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RESEARCH ARTICLE

Identifying unknown antibiotics with persistent and bioaccumulative properties and ecological risk in river water in Beijing, China

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Abstract

The goal of this study was to identify antibiotics with potential risk in river water of the megacity Beijing, China. This was accomplished by using a tiered approach that combined hazard (phase I) and monitoring-based risk (phase II) assessment. Ninety-five candidate antibiotics were screened and 31 was identified as hazardous during phase I assessment. Of these hazardous antibiotics, 29 were identified as persistent and 7 were identified as bioaccumulative antibiotics. Fluoroquinolones, macrolides, sulfonamides, and aminoglycosides account for over 80% of these hazardous antibiotics. During phase II, four antibiotics (erythromycylamine, cefotaxime, ampicillin, and fusidic acid) that were not previously reported were detected in the surface water sampled from four major rivers in Beijing, with concentrations ranging from not detected to approximately 300 ng/L. The ecological risk assessment showed that erythromycylamine, cefotaxime, and ampicillin posed low to high levels of risk to the aquatic organisms. To summarize, erythromycylamine, cefotaxime, and ampicillin were identified as priority antibiotics in rivers in Beijing, China. Our results demonstrated the necessity of conducting monitoring-based verification process in identification of priority antibiotics in a specific region.

Keywords Antibiotics · Persistence · Bioaccumulation · Toxicity · Pharmaceuticals · Priority

Introduction

Pharmaceuticals have attracted increasing concern from environmental scientists and ecotoxicologists in recent decades (Ankley et al. 2007; Daughton and Ternes 1999; Monteiro and Boxall 2010; Snyder et al. 2003), because they are specially-designed chemicals that have biological effects and are bioavailable. Extensive field investigations have demonstrated the wide distribution of pharmaceuticals in various environmental matrices worldwide (Arpin-Pont et al. 2016; Bu et al. 2013b; Daughton 2010; Ebele et al. 2017; Liu and Wong 2013; Sui et al. 2015). For example, since 1990 over 100 pharmaceuticals have been detected in surface water and sediment in China (Bu et al. 2013b), and up to approximately 300 have been detected around the globe (Howard and Muir 2011).

Albeit this, it is still a small fraction of presently-marketed pharmaceuticals. Our knowledge of the contamination status of pharmaceuticals in the environment needs to be further improved. It is unreasonable to test samples for all pharmaceuticals that are in use as it is extremely costly to monitor trace micropollutants in complex environmental matrixes. As a result, prioritization schemes are needed for a preliminary screening of pharmaceuticals, which allowing resources to be appropriately allocated on those which are most likely to cause greatest harm in aquatic environment. Studies conducted for identifying, ranking or prioritizing environmental pharmaceuticals are of great value and are urgently needed for both scientific research and environmental management (Boxall et al. 2012; Bu et al. 2013a; Bu et al. 2013b).

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According to the environmental risk assessment (ERA) proposed by the European Medicines Agency, persistence (P), bioaccumulation (B), and toxicity (T) are inherent properties of pharmaceuticals that were usually used in hazard-based screening procedure (Li et al. 2020). Multiple prioritization exercises have been performed based on these inherent properties during past few years (Berninger et al. 2016; Howard and Muir 2011; Sangion and Gramatica 2016) It has merit that the screening results could be directly applicable in other countries or regions. However, risk-based screening schemes were preferred as they were more realistic as environmental concentrations were usually considered. Several investigators have prioritized pharmaceuticals of potential concern based on either risk properties or risk estimates (Al-Khazrajy and Boxall 2016; Bu et al. 2020; Burns et al. 2017; Helwig et al. 2016; Ji et al. 2016; Mansour et al. 2016).

The bias existing in the screening results was inevitable for both hazard- and risk-based screening approach mentioned above. Hazard assessment did not consider that fact that the use profiles of pharmaceuticals and wastewater treatment infrastructures could be distinct between regions and countries (Veronica et al. 2018). On the other hand, in the risk-based screening practice, predictions of environmental concentrations were generally employed because of the limited availability of data on measured concentrations, which would bring great uncertainties to the results (Bu et al. 2020). These abovementioned facts emphasized the necessity of verifying the real risk of the identified targets in a specific region, but the in-situ monitoring-based verification process was seldom conducted among studies.

The aim of the present study was to identify antibiotics with potential risk in river water of the megacity Beijing, China by using a tiered approach that combined hazard- and monitoring-based risk assessment. Hazard-based screening could help us focus on some specific targets, and monitoring or measured data then would be obtained to further confirm the real risk. Specifically, the following procedure was established and applied to a list of current human-use antibiotics in China. Firstly, hazard assessment was conducted to identify P and B antibiotics, as well as those with high production volumes (HPV). Toxicity was not considered because it is still a major lack of chronic ecotoxicity data to assess impacts of the most pharmaceuticals in aquatic environments (Howard and Muir 2011). Secondly, these identified antibiotics were ranked by scoring their production volumes and P and B potential. The last steps were to develop a targeted analytical procedure for antibiotics with high ranks and to validate their occurrence and ecological risks in environmental samples. The identified antibiotics of high risks to the aquatic organisms would be valuable for further monitoring and developing proper emission reduction strategies in Beijing.

