Journal of Chromatography A 1649 (2021) 462225

Contents lists available at ScienceDirect

Journal of Chromatography A

journal homepage: www.elsevier.com/locate/chroma

Quality by design optimization of a liquid chromatographic-tandem mass spectrometric method for the simultaneous analysis of structurally heterogeneous pharmaceutical compounds and its application to the rapid screening in wastewater and surface water samples by large volume direct injection

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ARTICLE INFO

Article history:
Received 17 February 2021
Revised 27 April 2021
Accepted 28 April 2021
Available online 8 May 2021

Keywords:
LC-MS/MS
Analytical quality by design
Scheduled polarity switching
Matrix effect
Transformation products
Antibiotics

ABSTRACT

This study focused on the Analytical Quality by Design (AQbD) optimization of the chromatographic separation and mass spectrometric detection of a wide group of structurally heterogeneous model pharmaceutical compounds (PhCs) and transformation products (TPs), chosen to cover the challenging issues of the co-presence of compounds characterized by (i) a wide range of physicochemical properties, (ii) the same mass transitions, and (iii) different ionisation modes. Italian consumption of PhCs were also considered as election criteria of target analytes. Octadecyl and pentafluorophenyl stationary phases, acetonitrile/methanol ratios and acidity of the eluents, column temperature, initial organic phase percentage, and elution gradient were investigated by AQbD, aiming at optimizing critical resolutions, sensitivities, and analysis time. Statistically significant models were obtained in most cases with fitting and cross-validation coefficients in the ranges of 0.681-0.998 and 0.514-0.967, respectively. After optimization, the analysis of target analytes was performed in a single chromatographic run, adopting a mixed acquisition mode based on scheduled acquisition windows comprising both single polarity and continuous polarity switching. For most investigated analytes the method provided detection limits in the sub-ng/L to low ng/L range, meeting for macrolides the sensitivity requested by the "Watch List" 2018/840/EU. The optimized method was applied to the direct injection analysis of PhCs and TPs in four wastewater treatment plant (WWTP) effluents and surface water (SW) samples collected in the receiving water bodies. Absolute values of matrix effect were found to be far higher than 20% for most target analytes in most samples. Seventeen PhCs and two TPs were quantified in at least one sample, at the wide concentration range of about 1-3200 ng/L. The most occurring PhCs in both WWTP effluents and SWs were levofloxacin (202-1239 and 100-830 ng/L), furosemide (865-3234 and 230-880 ng/L), ketoprofen (295-1104 and 270-490 ng/L), and ibuprofen (886-3232 and 690-1440 ng/L).

1. Introduction

Modern environmental analytical chemistry constantly deals with the development of innovative, multiresidue and high-

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https://doi.org/10.1016/j.chroma.2021.462225
0021-9673/