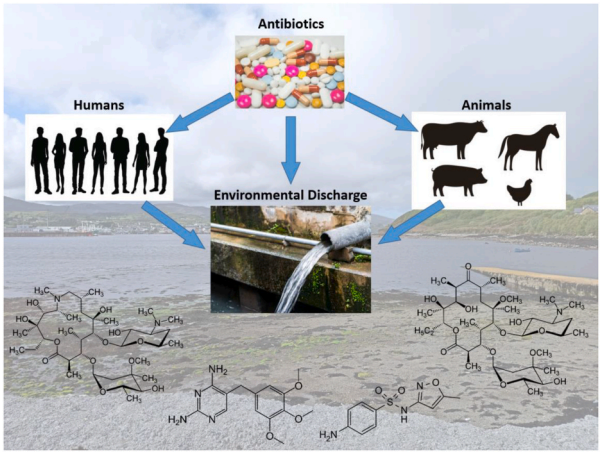
HIGHLIGHTS

- Clarithromycin of highest prevalence in sediment samples assessed.
- Low to moderate ecotoxicological risk for clarithromycin and sulphamethoxazole.
- Partitioning behaviour between sediment & water of importance to ecotox. risk.
- Ireland shows low concs. of antibiotics compared to similar studies worldwide.
- Ciprofloxacin also of potential ecotox. risk, but requires further assessment.

GRAPHICAL ABSTRACT



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ABSTRACT

This study assesses the concentrations of a range of antibiotics in riverine and transitional sediments in Ireland. A selection of 12 macrolide, fluoroquinolone, sulphonamide, and diaminopyrimidine antibiotics were quantified in 80 grab surficial sediment samples from around Ireland, selected to investigate areas of potentially higher pollution risk (agriculture, aquaculture, industrial emissions, and wastewater emission points) as well as isolated areas where there are no known pollution sources. Several of the macrolides and sulphonamides/trimethoprim were generally detected more frequently above limits of quantification (LoQ). Fluoroquinolones, while frequently detected above limits of detection (LoD), concentrations were mostly below method LOQs. The most prevalent antibiotic detected was clarithromycin, found at the highest mean concentration (6.65 ng/g) and detected in ~90 % of samples. Comparing levels of quantified antibiotics to levels reported internationally, Ireland is at the lower end for all quantified antibiotics. This is with the notable exception of clarithromycin, which is higher than levels found in comparable studies in Italy, Spain, France, and Argentina. Higher levels of

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total antibiotics (49.3 ± 24.7 ng/g) were found to be present immediately adjacent to wastewater emission points while moderate degrees of contamination (9.0 ± 9.7 ng/g) were also linked to wastewater, aquaculture, or agricultural pressures. Based on risk quotients calculated from available sediment PNECs taken from the NORMAN ecotoxicology database, clarithromycin was also the only compound to be present at concentrations indicative of a "moderate" degree of environmental risk, with most of the remaining falling below this threshold. Ciprofloxacin was ostensibly found to be of a "high" degree of environmental risk; however, this is based on only a single sample quantified above the LoQ. Overall, antibiotic sediment concentrations suggest a low ecotoxicological risk for most of the target antibiotics, although clarithromycin, ciprofloxacin, and sulfamethoxazole warrant further monitoring in sediments. A final notable finding is the differences in partitioning behaviour of antibiotics between water and sediment: clarithromycin is more likely to be detected in sediment while sulfamethoxazole partitions more to water. Such partitioning behaviour should therefore be taken into consideration for any subsequent monitoring programmes.

1. Introduction

Antimicrobials encompass a wide range of chemicals which act against various microbes such as fungi, viruses, and bacteria. Under this umbrella, antibiotics are specifically used to treat bacterial infections in humans and animals. However, the high usage of antimicrobials has resulted in increased instances of antimicrobial resistance (AMR) whereby continued exposure of microbes to antimicrobials results in the growth and proliferation of drug-resistant strains (WHO, 2022a). One of the major drivers of AMR is overuse of broad-spectrum antibiotics such as azithromycin, clarithromycin, ciprofloxacin, and sulfadiazine and there are a myriad of factors – from a lack of access to suitable medications, to overburdened healthcare systems, to fears of litigation for under-treating or under-prescribing medication – which are suspected to have contributed to the over-prescription of antibiotics in particular (Tarrant et al., 2021). Though undoubtedly versatile and effective, their overuse has been directly linked to the propagation of more resistant strains of bacteria, such as the excessive use of the methicillin inadvertently leading to the proliferation of methicillin-resistant *Staphylococcus aureus* (Harkins et al, 2017), as well as similar instances in other common bacterial infections such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Neisseria gonorrhoea* (WHO, 2019). Besides the risk of promoting the growth of resistant bacterial strains, the release of these antibiotics into the environment is also of direct ecotoxicological concern: adversely affecting photosynthesis and mitochondria in plants as well as delaying germination and reducing biomass in agricultural soils (Polianciuc et al, 2020).

Assessing the modes of release of antibiotics into the environment and assessing the degree of risk to ecological systems (including the proliferation of AMR) is an under-studied topic (Wang et al, 2023). Environmental pollution of antibiotics is recognised by the World Health Organisation as "… *critical for combatting rising levels of drug resistance*" (WHO, 2022b). The presence of antibiotics in environmental matrices such as sediments has been linked to increasing instances of antibiotic-resistant bacteria (BIO IS, 2013; Polianciuc et al, 2020; Wang et al, 2023), while their presence in water and sediment phases has also been linked to the distribution of antibiotic-resistant genes and mobile genetic elements (Chen et al, 2019; Wu et al, 2023). The bioavailability of these antibiotics is a major factor in their release into the environment. For example, ciprofloxacin has reported uses in cattle as well as domestic animals as a broad-spectrum antibiotic to treat a variety of infections [Mercer, 2022a; O'Sullivan et al, 2019; Papich, 2017]. However, the bioavailability in cattle and domestic animals has been shown to be less than 20 %, leading to a large non-metabolised fraction being excreted in waste (Mercer, 2022a). These bioavailabilities can vary widely depending on their class and the animal or human being treated (Chakwenya et al., 2002; Pitman et al., 2019; Mercer, 2022b). The release of antimicrobials into the environment is largely attributed to the discharge of wastewater following administration to humans and animals (Carvalho and Santos, 2016).

In Ireland, roughly three times as many antibiotics are used in human healthcare compared to veterinary applications (O'Sullivan et al, 2019). β-Lactam antibiotics such as penicillin constitute most antimicrobial use in humans in Ireland, while tetracyclines are dominant in animals, predominantly from use in the agricultural sector; the remaining share of antibiotics used in both humans and animals are spread among a wide array of antibiotics including diamino-pyrimidines, fluoroquinolones, lincosamides, macrolides (second most utilised in humans), and sulphonamides (second-most utilised in animals) (O'Sullivan et al, 2019). While penicillins dominate the market and relatively large fractions are shown to be excreted in urine after ingestion (Morris et al, 2008; Bryskier, 2005), they are thought to be of low environmental concern due to their short half-lives in aqueous environments and susceptibility to several modes of degradation (Hirsch et al, 1999; Monahan et al, 2022). By contrast, macrolides, fluoroquinolones, and sulphonamides (the lattermost typically used in conjunction with trimethoprim (Kemnic and Coleman, 2022)) are shown to be much more environmentally persistent and resistant to biodegradation (Morris et al, 2008). A recent study in Ireland concluded that macrolides were expected to be of the highest environmental risk, with quinolones, pyrimidines, tetracyclines, and sulphonamides expected to represent lower risk. (Rodriguez-Mozaz et al, 2020). This study further shows that a selection of these antibiotics are present in the effluent from Irish wastewater treatment plants (WWTPs) while O'Flynn (2024) report on their presence in river water.

