K54 New Strategies to Apply LC/MS/MS for the Quantitation and Confirmation of Hundreds of Substances Relevant in Forensic Toxicology

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The goal of this presentation is to present the comparison of different LC/MS/MS technologies used for screening and followed by library searching to detect drugs of abuse and pharmaceuticals.

This presentation will impact the forensic science community by demonstrating how LC/MS/MS will replace LC/UV screening methods.

Introduction: With about 5% of the population between the ages of 15 and 64 (~200 million people) using illicit drugs, and thousands of drug intoxications per year in the western world alone, fast screening methods for drugs and pharmaceuticals are necessary for the detection of xenobiotics in forensic intoxication cases. Screening methods usually include immunoassay tests, available only for a small number of substance classes, Gas Chromatography (GC) especially with Mass Spectrometric (MS) detection, or Liquid Chromatography (LC) with Ultraviolet (UV) detection. While GC requires typically extensive clean-up steps with derivatization, LC is ideally suited for polar compounds but UV detection lacks the necessary specificity and methods require long run times to minimize the potential for co-elution. Since 1999, screening for drugs with LC/MS and LC/MS/MS has made progress with mass spectral library searching to confirm detected drugs.

Experimental and Results: This presentation compares LC/MS(/MS) screening strategies using different mass spectrometric detection techniques such as Time of Flight (TOF), Single and Triple Quadrupole, Ion Trap and Hybrid Triple Quadrupole Linear Ion Trap. These MS technologies are compared regarding their ability to screen for a large number of compounds, sensitivity, selectivity, and the possibility of using mass spectral libraries to confirm the presence of detected analytes. Additionally the possibility of transferring once generated libraries to other instruments is discussed. A mass spectral library with more than 1200 substances was generated by injection of standard solutions using standardized Collision Energies (CE) of 20, 35, and 50. In addition a CE of 35V with a Collision Energy Spread (CES) of 15V was used. Data presented were acquired on different mass spectrometers including API 3200™, 3200 Q TRAP® and QSTAR® LC/MS/MS systems in different quadrupole, TOF, and ion trap scan modes. Electrospray Ionization (ESI) was used to ionize all investigated compounds including drugs of abuse, pharmaceuticals, and metabolites. A Shimadzu Prominence HPLC with reversed phase column was used with a standard eluent of water and acetonitrile with a buffer of formic acid and ammonium formate.

Comparative analysis of 300 compounds and extracts of urine and blood sample were used to investigate different MS technologies and their advantages and disadvantages when used for the screening in forensic toxicology.

Conclusion: It was found that the combination of highly selective and sensitive Multiple Reaction Monitoring and fast and sensitive Enhanced Product Ion Scan on a Hybrid Triple Quadrupole Linear Ion Trap is the most powerful LC/MS/MS technique to screen for a large number of unknown compounds and confirm their presence by library searching in forensic samples.

LC/MS/MS, Screening, Library Searching

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