Poster

[P27-7] P27-7: Assay

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[P27-7-1] Using MRM spectrum mode in quantitative clinical toxicological screening

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Background

To reduce false negative and false positive reporting in clinical toxicology two approaches were considered. The first approach acquired data in a multi-targeting screening mode in which threshold triggered MS/MS product ion scans were acquired at three collision energies to enable spectral based library searching. The alternative approach explored acquiring a higher number of MRMs specific for each target compound (up to 6 transitions) to generate a product ion spectrum. In both cases, the product ion spectrum can be used to increase the confidence in target compound identification using a library match score. This paper highlights the advantages of both techniques in reducing false positive reporting in clinical toxicology

Methods

Methods were developed to screen whole blood, plasma and urine for antipsychotics, benzodiazepines, cannabinoids, amphetamines and opioids (5-500ug/L). Samples were prepared by QuEChERS with inclusion of internal standard compounds to normalise sample matrix effects. Analysis was performed by reversed phase UHPLC separation (Nexera LC, LCMS-8060, Shimadzu Corporation).

Results

This study presents two different approaches for library screening. The first approach uses product ion scan data with library searching against MS/MS spectra. MS/MS product ion scans at three collision energies were threshold triggered based on multiple reaction monitoring (MRM) intensity. This approach was compared to an alternative approach which explored using MRM Spectrum mode. In this workflow, 5-10 optimized fragment ion transitions were monitored for each target compound (as opposed to a conventional approach using 2-3 fragment ions). By acquiring a high number of fragment ion transitions, each target compound had a corresponding optimized fragmentation spectra which could be used in routine library searching and compound verification using reference library match scores.

Conclusions

MRM Spectrum mode was applied to quantify and identify panels of toxicology compounds without compromising limits of detection, linearity or repeatability. We conclude that simultaneous measurement of numerous MRM transitions by using fast dwell and pause times enabling Library ID by MRM Spectrum mode offers an alternative approach to Library screening.