Neutral loss screening of mercapturic acids – compensating matrix effects by post column infusion

ROBERT BLOCH1,2, MERLE PLASSMANN3, WERNER BRACK1, AND MARTIN KRAUSS1

1Helmholtz Centre for Environmental Research - UFZ, Department of Effect-Directed Analysis, Permoserstr. 15, 04318 Leipzig, Germany , [robert.bloch@ufz.de](mailto:robert.bloch@ufz.de)

2RWTH Aachen University, Institute for Environmental Research (Bio V), Worringerweg 1, 52074 Aachen, Germany

3Stockholm University, Department of Environmental Science and Analytical Chemistry, Svante Arrhenius Väg 8, 11418 Stockholm, Sweden

One of the major challenges for modern medicine is the prevention and treatment of so-called civilization diseases such as dementia or allergies. These diseases might be influenced by electrophilic stress in the human body, caused by the daily uptake of chemicals from air, water, and food, as well as the application of cosmetics and pharmaceuticals. In this study, we characterized the electrophilic burden by analysing mercapturic acids (MA) which are breakdown products of glutathione conjugates. We established an untargeted neutral loss screening method for the analysis of MA in human urine using direct injection liquid chromatography – tandem mass spectrometry (LC-MS/MS). Because urine is a very complex and diverse matrix, there is a high variation in ionization efficiency within and between different samples. This results in poor comparability of samples and distortion of signal intensities. Therefore, matrix effects were monitored by constant post column infusion of an isotope-labelled standard, making it possible to compensate intra- and inter-sample deviations in ion suppression. We analysed 20 urine samples of pregnant women to characterize the individual electrophilic stress levels and found a large variation both in the mercapturic acid composition and in the matrix effect profiles. Whereas most matrix components cause ion suppression, we observed few cases of signal enhancement, too. By analysing spiked samples we can show that peak intensity variance decreases significantly when matrix effects are compensated. In addition, the signal-to-noise ratio can be improved for most peaks. With neutral loss scanning, MA can be used for fingerprinting a person’s electrophilic burden, providing more information than the quantification of few biomarkers in a targeted analysis. The high diversity of the individual MA profiles is an indication for the multiplicity of possible risk factors. In conclusion, both MA screening and matrix compensation are promising tools for the evaluation of human exposure to chemicals and the identification of so far unknown, but potentially harmful compounds.