1 Manuscript submitted to Environmental Pollution-2016-02-18

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10 Occurrence of Illicit Drugs in Surface Waters in China

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12 **Kaiyang Li, Peng Du, Zeqiong Xu, Tingting Gao, Xiqing Li***

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14 Laboratory of Earth Surface Processes, College of Urban and

15 Environmental Sciences, Peking University, Beijing, 100871, P. R. China

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* Corresponding author, e-mail: xli@urban.pku.edu.cn, phone/fax: 86-10-62753246

Abstract

Illicit drugs have been recognized as a group of emerging contaminants. In this work, occurrence of common illicit drugs and their metabolites in Chinese surface waters was examined by collecting samples from 49 lakes and 4 major rivers across the country. Among the drugs examined, methamphetamine and ketamine were detected with highest frequencies and concentration levels, consistent with the fact that these are primary drugs of abuse in China. Detection frequencies and concentrations of other drugs were much lower than in European lakes and rivers reported in the literature. In most Chinese surface waters methamphetamine and ketamine were detected at concentrations of several ng L^{-1} or less, but in some southern lakes and rivers, these two drugs were detected at much higher concentrations (up to several tens ng L^{-1}). Greater occurrence of methamphetamine and ketamine in southern surface waters was attributed to greater abuse and more clandestine production of the two drugs in southern China.

Capsule Abstract:

Methamphetamine and ketamine are the primary illicit drugs detected in surface waters in China, with concentrations up to several tens ng L^{-1} in some southern rivers and lakes.

Introduction

Abuse of illicit drugs (e.g., cocaine, heroin) is a worldwide problem (UNODC, 2014). Similar to legal pharmaceuticals, illicit drugs are not completely metabolized by the human body and typically enter sewage unchanged or as metabolites or conjugates (Zuccato et al., 2008a). Occurrence of illicit drugs and metabolites in wastewater has been widely observed across the globe, with concentrations up to $\mu\text{g L}^{-1}$ level (Chiaia et al., 2008; Postigo et al., 2008; Pal et al., 2013). However, their complete removal can rarely be achieved during wastewater treatment (e.g. Postigo et al., 2010; Evgenidou et al., 2015; Postigo et al., 2008; Pal et al., 2013). As a result, part of excreted illicit drugs and metabolites would enter receiving waters through effluent discharge. In regions where sewage treatment facilities are not available, excreted illicit drugs may enter receiving waters through direct sewage discharge. Illicit drugs may also enter receiving waters via direct dumping by clandestine manufacturers and/or drug dealers. Thus, illicit drugs and metabolites have recently been recognized as a group of emerging contaminants of concern (Zuccato et al., 2008b; Pal et al., 2013).

The potential health and eco-toxicological risks illicit drugs may pose have prompted investigations on its occurrence in surface waters in many European countries, such as Italy (Zuccato et al., 2005; Zuccato et al., 2008a), Switzerland (Berset et al., 2010), England (Kasprzyk-Hordern et al., 2008, 2009; Baker and Kasprzyk-Hordern, 2013), Spain (Huerta-Fontela et al., 2008; Boleda et al., 2009; Postigo et al., 2010; Vazquez-Rog et al., 2010; Vazquez-Rog et al., 2012; Martínez

Bueno et al., 2011; Valcárel et al., 2012). Cocaine (COC) and its metabolite benzoylecgonine (BE), morphine (MOR), codeine (COD), methamphetamine (METH), amphetamine (AMP), 3,4-methylenedioxymethamphetamine (MDMA), 3,4-methylenedioxyamphetamine (MDA), methadone (MTD) and its metabolite 2-ethylidene -1,5-dimethyl-3,3-diphenyl-pyrrolidine (EDDP), ketamine (KET) and its metabolite norketamine (NK) were all detected, at different concentrations and frequencies, in the rivers and lakes examined.

Reports on the occurrence of illicit drugs in surface waters in countries and regions outside Europe are scarce. Bartelt-Hunt et al. (2009) examined the occurrence of METH in surface waters influenced by wastewater treatment plants (WWTP) in Nebraska. Lin et al. (2014) examined the occurrence of ketamine (KET) and its metabolite norketamine (NK) in surface waters in Taipei and Kaohsiung-Pingtung areas of Taiwan. KET was detected at the overwhelming majority of sampling points, with concentrations up to 420 ng L⁻¹. KET concentrations were in overall much higher in surface waters in Taipei relative to the Kaohsiung-Pingtung area, likely due to the four-fold greater population density of the former area. Jiang et al. (2015) reported detection of AMP, KET, and MDMA in coastal waters of southwestern Taiwan, with frequencies of 15%, 27%, and 15% (n=52), and mean concentrations of 6.88, 3.69, and 0.51 ng L⁻¹, respectively.