Materials and methods

Antibiotics

We obtained the data for the antibiotics to be screened from China Medical Statistics (MIIT 2012; MIIT 2013; MIIT 2014; MIIT 2015; MIIT 2016). We focused on only antibiotics to reduce the workload associated with targeted analysis of micropollutants in environmental samples. Antibiotics were selected also because they are among the most extensively studied pharmaceuticals, which would help prove or disprove the hypothesis we tested in this study. The selected antibiotics were cross referred according to the name and Chemical Abstract Service Registry Number (CASRN) of each antibiotic, to ensure the accurate citation, by searching in multiple sources, including PubChem (https://pubchem.ncbi.nlm.nih.gov/) and SciFinder (https://scifinder.cas.org). The CASRN was used as the unique identifier and is cited throughout the study.

Ninety-five antibiotics were extracted and data such as on therapeutic group and production volume were compiled. The 95 antibiotics fell into 11 categories, including cephalosporins, β-lactams, macrolides, fluoroquinolones, sulfomides, aminoglycosides, tetracyclines, trimethoprims, amphenicols, lincosamides and other antibiotics. This abovementioned information is provided in Supporting Information Tables S1 and S2.

Overview of the identification scheme

As shown in Fig. 1, the method to screen prioritized antibiotics comprised two parts, Phase I and Phase II. In Phase I, we identified candidate antibiotics on the basis of their potential for being persistent and/or bioaccumulative, as well as their production volume and we then scored them for ranking. Phase II used target analysis and risk assessment to validate the occurrence of the high-risk antibiotics in environmental samples. Specific procedures that were used are described in the following sections.

Identification of HPV, P, and B antibiotics

A binary classification of antibiotics was performed to identify HPV, P and B chemicals. We obtained production volume of each antibiotic from China Medical Statistics (MIIT 2012; MIIT 2013; MIIT 2014; MIIT 2015; MIIT 2016). Production volumes were summed for a particular antibiotic if it was involved in two or more combined medicines. The average volume of each antibiotic between 2011 and 2015 was calculated. If the annual production volume of 1000 t was exceeded, the antibiotic was listed as an HPV chemical (EC 2003).

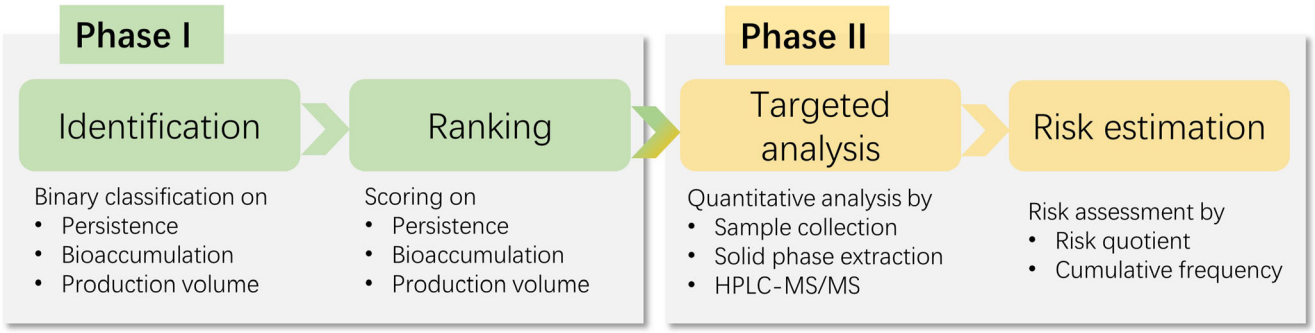

Fig. 1 Screening strategy and process of antibiotics

The identification of antibiotics that have P and B potential was done according to the method established by Howard and Muir (2011). Briefly, an antibiotic was deemed as persistent if the probability value estimated from the BIOWIN1 module of the Estimation Program Interface (EPI) Suite™ software was less than 0.5 (USEPA 2018). The octanol/water partition coefficient (log K_{ow}) was used as the criterion characterizing bioaccumulation potential, which was estimated by the KOWWIN program of EPI Suite™ (USEPA 2018). The cut-off value was set at 3, which is relatively conservative among existing regulations (Hernando et al. 2011; Howard and Muir 2011). One antibiotic was marked as bioaccumulative if the cut-off value was exceeded.

