Ecotoxicology and Environmental Safety 154 (2018) 214–220

Contents lists available at ScienceDirect

Ecotoxicology and Environmental Safety

journal homepage: www.elsevier.com/locate/ecoenv

Investigation of pharmaceutically active compounds in an urban receiving water: Occurrence, fate and environmental risk assessment

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ARTICLE INFO

Keywords:
Pharmaceutically active compounds
Partitioning
Bioaccumulation
Ecological risk

ABSTRACT

Pharmaceutically active compounds (PhACs) recently have been recognized to constitute a health risk for aquatic ecosystems. The major pathways of PhACs to enter the aquatic environment are excretion and discharge of effluents through sewage treatment plants (STPs). The occurrence, bioaccumulation and risk assessment of lipophilic PhACs, including erythromycin, ketoconazole, indomethacin, diclofenac, gemfibrozil, bezafibrate, propranolol, carbamazepine, sertraline and 17α-ethinylestradiol were investigated in a river that receives effluents from STP. The results indicate that the PhACs were extensively existed in fish, sediment, suspended particulate matter (SPM), colloidal phase (5 kDa to 1 μm) and truly dissolved phase (< 5 kDa) water, with total concentration of ten PhACs (Σ_{10}PhACs) of ND-19.6 ng/g, 7.3–11.2 ng/g, 25.3–101.5 ng/g, 10.1–27.7 ng/L and 67.0–107.6 ng/L, respectively. The Σ_{10}PhACs for particulate and water samples collected from STP's outfall site were higher than those collected from upstream and downstream, indicating that the STP is an important PhACs source of river. However, the Σ_{10}PhACs in sediment showed no significant statistical differences in the sampling area, and which was 3.5–9.5 times lower than those in SPM samples. The colloidal phase contributed 2.5–28.5% of erythromycin, 5.8–45.6% of ketoconazole, 8.4–32.2% of indomethacin, 7.0–21.4% of diclofenac, 11.6–36.9% of gemfibrozil, 10.2–45.9% of bezafibrate, 5.9–16.8% of propranolol, 1.9–11.1% of carbamazepine and 1.1–23.8% of sertraline in the aquatic environment. This suggests that aquatic particulates (e.g., colloids and SPM) maybe an important carrier for PhACs in the aquatic system. In general, the Σ_{10}PhACs in the tissues of fish were in order as follows: kidney > brain > liver > gill > muscle. Based on truly dissolved concentrations of PhACs in the water, bioaccumulation factors were between 3.7 and 2727.3 in the fish tissues, sertraline exhibited bioaccumulation potential. In all the risk assessments, erythromycin could cause most harmful adverse health effects for the most sensitive algae group based on the acute and chronic data. In addition, the risk quotient values for diclofenac toward fish were higher than 1. These results indicate that the PhACs pose a potential risk to the aquatic organisms, especially for chronic risk.

1. Introduction

Pharmaceutically active compounds (PhACs) have been growing attention over the years as emerging contaminants (Garcia-Ivars et al., 2017). It is generally thought that freshwater environment is a major sink of different types of organic pollutions (Kleywegt et al., 2016). Considering the pathways by which PhACs enter into the freshwater environment, the discharge of sewage treatment plant (STP) effluent plays a major role due to the incomplete removal of PhACs in STP facilities (Kasprzyk-Hordern et al., 2009). Because of the continuous entrance of PhACs into the aquatic environment, PhACs have been found widely throughout the world, including raw water sources for drinking water treatment plants (Bu et al., 2013; Liu and Wong, 2013). Most of these studies focused on the aqueous phase, which have been traditionally subdivided into dissolved and particulate fractions by filter membrane of 0.7 or 1.0 μm. However, dissolved fraction can be further divided into truly dissolved phase and colloidal fraction. Colloids were a significant storage site for PhACs and can regulate the environmental behaviour of PhACs (Duan et al., 2013a). Previous studies shown that colloidal organic carbon contributed to 76% fraction of total organic carbon in aquatic environments, and the colloidal phase can accounted for 4.7–49.8% of antibiotics PhACs in the dissolved phase (Cheng et al., 2017). Colloidal adsorption of PhACs should influence their mobility, reactivity and bioavailability (Yang et al., 2011). Therefore, the occurrence and distribution of PhACs in multi-phase in the aquatic environment need to be evaluated to improve the knowledge of PhACs

