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RESEARCH ARTICLE

Illicit drugs and their metabolites in 36 rivers that drain into the Bohai Sea and north Yellow Sea, north China

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Abstract Illicit drugs and their metabolites have recently been recognized as an emerging group of contaminants due to their potential ecotoxicological impact in aquatic ecosystems. To date, information on the occurrence of these compounds in the aquatic environment of China remains limited. In this study, we collected surface water samples from 36 rivers in north China that discharge into the Bohai Sea and north Yellow Sea and measured the concentrations of amphetamine-like compounds, ketamines, cocainics, and opioids. The occurrence and spatial patterns of these substances show significant differences between the rivers and regions. Two designer drugs, methamphetamine (METH) and ketamine (KET), were the most abundant compounds detected in the entire set of samples (detection frequency of 92 and 69 %). The concentrations of METH and KET ranged from <0.1 to 42.0 ng L^{-1} (mean = 4.53 ng L^{-1}) and <0.05 to 4.50 ng L^{-1} (mean = 0.49 ng L^{-1}), respectively. The high detection frequencies of METH and KET are consistent with the fact that they are the main illicit drugs consumed in China. The high concentrations of these illicit drugs and their metabolites were found in areas that have a high population density. The riverine input of total illicit drugs into the Bohai Sea and north Yellow Sea was estimated to be in the range of 684 to 1160 kg per year.

Keywords Surface water · Illicit drug · Methamphetamine · Ketamine · River · Bohai Sea

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Introduction

Illicit drugs and their metabolites have recently been recognized as emerging organic contaminants in the environment due to the increase of production and demand (Castiglioni and Zuccato 2010). These compounds reach the receiving surface waters unaltered or slightly transformed via the effluents from wastewater treatment plants (WWTPs) (Bijlsma et al. 2014; Hernández et al. 2015; Zuccato et al. 2005). The contaminated surface waters can be used as drinking water; thus, the presence of illicit drugs is a matter of concern because of their high biological activity and psychoactive properties (Huerta-Fontela et al. 2008). Furthermore, once released into the aquatic environment, illicit drugs and their metabolites may cause potential risk to aquatic organisms. The effects on the aquatic environment are still unknown. In some cases, the toxicological responses to the transformation products of illicit drugs can be up to 100 times higher than to those of the parent compounds (Gonzalez-Marino et al. 2015). Therefore, the assessment of their concentrations in the aquatic environment is essential to

evaluate their potential ecotoxicological effects (Jones-Lepp et al. 2004; Rosi-Marshall et al. 2015).

In recent years, many studies have reported the occurrence and levels of illicit drugs and their metabolites in natural waters, especially in Europe (Baker and Kasprzyk-Hordern 2013; Fedorova et al. 2014; Koeck-Schulmeyer et al. 2011; Postigo et al. 2008a; Postigo et al. 2010; Rosa Boleda et al. 2009; Vazquez-Roig et al. 2013). Two cocainic compounds, cocaine (COC) and its metabolite benzoylecgonine (BE), have high detection frequencies and occur at high levels in the surface waters of Europe. Opioids and related compounds were also quantified in the majority of studies. Among amphetamine-type compounds, methylenedioxymethamphetamine (MDMA) and 3,4-methylenedioxyamphetamine (MDA) were identified in river waters; however, the detection frequencies of amphetamine (AMP) and methamphetamine (METH) were sporadic. The frequency of detection indicates the rate of consumption of illicit drugs in Europe (Thomas et al. 2012). The residual drug levels in the aquatic environment are the good indicators of illicit drug abuse. Consequently, they constitute an indirect tool to estimate drug abuse by the population at the community level (Zuccato et al. 2005).

To the best of our knowledge, limited reports of the occurrence of illicit drugs in river waters are available throughout China. In the present study, we analyzed the occurrence of illicit drugs in the aqueous phase as well as their spatial distribution in 36 rivers draining into the Bohai Sea and north Yellow Sea. Rivers are major input sources of illicit drugs to the sea. Coastal waters are considered to be the ultimate sink for sewage and other by-products of human activities. More importantly, illicit drugs in river water may pose an ecotoxicological risk in aquatic ecosystems. Some recent studies have shown that notable amounts of illicit drugs and their metabolites are transported to coastal areas via riverine inputs and WWTP effluents (Jiang et al. 2014). In this study, we analyzed 13 target compounds belonging to four different chemical classes: AMP-like compounds, ketamines, cocainics, and opioids. These compounds were selected as follows: (1) AMP, METH, MDMA, and MDA; (2) ketamine (KET) and its metabolite norketamine (NK); (3) COC and its BE; and (4) morphine (Mor) and its metabolite codeine (Cod), methadone (MTD) and its metabolite 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP), and the exclusive metabolite of heroin, 6-acetylmorphine (6-AM).