Scoring algorithm

The antibiotics identified in the above procedure were further ranked by scoring their production volume, BIOWIN1 probability value and log K_{ow}. This indicated the relative importance of the identified antibiotics. The score of each criterion i (which equals P, B, or production volume) for the antibiotic j was calculated according to Kumar and Xagoraraki (2010) using:

$$S_{i,j} = \frac{i_j - i_{\min}}{i_{\max} - i_{\min}}. \quad (1)$$

The overall score of each antibiotic was calculated as follows:

$$S_{\text{overall}} = S_{\text{PV}} W_{\text{PV}} + S_{\text{P}} W_{\text{P}} + S_{\text{B}} W_{\text{B}}, \quad (2)$$

where S_{overall} is the overall score of each antibiotic; S_{PV}, S_{P} and S_{B} represent the score for production volume, persistence and bioaccumulation, respectively; and W_{PV}, W_{P} and W_{B} are weighting factors and were equally set at one third. Note that a negative BIOWIN1 value was used for scoring purposes to ensure that the antibiotic that should receive the highest concern gets the largest score. The antibiotics were ranked according to their overall score. Thus, the highest score received a rank of 1. To focus limited analytical resources, two filters were applied here. First, antibiotics with a rank greater than 28 (bottom 30%) were excluded. Then, antibiotics that have been reported before would not be considered at the targeted analytical screening stage.

Targeted analytical screening

As the first step in this targeted analytical screening stage, we selected a subset of antibiotics for development of the analytical method. To include an antibiotic in this step, there had to be analytical standards available for high performance liquid chromatography with tandem mass spectrum (HPLC-MS/MS) analysis.

The second step was to collect surface water samples. Surface river water was chosen as the matrix for screening because most antibiotics are discharged into rivers with effluents of the wastewater treatment plant (WWTP) and are highly soluble in water. Four rivers in Beijing were selected for the targeted analytical screening (Fig. 2), including Liangma River, Tonghui River, Qing River and Liangshui River, which receive effluents from WWTPs of Jiuxianqiao, Gaobeidian, Qinghe and Xiaohongmen, respectively. Thirty surface water samples were collected in October 2017 along the riverside. At each sampling site, surface water (0–50 cm depth, > 2 L) was collected using a stainless sampler (5 L) and filtrated immediately using Millipore® glass microfibre filters (0.7 μm, EMD Millipore, Temecula, CA, USA). After that, they were preserved in amber glass bottles at 4 °C and analyzed within 48 h.

The third step involved analysis of environmental samples. Two 1-L aliquots of water were each adjusted to pH values of 2.5 and 7 and the water was extracted by solid phase extraction with Oasis® hydrophilic-lipophilic balance (HLB, 500 mg, 6 ml; Waters Corporation, Milford, MA, USA) cartridges, which were successively preconditioned with 8 ml of methanol and 8 ml of ultrapure water. After washed by 6 ml of ultrapure water, the cartridge was dried under vacuum for 30 min and eluted with 10 ml of methanol. We concentrated the extract under a gentle stream of nitrogen and, thereafter, we changed the solvent from methanol to ultrapure water for HPLC-MS/MS analysis.

