

# MULTIDIMENSIONAL ON-LINE SPE FOR UNDISTURBED LC-MS/MS ANALYSIS OF BASIC DRUGS IN BIOFLUIDS

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In bioanalytical LC-MS/MS matrix effects influencing the ionization process are a major concern with respect to the quality of the results obtained. In general such matrix effects are directly related to an insufficient sample clean-up of the biofluids.

In order to establish a generic and MS-adequate clean-up procedure for basic drugs present in biofluids (e.g. urine, plasma) we developed an analytical platform which consists of two small Solid Phase Extraction (SPE) columns and one conventional analytical HPLC column. The multidimensional (MD)-SPE method relies on the combination of a SPE column packed with a restricted access material (RAM) allowing size-exclusion and reversed phase chromatography (SEC-RPC) and a second SPE column packed with a mixed-mode phase (MMP) allowing ion exchange and hydrophobic interaction chromatography (IEX-HIC). For application and evaluation of this MD-SPE method 8 tricyclic antidepressants and two metabolites were chosen as model analytes.

In order to monitor matrix effects, i.e. ion suppression, postcolumn infusion experiments were performed and compared with a two-dimensional SPE column mode (SEC-RPC) [1]. In order to optimize the instrumental set-up and operation of such a 3-column switching platform we recently developed the High SPEed™ workstation in cooperation with CTC Analytics AG.

The MD-SPE method is highly efficient for removal of low and high molecular weight sample components which suppress ionization to varying extent. In addition electrospray ionization of the model analytes is not affected by inter- or intra-individual variations in the composition of the matrices investigated nor by the species the biofluids originate from.

Finally, we were able to demonstrate that this MD-SPE method has a generic potential with respect to on-line SPE of basic drugs having a pKa > 6.5 and a moderate to low polarity and being present in different biofluids.

[1] K. Georgi, K.-S. Boos, *Chromatographia* 63 (2006) 523-531