Occurrence and seasonal variations of antibiotic micro-pollutants in the Wei River, China

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Abstract

In this study, a systematic monitoring campaign of 30 antibiotics belonging to tetracyclines (TCs), macrolides (MLs), fluoroquinolones (FQs) and sulfonamides (SAs) was performed in the Xi'an section of the Wei River during three sampling events (December 2021, June 2022, and September 2022). The total concentrations of antibiotics in water ranged from 297 to 461 ng/L with high detection frequencies ranging from 45 to 100% for the various antibiotics. A marked seasonal variation in concentrations was apparent with total antibiotic concentrations being 1.5 and 2 times higher than those in the summer and autumn seasons, respectively. The main contaminants in both winter and summer season were FQs, but in the autumn SAs were more abundant, suggesting seasonal sources or more effective runoff for certain antibiotics during periods of rainfall. Combined analysis using redundancy and clustering analysis indicated that the distribution of antibiotics in the Wei River was affected by the confluence with dilution of tributaries and outlet of domestic sewage. Ecological risk assessment based on risk quotients (RQs) indicated that most antibiotics in water samples posed insignificant risk to fish and green algae, insignificant to low risk to Daphnia. The water-sediment distribution coefficients of SAs were higher than those of other antibiotics indicating that particle-bound runoff could be a significant source for this class of antibiotics.

Key words: antibiotics, seasonal variation, spatiotemporal distribution, urban river, ecological risk

1. Introduction

Emerging contaminants, such as pharmaceuticals, have attracted increasing concern due to their widespread occurrence, and potential deleterious effects on microbial populations (Li et al., 2022; Wilkinson et al., 2022). Among pharmaceuticals detected in the environment, antibiotics are the most abundant groups, and can be considered as “pseudopersistent” due to their continual input into the environment (Jia et al., 2018).

China is one of the world's largest producers and consumers of antibiotic products and it has been estimated that approximately 2.48×10^5 tonnes of antibiotics were produced in 2013, with 1.62×10^5 tonnes consumed, and an estimated 5.0×10^4 tonnes were believed to have been released into water and soil environments (Zhang et al., 2015). The majority of antibiotics are used in livestock and human medical applications, however, most antibiotics that are consumed are not completely metabolized with ~80-90% excreted via urine and faeces as the parent chemical or metabolites, conjugates or both (Bound and Voulvoulis, 2004; Kümmerer, 2009). In turn this environmental release is contributing to widespread antibiotic resistance in pathogens that represent a risk to human health and the environment (Hou et al., 2023; Nandi et al., 2023).

Due to the risks posed by antibiotic pollution, particularly in the aquatic environment, there are a growing number of studies that have assessed their occurrence in river systems (Wang et al., 2023; Wilkinson et al., 2022), lakes (Jia et al., 2023; Liu et al., 2018) and groundwater (Huang et al., 2020a). Various antibiotics, such as tetracyclines (TCs), fluoroquinolones

(FQs), macrolides (MLs), and sulfonamides (SAs) have been detected in urban river systems in China (Chen et al., 2018; Jia et al., 2018; Zhang et al., 2020)., although there are substantial variations in the antibiotic type and concentrations depending on the river system in question. In the Wenyu River in Beijing, TCs, MLs and FQs constituted the main antibiotic families, with the concentrations ranging from ND-1430.30 ng/L (Zhang et al., 2015), whereas elsewhere the FQs were the most abundant and had concentrations ranging from ND-214 ng/L in the Liaohe River (Qin et al., 2015) and 6.36-463 ng/L in the Pearl River (Li et al., 2018a).

Xi'an is a city with a total population of 13 million in 2021, and the Wei River stands as the largest river that flows through it. The Wei River receives treated municipal wastewater as well hospital wastewater, with evidence that antibiotics are not fully removed during the wastewater treatment process (Tran et al., 2018; Wang et al., 2019b). With an escalating population and swift urbanization of Xi'an, then contamination of freshwaters with antibiotics is likely to continue and possibly increase, particularly in light of the rising consumption of antibacterial agents within hospitals (Yan et al., 2018) as well as livestock farms that occur in the Wei watershed (Jia et al., 2018). Given the ongoing potential influx of antibiotics into the urban river environment (Chen et al., 2018), their adverse impact on non-target organisms (Burns et al., 2018), and their potential contribution to the development of genetic resistance and antibiotic-resistant bacterial strains (Zhao et al., 2021), heightened water monitoring becomes imperative.

The aims of this study were to: (1) determine the occurrence and spatiotemporal distribution of antibiotics in the Wei River system (as it flows through the Xi'an and Xianyang city regions); (2) explore seasonal and environmental factors that influence antibiotic contamination; and (3) to evaluate the sources of antibiotics and the environmental risks posed to key aquatic organisms.

2. Materials and methods

2.1. Chemicals and reagents

A range of antibiotics were chosen based on their prior detection or expected occurrence in surface water (Huang et al., 2020b; Jiang et al., 2021; Wang et al., 2019a). Non-labelled antibiotic standards including 3 TCs, 5 MLs, 14 SAs, 8 FQs and isotopic internal standards (tetracycline-d_4, roxithromycin-d_7, sulfamethoxazole-d_4 and ciprofloxacin-d_8) were acquired from Sigma-Aldrich (St. Louis, USA). Chemical reagents used in this study, such as acetonitrile, methanol and formic acid were of HPLC grade. The detailed information of 30 target antibiotics were shown in Table S1. Their corresponding isotopic internal standards can be found in Table S2.

2.2. Study sites and sample collection

The Wei River, a primary tributary of the Yellow River situated in northwestern China (Fig. 1), holds a pivotal role in Shaanxi Province's social and economic development.

Approximately 64% of the population, 56% of the agricultural land, 72% of the irrigation area, and 82% of the total industrial output value in Shaanxi Province are within the Wei River watershed (Song et al., 2015). This region faces significant challenges due to substantial sewage effluents and animal waste discharge, potentially containing diverse antibiotics. As per data from the Shaanxi Provincial Environmental Protection Bureau, there are 245 sewage discharge points along both banks of the Wei River, contributing over 700 million tonnes of sewage annually (Li et al., 2013).