To accompany this previous data of antibiotics in surface water and WWTP effluent, this study aims to investigate the presence of a selection of antibiotics in Irish sediments in order to: provide an estimate of the degree of risk to the Irish environment based on their measured concentrations and ecotoxicities; investigate the partitioning behaviours of selected antibiotics in sediment and water; attempt to identify prominent sources of environmental release of antibiotics; and identify priority pollutants for further investigation and further monitoring. Presented here is the first ever study of antibiotics in Irish sediments, as well as (to the authors' knowledge) the largest ever study of concentrations of antibiotics in inland and transitional sediments in Europe, and the first to assess levels of difloxacin and levofloxacin in sediments.

2. Materials and methods

2.1. Antibiotics under investigation

As outlined in *Section 1*, the antibiotic classes of particular relevance to environmental contamination in Ireland are fluoroquinolones, macrolides, and sulphonamides (along with their common synergist, trimethoprim). Included in the list of analytes are the following antibiotics: azithromycin, clarithromycin, and erythromycin which had been listed as "watch-list" chemicals under the Water Framework Directive (WFD) 2000/60/EC and for which exist draft environmental quality standards per the Environmental Quality Standards (EQS) directive 2008/105/EC (SCHEER, 2022a, 2022b, 2022c); trimethoprim, sulfamethoxazole, ciprofloxacin, and ofloxacin, which have been or are currently watch-list chemicals under the WFD (EU 2015, 2018, 2020, 2022); as well as difloxacin, enrofloxacin, levofloxacin, roxithromycin, and sulfadiazine, additional fluoroquinolones, macrolides, and

sulfadiazines which are commonly-used in Irish veterinary and human health applications (O'Sullivan et al, 2019) (*SI 1*).

2.2. Sample collection

A total of 80 sediment samples were collected from inland (n = 61) and transitional (n = 19) waters across Ireland in 2023 for analysis of the antibiotics outlined above. The full details of this sampling campaign are reported elsewhere (*Sharkey et al, 2024*). Briefly, approximately 1 kg aliquots of sediments were collected from inland and transitional sites (*SI 2*) prior to homogenisation, wet sieving to a maximum grain size of 2 mm, and freeze-drying under a 0.133 mBar vacuum to a uniform temperature of −40 °C over a period of approximately six days. Samples were then sealed using parafilm and screw-top caps, and stored at −20 °C prior to analysis. Additional metadata for statistical analysis (*Section 2.6*) including water body type and river flow speed were obtained from the Environmental Protection Agency's Geographic Information System (https://gis.epa.ie/EPAMaps/Water), while population densities at sampling locations were obtained from the central statistics office (https://www.cso.ie/).

2.3. Chemicals and standards

Fourteen individual native antibiotic standards (erythromycin, clarithromycin, roxithromycin, azithromycin, lincomycin, trimethoprim, sulfamethoxazole, sulfadiazine, norfloxacin, enrofloxacin, ofloxacin, levofloxacin, difloxacin, and ciprofloxacin) and six labelled standards (d_3-erythromycin, d_3-azithromycin, d_4-sulfamethoxazole, d_3-ofloxacin, d_8-ciprofloxacin, and d_3-difloxacin) were supplied by Wellington Laboratories (Guelph, Canada).

SPE columns Oasis HLB 6 cc, 200 mg (Waters, USA), optima grade methanol, optima grade acetonitrile (ACN), optima grade water (Fisher Scientific, Loughborough, UK), citrate buffer solution 0.2 M pH 4 (Generon Ltd, Slough, UK), Na_2EDTA Molecular Biology Grade (Promega UK, Chilworth, UK), and formic acid (≥98%) (Sigma-Aldrich, Burlington, USA) were purchased for extraction and analytical procedures.

2.4. Sample extraction

Antibiotics laboratory extraction and clean up method was applied to sediment samples involved accurately weighing ca. 2 g aliquots of sample treated with 50 ng isotopically labelled antibiotics (d_3-erythromycin, d_3-azithromycin, d_4-sulfamethoxazole, d_3-ofloxacin, and d_8-ciprofloxacin) as internal (or surrogate) standards (IS). The samples were extracted using 3 sequential cycles of ultrasonication and vortexing using 5 mL citrate buffer (pH 4) with ACN (1:1, v/v) and 0.2 g of Na_2EDTA. The extract was centrifuged at 3000 RPM for 10 min and the three supernatants were combined (15 mL total) and filtered through a 0.7 μm glass fibre filter (GF/F, Whatman) and diluted to 60 mL with water (optima grade). The diluted samples were then loaded onto preconditioned and equilibrated Oasis HLB SPE cartridges (200 mg, Waters, USA), washed with 10 mL of optima grade water, then dried under vacuum for ca. 20 mins to remove excess water. Samples were then eluted using 10 mL methanol with 0.1 % formic acid under light vacuum. The eluent was gently evaporated to incipient dryness under a gentle stream of nitrogen and reconstituted in 0.5 mL water/methanol with 0.1 % formic acid (1:1, v/v) (optima grade) with 10 ng of recovery determination (or syringe) standard (RDS, d_3-difloxacin). The final 0.5 mL extract was transferred to a 1.5 mL amber vial and stored at −20 °C until analysis via Ultra High-Performance Liquid Chromatography Time of Flight Mass Spectrometry (UHPLC-TOF-MS).

2.5. Instrumental analysis

A 5 μL aliquot of the sample extract was injected into a Sciex Exion UHPLC coupled to a Sciex 5600+ triple TOF MS fitted with an Accucore RP-MS (internal diameter: 2.1; length: 100 mm; particle size: 2.6 μm, Thermo Scientific). Using a flow rate of 0.4 mL/min, a mobile phase gradient was ramped from 98 % Mobile Phase A (2 mM ammonium acetate in optima grade water), 2 % mobile phase B (optima grade MeOH with 0.1 % formic acid) to 98 % mobile phase B over 11 min. This was held for 1 min before equilibrating back to 2 % mobile phase B for 3.5 min. The triple TOF MS was operated in MS/MS mode equipped with a Turbo V source operated in positive mode using electrospray ionisation at a voltage of 5500 V. The curtain gas was set at 25 psi, whilst the nebuliser gas (source gas 1) was set at 45 psi and the drying gas (source gas 2) at 45 psi. Five-point calibration was conducted using standard solutions of known concentration (see *SI* 3). The collision-activated dissociation (CAD) gas was set to medium and the temperature to 350 °C. Manual mass calibration was performed on the instrument prior to the injection of each batch of samples using a Sciex calibrant delivery system (CDS) to ensure a starting mass accuracy of <1 ppm. An automated calibration was also performed after every 5 injections to ensure ongoing mass accuracy throughout each run. Quantification of individual antibiotics was performed in Multiquant 3.0.2 using appropriate mass transitions (for details see *SI 4*).

