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Occurrence, elimination, enantiomeric distribution and intra-day variations of chiral pharmaceuticals in major wastewater treatment plants in Beijing, China

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ABSTRACT

The occurrence, eliminations, enantiomeric distribution and intra-day variations of five chiral pharmaceuticals (three beta-blockers and two antidepressants) were investigated in eight major WWTPs in Beijing, China. The results revealed that metoprolol (MTP) and venlafaxine (VFX) were of the highest concentrations among the five determined pharmaceuticals with mean concentrations of 803 ng L^{-1} and 408 ng L^{-1}, respectively in influents, and 354 ng L^{-1} and 165 ng L^{-1} in effluents, respectively. Their removal efficiencies, intra-day concentration changes and enantiomeric profiles during wastewater treatment were further analyzed. Loads of these two chiral pharmaceuticals were also studied to reveal drug use pattern. A/A/O+MBR (anaerobic/anoxic/oxic + membrane bio-reactor) followed by joint disinfection treatment process exhibited the high removal efficiencies. No or weak enantioselectivity was observed in most WWTPs. However, obvious enantiomeric fraction (EF) changing of MTP was observed in WWTP3 employing A/A/O+MBR. Intra-day concentration fluctuations of MTP were smaller than VFX. A quick response to sudden rise influent concentration of MTP was observed in WWTP1 effluent but EF response lagged behind. Similar bihourly EF variations in influents and effluents were also observed in most WWTPs for MTP and VFX in consideration of hydraulic residence time (HRT).

1. Introduction

Pharmaceutically active compounds (PhACs) have raised more and more concern due to their increasing production and usage, frequent detection and potential threat to ecosystem and human health (Kasprzyk-Hordern, 2010). However, there is a shortage of information about the environmental occurrence, transport and fate for many pharmaceuticals. The lack of relative data was partly a result of a shortage of suitable and standard sampling methods and analytical methods (Kasprzyk-Hordern, 2010; Ort et al., 2010; Petrie et al., 2017).

More than half of the currently used drugs are chiral compounds. The consumption of chiral drugs have been increasing by over 60% since 2000 (Lin et al., 2011). The enantiomers of a chiral drug have similar physicochemical properties but different biological properties such as pharmacology (Liu and Gu, 2011), pharmacokinetics (Dong et al., 2011), metabolism and toxicology (Yang and Bu, 2011). Therefore, the enantiomeric composition can change significantly after absorption, distribution, metabolism and excretion from human or animal bodies. Due to some differences in their spatial structure and in the interaction with different bio-targets, enantiomers could vary much in toxicity (Kasprzyk-Hordern, 2010; Stanley et al., 2007; Tiritan et al., 2016).

Chiral drugs are introduced into the environment as a result of human actions. Most of them (including consumed and unconsumed chiral drugs) are gathered into wastewater treatment plants (WWTPs) and undergo both biotic and abiotic processes. However, municipal WWTPs are not specially designed to remove them and

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their removal efficiencies largely depend on the treatment process (MacLeod and Wong, 2010). Biodegradation processes of chiral drugs in WWTPs were regarded as important enantioselective processes and may lead to enrichment or depletion of one specific enantiomer. In turn, the changes in enantiomeric fraction (EF) value, which is used for quantifying enantiomeric composition, were also indications of the effectiveness of the biological processes (Hashim et al., 2010; Souchier et al., 2016). Unfortunately, the removal performances of different treatment techniques and enantioselectivity of chiral drugs during wastewater treatment were seldom studied.

In addition, as WWTP effluents are considered a main point source of pharmaceuticals, it is necessary to develop environmental legislation supported by credible monitoring data-sets (Petrie et al., 2017). Separation and analytical methods of enantiomers has been limitedly studied in some previous researches (Camacho-Munoz and Kasprzyk-Hordern, 2017; Camacho-Munoz et al., 2016; Ribeiro et al., 2012, 2014). Meanwhile, suitable and feasible sampling strategy ought to be carefully designed but has always been neglected during monitoring campaign. Traditional instantaneous grab sampling method has been widely used in previous studies. However, this approach has limitations as it may only represent a stochastic concentration at the moment, (Petrie et al., 2015) so it may lead to an inaccurate and biased result. Ort et al. assessed uncertainties associated with different sampling modes and recommended a 5-min or shorter sampling frequency to account for intra-day fluctuations in influents of WWTPs (Ort et al., 2010), which indicated that a composite sampling approach should help to get more accurate information. Time proportional composite sampling was applied in this study to investigate within day variability of 5 chiral drugs.

China is the largest pharmaceutical producer in the world and the proportion of pharmaceutical production in China is more than 20% of the total world production. The pharmaceutical production in China has tripled from 2003 to 2011. In addition, Beijing, as the capital of China, is one of the international city in the world, with a large population and rapid economic growth, and faces various environmental issues (Liu and Wong, 2013). To date, there were few studies concerning the occurrence, removal, spatial and temporal distribution of pharmaceuticals in WWTPs in China, especially in Beijing (Li et al., 2013; Liu et al., 2017; Sui et al., 2010, 2011; Zhou et al., 2010). In these available studies, all of them focused on occurrence and removal of pharmaceuticals, including some chiral drugs but without chiral analysis, and a limited number of WWTPs were investigated under the same sampling and experimental conditions. Additionally, intra-day concentration, EF and load variations could not be fully demonstrated by the commonly used grab sampling in these studies.

