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Detection, occurrence and fate of 22 psychiatric pharmaceuticals in psychiatric hospital and municipal wastewater treatment plants in Beijing, China

Shengliu Yuan [a,b], Xiaoman Jiang [a,*], Xinghui Xia [a], Haixia Zhang [b], Shaokui Zheng [a,*]

[a] School of Environment, MOE Key Laboratory of Water and Sediment Sciences/State Key Lab of Water Environment Simulation, Beijing Normal University, Beijing 100875, China
[b] College of Chemistry and Chemical Engineering, Key Laboratory of Nonferrous Metal Chemistry and Resources Utilization of Gansu Province, Lanzhou University, Lanzhou 730000, China

HIGHLIGHTS

- We developed LC–MS/MS analysis of 22 common psychiatric pharmaceuticals in wastewater.
- Higher influent pharmaceutical concentrations were observed in P-WWTPs than M-WWTPs.
- Higher effluent pharmaceutical concentrations in P-WWTPs with higher removals.
- Pharmaceutical removals mainly happened in the secondary treatment of these WWTPs.

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ABSTRACT

The liquid chromatography–electrospray ionization-tandem mass spectrometer (LC–MS/MS) method coupled with an automated solid-phase extraction procedure has been developed to identify 22 psychiatric pharmaceuticals, including seven anxiolytic-sedative-hypnotics, six antidepressants, and nine anti-schizophrenia drugs, in wastewater samples from two psychiatric hospital wastewater treatment plants (P-WWTPs) and three municipal wastewater treatment plants (M-WWTPs) in Beijing, China. Analyte recoveries from spiking experiments in the WWTP influent and effluent at three concentrations ranged from 70% to 110%, excluding sulpiride, ziprasidone, and olanzapine. Method detection limits for five, eight, and nine analytes in the WWTP influent and effluent were 20–80, 1–16, and <1 ng L^{-1}, respectively. High psychiatric pharmaceutical concentrations (e.g., ~942 ng L^{-1}oxazepam, 5552–12,782 ng L^{-1} clozapine, 2762–9832 ng L^{-1}sulpiride, and 2030–4967 ng L^{-1}quetiapine) were frequently observed in P-WWTP influent compared to M-WWTPs. Although P-WWTPs typically had higher removal rates, significantly higher concentrations of the target compounds were observed in the P-WWTP secondary effluent than in the M-WWTP influent (e.g., ~752 ng L^{-1}oxazepam, ~8183 ng L^{-1} clozapine, ~10,833 ng L^{-1} sulpiride, and ~1168 ng L^{-1}quetiapine). Thus, the discharge control of psychiatric pharmaceuticals from psychiatric hospitals requires improvement.

1. Introduction

In the last two decades, pharmaceuticals and personal care products (PPCPs), a large and diverse group of organic compounds consisting of human and veterinary drugs and consumer products, have received growing international concern for their pseudo-persistent properties and their potential impact on ecosystems and human health, even at trace concentrations (e.g., ng L^{-1}) (Shao et al., 2009; Kosma et al., 2010). Psychiatric pharmaceuticals, such as sedatives-hypnotics-anxiolytics (including antiepileptics), antidepressants, and anti-schizophrenia drugs, directly act on the central nervous system and disrupt neuro-endocrine signaling, and are among the most prescribed active substances globally (Calisto and Esteves, 2009; Calisto et al., 2011). For example, 35 of the top 200 prescriptions in the USA in 2010 were psychiatric pharmaceuticals, including 17 sedatives-hypnotics-anxiolytics, 16 antidepressants, and two anti-schizophrenia drugs (http://www.rxlist.com/script/main/hp.asp). The recent presence of psychiatric pharmaceuticals in various environmental matrices and their high persistence and toxicity to non-target organisms justifies them as newly emerging environmental pollutants (for a detailed description, see a review by Calisto and Esteves (2009)). For example, the sedative-hypnotic diazepam (the most extensively studied psychiatric pharmaceutical) has been found in all environment

* Corresponding authors. Tel.: +86 10 58809266.
E-mail addresses: jiangxiaoman@bnu.edu.cn (X. Jiang), zshaokui@yahoo.com.cn (S. Zheng).

