K7 Differential Mobility Spectrometry as a Tool to Improve Mass Spectral Library Searching Scores by Removal of Isobaric Interferences

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After attending this presentation, attendees will understand how differential mobility spectrometry (DMS) can be used advantageously to pre-separate isobaric compounds and therefore allow the removal of interfering peaks in generated MS/MS spectra that are used in library searching; improving the purity scores obtained for the library hit.

This presentation will impact the forensic science community by enabling a more confident confirmation of the identification of drug compounds in urine.

Rapid and reliable screening methods for drugs of abuse are required for the detection of xenobiotics in forensic intoxication cases. Multi-targeted screening by LC/MS/MS uses MRM triggered Information Dependent Acquisition (IDA) MS/MS spectra, which are used to confirm the identity of detected drugs based on mass spectral library searching.

Matching MS/MS spectra generated from real samples to library spectra can be impeded by the presence of interfering isobaric compounds in the sample matrix. These isobaric interferences having similar m/z to the analyte will fragment producing extra peaks in the sample spectrum not present in the library spectrum. This results in a reduced score and reduced confidence rating.

DMS separates ions on the basis of the difference in their migration rates under high versus low electric fields and requires the application of an intense asymmetric electric field known as the DMS separation field, typically in the megahertz frequency range. Ion filters based on planar DMS can be integrated with the inlet configuration of most mass spectrometers and are able to enhance the quality of mass analysis by reducing chemical noise and pre-separating ions of similar mass. Using this technology, we have shown the separation of isobaric interferences that, in the absence of the device, would have been transmitted into the mass spectrometer and fragmented at the same time as the analyte.

Data was obtained using a linear ion trap system coupled with an LC system. The ion source region of the mass spectrometer was modified for incorporation of various DMS analyzers. The standard ceramic orifice plate was replaced with a modified ceramic plate that included provisions for sealing a DMS cell. The mass spectrometer analysis consisted of an MRM detection using scheduled MRM algorithm and product ion dependent scans using the linear ion trap, automatically triggered to collect full scan MS/MS fragmentation spectra. The MS/MS data were collected using low, medium, and high energy fragment ions. A 1250 compound Forensic Drug Library was searched to provide identification and confirmation.

Comparisons of IDA triggered product ion spectra generated from urine samples both with and without the use of the DMS were made. An improvement in the MS/MS spectrum generated with the use of DMS was seen for amphetamine detected in urine, by removal of the interfering ions at m/z 77, 107, and 109. This improved the quality of the spectrum for searching against the forensic drug library, producing 100% purity score for an amphetamine match when compared to only 40% when performing the same experiment, on the same sample but without the use of the DMS device. Other examples where improvements in MS/MS spectra were gained by the use of the DMS device, compared to without using the device, included product ion spectra triggered for m/z ions that corresponded to lidocaine, indomethacin, and fentanyl. Library match purity scores for these compounds improved from 79 to 90%, 14 to 78% and 32 to 89% respectively, allowing for a higher confidence in the identification of these compounds. Comparisons of product ion spectra generated from urine samples both with and without the use of the DMS show that fragment ions are detected and falsely represented in the resulting product ion spectrum in those experiments performed without the use of the DMS. The DMS, therefore, removes these isobaric interferences, improving the mass spectral library searching scores.

Differential Mobility Spectrometry, Drug Screening, LC/MS/MS

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