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# Occurrence and environmental implications of pharmaceuticals in Chinese municipal sewage sludge

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## HIGHLIGHTS

- Pharmaceutical residuals were analyzed for sludge samples from 45 sewage treatment plants in China.
- Fluoroquinolone and tetracycline were the dominant antibiotics.
- Other pharmaceuticals such as ketoprofen and ibuprofen also in significant presence.
- Poor agreement found between the detected and predicted concentrations.

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## ABSTRACT

The presence of pharmaceuticals in aquatic environment has become a topic of concern because of their potential adverse effects on human health and wildlife species. A total of 45 dewatered sewage sludge samples were collected throughout China and analyzed for 30 commonly consumed pharmaceutical residues. Ofloxacin was found to be the dominant contaminant with concentrations up to 24760 μg $kg^{-1}$, followed by oxytetracycline (5280 μg $kg^{-1}$), norfloxacin (5280 μg $kg^{-1}$) and ketoprofen (4458 μg $kg^{-1}$). The concentration of pharmaceutical residues varied greatly depending on the operation conditions of wastewater treatment plants and sampling locations. Poor agreement was found between the predicted (calculation based on the annual consumption and coefficient of sludge water partition) and detected concentrations of the pharmaceuticals indicating that the occurrence of pharmaceutical residues was affected by various factors such as loading rates, sewage properties and the chemical properties such as the contribution from polar groups. National wide fate and ecotoxicity study is required for the development of control strategies.



## 1. Introduction

Pharmaceuticals as emerging organic pollutants have received increasing attention by the scientific community in recent years, due to their frequent occurrence in the environment and associated health risks (Ellis, 2006; Kümmerer, 2009). These contaminants are observed at concentrations of several nanograms per liter in the aquatic environment as a result of human and animal activities (Kolpin et al., 2002; Kaplan, 2012). Although found in trace levels, some therapeutic compounds such as synthetic sex hormones and antibiotics have been found to cause adverse effects on aquatic organisms (Kristiansson et al., 2011; Lee et al., 2012). In addition, pharmaceuticals may accumulate and cause irreversible changes in wildlife and humans (Daughton and Ternes, 1999).

Most pharmaceuticals are likely to persist in wastewater systems due to their hydrophilic properties. The polar functional groups (carboxylic moieties, aldehydes and amines) of these compounds may interact with suspended organic materials and lead to their high concentration in sewage sludge (Ternes et al., 2004; Carballa et al., 2008). Due to the lack of reliable analytical methods, most previous studies have focused on the water phase of pharmaceuticals in sewage (Ort et al., 2010; Bailly et al., 2013). In fact, most biological wastewater treatment plants have high removal efficiencies for pharmaceuticals resulting from the sorption and sedimentation of these products into the sludge (Jelic et al., 2011; Jia et al., 2012). The majority of pharmaceuticals in sludge are likely to be discharged into terrestrial environment after sludge disposal, causing serious environmental problems in some cases (Martín et al., 2012a,b). Agricultural use and land-fill are two major

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sludge disposal practices worldwide (Kelessidis and Stasinakis, 2012), which may contaminate food chain and water supply. The presence of pharmaceuticals in sewage sludge therefore becomes an important issue in China which produces more than 10 million tonnes of dry sludge every year with more than 70% of which are landfilled or used in the agricultural sector (40%) (Chen et al., 2012a).

Previous studies have shown that the level of pharmaceuticals varied greatly in the sewage sludge ranging from several micrograms per kilogram to milligrams per kilogram depending on the sampling point and properties of the compounds (Miao et al., 2005; Nieto et al., 2007; McClellan and Halden, 2010). Among all studied pharmaceuticals, antibiotics have been on the priority list due to the antibiotic-resistance genes found in bacteria (Gao et al., 2012). Research shows that tetracyclines, fluoroquinolones, sulfonamides and macrolides are the dominant antibiotic classes presented in sewage sludge samples in the United States (McClellan and Halden, 2010), Canada (Miao et al., 2005), Spain (Nieto et al., 2007; Radjenović et al., 2009), Germany (Ternes et al., 2005), Switzerland (Göbel et al., 2005) and China (Yu et al., 2011; Jia et al., 2012). However, most recent investigations on pharmaceuticals in sewage sludges have been limited to the development of analytical methods, or often restricted to one sewage treatment plant (Nieto et al., 2007; Yu et al., 2011), therefore, providing little information on the occurrence of pharmaceuticals in sewage sludge. Pharmaceuticals other than antibiotics should also be studied because of their high concentrations and potential adverse effects on human health (Williams and Brooks, 2012). Therefore, the present study was designed to investigate 30 different pharmaceutical compounds of therapeutic classes in sewage sludge samples collected from wastewater treatment plants across 13 provinces (20 cities) in China. The national load of pharmaceutical products discharged into the environment was also estimated.