Methods

Chemicals

High-purity (>97 %) standard solutions of the target compounds (METH, AMP, MDMA, MDA, KET, NK, COC, BE, Mor, Cod, MTD, EDDP, and 6-AM) and their deuterated analogues (METH-d8, AMP-d8, MDMA-d5, MDA-d5, KET-d4, NK-d4, COC-d3, BE-d3, Mor-d3, Cod-d6, MTD-d9, EDDP-d3, and 6-AM-d6) used as internal standards (purity >98 %) were purchased from Cerilliant (Round Rock, TX, USA). Individual stock solutions were prepared by diluting each analyte solution with acetonitrile (AcN) (HPLC grade, Fisher Science). Working standard mixtures were prepared at different concentrations by the appropriate dilution of the individual stock solutions with AcN. All of the stock and working standard solutions were stored in the dark at −20 °C. High-purity water was prepared with a Milli-Q system (Millipore, MA, USA). Oasis MCX (60 mg, 3 mL) solid-phase extraction (SPE) cartridges were purchased from Waters Corporation (Milford, MA, USA). A CNW™ SPE vacuum manifold (CNW Technologies GmbH) was used for the SPE clean-up processes. Ammonium hydroxide (NH_4OH) was purchased from Sinopharm Chemical Regent Co. Ltd. (Beijing, China). Ammonium acetate (HPLC grade) was obtained from CNW Technologies GmbH (Düsseldorf, Germany).

Sampling

Water samples were collected from 36 major rivers in the Bohai Sea and north Yellow Sea region in September 2015 to investigate the concentrations and distribution characteristics of illicit drugs in these rivers. There were no rainfall events during the sampling event. The rivers were chosen based on their water loading volume and length. The total water volume of these 36 rivers accounted for approximately 96 % of all the rivers emptying into the Bohai Sea and the north Yellow Sea. The Bohai Sea is a semi-enclosed Chinese water body and a huge amount of domestic sewage and industrial waste water pouring into it every year. The river basins in the study area called the “Bohai rim economic cycle” have a population of 0.26 billion people, which accounts for 28.5 % GDP of China. The total watershed area is approximately 1,412,581 km^2 and encompasses four provinces, Liaoning, Hebei, Tianjin, and Shandong, which account for nearly 15 % of the total population.

To avoid the influence of salt water, sampling sites were chosen as close to the river mouth as possible. The water sampling procedure was based on the Chinese National Standard Technical Specifications Requirements for Monitoring of Surface Water and Waste Water. Before sampling, one transect with three to five stations was set at each river, and the number of stations was chosen according to the river width. A stainless steel bucket was used to collect surface river water. Three to five 10-L water samples were mixed together in one 60-L stainless steel barrel, and finally, 0.5-L mixed water was stored in polyethylene terephthalate (PET) bottles. The pH was adjusted to 2.0 with 37 % HCl. The PET bottles were rinsed with Milli-Q water and then rinsed with

river water three times. They were then filled to the top to eliminate air bubbles.

Analysis

Extraction, purification, concentration, and analysis followed the methods described in previous studies (Du et al. 2015; Li et al. 2014). Briefly, water (50 mL) was filtered through a glass filter (0.45 μm) to remove particles. Then, deuterated labeled internal standards for quantification were added and a SPE clean-up set with Oasis MCX cartridge was applied. The cartridges were conditioned consecutively with methanol, high-purity water, and high-purity water at pH = 2. The extracts were allowed to enter the preconditioned SPE cartridge connected to a vacuum pump. After the cartridge was dried, elution was performed with 4 mL of methanol and 4 mL of 5 % NH_3 in methanol. The eluate was evaporated and redissolved in 200 μL of AcN and 200 μL of AcN/5 M ammonium acetate in water (90/10, *v*/*v*).