Mainland China has seen rapid increases in illicit drug use in the past quarter century. The number of registered drug users has more than doubled in the past five years (Office of China National Narcotic Control Commission, 2014). Drug seizures

(especially of METH) have also increased significantly in recent years. Recent studies revealed that METH loads in Chinese wastewater were lower than in Norway, Czech Republic, Australia, and some American cities, but were higher than in most other countries, such as Spain, Italy, and Belgium (Usman et al., 2014; Li et al., 2014; Du et al., 2015). KET loads in wastewaters in south China were lower than in Taiwan, but were much higher than in countries other than China. The objective of this work was to examine, for the first time, the occurrence of illicit drugs in Chinese surface waters. For this purpose, samples were collected from major Chinese lakes and rivers. Twelve drugs of abuse and metabolites (METH, AMP, KET, NK, MOR, COD, COC, BE, MDMA, MDA, MTD, EDDP) were analyzed using LC-MS/MS. The primary illicit drugs in Chinese surface waters and spatial variations in their occurrence were revealed.

Materials and Methods

Sample collection

Surface water samples were collected from 4 major rivers of China, the Yangtze River, the Pearl River, the Songhua River, and the Yellow River. The Yangtze River, also called Changjiang, is the longest river of the country (6,300 km long), flowing from the glaciers on the Qinghai-Tibet Plateau eastward across southwest, central and eastern China before emptying into the East China Sea at Shanghai. The Pearl River originates in Yunan province in southwest, flows about 2,414 km through Guangxi and Guangdong provinces, and empties into the South China Sea. The Songhua River

is the largest tributary of the Heilong River, flowing about 1,434 km from Changbai Mountains through Jilin and Heilongjiang provinces in Northeast China. Originating in the Bayan Har Mountains in Qinghai province, the 5,464 km-long Yellow River flows through nine provinces in northwest and north China, and empties into the Bohai Sea. The four rivers rank 1 to 4, in order, in annual discharge (30,165, 10,585, 2,463, and 2,096 m³ s⁻¹, respectively).

Given the lengths of the rivers, comprehensive sampling across each river was prohibited by cost and manpower. In this work, 5-6 grab samples were collected at each river, from upstream to downstream of the urban area of a major city through or near which a river flows. The cities are Wuhan (the Yangtze River), Guangzhou (the Pearl River), Haerbin (the Songhua River), and Yinchuan (the Yellow River), which are capitals of Hubei, Guangdong, Heilongjiang, and Ningxia provinces, respectively. Samples were collected at points that were at least 3 m from river banks. At the Songhua and Yellow Rivers, sample collection was performed once on May 4th and 13th of 2015, respectively. At the Yangtze and Pearl Rivers, samples were collected twice, on July 3-4th and July 11-12th of 2015, respectively. The locations of the sampling points, cities, and rivers are presented in [Figure 1](#).

Surface water samples were also collected from 49 major lakes across China ([Figure 2](#)) in a sampling campaign conducted from July to September, 2014. The lakes include the largest lakes of the country, such as Poyang Lake in Jiangxi province and Dongting Lake in Hunan province, and small lakes within cities, such as Xihu in Hangzhou and Xuanwuhu in Nanjing. Among the lakes, Longchi Lake (LCH),

Dianchi (DC), Erhai (EH), Xuanwuhu (XWH), Donghu(DH), Taihu (TH), Luomahu (LMH), Chaohu (CH), Dongting Lake (DTH), Poyang Lake (PYH), Xihu (XH), Hengshui Lake (HSH), and Henghu (HH) are either within or close to cities (with distances <10 km). The other 36 lakes, such as Qinghai Lake, are far from large cities. Samples were collected with boats and using Hydro-BIOS Integrating Water Sampler (2.5L) at locations that are at least 500 m from shores in all lakes but Namucuo in Tibet (where samples were collected at the lake shore). At each sampling location, four sub-samples were collected within a surrounding area of about 10000 m² and mixed on spot to constitute a composite sample of that location. The longitudes and latitudes of the sampling locations are presented in [Table 1](#).

