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Contamination profiles and mass loadings of macrolide antibiotics and illicit drugs from a small urban wastewater treatment plant

Bommanna Loganathan [a], Malia Phillips [a], Holly Mowery [a], Tammy L. Jones-Lepp [b,*]

[a] Department of Chemistry and Center for Reservoir Research, Murray State University, Murray, KY 42071-3346, USA
[b] USEPA/ORD/NERL-ESD, P.O. Box 93478, Las Vegas, NV 89193-3478, USA

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ABSTRACT

Information is limited regarding sources, distribution, environmental behavior, and fate of prescribed and illicit drugs. Wastewater treatment plant (WWTP) effluents can be one of the sources of pharmaceutical and personal care products (PPCP) into streams, rivers and lakes. The objective of this study was to determine the contamination profiles and mass loadings of urobilin (a chemical marker of human waste), macrolide antibiotics (azithromycin, clarithromycin, roxithromycin), and two drugs of abuse (methamphetamine and ecstasy), from a small (<19 mega liters day^{-1}, equivalent to <5 million gallons per day) wastewater treatment plant in southwestern Kentucky. The concentrations of azithromycin, clarithromycin, methamphetamine and ecstasy in wastewater samples varied widely, ranging from non-detects to 300 ng L^{-1}. Among the macrolide antibiotics analyzed, azithromycin was consistently detected in influent and effluent samples. In general, influent samples contained relatively higher concentrations of the analytes than the effluents. Based on the daily flow rates and an average concentration of 17.5 ng L^{-1} in the effluent, the estimated discharge of azithromycin was 200 mg day^{-1} (range 63–400 mg day^{-1}). Removal efficiency of the detected analytes from this WWTP were in the following order: urobilin > methamphetamine > azithromycin with percentages of removal of 99.9%, 54.5% and 47%, respectively, indicating that the azithromycin and methamphetamine are relatively more recalcitrant than others and have potential for entering receiving waters.

1. Introduction

The occurrence of pharmaceutical and personal care product (PPCP) residues in the environment has received considerable attention in recent years as these compounds have been implicated for negative effect on biota and the ecosystem. PPCPs are considered emerging environmental pollutants, and have been detected in groundwater, surface water and municipal wastewater, fish and biosolids (Snyder et al., 2001; Kolpin et al., 2002; Mottaleb et al., 2004; Osemwengie and Gerstenberger, 2004; Petrovic et al., 2006; Kinney et al., 2006; Pedrouzo et al., 2007; Cuderman and Heath, 2007; Jones-Lepp and Stevens, 2007). Earlier studies have implicated the presence of PPCPs in the development of antibiotic resistant bacteria, feminization of male fish, and acute toxicity and genotoxicity in aquatic organisms (Jobling et al., 1998; Daughton and Ternes, 1999; Daughton, 2001; Schwartz et al., 2003; Nash et al., 2004; Isidori et al., 2005; Jobling et al., 2006; Schwartz et al., 2006; Horii et al., 2007; Kostich and Lazorchak, 2008). Many pharmaceuticals are designed to be persistent and lipophilic so that they can retain their chemical structure in the organism (usually human or domesticated animals) long enough to do their therapeutic work. Consequently, after they are excreted such chemicals can persist in the environment and enter the food chain through bioaccumulation and biomagnification (Daughton and Ternes, 1999; Daughton, 2003). For example, macrolide antibiotics, drugs that are used for therapeutic treatment of infectious disease in humans, have been reported in wastewaters, surface waters, sediments, biosolids, and in aquatic organisms (Hirsch et al., 1999; McArdell et al., 2003; Jones-Lepp et al., 2004; Kim and Carlson, 2007; Jones-Lepp and Stevens, 2007; Ramirez et al., 2007). While the ecotoxicological significance of drugs in environmental matrices, particularly water, has not been closely examined, it can only be surmised that these substances have the potential to adversely affect biota (e.g., bacteria, fish, amphibians, etc.) that are continuously exposed, even at very low levels. Further, the occurrence of antibiotic-resistant bacteria in waters receiving wastewater effluents is of great concern (Miyabara et al., 1995; Schwartz et al., 2003, 2006).