A liquid chromatography (UFLCXR-LC, Shimadzu, Japan) coupled with an API 4000 triple quadrupole mass spectrometry (AB SCIEX, USA) (LC-MS/MS) was used to analyze the samples. The injection volume was 5 μL. Targeted analytes were chromatographically separated using a Phenomenex Gemini C 18 column (3.5 μm, 100 mm × 2 mm) at a flow rate of 0.3 mL min^{-1}. Eluents used for the separation included 30 mM ammonium formate in ultrapure water with pH adjusted to 3 using formic acid (98 % in water) (eluent A) and 0.1 % formic acid in AcN (eluent B). The elution gradient was as follows: 0–0.1 min: 5 % B; 0.1–3.0 min: 30 % B; 3.0–5.0 min: 80 % B; 5.0–7.5 min: 90 % B; 7.5–7.6 min: 5 % B; and 7.6–13.0 min: 5 % B.

Multiple reaction monitoring mode with positive electrospray ionization was used to identify and quantify the masses of the analytes. The collision energy and tube lens offset were optimized for each analyte and surrogate separately. Positive ionization electrospray with nitrogen as the cone and desolvation gas was used. Identification and quantification were performed using two characteristic transitions for the analyzed compounds. Quantification was performed using a seven-point calibration curve (r^2 0.9960–0.9999) spanning the range of the anticipated analyte concentrations in the samples. The limits of detection (LOD), limits of quantification (LOQ), and recoveries are listed in Table 1.

Results and discussion

Concentrations in surface river water

The concentrations (mean, median, and concentration range) and frequency of detection of all the illicit drugs and their metabolites tested in this study are shown in Table 1. The illicit drugs and their metabolites are detected in 34 out of 36 samples, and their concentrations vary between LOQ and 43.9 ng L^{-1} (Table 2). Among all of the investigated compounds, only MDMA, MDA, 6-AM, and Mor are not detected. Current research related to the stability of commonly investigated drugs indicates that MDMA and MDA are rather stable compounds (McCall et al. 2016). The absence of MDMA and its metabolite MDA indicates a low prevalence rate in China. These findings are in accordance with the China Food and Drug Administration report (CFDA 2015). The low stability of 6-AM and Mor may be the reason for their absence in surface waters.

The most abundant and ubiquitous compounds are METH and KET, which are present in most of the investigated surface water samples. Their detection frequencies are 92 and 69 %, respectively. The METH concentrations account for 72 % of the total compounds and vary between <0.1 and 42.0 ng L^{-1}, with a median value of 1.90 ng L^{-1}. The median KET concentration is 0.145 ng L^{-1}, ranging from 0.052 to 4.50 ng L^{-1}. The metabolite of KET, NK, is also positively identified in 25 % of the investigated river water samples, but the detected levels do not surpass 1.50 ng L^{-1}. The remaining detected compounds, AMP, Cod, COC, BE, Med, and EDDP, are present in less than 25 % of the samples at levels up to 16.2 ng L^{-1}. The concentrations of illicit drugs and their metabolites in natural surface waters can be affected by many factors, such as consumption and stability. METH and KET are the two most commonly found compounds in natural surface waters. Accordingly, our data indicate the extensive presence of these compounds in surface waters in China. This finding is consistent with the fact that these drugs are the most used (Du et al. 2015). This finding is also in accordance with previous studies that those two drugs are most found in influent, effluent, and surface water in Chinese WWTPs (Du et al. 2015; Khan et al. 2014; Li et al. 2014; Li et al. 2016; Lin et al. 2010). Du et al. (2015) reported METH and KET concentrations in wastewater samples from 36 WWTPs in 18 major Chinese cities. The concentrations of METH (1.90 ng L^{-1}) and KET (0.145 ng L^{-1}) in surface water in this study are much lower than those in the influent (median values 179 and 20.1 ng L^{-1}) and effluent (median values 16.1 and 14.7 ng L^{-1}) samples (Fig. 1). These data suggest that the concentrations in surface water beyond the median values for the effluent may originate from direct illicit disposal and/or untreated wastewater. In addition to high consumption, the high stability of two drugs plays a vital role in their widespread occurrence in surface waters. It is noteworthy that drugs can also be degraded though a variety of processes, e.g., photolysis and biodegradation that occur during treatment

Table 1 Limits of detection (LOD), limits of quantification (LOQ), recoveries, frequencies of detection, and concentrations of the target drugs and their metabolites in surface river water

