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ORIGINAL PAPER

A Systematic Workflow of Data Mining Confirms Widespread Occurrence of Antibiotic Contamination in Freshwater Reservoirs

Zhao-Feng Guo[1,2,3] · Wiebke J. Boeing[4] · Yao-Yang Xu[1,3] · Edoardo Borgomeo[5] · Dong Liu[1,2,3] · Yong-Guan Zhu[1,3]

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Abstract
Antibiotic residues in reservoirs threatens ecosystems and human health. Whereas numerous studies have been conducted on their occurrence and distribution, overall quantitative and comparative analysis of antibiotic contamination in reservoirs is challenging due to scattered data and scale differences. Here, we integrate antibiotic data from 520 samples in 80 reservoirs and provide an overview of the distribution, determinants, and potential risks of these emerging contaminants in reservoirs at a cross-continental scale. A total of 69 antibiotics were detected in reservoirs, with sulfonamides, fluoroquinolones, tetracyclines, macrolides, and β-lactams occurring more frequently. Concentration and type of antibiotics varied among continents and reservoirs between data generated from sediment and water. Geographic location, seasonal variation, artificial impervious area around the reservoir, reservoir characteristics, and water quality also influenced reservoir antibiotic distributions. These factors enhanced the explanatory power of antibiotic distribution through linear or non-linear interactions. Cumulative risk for 44 antibiotics in reservoirs is low, but it is essential to further assess the environmental behavior and integrated risk of antibiotics from an interdisciplinary perspective and at the human-food chain-ecosystem interface, particularly antibiotic resistance under "One Health" framework.

Keywords Reservoirs · Antibiotics contamination · Distribution · Determinants · Risk assessment · Data mining

Introduction

The amounts of antibiotics used each day is increasing (Bhagat et al. 2020). Global antibiotic consumption was 131,000 tons in 2013 and is predicted to reach 200,000 tons per year by 2030 (Klein et al. 2018). Antibiotics are partially utilized, and residual antibiotics and their metabolites eventually reach and stay in aquatic ecosystems through pathways such as runoff and effluent discharge (Tran et al. 2018). Due to massive inputs and pseudo-persistence, antibiotics inevitably accumulate in waters and sediments and pose a potential hazard to aquatic ecosystems (Nijsingh et al. 2019; Pruden. 2014). Unregulated production and consumption of antibiotics in less developed countries will further exacerbate this water safety problem (Talib and Randhir. 2016). Accumulation of antibiotics in natural systems poses an increasing threat to global health.

Persistent accumulation of antibiotics in reservoirs has many negative effects on ecosystem structure and function, such as reduction in microbial diversity and altered nutrient cycling (Szymańska et al. 2019; Kovalakova et al. 2020). Antibiotic-microbial interactions can enrich for antibiotic-resistant bacteria and antibiotic resistance genes in the environment (Zhu et al. 2013; Booth et al. 2020) and increase health risks to aquatic organisms (Sharma et al. 2016) and public health (Berendonk et al. 2015). Even low levels of antibiotics have high biological activity (Zainab et al. 2020). As such,

✉ Yao-Yang Xu
yyxu@iue.ac.cn

1 Key Laboratory of Urban Environment and Health, Ningbo Observation and Research Station, Institute of Urban Environment, Chinese Academy of Sciences, Xiamen 361021, China

2 University of Chinese Academy of Sciences, Beijing 100049, China

3 Zhejiang Key Laboratory of Urban Environmental Processes and Pollution Control, CAS Haixi Industrial Technology Innovation Center in Beilun, Ningbo 315830, China

4 Department of Fish, Wildlife & Conservation Ecology, New Mexico State University, Las Cruces, NM 88003, USA

5 Environmental Change Institute, University of Oxford, Oxford OX1 3QY, UK

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direct exposure to low levels of antibiotics can be hazardous to human health.

Distribution of antibiotics in reservoirs and factors influencing those distributions have been investigated in many countries including Iran, China, Spain, and Mexico (Javid et al. 2016; Marti et al. 2018; Perez-Coyotl et al. 2019; Xu et al. 2020). However, there is a lack of overall knowledge on the differences in reservoir antibiotic distribution at large scales. This is not only attributed to variation in methods and explanatory factors studied, but may also be due to basic attributes such as reservoir capacity and catchment area (Janssen et al. 2021).

Exposures to emerging contaminants in water systems such as municipal wastewater and rivers on a global scale have been assessed (Hendriksen et al. 2019; Guo et al. 2021; Kumari and Gupta. 2022; Wilkinson et al. 2022). In these studies, reuse of data provides additional information on occurrence of emerging contaminants at multidimensional scales that can resolve different risk patterns among geographic areas. In contrast, existing studies are scattered and localized, and not sufficient to draw generalized conclusions. Integration of existing raw data from different studies can reveal patterns and facilitate scientific breakthroughs (Uzzi et al. 2013; Pierce et al. 2019).

The number of studies on antibiotic contamination in reservoirs has increased in the last decade. A full and systematic review of data from these published studies can lead to both, meaningful conclusions as well as identification of gaps and future research directions (Sharma et al. 2021). Here, we collated datasets from 520 samples from 80 different reservoirs to (i) reveal differences in the distribution of antibiotic contamination in reservoirs; (ii) elucidate determinants of antibiotics and their interactions; and (iii) assess risks from antibiotics to reservoir ecosystems and human health. Through constructed datasets and proposed systematic workflow, we demonstrated and informed the spatiotemporal scopes of monitoring, integrated risk assessment, internal and external drivers, and data sharing for reservoir antibiotics, facilitating the understanding of the current status of antibiotic contamination and its mechanisms for polluting reservoir ecosystems. Therefore, we are able to provide theoretical knowledge on how to control antibiotic contamination and reduce potential risks for reservoirs. In brief, this study provides enlightening and vibrant field for research on emerging contaminants in the aquatic environment in terms of systematic methodology, dataset integrity, and data-intensive discoveries.

Materials and Methods

We constructed a workflow to provide a comprehensive overview of antibiotic contamination and impacts in reservoirs from a cross-continental perspective (Fig. 1). We collected, processed, and statistically analyzed data from the literature on reservoir antibiotics. First, we retrieved literature on antibiotics, screened it for relevance and data availability, and extracted data. Acquired data were then categorized according to the environmental media (water vs sediment) and geographical location of the study. Finally, we analyzed data using multivariate statistical methods to visualize the current status of antibiotic contamination in reservoirs and to identify driving mechanisms. Mapped Sankey diagrams visualize the specific workflow of data resource mining, enabling a detailed understanding of existing research landscape and identifying research directions that need to be filled (Lupton and Allwood. 2017).