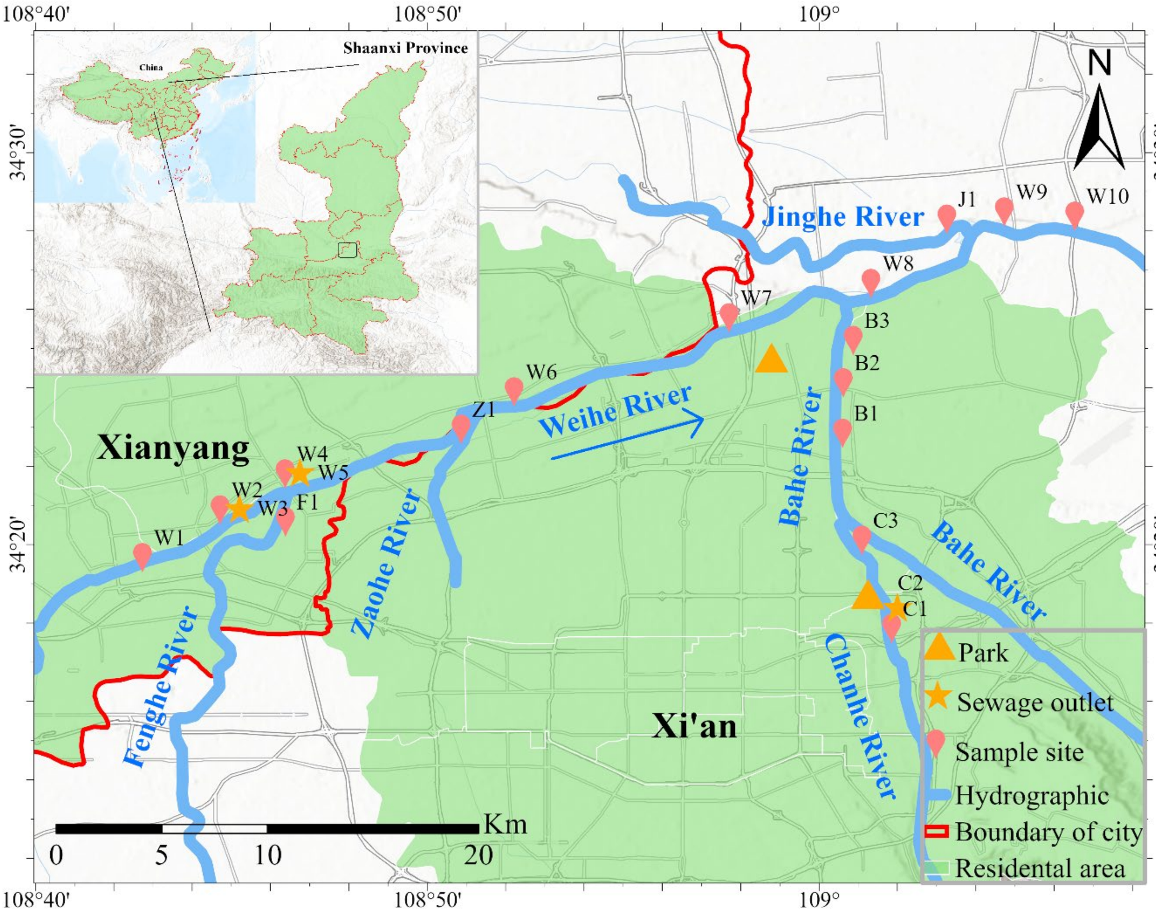


Fig.1. Study area and sampling sites.

Based on temperature, rainfall, and hydrological characteristics of the monitoring area in different months, three sampling campaigns were undertaken: December 2021 (winter season), June 2022 (summer season) and September 2022 (autumn season). During each campaign surface water was collected at 19 sampling sites along the Wei River. The detailed sampling sites are shown in Fig.1. The climate in the region is characterized as temperate continental monsoon with a mean annual precipitation of 610 mm approximately, 80% of which falls between June and October (Fig. S1). Sediment samples were also obtained at the same sites during the winter and summer seasons. The sampling sites along the Wei River, from upstream to downstream, were W1 to W10, with other tributary rivers represented by the letters F (Feng River), Z (Zao River), C (Chan River), B (Ba River) and J (Jing River). All tributaries flow into the Wei River, and sampling sites were chosen approximately 1 kilometer upstream from their confluence with the Wei River. W3, W5 and C2 were situated at the discharge points of effluents from two residential WWTPs (W3 and C2) and an industrial area (W5). In order to collect surface water (0.5 m below the water surface), grab sampling was conducted using 1000 mL prewashed brown glass bottles. Sediment samples (the top 5 cm layer) were obtained using a stainless-steel grab sampler with samples wrapped in aluminium foil and placed into polyethylene plastic bags. Triplicate samples comprised >10% of the total sample numbers. The water samples were analysed in the laboratory as soon as possible, and the sediment samples were stored at -20 ºC for subsequent analysis. The sampling and transportation procedures for each monitoring campaign were validated to be contamination-free through the use of field blanks employing Milli-Q water.

2.3. Analysis of environmental factors and antibiotics

The water temperature (WT), electrical conductivity (σ), total dissolved solids (TDS), salinity and pH were measured onsite at each sampling point using a multi-parameter water quality checker (DDBJ-350F, Lei-ci, China). The total organic carbon (TOC) of water was detected by TOC analyser (Vario cube, Elementar, German).

Each water sample (1 L) was filtered through a 0.22 μm fiberglass paper. Then 1 g EDTA-2Na and 50 mg ascorbic acid was added to the filtrate to remove metal ions and prevent target oxidation of target compounds; the sample pH was adjusted to 4 with HCl. After addition of 100 ng isotopically labeled standards, the samples were subjected to solid phase extraction (SPE) (Oasis, HLB cartridges, 500 mg, 6 mL). SPE cartridges were activated with 12 mL methanol, 6 mL ultrapure water and 6 mL ultrapure water (pH 4) prior to sample elution. The SPE cartridges were subsequently washed with 6 mL of ultrapure water, dried under vacuum and eluted with 10 mL of methanol. The eluent was concentrated to 100 μL under a gentle nitrogen stream, and the volume was reduced to 1.0 mL with methanol, then filtered through 0.22 μm nylon membrane before HPLC-MS/MS analysis. The sediment samples underwent sieving using a 2 mm mesh after freeze drying. Then 5 g dry sediment was spiked with 100 ng isotopically labeled standards. Antibiotics were extracted by ultrasonic extraction (30 min) using 20 mL acetonitrile and centrifuged at 3000 rpm for 5 min. The extraction process with acetonitrile was repeated twice. All the extracted solutions were combined and diluted to 1 L with ultrapure water before SPE. The extraction conditions mirrored those utilized for the water samples.

The target antibiotics were measured by an HPLC triple-quadrupole mass spectrometer (Agilent 1260 HPLC – Agilent 6470 MS/MS) equipped with the high-efficiency electron spray ionization (ESI). The HPLC condition was referenced from (Jiang et al., 2021), and the MS/MS parameters are outlined in Table S3. The method detection limit (MDL) and method quantitative limit (MQL) were determined as previously described (Cao et al., 2022) (summarized in Table S2). The recoveries of spiked target compounds and recoveries of isotopically internal labelled standards ranged from 70-120%. The relative standard deviations of the triplicate samples were <30%.

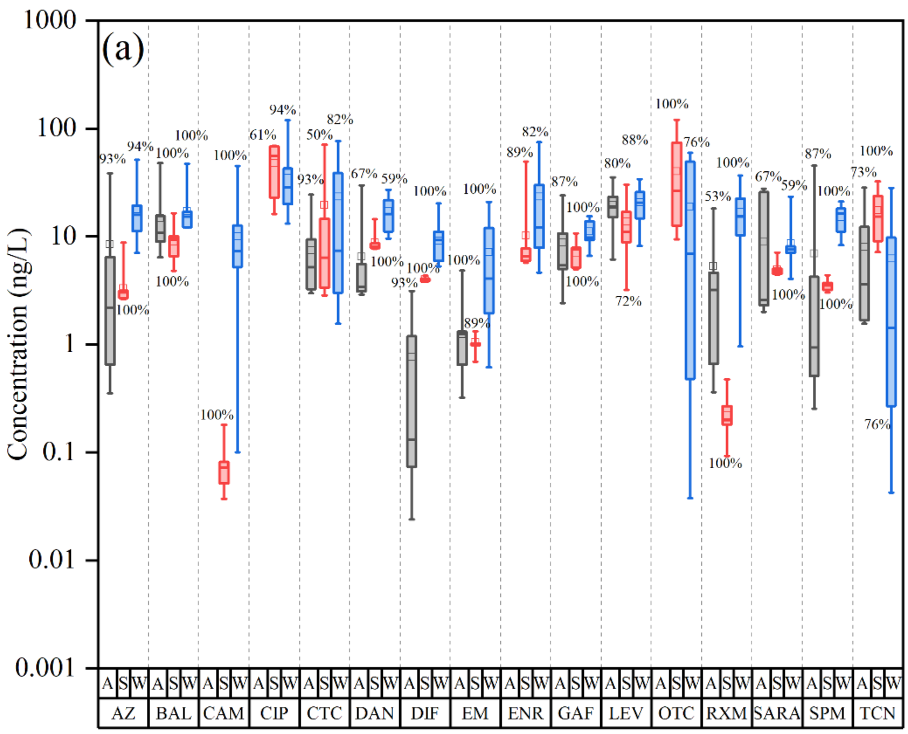
2.4. Statistical analysis and environmental risk assessment

To delineate the primary sources of antibiotic pollutants, then clustering analysis was used on the data along with redundancy analysis (RDA) to illuminate the link between antibiotic concentration levels and environmental factors. The clustering, RDA and circos-plots were conducted using the OriginPro 2024 (Learning Edition) software. The ecological and human health risks posed by antibiotics in the aquatic environment were assessed utilizing the risk quotient (RQ) method (Text S1).

