Poster

[P26-10] P26-10: Assay of toxicants

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[P26-10-3] Quantitative screening using liquid chromatography-tandem mass spectrometry with MS/MS library based identification

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Background

Multi Target Screening (MTS) methods uses threshold triggered multiple reaction monitoring (MRM) and MS/MS product ion scans at different collision energies (CE) to confirm the compound identification based on mass spectral library searching. They are useful in clinical and forensic toxicology. We aimed at (i) developing a MTS method for most commonly observed compounds including: antidepressants, anxiolytics, drugs of abuse, analgesics and antipsychotics; (ii) testing its performances at infra-therapeutic, therapeutic and toxic concentrations (quantitative approach).

Methods

The MS/MS library was created using certified reference materials and included electrospray spectral data on over 1200 compounds in both positive and negative ion modes and using a broad range of CE from 10 to 60eV. Samples were prepared by a QuEChERS procedure with inclusion of 10 internal standards. Analysis was performed by reversed phase UHPLC separation (Nexera LC, Shimadzu Corporation) using a Restek Biphenyl 2.7um 2.1x100mm column, followed by MRM triggered product ion scan MS/MS (LCMS-8060, Shimadzu Corporation). A panel of 71 compounds was used to test both the library search and the quantitative performances. Whole blood samples were prepared in triplicate at a concentration range 1-1000 ug/L (calibration curves typically ranged 5-500 g/L).

Results

Spectral Library information was registered for CE 10, 35 and 55V and the library included spectra for each CE and a separate library for merged spectra. All compounds of the test panel were detected and positively identified using product ion scan MS/MS with library based searching. The approach also resulted in good quantitative data: regression coefficients (r^2) greater than 0.99 for all compounds. For example, flurazepam, temazepam and diazepam spiked at 20 and 100g/L, yielded accuracy from 95 to 109% and RSD% in repetability <8% (n=5). The whole procedure required 1 hour: about 45min for sample preparation and 12 min for the LC-MS/MS acquisition.

Conclusions

A spectral based library of more than 1200 compounds has been created on a triple quadrupole mass spectrometry platform. A MRM triggered product ion spectra method to identify and quantify a panel of compounds commonly found in clinical and forensic toxicology was successfully applied to a representative panel of compounds.