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matrices (wastewaters, surface, ground and drinking waters, soils, sediments, bio-solids, and tissue) (Calisto et al., 2011), and Pascoe et al. (2003) described its visible adverse effects (deficient regeneration of polyps) on an aquatic invertebrate sedentary organism (*Hydra vulgaris*) at concentrations of 10 μg L^{-1}. Carbamazepine, an antiepileptic, was found to be potentially harmful to aquatic organisms with acute toxicity for Daphnia at 17 mg L^{-1} and midges at 34 mg L^{-1}, and with growth inhibition for Daphnia at 13 mg L^{-1} and midges at 9 mg L^{-1} (Till, 2005).

Since the discharge from wastewater treatment plants (WWTPs) is an important pathway for the entrance of pharmaceuticals into environmental matrices (Sui et al., 2010), the ability to detect these psychiatric pharmaceuticals, as well as understand their occurrence and fate in WWTPs, is crucial to assess their environmental concentrations. Gracia-Lor et al. (2011) identified two sedatives-hypnotics (lorazepam, alprazolam), one antidepressant (venlafaxine), and one anti-schizophrenia drug (olanzapine) at mg L^{-1} concentrations in WWTP influent and effluent in Spain. Schultz et al. (2010) identified 10 antidepressants (fluoxetine, norfluoxetine, sertraline, norsertraline, paroxetine, citalopram, fluvoxamine, duloxetine, venlafaxine, and bupropion) present at ng L^{-1} concentrations in WWTP effluent and downstream from WWTPs in Boulder, Colorado, USA. Gomez et al. (2006) investigated the occurrence of one antiepileptic (carbamazepine) and two antidepressants (fluoxetine and paroxetine) in hospital WWTP effluent. Sedative-hypnotic-anxiolytics and antidepressants are among the most widely investigated psychiatric pharmaceutical groups in WWTPs. Despite the increasing interest, there is little information available on the majority of psychiatric pharmaceuticals (particularly anti-schizophrenia drugs) in WWTPs. Furthermore, wastewater from psychiatric hospitals, the centralized administrators of psychiatric pharmaceuticals, is a very important source of psychiatric pharmaceuticals in environmental matrices. However, there is also a serious lack of information on pharmaceutical occurrences in psychiatric hospital wastewater and their fate in subsequent WWTPs.

In this study, we developed an analytical method using liquid chromatography–electrospray ionization-tandem mass spectrometer (LC–MS/MS) coupled with solid-phase extraction (SPE) for the quantification of 22 common psychiatric pharmaceuticals, including seven anxiolytic-sedative-hypnotics (anxiolytics: alprazolam, lorazepam, oxazepam, clonazepam; sedative-hypnotic: zaleplon; carbamazepine; trihexyphenidyl), six antidepressants (citalopram, fluvoxamine, sertraline, paroxetine, clomipramine, fluoxetine), and nine anti-schizophrenia drugs (sulpiride, risperidone, olanzapine, clozapine, ziprasidone, aripiprazole, perphenazine, chlorpromazine, quetiapine). Subsequently, the occurrence and fate of these 22 psychiatric pharmaceuticals in two psychiatric hospital WWTPs (P-WWTPs) and three municipal WWTPs (M-WWTPs) with different biological treatment processes in Beijing, China, were investigated. To the best of our knowledge, this work is the first reported identification of the majority of 22 psychiatric pharmaceuticals in WWTP wastewater samples.

