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Carbamazepine in municipal wastewater and wastewater sludge: Ultrafast quantification by laser diode thermal desorption-atmospheric pressure chemical ionization coupled with tandem mass spectrometry

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ABSTRACT

In this study, the distribution of the anti-epileptic drug carbamazepine (CBZ) in wastewater (WW) and aqueous and solid phases of wastewater sludge (WWS) was carried out. A rapid and reliable method enabling high-throughput sample analysis for quicker data generation, detection, and monitoring of CBZ in WW and WWS was developed and validated. The ultrafast method (15 s per sample) is based on the laser diode thermal desorption-atmospheric pressure chemical ionization (LDTD-APCI) coupled to tandem mass spectrometry (MS/MS). The optimization of instrumental parameters and method application for environmental analysis are presented. The performance of the novel method was evaluated by estimation of extraction recovery, linearity, precision and detection limit. The method detection limits was 12 ng L^{-1} in WW and 3.4 ng g^{-1} in WWS. The intra- and inter-day precisions were 8% and 11% in WW and 6% and 9% in WWS, respectively. Furthermore, three extraction methods, ultrasonic extraction (USE), microwave-assisted extraction (MAE) and accelerated solvent extraction (ASE) with three different solvent condition such as methanol, acetone and acetonitrile:ethyle acetate (5:1, v/v) were compared on the basis of procedural blank and method recovery. Overall, ASE showed the best extraction efficiency with methanol as compared to USE and MAE. Furthermore, the quantification of CBZ in WW and WWS samples showed the presence of contaminant in all stages of the treatment plant.

1. Introduction

Large volumes of pharmaceuticals are used for the prevention, diagnosis and treatment of diseases in human and animals. The worldwide average per capita consumption of active pharmaceutical ingredients per year is estimated to be about 15 g and in industrialized countries, the value is expected to be in between 50 and 150 g [1]. Due to their extensive use, presence in the aquatic environment and potential for impacts on wildlife and humans, pharmaceutical compounds are becoming an environmental issue [2]. Therefore, study of the fate of these compounds is becoming very important component of assessing the environmental risks associated with them.

Carbamazepine (CBZ) is one such important drug used: (i) as an antieliptic and anticonvulsant; (ii) for the treatment of epilepsy, as well as for various psychotherapeutic applications and; (iii) in combination with other drugs for the treatment of alcohol withdrawal [3]. The physico-chemical and pharmacological properties of CBZ are summarized in Table 1. CBZ has been proposed as an anthropogenic marker in water bodies [6]. Annually, about 1014 t of CBZ is consumed worldwide (estimated value is in accordance with Intercontinental Marketing Services (IMS) Health data: 942 t of CBZ were sold in 2007 in 76 major countries which are believed to account for 96% of the global pharmaceutical market) and this yields to more than 30 t of CBZ which have to be removed from effluents [7]. In Canada, approximately 28 t of CBZ was sold as prescriptions in 2001 [8].

Following human administration (excreted unchanged and/or as metabolies with feces and urine), CBZ has been detected in wastewater (WW) and wastewater sludge (WWS). Studies in Europe and North America have shown that CBZ is one of the most frequently detected pharmaceuticals in wastewater treatment plants (WWTPs) effluents and in river water [9–11]. As WWTPs provide the first and perhaps the most important opportunity for removing CBZ that are destined for discharge into the environment, it is important to characterize the fate

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Table 1
Physico-chemical and pharmacological properties of CBZ.

Molecular formula, CAS No. and molecular weight	$C_{15}H_{12}N_2O$, 298-46-4 and 236.27 g mol^{-1}
Water solubility[a]	17.7 mg L^{-1} (20 °C)
Log K_{ow} (octanol-water partitioning)[a]	2.45
Henrys law constant[a]	1.09×10^{-5} Pa m^3 mol^{-1} (25 °C)
p*K*a	Neutral
Melting point	189–193 °C
Usage	Analgesic, anticonvulsant, antimanic agent
Elimination half-life[b]	25–65 h
Appearance	White, light yellowish powder
Toxicity	Mild ingestion cause vomiting, drowsiness, ataxia, slurred speech, nystagmus, dystonic reactions, and hallucinations. Severe intoxications may produce coma, seizures, respiratory depression and hypotension
Affected organisms	Human and aquatic organisms

[a] [4].
[b] [5].

of CBZ during the treatment of municipal wastewater. The most important process to study the fate of CBZ in WW and WWS includes to know whether CBZ will primarily enter the aquatic or terrestrial environment or get partitioned from aqueous sewage into sludge and disposed with further application of sludge. Several groups have investigated the elimination of CBZ during sewage treatment and also fate of the compound in different contaminated media including WW and WWS [12,13]. However, to the best of our knowledge there have been no studies conducted on partitioning of CBZ in different compartment of WWTPs which is very important to know the fate of compound and to select different treatment processes for effective degradation of compound.

