CARBAMAZEPINE CONCENTRATIONS IN NATURAL WATERS AND WASTEWATER TREATMENT PLANT SAMPLES

Sajwan K[1]*, Johnson R[1] , Peng S[2] , Loganathan BG[2]

[1]Savannah State University, 3219 College Street, Savannah, GA 31404, USA; [2]Murray State University, 1201 Jesse D Jones Hall, Murray, KY 42071, USA

Introduction

Carbamazepine is a drug primarily used in the treatment of epilepsy, trigeminal neuralgia, pain syndromes and diabetes insipidus etc. Several pharmaceutical and personal care products are being reported in streams, rivers and lake waters[1,2]. Many PPCPs, including carbamazepine have persistent properties that make them remain biologically active after they leave the body or are disposed in landfills and waters. Due to persistent and lipophilic properties, these compounds do not degrade and enter the food chain through bioaccumulation and biomagnifications[3,4]. Presence of pharmaceuticals in municipal wastewater, stream, and river waters is an increasing concern, likely to have adverse effects on aquatic organisms and our drinking water supply[5,6]. Carbamazepine is used worldwide as anticonvulsant and as analgesic. Several disorders including physical and mental illness, including epilepsy, trigeminal neuralgia, pain syndromes and diabetes insipidus, can be controlled by carbamazepine[7,8]. As one of the most frequently prescribed drug, carbamazepine (5H-dibenz[b,f]azepine-5-carboxamide) was first synthesized by Schindler in the 1960s[9,10]. It became a commercial drug later with several brand names of Tegretol, Carbatrol, Tegretol XR, Epitol *etc.* in different countries[11]. The formula is $C_{15}H_{12}N_2O$, and the chemical structure is shown in 0 with molecular weight of 236.27. Carbamazepine is practically insoluble in water of 17.7 mg/L at 25 °C,[12] however, it can dissolve in methanol, tetrahydrofuran, ethanol and acetone at room temperature[13]. The mechanism of action of this compound is to interface and stabilize voltage-gated sodium channels, preventing brain cell from over activated state[10]. However, the risks of using carbamazepine include toxic epidermal necrolysis (TEN) and Stevens-Johnson Syndrome (SJS). It is about 0.01-0.06% new patients using this drug get this negative effect[7]. Carbamazepine's unique properties prevent this compound from biodegradation and rarely eliminated during wastewater treatment process[14]. Very limited information is available on carbamazepine in stream and river waters and wastewater treatment plant samples. The objective of this study was to determine the levels of carbamazepine in water samples from wastewater treatment plant (WWTP) samples from Murray, Bee Creek, and Clarks River and five WWTP from Savannah, Georgia.

Murray is a small town located in western Kentucky with a population of approximately 30,000 people. Murray is also home of the Murray State University, several pharmacies, private clinics and the Murray Calloway County Hospital. The wastewaters from these facilities carry pharmaceutical residues that are transported along with waste to the local wastewater treatment plant. Savannah is a port city situated on the southeastern United States with a population of over 300,000 people. There are five major wastewater treatment plants process the wastewaters from the city of Savannah residential, commercial and industrial operations. Considering the nature of population of these towns, the use of carbamazepine is highly possible. Based on the above attributes, we hypothesize that detectable levels of carbamazepine may be found in water samples from these locations.

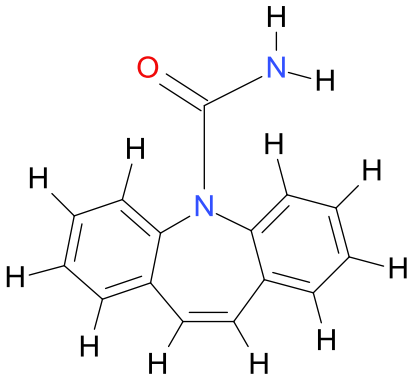

Figure 1. Structure of Carbamazepine

Materials and Methods

Water samples were collected from various water resources in Murray and five WWTPs from Savannah, Georgia to study carbamazepine contamination levels. Three regions were selected for sampling in Murray, WWTP,. Bee Creek and Clarks River. Sampling locations in Savannah include: The WWTPs from The President Street, Wilshire Street, Cross Roads, Georgetown and Tybee Island.Were also selected for monitoring this pharmaceutical chemical. Sampling dates were chosen from October 2010 through March 2011, occurring in fall, winter and spring. Samples were collected using pre-cleaned I-Chem bottles and transported to lab in ice. Samples filtered through the Millipore apparatus with pre-ashed glass fiber filters of 0.45 µM under vacuum. Water samples passed through solid phase extraction (SPE-HLB) cartridges (purchased from Waters Corporation, MA, USA) under vacuum condition with a flow rate of 10 mL/min. The analytes were eluted using methanol:acetic acid 99:1 ratio solution. Analyte elution was performed by 4×5 mL solution using elution manifold. The eluant was evaporated to 1 mL using a gentle stream of nitrogen gas. ELISA method (Abraxis ELISA kit, Il, USA) was used to quantitate carbamazepine in the water samples. Absorbance was measured using a M6+ 450 nm filter Mini Photometer.

Results and discussion

Table 1 and Table 2 shows carbamazepine levels in water samples from MWWTP, Bee Creek, Clarks River and Red Duck Creek from western Kentucky and WWTPs from Savannah, Georgia. Measurable levels of carbamazepine were detected in all samples analyzed. Concentrations of carbamazepine ranged from 11.4 ng/L (Site F of Red Duck Creek) to 35.2 ng/L (WWTP effluent). The concentrations were similar in Bee Creek, Clarks River and Red Duck (Range: 11.4-20.0 ng/L). Carbamazepine levels in effluent of WWTP were about two times higher than all other sites (Range: 26.6-35.2 ng/L).