Data Collection and Preprocessing

To obtain data on antibiotics in reservoirs, we conducted a systematic search of the peer-reviewed literature in the Web of Science database. The Web of Science database was chosen because it is a world-leading and authoritative citation database and includes many high-impact international academic journals on environmental research topics, providing access to the most complete peer-reviewed publication possible. Search topics were (“reservoir” OR “dam”) AND (“antibiotic*” OR “sulfonamides” OR “tetracyclines” OR “fluoroquinolones” OR “macrolides” OR “β-lactams” OR “pharmaceutical*”). The language of our search was limited to English and peer-reviewed research and review journal articles published before June 2021 were included. A total of 2812 articles were retrieved. From those articles, we manually screened 44 studies where antibiotic concentrations in reservoirs were monitored in the field. Of these, data from 3 studies were reused from previous publications and were excluded. Of the remaining 41 studies, 39 investigated antibiotic concentrations in waters or sediments of reservoirs, whereas only 2 studies were conducted on aquatic organisms. Therefore, for our comparative analysis, we only considered antibiotic data from reservoir waters and sediments.

From the 39 selected studies, we extracted data on (i) geographic coordinates of sampling sites, environmental media (water versus sediment), and sampling date; (ii) basic reservoir characteristics such as water level, size of reservoir catchment area, and reservoir water storage capacity; and (iii) antibiotic concentrations and other environmental parameters. Relevant information provided in the supplementary materials accompanying the respective journal articles was also included in our search during the data extraction process. Antibiotic concentrations below detection limit or not detected were counted as zero. For sampling sites without indicated coordinates, we estimated latitude and longitude of sampling sites using Google Earth based on the description and sampling schematic information in the article. For the data presented as figures, we extracted

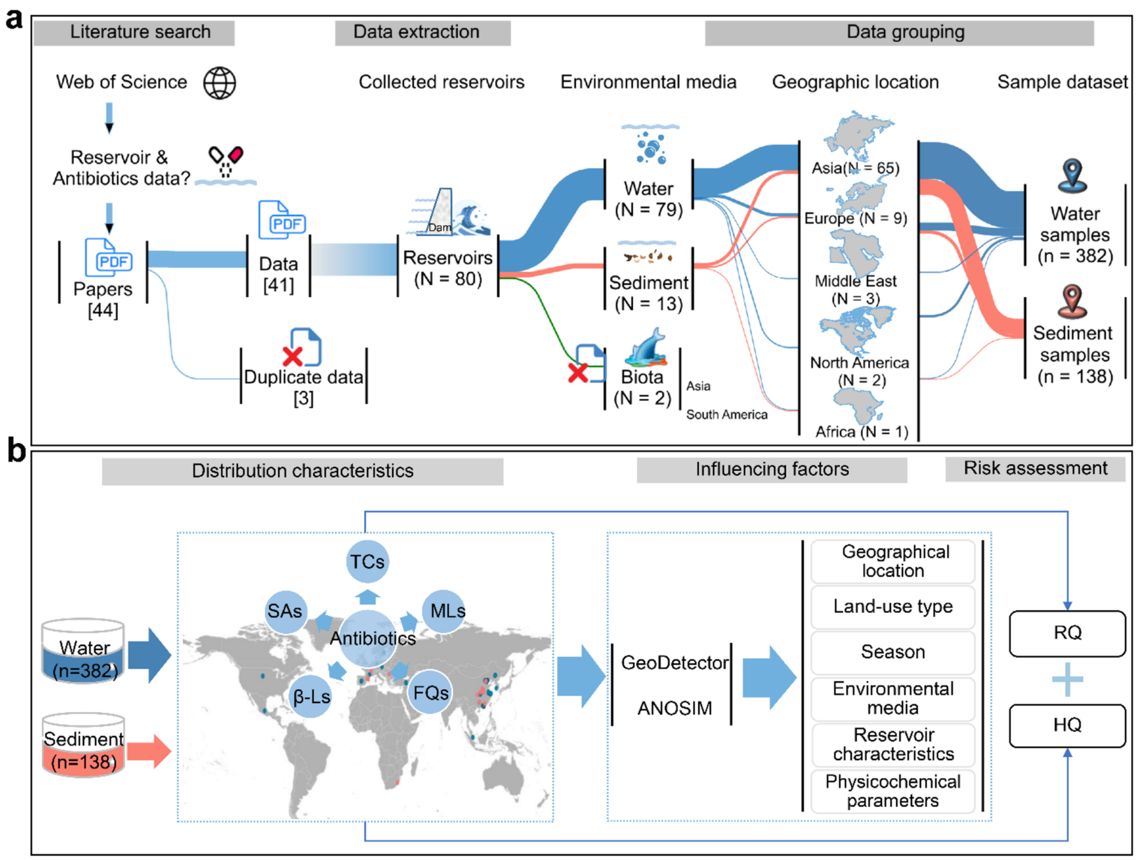


Fig. 1 Workflow of data collection and preprocessing **a** and statistical analysis **b**. *WOS* Web of Science; *SAs* Sulfonamides; *TCs* Tetracyclines; *MLs* Macrolides; *FQs* Fluoroquinolones; *β-Ls* β-lactams; *RQ* Risk Quotient; *HQ* Health Risk Quotient

data using Getdata Graph Digitizer (version 2.26). Artificial impervious areas of 500 m around the sampling sites were derived from the Finer Resolution Observation and Monitoring-Global Land Cover database (FROM-GLC 2017v1; http://data.ess.tsinghua.edu.cn/fromglc2017v1.html).

In total, we obtained 520 sample data from 39 studies in 80 different reservoirs. This included 382 water samples and 138 sediment samples. Given data accessibility and studies comparability, a novel dataset containing a total of 11 parameters including basic reservoir characteristics, geographic sampling locations, sampling date, and hydrological parameters, in addition to antibiotics, was obtained (Table S1).

Statistical Analysis

Identification of Determinants

Analysis of Similarities (ANOSIM) was used to test the significance of differences in the distribution of antibiotic concentrations between different environmental media (water and sediment). The coupled effects of 11 factors on the distribution of antibiotic concentrations in reservoirs were assessed using the GeoDetector model (Wang et al. 2010). The GeoDetector model reveals both, the driving force of single factor (x_i) (factor detector) and quantifies the explanatory power of two-factor interaction ($x_1 \cap x_2$) on the distribution of antibiotic concentration (interaction detector) by detecting spatial heterogeneity (Wang et al. 2016). The degree of explanatory power of x_i on the distribution of y is measured by the q-value (explanatory power: $q \times 100\%$). q-value range from [0, 1]. The larger the q-value, the stronger the explanatory power of x_i for y. It is calculated as follows Eq. (1):

$$q = 1 - \frac{\sum_{h=1}^{L} N_h \sigma_h^2}{N\sigma^2} \tag{1}$$

where $h = 1, \ldots, L$ is the classification of x. N_h and N are the numbers of classification in class h and the total, respectively. σ_h^2 and σ^2 represent the variance of microplastic distribution in the h class and the total, respectively.