Very few studies have examined the contamination profiles and mass loadings of wastewater treatment plants (WWTPs) for prescribed and illicit drugs. For human-use antibiotics, WWTPs are considered the major source of release into the environment due

* Corresponding author. Tel.: +1 702 798 2144; fax: +1 702 798 2142.
E-mail address: jones-lepp.tammy@epa.gov (T.L. Jones-Lepp).

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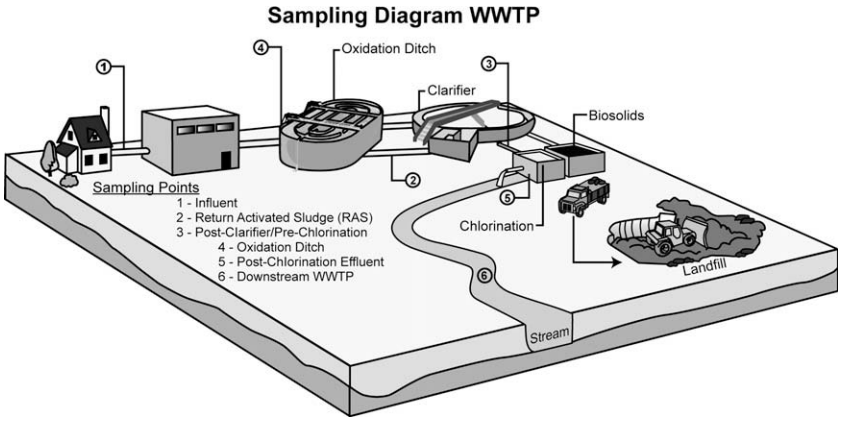

Fig. 1. Simplified diagram of Murray WWTP and sampling points.

to the partial removal efficiency in the treatment process (Kim and Carlson, 2007). The objectives of this research were to measure the contamination profiles and environmental loadings of three antibiotics and two illicit drugs from a small urban wastewater treatment plant in Kentucky. The target compounds were the macrolide antibiotics azithromycin, clarithromycin, and roxithromycin, and two illicit drugs methamphetamine and ecstasy (3,4-methylene dioxymethamphetamine, MDMA). We also measured urobilin as a chemical marker of human waste. Wastewater samples were collected during different times of the year to determine if seasonal differences occur in concentrations of the target analytes, and from different points within the WWTP to examine the removal efficiency of target compounds during the treatment process, and to determine the final amount of these compounds entering into receiving waters. The samples collected for this study were comprised of influent, effluent, return activated sludge (RAS), the oxidation ditch, and before and after chlorination, see Fig. 1.

The WWTP used in this study has a capacity to process 20 mega liters day^{-1} (MLd) of wastewater per day. Primarily, the combined sources of wastewater into this treatment plant are from homes, a hospital, university dormitories, and a small fraction of commercial and industrial sewage. This town has a local population of approximately 15,099 people (2002 US Census), throughout the year (MCC Community Profile, 2007), a considerable portion of which are retirees, and then an influx of university students (10,275 students, academic year 2006–2007) during the academic year (mid-August–mid-May). Significant population fluctuations (about 40%) occur during a calendar year, especially during winter and summer breaks, during which the student population is at its minimum. Considering the nature of population, including elderly (retirement community) and university students, the use of antibiotics and illicit drugs are highly possible. According to recent Murray State statistics, twenty-two possessions of marijuana, twenty possession of drug paraphernalia, one drug trafficking within 1000 yards of the university were reported, and drug-related violations are showing an increasing trend since 2005 (second only to theft) (Phelps, 2008a,b).