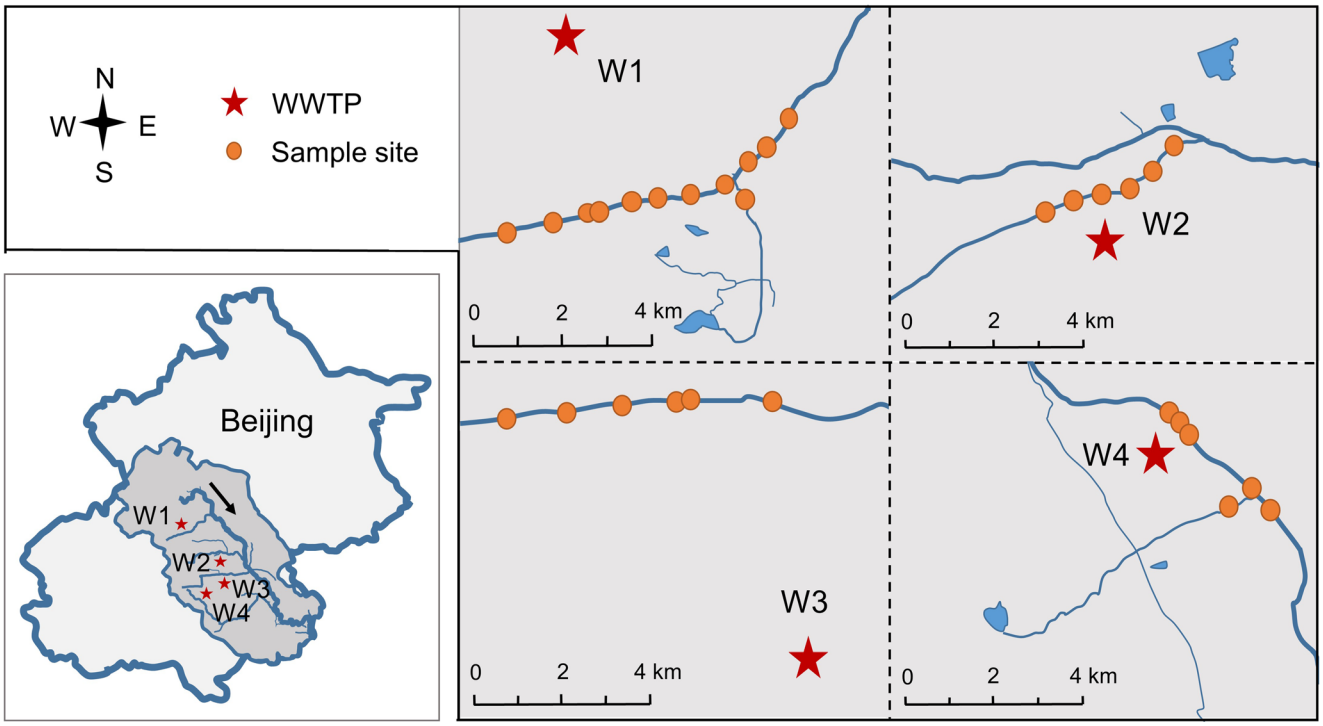

Fig. 2 Schematic diagram showing the locations of the sampling sites

The fourth step was to test whether the selected antibiotics could be detected by HPLC/MS-MS. Standard solutions were prepared in acetonitrile and water. Targeted analysis was conducted by a Shimadzu HPLC (LC-30A, Shimadzu Corporation, Kyoto, Japan) coupled with a triple stage quadrupole (TSQ) MS (LCMS-8030, Shimadzu Corporation, Kyoto, Japan), which were operated in electrospray ionization (ESI) mode. We developed HPLC-MS/MS methods. More details on instrumental parameters can be found in Table S3.

ERA

ERA was performed for selected antibiotics in surface water mainly on basis of the method stated by Huang et al. (2018) that calculated the probabilistic distribution of risk quotient (RQ). The RQ was calculated for the selected antibiotic from the following equation:

$$\mathrm{RQ} = \frac{\mathrm{MEC}}{\mathrm{PNEC}_{\mathrm{lowest}}}, \quad (3)$$

where MEC was measured environmental concentrations, $\mathrm{PNEC}_{\mathrm{lowest}}$ was the predicted no-effect concentrations that were derived on the basis of the most sensitive endpoint. Risk categorization for selected antibiotics was divided into three scenarios: when $\mathrm{RQ} \le 0.1$, low risk to organisms; when $0.1 \le \mathrm{RQ} \le 1$, moderate risk to organisms; when $\mathrm{RQ} > 1$, high risk to organisms. Monte Carlo simulation was employed to calculate distribution curves and the probabilities of RQ exceeding one particular value. The simulation was run 5000 times with Oracle Crystal Ball (Version 11.2), a software add-in in Microsoft Excel 2013.

Results and discussion

Identification of P&B antibiotics

The results of identification are summarized in Table S1. The estimated values were provided by BIOWIN1 and KOWWIN models as the measures of P and B, respectively. EPI Suite™ predicted values that ranged from −2.5405 to 2.0203 for BIOWIN1 and −8.36 to 6.75 for log K_{ow} for the 95 antibiotics (Table S1). Of these antibiotics, 29 were identified as P and 7 as B. Five antibiotics were common to these two groups (P&B chemicals), namely sulfasalazine, flucloxacillin, erythromycylamine, clarithromycin and azithromycin, leaving 31 antibiotics that were rated as P and/or B (Table S1).

The 31 identified antibiotics fell into six main therapeutic groups, including 10 fluoroquinolones (32%), 7 macrolides (23%), 5 sulfonamides (16%), 4 aminoglycosides (14%), 2 β-Lactams (6%), and 3 other antibiotics (12%) (Fig. 3a). As shown in Fig. 3b, it was noted that all the candidates of fluoroquinolones and macrolides were finally classified as priorities in the present study. The majority candidates of sulfonamides (71%) were on the priority list, while the corresponding percentages for β-Lactams, aminoglycosides and other antibiotic were 12%, 30% and 50%, respectively. The results demonstrated that fluoroquinolones, macrolides and