3. Results and discussion

3.1. Profiles of antibiotics in the Wei River

As shown in Fig. 2 and Table S4, a total of 30 antibiotics were detected in the surface water of the Wei River during the three sampling campaigns, with individual concentrations ranging from <MDL -145.21 ng/L. The order of total concentrations among various antibiotic groups was as follows: FQs (11.09-216.12 ng/L), SAs (11.64-146.46 ng/L), TCs (nd-127.77 ng/L) and MLs (1.11-105.63ng/L). The antibiotics consistently displaying the highest concentrations (mean >50 ng/L) were CIP, ENR, SMR, CTC, OTC and AZ. All the detected antibiotics had mean concentrations >1 ng/L, in at least one season. Overall, the antibiotics were consistently and extensively detected throughout the watershed, indicting an abundance of antibiotic sources in this region.



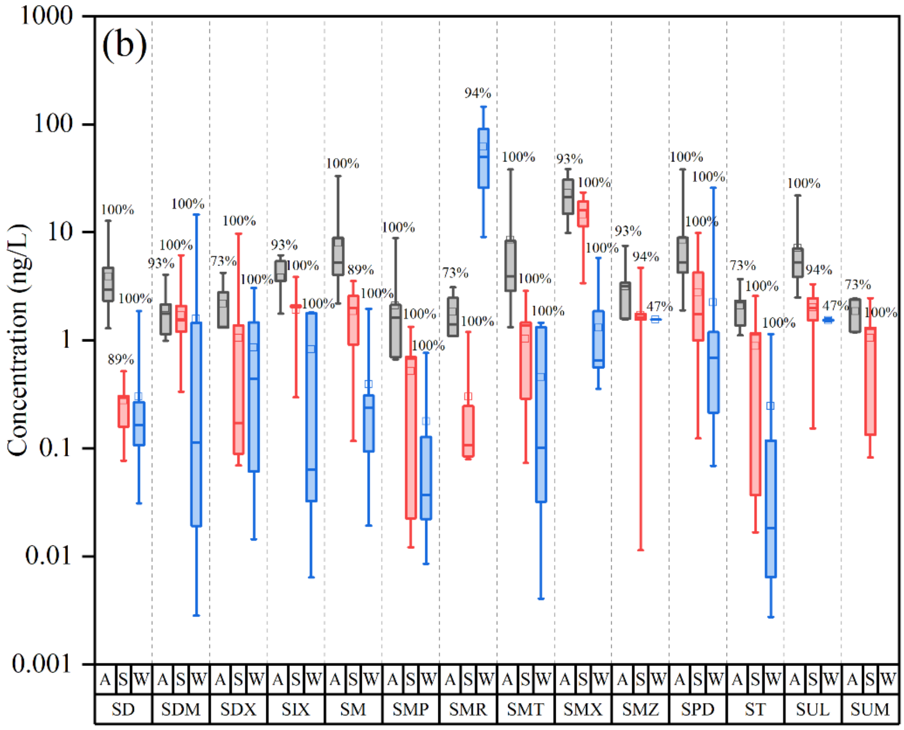
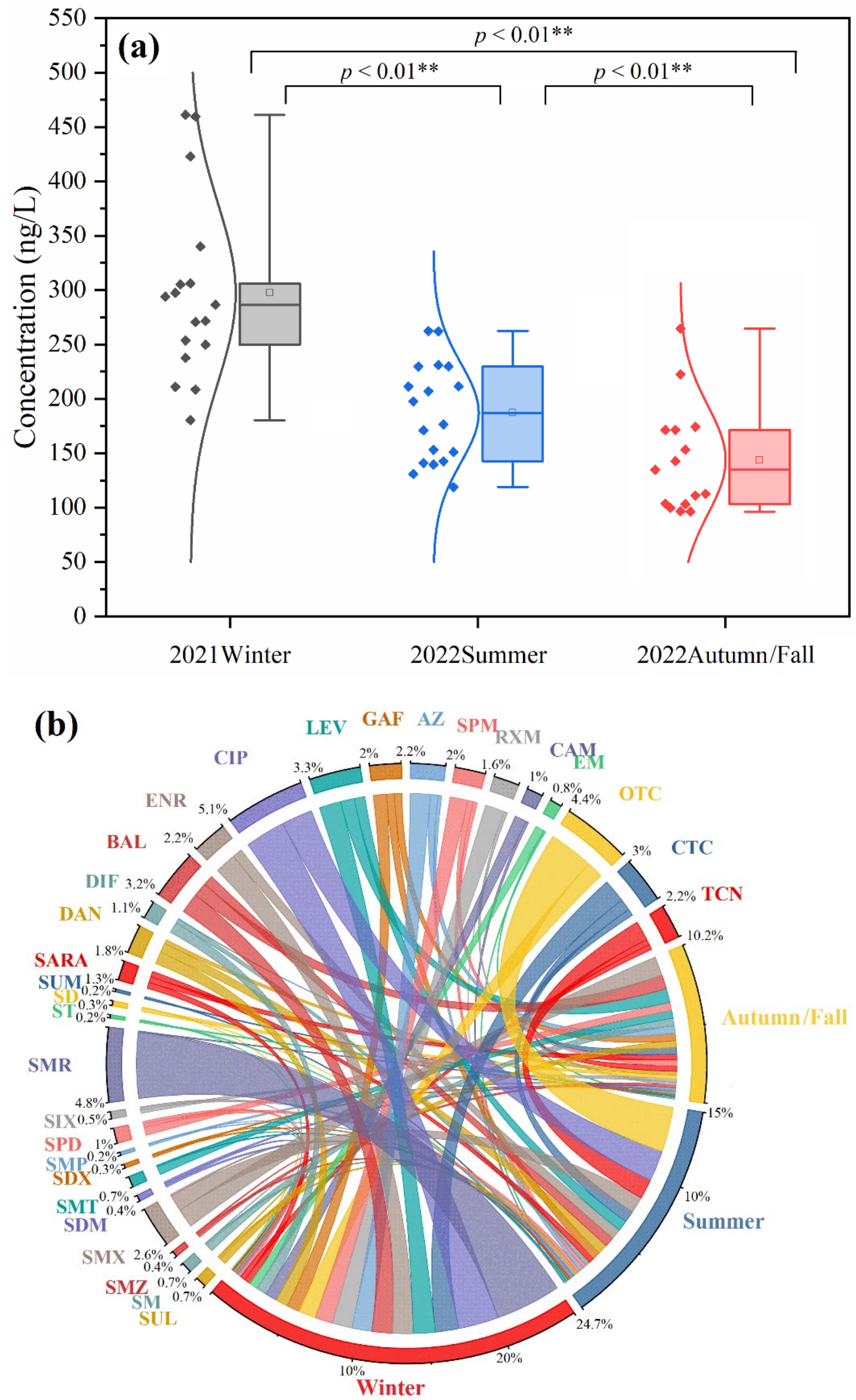


Fig.2. Occurrence of antibiotics in surface water: (a) TCs, MAs and FQs; (b) SAs. Above each corresponding boxplot, the detection frequency of each compound is marked. The box signifies the 25th and 75th percentiles, while the whiskers illustrate the 10th and 90th percentiles. Within each box, the solid horizontal line portrays the median, and the square denotes the mean. The x-axis label notation is as follows: W for winter, S for summer, and A for autumn.