2.6. Data analysis and risk assessment

For comparisons of mean concentrations determined with various metadata recorded (Inland vs transitional waters, population density, and river speed), non-parametric statistical tests are used as data do not follow a normal distribution. For two sample means Mann-Whitney U tests are used while for greater number, Kruskal Wallis H tests are used (confidence interval of 95 %, Significance Level (p) of 0.05). Where data are recorded to be below the limits of detection (LoQ), proxy values are determined using (LOQ x Detection Frequency). Where appropriate and noted, graphed data omit data points below LOQ and reports the statistical metrics along with the detection frequency for the relevant parameter(s).

Risk Quotients (RQs) are employed to evaluate ecotoxicological risks for targeted compounds in sediment samples collected in inland and transitional sediments in 2023. RQs were calculated per the following equation:

$$RQ = \frac{MEC_{95}}{Lowest\ PNEC}$$

where MEC_{95} is the 95th percentile of the maximum measured environmental concentration and lowest predicted no-effect concentration (PNEC) in sediments are taken from the Norman Ecotoxicology Database (www.norman-network.com/nds/ecotox). Degree of risk is assessed based on resulting risk quotient: RQ > 1 – high risk; 1 > RQ > 0.1 – moderate risk; RQ < 0.1 – low risk (Carvalho et al, 2015).

3. Results and discussion

3.1. Concentrations of antibiotics in Irish sediments

No statistically significant differences were seen in inland sediment concentrations compared to transitional sediment concentrations in this study (*SI 6*); therefore, for the purposes of reporting and statistical analysis, data will be considered as a single dataset with n = 80 samples. Table 1 reports summary statistics for the target antibiotics in inland and transitional sediment samples. At least one antibiotic was detected at concentrations above the method LoD in all samples, and at least one antibiotic was quantified in 77/80 samples at concentrations above the LoQs. The detection frequency differed significantly across the analytes with ciprofloxacin and enrofloxacin being quantified in only one sample apiece, while clarithromycin was detected in 87.2 % of samples. Only a few analytes were detected at a relatively high (>20 %) detection frequency: Clarithromycin was by far the most frequently detected (87.2

Table 1
Summary statistics of concentrations (ng/g) of antibiotics quantified in inland and transitional sediments collected from locations around Ireland in 2023. "n" = number of samples analysed (note: antibiotics were not quantified in some samples due to interference). "DF" = percentage of samples detected above the limit of quantification. "Range" shows the Limit of Quantification for each substances as the minimum value. "PNEC" - Predicted No-Effect Concentration. "% (RQ > 0.1)" - percentage of samples above a Risk Quotient of 0.1 (i.e. of 'moderate' risk or higher – see Section 3.3).

Antibiotic	n	Mean	LOQ	Median	Range	DF (%)	*PNEC*	% (RQ > 0.1)
Trimethoprim (TRI)	78	0.170	0.087	<LOQ	<LOQ - 9.14	20.5	*872*	0
Ciprofloxacin (CIP)	79	< LOQ	5.04	<LOQ	<LOQ - 7.76	1.27	*1.49*	1.27
Difloxacin (DIF)	80	< LOQ	0.344	<LOQ	<LOQ - 1.27	5.00	*40.4*	0
Enrofloxacin (ENR)	80	< LOQ	0.977	<LOQ	<LOQ - 5.66	1.25	*40.8*	1.25
Levofloxacin (LEV)	80	< LOQ	0.647	<LOQ	<LOQ - 1.88	10.0	*188*	0
Ofloxacin (OFL)	80	< LOQ	0.355	<LOQ	<LOQ - 2.72	12.5	*35.3*	0
Azithromycin (AZI)	80	0.185	0.093	<LOQ	<LOQ - 5.36	38.8	*40.8*	1.25
Clarithromycin (CLA)	78	6.65	0.411	3.79	<LOQ - 78.5	87.2	*269*	5.13
Erythromycin (ERY)	78	<LOQ	0.156	<LOQ	<LOQ - 1.88	14.1	*657*	0
Roxithromycin (ROX)	78	<LOQ	0.333	<LOQ	<LOQ - 4.46	7.69	*129*	0
Sulfamethoxazole (SME)	80	0.077	0.047	<LOQ	<LOQ - 0.33	33.3	*3.97*	2.50
Sulfadiazine (SDI)	78	<LOQ	0.074	<LOQ	<LOQ - 0.98	8.97	*7.28*	0

%), followed by azithromycin (38.8 %), sulfamethoxazole (33.3 %), and trimethoprim (20.5 %). There were similarly no statistically significant correlations based on relative population size of the surrounding area where samples were collected nor the relative water speed (*SI 7, 8*).

As outlined in *Section 1*, the discharge of wastewaters originating from humans and animals is suspected as being the major source of antibiotics entering the environment. This conforms with results garnered here with samples collected in the immediate vicinity of wastewater emission points (<0.1 km) showed levels of total antibiotics (49.3 ± 24.7 ng/g) which were significantly higher ($p < 0.01$) than those taken well-isolated (<5 km) from emission points (4.7 ± 3.8 ng/g). Two notable exceptions of these "isolated" samples showed comparatively high concentrations of clarithromycin (>10 ng/g): the first river site (*SI 2.1* – Sample 18) being noted by the EPA as having significant aquaculture pressures, where antibiotics are commonly used (Cherian et al, 2023); and the other (*SI 2.1* – Sample 64) as having significant agricultural pressures, where antibiotic residues from cattle treatment as well as run-off from wastewater-derived biosolids (Rodriguez-Mozaz et al, 2020; Uisce Éireann, 2024) used on farmland could lead to environmental contamination. Samples in an intermediate range from wastewater emission points (0.1–5 km) have more moderate degrees of contamination with a broader range (9.0 ± 9.7 ng/g) with the higher concentrations coinciding with high population equivalent, wastewater treatment emissions and agricultural or aquaculture pressures [EPA, 2024].