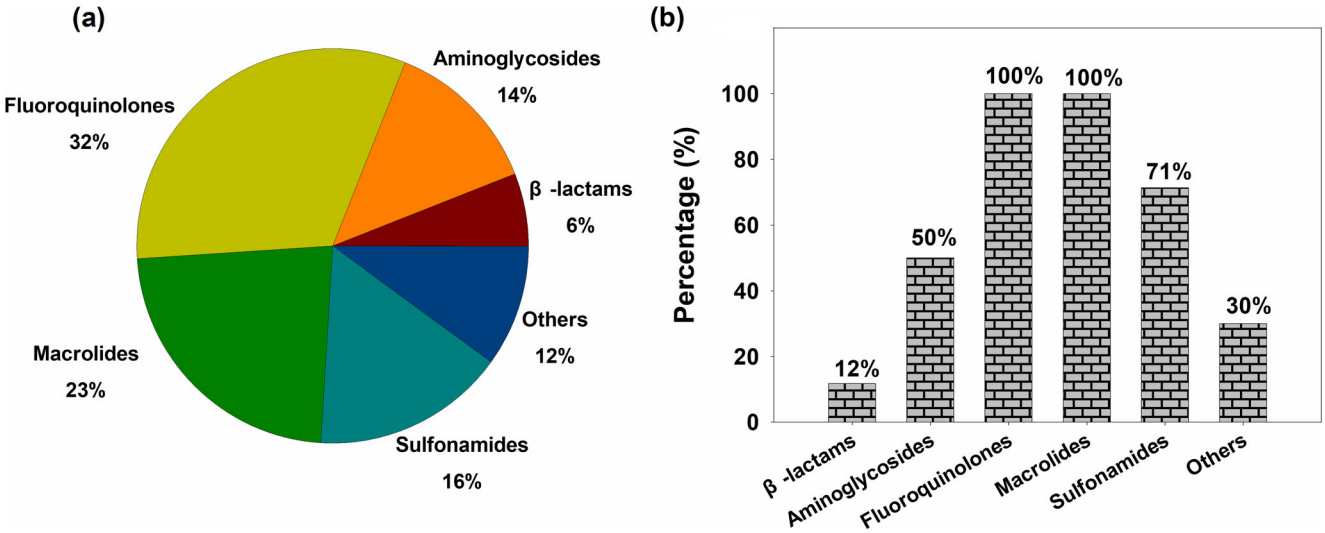

Fig. 3 Characterization of priority antibiotics by therapeutic classes: **a** contribution of each therapeutic class to the priority antibiotics and **b** percentage of priority antibiotics to the total number of candidate antibiotics in different therapeutic classes

sulfonamides should be paid more attention to. All fluoroquinolone candidates to be screened were categorized as P because the substructure of aromatic fluorine exists in these antibiotics. Macrolides were all deemed as P by our classification because they commonly possess substructures such as those of tertiary amine and aliphatic ether. At the same time, macrolides had relatively higher estimated log K_{OW} values. Of the seven antibiotics classified as B, three were macrolides. Five of the seven studied sulfonamides were classified as P because they have a substructure of aromatic amine (which suggests persistence). Conversely, none of the candidates of amphenicols, cephalosporins, lincosamides, tetracyclines, and trimethoprims was finally classified as P or B (Table S2).

P&B antibiotics identification results were significantly influenced by different screening criteria and estimation parameters among studies. Both we and Howard and Muir (2011) employed the same prioritization for P and/or B properties. Of the 95 antibiotics in the present study, 22 were in their candidate database, of which 15 were estimated to be P or B antibiotics and 6 were commonly identified as neither P nor B pharmaceuticals. Only one pharmaceutical, chloramphenicol, was listed as a persistent contaminant in Howard and Muir (2011) but not in this current study. This difference could be explained by the fact that another criterion to indicate potential persistence was used in their study but not in ours. This criterion was that the results of BIOWWIN5 models from EPI Suite™ were less than 0.5. Li et al. (2020) ranked 100 pharmaceuticals in China in terms of their occurrence, persistence, bioaccumulation and toxicity. Twenty-five of our candidate antibiotics are also included in their list of pharmaceuticals. Ten of the 25 antibiotics were commonly marked as P or B. Eight were identified as neither P nor B in either Li and co-workers or our study. Of the remaining seven candidate antibiotics, sulfadiazine and sulfamethoxazole were only screened as P in the present study and five antibiotics (benzylpenicillin, oxytetracycline, ceftriaxone, tetracycline, and doxycycline) were identified only as P by Li et al. (2020). A discrepancy in parameters for identifying "persistent" could explain the difference in screening results. In Li et al.'s (2020) study, candidate antibiotics were marked as P if the probability value estimated by the BIOWIN2 module of EPI Suite™ was less than 0.5 or the value estimated by the BIOWIN6 module was less than 0.5 and that of the BIOWIN3 module was less than 2.2. In our study, this was the case only when the probability value estimated by the BIOWIN1 module was less than 0.5. Zhou et al. (2014) screened 126 pharmaceuticals found in wastewater entering urban aquatic environments in China. Twenty of these were also listed in our candidate database. Seven out of the 20 candidate antibiotics were commonly marked as P&B in both studies and three antibiotics (cefotaxime, clindamycin, cefaclor) were identified as neither P nor B. Of the remaining 10 antibiotics, 6 antibiotics (sulfasalazine, chlortetracycline, spiramycin, enoxacin, lomefloxacin, and cloxacillin) were screened as P only by the present study but not in Zhou et al. (2014). Four antibiotics (chloramphenicol, amoxicillin, tetracycline and oxytetracycline) were assigned as P in the former study but not in ours. Differences in parameters for identifying persistence result in the discrepancy in screening results. In Zhou et al.'s (2014) study, the pharmaceuticals were marked as P if their half-life values exceed 30 days, which was not the case in our study. Of the nine initial overlapping candidate antibiotics, erythromycin and azithromycin were commonly marked as P&B and ampicillin and doxycycline were commonly identified as neither P nor B antibiotics, in both in our study and Mansour et al. (2016), which used a range of indexes including exposure, persistence, bioaccumulation and toxicity as well as the ERA approach in the Middle East and North Africa region.