The explanatory power of two-factor interactions is expressed as $q\ (x_1 \cap x_2)$. By comparing q-values of the two factors [$q\ (x_1)$ and $q\ (x_2)$] with $q\ (x_1 \cap x_2)$, we can determine whether the explanatory power of the two-factor interaction on antibiotic concentration is enhanced or diminished, or whether they affect each other independently. The five interaction types between two factors are described by Xu et al. (2021) (see Text S1 for details).

Assessment of Ecological and Health Risks

We assessed ecological risks and health risks of antibiotics using risk quotient values (RQ) and health risk quotient (HQ_i). While considering the risk of individual antibiotics, we also calculated the cumulative risk effect of target antibiotics on reservoir organisms as well as human health (for detailed information, see Text S2).

ANOSIM was conducted with the vegan and ggplot2 packages of R software and Geodetector models with the Geodetector packages of R software (version 3.5.3). The distribution map of antibiotic concentrations and risk was plotted in ArcGIS (version 10.5).

Results

Occurrence and Distribution of Antibiotics in Reservoirs

Data on antibiotic concentrations were collected from 520 samples in 80 reservoirs, covering five geographical regions in 14 countries (Fig. 1a). Previous studies detected antibiotics in reservoirs located in Asia (65 reservoirs), Europe (9), Middle East (3), North America (2), and Africa (1). No data on antibiotics in reservoir waters or sediments located in Oceania and South America were found. The environmental media studied were mainly reservoir waters or sediments (39 studies), while less attention has been paid to aquatic organisms (2 studies).

A total of 69 antibiotics were detected across all samples (Fig. 2a and b). Of these, 69 antibiotics were found in waters, with a range of 1–32 antibiotics per sample (Fig. 2a). Asia had the largest number of antibiotic species identified in reservoir waters, with a total of 66 antibiotics, followed by European with 20 antibiotics. In the remaining three regions < 6 antibiotics were detected. Fewer antibiotic species were found in sediments (total of 25), with a range of 2–20 antibiotics detected per sample. Similarly, the largest number of antibiotic types was identified in reservoir sediments from Asia, with 24 antibiotics. Antibiotics were classified into the following types: sulfonamides (SAs), fluoroquinolones (FQs), tetracyclines (TCs), macrolides (MLs), β-lactams (β-Ls), and others (lincomycin, chloramphenicol, nitroimidazoles, and polypeptides). The first five types of antibiotics were found more frequently in water samples than in sediments, especially sulfonamides, which have low degradation rates, high water solubility, and are not easily adsorbed to sediments (Fig. 2c). Lincomycin and chloramphenicol were detected more regularly in waters, with frequencies of 42% and 15% of the total water samples, respectively.

According to European and American regulations, antibiotic drug residues in water exceeding 10 ng/L trigger an environmental risk assessment, while concentrations above 100 ng/L require an impact study (Le Page et al. 2017). We calculated concentrations across all 80 reservoirs for each antibiotic species. Less than half of the concentration of antibiotics in waters exceeded 10 ng/L (46 antibiotics; Fig. 2a). The concentrations ranged from 10 to 100 ng/L for 18 antibiotics. There were five antibiotics above 100 ng/L, including four tetracyclines (tetracycline, epitetracycline, 4-epianhydrotetracycline, and anhydrotetracycline) and one fluoroquinolone (ciprofloxacin). Among them four tetracyclines had abnormally high concentrations but low detection frequencies, while ciprofloxacin was detected more frequently. In sediments, only one antibiotic had a concentration of less than 1 ng/g (Penicillin G; Fig. 2b). Fourteen antibiotics found had concentrations between 1 and 10 ng/g, and 8 antibiotics ranged from 10 and 100 ng/g. Only two antibiotics had concentrations above 100 ng/g, including norfloxacin and metronidazole.

Concentrations and species of antibiotics in waters varied across continents and reservoirs (Fig. 3a, Table S1). The highest total concentrations of antibiotics were found in waters of Keban and Karakaya Reservoir (Turkey; Middle East), with a median value of 9.59×10^4 ng/L and 3.71×10^4 ng/L, respectively. Notably, tetracyclines were found in individual samples from Keban Reservoir in concentrations up to 1.88×10^5 ng/L. Fewer antibiotic species were detected in North America. The Madín Reservoir in Mexico, which receives domestic wastewater (Perez-Coyotl et al. 2019), had a median antibiotic concentration of 279 ng/L and was dominated by β-lactams. The median concentrations of reservoir antibiotics in Europe and Asia were 20.7 ng/L (mean ± standard deviation: 313.3 ± 327.4 ng/L) and 43.3 ng/L (mean ± standard deviation: 320.5 ± 628.8 ng/L). Antibiotics in reservoir waters in Asia were dominated by fluoroquinolones and sulfonamides, followed by tetracyclines and macrolides. In Europe regions, macrolides and sulfonamides made up the largest percentages of antibiotics in reservoir waters. Henley Reservoir in South Africa had a total antibiotic concentration of 391 ng/L consisting mainly of sulfonamides and macrolides.

Antibiotic concentrations in different reservoir sediments ranged from not detected (ND) to 1340 ng/g (Fig. 3b). Antibiotic species in sediments of Henley Reservoir (South Africa) differed greatly from those in waters, with metronidazole (1,250 ng/g) accounting for more than 90% of the total concentration and the rest being sulfonamides (Table S1). The longer hydraulic residence time