Compounds	Abbrev.	LOD (ng L^{-1})	LOQ (ng L^{-1})	Recovery (%)	Frequency (%)	Concentration (ng L^{-1})		
						Mean	Median	Range
Methamphetamine	METH	0.03	0.1	90	92	4.53	1.90	0.1–42.0
Amphetamine	AMP	0.03	0.1	105	8	2.12	1.68	1.41–3.26
3,4-Methylenedioxymethamphetamine	MDMA	0.02	0.05	111	–	–	–	–
3,4-Methylenedioxyamphetamine	MDA	0.03	0.10	98	–	–	–	–
Ketamine	KET	0.02	0.05	95	69	0.495	0.145	0.052–4.50
Norketamine	NK	0.02	0.05	86	25	0.645	0.488	0.184–1.50
Cocaine	COC	0.02	0.05	110	19	5.71	6.81	0.053–12.9
Benzoylecgonine	BE	0.02	0.05	107	22	5.21	3.85	0.070–16.2
Codeine	Cod	0.03	0.10	88	8	1.19	0.986	0.829–1.76
Methadone	MTD	0.02	0.05	87	8	0.192	0.141	0.123–0.313
2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine	EDDP	0.02	0.05	91	8	0.260	0.248	0.216–0.317
Morphine	Mor	0.02	0.05	104	–	–	–	–
6-Acetylmorphine	6-AM	0.03	0.10	85	–	–	–	–

and/or in the environment. However, METH and KET are stable under direct photolysis (Lin et al. 2013) and biodegradation (McCall et al. 2016).

The seasonal variations of presence of illicit drugs in influent, effluent, and flow rates in river water also influence on the concentrations of illicit drugs in surface water. Li et al. (2014) found that the METH concentrations in influent and effluent in Beijing were slightly higher in summer than in early winter. Postigo et al. (2010) also reported that the collective use of illicit drugs was more intense in summer than in fall. The increase use and, thus, release of these drugs may induce high discharge rate into the aquatic environment. However, the high flow rate in summer may dilute the emission of illicit drugs, leading to relatively stable mass load in rivers during different seasons (Kasprzyk-Hordern et al. 2008). In this study, we collected water samples in one sampling campaign. Further study is warranted to investigate seasonal variations of concentrations in surface water.

Comparison with other studies

Contrary to previously published finding, illicit drug compound contamination in China shows different profile than in Europe. The highest detection frequencies for surface water in Europe correspond to COC and its major metabolite BE, which were commonly detected at high levels. The frequency of detection indicates both a high and steady consumption of COC in this region. Opioids are present in surface water at lower concentrations than BE and COC (Postigo et al. 2008b). The measured concentrations of METH in surface water from 36 rivers in China were in accordance with earlier reported levels (range <0.2–2.87 ng L^{-1}) in surface water from Spain (Maria et al. 2008; Postigo et al. 2008a), Switzerland, British, and Italy (Zuccato et al. 2008). However, the detection frequency of METH in this study is higher than that in European countries (Baker and Kasprzyk-Hordern 2013; Boles and Wells 2010; Postigo et al. 2010; Vazquez-Roig et al. 2012; Zuccato et al. 2008).

Spatial variation of illicit drugs in river water

Concentrations at the various sampling sites are shown in Fig. 2. An elevated METH concentrations in surface water >16.1 ng L^{-1} may be caused by direct disposal and/or untreated wastewater. We suspect that the high METH concentration at three sampling sites is affected by direct disposal. The high METH concentrations are found in water samples collected from Daqing River (42.0 ng L^{-1}) and Yalu River (17.2 ng L^{-1}). The sample sites are located in Gaizhou and Dandong cities in Liaoning province, approximately 3 and 6 km upstream of the WWTPs, respectively. Therefore, the high METH concentrations in these sampling locations have been affected by direct disposal and/or untreated wastewater. The Jiehe River runs through Zhaoyuan city, Shandong province, where the METH concentration is 23.8 ng L^{-1}. The sampling site is located 3.5 km downstream of the WWTP. Therefore, both treated and untreated wastewater and/or direct disposal influenced this sampling location.