Of the remaining five antibiotics, sulfadiazine, ciprofloxacin and ofloxacin were estimated as P&B by our study but not in the previous study. Amoxicillin and cefixime were identified as P in Mansour et al. (2016) but not in our research. Discrepancies between the two studies could have resulted because the previous study estimated antibiotics as P by ranking the pharmaceutical removal ability of WWTP and using organic carbon to water partition coefficients (log K_{OC}) of candidate antibiotics, which were greatly different from ours. After comparing researches, we found that a discrepancy existed in the selection of evaluation parameters and the definition of screening criteria, which affected identification results.

We also included HPV antibiotics for further ranking as highly frequent use would also lead to a lasting existence (pseudo-persistence) of antibiotics in the environment (Daughton and Ternes 1999). Consequently, 11 HPV antibiotics were identified. Of these, only ciprofloxacin was potentially persistent and the rest all escaped from the P and B filters. Combining P and/or B chemicals, the identification procedure produced a list of 41 antibiotics for further ranking (Table S1).

Ranking

According to the overall score of 41 hazard antibiotics based on P, B and PV (Fig. 4), we selected the 28 top-ranked antibiotics to focus our limited available analytical resources, removing 13 P and/or B chemicals despite that they were previously mostly not reported. However, these antibiotics also have the potential of being emerging contaminants and each should be characterized for its environmental relevance in the future. Of the 28 top-ranked antibiotics, 20 have been found at least once in previous studies conducted in China (Bu et al. 2013b; Liu and Wong 2013; Sui et al. 2015; Sui et al. 2012).

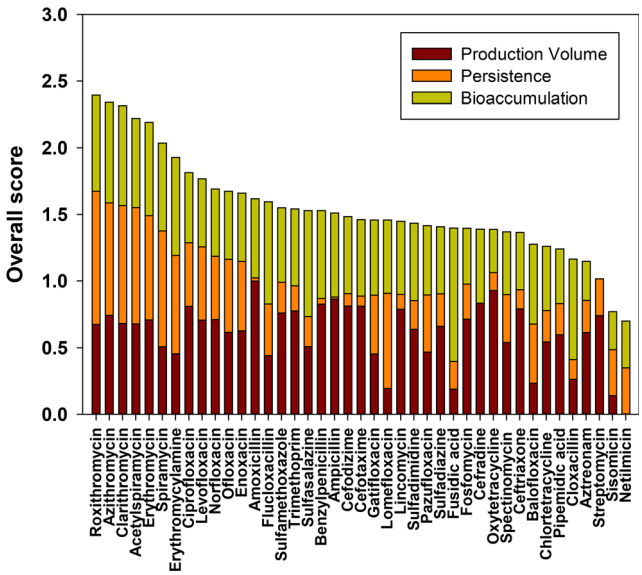

Fig. 4 Overall score of priority antibiotics

In summary, as shown in Fig. 4, eight of the antibiotics were passed onto the targeted analytical screening stage, namely erythromycylamine (rank 7), flucloxacillin (rank 14), sulfasalazine (rank 17), ampicillin (rank 19), cefodizime (rank 20), cefotaxime (rank 21), pazufloxacin (rank 26), and fusidic acid (rank 28).

Targeted analysis

Of the eight antibiotics we selected because of the P and B assessment, we selected five for analytical method development. Flucloxacillin and pazufloxacin were not selected because analytical standards were not available at the time of method development. Cefodizime was not selected because its production in China decreased sharply from 8850 t in 2011 to around 20 t since 2012, which makes it less relevant for inclusion as one of the analytical targets.