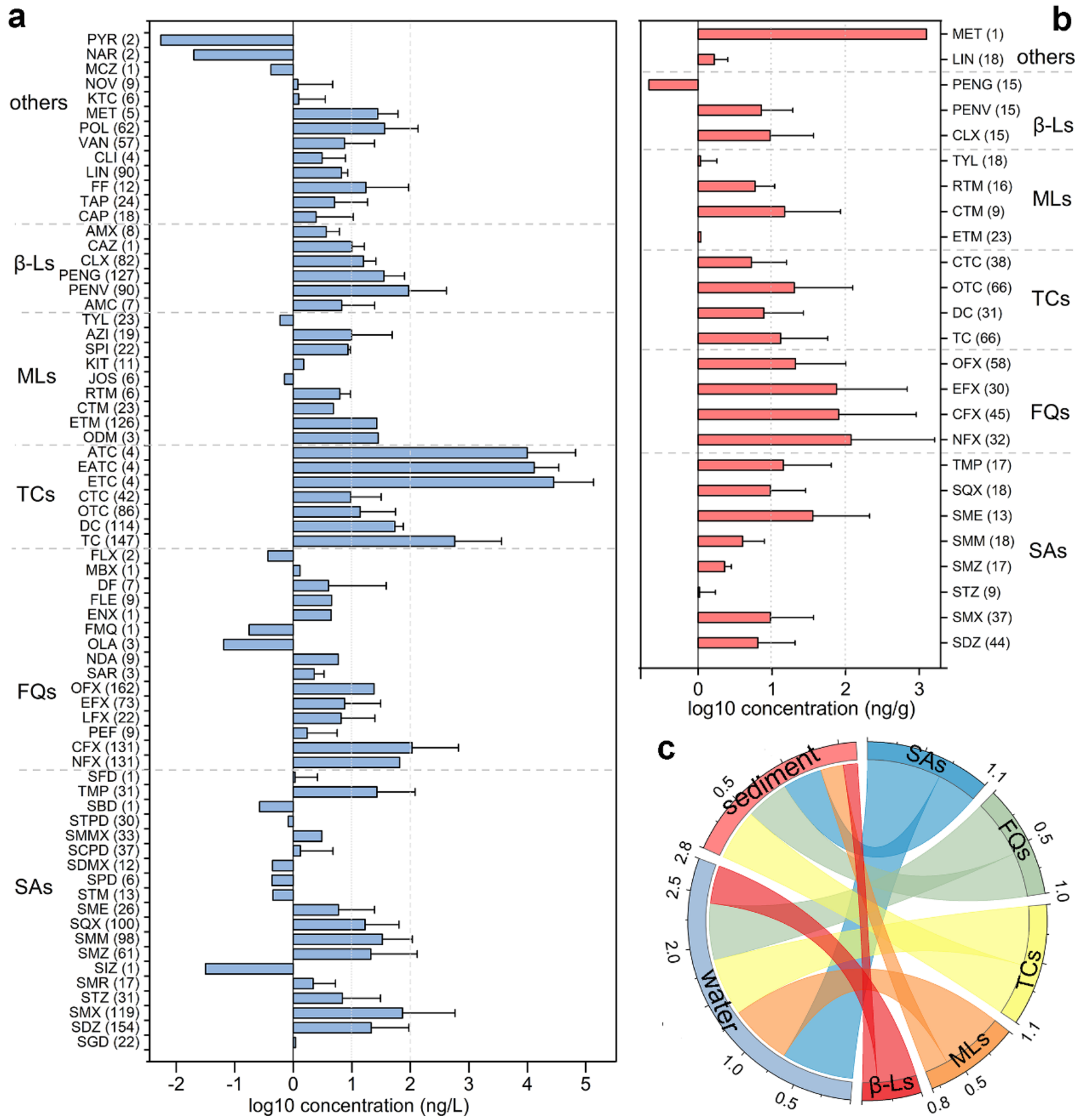


Fig. 2 The concentrations of individual antibiotics in reservoir waters **a** and sediments **b** Log10 values; error bars are standard deviations, and values in parentheses are detection frequencies of the corresponding antibiotics. Abbreviations of individual antibiotics can be found in Table S1. **c** The total frequency of detection of five types of antibiotics in water and sediment samples

of Henley Reservoir might lead to increased metronidazole in its sediment. Antibiotic concentrations in Europe were relatively low, with a median value of 5.73 ng/g (mean ± standard deviation: 20.5 ± 0.4 ng/g). Compared to other European reservoirs, Foix Reservoir in Spain which is used for agricultural irrigation had higher antibiotic concentrations of 69.63 ng/g and was dominated by macrolides. In Asian reservoirs, median concentration of antibiotics was 10.11 ng/g (mean ± standard deviation: 128.8 ± 189.8 ng/g) and the main types were fluoroquinolones and tetracyclines.

Determinants of Antibiotic Distribution

Determinants and the degree to which they influence antibiotic distribution were inconsistent between environmental media (water vs sediment) even for the same type of antibiotic (Fig. 4a–e). For example, sulfonamides in waters mainly responded to reservoir catchment area (explanatory power: 18%) and storage capacity (17%) but were insensitive to water quality parameters like pH and water temperature. In contrast, hydraulic residence time (53%), artificial impervious area (23%), and water quality significantly affected