KET shows a similar spatial pattern with METH, except these three sampling sites (Fig. 2). The rivers in Tianjin province show higher concentrations and detection frequencies than the other three rivers. Even COC,

Table 2 Names of rivers, location, flow rate ($\times 10^8$ m^3 $years^{-1}$), and mass load (kg $year^{-1}$) of the illicit drugs and their metabolites

No.	Name	Province	Flow	METH	AMP	KET	NK	COC	BE	Cod	Med	EDDP	Total
1	Fuzhou River	Liaoning	2.37	0.11	–	0.01	–	–	–	–	–	–	0.12
2	Biliu River	Liaoning	9.00	–	–	–	–	–	–	–	–	–	–
3	Dayang River	Liaoning	9.8	0.43	–	–	–	–	–	–	–	–	0.43
4	Yalu River	Liaoning	191	327	32.0	1.15	–	–	–	–	–	–	360
5	Daqing River	Liaoning	0.03	0.13	–	–	–	–	–	0.01	–	–	0.13
6	Daliao River	Liaoning	46.6	16.6	–	0.41	–	–	–	–	–	–	17.05
7	Shuangtaizi River	Liaoning	39.5	11.2	–	0.28	–	–	–	–	–	–	11.5
8	Nansha River	Liaoning	1.27	0.1	–	–	–	–	–	–	–	–	0.1
9	Liugu River	Liaoning	6.02	0.18	–	–	–	–	–	–	–	–	0.18
10	Tanghe River	Hebei	0.34	0.16	–	–	–	–	–	0.03	–	–	0.19
11	Daihe River	Hebei	0.51	0.05	–	–	–	–	–	–	–	–	0.05
12	Yanghe River	Hebei	0.28	0.01	–	–	–	–	–	–	–	–	0.01
13	Luanhe River	Hebei	29.0	3.85	–	–	–	–	–	–	–	–	3.85
14	Shahe River	Hebei	4.95	–	–	–	–	–	–	–	–	–	–
15	Douhe River	Hebei	13.1	4.74	–	–	–	–	–	–	–	–	4.74
16	Jiyun River	Tianjin	15.9	4.25	–	2.16	0.77	–	–	–	–	–	7.18
17	Yongdingxin River	Tianjin	0.712	0.41	–	0.04	0.02	0.51	1.15	–	0.02	–	2.15
18	Chaobai River	Tianjin	15	3.33	–	0.59	1.06	–	–	–	–	–	4.99
19	Haihe River	Tianjin	2.85	2.92	–	0.08	0.05	3.68	2.82	–	0.04	0.07	9.66
20	Dagupaiwu River	Tianjin	4.76	3.72	–	1.19	0.3	–	–	–	0.07	0.1	5.38
21	Duliujian River	Tianjin	9.77	0.39	–	0.1	–	6.65	4.05	–	–	–	11.2
22	Qingjinghuang River	Tianjin	NA	–	–	–	–	–	–	–	–	–	–
23	Ziya River	Tianjin	3.09	1.65	–	1.39	0.39	0.02	–	–	–	0.1	3.55
24	Xuanhui River	Shandong	0.44	0.09	–	0.01	–	–	–	–	–	–	0.1
25	Zhangweixin River	Shandong	7.55	0.28	–	0.06	–	4.44	2.68	–	–	–	7.46
26	Majia River	Shandong	2.93	0.52	–	–	–	–	–	–	–	–	0.52
27	Dehuixin River	Shandong	1.23	0.18	–	0.01	–	–	–	–	–	–	0.18
28	Tuhai River	Shandong	8.97	0.31	–	0.15	0.19	–	–	–	–	–	0.65
29	Yellow River	Shandong	283	8.14	–	6.27	–	202	216	–	–	–	432
30	Zimai River	Shandong	2.58	0.22	–	0.03	0.12	–	–	–	–	–	0.37
31	Xiaoqing River	Shandong	8.78	2.83	–	0.39	–	–	0.09	–	–	–	3.31
32	Tahe River	Shandong	NA	–	–	–	–	–	–	–	–	–	–
33	Mihe River	Shandong	4.23	–	–	0.1	–	–	0.03	–	–	–	0.13
34	Yuhe River	Shandong	0.05	0.04	–	–	–	–	–	–	–	–	0.04
35	Jiehe River	Shandong	2.46	5.85	0.8	0.03	–	–	–	0.2	–	–	6.89
36	Jiahe River	Shandong	6.15	1.85	–	0.09	–	–	–	–	–	–	1.94

METH methamphetamine, *AMP* amphetamine, *KET* ketamine, *NK* norketamine, *COC* cocaine, *BE* benzoylecgonine, *Cod* codeine, *MTD* methadone, *EDDP* 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine, *Mor* morphine, *NA* not available

BE, Med, and EDDP in Tianjin have higher detection frequencies than in the other three provinces (Fig. 3). This difference could be attributed to the population density along the watershed area. The concentration trend of the total targeted compounds is in agreement with the population density estimation for Tianjin (1269 people km^{-2}) > Shandong (623 people km^{-2}) > Hebei (391 people km^{-2}) > Liaoning (297 people km^{-2}). We analyzed the relationship between population density and median concentrations for AMP-like compounds, KET, cocainics, and total compounds in water collected from four different provinces (Fig. S1). Opioids were not included in this analysis because their detection frequency in surface water is low. Significant relationships were found between population density and median concentrations for AMP-like compounds ($r^2 = 0.917$), KET ($r^2 = 0.970$), cocainics (0.915), and total compounds ($r^2 = 0.970$). Higher population density areas experience high drug use, suggesting higher emissions of illicit drugs and their metabolites into the aquatic environment.