Surface water samples were analyzed for four of these antibiotics that had satisfactory recovery during our pre-treatment. These were erythromycylamine (CASRN 026116-56-3), ampicillin (CASRN 000069-53-4), cefotaxime (CASRN 063527-52-6) and fusidic acid (CASRN 006990-06-3). The fifth antibiotic, sulfasalazine (CASRN 000599-79-1), was poorly recovered regardless of whether the water samples were acidified.

All analyzed targets, except fusidic acid, were found in water samples at varying concentrations. The analytical method specially identified these targets that retention time and extracted spectra were both matched with that of standards. This is illustrated by comparing the chromatograms and mass spectra in a standard, a spiked sample and a water sample in Fig. S1 to S3 for erythromycylamine, ampicillin, and cefotaxime.

Recovery tests were run to confirm the performance of our established method. Water samples were spiked with known amounts of targeted antibiotics at three concentration levels. It has been found that he determined concentrations were well in accordance with the spiked values at each spiked level (Table S4), indicating that the analytical method had good reproducibility and recovery. No targeted antibiotics were identified when procedural blanks were run. The limit of detections (LODs) and quantifications (LOQs) for the four detected antibiotics ranged from 0.05 to 0.86 ng/L and 0.16 to 2.16 ng/L, respectively. Furthermore, the method detection limits (MDLs) of erythromycylamine, ampicillin, cefotaxime and fusidic acid were 0.13 ng/L, 0.43 ng/L, 0.66 ng/L, and 3.97 ng/L, respectively, with an assumed extract volume of 1 ml and a water sample of 1 L. These data for each individual compound are provided in Table S4 and indicated that the analytical method is sensitive and reliable.

The results of the targeted analytical screening of the four antibiotics in water samples from the four selected rivers are summarized in Table 1. Erythromycylamine was detected at almost all sampling sites at concentration levels from < 0.13 to 299 ng/L, followed by cefotaxime with concentrations ranging from < 0.66 to 12.4 ng/L. Another antibiotic, ampicillin, was detected in 42% of the sampling sites, with the highest concentration of 18.0 ng/L in Tonghui River. Generally, antibiotic concentrations were higher in water samples from Tonghui River and Qinghe River than in water samples collected from the other two rivers. Such a trend can be explained because the former two were both drainage rivers connected to large scale WWTPs. These data provided clear and strong evidence that the three antibiotics are present in surface water as environmental contaminants. However, we were unable to detect fusidic acid in our sampling campaign. This could be attributed to some factors that we will discuss later. Positive results from the targeted analytical screening procedure strongly indicated that persistence and bioaccumulation are useful indicators for identifying environmental contaminants.

Risk assessment

The cumulative probabilities of RQs are shown in Fig. 5. The risk posed by ampicillin to the surface water in Beijing was much greater than the risks posed by erythromycylamine and cefotaxime. For ampicillin, the probability of RQ exceeding 0.1 was 74.0% and of RQ exceeding 1.0 was 4.38%, which suggested that organisms were most likely to be exposed to ampicillin at a moderate risk and might even be exposed at a high risk. High excretion (80%) and low wastewater treatment plant removal (1.94%) (Bu et al. 2020), as well as higher consumption, contributed to the high risk of this an "anti-infective for systemic use" drug. For erythromycylamine, the probabilities of RQ exceeding 0.01, 0.1, and 1 were 99.46%, 44.1%, and 0.16%, respectively. This illustrated that organisms had a probability of nearly half to being exposed to erythromycylamine at a relatively moderate risk. A well-known active metabolite of erythromycin, erythromycylamine has long half-life, high tissue concentrations (Geerdes-Fenge et al. 1997) and high production volume in China (26,384 kg/year). These properties facilitate its ecological risk to organisms. The RQ of cefotaxime was lower than 0.001, which suggested that the risk of organisms exposed to the cefotaxime could be ignored. However, considering that cefotaxime was estimated to be an HPV antibiotic with a high detection frequency (83%) in surface water samples (Table 1), it still could have a great impact on the environment. Therefore, we assessed ampicillin, erythromycylamine and cefotaxime to be the priority antibiotics in Beijing, China.