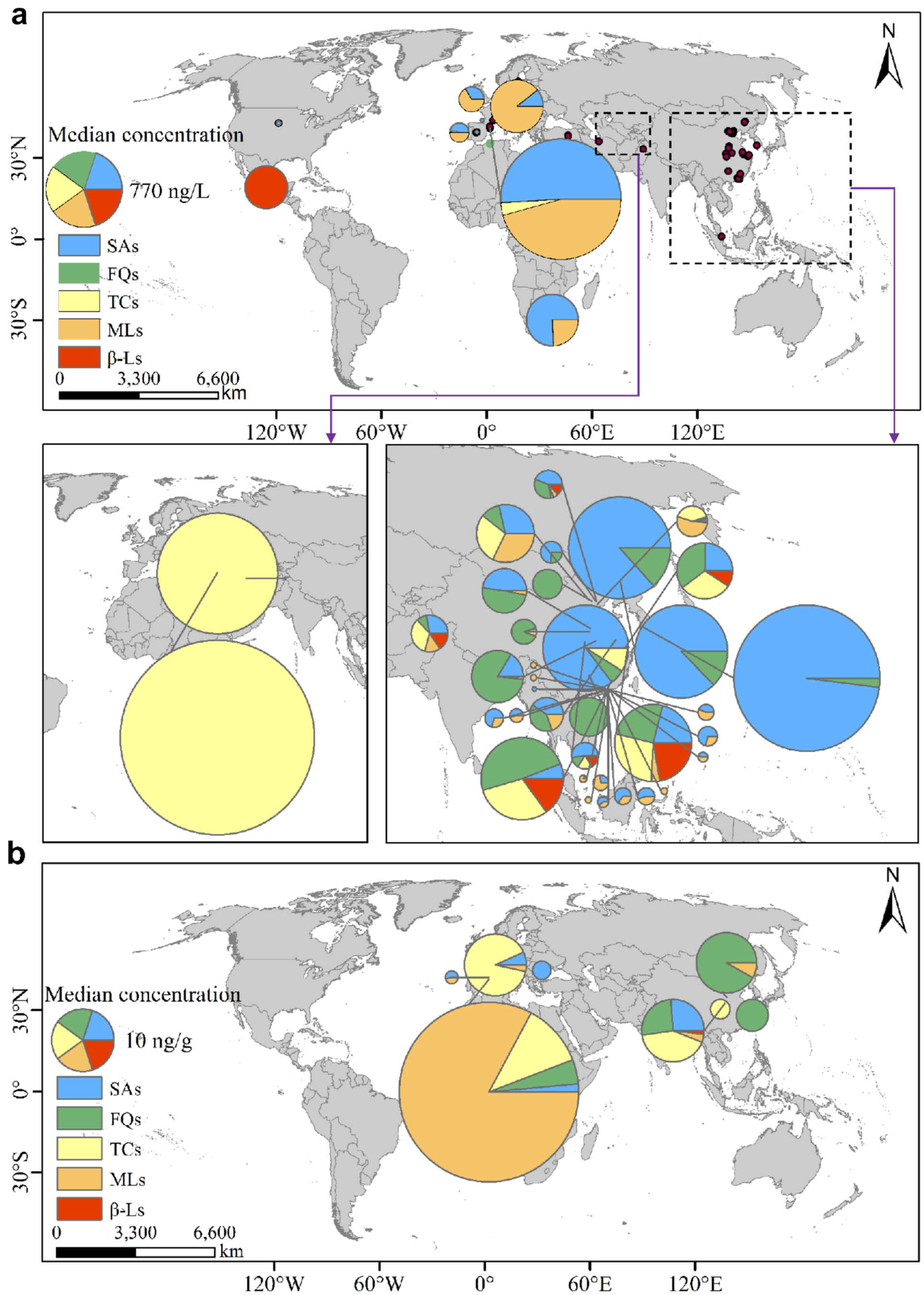


Fig. 3 Spatial distribution of median concentrations of sulfonamides (SAs), fluoroquinolones (FQs), tetracyclines (TCs), macrolides (MLs) and β-lactams (β-Ls) in reservoir waters **a** and sediments **b**

distribution of sediments sulfonamide ($p < 0.05$; Fig. 4a). Differences like this contributed attributed to the significant effect of environmental media on antibiotic distribution ($r = 0.06$, $p = 0.01$). Furthermore, variability of antibiotic distribution in waters was higher than in sediments (Fig. 4f).

The factors driving distribution and degree of influence vary among different types of antibiotics. In reservoir waters, the most influential factors that dominated distribution of sulfonamides and fluoroquinolones were reservoir catchment area and storage capacity. But these single factors were much stronger drivers for fluoroquinolones (52% and 32% explanatory power, respectively) than for sulfonamides (Fig. 4a and b). Secondary factors impacting sulfonamides were artificial impervious area and hydraulic residence time and for fluoroquinolones included reservoir level, artificial impervious area, and seasonal variation. Geographic location was a determinant for tetracyclines (33%, $p < 0.05$), followed by reservoir characteristics (water level, size of reservoir catchment area, and reservoir water storage capacity), all with less than 10% explanatory power (Fig. 4c). Similarly, geographic location and basic reservoir characteristics had some influence on macrolides, but all had less than 10% explanatory power (Fig. 4d). All 11 factors selected, except dissolved organic carbon, had significant effects on β-lactams, especially hydraulic residence time (39%) (Fig. 4e).

In sediments, hydraulic residence time explained 53% of distribution of sulfonamide antibiotics. Seasonal variation and reservoir catchment area had a greater impact on fluoroquinolones, with an explanatory power of 59% and 39%, respectively. Reservoir catchment area and storage capacity were the dominant factors for tetracyclines and macrolides, with explanatory power of more than 50% for both types of antibiotics. The influence of reservoir catchment area on β-lactams was significant with a contribution of 37%.

Factor interactions occurred between parameters of the same as well as different types of antibiotics and mostly showed two-factor linear or non-linear enhancement effects. For instance, the interactions between reservoir catchment area and ten other factors all had an explanatory power of more than 50% for fluoroquinolones in waters (Fig. 4b). In particular, non-linear enhancing effects of reservoir catchment area and seasonal variation; catchment area and artificial impervious area; storage capacity and seasonal variation; water level and seasonal variation all had explanatory power at or above 80% for fluoroquinolones. Some single factors might have significant interactions with other factors even if they have no significant effect on a particular type of antibiotics.

GeoDetector's risk detector demonstrated that reservoirs located in subtropical and temperate regions were sinks for antibiotics (Table S4 and S5). Although artificial impervious area is an indicator of urbanization and human settlement (Gong et al. 2020), the percentage of artificial impervious area was not proportional to antibiotic concentrations in reservoirs' catchments. Sulfonamides and fluoroquinolones concentrations were higher in spring than in other seasons, while β-lactams tended to have higher concentration levels in winter. In sediments, concentrations of fluoroquinolones and tetracyclines were more likely to pose a potential risk in spring. Acidity and low temperatures both favored the preservation of antibiotics in sediments (Table S5).

Risks of Antibiotics to Ecosystem and Human Health

Most of the individual antibiotics had RQ values less than 0.01 (Table S6). However, 19 antibiotics posed risks to aquatic organisms in an individual or multiple reservoirs, including 7 sulfonamides, 1 fluoroquinolone, 5 tetracyclines, 3 macrolides, and 3 β-lactams. Of these, sulfamethoxazole and erythromycin posed a low to moderate risk to invertebrates / fish in dozens of reservoirs located in the Eurasian region. Sulfamethoxazole posed a high risk to invertebrates (RQ = 1.03) and medium risk to fish (RQ = 0.16) in Yeongsan Reservoir (Korea). Tetracycline, 4-epianhydrotetracycline, and Anhydrotetracycline presented a very high risk to three groups of aquatic organisms (RQ = 1.13–7.64 for algae; 1.52–20.38 for invertebrates; 1.01–4.17 for fish) in Keban and Karakaya Reservoirs (Turkey). Amoxicillin posed a high risk (RQ = 1.82) to algae in Qingcaosha Reservoir (China) and should be controlled as a priority.