Once collected, both river and lake samples were acidified to pH=2 using HCl and frozen at a local laboratory. The samples were then shipped to our own laboratory with ice and remained frozen upon arrival. The river and lake samples were stored at until analysis –20 °C(for less than three weeks and three months, respectively).

Analysis

Standards of illicit drugs as well as their deuterated internal standards were purchased from Cerilliant (Round Rock, TX, USA). After the river and lake samples were thawed, 200 ml of each sample was filtered using glass fiber membranes (Shanghai Hongguang Industrial Corporation Limited) to remove solid particles, followed by adding deuterated internal standards (10 ng each). An Oasis MCX cartridge was conditioned in sequence with 6 mL of methanol (MeOH), 4 mL of deionized water, and 4 mL of deionized water at pH=2. Sample was then loaded to the

cartridge at a flow rate of 2-3 mL/min. After drying under vacuum, the cartridge was eluted in sequence with 4 mL of MeOH and 4 mL of 5% NH₃ in MeOH. The eluate was evaporated to dryness with gentle nitrogen stream and re-dissolved in 200 µL acetonitrile (AcN)/water (5/95, v/v). A further cleaning step was performed using a 0.22 µm centrifugal filter (VWR International, Radnor, PA, USA).

Compound separation was achieved using a UFLCXR-LC system (Shimadzu, Japan) with a Phenomenex Gemini C18 column (100 mm × 2 mm, 3 µm). An injection volume of 5 µL was adopted. For METH, AMP, KET, NK, the mobile phase was composed of 30 mM ammonium formate in ultrapure water with pH adjusted to 3 using 98% formic acid (A) and 0.1% formic acid in AcN (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; 7.6-13.0 min: 5% B. For the remaining compounds (COC, BE, etc.), the mobile phase was composed of 30 mM ammonium formate in ultrapure water with pH adjusted to 3.5 using 98% formic acid (A) and methanol (B). The elution gradient was: 0-0.1 min: 5% B; 0.1-3.0 min: 30% B; 3.0-5.0 min: 80% B; 5.0-9.5 min: 95% B; 9.5-14.0 min: 5% B. The flow rate for both mobile phases was controlled at 0.3 mL/min.

MS determination of the target analytes was performed using an API 4000 triple quadrupole mass spectrometer (AB SCIEX, USA) equipped with an electrospray interface operating in positive ionization mode. MS acquisition was carried out in selected reaction monitoring (SRM) mode. MS conditions used to register target compounds, limits of detection (LODs) and limits of quantification (LOQs) achieved

for each analyte, as well as other method validation parameters (recoveries, matrix effects, repeatability) are provided in Table 2.

Results and Discussion

Occurrence in lakes

AMP, COC, BE, and MOR were below detection limits in all lakes. COD and MDA were detected in two lakes, with concentrations of 2.4 ng L⁻¹ in Dianchi and 0.3 ng L⁻¹ in Poyang Lake, 2.7 ng L⁻¹ in Dianchi and 1.9 ng L⁻¹ in Erhai, respectively (Table 1). MTD and EDDP were detected in only one lake, Dianchi, with concentrations of 1.8 ng L⁻¹ and 1.9 ng L⁻¹, respectively. The detection frequencies of COC, BE, COD, MOR, MTD, EDDP, MDA were much lower than in lakes in Switzerland and Italy (Zuccato et al., 2008b; Berset et al., 2010).

METH was above its method LOQ in 9 lakes. The highest concentration was found in Dianchi. (95.9 ng L⁻¹). KET and NK concentrations were quantified in 20 and 18 lakes, respectively, with the highest concentrations found also in Dianchi (12.6 ng/L for KET and 5.6 ng/L for NK). In lakes other than Dianchi, METH, KET, and NK were either below LODs or below 4.0 ng L⁻¹. The detection frequency of METH in Chinese lakes is higher than in Switzerland and Italy (Zuccato et al., 2008b; Berset et al., 2010). High detection frequencies of METH and KET (and its metabolite NK) in Chinese lakes are consistent with the fact METH and KET are the two primary illicit drugs in China (Du et al., 2015). Higher detection frequencies of KET relative to METH may be explained by the fact that removal of KET by wastewater treatment

is low (Du et al., 2015; Yargeau et al., 2014; Andrés-Costa et al., 2014), whereas near complete removal of METH was observed at most sewage treatment plants in China (Li et al., 2014; Du et al., 2015).