3.2. Comparison of antibiotics in different environmental matrices in Ireland

Next to penicillins, macrolides (such as clarithromycin) were likely to present the greatest risk to the Irish environment based on the ecotoxicological risk, due to extensive use in humans, and its relatively high half-life in sewage entering the environment (mean of 46.91 days; Monahan et al, 2022). The comparatively high use rate in humans is reflected in results reported herein showing that clarithromycin and, to a lesser extent, azithromycin, are dominant in sediment samples. However, other data reported from Ireland may point to uptake into different environmental compartments being a significant consideration. Fig. 1 shows a comparison between the relative levels of five antibiotics reported in sediments (this study), river waters (O'Flynn, 2024), and WWTP effluents (Rodriguez-Mozaz et al, 2020). Effluents from WWTP broadly conform to reported antimicrobial usage: the macrolides clarithromycin and azithromycin being dominant (high usage in humans and moderate usage in animals), with trimethoprim/sulpha-antibiotics

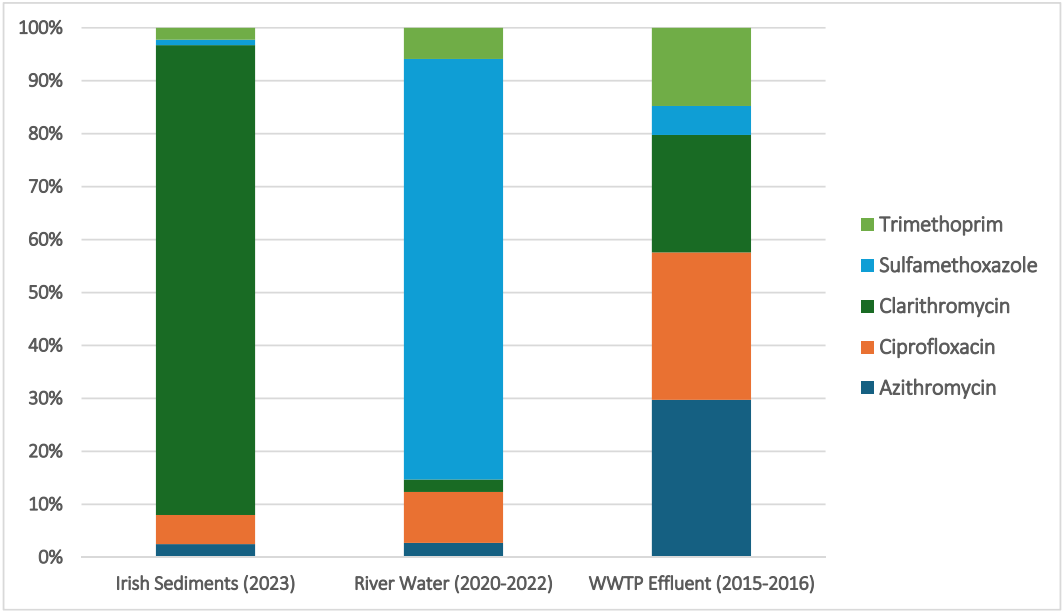

Fig. 1. Relative abundance of antibiotics in Irish sediments (this study) compared to composition of river water (O'Flynn, 2024) and WWTP effluents (Rodriguez-Mozaz et al, 2020). Stated years refer to the year of collection.

(major use in animals, very minor use in humans) and fluoroquinolones (minor use in both humans and animals) showing up secondarily. Comparing levels and distribution in the environmental compartments, clarithromycin is much more abundant in sediment samples while sulfamethoxazole is more prevalent in water samples. This is reflected in the octanol:water partitioning coefficients (Log K_{OW}) of the compounds, with sulfamethoxazole being much more hydrophilic (Log K_{OW} = 0.7–0.89) than clarithromycin (Log K_{OW} = 1.7–3.16) (https://pubchem.ncbi.nlm.nih.gov/). The low ecotox. risk for the majority of antibiotic residues assessed herein may therefore not translate to an equivalent risk in other environmental compartments. The partitioning behaviour of antibiotics should therefore be taken into consideration for further antibiotic residue assessment and monitoring.

3.3. Ecotoxicological implications of concentrations of antibiotics in Irish sediments

For the majority of samples analysed, antibiotic concentrations were below the "low risk" threshold when compared to available sediment PNECs, with the exception of clarithromycin and sulfamethoxazole where several samples each were shown to be in the "moderate" risk category (0.1 < RQ < 1). Azithromycin, enrofloxacacin and ciprofloxacin were similarly in the low risk category, with only a single sample apiece being above the 0.1 RQ threshold for low risk (Fig. 2; Table 2). However, as outlined in *Section 3.2*, the matrix into which antibiotics partition may be a significant factor in relative risk to different compartments. For example, based on results from O'Flynn (2024) and the results of his study on surface water along with PNECs in surface water from the NORMAN database: levels of sulfamethoxazole are of moderate risk in both water and sediment samples; clarithromycin is of moderate risk in sediment and low risk in water; and ciprofloxacin is potentially of high risk in sediments, but low risk in water.

Across all of the samples analysed, a proportion of compounds were detected below the method LOQs (ca. between 13 and 99 % – Table 1). In the majority of cases, the LOQs permitted comparison of quantified levels with available PNECs for each compound. However, in the case of ciprofloxacin, the LOQ exceeded the PNEC and in only one sample was ciprofloxacin quantified above the LOQ and therefore the PNEC (Fig. 3) though a further 18 % of samples indicated the presence of ciprofloxacin above the LOD. Clearly, for ciprofloxacin, a more sensitive analytical method is required to fully assess the environmental risk this compound may present. Overall, results appear to conform with Monahan et al. (2022): macrolides such as clarithromycin being of a higher environmental risk compared to fluoroquinolones and trimethoprim. However, sulphonamides were also flagged by this model as being low-risk, though were detected with moderate frequency here (46.2 %) and just below the low-risk threshold based on the calculated MEC_{95} (0.094). The RQs determined for clarithromycin and Sulfamethoxazole in these sediments may therefore indicate a relatively low-risk for biota. However, further environmental assessments would be beneficial investigating regional hotspots which may be of higher concern for biota, particularly for clarithromycin due to its ubiquity in sediments.

Table 2
– Risk quotients determined from lowest predicted no-effect concentrations (PNECs) taken from the NORMAN Toxicological Database (as of June 6, 2024) using 95th percentile concentrations (see Section 2.6). QSAR (Quantitative Structural Activity Relationship) utilised for determining PNEC where experimental ecotoxicology value not yet determined. * Based on a single sample which was determined above the LoQ.

Antibiotic	PNEC (ng/g)	PNEC Determination	95th percentile Conc. (ng/g)	RQ (95th percentile)
Trimethoprim	872	Experimental	0.24	0.0003
Ciprofloxacin	1.49	Experimental	2.2*	1.48*
Difloxacin	40.4	QSAR	0.35	0.009
Enrofloxacin	40.8	QSAR	0.35	0.009
Levofloxacin	188	Experimental	1.1	0.006
Ofloxacin	35.3	QSAR	0.48	0.014
Azithromycin	40.8	Experimental	0.46	0.011
Clarithromycin	269	Experimental	27	0.101
Erythromycin	657	Experimental	0.21	0.0003
Roxithromycin	129	QSAR	0.56	0.004
Sulfamethoxazole	3.67	Experimental	0.35	0.094
Sulfadiazine	7.28	Experimental	0.13	0.018