## 2. Materials and methods

### 2.1. Chemicals and standards

The analytical standards were obtained from Sigma–Aldrich Corp., (St. Louis, MO). The internal standards of mecoprop-3d, atrazine-5d, chloramphenicol-5d, N,N-diethyl-meta-toluamide-7d (DEET-7d), ofloxacin-d8, and enythromycin-$^{13}$C & d4 were purchased from Dr. Ehrenstorfer GmbH (Augsburg, Germany). $^{13}$C-phenacetin was obtained from Sigma–Aldrich and gemfibrozil-6d from Toronto Research Chemicals Inc., (Toronto, Canada). HPLC grade methanol and formic acid were provided by Thermo Fisher (Hampton, NH) and analytical grade citric acid-monohydrate and sodium phosphate-dibasic anhydrous by Sinopharm Chemical Reagent Co., Ltd., Shanghai, China. Ultra-pure water was prepared with a Milli-Q water purification system (Millipore, Billerica, MA). All the pharmaceutical compounds were dissolved in methanol and stored in a freezer at 4 °C. Working solutions were prepared immediately before use by diluting the stock solutions.

Oasis HLB cartridges (6 mL/500 mg) were purchased from Waters Corp., Milford, MA, glass microfiber filters (GF/F) from Whatman Ltd., (Maidstone, Kent, UK) and syringe-driven filters (PTFE) from Millipore, Billerica, MA.

### 2.2. Sample collection

A total of 45 sewage sludge samples were collected from 20 cities in 13 provinces of China (Fig. 1). More information regarding the wastewater treatment plants is given in the Supplemental material (Table S2). Sewage sludge samples were collected directly from dewatering machines in the sewage treatment plants. Five discrete samples were collected from each wastewater treatment plant and then mixed together to get a composite one. About 500 g sludge from each final sample was taken by the quadripartite method and transported to the laboratory and stored at −20 °C prior to analysis. To assess the sorption behaviors of pharmaceutical products present in sewage sludge, wastewater samples were also collected from 7 sewage treatment plants located in Beijing. Wastewater samples (2 L in duplicates) were collected in pre-washed amber glass bottles using the grab sampling technique and transported to the laboratory immediately. The samples were filtered through glass microfiber filters (GF/F, Whatman) to remove particulate matters and stored at 4 °C before the extraction of pharmaceuticals.

### 2.3. Sample preparation

Sludge samples were subjected to pressurized liquid extraction (PLE) method following the procedures as described by Nieto et al. (2007) and Chen et al. (2012b). Briefly, the sludge was homogenized, frozen, lyophilized and passed through a 0.45 mm sieve before spiking with the internal standards. Samples were extracted with methanol/EDTA-McIlvaine buffer (50/50, v/v) using accelerated solvent extraction system (PLE2000) equipped with 22 mL capacity of stainless-steel cells. The extract was diluted to 500 mL with Mili-Q water and then cleaned up. Each sample was extracted with Oasis HLB cartridges (500 mg/6 mL) and the eluate was concentrated and filtered through a 0.20 μm PTFE syringe filter.

Wastewater samples (500 mL) were filtered and spiked with internal standards and then extracted using SPE method. The detailed information on SPE method for sewage sludge preparation and wastewater extraction was given by Chen et al. (2012b,c).

### 2.4. HPLC and MS–MS system

The pharmaceutical residues were separated and quantified using high-performance liquid chromatography (HPLC: Ultimate 3000, Dionex, Sunnyvale, CA) followed by electrospray ionization and tandem mass spectrometry (ESI-MS/MS, API3200, AB Sciex, Framingham, MA). ESI-MS/MS parameters such as declustering potential (DP) and collision energy (CE) for each compound were optimized by continually injecting standard solution with a syringe pump. The ESI conditions were set at optimum values to obtain acceptable sensitivity and selectivity for the compounds analyzed (Table S1 in Supplemental material). Among all the fragmented product ions, only two characteristic ions were performed in the MRM monitoring system. The most intensive fragment ion was used for quantification and the less intensive was used for qualification to avoid possible misidentification in the matrix (Table S1 in Supplemental material).

The gradient separation and the HPLC conditions were performed by three chromatographic columns (Capcell PAK C18, Agilent XDB C18 and Waters XBridge C18) using a mixed standard solution carried by different mobile phases as well as mobile phase additive (formic acid or ammonium acetate). Operational parameters and mobile phase additives were optimized frequently by adjustment and comparison to increase sensitivity and reduce signal suppression for each compound. This information also can be found in Table S1 (Supplemental material).

### 2.5. Predicted concentrations of pharmaceuticals in sewage sludge

The calculation procedures for predicted concentrations in sewage sludge ($C_{sludges}$) was carried out for the studied compounds using the following equations as described by Stuer-Lauridsen