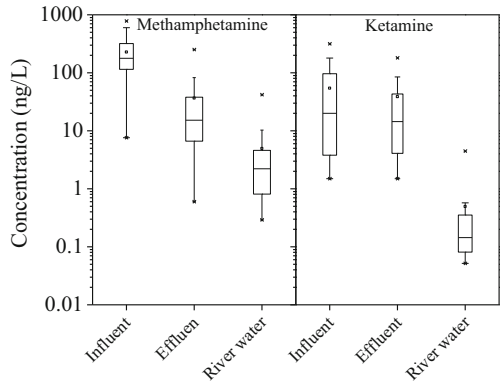

Fig. 1 Concentrations of methamphetamine and ketamine in the influent, effluent, and river water samples. Influent and effluent concentrations were measured from 36 WWTPs in 18 major Chinese cities reported by Du et al. (2015). The *bottom* and *top of the boxes* represent the 25th and 75th percentiles of values, respectively. The *solid horizontal line within each box* represents the median value. The *little box* represents the mean value. The *lower whisker* is equal to the minimum values. The *upper whisker* is equal to the maximum values

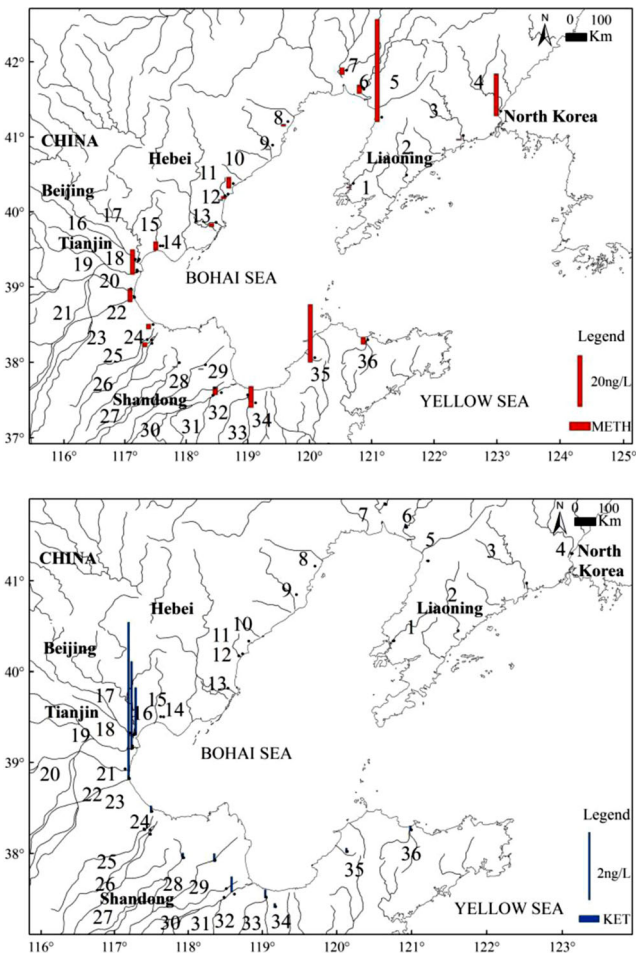

Fig. 2 Spatial pattern of methamphetamine (METH) and ketamine (KET) in 36 rivers draining into the Bohai Sea and north Yellow Sea. The number of rivers is listed in Table 2. METH and KET are represented by *red* and *blue*

Drug loads in rivers and the uncertainty analysis

Runoff into riverine systems plays an important role in the transport of anthropogenic pollutants from terrestrial sources to the ocean (Wang et al. 2015). To obtain the mass load of illicit drugs into Bohai Sea and north Yellow Sea through runoff, we calculate the mass load (m) using the concentrations of illicit drugs and the annual runoff for all rivers.

$$m = \sum_{i=1}^{n} F_i C_i$$

where F_i is the annual runoff for river i, C_i is the concentration of illicit drugs in water, and n is the number of the rivers, from 1 to 36.