3.4. Comparison of concentrations of antibiotics in Irish and international sediments

Table 3 compares antibiotic concentrations recorded in this study

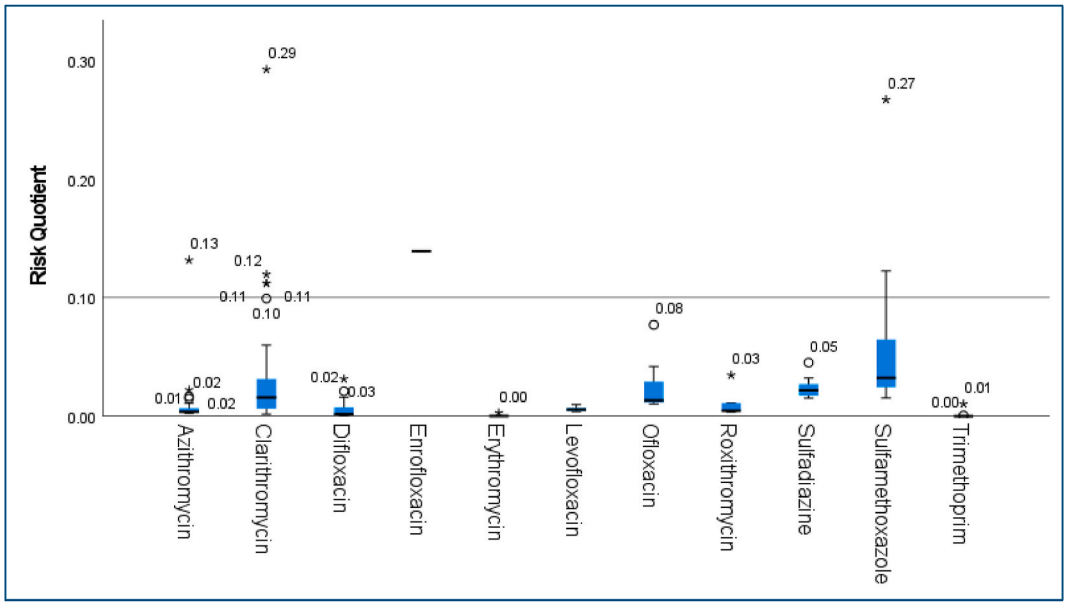

Fig. 2. Box plot of individual Risk Quotients (RQ) for individual samples (ciprofloxacin omitted for clarity; see Fig. 3 for plot including ciprofloxacin). Blue shaded bars with central black lines denote the median and interquartile range (IQR); lower whiskers denote minimum values; upper whiskers denote [1.5 × IQR]; open circles denote outliers (>1.5 × σ); stars denote extreme outliers (>3 × σ); solitary bars denote single value detected above LOQ.

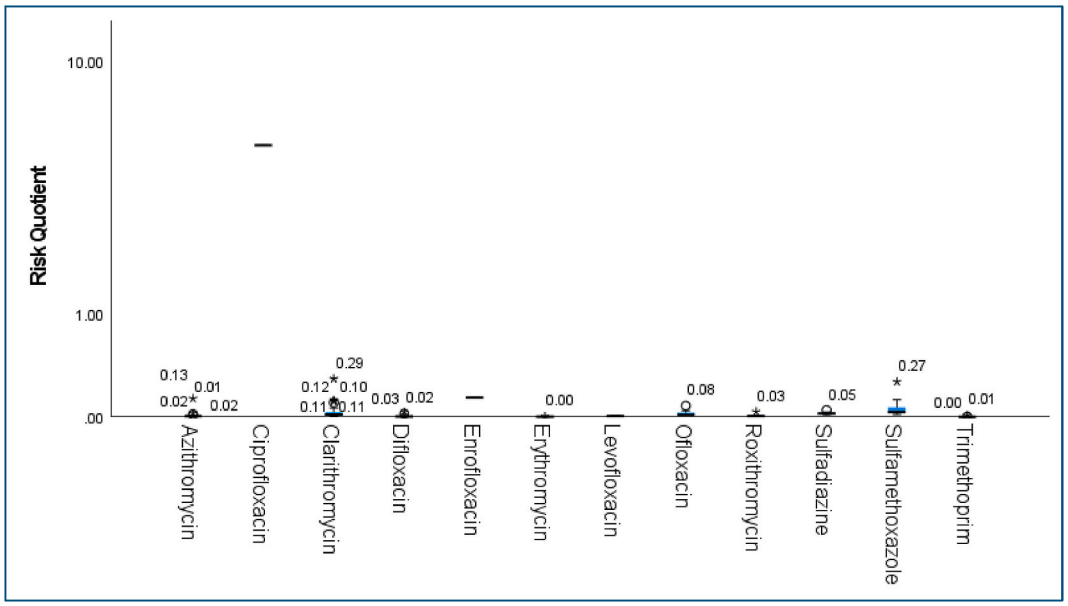

Fig. 3. Box plot of individual Risk Quotients for individual samples (including ciprofloxacin sample). Blue shaded bars with central black lines denote the median and interquartile range (IQR); lower whiskers denote minimum values; upper whiskers denote [1.5 × IQR]; open circles denote outliers (>1.5 × σ); stars denote extreme outliers (>3 × σ); solitary bars denote single value detected above LOQ.

Table 3
Comparisons of mean antibiotic concentrations (ng/g) in Irish sediments with similar studies conducted worldwide. Note that Levofloxacin and Difloxacin are omitted as suitable data for comparison could not be located. (a) Year stated denotes the collection date as opposed to journal publication date. In descending order: Pizzini et al (2024); Siedeleicz et al. (2018); Da Silva et al. (2011); Feitosa-Felizzola and Chiron (2009); Kairigo et al. (2020); Valdés et al (2021); Deng et al (2018); Liu et al (2016); Chen and Zhou (2014); Zhou et al (2011); Kim and Carlson (2006).

Study [a]	TRI	CIP	ENR	OFL	AZI	CLA	ERY	ROX	SME	SDI
This Study 2023 (n = 80)	0.170	<5.04	<0.977	<0.355	0.093	6.65	<0.156	<0.333	0.077	<0.074
Italy 2019–2021 (n = 26)	–	<17.1	–	–	7.099	0.285	1.219	–	–	–
Poland 2011–2013 (n = 61)	1.851	–	–	–	–	–	0.135	–	20.11	–
Spain 2009 (n = 20)	0.270	–	–	–	–	1.408	2.718	–	–	0.430
France 2008–2009 (n = 12)	–	–	–	–	130.4	1.71	–	–	–	–
Kenya 2019 (n = 9)	1.678	12.49	–	–	–	–	–	–	8.311	–
Argentina 2016 (n = 10)	<0.8	–	–	6.0	3.2	0.96	–	<0.1	<0.6	<0.7
Hong Kong 2016 (n = 20)	–	0.986	–	0.355	–	–	–	0.279	0.267	–
China (Bohai Sea) 2014 (n = 35)	–	12.9	19.9	7.6	–	–	–	2.5	–	–
China (Shanghai) 2012	–	–	3.2	4.1	–	–	10.2	1.9	0.2	0.4
China (North East) 2011 (n = 94)	1.187	40.05	0.177	20.07	–	–	–	4.267	<0.65	0.713
USA 2003–2005 (n = 20)	–	–	–	–	–	–	–	2.1	1.6	–

