Assessment of Three Time-of-Flight/Mass Spectrometry (TOF/MS) Drug Screening Technologies Using Different Fragmentation Modes

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After attending this presentation, attendees will be able to describe and distinguish between three different fragmentation techniques in Liquid Chromatography/Time-Of-Flight/Mass Spectrometry (LC/TOF/MS) instrumentation and assess their utility for different types of toxicological analyses.

This presentation will impact the forensic science community by describing novel approaches to improving the sensitivity and specificity of emerging TOF/MS instrumentation in the forensic toxicology laboratory and by assisting laboratory managers and technical staff in selecting the appropriate instrumentation for specific analyses.

There is increasing interest in the use of High Resolution Accurate Mass Spectrometry (HRAMS) for toxicological drug screening.LC/TOF is a very powerful technique due to its increased specificity and sensitivity over immunological screening, its ease of sample preparation, and rapid run time compared to traditional Gas Chromatography/Mass Spectrometry (GC/MS) screening, and its capabilities for retrospective data analysis. Analysis by LC/TOF can be performed in multiple modes, all of which use a calculated exact mass based on the chemical formula of the parent compound and an expected retention time to identify analytes. Fragmentation allows for additional data characteristics to be used for identification thus eliminating some of the false positives caused by artifacts, minor metabolites, degradation products, drug analogs, and isomers. These false positives may lead to unnecessary confirmatory testing and/or an excess of candidate compounds requiring thorough data evaluation for a simple presumptive screening identification.

Three ionization modes were evaluated using an Agilent 1290 HPLC/6530 QTOF mass spectrometer with Jet Stream® technology for the screening of spiked postmortem samples and samples collected from an Electronic Dance Music (EDM) festival population for novel psychoactive substances as well as therapeutic drugs and traditional drugs of abuse. The modes were conventional Quadrupole Time-of-Flight (QTOF) and two All-Ions ionization modes: Collision-Induced Dissociation in the Source (CIDS) and Collision-Induced Dissociation in the Collision Cell (CIDCC). The conventional QTOF mode uses targeted MS/MS analysis, while the CIDS and CIDCC All-Ions modes provide fragmentation data through the use of alternating fragmentor voltages in the source or collision energies in the collision cell, respectively. The elution profiles of each of the ions, parents, and fragments are correlated for use in compound identification.

The All-Ions modes proved more advantageous for screening than the QTOF mode, especially for analytes present at lower concentrations. The QTOF mode is a data-dependent acquisition mode in which the MS/MS data collected for a particular sample is dependent on the precursor ions detected

through MS data collection within the same injection. This leads to an increase in analysis time, a decrease in sensitivity, and an overall decrease in the amount of information obtained from a single injection; fewer data points are collected for each ion observed. The All-Ions CIDCC mode is similar to the QTOF mode in that the collision cell of the QTOF is utilized to generate mass spectra of precursor and fragment ions while the fragmentor voltage in the source is maintained at a low level preventing fragmentation prior to the collision cell; however, in this mode, the quadrupole is not used to filter for precursors observed; all ions within the mass range are passed to the analyzer for the entire run. The All-Ions CIDS mode cycles through the low and two higher source fragmentor voltages with the collision cell turned off thus allowing for collection of QTOF-like data using a conventional TOF instrument. Overall, both All-Ions modes performed better than the QTOF mode for broad-spectrum toxicological drug screening.