The results showed that the total drug mass load was estimated to be 896 kg year^{-1} (Table S2). Due to large annual flow rates, the Yellow River and Yalu River are found to steadily carry almost 432 and 360 kg of illicit drug equivalents per year, respectively. However, they carry different illicit drugs. The Yellow River mainly carries COC and BE (418 kg year^{-1}), and the Yalu River mainly carries METH (371 kg year^{-1}). The total riverine input of METH is estimated to be 401 kg year^{-1}, and the Yalu River load accounts for almost 82 % of the total input (Fig. 4). The mass load results indicate that the Yalu River carries 1.1 kg of METH daily. This suggests approximately 36,700 doses per day, assuming 30 mg as an average dose. If METH users abuse the drug daily, the estimated prevalence of METH use reaches 1.3 % in this region. There are two major cities in this region, Dandong city, China, with a population of 2.46 million people, and Xinyizhou city, North Korea, with a population of 0.352 million people. This value (best estimate = 0.6 %, range of 0.2–1.3 %) reaches the upper level of the use of AMP-like compounds in East and South-East Asia (UNODC 2015). Because this river is flowing along the border of China and North Korea, drug manufacturing may be a potential source of METH in this area.

It should be noted that the estimation of the annual load carried by these rivers was based on the illicit drugs in the dissolved phase and one single sampling campaign in each river. The amount of these illicit drugs and their precipitated metabolites was relatively low compared to the amount in the dissolved phase (Baker and Kasprzyk-Hordern 2011; Metcalfe et al. 2010; Senta et al. 2013). Therefore, we only considered the concentrations of dissolved compounds for the estimation of the mass load. In addition, the observed concentrations cannot remain constant throughout the year due to different flow rates observed during dry and wet seasons. The annual runoffs change due to climate changes and increasing human activities. There is a degree of uncertainty in the estimation of the mass load due to the use of fixed-point values for the concentrations and runoff. To quantify this