with those in sediments elsewhere. Within the EU, Ireland appears to be on the lower range of reported antibiotic concentrations in sediments, with the notable exception of clarithromycin which was detected at higher average concentrations than in comparable studies and with a high detection frequency (Ireland – 89.7 %, n = 80; Italy – 11.5 %, n = 26; Spain – 75.0 %, n = 20; and France – 100 %, n = 12). The French and Spanish studies were conducted 15 years ago and, globally antibiotic usage has increased by approximately 46 % between 2000 and 2018 (Browne et al, 2021); therefore, concentrations in sediments have likely risen concomitantly. Concentrations in Ireland appear to be at the lower end of those reported worldwide with only Spain and the USA being lower, again with the caveat that increasing use of antimicrobials worldwide during that period may affect that comparison. Internationally, a greater focus is placed on the fluoroquinolones and sulphonamides, with Roxythromycin being the only macrolide to be regularly assessed in these studies (of the antibiotic residues included herein). Though reliable statistics on the market share of antibiotic classes is not available, the variances observed in Fig. 4 indicates that significant inter-regional differences in the environmental uptake – and therefore environmental risk – exist. This is likely based on regional requirements for example: the use of macrolides to treat pneumonia (One Health Trust, 2012; Hinnerskov et al., 2011) in more affected areas such as Ireland and Argentina (Dadonite and Roser, 2019); the reportedly high use of macrolides in France (Adriaenssens et al., 2021; Le Baron et al., 2024); and the use of fluoroquinolones in swine (Hayer et al, 2022), and China's dominance of the global pork production market (USDA, 2024). This therefore highlights the need for targeted regional assessments and monitoring of antibiotics based on regional usage.

4. Conclusions

Overall, concentrations of antibiotics in Irish sediments appear to be at the lower end of those detected in similar studies worldwide, with the exception of clarithromycin, which is present at higher concentrations than hitherto reported internationally. Clarithromycin was by far the most frequently detected antibiotic in this study. Lower concentrations of antibiotics were found in sediments isolated from wastewater emission points and low population centres. In contrast, higher concentrations were found in samples directly adjacent to wastewater emission points, and could potentially be attributed to certain specific regional activities such as agriculture, aquaculture, and dairy processing. Based on the concentrations found and available sediment PNECs, most

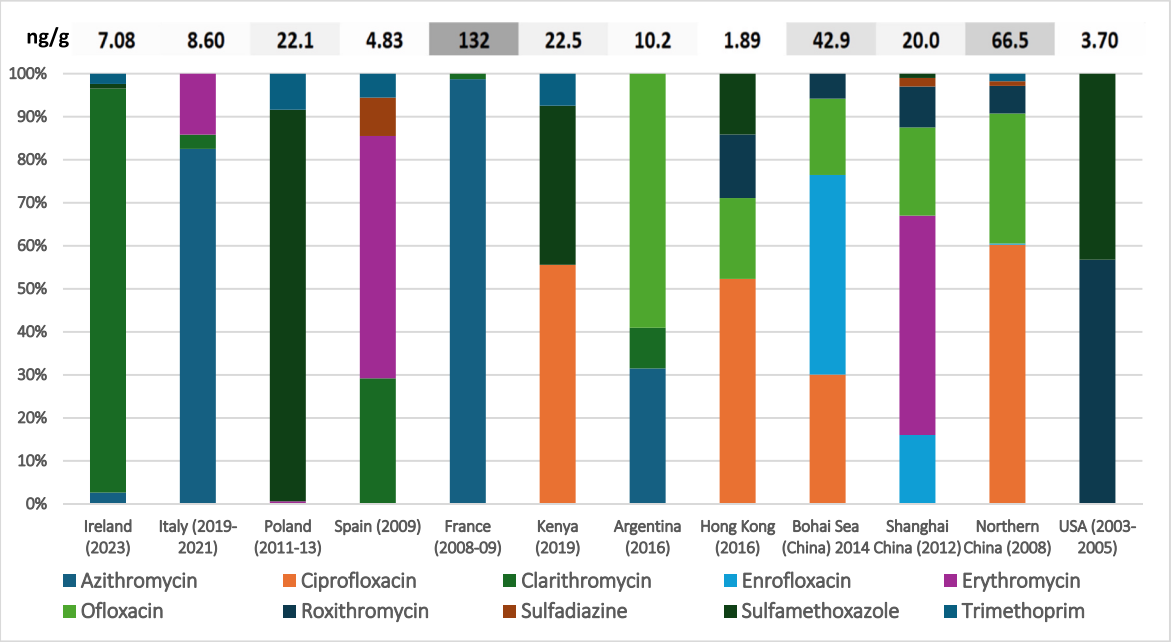

Fig. 4. Comparisons of mean concentrations of antibiotics in Irish sediments with similar studies conducted worldwide. Values above the bars represent total average antibiotic concentrations quantified in each study. Citations given in Table 3.

antibiotics assessed here appear to present low ecotoxicological risk in terms of their measured concentrations in sediments, with the exception of clarithromycin, sulfamethoxazole, and, potentially, ciprofloxacin (for which the method limit of quantification exceeded the PNEC). This does not however necessarily indicate that other antibiotics are of low environmental risk overall, as the partitioning behaviour of these antibiotics into different matrices highlight that different environmental compartments may be at greater risk depending on the individual compounds. Future monitoring programmes should therefore focus on those antibiotics shown here to be of moderate or high ecotoxicological risk, while taking care to consider the risks of individual compounds in different environmental compartments.

CRediT authorship contribution statement

Martin Sharkey: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **William A. Stubbings:** Writing – original draft, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Stuart Harrad:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Funding acquisition, Conceptualization. **Mark G. Healy:** Writing – review & editing, Project administration, Methodology, Funding acquisition, Conceptualization. **Shijie Wang:** Investigation, Formal analysis. **Jingxi Jin:** Investigation, Formal analysis. **Ann Marie Coggins:** Writing – review & editing, Supervision, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2024.143793.

Data availability

Data will be made available on request.

References

Adriaenssens, N., Bruyndonckx, R., Versporten, A., Hens, N., Monnet, D.L., Molenberghs, G., Goossens, H., Weist, K., Coenen, S., 2021. Consumption of macrolides, lincosamides and streptogramins in the community, European Union/European Economic Area, 1997-2017. J. Antimicrob. Chemother. 12 (20), 30–36.

BIO, I.S., 2013. "Study on the environmental risks of medicinal products". Final Report prepared by BIO Intelligence Services for the European Commission Executive Agency for Health and Consumers. https://health.ec.europa.eu/document/download/592edea4-27d9-4b36-933a-6009057960c1_en, 06-08-24.

Browne, A.J., Chipeta, M.G., Haines-Woodhouse, G., Kumaran, E.P.A., Hamanadi, B.H. K., Zaraa, S., Henry, N.J., Deshpande, A., Reiner Jr, R.C., Day, N.O.J., Lopez, A.D., Dunachie, S., Moore, C.E., Stergachis, A., Hay, S.I., Dolecek, C., 2021. Global antibiotic consumption and usage in humans, 2000-18: a spatial modelling study. Lancet 5 (12), 893–904.