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https://doi.org/10.1016/j.ecoenv.2018.02.052
Received 10 December 2017; Received in revised form 12 February 2018; Accepted 15 February 2018

risk and fate in the aquatic environment.

Most PhACs are designed to interact with specific pathways and processes (e.g. specific receptor, enzyme or biological process) in target humans and animals, which may bring about some negative effects on the physiological processes in the organisms (Boxall et al., 2012; Liu et al., 2015a). Responses such as development, reproduction and up- or down-regulation of genes have been observed in organisms exposed to PhACs (Boxall et al., 2012). An investigation completed by 535 environmental scientists from 57 countries on the most pressing knowledge gaps around the risk of PhACs in the environment showed that the effects of long-term exposure to low concentrations of PhACs mixture on nontarget organisms were ranked as one of the most priority researches (Rudd et al., 2014). However, environmental risks from PhACs are still often assessed substance-by-substance, neglecting possible interaction effects triggered by mixtures, which may underestimate the actual impacts of the PhACs in the environment.

The objectives of this study were to investigate the occurrence, multi-phase distribution and bioaccumulation of ten PhACs in an urban STP receiving river in Nanjing, China. The environmental implications of each individual component and the mixtures of the detected PhACs on algae, daphnids and fish were also evaluated by employing the risk quotient method. The ten PhACs investigated in this study include antibiotic erythromycin (ERY), antifungal ketoconazole (KCZ), anti-inflammatories diclofenac (DIC) and indomethacin (IMC), b-blocker propranolol (PRO), anti-epileptic carbamazepine (CBZ), lipid regulators gemfibrozil (GFB) and bezafibrate (BZB), antidepressant sertraline (SER) and steroid hormone 17a-ethinylestradiol (EE2).

2. Materials and methods

2.1. Chemicals

The standards of ERY, KCZ, DIC, IMC, PRO, CBZ, GFB, BZB, SER and EE2 were obtained from Dr. Ehrenstorfer (Augsburg, Germany). LC/MS grade methanol, formic acid, and acetone were purchased from Merk Corporation (Darmstadt, Germany). Standard stock solutions of the individual PhAC were prepared in methanol at a 50 mg/L concentration and stored at 4 °C.

2.2. Sample collection

Four sampling sites were selected at an STP effluent outfall, the upstream (200 m) and downstream (100 m, 800 m and 3 km) represented by symbol S1, S2, S3 and S4, respectively. Surface water was collected in 1 L brown glass bottle, which was pre-cleaned by methanol and deionized water. The sampling campaign was conducted in November 2016, according to the technical specification requirements for monitoring of surface water and wastewater (SEPAC, 2003). The top 5-cm layer of sediments collected using a stainless steel grab sampler was scooped using a precleaned stainless steel scoop. The collected sediments samples were wrapped in a tinfoil and enclosed in ziplock bags to avoid pollutant losses. After transporting on drikold to the laboratory, sediments were each lyophilized at − 60 °C and stored at − 20 °C until pre-processing (within 48 h). The pH of the sediments was measured in 0.01 M $CaCl_2$ using pH meter. The total organic carbon (TOC) in the sediments was measured using an Aurora Model 1030 TOC analyzer (OI Analytical, USA). Sediment texture was analyzed using a SEDIMA 4–12 Particle Size Analyzer (UGT Scientific Instruments, Germany). Common carp (*Cyprinus carpio*) were captured with hook and line in November 2016. To collect sufficient amount of fish, 4 anglers were simultaneously fished ranging from 200 m to 3 km downstream of the STP outlet for 4 h. After the capture, the fish were anesthetized using tricaine methanesulfonate. All the fish samples were transported immediately to the laboratory in a cooler with drikold, and completed sample pre-processing within 48 h.