In comparison with other studies investigating antibiotics in freshwater systems (Table S5, S6), Jiang et al. (Jiang et al., 2021) reported concentrations of 61 PPCPs (including 40 antibiotics) in the Yangtze River Delta. The maximum concentration of 596 ng/L (SUL) was ~27 fold higher than that reported in this study (21.86 ng/L), with the overall mean value of the various collection events ~4 fold higher. It is noteworthy that the Yangtze River Delta receives significant livestock farming runoff and wastewater which may have contributed to the relatively higher concentrations compared to this study. In an earlier study, Wang et al. (Wang et al., 2019a) also measured antibiotics in the Wei River during a spring (May) sampling campaign. The range of detected concentrations (nd-270.60 ng/L) was comparable to this study. Generally, antibiotics were detected within the concentration range of several ng/L to hundreds of ng/L, with 90% of all compounds were <100 ng/L. This aligns with antibiotic concentrations reported in other prominent rivers across China over the last 10 years or so (Li et al., 2018b).

3.2. Temporal variation of antibiotics in the Wei River

Fig. 3a illustrates the seasonal profile of antibiotic concentrations in the Wei River. The total (Σ–antibiotics) concentrations follow the order: winter > summer > autumn, and pair-sample analysis confirms significant differences (*t*-test, $p < 0.01$) in the distribution of antibiotic concentrations between seasons. This contrasts with the trend in rainfall (highest during the autumn) (Fig. S1), indicating the likely effect of dilution on the antibiotic concentrations (Ding et al., 2017; Li et al., 2019). Moreover, higher temperatures, increased flow, intensified light exposure, and heightened microbial activity contribute to accelerated abiotic and biotic degradation processes, may cause concentrations of many antibiotics to fall during the summer and early autumn seasons (Li et al., 2018a; Lindholm-Lehto et al., 2016; Ma et al., 2017; Wang et al., 2017). In addition, two outlets of residential WWTPs (W3) and industrial effluents (W5) were closed during the sampling collection of the autumn sampling campaign. Both outfalls are in the upstream of this study area, which may have contributed significantly to the overall reduction in the antibiotic concentrations.


(a)
Concentration (ng/L)
0
50
100
150
200
250
300
350
400
450
500
550
p < 0.01**
p < 0.01**
p < 0.01**
2021Winter
2022Summer
2022Autumn/Fall
(b)
CIP
LEV
GAF
AZ
SPM
RXM
CAM
EM
OTC
CTC
TCN
ENR
BAL
DIF
DAN
SARA
SUM
SD
ST
SMR
SIX
SPD
SMP
SDX
SMT
SDM
SMX
SMZ
SM
SUL
3.3%
2%
2.2%
2%
1.6%
1%
0.8%
4.4%
3%
2.2%
10.2%
5.1%
2.2%
3.2%
1.1%
1.8%
1.3%
0.2%
0.3%
0.2%
4.8%
0.5%
1%
0.2%
0.3%
0.7%
0.4%
2.6%
0.4%
0.7%
0.7%
Autumn/Fall
15%
10%
Summer
24.7%
20%
10%
Winter

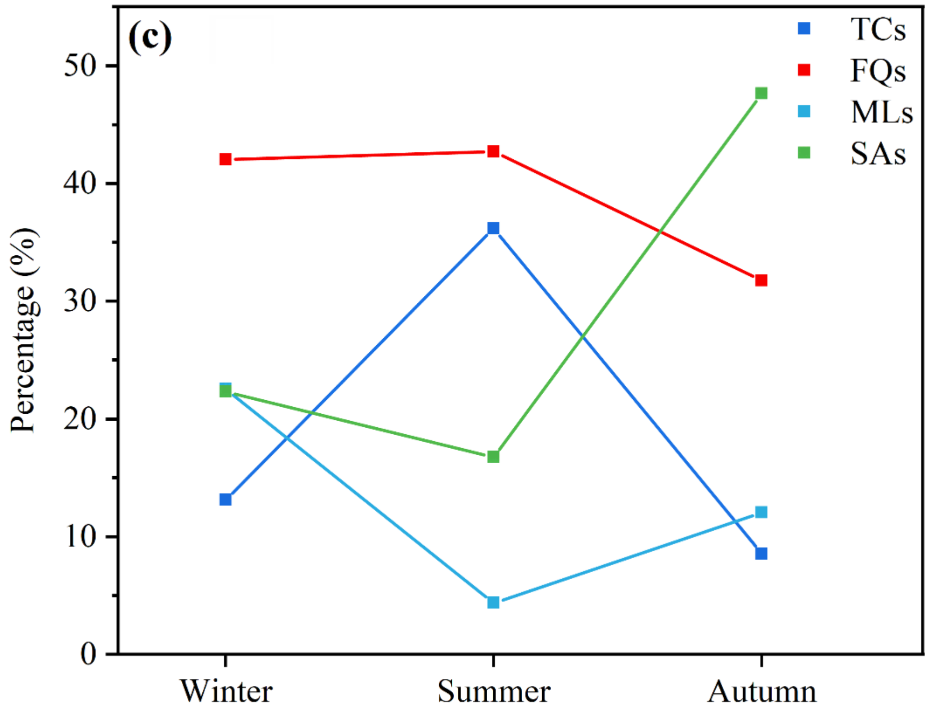


Fig. 3. Temporal variation of antibiotics in 2021 (winter season) and 2022 (summer season and autumn season): (a) Boxplot of total concentration; (b) circos-plot of antibiotic composition; (c) proportion of antibiotic distributions along different seasons.

The distributional relationship between the various antibiotics and the different seasons are visualized using a circos-plot in Fig. 3b. Compared with the summer and autumn seasons, the residual of antibiotics was much higher during the winter. FQs were generally dominant in two seasons, comprising 42.0% and 42.7% of total concentration in winter and summer seasons, respectively. As the typical antibiotics to treat bacterial pathogens, FQs are extensively used in both human and veterinary medicine. For example, the CIP annual usage reached 5340 t in China in 2013, positioning it as the sixth most utilized antibiotic (Zhang et al., 2015). In the four categories of antibiotics, MLs are widely used in the treatment of respiratory tract infections in humans, driven by seasonally (winter) associated pathologies.

MLs concentrations were found to be the highest during winter and this was also observed by (Zhao et al., 2017) who reported seasonal trends in the Yangtze River estuary. In contrast, SAs accounted for 47.6% of the total antibiotic concentration notably during the wetter autumn season. Amidst high precipitation, elevated humidity, and fluctuating temperatures during summer in the Xi'an city area, there's a heightened potential for livestock disease, potentially leading to increased usage and subsequent discharge of SAs. SAs find extensive use as antibacterial agents in poultry and aquaculture, primarily owing to their cost-effectiveness (Chen et al., 2018). In the Haihe River basin, (Luo et al., 2011) reported that SAs in the soil or associated manure could be transported into river water through efficient surface runoff during the autumn, especially as SAs exhibit relatively low rates of partitioning to organic matter. SAs are rarely used in clinical treatment (humans) due to their side effects; thus, it is considered that they are representative of livestock sources. However, in the study, FQs used predominantly as human antibiotics were detected at relatively high levels in the two seasons. Fewer antibiotics accompanied by lower concentrations in the rivers were found during the autumn (Fig. 3b), which is consistent with findings of (Ma et al., 2017; Sui et al., 2011).

The highest concentrations observed during the winter months could be linked to the seasonal consumption pattern. Numerous studies have indicated that antibiotic consumption peaks during winter, a time when animals (and humans) are more prone to bacterial infections (Ben et al., 2017; Looft et al., 2012; Wang et al., 2019b). OTC and CIP were the primary antibiotics detected during the summer, constituting approximately 21.4% and 14.8% of the total concentration, respectively (Fig. 3b). The average detection frequency of OTC across a broad array of study sites has been noted to be around 50% (Hughes et al., 2013), whereas in this study OTC was detected in all water samples (e.g. 100%) potentially due to its usage for both human medical and animal veterinary purposes (Table S1).