Bryskier, A., 2005. Antimicrobial Agents: Antibacterials and Antifungals. American Society for Microbiology (ASM), Washington DC, USA.

Carvalho, R.N., Ceriani, L., Ippolito, A., Lettieri, T., 2015. Development of the first watch list under the environmental quality standards directive. JRC Technical Report,

European Commission. https://publications.jrc.ec.europa.eu/repository/handle/JRC95018, 14-11-24.
Carvalho, I.T., Santos, L., 2016. Antibiotics in the aquatic environments: a review of the European scenario. Environ. Int. 94, 736–757.
Chakwenya, J., Lakritz, J., Tyler, J., Fales, W.H., James-Kracke, M., Smith, K., Holle, J., 2002. Pharmacokinetics and bioavailability of trimethoprim-sulfamethoxazole in alpacas. J. Vet. Pharmacol. Therapeut. 25 (5), 321–327.
Chen, K., Zhou, J.L., 2014. Occurrence and behaviour of antibiotics in water and sediments form the Huangpu River, Shanghai, China. Chemosphere 95, 604–612.
Chen, Y., Li, P., Huang, Y., Yu, K., Chen, K.H., Cui, K., Huang, Q., Zhang, J., Yew-Hoong Gin, K., He, Y., 2019. Environmental media exert a bottleneck in driving the dynamics of antibiotic resistance genes in modern aquatic environment. Water Res. 162, 127–138.
Cherian, T., Ragavendran, C., Vijayan, S., Kurien, S., Peijnenburg, W.J.G.M., 2023. A review on the date, human health and environmental impacts, as well as regulations of antibiotics used in aquaculture. Environ. Adv. 13, 100411.
Da Silva, B.F., Jelic, A., López-Derna, R., Mozeto, A.A., Petrovic, M., Barceló, D., 2011. Occurrence and distribution of pharmaceuticals in surface water, suspended solids and sediments of the Ebro Rover basin, Spain. Chemosphere 85 (8), 1331–1339.
Dadonite, B., Roser, M., 2019. Pneumonia. Our World in Data. Available at: ourworldindata.org/pneumonia.
Deng, W.-J., Li, N., Ying, G.-G., 2018. Antibiotic distribution, risk assessment and microbial diversity in river water and sediment in Hong Kong. Environ. Geochem. Health 40, 2191–2203.
EPA, 2024. EPA Geoportal Site – Water Maps. Environmental Protection Agency of Ireland. Available at: https://gis.epa.ie/EPAMaps/Water, 02-11-24.
EU, 2015. Commission Implementing Decision (EU) 2015/495 of 20 March 2015 establishing a watch list of substances for Union-wide monitoring in the field of water policy pursuant to Directive 2008/105/EC of the European Parliament and of the Council. Off. J. Eur. Union 78, 4–42, 24.3.2015.
EU, 2018. Commission Implementing Decision (EU) 2018/840 of 5 June 2018 establishing a watch list of substances for Union-wide monitoring in the field of water policy pursuant to Directive 2008/105/EC of the European Parliament and of the Council. Off. J. Eur. Union 141, 9–12, 7.6.2018.
EU, 2020. Commission Implementing Decision (EU) 2020/1161 of 4 August 2020 establishing a watch list of substances for Union-wide monitoring in the field of water policy pursuant to Directive 2008/105/EC of the European Parliament and of the Council. Off. J. Eur. Union 257, 32–35, 6.8.2020.
EU, 2022. Commission Implementing Decision (EU) 2022/1307 of 22 July 2022 establishing a watch list of substances for Union-wide monitoring in the field of water policy pursuant to Directive 2008/105/EC of the European Parliament and of the Council. Off. J. Eur. Union 117–120, 26/07/2022.
Feitosa-Felizzola, J., Chiron, S., 2009. Occurrence and distribution of selected antibiotics in a small Mediterranean stream (Arc River, Southern France). J. Hydrol. 364 (1–2), 50–57.
Harkins, C.P., Pichon, B., Doumith, M., Parkhill, J., Westh, H., Tomasz, A., de Lencastre, H., Bentley, S.D., Kearns, A.M., Holden, M.T.G., 2017. Methicillin-resistant *Staphylococcus aureus* emerged long before the introduction of methicillin into clinical practice. Genome Biol. 18, 130.
Hayer, S.S., Casonova-Higes, A., Paladino, E., Elnekave, E., Nault, A., Johnson, T., Bender, J., Perez, A., Alvarez, J., 2022. Global distribution of fluoroquinolones and colistin resistance and associated resistance markers in *Escherichia coli* of swine origin – a systematic review and meta-analysis. Front. Microbiol. 13, 834793.
Hinnerskov, M., Therkildsen, J.M., Cordoba, G., Bjerrum, L., 2011. Macrolide overused for treatment of respiratory tract infections in general practice. Dan. Med. Bull. 58 (11), A4356.
Hirsch, R., Ternes, T., Haberer, K., Kratz, K.-L., 1999. Occurrence of antibiotics in the aquatic environment. Sci. Total Environ. 225 (1–2), 109–118.
Kairigo, P., Ngumba, E., Sundberg, L.-R., Gachanja, A., Tuhkanen, T., 2020. "Occurrence of antibiotics and risk of antibiotic resistance evolution in selected Kenyan wastewaters, surface waters and sediments". Sci. Total Environ. 720, 137580.
Kemnic, T.R., Coleman, M., 2022. "Trimethoprim Sulfamethoxazole". StatPearls (Internet). StatPearls Publishing, Treasure Island (FL).
Kim, S.-C., Carlson, K., 2006. Temporal and spatial trends in the occurrence of human and veterinary antibiotics in aqueous and river sediment matrices. Environ. Sci. Technol. 41 (1), 50–57.
Le Baron, Q., Bourneau-Martin, D., Babin, M., Gouraud, A., Tauber, M., Fresse, A., Lebrun-Vignes, B., Delaunay, J., Morisset, M., Briet, M., 2024. Cross-reactivity among and between macrolides, lincosamides, and streptogramins: study on the French pharmacovigilance database. Fund. Clin. Pharmacol. 38 (5), 988–997.
Liu, X., Zhang, H., Lu, L., Fu, C., Tu, C., Huang, Y., Wu, L., Tang, J., Luo, Y., Christie, P., 2016. Levels, distributions and sources of veterinary antibiotics in the sediments of the Bohai Sea in China and surrounding estuaries. Mar. Pollut. Bull. 109 (1), 597–602.
Mercer, M.A., 2022a. Quinolones, including fluoroquinolones, use in animals. In: Merck Veterinary Manual. Merck & Co Inc, Whitehouse Station, NJ.
Mercer, M.A., 2022b. "Macrolide Use in Animals". Merck Veterinary Manual. Merck & Co Inc, Whitehouse Station, NJ.
Monahan, C., Harris, S., Morris, D., Cummins, E., 2022. A comparative risk ranking of antibiotic pollution from human and veterinary antibiotic usage – an Irish case study. Sci. Total Environ. 826, 154008.
Morris, D., Harris, S., Morris, C., Commins, E., Cormican, M., 2008. EPA Report No. 162 – Hospital Effluent: Impact on the Microbial Environment and Risk to Human Health. Environmental Protection Agency of Ireland, Dublin, Ireland.