Table 1. Concentrations of carbamazepine in Clarks River samples, Bee Creek and Murray Wastewater Treatment Plant (MWTTP) collected from October 2010 to March 2011.

No.	Date of Sampling	Clarks River (ng/L)		Bee Creek (ng/L)		MWWTP (ng/L)
		Square Holland	I-94	Upstream	Downstream	Effluent
1	10/21/2010	15.7	17.9	13.5	16.0	33.7
2	11/5/2010	17.4	17.6	14.6	15.4	29.4
3	3/11/2011	16.8	17.2	13.7	17.9	35.2
Mean	-	16.6	17.6	13.9	16.4	32.8

Table 2. Concentrations of Carbamazepine in Wastewater Treatment Plant samples from Savannah, Georgia..(Int: Interfrence, NA: Not analyzed).

Survey No.	WWTP Location	Influent (ng/L)	Effluent (ng/L)
1	President Street	Int	330
2	Wilshire Street	Int	226
3	Cross Roads	Int	270
4	George Town	Int	310
5	Tybee Island	NA	199

Carbamazepine concentrations in Murray were shown in Table 1. Carbamazepine concentrations ranged from 15.7 ng/L to 17.9 ng/L in Clarks River, and concentrations in Clarks River at I-94 bridge, which is close to downtown, were higher than in Clarks River at Square Holland Road through each event. Carbamazepine concentrations ranged from 13.5 ng/L to 17.9 ng/L in Bee Creek, and concentrations in upstream were lower than in downstream through each event. This is reasonable that water from MWWTP combined Bee Creek in downstream. Carbamazepine concentrations ranged from 29.4 ng/L to 35.2 ng/L in MWWTP, and concentrations in Effluent were understandably about twice higher than other sites.

Carbamazepine concentrations in effluent water samples from Savannah, Georgia were shown in Table 2. Due to matrix effect (Int. :interference), influent samples were unable analyze and determine the analyte concentrations. In effluent samples, carbamazepine concentrations ranged from 199 ng/L to 330 ng/L, Variation in concentration indicate various amounts of input of carbamazepine in these WWTPs. Carbamazepine concentrations in WWTP samples from Savannah were one order magnitude higher than Murray WWTP and natural water samples.

In conclusion, measurable levels of carbamazepine were detected in all samples analyzed. Carbamazepine levels in WWTPs in Savannah, Georgia were considerably higher than all other sites. Occurrences of carbamazepine in Bee Creek and Clark River waters indicate that this pharmaceutical chemical is a contaminant in the regional waters. Further studies with more number of samples are needed to determine environmental distribution, behavior and fate of carbamazepine in western Kentucky Watershed.

References

1. Snyder S, Kelly K, Grange A, Sovocool G, Snyder W, Giesy J. (2001). Pharmaceuticals and personal care products in the waters of Lake Mead, Nevada. In: Daughton C., Jones-Lepp, T. (Eds.). Pharmaceutical and Personal Care Products in the Environment-Scientific and Regulatory Issues, American Chemical Society Symposium Series 791, Washington D.C., pp.116-139
2. Kolpin D, Furlong E, Meyer M, Thurman E, Zaugg S, Barber L, Buxton H. (2002). *Environ. Sci. Technol*. 36: 1202-11
3. Daughton C, Ternes T. (1999). *Environ. Health Perspect*. 107 (suppl. 6): 907-38
4. Daughton C. (2003). Chemicals from pharmaceuticals and personal care products. In: Dasch, E.J. (Ed.), Water: Science and Issues, Vol. 1. Macmillan Reference, New York, USA, pp. 158-164
5. Loganathan BG, Phillips M, Mowery H, Jones-Lepp TL. (2009). *Chemosphere* 75: 70-77
6. Jones-Lepp T, Alvarez D, Loganathan BG. (2011). On the Frontier: Analytical chemistry and the occurrence of illicit drugs in surface waters in the United States. In. Illicit Drugs in the Environment: Occurrence, Analysis, and Fate Using Mass Spectrometry. Eds. S. Castiglioni, E. Zuccato, R. Fanelli. John Wiley & Sons, Inc. pp 171-88

7. Novartis (2010). Tegretol Medication Guide. T2011-31/T2011-32. Novartis Pharmaceutical Corporation, East Hanover, New Jersey, USA.
8. Okuma T, Kishimoto A. (1998). *Psychiatry arid Clinicd Nerosciences* 52: 3-12
9. Schindler, W. (1960). New N-heterocyclic compounds. U.S. Patent 2,948,718
10. Benes J, Parada A, Figueiredo AA, Alves P C, Freitas A P, Learmonth DA, Cunha RA, Garrett J, Soares-da-Silva P. (1999). Anticonvulsant and Sodium Channel-Blocking Properties of Novel 10,11-Dihydro-5H-dibenz[b,f]azepine-5-carboxamide Derivatives. *J. Med. Chem.* 42: 2582-87
11. Carbamazepine. Retrieved April 28, 2011, from http://www.drugs.com/ingredient/carbamazepine.html
12. Oetken M, Nentwig G, Lçffler D, Ternes T, Oehlmann J. (2005). *Arch. Environ. Contam. Toxicol.* 49: 353–61
13. Liu W, Dang L, Black S, Wei H. (2008). *J. Chem. Eng. Data*. 53: 2204–206
14. Kosjek T, Andersen HR, Kompare B, Ledin A, Heath E. (2009). *Environ. Sci. Technol.* 43: 6256–61.