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Representative input load of antibiotics to WWTPs: Predictive accuracy and determination of a required sampling quantity

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ABSTRACT

Predicting the input loads of antibiotics to wastewater treatment plants (WWTP) using certain input data (e.g. prescriptions) is a reasonable method if no analytical data is available. Besides the spatiotemporal uncertainties of the projection itself, only a few studies exist to confirm the suitability of required excretion data from literature. Prescription data with a comparatively high resolution and a sampling campaign covering 15 months were used to answer the question of applicability of the prediction approach. As a result, macrolides, sulfamethoxazole and trimethoprim were almost fully recovered close to 100% of the expected input loads. Nearly all substances of the beta-lactam family exhibit high elimination rates during the wastewater transport in the sewer system with a low recovery rate at the WWTP. The measured input loads of cefuroxime, ciprofloxacin and levofloxacin fluctuated greatly through the year which was not obvious from relatively constant prescribed amounts. The latter substances are an example that available data are not per se sufficient to monitor the actual release into the environment. Furthermore, the extensive data pool of this study was used to calculate the necessary number of samples to determine a representative annual mean load to the WWTP. For antibiotics with low seasonality and low input scattering a minimum of about 10 samples is required. In the case of antibiotics exhibiting fluctuating input loads 30 to 40 evenly distributed samples are necessary for a representative input determination. As a high level estimate, a minimum number of 20–40 samples per year is proposed to reasonably estimate a representative annual input load of antibiotics and other micropollutants.

1. Introduction

Input loads of antibiotics into the sewer system and the environment are often estimated using information on nationwide productions, sales or prescribed amounts (Bendz et al., 2005; Choi et al., 2008; Gobel et al., 2005). If applying this approximation method, it has to be taken into account that the catchments of wastewater treatment plants (WWTP) can vary significantly in amounts of actually administered

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antibiotics due to socio-economic reasons. Li and Zhang carried out an evaluation of prescription data of antibiotics from different districts in Hong Kong and stated that a breakdown of district- or nation-wide prescriptions to single catchments is not acceptable to sufficiently estimate input loads (Li and Zhang, 2011). In addition to local variations regarding drug administration further uncertainties arise through the necessary use of substance-specific excretion rates. Those pharmacokinetic information are based on only a few pharmacological studies and have been rarely validated in practice (Ghosh et al., 2009). One of the few studies comparing predicted and measured influent was carried out for trimethoprim at the Kälby WWTP in Sweden (Bendz et al., 2005). As a result the theoretical load was almost 5 times higher than the measured value. Reasons for the discrepancy were not provided. At a Swiss WWTP about 50% and 75% of predicted sulfamethoxazole and trimethoprim loads were determined, respectively, taking a sum of 8 samples in 2002 (March) and 2003 (February, November) (Gobel et al., 2005). Investigated macrolides azithromycin, clarithromycin and roxithromycin were fully recovered by the measurement. Those investigations provide important information on the reliability of applied extrapolation methods for load determination but also raise the question of an appropriate sample quantity in this field of investigations. For example, grab samples and short-term composite samples (2 h, 4 h etc.) were shown to be not suitable for input load characterization due to high fluctuations within one day (Coutu et al., 2013; Li and Zhang, 2011). In this context, most of the previous investigations with the aim of determining antibiotic input loads used a comparatively low number of input samples. Zhou et al. used each 2 h time-integrated samples on two consecutive days to perform a mass balance analysis of two WWTP in South China during May and November 2010 (Zhou et al., 2013). Plosz et al. (2010) and Gao et al. (2012) used 6 h-, 8 h- and 24 h-composite samples (three of each type) to investigate input load dynamics and evaluate the contributing processes for pharmaceutical removal, respectively (Gao et al., 2012; Plosz et al., 2010). Four 24 h-composite samples were used to investigate the elimination pathways of antibiotic loads in a Chinese WWTP (Li et al., 2013). A total of eight 24 h-composite (flow proportional) samples were taken to determine the mean input load to the WWTP Kloten-Opfikon, near Zurich, Switzerland (Gobel et al., 2005). By far the highest number of 24 h-mixed composite samples was taken to examine temporal dynamics of antibiotics in the WWTP Lausanne, Switzerland. A total of 84 samples were evenly distributed over the year to capture the seasonality of antibiotics (Coutu et al., 2013).

The current state of knowledge poses two main questions regarding the determination of the representative input load of antibiotics to WWTP:

1. Is the extrapolation of suitable input data (production, sales or prescriptions) in combination with the excretion rate sufficiently accurate to estimate the input loads to WWTPs?
2. What is the appropriate number of samples to determine the characteristic input loads of WWTP, in case alternative input data are not available?

In order to provide answers to the above questions an intensive monitoring program was carried out at the WWTP Dresden-Kaditz taking daily samples over a period of 15 months. The determined input loads were compared to predicted values based on in- and outpatient prescription data for the catchment area of the WWTP. This comprehensive information give insights into load fluctuations of antibiotics at WWTP inflows and establish a solid basis to evaluate excretion rates from literature. Proceeding from the pool of high resolution data a substance specific estimation on the minimal number of samples which satisfactorily describes the annual mean load was carried out.

2. Materials and methods

2.1. *Ambulance and clinical prescription data*

A total of 14 antibiotics were investigated covering the following classes: macrolides (azithromycin, clarithromycin, roxithromycin), tetracyclines (doxycycline), cephalosporins (cefuroxime, cefotaxime), sulfonamides (sulfamethoxazole + trimethoprim), lincosamide (clindamycin), penicillins (penicillin V, piperacillin, amoxicillin) and fluoroquinolones (ciprofloxacin, levofloxacin).

The projection model is based on in- and outpatient prescription data. Outpatient prescription data were provided by the AOK PLUS, the largest statutory health insurance company in the district of Saxony, Germany. About 41% of the population in Dresden is insured by the AOK PLUS while the remaining part is being held by other statutory and private health insurance companies. Ambulant data are available weekly for 2005–2012. Inpatient prescriptions were available for three major hospitals covering about 65% of hospital beds in the catchment area of the WWTP Dresden-Kaditz. Hospital prescription data are available for 2011 and 2012 on a quarterly or monthly basis, depending on the institution. The projection factor of stationary prescriptions to the entire catchment area was calculated to 100%/65% = 1.54. Comparing the amounts of in- and outpatient prescribed amounts it can be stated that most antibiotics are predominantly prescribed in the ambulant sector. The projected amounts of all hospitals constitute less than 30% of the total prescriptions (=sum of in- and outpatient loads) in the catchment area (see Fig. 1). Levofloxacin (40%), cefuroxime (80%), piperacillin (100%) and cefotaxime (100%) are exceptional cases and hospitals are considered to be the main contributors to the overall administration, regarding those substances.

In most cases hospital antibiotics are constantly applied throughout the year. The standard deviations of mentioned high-impact substances are less than 17% and justify the assumption of an even (constant) administration in hospitals. The prescription characteristic of remaining antibiotics with higher standard deviations SD (roxithromycin: 77%, amoxicillin: 61%, clarithromycin: 49%, doxycycline: 42%, azithromycin: 38%, ciprofloxacin: 27%, clindamycin: 25%) will also be assumed to be evenly distributed over the year since no repeating seasonal pattern is evident and their impact on the total input to the catchment area is negligible.