

Fast polarity switching and MRM triggered automatic MS/MS applied to benzodiazepines and their metabolites in clinical and forensic analysis

MS/MS library matching

Using a polarity switching speed of 15msec and a scan speed of 15,000u/sec, product ion spectra were generated in both positive and negative ionization which could be matched against a user library of 70 compounds an

automated aid to screening and compound identification. Fast polarity switching helps to provide information rich product ion spectra resulting in better detection and identification for each benzodiazepine.

Type	Event#	+/-	Compound Name	n/z	Time (2.898 min - 5.711 min)
MRM	19	+	66 N-desmethylzopiclone	375	
- Product Ion Scan	20	+	66 N-desmethylzopiclone	100	
MRM	21	+	57 7-acetamidonimetazepam		
- Product Ion Scan	22	+	57 7-acetamidonimetazepam		
MRM	143	-	57 7-acetamidonimetazepam		
- Product Ion Scan	144	-	57 7-acetamidonimetazepam		
MRM	23	+	63 4-hydroxytriazolam	350	
- Product Ion Scan	24	+	63 4-hydroxytriazolam	100	
MRM	25	+	44 clonazepam Y-1024	321	
- Product Ion Scan	26	+	44 clonazepam Y-1024	100	

Figure 3. Method set-up for accelerated benzodiazepine analysis using overlapping MRM/product ion scan acquisitions in both positive and negative mode (17 of 70 compounds were set both positive and negative mode).

Ch	Precursor m/z	Product m/z	Dwell Time (msec)	Q1 Pre Bias(V)	CE	Q3 Pre Bias(V)
Ch1	375.20	245.10	25.0	-14.0	-21.0	-20.0
Ch2						
Ch3						
Ch4						

Event Time: 0.028 sec Q1 Resolution: Unit Advanced Settings...

Q3 Resolution: Unit

Use as Survey Event Survey Event Settings...

Dependent Event: Product Ion Scan Add

Start m/z: 50.00 End m/z: 400.00

Precursor Ion m/z: 100.00 Collision Energy: -15.0 v

Scan Speed: 15000 u/sec Event Time: 0.030 sec Q1 Resolution: Unit Advanced Settings...

Q3 Resolution: Unit

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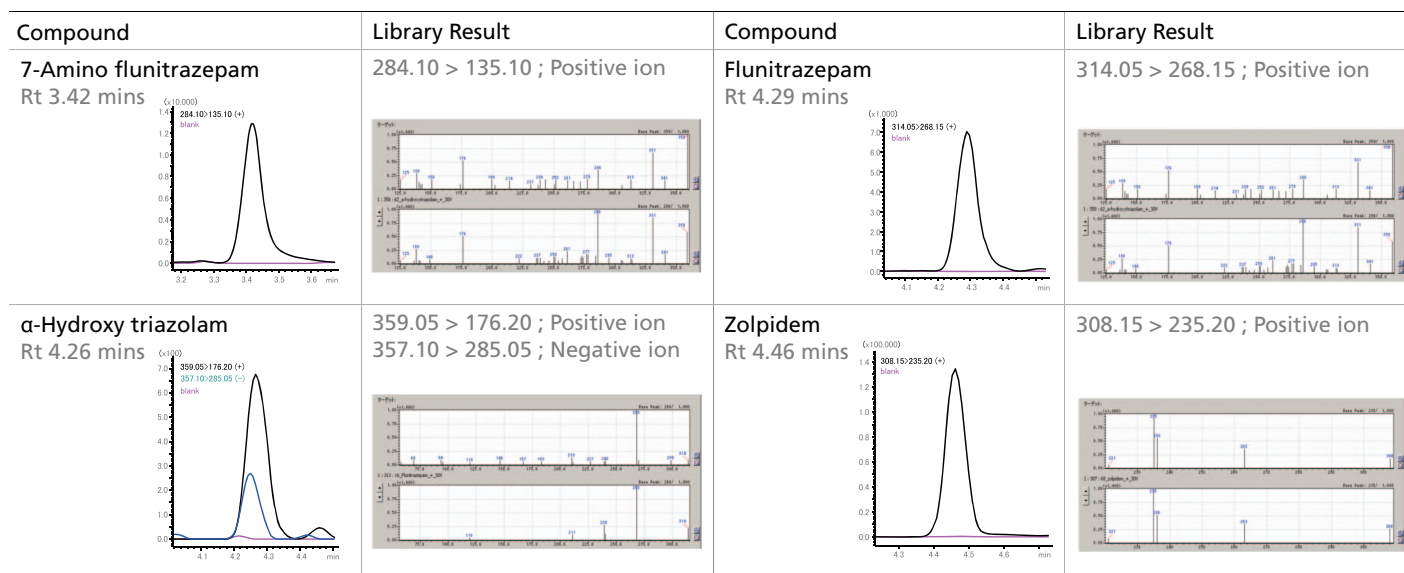


Figure 4. MRM chromatograms of 4 compounds (each 100 ng/mL) spiked into urine and analyzed by Nexera using Shim-pack XR-ODS III coupled to LCMS-8030 after sample preparation. As the LC/MS/MS system has a high speed of data acquisition, the assay generates both MRM and Product Ion Scan (MS/MS) spectra resulting in quantitative data and library searching/product matching to help product confirmation. Fast polarity switching helps to provide information rich product ion spectra resulting in better detection and identification for each benzodiazepine.

Conclusion

- With Nexera using Shim-pack XR-ODS III coupled to LCMS-8030 provides significant advantage over other method for benzodiazepine analysis: fast analysis time (all compounds are eluted in a retention window less than 3 minutes) and detected in both positive and negative ion using a single analytical run.
- To help forensic chemists this high speed MRM triggered automatic MS/MS and a new method package and database enabled simultaneous screening and quantification of benzodiazepines and their metabolites.
- This method will be applied to the forensic analysis of urine samples taken to confirm administration in cases of benzodiazepine abuse.

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