APPLICATION OF SUSPECT SCREENING APPROACH FOR DETECTION DRUG GLUCURONIDES IN WASTEWATER TREATMENT

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Analysis of polar organic contaminants in wastewaters (WW) usually relies on a target approach which involves commonly the use of reference standards to quantify a set of analytes using low-resolution mass spectrometry (MS). In the case of polar contaminants, this task has been carried out mainly with liquid chromatography instruments coupled to mass spectrometry (LC-MS) generally triple quadrupole instruments, which detect only a limited number of analytes without the possibility of a retrospective analysis of data. In contrast to this classical target analysis, the suspect screening has very good prospects as it involves a more comprehensive overview of the contamination of urban wastewaters and of any other environmental sample of great complexity. The recent introduction of very sensitive high-resolution MS platforms and the development of specific software essential for efficient and automated processing of MS data, has been laid the groundwork to a successful non-targeted analysis. Not only can such data be examined for the presence of any known analyte (using elemental composition, isotope pattern, adducts and fragmentation information as well as chromatographic retention behavior as criteria for compound identification) but reported or predicted metabolites can be included in the databases and will be search in any kind of sample.

Pharmaceuticals prior entering in the wastewater treatment plants (WWTP) are already biotransformed in humans which lead to metabolites with different chemical structures and physico-chemical properties than their parent compounds. They are metabolized by an array of drug-metabolizing enzymes such as cytochrome P450 (CYP), UDP-glucuronosyltransferase (UGT), and glutathione S-transferases which are present in the human liver at high abundance. After excretion of pharmaceuticals in conjunction with their human metabolites and their discharge into the sewer, they enter in wastewater treatments plants (WWTP) and they can be also biotransformed by secondary treatments. Some authors have been proposed that some glucuronides of the pharmaceuticals can be cleavage in the WWTP treatment. However, little evidence has been published as regards metabolic pathways in complex microbial communities of the glucuronides of pharmaceuticals like those encountered in the aeration tank of the activated sludge treatment. In our previous work[1], we have detected by chance some non-predicted transformation products of lamotrigine glucuronide in wastewater effluent using FISH program.

Against this background, the present study aimed at investigating the biodegradation of some selected glucuronides (lamotrigine-N2-glucuronide, sulfamethoxazole-N1-glucuronide, propranolol-O-glucuronide, tamazepam-O-glucuronide, diclofenac-acyl-glucuronide and atorvastatin-O-glucuronide) under controlled laboratory settings in order to gain further insight into the biodegradability and metabolic pathways of the selected compounds. The samples from the biodegradation studies were screened for the presence of stable intermediates and these were characterized by Q-exactive-Orbitrap-MS of unusual microbial transformation products. Differences in occurrence patterns of several glucuronides of pharmaceuticals have been observed in influent and effluent samples. Further examination of mass spectral data of N-glucuronides has revealed the presence of closely related compounds in a wastewater-dependent manner. Lab-scale biodegradation studies with mixed liquor have demonstrated the conversion of the N-glucuronides of sulfamethoxazole and lamotrigine into various species; lamotrigine glucuronide formed three stable TPs: lamotrigine, oxo-lamotrigine and and TP429

formed from the oxidation of the benzylic acid of the glucuronic acid; identification of the transformation products of sulfamethoxazole is under way. In this work, the applicability of suspect analysis for the screening of target pharmaceuticals and their glucuronides as well as their identified TPs in wastewaters was evaluated. Following generic sample preparation on solid-phase extraction sorbents with different selectivities, extracts were analyzed by ultra-performance liquid chromatography (UPLC) coupled to electrospray high-resolution MS on a Q-Exactive instrument. Detection of novel transformation products in real sewage samples has highlighted the usefulness of HR-MS suspect screening in combination with biodegradation studies.

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