In Fig. 3c, variations in antibiotic proportion across different seasons are depicted. Specifically, TCs exhibit a notable increase during the summer, whereas MLs and SAs demonstrate a declining pattern. This can be attributed to the widespread use of TCs, particularly as growth promoters in both livestock and aquaculture during the summer season (Liu et al., 2017). Transitioning to autumn in Xi'an, characterized by high temperatures and humidity, there is a heightened susceptibility to livestock diseases. Fig. 3c illustrates a significant increase in the proportion of SAs during the autumn. SAs are commonly employed in animal husbandry and aquaculture to combat bacterial infections (Shen et al., 2023). It can be seen that during both summer and autumn, the use of veterinary drugs in the surrounding area emerges as the primary source of antibiotic contamination. However, a shift is observed in the winter season, with FQs occupying a larger proportion due to their usage in human therapeutic contexts. Winter, marked by a heightened incidence of seasonal viral and bacterial-induced influenza, consequently, leads to increased discharge of such antibiotics into municipal wastewater.

When antibiotics are introduced into freshwater systems, they undergo physical and chemical processes such as sedimentation and degradation. The degradation mechanism of antibiotics influences their final occurrence in the environment. There are various mechanisms of antibiotic degradation in the environment, which can be biotic and/or non-biotic, and dependent on the physicochemical properties and environmental conditions such as pH, TOC, temperature (Kümmerer, 2009; Wohde et al., 2016). Therefore, providing information about the correlations between antibiotic concentrations and water parameters is essential but also presents a major challenge, especially concerning analytical determinations and forecasting development trends. RDA is an effective statistical way to predict the correlation between antibiotic occurrence and environmental parameters. As shown in Fig. 4, the antibiotics and selected environmental factors accounted 89.2% of the total variance observed in the antibiotics. The three sampling events were distributed or grouped into four quadrants based on the influence of different environmental factors (Table S7). The concentration of TCN and OTC, for example, showed a significant relationship with pH, while a positive relationship was observed between most of the FQs and TOC, TDS, σ and salinity. There was a negative relationship between MLs and pH, and the SAs are inversely related to TOC, TDS, σ and salinity. Several studies have demonstrated that pH is an important factor that affects the ionisation status of antibiotics in solution (Huang et al., 2020b; Liu et al., 2016), with ionised or neutral forms of the chemicals showing quite different sensitivities to partitioning and photodegradation processes, which in turn will influence their removal and hence longevity in the water column (Ge et al., 2018; Ge et al., 2019a). Recent studies have underscored the significance of transformation products of MLs in the aquatic environment driven in the main by hydrolysis (Montone et al., 2024). Changes in pH affect the hydrolytictendencies of many antibiotics , subsequently influencing the direction and efficiency of aqueous degradation. Moreover, the degradation of TCs, in contrast to other antibiotics, is significantly influenced by the pH and temperature of the surface water (Doi and Stoskopf, 2000). An increase in temperature generally favors most degradation processes. This observation aligns with the phenomenon depicted in Fig. 4, where water temperature (WT) exhibits a negative relationship with most antibiotic concentrations.

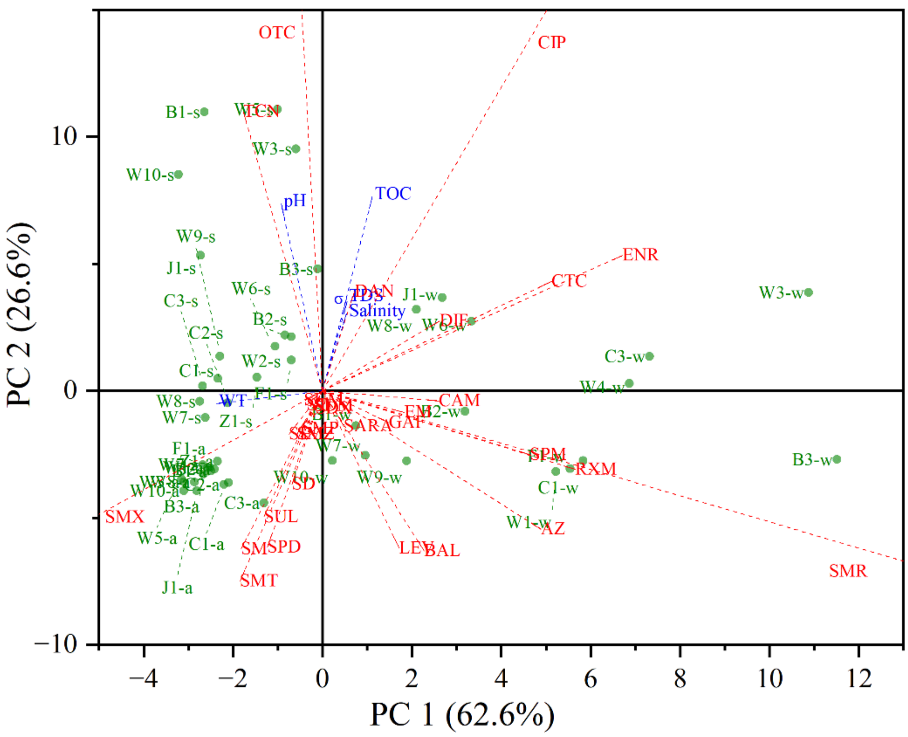


Fig. 4. Redundancy analysis (RDA) of the relationships between environmental factors (blue arrows) and the concentrations of antibiotics (red arrows). (WT: water temperature; TOC: total organic carbons; TDS: total dissolved solids; σ: electrical conductivity, besides, the green fill of point represents samples in winter season(w), summer season(s), autumn season(a)).

Many studies have now consistently indicated that antibiotic levels in freshwater systems are generally higher in winter than in summer (Burns et al., 2018; Li et al., 2018a). The reasons for temporal variations vary across studies. Some studies attribute lower contaminant levels to increased river flow or discharge during high-water flow periods, which serves to dilute contaminant levels (Kasprzyk-Hordern et al., 2008; Kolpin et al., 2004). Alternatively, some suggest that higher antibiotic concentrations during winter might align with increased winter usage patterns (Sun et al., 2014) or reduced biodegradation processes during this season (Moreno-González et al., 2014). However, other factors are likely to influence concentrations in water courses. For example, after rainfall incidents local surface waters can be polluted by runoff from fields treated with digested sludge or livestock slurries, confounding seasonal trends in antibiotic concentrations that might have been observed elsewhere (Bernot et al., 2013; Jiang et al., 2021). Surface runoff from rainfall can result in two distinct outcomes, the dilution effect and the introduction of pollution. The pollution status of the area surrounding the river determines which of these two effects is the dominant factor in the area. Based on the results of our study, the level of antibiotic pollution in the Wei River was significantly lower during the summer and autumn seasons. Therefore, it is more likely that surface runoff is carrying large amounts of rainwater to the Wei River, thereby diluting the original antibiotic concentration in the river, rather than transporting large quantities of these pollutants into the Wei River. Furthermore, several factors are proposed that account for seasonal variation in antibiotic concentrations including: usage patterns (Ma et al., 2017), ambient water temperature (Azzouz and Ballesteros, 2013), light intensity (Ge et al., 2019b), and microbial activity (Xu et al., 2011). Given the higher concentrations during low-flow periods in this study, we posit that flow, or more precisely, its dilution effect, seem to be a primary driver influencing the observed seasonal variability.