Furthermore, the measurement problems associated with quantification of these pharmaceutical compounds including CBZ in WW and WWS is to detect the analyte in trace levels (ng L^{-1} or below) and to avoid the impact on the analyte signals caused by matrix components. Identification and quantification of different pharmaceutical compounds including CBZ are usually performed by LC or GC-MS/MS [13,14]. To reduce sample preparation, analysis time and concentration of organic solvents (during quantification), the development of an ultrafast method for the analysis of CBZ in WW and WWS has been carried out using a laser diode thermal desorption (LDTD) coupled to an atmospheric pressure APCI source for tandem mass spectrometry (MS/MS). LDTD-APCI-MS/MS analysis has been recently developed to enhance the high throughput capacity in MS by reducing LC-MS/MS runs of 5 to 30 min to 10 to 30 s in LDTD-APCI-MS/MS run [15].

In this study, we developed a suitable ultrafast method based on LDTD-APCI-MS/MS method for quantification of CBZ in WW and WWS which has never been studied earlier. Furthermore, three extraction methods namely, ultrasonic extraction (USE), microwave-assisted extraction (MAE) and accelerated solvent extraction (ASE) were compared for extraction of CBZ from WWS by spiked recovery experiments. Furthermore, the concentration of CBZ was monitored in WW and WWS at various stages of treatment in the WWTP for the Quebec City, Qc, Canada.

2. Materials and methods

2.1. Chemicals

CBZ was obtained from Sigma Aldrich (St Louis, MO, USA). The internal standard (IS), carbamazepine-d_{10} was purchased from C/D/N Isotopes Inc. (Montreal, Quebec, Canada). HPLC-grade methanol (MeOH), acetonitrile, ethyl acetate, and acetone, were purchased from Fisher Scientific (Ontario, Canada). Sep-Pak Plus C18 environmental cartridges used for solid phase extraction (SPE) clean-up was purchased from Waters (Milford, MA, USA). HPLC grade water was prepared in the laboratory using a Milli-*Q*/Milli-RO Millipore system (Milford, MA, USA).

2.2. Wastewater treatment plants and sampling

Samples were collected from Quebec Urban Community (CUQ) wastewater treatment plant (Beauport, Quebec city, Quebec, Canada) which receives wastewater originating from domestic zones, industries, commercial enterprises and institutions present in the city. The eastern station of WWTP serves a population of 528,016 (2006 estimate) and has a treatment capacity of 400,000 m^3 day^{-1}. The CUQ treatment plant accomplishes primary and physical-chemical treatment of sewage before discharging the treated water into the Saint-Lawrence River.

Samples of WW and WWS were collected as grab samples during the sampling periods (August 20th, 21st, 22nd, 23rd, 24th, 2011). Fig. 1 represents a schematic of the treatment process and the different sampling locations. Samples were collected in pre-cleaned glass amber bottles with aluminum foil-lined caps. After sample collection, in order to study the partitioning of CBZ in WWS, the liquid fraction of WWS was separated from the solid fraction by centrifugation at 7650 *x* g for 15 min. Later, WWS (primary sludge, secondary sludge, mixed sludge, dewatered sludge) and the solid fraction of WWS (primary sludge solids, secondary sludge solids and mixed sludge solids) were stored at 4 ± 1 °C in a cold room until preparation for analysis, which generally occurred within 24 h of collection. Furthermore, WW (influent, grit influent, effluent) and liquid fraction of WWS (primary sludge liquid, secondary sludge liquid and mixed sludge liquid) samples were filtered through a 0.45 μm glass-fiber (Fisherbrand G6 filter circles, Fisher Scientific, Ontario, Canada) and immediately stored at 4 ± 1 °C until analysis.

2.3. Extraction

Different WWS and solid fraction of WWS were frozen using liquid nitrogen prior to lyophilization by the freeze-dry system (Dura Freeze Dryer, Kinetics). Three types of extraction methods, ultrasonic extraction (USE), microwave-assisted extraction (MAE) and accelerated solvent extraction (ASE) were carried out in order to optimize the extraction method for higher recovery of CBZ from WWS. The experiments were carried out by spiking the known concentration of CBZ (100 ng g^{-1}) to WWS samples.