Among the 49 lakes sampled in this study, the numbers of lakes in the north and south of Yangtze River are about the same (24 vs. 25). Among the 9 lakes where METH was detected, 3 and 6 lakes were in north and south China, respectively (Table 1). The north-south difference in occurrence of KET in Chinese lakes was even more pronounced. KET and NK were detected in 17 and 16 southern lakes, respectively, whereas the two compounds were detected in only 4 and 3 northern lakes, respectively (Table 1). Much higher detection frequencies of KET and NK in southern lakes is consistent with much higher prevalence of KET abuse in the south, as revealed by wastewater analysis (Du et al., 2015). Occurrence of METH and KET was also related to the distances between the lakes and large cities. The detection frequency of METH in lakes within or near cities was 36% (4 out of 13), whereas METH was detected in 17% (6 out of 36) of lakes far from cities (Table 1). KET and NK were detected in 77% of lakes within or near cities, whereas detection frequencies in lakes far from cities were 46% and 33%, respectively (Table 1). Clearly, occurrence of METH and KET in lakes increased with increasing population density around the lakes.

Occurrence in rivers

In general, detection frequencies and concentrations levels of MTD, EDDP, MDMA, MDA, MOR, COD, COC, and BE were low in the four rivers examined,

albeit higher than those in Chinese lakes. MTD, MOR, and MDA were not detected in any river (Table 3). EDDP was above LOQ at all sampling points in the Yellow River and the five downstream points in the Pearl River. The maximum EDDP concentration in the two rivers was 0.4 ng L^{-1} . MDMA was detected only in the Pearl River (at all points), with concentrations ranging from 0.4 to 1.3 ng L^{-1} . COC and BE concentrations ranged from 0.2 - 0.7 ng L^{-1} and 0.8 - 1.4 ng L^{-1} in the Yangtze River, respectively. BE was also detected at concentration level below 1 ng L^{-1} at the two downstream points in the Pearl River. The two compounds were below detection limits in the other rivers. Detection frequencies of COD in both Yellow and Pearl Rivers were 100%, with concentration ranges of 1.1 - 2.2 ng L^{-1} and 0.5 - 2.1 ng L^{-1} , respectively. COD was also detected at two downstream points of the Songhua River and at three points in the Yangtze River. The overall low occurrence of these compounds (compared to those of METH and KET) in Chinese lakes and rivers is consistent with their low use that was demonstrated by the observation that concentrations of these compounds were very low or even below detection limits in wastewater in China (Usman et al., 2014).

Since water samples in this study were collected at river segments that flow through or near major cities, concentrations of above mentioned compounds observed here likely represent the highest levels in major Chinese rivers. However, detection frequencies and concentration levels of these compounds were much lower than those in European rivers. For example, COC and BE were detected at frequencies up to 100% and concentrations up to 60 and 346 ng L^{-1} , respectively, in Ebro, Tagus, Henares, and

Llobregat rivers in Spain (Huerta-Fontela et al., 2008; Boleda et al., 2009, Postigo et al., 2010, Martínez Bueno et al., 2011), Thames and Taff rivers in England (Zuccato et al., 2008b; Kasprzyk-Hordern et al., 2009); and Olona, Lambro, Po, and Arno rivers in Italy (Zuccato et al., 2008b). MTD and EDDP were detected at most sampling points with concentrations up to 18.1 and 64 ng L⁻¹, respectively, in the Tagus and Llobregat rivers in Spain (Boleda et al., 2009; Valcárel et al., 2012), Swiss rivers and creeks (Berset et al., 2010), and the Olona, Lambro, Po, and Arno rivers in Italy (Zuccato et al., 2008b). Similarly, higher detection frequencies and concentration levels of MOR and COD were also observed in the Ebro and Llobregat rivers in Spain (Boleda et al., 2009; Postigo et al., 2010), Swiss rivers and creeks (Berset et al., 2010), and the Olona, Lambro, Po, and Arno rivers in Italy (Zuccato et al., 2008b). MDMA was detected in the Ebro, Tagus, and Llobregat rivers in Spain (Huerta-Fontela et al., 2008; Boleda et al., 2009; Postigo et al., 2010), the Thames River in England (Zuccato et al., 2008b), Swiss rivers and creeks (Berset et al., 2010), and the Olona, Lambro, Po, and Arno rivers in Italy (Zuccato et al., 2008b). Lower occurrence in the four Chinese rivers may partly be because of much greater dilution factors at the rivers (due to much greater stream flows) relative to the European rivers examined. Low use of the compounds in China (as evidenced by low loads in Chinese wastewater) (Usman et al., 2014) relative to Europe (e.g., Postigo et al., 2010; Baker and Kasprzyk-Hordern, 2011) is another important contributor to the low occurrence in Chinese rivers.

