Identification and Fate of Known and Unknown Transformation Products of Pharmaceuticals in the Aquatic System

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Monografía

"Pharmaceuticals which are used worldwide are designed to facilitate the life for the human society and have an important role in treatment and prevention of disease for both humans and animals. They are ubiquitous in the aquatic environment and are mainly derived from municipal wastewater treatment plants (WWTPs) due to their low removal rate. Therefore, their presence in the environment is directly linked to the human impact. Various biological and abiotic processes in the environment can transform them to transformation products (TPs). In many cases, transformation is already initiated in the human body by a variety of drug-metabolizing enzymes. The metabolites formed through human metabolism present some modifications in their chemical structures that can differ in physicochemical properties to their parent compound. Once they are excreted from the human body, both the unmetabolised parent drug and their metabolites enter WWTPs by means of the sewer system. Since the WWTPs are not designed to remove completely pharmaceutical residues, the fraction not removed after the treatment will eventually end up in the receiving water bodies. Consequently, due to pharmaceutical transformations in the human body, biotransformations in WWTPs and phototransformations in surface water, they can potentially produce a high number of TPs in real world samples which makes their identification a challenge. In this thesis, two different approaches (TPs profiling and suspect screening) based on high resolution mass spectrometry (HRMS) for the detection and identification of TPs of pharmaceuticals were investigated. TPs profiling approach was applied for the identification of phototransformation products of an antiviral zanamivir (ZAN) in batch reactors filled with surface water. On the other hand, suspect screening approach was applied for evaluation of transformation, prioritization and identification of photoTPs of six iodinated contrast media in surface water. Finally, a combination of suspect and TPs profiling approach was applied for the detection of TPs of an anticonvulsant lamotrigine and its main human metabolite lamotrigine N2-glucuronide which were formed as the result of their degradation in both activated sludge and pH dependent hydrolysis. The TPs profiling approach for evaluation of these transformations is illustrated in the example of photodegradation of an antiviral ZAN with identification of its TPs in surface water (Chapter 3.). Here a set of lab- scale experiments was performed in order to determine the susceptibility of ZAN towards photodegradation under simulated and natural sunlight. The identification of the TPs was performed using hydrophilic interaction liquid chromatography coupled to high resolution mass spectrometry (HILIC-HRMS) where four photoTPs were tentatively identified and their proposed structures were rationalized by photolysis

mechanisms. Kinetic experiments showed that photodegradation kinetics of ZAN in surface waters would proceed with slow kinetics since upon exposure of aqueous solutions of surface water (20 (So(Bg L-1) to simulated sunlight, ZAN was degraded with t1/2 of 3.6 h. Under natural sunlight irradiating surface water, about 30 % of the initial concentration of the antiviral disappeared within 18 days. However, when ZAN and its TPs were retrospectively screened from surface water extracts, neither the parent nor the TPs were detected. The results of this TP profiling used for the identification of TPs of ZAN, although straightforward, suggests that it is not suitable when dealing with a considerably elevated number of TPs formed in batch experiments. However, time and effort needed to be optimised for the structure elucidation of 108 photoTPs of six iodinated contrast media (ICM) (Chapter 3.). Again, the photodegradation study was performed in surface water spiked with the ICMs using a sunlight lab-scale simulator. 108 TPs were generated and each photoTP was characterised by its unique exact mass of the molecular ion and retention time and added to a suspect list. Once t

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