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Detection of pharmaceuticals and phytochemicals together with their metabolites in hospital effluents in Japan, and their contribution to sewage treatment plant influents

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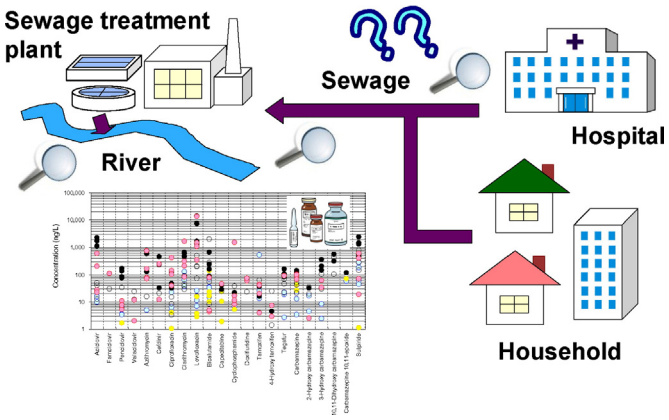
HIGHLIGHTS

- 41 PPs including metabolites in hospital effluent were surveyed.
- Detection level ranged widely from ng/L to μg/L (maximum, 92 μg/L).
- Mass balance of each PP was evaluated by mass fluxes.
- Contribution of PPs in the hospital to STP influent varied from <0.1% to 14.8%.
- Ozone treatment at STPs was effective for the removal of PPs targeted in this study.

GRAPHICAL ABSTRACT



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ABSTRACT

The occurrence of 41 pharmaceuticals and phytochemicals (PPs) including their metabolites was surveyed in hospital effluent in an urban area of Japan. A detailed survey of sewage treatment plant (STP) influent and effluent, and river water was also conducted. Finally, mass balances with mass fluxes of the target PPs through the water flow were evaluated and the degree of contribution of hospital effluent to the environmental discharge was estimated.

The results indicate that 38 compounds were detectable in hospital effluent over a wide concentration range from ng/L to μg/L, with a maximum of 92 μg/L. The contributions of PPs in the hospital effluent to STP influent varied widely from <0.1% to 14.8%. Although almost all of the remaining components could be removed below 1.0 ng/L at STPs by the addition of ozone treatment, a number of PPs still remained above 10 ng/L in STP effluent. These findings suggest the importance of applying highly developed treatments to hospital effluents and at STPs in the future to reduce the environmental risks posed by PPs. To our knowledge, this is the first demonstration of the presence of two conjugated metabolites of acetaminophen, acetaminophen glucuronide and acetaminophen sulfate, as well as of loxoprofen and loxoprofen alcohol, in hospital effluent, STP, and river waters.

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1. Introduction

An emerging problem of pollution of river environments by pharmaceuticals and phytochemicals (PPs) has begun to receive a large amount of attention worldwide (López-Serna et al., 2013; Vasquez et al., 2014; Evgenidou et al., 2015).

Extensive studies on the occurrence and behavior of pollutants in rivers and sewage treatment plants (STPs) (López-Serna et al., 2013; Oliveira et al., 2015), including environmental risk assessments (Komori et al., 2013; Ågerstrand et al., 2015), have triggered anxiety regarding the potential appearance of drug-resistant microorganisms in the water environment (Kümmerer, 2009b; Adachi et al., 2013). Moreover, there is concern that PPs could inhibit algal growth (Aristilde et al., 2010) or have antibacterial effects, and that anti-cancer drugs could have ecotoxicological effects on aquatic organisms (Besse et al., 2012; Booker et al., 2014; Toolaram et al., 2014).

Because pharmaceuticals are designed to have specific physiological effects on targeted body areas, they have high polarity to make them easily discharged from the body (Daughton and Ternes, 1999; Kolpin et al., 2002). As a result, they tend not to be removed during the traditional sewage treatment process, which is centered on biological treatment (Kümmerer, 2009a; Onesios et al., 2009; Michael et al., 2013). In addition, pharmaceuticals are used constantly in hospitals to treat disease. In the past, studies of the occurrence of pharmaceuticals in hospital effluents, and of the development of water treatment systems for these chemicals, have been reported mainly from Europe (Santos et al., 2013; Al Aukidy et al., 2014; Verlicchi et al., 2015) and the United States (Nagarnaik et al., 2010; Oliveira et al., 2015).

The quantity of pharmaceuticals used in Japan is the second largest in the world after that used by the United States (Ministry of Health Labour and Welfare, Japan, 2013). The high coverage (more than 90% of urban areas) of sewerage systems in Japan (Japan Sewage Works Association, 2014) and the transfer of both domestic waste and hospital effluent into sewerage systems indicate the importance of STPs as loading sources of pollutants in river environments. The contributions of not only pharmaceutical components including endocrine-disrupting chemicals such as estrogen as pollutant loads are reported in a range from 50% to nearly 100% due to STPs (Azuma et al., 2013; Kumar et al., 2014). The STPs are responsible for the reduction of the levels of PPs in sewage based on the result of the stability of cytostatic agents in STP influents after their discharge from hospitals (Ferrando-Climent et al., 2013). Nevertheless, to our knowledge, no study has yet surveyed both pharmaceuticals and phytochemicals in hospital effluents in Japan (Verlicchi et al., 2015), and their occurrence and contribution to STP influents are mostly unknown. Moreover, the presence of not only pharmaceuticals but also their active metabolites in sewage and river water was pointed out by several researchers. For example, in the case of the anti-cancer drug tamoxifen for breast cancer, 4-hydroxytamoxifen was also detected as its active metabolite in sewage and river waters (Borgatta et al., 2015; Orias et al., 2015), but their distribution in hospital effluents is limited worldwide.