METH and KET were detected with much higher frequencies and concentration

levels in the four rivers than other compounds examined. Both drugs were detected in all the four rivers. North-south difference in occurrence of the two drugs in rivers was also evident, as in lakes (Figure 3, Table 3). KET was above LOQ at two sampling points in the Songhua and Yellow Rivers, respectively, whereas in Yangtze and Pearl Rivers KET was detected at all sampling points (Table 3). KET concentrations ranged from below LOD to 0.4 ng L⁻¹ in the Songhua and Yellow Rivers. In contrast, KET concentrations ranged from 1.8-3.7 ng L⁻¹ and 9.9-21.7 ng L⁻¹ in the Yangtze and Pearl Rivers, respectively. NK, the metabolite of KET, was detected only in the Yangtze and Pearl Rivers, with concentration ranges of 0.4-1.0 ng L⁻¹ and 3.1-6.5 ng L⁻¹, respectively. The KET concentration range in the Yangtze River was similar to that in river waters in Taipei area (Lin et al., 2014). The concentration range in the Pearl River was roughly at the same level as in a major river in UK that receives discharges from multiple wastewater treatment plants, and in surface waters of the natural park of Pego-Oliva Marsh in Valencia (Spain) (Vazquez-Rog et al., 2012; Baker and Kasprzyk-Hordern, 2013).

METH concentrations ranged from below LOD to 3.9 ng L⁻¹ and 0.8-1.7 ng L⁻¹ in the Songhua and Yellow Rivers, respectively. In contrast, METH concentrations ranged from 1.4-2.8 ng L⁻¹ and 17.4-58.2 ng L⁻¹ in the Yangtze and Pearl Rivers, respectively. In addition, in the Yangtze and Pearl Rivers, the inter-day variation of concentrations at a particular sampling point was not significant, as was the case for KET. AMP, mainly arising from METH metabolism (Li et al., 2014), was detected only in the Pearl River, with a concentration range of 0.5-1.4 ng L⁻¹. Detection

frequencies and concentration levels of METH were much higher than in rivers in Italy, Switzerland, Spain and England. This is consistent with the fact that overall METH abuse in these countries is much lower than in China (Du et al., 2015). The highest METH concentration observed in this study was lower than that (62.6 ng L⁻¹) reported by Bartelt-Hunt et al. at downstream of a WWTP at Hasting, Nebraska (Bartelt-Hunt et al., 2009).

METH concentrations increased progressively from upstream (<LOQ) to downstream sampling points in the Songhua River. This is likely due to release (e.g., via effluent discharge) from the city of Haerbin it flows through, as indicated by METH concentration increase from upstream (SH3, 1.4 ng L⁻¹) to downstream (SH4, 3.0 ng L⁻¹) of the largest sewage treatment plant of the city (Figure 1 and 3). However, no clear upstream-downstream trend was observed in the other three rivers, which was also true for KET. In the three rivers, both METH and KET concentrations at the first upstream points were even higher than at certain downstream points. This observation indicates that significant amounts of METH and KET in the river segments near the cities were carried from upstream segments.

The north-south difference in KET occurrence in rivers and lakes is understandable in a sense that KET abuse in China mainly occur in provinces in the south of the Yangtze River (Du et al., 2015). However, significantly lower METH concentrations in northern lakes and rivers cannot be explained by the difference in METH abuse between the North and South. Previous study indicates there was no clear geographic pattern in METH abuse in major cities across China (Du et al., 2015).

