

SUSPECT SCREENING OF HUMAN METABOLITES OF PHARMACEUTICALS IN WASTEWATER USING LC-HRMS/MS

BLETSOU A.A.¹, GAGO-FERRERO P.¹, SCHYMANSKI E.L.², AALIZADEH R.¹, SINGER H.², HOLLENDER J.^{2,3} and THOMAIDIS N.S.¹

¹ National and Kapodistrian University of Athens, Department of Chemistry, Laboratory of Analytical Chemistry, Panepistimiopolis 157 71, Athens, Greece, ² Environmental Chemistry Department, Swiss Federal Institute of Aquatic Science and Technology (Eawag), Überlandstrasse 133, 8600 Dübendorf, Switzerland, ³ Institute of Biogeochemistry and Pollutant Dynamics, ETH Zurich, Universitätstrasse 16, 8092 Zurich, Switzerland
E-mail: pgago@chem.uoa.gr

A large number of organic contaminants and related transformation products (TPs) are present in wastewater. Target analysis methodologies can only detect a very small fraction of these substances, due to analytical limitations, the absence of standards for all suspected substances and lack of knowledge about the presence of many compounds. However, advances in high resolution mass spectrometry (HRMS) have opened up new horizons in the field of complex samples analysis [1]. The application of suspect screening, with suspected substances based on prior information but with no reference standards available, greatly increases the number of substances that can be tentatively identified.

This work describes the development of an integrated workflow based on liquid chromatography coupled to a quadrupole-time-of-flight mass spectrometer (LC-QToF-MS) to detect suspect compounds in wastewater. To demonstrate this, an in-house database with eight high consumption pharmaceuticals (amisulpride, atenolol, clarithromycin, metformin, niflumic acid, ranitidine, tramadol and venlafaxine), plus nicotine and their related human metabolites (297, in total) was developed, based on a metabolite prediction software (Metabolite Predict, Bruker) and pharmacokinetic literature. The tentative identification of these compounds was based on the evaluation of criteria such as blank signal presence, mass accuracy, isotopic pattern, presence of adduct ions, a peak score and MS/MS spectrum interpretation, including comparisons with MS databases (e.g. MassBank, NIST). The chromatographic retention time plausibility, using an in-house developed QSPR prediction model, was also considered.

Apart from the aforementioned criteria, new specific strategies for the identification of metabolites were applied in order to obtain extra confidence including the comparison of the concentration trends of the metabolite and the parent compound at different daily hours or the complimentary use of HILIC. Following these procedures 13 metabolites were tentatively identified with high peak intensities in wastewater samples from the wastewater treatment plant of Athens (Greece). Seven of these substances were finally confirmed through the use of the corresponding standards (amisulprid-N-Oxide, atenolol acid, N-desmethyl clarithromycin, cotinine, hydroxyl cotinine, ranitidin-S-oxid and guanyurea), showing the good performance of the developed approach.

Keywords: Emerging pollutants, pharmaceuticals, metabolites, suspect screening, high resolution mass spectrometry, QTOFMS.

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