Given this situation, a group of PPs whose pollution status in the aquatic environment was unknown was selected and surveyed in hospital effluent in an urban area of Japan. In addition, a similar survey was conducted for influent and effluent of an STP that treated sewage from a targeted hospital and surrounding households and river water. Estimation of mass fluxes and their correspondence with mass balances were further made to get information of the effects of transfer of PPs and their metabolites from the hospital to its effluent and then to STP inflows.

2. Materials and methods

2.1. Target PPs

For the analysis 41 PPs grouped into 9 therapeutic classes were selected on the basis of previously detected levels and frequencies of detection in hospital effluent, sewage, and river water (López-Serna et al., 2013; Azuma et al., 2015; Oliveira et al., 2015). The names of the target compounds were listed as follows by typifying into each constituent class: (1) anti-virals (acyclovir, famciclovir, penciclovir, and valaciclovir); (2) anti-bacterials (azithromycin, cefdinir, ciprofloxacin, clarithromycin, and levofloxacin); (3) anti-cancers (bicalutamide, capecitabine, cyclophosphamide, doxifluridine, tamoxifen, 4-hydroxytamoxifen, and tegafur); (4) psychotropics (carbamazepine, 2-hydroxy carbamazepine, 3-hydroxy carbamazepine, 10,11-dihydroxy carbamazepine, carbamazepine 10,11-epoxide, and sulpiride); (5) analgesic–antipyretics (acetaminophen, acetaminophen glucuronide, acetaminophen sulfate, ethenzamide, ibuprofen, indomethacin, loxoprofen, and loxoprofen alcohol); (6) bronchodilators (caffeine and theophylline); (7) anti-pruritic (crotamiton); (8) herbal medicines (berberine and puerarin); and (9) phytoestrogens (daidzein, daidzin, genistein, genistin, glycitein, and glycitin). The physicochemical properties of the target PPs, are also shown in Table S1. All analytical standards were of high purity (>98%) and were purchased from AdooQ BioScience (Irvine, CA, USA), Cayman Chemical (Michigan, Ann Arbor, USA), LC Laboratories (Woburn, MA, USA), LKT Laboratories (St. Paul, MN, USA), Santa Cruz Biotechnology, Inc. (Santa Cruz, CA, USA), Sigma-Aldrich (St. Louis, MO, USA), and Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan).

Individual standard stock solutions at 10 mg/L were prepared in methanol and stored at −20 °C. These standard solutions were used to prepare a minimum of six calibration curve solutions in a 90:10 (*v*/*v*) mixture of 0.1% formic acid solution in methanol.

2.2. Sampling

Location of the present survey was settled in the middle region on the right bank of the Yodo River in the Kansai region of Japan. The main hospital is located in Takatsuki City, the midpoint urban city between Kyoto and Osaka, and has the number of beds 477 and a mean number of patients 1100 persons/day. The flow rate of hospital effluent ranged from 426 to 503 m^3/day (mean, 460 m^3/day). The STP is located in the lower reaches of the sewage system which connects the hospital. The STP disposed of municipal sewage from 420,000 people at 134,000 m^3/day (annual mean value). The STP has one influent site and two effluent sites which differed in treatment: one is introduced from a conventional activated sludge (CAS) and Step AO followed by chlorination for disinfection (132,000 m^3/day), and the other consisting of a partial CAS and Step AO followed by ozonation (contacting with 8.6 mg ozone/L for 100 min) (2000 m^3/day). Sludge retention times for CAS and AO were 9 and 8 days, respectively. Hydraulic retention times for CAS and AO were settled as 7 and 6 days, respectively. Chlorination was conducted for 15 min at 1.5 mg NaClO/L. The final site for sampling river water is located about 1 km downstream from the site where the STP effluent entered the river. The mean river flow rate was 196,000 m^3/day and its deviation was estimated as 10% (Azuma et al., 2012).

Because four clear cut different seasons (spring, summer, autumn and winter) are present in the sampling district and no unexpected epidemic was spread during the experimental years, frequency of the sampling was set to four, one day each in an individual typical climate season, to fit for the present study. This sampling frequency was also determined based on the previous surveying reports (Kumar et al., 2011; Hanamoto et al., 2013). The survey was conducted on April 11 (spring), July 15 (summer), December 18 (late autumn), and February 27 (winter) in 2014 to 2015. We used glass bottles containing ascorbic acid (1 g/L) as a preservative to collect 500-mL samples of hospital effluent, STP influent, STP effluent, and river water (Kumar et al., 2009).

For sampling the hospital effluent there was no space enough to settle composite samplers at the sampling location and no power supply was available in the same area. Similarly, no composite sampler