Accordingly, we designed and conducted a high-frequency continuous composite sampling campaigns in eight major WWTPs in Beijing. Four different treatment processes were applied in these WWTPs, which are the perfect case scenarios to compare the elimination capability. Five typical chiral drugs were selected as target analytes according to previous studies, including three beta-blockers and two antidepressants. The main aim of this study was to know better about diurnal behavior of selected five chiral pharmaceuticals during wastewater treatment, provide useful information of chiral drugs and their enantioselectivity in WWTPs. The major objectives of this work were the following: (i) To determine concentrations of five chiral drugs and analyze their occurrences and eliminations; (ii) To evaluate enantioselectivity behavior and enantiomer distribution in both raw wastewater and treated wastewater; (iii) To gain an insight to intra-day concentration and enantiomeric variations of target chiral pharmaceuticals with HRT-adjusted; (iv) To analyze drug use pattern both in temporal and spatial scales.

2. Material and methods

2.1. Chemicals and materials

Target pharmaceuticals, atenolol (ATN), metoprolol (MTP), propranolol (PHO), venlafaxine (VFX) and fluoxetine (FLX), were purchased from Sigma-Aldrich (Steinheim, Germany) and information on their molecular and physicochemical properties are detailed in Table S1. Surrogate standards atenolol-d7 and fluoxetine-d5 were obtained from Sigma-Aldrich. Metoprolol-d7, propranolol-d7 and venlafaxine-d6 were purchased from Toronto Research Chemicals Inc. (Toronto, Canada). ^{13}C-Atracine as instrumental internal standards were obtained from Dr. Ehrenstorfer (Augsburg, Germany). Methanol (MeOH) and formic acid (HPLC grade) were purchased from Fisher Scientific (Loughborough, Leicestershire, UK). Ammonium acetate (NH_4OAc) was provided by Fluka (Buchs, Switzerland). Ultrapure water was of 18.2 MΩ quality (Millipore, USA). Na_2EDTA and L-Ascorbic acid, obtained from Yongda Chemical Inc. (Tianjin, China), were added before extraction to prevent the degradation of target chemicals. Oasis HLB (200 mg, 6 mL) solid phase extraction (SPE) cartridges were purchased from Waters (Manchester, UK).

2.2. WWTPs sampling

The influent and effluent samples were collected from 8 WWTPs in Beijing during November 2016 through January 2017 using SD 900 portable samplers (HACH, CO, USA). Saturated mercuric chloride solution was added in advance in each container to restrain biodegradation. A 150 mL aliquot of wastewater was collected every 10 min, 6 composite samples were deposited into 1 L polypropylene bottles (6 samples per bottle), and 2-h samples were mixed as one in the laboratory. All samples were brought back to laboratory immediately, stored in refrigerator at 4 °C(Brett J. Vanderford et al., 2011; De Wever et al., 2007; Kasprzyk-Hordern et al., 2010; Nelson et al., 2011; Petrie et al., 2017; Wick et al., 2009) and treated within 24 h.

The 8 WWTPs are located at the central area of Beijing and account for more than 80% wastewater treatment capacity. Their catchment areas are shown in Fig. 1. The primary treatment processes of the 8 WWTPs are the same. The main differences among these WWTPs are secondary treatment and advanced treatment processes: WWTP1 employs biological aerated filter + anoxic/oxic (A/O) + cloth-media filter + joint disinfection with ozone and sodium hypochlorite (Type A); WWTP2 adopts oxidation ditch (OD) + A/O + cloth-media filter + contact tank with ozone and sodium hypochlorite (Type B); WWTPs 3, 4 and 5 employ anaerobic/anoxic/oxic (A/A/O) + membrane bio-reactor + joint disinfection with ozone and sodium hypochlorite (Type C) and in WWTPs 6, 7 and 8, A/A/O + contact tank with sodium hypochlorite is adopted (Type D). More details, including population equivalent (PE), hydraulic retention time (HRT), daily capacity, catchment areas and treatment processes, are shown in Table S2.

2.3. Sample preparation and analysis

In brief, samples (raw wastewater: 100 mL; treated wastewater: 200 mL) were filtered through glass fiber filters (GF/F. 47 mm, Whatman, Kent, UK) and loaded onto pre-conditioned Waters Oasis HLB cartridges, which were dried and eluted using 2 × 4 mL 50:50 (v: v) MeOH: H_2O. The mixed surrogate standards (50 ng of each compound) were spiked into samples before passing through the HLB cartridges. The extracts were dried under nitrogen and reconstituted in 500 μL 50:50 (v: v) MeOH: H_2O with 0.025% HCOOH and 50 ng internal standard. All the samples were filtered