The six compounds studied, Fig. 2 were chosen for their amenability to the methodologies used, and for socially-related reasons. Azithromycin is the most widely prescribed antibiotic (of any kind) in the United States (US), and has been in the top 10 for the last six years (2001–2007) (http://drugtopics.modernmedicine.com/drugtopics/data/articlestandard//drugtopics/072008/491181/article.pdf and http://www.rxlist.com, top 200 prescribed drugs); clarithromycin is in the top 200 prescribed drugs (http://www.rxlist.com, top 200 prescribed drugs); roxithromycin, while not prescribed in the US, is widely used in Latin America and Europe, thereby lending itself as a marker of the importation of drugs by other than traditional means. The two illicit drugs (methamphetamine and MDMA) were chosen because of their reported use and limited environmental occurrence data (Zuccato et al., 2005; Jones-Lepp et al., 2004) and verifiable usage in the United States, especially MDMA amongst young adults (last accessed 31 July 2007, http://www.usdoj.gov/dea/pubs/states/kentucky.html). Urobilin, previously studied as a chemical marker of human waste, was measured throughout the study for correlation to the extraction efficiencies, and was helpful in understanding removal efficiency of the WWTP (Jones-Lepp and Stevens, 2007).

2. Materials and methods

2.1. Materials

2.1.1. Drug standards

Azithromycin [(2*R*-(2R*,3S*,4R*,5R*,8R*,10R*,11R*,12S*,13S*,14R*)]-13-[(2,6-dideoxy-3-C-methyl-3-*O*-*methyl*-α-L-*ribo*-hexopyranosyl)oxy]-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-*xylo*-hexopyranosyl]oxy]-1-oxa-6-azacyclopentadecan-15-one; CASRN 83-905-01-5], roxithromycin [3R,4S,5S,6R,7R,9R,11S,12R,13R,14R)-6-[(2S,3R,4S,6R)-4-dimethylamino-3-hydroxy-6-methyl-oxan-2-yl] oxy-14-ethyl-7,12,13-trihydroxy-4-[(2S,4R,5S,6S)-5-hydroxy-4-methoxy-4,6-dimethyl-oxan-2-yl]oxy-10-(2-methoxyethoxymethoxyimino)-3,5,7,9,11,13-hexamethyl-1-oxacyclotetradecan-2-one; CASRN 80214-83-1], and clarithromycin [6-(4-dimethylamino-3-hydroxy-6-methyl-tetrahydropyran-2-yl)oxy-14-ethyl-12,13-dihydroxy-4-(5-hydroxy-4-methoxy-4,6-dimethyl-tetrahydropyran-2-yl)oxy-7-methoxy-3,5,7,9,11,13-hexamethyl-1-oxacyclotetradecane-2,10-dione; CASRN 81103-11-9] were obtained from U.S. Pharmacopeia (Rockville, MD, USA) and Sigma–Aldrich (St. Louis, MO, USA). Methamphetamine [(α*S*)-*N*,α-dimethylbenzeneethanamine; CASRN 537-46-2], and MDMA [*N*,α-dimethyl-1,3-benzodioxole-5-ethanamine (also known as 3,4-methylene dioxymethamphetamine; CASRN 42542-10-9] were obtained from Cerilliant Corporation (formerly Radian Co., Round Rock, TX).

d-Urobilin IX hydrochloride [(21H-biline-8,12-dipropanoic acid, 3,18-diethyl-1,4,5,15,16,19,22,24-octahydro-2,7,13,17-tetramethyl-1, 19-dioxo-monohydrochloride, (4R, 16R)-(9Cl); CASRN 28925-89-5] was obtained from Frontier Scientific (Logan, UT, USA).

Stock standard solutions were individually prepared in HPLC-grade methanol (Burdick & Jackson, Muskegon, MI, USA, or equivalent) and stored in darkness at 4 °C. A high-level standard mix containing the macrolide antibiotics, urobilin, and the illicit drugs (at 10 or 20 ng μL^{-1}), in methanol, was prepared quarterly, and a