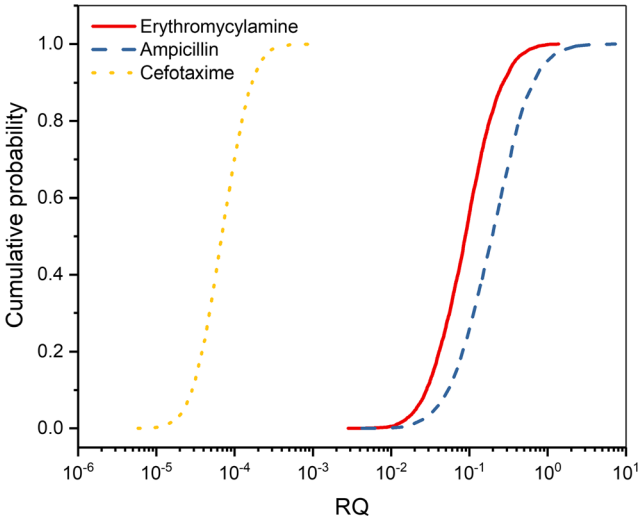

Fig. 5 Cumulative probability of RQs for the detected antibiotics in surface waters

It can be found that fusidic acid was identified as hazardous antibiotics, but nearly no ecological risk was posed by it in our investigated rivers in Beijing. On the other hand, in our previous study based on a national-scale assessment of the risk of human use pharmaceuticals, we estimated that ampicillin was a pharmaceutical with low risk (Bu et al. 2020). The discrepancy in ERA results between the previous and current study came about because of the difference in pharmaceutical consumption between the national scale and the local scale. Especially for highly populated regions, the predicted concentration at the national scale did not well-reflect the MEC level at local scale. These findings demonstrated that monitoring-

Table 1 Levels of erythromycylamine, ampicillin, cefotaxime, and fusidic acid in water samples collected from four rivers in Beijing

Contaminant	DF (%)[a] ($n = 30$)	Concentration (ng/L)				PNEC (ng/L)
		Liangma River ($n = 6$)	Tonghui River ($n = 6$)	Qing River ($n = 12$)	Liangshui River ($n = 6$)	
Erythromycylamine	97	1.83–23.2	58.6–299	< 0.13–154	3.90–31.3	390
Ampicillin	37	< 0.43–2.37	< 0.43–18.0	< 0.43–3.47	< 0.43	10
Cefotaxime	83	< 0.66–1.23	5.03–10.2	< 0.66–5.41	4.74–12.4	45,500
Fusidic acid	0	< 3.97	< 3.97	< 3.97	< 3.97	-

[a] Detection frequency, DF, denotes the percentage that the number of samples in which the concentrations of targets were higher than LOQ over the total number of samples

based risk screening is of urgent need, especially for a specific region.

As for the verified priority antibiotics, the following measures should be taken as a follow up to mitigate risks. Firstly, minimizing individual antibiotics overuse should be advocated to mitigate ecological risk of antibiotics in the aquatic environment (Chen et al. 2019). Secondly, it is crucial to define and take stricter sewage discharge regulations for the antibiotics that have been found to be of high risk (Peng et al. 2017; Zhang et al. 2016). Thirdly, refining waste water treatment processes to those priority antibiotics with poor removal efficiencies is of great importance. Last but not least, it is necessary to conduct routine monitoring for these newly identified antibiotics to reveal the long-time occurrence levels and the associated risks.

Limitations

Some limitations are associated with the present study. We only selected 28 out of 41 P&B pharmaceuticals for further screening because of resource limitations. For the remaining 13 P&B pharmaceuticals, it is unknown how many have been reported in the environment. Therefore, it is crucial that monitoring and risk assessment are performed to improve the control of the remaining unanalyzed P&B pharmaceuticals. Additionally, the number of samples was relatively small and collection was mainly concentrated near wastewater treatment plants, so there was insufficient coverage of the water bodies in the Beijing region. More work should be done to further characterize the risk of these identified antibiotics.

Conclusions

This paper presented a case study for identifying priority antibiotics in rivers in Beijing, China. Of the 95 screened antibiotics, 29 were rated as P and 7 were rated as B. Fluoroquinolones, macrolides, sulfonamides and aminoglycosides accounted for the majority of these hazardous antibiotics. The targeted analytical method was successfully developed for four hazardous antibiotics and used to determine their presence in 30 surface waters from four rivers in Beijing, with concentrations ranging from not detected to approximately 300 ng/L. Results of the ecological risk assessment showed that three antibiotics, namely erythromycylamine, cefotaxime and ampicillin, which were never been reported previously in Beijing (or even in China), were finally selected as priorities in Beijing. The present study illustrated the necessity of conducting monitoring-based verification process in identification of priority antibiotics in a specific region.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11356-020-11611-4.

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Authors' contributions Qingwei Bu designed, planned, conceptualized, performed the analysis, drafted the original manuscript, funding acquisition, and project administered, Hongmei Cao was involved in performing the analysis, and drafting the original manuscript; Qingshan Li and Handan Zhang were involved in statistical analysis, and proofreading; Weiwei Jiang was involved in planning and designing the research; Gang Yu was involved in interpretation, and consultation to write a draft manuscript. All authors have approved the final version of the manuscript.

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Data availability The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Ethical approval Not applicable.

Consent to participate Not applicable.

Consent to publish Not applicable.

Competing interests The authors declare that they have no competing interests.

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