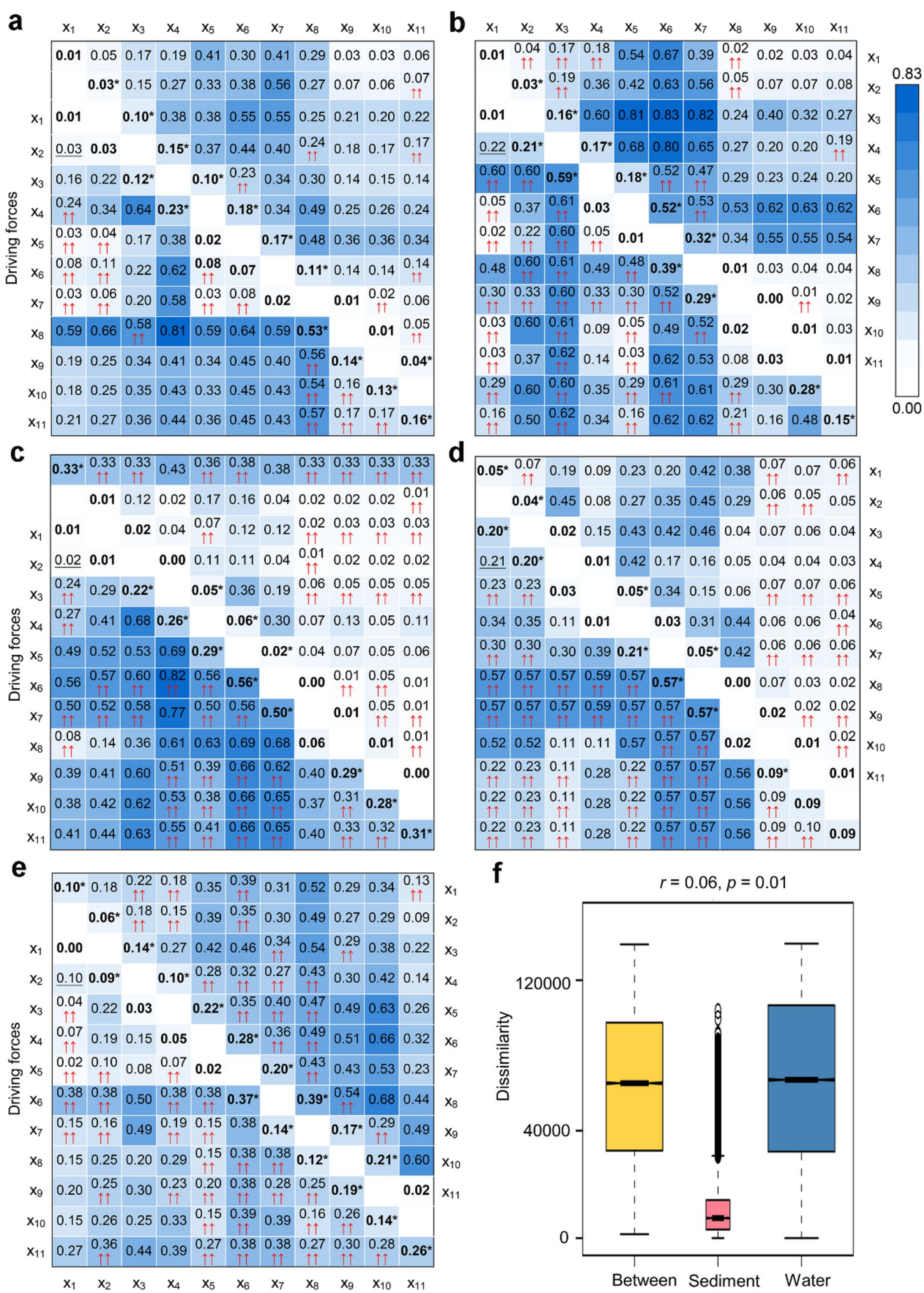
Qingcaosha, Keban, and Karakaya Reservoir were all at high risk of negatively impacting aquatic organisms due to antibiotic contamination (Fig. 5a). Additionally, there were 14 other reservoirs with a low risk for algae when considering cumulative risk effects. Invertebrates were more sensitive to antibiotic contamination and a higher proportion of reservoirs posed medium and low risks to them. A total of 27 reservoirs had $\sum$RQ values in the range of 0.01–0.09, 23 of which are located in China (Fig. 5b). There were 9 reservoirs with moderate risk and three with high-risk potential for invertebrates. $\sum$RQ values for invertebrates in Keban, Karakaya, and Yeongsan Reservoir were as high as 34.18, 19.08, and 1.17, with a very high ecological risk. Low, moderate, and high risks to fish existed in 14, 4, and 2 reservoirs, respectively (Fig. 5c). Both Keban and Karakaya Reservoirs had $\sum$RQ values greater than 3.50, with high-risk potential for fish.

Concentrations of 30 antibiotics were generally low enough so as to not pose a risk to humans. Except for epitetracycline (Keban Reservoir) for which the risk to small infants (< 3 months) needs further assessment (HQ = 0.25), all individual antibiotics had HQ values less than 0.20 (Table S7). Among the different age groups, infants (< 12 months) are more sensitive to antibiotic contamination, followed by children (1–11 years). Geographically, $\sum$HQ values for reservoirs in the European region were lower than those in the Middle Eastern and Asian regions (Fig. S1). In Asia, the cumulative health risk values for target antibiotics in reservoir waters were less than 0.20. In the waters of Keban and Karakaya reservoirs, the cumulative health risk value for toddlers (< 2 years old) due to high concentrations of tetracyclines exceeded 0.20.

Discussion

Antibiotics Distribution in Reservoirs and Its Determinants

The range of antibiotic concentrations in waters and sediments of different reservoirs spanned 1–5 and 2–3 orders of magnitude, respectively. The highest total antibiotic concentration and the highest abundance of tetracyclines were detected in reservoir waters in the Middle East. High levels of antibiotic concentrations were detected in reservoir sediments in South Africa, while sediment antibiotic


a
b
c
d
e
f
Driving forces
0.83
0.00
r = 0.06, p = 0.01
Dissimilarity
120000
40000
0
Between
Sediment
Water

◀**Fig. 4** Driving forces for sulfonamides **a**, fluoroquinolones **b**, tetracyclines **c**, macrolides **d**, and β-lactams **e** in waters (upper triangle; secondary y-axis) and sediments (lower triangle; primary x-axis). The *q*-values in bold font are driving forces for a single factor, and the other q-values were calculated for two-factor interaction. "*" represents statistically significant differences at $p < 0.05$ level. Underline values indicate the two-factor are independent of each other. "↑↑" indicate a two-factor enhancement effect and the rest are non-linearly enhanced. X_1—geographic location, X_2—latitude, X_3—season, X_4—artificial impervious area, X_5—water level, X_6—reservoir catchment area, X_7—reservoir capacity, X_8—hydraulic residence time, X_9—pH, X_{10}—water temperature, X_{11}—total organic carbon. **f** Analysis of similarity (ANOSM) to examine differences of antibiotics in waters and sediments

concentrations were relatively low in Europe. China has a high frequency of detection of different types, which may be explained by the high production and consumption of antibiotics (Schoenmakers. 2020). Different types of antibiotics used and consumption patterns of different countries / regions (Kummerer. 2009) and different levels of awareness about antibiotics risk and related environmental testing might be the main reason for geographical differences detected in this study.