O'Flynn, D., 2024. Determination of Pharmaceuticals in Irish Aquatic Ecosystems: an Evaluation of Occurrence and Risk. PhD Thesis. Dublin City University. Available at: https://doras.dcu.ie/29350/1/Dylan%20O%27Flynn%20PhD%20thesis.pdf.
O'Sullivan, M., Burns, K., Slowey, R., Byrne, W., Sammin, S., 2019. Ireland – One Health Report on Antimicrobial Use and Antimicrobial Resistance. Department of Health/Department of Agriculture, Food, and the Marine. Available at: https://www.gov.ie/en/publication/98f5bb-one-health-report-on-antimicrobial-use-antimicrobial-resistance/, 06-08-24.
One Health Trust, 2012. Macrolide antibiotic use is increasing in developing countries. One Health Trust. Available at: https://onehealthtrust.org/publications/infographics/macrolide-antibiotic-use-increasing-developing-countries/, 13-11-24.
Papich, M.G., 2017. Ciprofloxacin pharmacokinetics in clinical canine patients. J. Vet. Intern. Med. 31 (5), 1508–1513.
Pitman, S.K., Hoang, U.T.P., Wi, C.H., Alseikh, M., Hiner, D.A., Percival, K.M., 2019. Revisiting oral fluoroquinolones and multivalent cation drug-drug interactions: are they still relevant? Antibiotics (Basel) 8 (3), 108.
Pizzini, S., Giubilato, E., Morabito, E., Barbaro, E., Bonetto, A., Calgaro, L., Feltracco, M., Semenzin, E., Vecchiato, M., Zangrando, R., Gambaro, A., Marcomini, A., 2024. Contaminants of emerging concern in water and sediment of the Venice Lagoon, Italy. Environ. Res. 249, 118401.
Polianciuc, S.I., Gurzau, A.E., Kiss, B., Stefan, M.G., Loghin, F., 2020. Antibiotics in the environment: causes and consequences. Med. Pharm. Rep. 93 (3), 231–240.
Rodriguez-Mozaz, S., Vaz-Moreira, I., Giustina, S.V.D., Llorca, M., Barceló, D., Schubert, S., Berendonk, T.U., Michael-Kordatou, I., Fatta-Kassinos, D., Martinez, J. L., Elpers, C., Henriques, I., Jaeger, T., Schwartz, T., Paulshus, E., O'Sullivan, K., Paranen, K.M.M., Virta, M., Do, T.T., Walsh, F., Manaia, C.M., 2020. Antibiotic residues in final effluents of European wastewater treatment plants and their impact on the aquatic environment. Environ. Int. 140, 105733.
SCHEER, 2022a. Draft environmental quality standard for priority substances under the water Framework directive – azithromycin. Scientific Committee on Health, Environment and Emerging Risks (SCHEER). Available at: https://health.ec.europa.eu/publications/draft-environmental-quality-standards-priority-substances-under-water-framework-directive-3_en, 06-08-24.
SCHEER, 2022b. Draft environmental quality standard for priority substances under the water Framework directive – clarithromycin. Scientific Committee on Health, Environment and Emerging Risks (SCHEER). Available at: https://health.ec.europa.eu/publications/draft-environmental-quality-standards-priority-substances-under-water-framework-directive-2_en, 06-08-24.
SCHEER, 2022c. Draft environmental quality standard for priority substances under the water Framework directive – erythromycin. Scientific Committee on Health, Environment and Emerging Risks (SCHEER). Available at: https://health.ec.europa.eu/publications/draft-environmental-quality-standards-priority-substances-under-water-framework-directive-0_en, 06-08-24.
Siedeleicz, G., Bialk-Bienlinska, A., Borecka, M., Winogradow, A., Stepnowski, P., Pazdro, K., 2018. Presence, concentrations and risk assessment of selected antibiotic residues in sediments and near-bottom waters collected from the Polish coastal zone in the southern Baltic Sea – summary of 3 years of studies. Mar. Pollut. Bull. 129 (2), 787–801.
Sharkey, M., Wang, S., Harrad, S., Stubbings, W.A., Healy, M.G., Coggins, A.M., 2024. Legacy and emerging flame retardants in sediments and wastewater treatment plant-derived biosolids. Sci. Total Environ. 954, 176582.
Tarrant, C., Colman, A.M., Jenkins, D.R., Chattoe-Brown, E., Perera, N., Mehtar, S., Nakkawita, W.M.I.D., Bolscher, M., Krockow, E.M., 2021. Drivers of broad-spectrum antibiotics overuse across diverse hospital contexts – a qualitative study of prescribers in the UK, Sri Lanka and South Africa. Antibiotics (Basel) 10 (1), 94.
Uisce Éireann, 2024. What is the regional biosolids storage facility? Uisce-Éireann. Available at: https://www.water.ie/projects/local-projects/regional-biosolids-storag/faqs, 13-11-24.
USDA, 2024. Production – Pork. U.S. Department of Agriculture – Foreign Agriculture Service. Available at: https://fas.usda.gov/data/production/commodity/0113000, 13-11-24.
Valdés, M.E., Santos, L.H.M.L.M., Castro, M.C.R., Giorgi, A., Barceló, D., Rodríguez-Mozaz, S., Amé, M.V., 2021. Distribution of antibiotics in water, sediments ad biofilm in an urban river (Córdoba, Argentina, LA). Environ. Pollut. 269, 116133.
Wang, W., Weng, Y., Luo, T., Wang, Q., Yang, G., Jun, Y., 2023. Antimicrobials and the resistances in the environment: ecological and health risks, influencing factors, and mitigation strategies. Toxics 11 (2), 185.
WHO, 2019. Antimicrobial Resistance. World Health Organisation. Available at: https://www.who.int/europe/news-room/fact-sheets/item/antimicrobial-resistance, 06-08-24.
WHO, 2022a. Global Antimicrobial Resistance and Used Surveillance System (GLASS) Report 2022. World Health Organisation. Available at: https://iris.who.int/bitstream/handle/10665/364996/9789240062702-eng.pdf?sequence=1, 06-08-24.
WHO, 2022b. World Leaders and Experts Call for Action to Protect the Environment from Antimicrobial Pollution. World Health Organisation. Available at: https://www.who.int/news/item/02-03-2022-world-leaders-and-experts-call-for-action-to-protect-the-environment-from-antimicrobial-pollution, 06-08-24.
Wu, Y., Li, S., Hu, J., Chen, Q., Sun, W., 2023. Wastewater treatment plant effluents exert different impacts on antibiotics resistome in water and sediment of the receiving river: metagenomic analysis and risk assessment. J. Hazard Mater. 460, 132528.
Zhou, L.-J., Ying, G.-G., Zhao, J.-L., Yang, J.-F., Wang, L., Yang, B., Liu, S., 2011. Trends in the occurrence of human and veterinary antibiotics in the sediments of the Yellow River, Hai River and Liao River in northern China. Environ. Pollut. 159 (7), 1877–1885.