After the delivery to the laboratory, the water samples were filtered through pre-baked (4 h; 450 °C) 1.0 μm-glass fiber filters. The suspended particulate matters (SPM) were collected from the 1.0 μm-glass fiber membranes and stored in an airtight container after being freeze dried. The filtrate was further divided into colloidal (i.e. 5 kDa to 1.0 μm) and truly dissolved fractions (i.e. < 5 kDa) by cross-flow cell (SEPA CF, Sterlitech, USA), whose main part was a polyether sulfone membrane with a pore size of 3 nm (5 kDa). The fish were sacrificed by rapid decapitation, and their brain, liver, kidney, gill and muscle tissues were dissected and weighed. All the tissues were washed by 0.15 M KCl, blotted onto filter paper after 1 min, and subsequently stored in a liquid nitrogen tank.

2.3. Sample extraction and instrument analysis

The methods for the extraction and analysis of the PhACs in the aqueous samples, sediment and fish tissues was described elsewhere (Xie et al., 2017). Briefly, solid-phase extraction system was used to extract aqueous samples (i.e. soluble phase, colloidal phase and filtrate) using HLB cartridges (500 mg, Waters, Massachusetts, USA), and eluted using a mixed solution of methanol/acetone (1:1). Solid matrix samples, including biota, sediment and SPM samples were extracted by pressurized liquid extraction (Dionex ASE 350 system) using methanol/acetone (1:1), followed by purification using HLB cartridge. The PhACs were analyzed using Waters Acquity ultra-high performance liquid chromatograph coupled with a Waters Acquity Xevo TQ triple quadrupole mass spectrometer. The analyzer confirmed and quantified by mass spectrum of triple quadrupole in the multiple reaction monitoring (MRM). The analyzer Additional details on the analytical procedures used are given in the Supplementary information (SI) Tables S1 and S2. The physicochemical properties of the ten PhACs are listed in the Table S3.

2.4. Quality assurance/quality control (QA/QC)

The quantification of PhACs was carried out through matrix-matched external standard method. The limit of detection (LOD) and limit of quantitation (LOQ) were used to evaluate the method sensitivity. The LODs of the PhACs in the water and biota samples were 0.01–0.34 ng/L and 0.02–1.12 ng/g, respectively. The LOQs of the PhACs were 0.04–1.1 ng/g in the water and 0.05–3.62 ng/g in the biota. The calibration curves showed good linearity in concentration range of 0.5–500 ng/mL ($R^2 > 0.998$). Satisfactory recoveries of the PhACs in the matrix spikes were obtained in the range of 76–109% for the water samples and 70–104% for the biota samples, and the relative standard deviations were less than 20%.

2.5. Parameter measurement and statistical analysis

Eco-toxicity of PhACs in the truly dissolved fractions of water phase was assessed using the risk quotient (RQ) on non-target organisms, which was widely used to evaluate the risk properties of Pharmaceuticals recently (Backhaus and Karlsson, 2014). Detailed calculation methods are described in SI. The regression analysis on the MRQ_{STU} versus $MRQ_{PEC/PNEC}$ was performed by SigmaPlot 12.5. A P value of 0.05 was used for the test significance.

3. Results and discussion

3.1. Occurrence of PhACs in the receiving river

3.1.1. Sediment

The PhAC concentrations in the conventional sediment, SPM and dissolved phase of receiving river were presented in Fig. 1. Eight of the ten PhACs (excluding CBZ and GFB) were detected in all sediment samples. The total concentrations of eight PhACs (Σ_8PhACs) in sediment samples ranged from 7.32 to 11.2 ng/g on a dry weight basis (dw).