Antibiotics distribution in reservoir waters and sediments showed different influence patterns due to differences in environmental media. The explanatory power of reservoir characteristics (water level, size of reservoir catchment area, and reservoir water storage capacity), seasonal variations, and water quality parameters on distribution of antibiotics in reservoir sediments was stronger compared to waters. In particular, reservoir characteristics, latitude and geographical location had significant and strong effects on macrolide antibiotics in sediments. However, 11 considered single factors all had a small effect on macrolides in waters. Factor interactions, such as reservoir capacity and latitude as well as reservoir capacity and seasonal variation, all had a greater coupling effect on macrolides in waters. This suggests that waters, as the most direct receptors of contaminants, are more diverse in their antibiotic sources and influencing factors. Thus, mitigation of antibiotic contamination in reservoir waters is more urgent compared to sediments. Water quality parameters affect sorption, desorption, transformation, and diffusion of antibiotics in water and sediment media (Rico et al. 2012). When one of these water quality factors was altered, antibiotics were likely to migrate and transform in the water–sediment interface (Hu et al. 2018).

Antibiotics in reservoirs varied seasonally. Sulfonamides, fluoroquinolones, and β-lactams were usually high in winter/spring than in summer or fall. This may be attributed to low temperature or weaker light intensities that are not conducive to antibiotic degradation (Singh et al. 2019; Chen et al. 2020). Besides, winter and spring are high incidences of some livestock and poultry diseases among others, and antibiotics such as sulfonamides, tetracyclines, and fluoroquinolones, which are commonly used to treat or prevent diseases, will be used in large quantities during these seasons and enter into waters through excretion (Suda et al. 2014). However, macrolides showed no significant seasonal variation either in waters or in sediments. Interactions of season and latitude as well as season and reservoir characteristics had a higher explanatory power for macrolides. Consequently, different types of antibiotics are influenced by different factors and need to be considered separately when exploring their pollution mechanisms (Liu et al. 2022).

The influence of reservoir characteristics on antibiotic concentration was not simply linear and different types of antibiotics exhibited different influence patterns. For example, small reservoirs were more likely to accumulate sulfonamides, but their antibiotic contamination levels increased with further reduction in reservoir capacity. This suggests that small reservoirs located in densely populated areas might have higher levels of contamination due to low dilution.

Effects of Antibiotics and Their Risks

Most antibiotics had negligible risk potential for aquatic organisms in reservoirs, but the potential risks of sulfamethoxazole, sulfamethazine, erythromycin and amoxicillin for aquatic organisms in Eurasian reservoirs requires attention. Among them, erythromycin has been listed as a priority contaminant for control in the EU (Szekeres et al. 2018) and is a bioaccumulative chemical that requires strict control of its thresholds in reservoirs. Invertebrates were at low risk in 34%, at moderate risk in 11%, and at high risk in 4% of the total number of reservoirs investigated. Fish were at low risk in 18%, at moderate risk in 4%, and at high risk in 3% of all reservoirs evaluated. The probability of algae exposed to antibiotic contamination risk was relatively low, with 18% at low risk and 4% at high risk. Keban and Karakaya Reservoirs in Turkey posed a high risk to all three groups of organisms due to their abnormally high levels of four tetracycline antibiotics caused by aquaculture wastewater discharges (Topal and Topal. 2016).

Overall, the 30 antibiotics assessed in this study did not pose a risk to human health through drinking water consumption. This is consistent with other studies that have assessed health risks of antibiotics in reservoirs, where antibiotics pose a negligible risk to human health (Gaffney et al. 2015; Chen et al. 2020).

However, there was a wide range of antibiotics in reservoirs, and combined effects and long-term risks due to their interactions has not been considered. Even at currently accepted environmentally safe concentration levels, antibiotics may still cause effects such as spread of bacterial resistance and disruption of ecosystem balance, leading to risks that are unforeseen and beyond those triggered

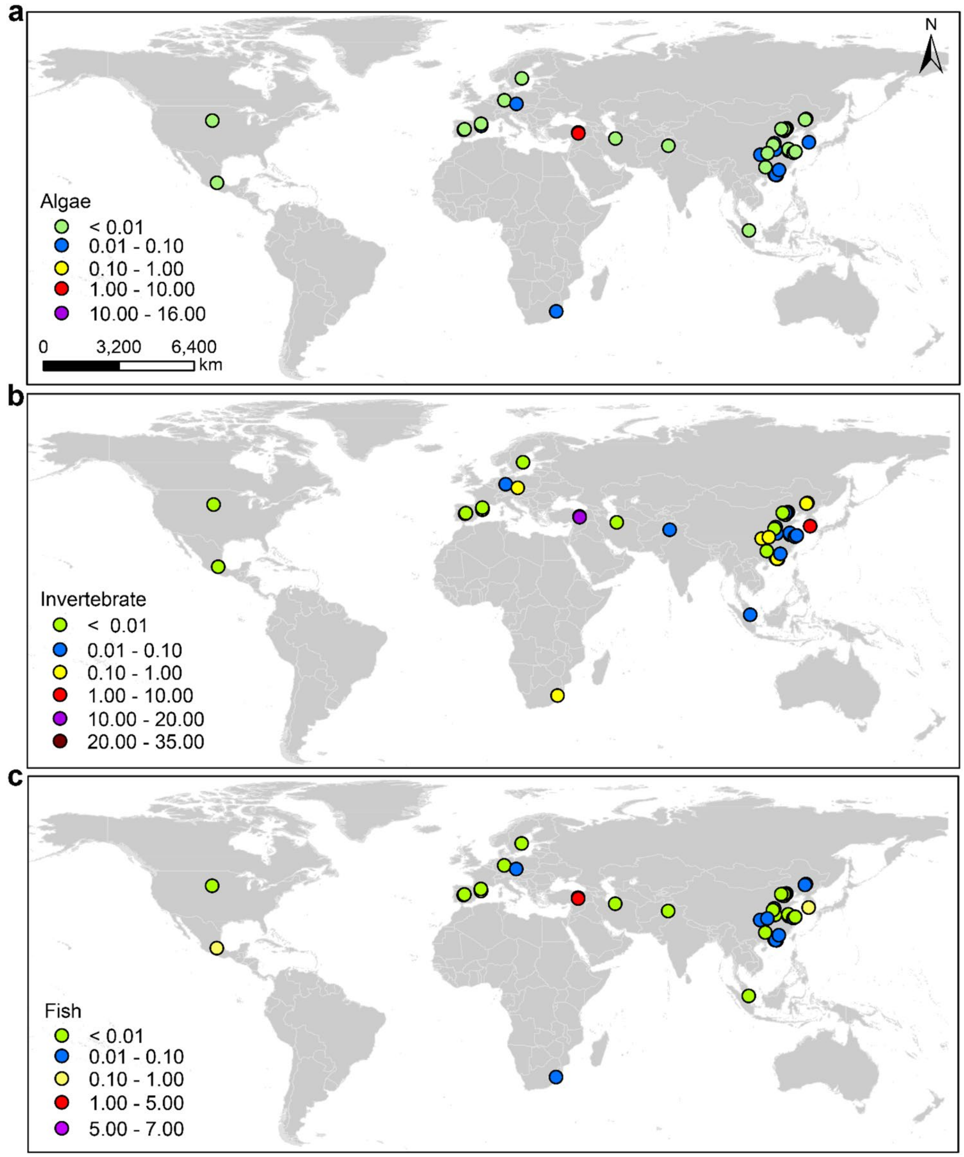


Fig. 5 Spatial distribution of cumulative risk quotient (∑RQ) of antibiotics in reservoir waters for algae **a**, invertebrates **b**, and fish **c**