3.3. Spatial distribution of antibiotics in the Wei River

In general, total antibiotic concentrations gradually decreased from upstream to downstream during the both the winter and summer sampling months (Fig. 5 a and b). During these seasons, the total concentration at the upstream sampling points (W1-W5, 170.99-461.14 ng/L) was statistically significantly higher than the midstream (W6 and W7, 139.54-306.07 ng/L) and downstream sample sites (W8-W10, 142.62-297.39 ng/L). On the one hand, there were identifiable potential sources and hotspots of contamination near the upstream area. The highest concentration of total antibiotics was 461.14 ng/L at site W3 in winter and 262.42 ng/L at site W5 in summer. These two sites were influenced by a major domestic sewage outlet and an industrial area sewage outlet, respectively. Moreover, the population density increases from upstream to downstream (Wang et al., 2019a), and the detected antibiotics exhibited a similar pattern in both winter and summer seasons. On the other hand, the middle and downstream reaches might have been affected by dilution effects and in-stream degradation after many tributary rivers confluence (Burns et al., 2018). The Wei River in the study area is feed by four rivers, Feng River, Zao River, Jing River and Ba River. The combined average annual runoff of these four tributaries is about one-third that of the Wei

River. This dilution may have contributed to the continued weakening of pollutant concentrations down the Wei River. Nevertheless, the distribution of antibiotics within the watershed during the autumn season differed from that observed in winter and summer. As shown in Fig. 5c, the total concentrations of pollutants in the region were lower upstream than that of midstream and downstream. We noted that the sewage outlets nearby the W3 and W5 were all closed during the event of autumn season sampling, in the absence of point source pollution upstream, this was preliminarily inferred as being the pollution problems posed by possible tributaries will come to the fore.

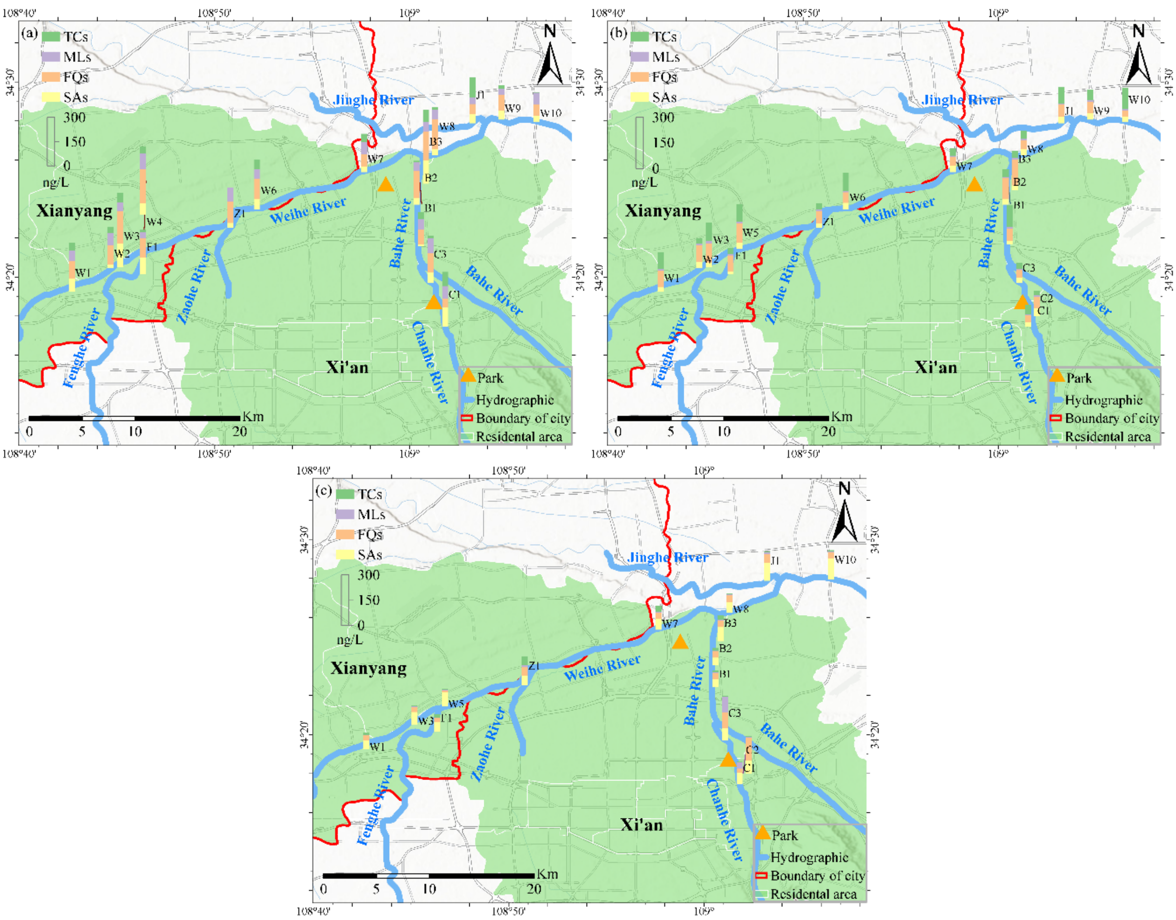


Fig. 5. Accumulative concentration of detected compounds at each sampling site at different seasons in water (a. winter season; b. summer season; c. autumn season).

As for the tributaries, the notably elevated antibiotic concentrations were detected in Ba River (including B1-B3), attributed to the presence of poultry and livestock breeding areas around the Baqiao District, as well as dairy cattle and aquaculture zones near the Weiyang District (Wang et al., 2019a). In addition, the concentration of antibiotics in B3 was higher than that of B2. They were situated upstream and downstream, respectively, of Xi'an ChanBa National Wetland Park. This park is open year-round for recreational activities for nearby residents, and fluctuations in antibiotic concentrations downstream may be linked to human activities within this area (Jia et al., 2018). In comparison to B1-B3, the concentration of antibiotic in W8 was lower. Site W8 is located one kilometre after the Ba River joins the Wei River. This suggests that the tributaries could effectively dilution partial antibiotics of main river streams that flow through residential. The antibiotics concentrations in C2 were much higher than C1 and C3, suggesting susceptibility to anthropogenic influences. This disparity could be due to factors like the impact of rubber dams (e.g., less water exchange) and phytoremediation by plants between the C2 and C3 (this area is a compact wetland park).

In order to highlight the distinctions among the various spatial sampling sites and trace their sources, the clustering was conducted based on the concentrations of individual antibiotics (Fig. 6), and the findings revealed that the monitoring sites could be categorized into four distinct groups. The site of red group (J1 in winter and summer) is located in the Jing River, which is the only tributary in this study that does not through human settlements. While the profiles of W9 and W10 (blue group) from downstream were closely related. These results suggested that the confluence of the clearer Jing River has played a major role in local to changing the water quality of the Wei River. In fact, there exists a renowned local attraction where observers on the shore can distinctly perceive the contrasting hues between the confluence of the Jing River and Wei River, and this demarcation remains discernible as it meanders downstream until the two rivers intermingle completely. The remaining two groups observed the first axis are the grey group and green group, suggesting similarities among these sites concerning both the distribution of antibiotics and seasonal environmental factors. The green one includes most of sampling site from winter, where W7-w and W8-w were closer to the middle circle and W3-w and W4-w are closer to the outside. These finding imply distinct sources of the antibiotics in the vicinity of the two tributaries, Ba River and Feng River. Most of the sampling sites from summer and autumn season were clustered in the grey group, but C1-a and C3-a were not close to either the cluster on the left representing the autumn season or the cluster on the right representing the summer season. There are some dams between these two sites, and maybe their influence on water pattern characteristics becomes more pronounced during periods of significantly increased precipitation.