Therefore it is unlikely that average use of METH per capital (including population in rural areas) is significantly different between the South and North. Given that there are fewer large rivers (each having much smaller stream flows) and lakes in the North relative to the South, overall greater METH occurrence is expected in northern rivers and lakes, if METH in the rivers and lakes mainly comes from human consumption. The greater detection frequencies and concentrations of METH in southern lakes and rivers are most likely caused by direct dumping arising from illegal manufacturing, as illegal production of synthetic illicit drugs are more active (evidenced by more seizures) in southern provinces. The very high METH and KET concentrations in the Pearl River at Guangzhou corroborate with the fact that illegal production of METH and KET are most active in Guangdong, as evidenced by greatest seizures in the province, compared with the rest of China ([Du et al., 2015](#)). In fact, METH concentrations in effluents of two major sewage treatment plants in Guangzhou during the river water sampling days were 40.2 ± 10.8 and 72.3 ± 20.8 ng L⁻¹, respectively. According to a local monitoring station, flows at two cross sections near sampling point 3 and 4 were 5.5×10^8 and 6.1×10^8 m³/d, respectively. Given that total municipal wastewater volume in the Guangzhou area was about 3.8 million cubic meters per day (according to www.dowater.com), effluents will be diluted by a factor of at least 150 (assuming all the effluents are discharged into the river). This means that even for Guangzhou, the provincial capital of Guangdong, the overall contribution of METH release into the Pearl River via effluent discharge is negligible, compared to the average concentration (31.1 ± 16.9 ng L⁻¹) in the river.

In summary, this work examined the concentrations of common illicit drugs and metabolites in major Chinese lakes and rivers. Since samples collected in a particular lake/river were limited, this work only provided a snapshot on the occurrence of these drugs in surface waters in China. The distribution of the drugs and metabolites in large lakes and along the entire lengths of the rivers was not known. Seasonal variations in the occurrence were not examined either. More sampling is required to close these gaps. Future research is also needed to examine the fate of the drugs and metabolites in the surface waters in China and to assess the potential ecological risks of these compounds.

Acknowledgements

This work was funded by the National Science Foundation of China (Grant No. 41371442 and 41401566). The authors wish to thank Prof. Fuli Xu's group at the College of Urban and Environmental Sciences of Peking University for their assistance in lake water collection. The authors also wish to thank two anonymous reviewers whose comments improved the manuscript.

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Figure captions

Figure 1. Locations of sampling points in the Songhua (SH), Yellow (Y), Yangtze (YZ), and Pearl (P) rivers.

Figure 2. Locations of lakes where grab samples were collected.

Figure 3. METH, AMP, KET, and NK concentrations in the Songhua (SH), Yellow (Y), Yangtze (YZ), and Pearl (P) rivers.

Figure 1

Figure 2

Figure 3

Table

Table 1. Sampling information and concentrations of illicit drugs in Chinese lakes. Concentrations of MOR, MDMA, COC, BE, AMP were below detection limits in all lakes and were not listed in the table.

[illegible]

Qinghaihu(QHH)	North	No	100.65278	36.70000	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
Yangzhuoyonghu(YZYH)	North	No	90.75556	29.26667	< LOD	< LOQ	< LOD	< LOD	< LOD	< LOD	< LOD
Namucuo(NMC)	North	No	91.06111	30.82833	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
Yangbajing(YBJ)	North	No	90.62500	30.20000	< LOQ	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
Hongfenghu(HFH)	South	No	106.44340	26.61389	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
Yilonghu(YLH)	South	No	102.62361	23.80139	0.2	0.1	< LOD	< LOD	< LOD	< LOD	< LOD
Qilanhu(QLH)	South	No	102.84222	24.30528	3.5	< LOD	< LOD	< LOQ	< LOD	< LOD	< LOD
Fuxianhu(FXH)	South	No	102.97986	24.54375	< LOD	< LOQ	< LOD	< LOD	< LOD	< LOD	< LOD
Baiyangdian(BYD)	North	No	116.08681	39.03194	2.4	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
Qiandaohu(QDH)	South	No	119.03403	29.64444	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
Hongzehu(HZH)	South	No	118.72639	33.49236	< LOD	0.3	0.1	< LOD	< LOD	< LOD	< LOD
Wabuhu(WBH)	South	No	116.96319	32.47986	< LOD	0.1	0.1	< LOD	< LOD	< LOD	< LOD
Dongjianghu(DJH)	South	No	113.39236	25.91528	< LOD	1.0	0.2	< LOD	< LOD	< LOD	< LOD
Longganhu(LGH)	South	No	116.12569	30.02222	< LOD	0.7	0.4	< LOD	< LOD	< LOD	< LOD
Danjiangkou(DJK)	South	No	111.60972	32.69722	< LOD	0.1	< LOD	< LOD	< LOD	< LOD	< LOD
Changhu(LH)	South	No	112.48472	180.50417	< LOD	0.7	0.4	< LOD	< LOD	< LOD	< LOD
Longzehu(LZH)	South	No	114.63194	30.33889	< LOD	0.4	0.1	< LOD	< LOD	< LOD	< LOD
Gangnanshuiku(GNSK)	North	No	114.06458	38.38056	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOQ
Zhaoyanghu(ZYH)	North	No	117.03611	34.98819	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
Weishanhu(WSH)	North	No	117.27500	34.79444	< LOQ	0.2	0.1	< LOD	< LOD	< LOD	< LOD
Dongpinghu(DPH)	North	No	116.32361	36.06458	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
Guantingshuiku(GTSK)	North	No	115.73194	40.41042	< LOQ	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD

Table 2. Analysis conditions, limits of detection (LOD, ng L⁻¹), limits of quantification (LOQ, ng L⁻¹), recovery (spike=2 ng), matrix effect (spike=2 ng), and repeatability (RSD %) of monitored chemical residues.

Chemical Residue	Retent - ion (min)	Precursor ion (m/z)	DP ^a (V)	Quantifier		Qualifier		LOD	LOQ	Recovery (%)	Matrix effect (%)	Repeatability	
				Product ion (m/z)	CE ^b (V)	Product ion(m/z)	CE ^b (V)					Inter-	Intra-
AMP	3.77	136.1	40	91.1	20	119.1	15	0.2	0.4	105.2±4.8	92.5±5.5	0.44	0.23
AMP- <i>d</i> ₈	3.73	144.1	40	97.1	22			-	-	-	-	-	-
METH	3.97	150.1	35	91.2	20	119.2	15	0.03	0.1	90.0±7.3	95.2±12.6	1.06	0.96
METH- <i>d</i> ₈	3.95	158.1	40	93.2	24			-	-	-	-	-	-
KET	4.39	238.1	50	207.1	20	125.1	38	0.03	0.1	94.8±9.4	98.7±2.6	0.55	0.73
KET- <i>d</i> ₄	4.38	242.1	60	129.1	37	-	-	-	-	-	-	-	-
NK	4.29	224.1	40	125.1	32	207.1	16	0.01	0.1	85.7±3.7	105.9±2.0	0.44	1.09
NK- <i>d</i> ₄	4.28	228.1	45	129.1	30	-	-	-	-	-	-	-	-
BE	5.48	290.1	108	105.1	40	168.1	26	0.2	0.5	106.9±4.5	105.1±5.2	0.15	0.22
BE- <i>d</i> ₃	5.47	293.2	93	171.2	27	-	-	-	-	-	-	-	-
COD	3.99	300.1	90	215.1	35	165.1	54	0.05	0.1	87.5±6.6	85.8±5.7	1.50	0.26
COD- <i>d</i> ₆	3.97	306.2	103	165.2	55	-	-	-	-	-	-	-	-
MOR	2.76	286.2	90	201.3	35	181.1	49	0.2	0.5	104.2±8.8	103.2±7.1	0.97	0.44
MOR- <i>d</i> ₃	2.74	292.1	90	181.1	51	-	-	-	-	-	-	-	-
COC	5.64	304.1	114	182.2	26	150.3	34	0.01	0.05	110.0±14.5	84.2±2.9	0.82	0.38
COC- <i>d</i> ₃	5.66	307.1	105	185.1	28	-	-	-	-	-	-	-	-
MDA	4.81	180.1	41	162.9	15	135.0	26	0.2	0.5	97.8±8.1	108.3±4.7	0.75	0.95
MDA- <i>d</i> ₅	4.96	185.1	55	168.0	14	-	-	-	-	-	-	-	-
MDMA	4.87	193.8	70	162.9	15	134.9	25	0.05	0.1	110.6±9.9	88.3±0.3	1.37	0.97
MDMA- <i>d</i> ₅	4.89	199.1	65	165.0	17	-	-	-	-	-	-	-	-
MET	6.52	310.3	65	105.1	40	265.1	20	0.04	0.1	87.4±3.4	110.4±1.1	0.57	0.28
MET- <i>d</i> ₉	6.55	319.3	60	268.2	22	-	-	-	-	-	-	-	-
EDDP	6.17	278.2	100	234.2	33	249.2	33	0.01	0.1	90.7±7.4	108.3±32.9	0.42	0.82

EDDP-d_3	6.17	281.2	100	234.2	33	-	-	-	-	-	-	-	-
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a: Declustering potential; b: Collision energy

Table 3. Concentrations of illicit drugs in the Songhua (SH), Yellow (Y), Yangtze (YZ), and Pearl (P) rivers. Concentrations of MOR, 6-AC, and MDA were below LOD in all the four rivers and were not listed in the table. Sampling numbers 1 to 5 (or 6) represent upstream to downstream sampling points in order.