by their toxic effect (Zhu et al. 2018). Notably, antibiotic occurrence has not been investigated in some reservoirs in less developed regions, but these regions are actually vulnerable and have a higher risk potential for antibiotic contamination due to limited water treatment capacity and poor sanitation (Singh et al. 2019; Ott et al. 2021). In order to compare and assess the level and combined risk of antibiotic contamination in reservoirs from different geographic regions, it is necessary to (i) build on an interdisciplinary perspective to obtain environmental behavior of antibiotics and to establish close collaborations with scientists and health professionals collecting clinical data (Larsson et al. 2018) and (2) to extend antibiotics sampling and monitoring efforts to regions of the world where data is lacking.

Challenges and Solutions

Our study shows that reservoirs in subtropical / temperate regions are more vulnerable to antibiotic contamination. Current antibiotic monitoring data are very limited for reservoirs located in Oceania, South America, and Africa. Additionally, the development and spread of antibiotic resistance have transcended species and boundaries to become an imminent "One Health" issues (Iskandar et al. 2020).

Antibiotics may be influenced by other factors, such as reservoir nutrients, dissolved oxygen, and distance of the sampling site from the dam. To obtain a global perspective on the dynamics of reservoir antibiotic distribution and their drivers in reservoirs, it is necessary to improve comparability among reservoir antibiotic studies and data accessibility.

Collecting and utilizing data from existing studies, addressing challenges associated with data-driven approaches (Eggimann et al. 2017), and encouraging routine monitoring of ecosystem antibiotics offer new possibilities for systematically elucidating global reservoir antibiotic contamination. Increased demand and willingness to share data could pave the way for cross-border regional cooperation, replication of transferable results, and deepening of existing research (Li et al. 2021). To encourage research reproducibility and data-sharing, adoption of a data availability survey tool in water resources field developed by Stagge et al. (2019) is expected to help authors and journals to self-assess and improve data accessibility and reusability.

Four priorities for future studies on antibiotic contamination in reservoirs are (Fig. 6): (i) expanding the scope of antibiotic contamination investigations in reservoirs; (ii) including reservoir, food chain, and human when studying antibiotic residues; (iii) paying attention to the influence of reservoir characteristics, socioeconomic parameters, and factor interactions on distribution of antibiotics in reservoirs; and (iv) improving comparability of studies and data accessibility. Addressing these issues will provide a more comprehensive insight into the interactions between antibiotics and environment as well as antibiotic contamination mechanisms from a global perspective that is not constrained by time, geography, and environmental conditions.

Conclusion

We constructed a systematic workflow to integrate 520 sample data from 80 reservoirs to demonstrate the distribution, determinants, and potential risks of antibiotic contamination in reservoirs at a cross-continental scale. The abundance and types of antibiotics in reservoirs varied widely across geographic regions. Reservoirs in subtropical/temperate regions should be considered critical control points for antibiotic contamination. Factors driving distribution of antibiotics in waters and sediments, and the extent of their influence varied primarily due to differences in environmental media. Antibiotics in reservoirs exhibited seasonal variations and residues of sulfonamides, fluoroquinolones and β-lactams were usually higher in winter/spring than in summer or fall. Reservoir characteristics were generally higher driving forces of antibiotics but were not simply linearly correlated with antibiotic concentrations. Reservoir antibiotics pose a negligible risk to human health, but aquatic organisms, especially invertebrates, have a high probability of being at low, moderate, or high risk for antibiotics that have been detected in several reservoirs. Given the fundamental role of reservoirs for drinking water supply and our inevitable exposure to antibiotic contamination into account, there is an urgent need to expand monitoring and further assess antibiotic contamination in reservoirs to develop priority contamination control measures. This data-driven workflow, a systematic methodology based on constructed datasets and multivariate statistical techniques, sets a good example for transforming data science into applicable information, thus providing data to support more effective antibiotic contamination control.

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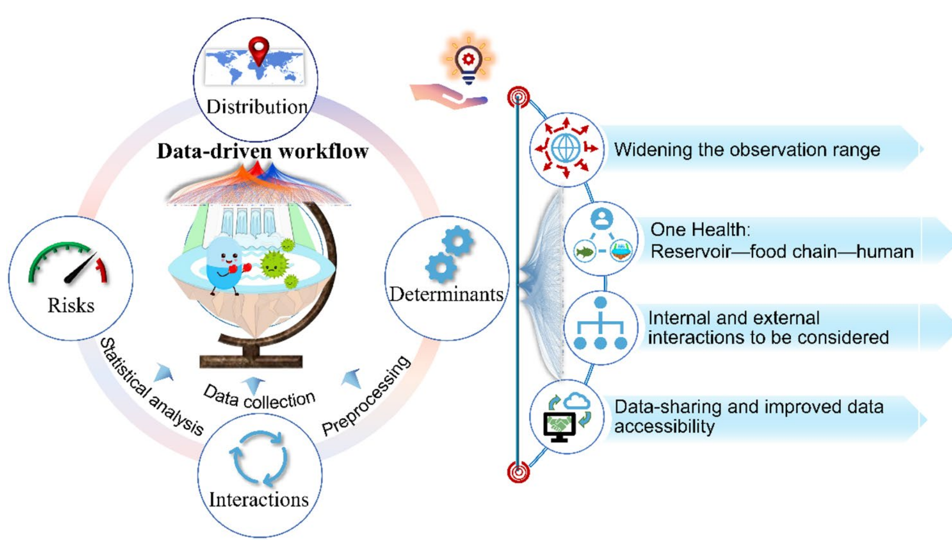

Fig. 6 Data-driven workflow and four priorities for future studies on antibiotic contamination in freshwater reservoirs

manuscript. The views expressed are those of the authors and do not necessarily reflect the views of MSTC and ANSO.

Author Contributions ZG: conceptualization, Methodology, Formal analysis, Writing & editing. WJB: Methodology, Formal analysis, Writing & editing. YX: conceptualization, Data curation, Visualization, Writing & editing, Supervision, Funding acquisition. EB: Analysis, and interpretation of data, Writing & editing. DL: analysis, Writing & editing. Y-GZ: writing, reviewing and editing.

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Data Availability The data supporting results and related information extracted from papers are available from the Supplementary Data file and at Zenodo: https://doi.org/ 10.5281/zenodo.5565706.

Declarations

Competing Interests We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

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