A Fast Polarity Switching LC-MS/MS Analysis of Benzodiazepines and Barbiturates

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Novel Aspects: Reliable and reproducible fast polarity switching LC-MS/MS analysis on pain management drugs

Key words: Fast polarity switching, positive and negative ionization, high-throughput LC-MS/MS analysis, IONICS 3Q 120 mass spectrometer

Introduction: ESI-LC-MS/MS has been widely used to monitor pain management drugs on a routine basis in many labs worldwide. Because some of these drugs ionize better in negative mode than that in positive electrospray ionization mode, the panel of interest usually is split into positive mode and negative mode panels. However, recent advancement in fast and robust polarity switching technology allows for high throughput, reliable implementation of methods in which all drugs are combined into one panel regardless of preferred ionization modes. The goal of this study is to demonstrate a fast, robust polarity switching ESI-LC-MS/MS method on an IONICS 3Q 120 triple quadrupole mass spectrometer.

Methods: The mixed barbiturates and benzodiazepine drug standards and analytical LC column were provided by Restek. 5 µL of diluted standard at various levels were loaded on a Raptor Biphenyl column (100X2.1mm, 2.7um) and eluted by a gradient method at a flow rate of 0.6 mL/min and a total LC cycle time of 6.5 minutes. The signal is detected by an IONICS 3Q 120 triple quadrupole coupled to a Shimadzu Prominence UPLC system. All solvents are HPLC grade. The 3Q system indicated is able to perform fast polarity switching (<15ms) with high ionization and ion sampling efficiencies. The separation and sensitivity reproducibility is monitored as a function of number of injection.

Preliminary Results:

All 14 compounds eluted within the 6.5 minutes run time showed good chromatogram separation and excellent peak shape. No sensitivity loss is found for 14 compound panel as compared to the run if split into two panels. The CVs were <5% for all analytes within intra-day run and <9%

within 3 series of inter-day run. The results indicate that the ESI-LC-MS/MS method with ultra-fast polarity switching using IONICS 3Q 120 mass spectrometer can greatly improve sample throughput in clinical pain management monitoring application.

The dwell time and pause time effect for co-eluting positive and negative mode ions will also be explored and discussed.

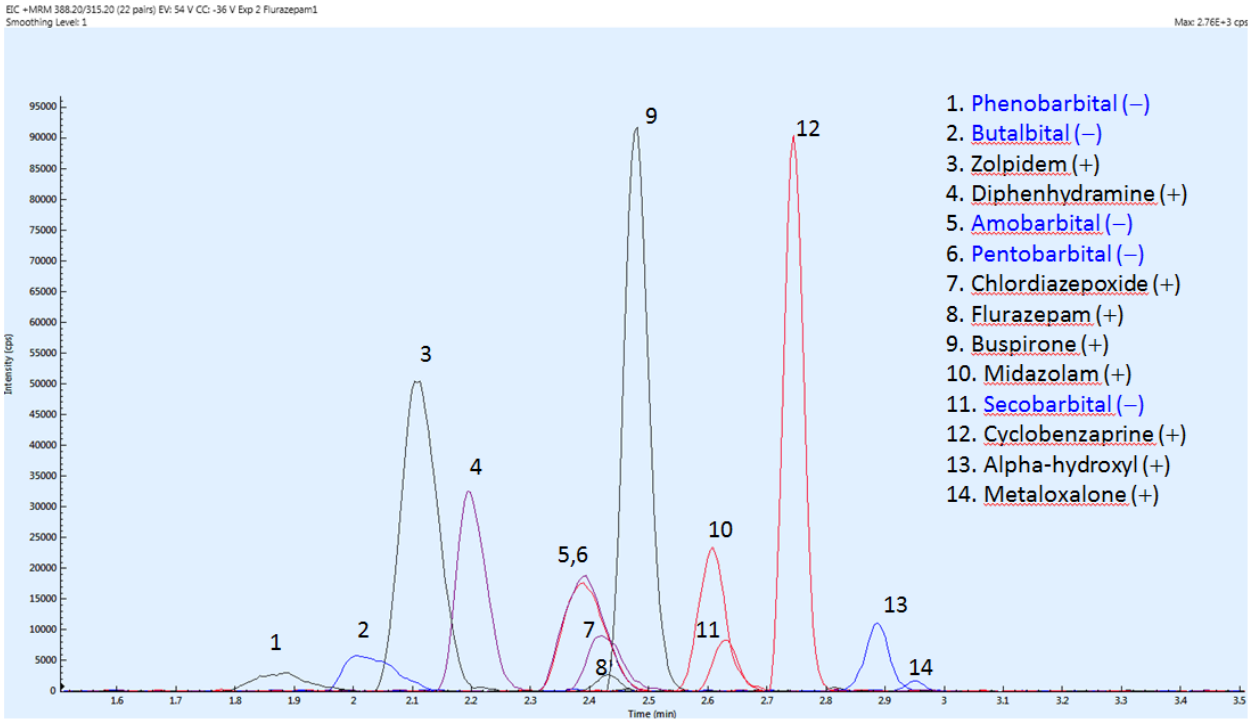

Fig.1. Overlaid chromatograms of 14 drugs with 5 and 9 in negative and positive modes, respectively.