Sampling points	Coordinates		Concentrations (ng L ⁻¹)								
	Longitude	Latitude	METH	AMP	KET	NK	BE	COD	COC	MDMA	EDDP
SH1	126.53139	45.75861	<LOQ	<LOD	0.1	<LOQ	<LOD	<LOD	<LOQ	<LOD	<LOD
SH2	126.61056	45.77917	0.5	<LOD	<LOQ	<LOQ	<LOD	<LOQ	<LOD	<LOD	<LOD
SH3	126.70056	45.81556	1.4	<LOD	<LOQ	<LOQ	<LOD	<LOQ	<LOD	<LOD	<LOD
SH4	126.71194	45.83583	3.0	<LOD	<LOQ	<LOQ	<LOD	0.5	<LOD	<LOD	<LOD
SH5	126.71049	45.84823	3.9	<LOD	0.1	<LOQ	<LOD	0.5	<LOD	<LOD	<LOD
Y1	106.52755	38.62007	1.7	<LOD	0.4	<LOD	<LOD	1.9	<LOD	<LOD	0.2
Y2	106.52306	38.49046	1.2	<LOD	0.1	<LOD	<LOD	2.1	<LOD	<LOD	0.1
Y3	106.48542	38.39822	1.3	<LOD	<LOD	<LOD	<LOD	2.2	<LOD	<LOD	0.1
Y4	106.40637	38.34474	1.3	<LOD	<LOD	<LOD	<LOD	2.0	<LOD	<LOD	0.3
Y5	106.34292	38.30995	0.8	<LOD	<LOD	<LOD	<LOD	1.1	<LOQ	<LOD	0.2
YZ1	114.24806	30.48250	2.1±0.4	<LOD	2.6±0.5	0.7±0.1	1.3±0.1	<LOD	0.7±0.5	<LOD	<LOQ
YZ2	114.28417	30.52940	1.9±0.5	<LOD	2.0	0.6±0.1	1.0±0.2	0.1	0.3±0.1	<LOD	<LOD
YZ3	114.28778	30.55000	1.3±0.5	<LOD	1.8±0.3	0.4	0.8±0.5	0.1	0.3±0.2	<LOD	<LOQ
YZ4	114.30528	30.57440	1.4±1.0	<LOD	2.6±2.2	0.3±0.1	1.0	<LOD	0.3±0.2	<LOD	<LOD
YZ5	114.33889	30.61670	1.9±1.8	<LOD	2.7±2.1	0.7±0.5	1.3±0.9	<LOD	0.2±0.2	<LOD	<LOD
YZ6	114.37806	30.64417	2.8±0.8	<LOD	3.7±0.6	1.0±0.1	1.4±0.4	0.1	0.7±0.3	<LOD	<LOQ
P1	113.20944	23.15670	26.0±8.2	0.7±0.2	16.7±0.5	4.8±0.1	<LOD	0.6±0.2	<LOQ	1.3±0.5	<LOD
P2	113.225	23.10694	20.0±7.4	0.5±0.2	14.2±3.2	3.9±0.6	<LOD	0.4±0.2	<LOD	1.3±0.3	0.1
P3	113.32361	23.05583	17.4±10.8	0.5±0.1	9.9±3.5	3.2±1.6	<LOD	0.4±0.2	<LOQ	0.6±0.6	0.1
P4	113.33056	23.11444	58.2±18.6	1.4±0.4	21.7±3.9	6.5±1.1	<LOD	2.1±0.4	<LOQ	0.7±0.2	0.4±0.2
P5	113.35528	23.11111	45.7±4.8	1.1	20.6±0.3	6.1±0.4	0.6	1.7	<LOQ	0.7±0.1	0.2
P6	113.42444	23.09611	19.4±1.0	0.6±0.2	10.5±1.2	3.1±0.2	0.5	0.7±0.1	<LOQ	0.4±0.1	0.1