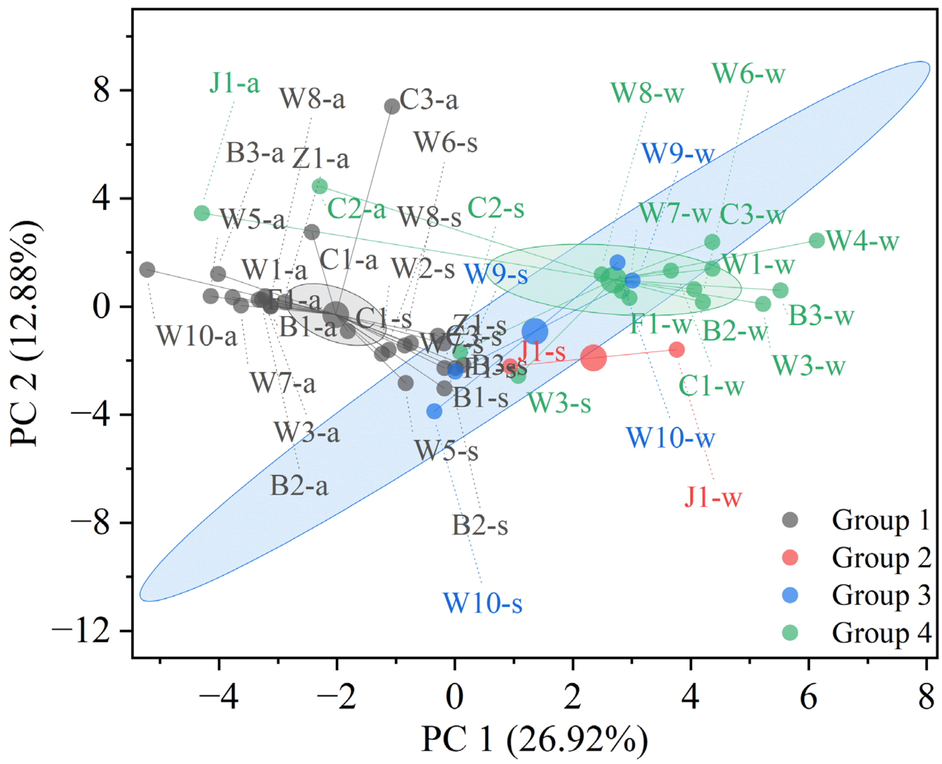


Fig. 6. Cluster analysis of the antibiotics at the Wei River sites, the colourful fill of point represents samples in winter season(w), summer season(s) and autumn season(a).

In essence, these findings highlight a range of environmental processes, including seasonal fluctuations, dilution, and in-stream degradation, each operating to varying degrees in adjacent rivers. Consequently, these processes contribute to distinct spatial patterns in antibiotic concentrations among different sampling sites. On the one hand, this seasonal difference is evident in the markedly different temperatures and flow between summer and winter. On the other hand, cluster plot also shows a substantial divergence between the occurrence of antibiotics before and after the confluence of the Jing River into the Wei River.

3.4. Ecological risk assessment

In this study, the RQs of the antibiotics for three target aquatic species were estimated, with an overview provided in Text S1. Generally, all antibiotics exhibited a negligible or insignificant risk to fish and green algae across the majority of river water samples (Fig. 7a), while presenting insignificant to low risk to Daphnia. The RQs derived from the Wei River were comparable to those derived from sampling conducted in 2016 (Wang et al., 2019a), but were >10 fold lower than those derived from other major rivers in China (Li et al., 2018b). Among individual antibiotics, SMR posed the highest risk to Daphnia during the winter and RQs very close to the medium risk threshold. In addition, AZ and SPM were deemed to present a low risk to Daphnia in winter and autumn seasons. Among the different types of antibiotics (Fig. 7b), SAs made a substantial contribution to the risk posed to Daphnia and fish in all seasons, primarily owing to their high chronic toxicity (Table S8). This is consistent with previous studies which have shown that SAs are more likely to have an ecotoxicological impact (Ding et al., 2017; Li et al., 2018a; Yan et al., 2013). TCs, FQs and MLs generally pose an insignificant risk to organisms across various trophic levels.

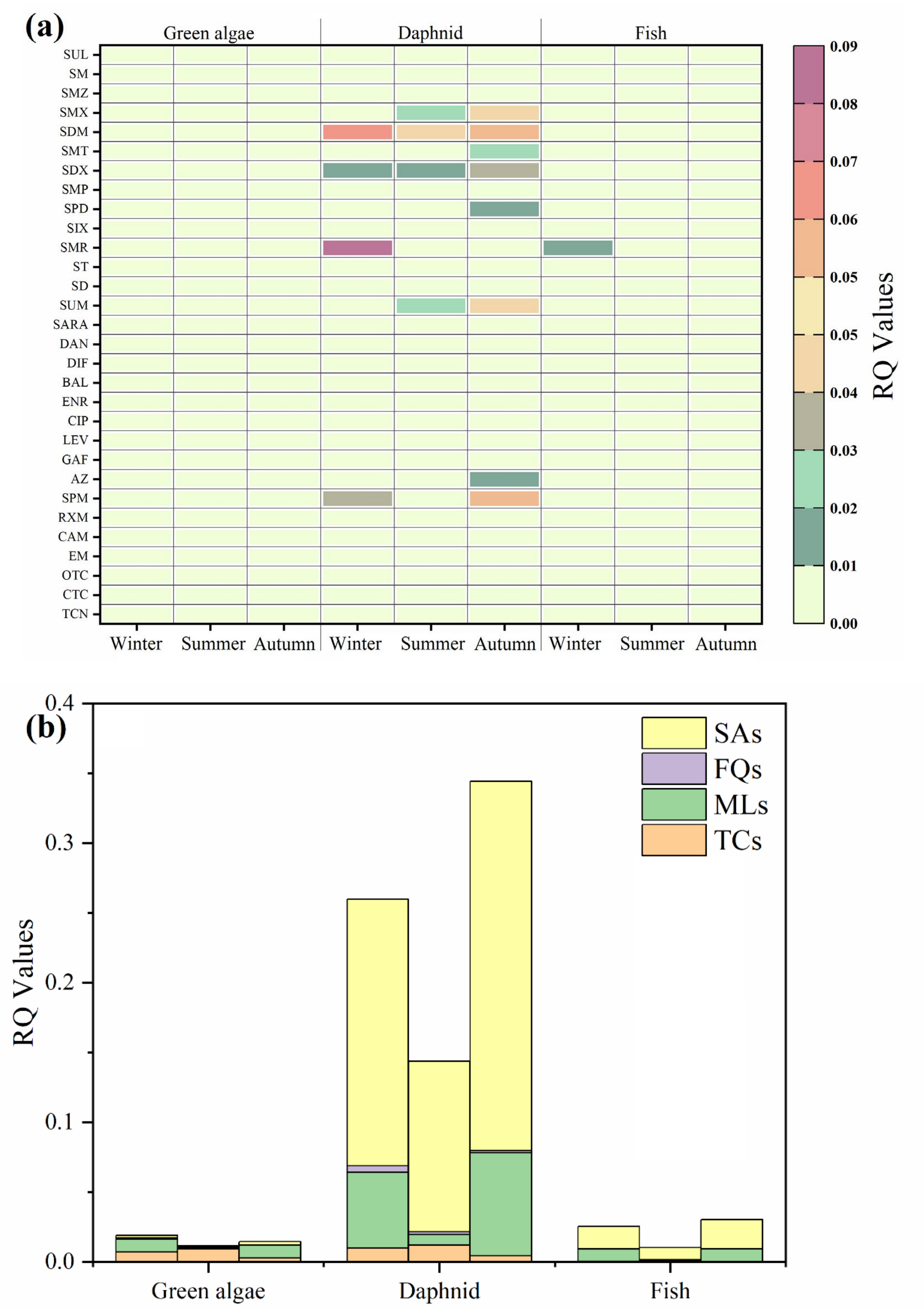


Fig. 7. RQ values for individual antibiotics (a) and selected antibiotic families (b) in water samples from the Wei River. Each group of bar-plots contains three columns representing the RQ values for the winter, summer, and autumn seasons, respectively.

The risk to all the considered organisms in river water were generally elevated during winter and autumn due to notably higher antibiotic concentrations during these seasons. SAs, AZ and SPM can therefore be considered as priority pollutants based on the ecological risk posed by these chemicals. The pervasive presence of antibiotics has raised concerns regarding the adverse ecological effects stemming from their "pseudo-persistence" and potential post-therapeutic effects on non-target aquatic organisms (Carlsson et al., 2006; Ma et al., 2016). Additionally, a major concern is the potential induction of resistant bacterial strains though exposure to low levels of multiple classes of antibiotics, posing a health threat to both humans and aquatic ecosystems (Ma et al., 2017). Furthermore, aquatic organisms are not exposed to a single substance but rather to a mixture ofantibiotics, pharmaceuticals and other chemicals , and the toxicity of such mixtures may increase due to synergistic actions, even if individual compounds display low acute or even low chronic toxicity (Backhaus et al., 2003; Silva et al., 2002). Therefore, to conduct a thorough risk assessment, there is a necessity to establish a conceptual framework that evaluates antagonistic and /or synergistic toxicity arising from a blend of antibiotics, in conjunction with the effects of other water constituents.