2. Experimental

2.1. Chemicals

Physicochemical properties and molecular structures of the 22 targeted psychiatric pharmaceuticals are shown in the Supplementary Materials (SM) (Table S1). Standards of risperidone, olanzapine, clozapine, citalopram, quetiapine, ziprasidone, paroxetine, fluvoxamine, aripiprazole, fluoxetine, oxazepam (1.0 mg mL^{-1} methanol), alprazolam (1.0 mg mL^{-1} methanol), clonazepam (1.0 mg mL^{-1} methanol), and lorazepam (1.0 mg mL^{-1} acetonitrile) were purchased from Cerilliant (Round Rock, TX, USA). Perphenazine, clomipramine, and sulpiride standards were purchased from Sigma Aldrich (St. Louis, MO, USA). Carbamazepine and sertraline were provided by AcrosOrganics (Morris Plains, NJ, USA) and Tokyo Chemical Industry (Shanghai, China), respectively. Chlorpromazine and trihexyphenidyl were supplied by Dr. Ehrenstorfer company (Augsburg, Germany), and zaleplon was provided by the National Institutes for Food and Drug Control (China). The purities of all analytical standards used in this study were ⩾98%. Approximately 10 mg of individual standard (except for oxazepam, lorazepam, clonazepam, alprazolam) was accurately weighed and placed in a 10 mL flask and then diluted to 10 mL with methanol. Stock solutions were stored at 4 °C. HPLC grade methanol, acetonitrile, and acetone were purchased from J.T. Baker (Deventer, Netherlands). Other chemicals and solvents were of analytical grade. Ultra-pure water was obtained by using an in-house Milli-Q Ultra-purewater system (Millipore, Bedford, MA, USA) for preparation of buffer solutions and mobile phases.

2.2. Sample collection

Table S2 in the SM summarizes the characteristics of the five investigated WWTPs in Beijing, China. In this study, five WWTPs were used for the primary treatment to remove particles (in P-WWTP2 and M-WWTP1) and the secondary biological treatment, which can be divided into the conventional activated sludge process (in P-WWTP1 and P-WWTP2), Anoxic/Oxic process (in M-WWTP1), Anaerobic/Anoxic/Oxic process (in M-WWTP2), and Anoxic/ Anaerobic/Oxic process (in M-WWTP3). During August and September 2011, grab samples of wastewater were collected five times at 0.5 m below the liquid surface of each tank of the five WWTPs. Subsequently, 150 mL P-WWTP wastewater (or 500 mL M-WWTP wastewater) was added into amber glass bottles precleaned by chromic acid lotion prior to immediate filtration through 0.45 μm microfiber filters and stored at 4 °C for less than 72 h until extraction.

2.3. SPE procedure

The SPE experimental procedure is shown in Table S3 in the SM. Aqueous samples were adjusted to pH value 7 using ammonia solution and spiked with 30 μL of analyte stock solutions. The extraction was subsequently conducted in a SPE-DEX fully automatable extraction system (Horizon Technology, Salem, NH, USA). The HLB extraction disks (47 mm, I.D.) (Horizon Technology) were conditioned with 5 mL methanol and 5 mL water. Subsequently, wastewater samples (adjusted to pH = 7 and mixed with methanol (1%, v/v)) were introduced to the disks at a flow rate of 100 mL min^{-1}. After washing twice with 5 mL 5% methanol solution, the disks were dried under vacuum for 3 min and eluted with 5 mL of 2% acetic acid methanol solution three times. The cycle time for a 500 mL sample is approximately 24 min. The final extracts were evaporated to dryness under a gentle nitrogen stream in a 40 °C water bath and reconstituted with 1 mL initial gradient mobile phase.

2.4. LC–MS/MS analysis

A 15 μL aliquot of each sample extract was separated using an Ultimate 3000 HPLC system (Dionex, Germering, Germany) equipped with an X-bridge C18 column (2.0 mm × 150 mm, particle size of 3.5 μm, Waters, Milford, MA, USA) and detected by an API 3200 triple quadrupole mass spectrometer (AB Sciex, Foster City, CA, USA) equipped with an electrospray ionization (ESI) source that was operated in positive mode. The column was maintained at 40 °C at a flow rate of 0.3 mL min^{-1}. Solvent A was 0.2%