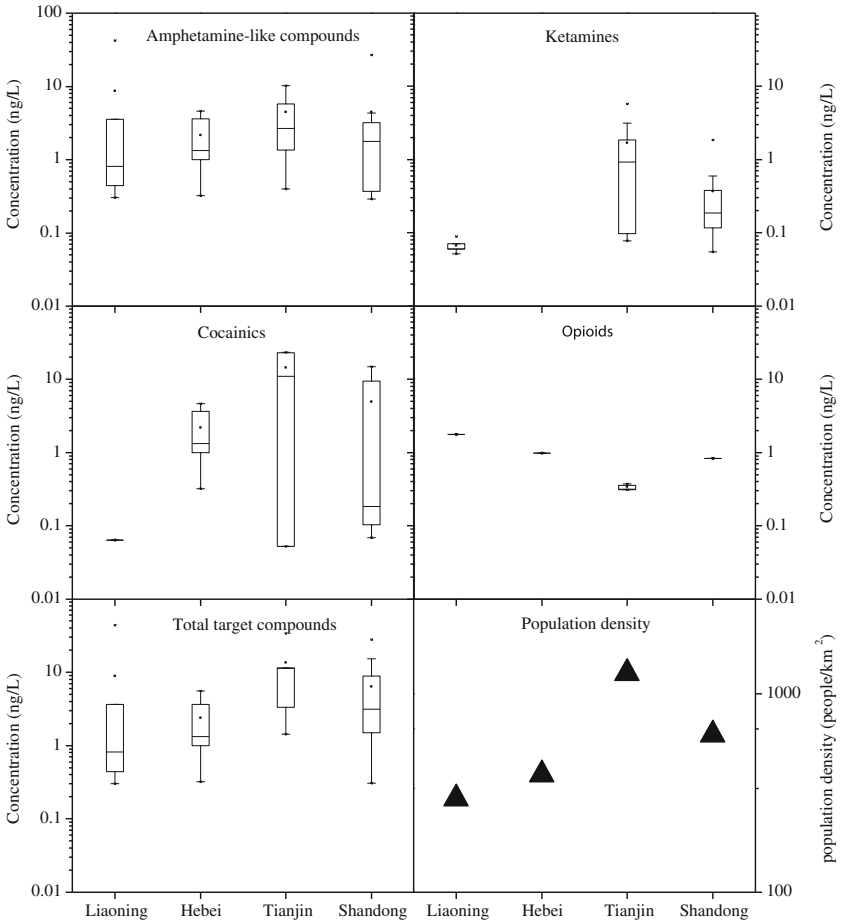

Fig. 3 Population density and concentrations of amphetamine-like compounds, ketamines, cocainics, and opioids in surface river water samples collected from four provinces of Liaoning, Hebei, Tianjin, and Shandong. Amphetamine-like compounds: amphetamine, methamphetamine, methylenedioxymethamphetamine, and 3,4-methylenedioxyamphetamine; ketamine and its metabolite norketamine; cocaine and its metabolite benzoylecgonine; opioids: morphine and its metabolite codeine, methadone and its metabolite 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine, and the exclusive metabolite of heroin, 6-acetylmorphine. The *bottom* and *top of the boxes* represent the 25th and 75th percentiles of values, respectively. The *solid horizontal line within each box* represents the median value. The *little box* represents the mean value. The *lower whisker* is equal to the minimum values. The *upper whisker* is equal to the maximum values

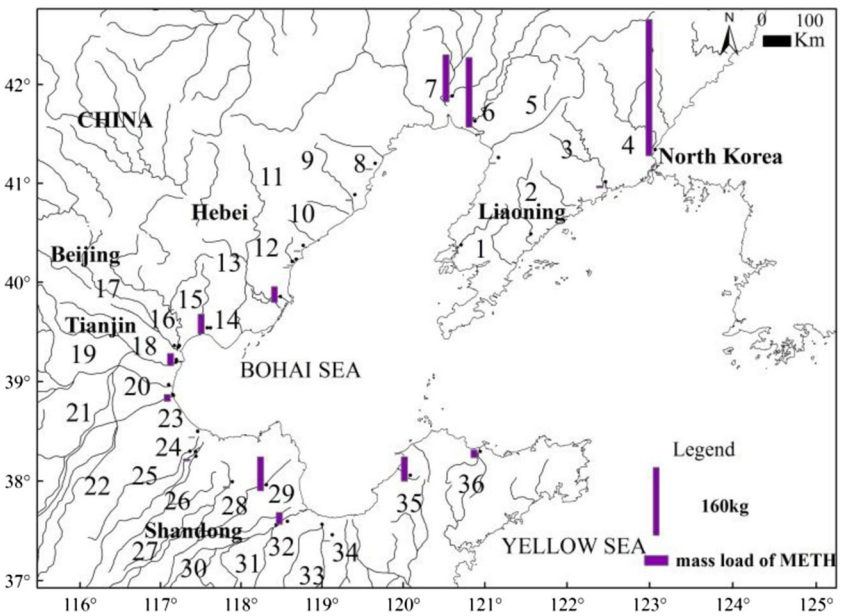

Fig. 4 Spatial distribution of mass load of methamphetamine (METH) per year in 36 rivers draining into the Bohai Sea and north Yellow Sea

uncertainty and its impact on the estimation of the expected mass loads, Monte Carlo simulation (Oracle Crystal Ball software, Version 7.3.1) was used to conduct the uncertainty analysis. Annual runoff was assumed to have a normal distribution, with a conservative estimate of a 10 % relative standard deviation. The concentrations of illicit drugs were taken as lognormal distribution, with a conservative estimate of a 30 % relative standard deviation. The uncertainty analysis showed that the mass load for total drugs (Fig. S2) and METH (Fig. S3) was estimated to be 884 (range 684–1160) and 387 kg (range 261–594) per year. A high mass load of illicit drugs may pose a potential ecotoxicological risk in these aquatic ecosystems.

Conclusions

In summary, the present work reports the occurrence of illicit drugs and their metabolite residues in natural surface waters from 36 rivers draining into the Bohai Sea and north Yellow Sea, north China. METH and KET are the most abundant illicit drugs found in these 36 rivers, reflecting the high prevalence of METH and KET use in China. Drug residue levels in the aquatic environment have also been proved as good indicators of illicit drug abuse. High concentrations of illicit drugs and their metabolites occurred in the areas that have a high population density. Monitoring the concentrations of illicit drugs in surface water is necessary to investigate the transport and fate of these compounds in the environment as well as their potential ecotoxicological significance in aquatic ecosystems. Further study should focus on the long-term monitoring of the variation of illicit drugs and their metabolites in rivers. The high mass load of METH in the Yalu River, on the border of China and North Korea, suggests that two governments should strengthen their cooperation and take measures to address drug trafficking and manufacturing.

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