3.5. Water-sediment distribution of antibiotics

The antibiotic concentrations of sediment samples were shown in Fig. 8 a and b. The concentrations of antibiotics in sediment were comparable between the winter and summer sampling periods (Fig. S2), and the total concentration for all the sites ranged from 3.34 ng/g to 17.26 ng/g in winter, 4.23 ng/g to 9.07 ng/g in summer. For the different kinds of antibiotics, more than 90% of the detectable concentrations were below 1.0 ng/g, which is significantly lower than the antibiotics concentration in the water. This phenomenon can be attributed to their high-water solubility and persistence in water (Hu et al., 2018; Li et al., 2014). The detection frequency was like that of the antibiotics in the overlying water, although TCN, OTC, CIP and ENR were not detected in either the winter or summer sampling campaigns. There weren't apparent seasonal variations in the antibiotic composition within the sediments, with no significant difference between the seasonal average concentrations of the antibiotics (pair-sample t-test, $p > 0.05$). This finding aligns with prior research (Li et al., 2018a; Zhou et al., 2011), suggesting that antibiotics adsorbed to sediments are relatively less influenced by seasonal fluctuations in antibiotic sources or removal processes in the overlying water column. The antibiotic concentrations in sediments of Wei River were several orders of magnitude lower than those reported in river sediments in China (Li et al., 2018b), but comparable to those observed in lake/reservoir sediments (Li et al., 2019).

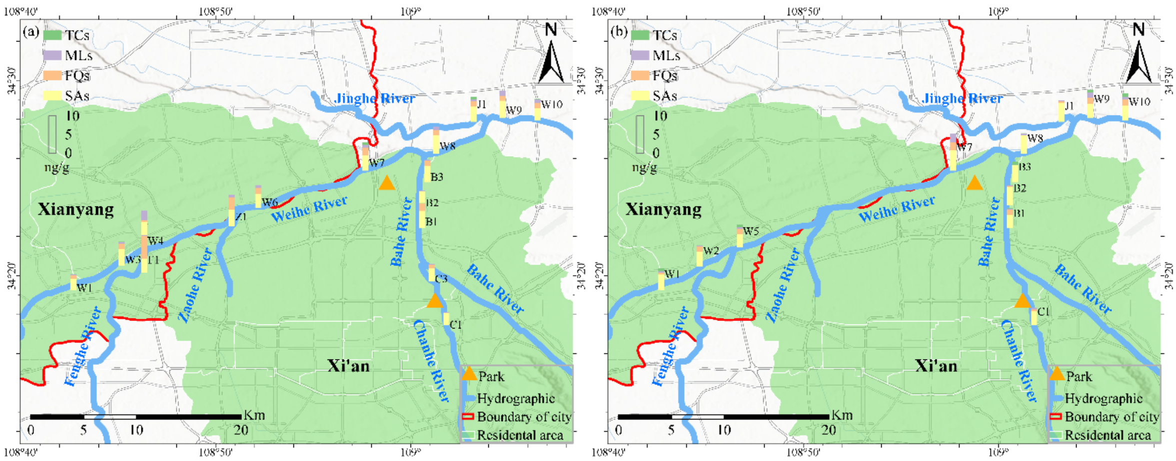


Fig. 8. Accumulative concentration of detected compounds at each sampling site at different seasons in

sediment (a. winter season; b. summer season).

The allocation of antibiotics between water and sediments in the Wei River was assessed by calculating distribution coefficients (K_p, L/kg), defined as C_s/C_w [where C_s represents the antibiotic concentration in the sediment (ng/kg) and C_w is the concentration in the river water (ng/L) (MacKay and Vasudevan, 2012)]. Only antibiotics with detection frequencies exceeding 50% in both water and sediments were chosen (Liang et al., 2013). As shown in Fig. S3 a and b, the calculated K_p ranged from 0.33 to 36398 L/kg, aligning generally with the findings of (Li et al., 2018a). The variability observed in K_p values is likely attributable to differences in the physicochemical properties of the antibiotics (e.g. aqueous solubility, ionisation state (pKa) and K_{OW} or hydrophobicity) as well as the properties of the sediments (e.g. organic matter content) (Chen et al., 2017; Li et al., 2018b; Liang et al., 2013; Luo et al., 2011). In addition, the K_p values were higher in winter than in summer, which may be due to the lower flows in the headwaters and tributaries as well as river velocities during winter, allowing sufficient time for the antibiotics to enter the sediments, resulting in higher K_p values (Hu et al., 2018).

4. Conclusions

In this study, 30 antibiotics were detected and measured over a two-year period in the Wei River in Xi'an, China. All the target compounds were detected during at least one season, and the average total levels in surface water were 297.44 ng/L, 187.08 ng/L and 143.90 ng/L in winter, summer and autumn, respectively, indicating the extensive usage of these antibiotics within the catchment. FQs were the dominant antibiotics in winter and summer season, while the SAs were the dominant in autumn season due to the differentiation of usage characteristics. In contrast to the wet seasons (summer and autumn), notably higher antibiotic concentrations were observed in river water during the dry season (winter), likely a result of dilution effects from increased water flow and enhanced antibiotic removal in the wet seasons. RDA highlighted correlations between antibiotic concentration and WT, σ, TDS, salinity, pH and TOC in the water. The antibiotic burden was most evident in the upstream region of the Wei River and its two tributaries (Chan River and Ba River) during both winter and summer. Derived risk quotients based on the measured water concentrations revealed that SAs pose a chronic ecological risk to freshwater invertebrates like Daphnia, but the overall level of risk is low.

Antibiotic pollution of urban rivers with a varied rural/urban watershed and hence varied sources of antibiotics cannot be ignored. There is a critical need for increased surveillance of antibiotics across a wider geographical area, particularly the implementation of long-term monitoring to track changes in antibiotic residues over different seasons and years. Such monitoring activities can yield vital information on trends in river pollution and assess the effectiveness of pollution control measures by comparing changes before and after their implementation. Furthermore, antibiotic pollution control policy and technology needs to be applied to protect river water from major point sources like waste effluent discharges. Various management practices and policies have resulted in different pollution trends in aquatic ecosystems. Recently, Jiang et al. (Jiang et al., 2021) reported on human activities related to water pollution controls in the Taige canal basin, China. Their results demonstrate effective control of antibiotic contamination in the study area, with methodologies aligning closely with the actual needs of the region, thus offering valuable lessonsfor the control of pharmaceuticals as part of catchment management plans.. However, their focus was primarily on a rural area. For towns and cities, particularly for Xianyang and Xi'an, the following measures are recommended: (a) implementing high-temperature aerobic biological fermentation of poultry excreta, particularly in livestock farms, especially in Baqiao District (located in Ba River and Chan River); (b) purifying wastewater from aquaculture through ecological purification ponds and constructed wetland, especially in Weiyang District (nearby the sites Z1 and W6); (c) enhancing existing centralized wastewater treatment plants with targeted facilities in the purification process, such as light degradation, which effectively mitigates antibiotics. Furthermore, it is essential to dynamically adjust pollution control policies and technologies through long-term monitoring efforts.

CRediT authorship contribution statement

Shengkai Cao: Conceptualization, Investigation, Methodology, Visualization, Formal analysis, Writing – original draft. **Peng Zhang**: Investigation, Formal analysis, visualization.

Crispin Halsall: Supervision, Writing – review & editing. **Linke Ge**: Conceptualization, Funding acquisition, Supervision, Writing – review & editing.

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.

Data Availability

Data will be made available on request.

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Supplementary data

Supplementary data associated with this article can be found in the supplementary material.

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