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Expansion of the MRM Toxicology Screening Methodology for Use With Waters Xevo TQ-S micro

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For forensic toxicology use only.

Abstract

This application brief describes an update of the nominal mass multiple reaction monitoring (MRM) screening method for toxicologically-relevant analytes.

Benefits

An enhancement of the positive ion MRM targeted screening method for use with the Waters Xevo™ TQ-S micro Mass Spectrometer (Figure 1), has led to improved coverage for novel psychoactive substances (NPS) and other new drug classes, including doping agents, and expands applicability of the method.

Figure 1. ACQUITY UPLC I-Class and Xevo TQ-S micro configuration.

Introduction

Tandem mass spectrometry has gained popularity over the years owing to its analytical sensitivity and selectivity, especially when used in MRM mode. MRM can be used for quantitative analysis as well as targeted qualitative screening. Consequently, over the years, Waters scientists have acquired significant experience in MRM analysis

and have collectively developed large, targeted databases to address the needs of differing market areas.

Broad screening techniques that can detect a wide variety of toxicants in highly complex biological matrices are very much in demand in forensic toxicology laboratories, however, analysts often do not have the significant resources required to develop methods themselves, therefore reliable, ready-to-implement solutions are valuable. At Waters, we have provided and supported, ready-to-implement MRM based toxicology screening solutions for almost two decades. These have been applied on a number of our tandem mass spectrometers including the Xevo TQD and latterly, the TQ-S micro.[1–3] The solutions include optimized quantifier and qualifier transitions and proven, dedicated chromatographic methods that maximize sensitivity for positive and negatively-ionizing analytes. Here we describe a further development of the popular Xevo TQ-S micro method.

Experimental

Materials

Certified reference materials (CRM) were obtained from Merck (Dorset, UK). Authentic drug-free urine was collected from volunteers and pooled.

Test Substances

Individual solutions of CRM were prepared at 2000 ng/mL, by dilution with 5 mM ammonium formate pH 3 (mobile phase A), to yield solutions for tuning and verifying analyte retention times.

Data Acquisition

Each compound was tuned to determine the optimum cone voltage (CV) and collision energies (CE) for quantifier and qualifier MRM transitions. To verify these new transitions and to establish the retention time (RT) for each new compound, data were acquired using the chromatographic method that is supplied with the Forensic Toxicology Screening solution.[4] The Xevo TQ-S micro Mass Spectrometer was used in electrospray positive ionization (ESI+) mode.

Results and Discussion

Approximately 200 toxicologically-relevant analytes were individually optimized in ESI+. Once tested, quantifier and qualifier transitions, together with the associated RT were added into the MRM method. For ease of use, the data for each analyte was added in an individual function.

Drug mixtures were subsequently analyzed to further verify the method. A test sample containing 10 benzimidazoles were spiked into a pooled blank urine sample at 500 ng/mL and was subsequently diluted 10-fold with mobile phase A and vortex-mixed prior to analysis. Figure 2 details the 10 benzimidazoles which were detected using the Xevo TQ-S micro Mass Spectrometer.

This latest expansion of the MRM screening method has effectively doubled the analyte coverage for substances which ionize in positive ionization mode. The development has improved the overall coverage for NPS and other new drugs, such as designer benzodiazepines, psychedelic tryptamines, benzimidazoles, and fentanyl analogs, while the inclusion of beta blockers, diuretics, steroids, and receptor modulator drugs, will expand the applicability to sports doping analysis.

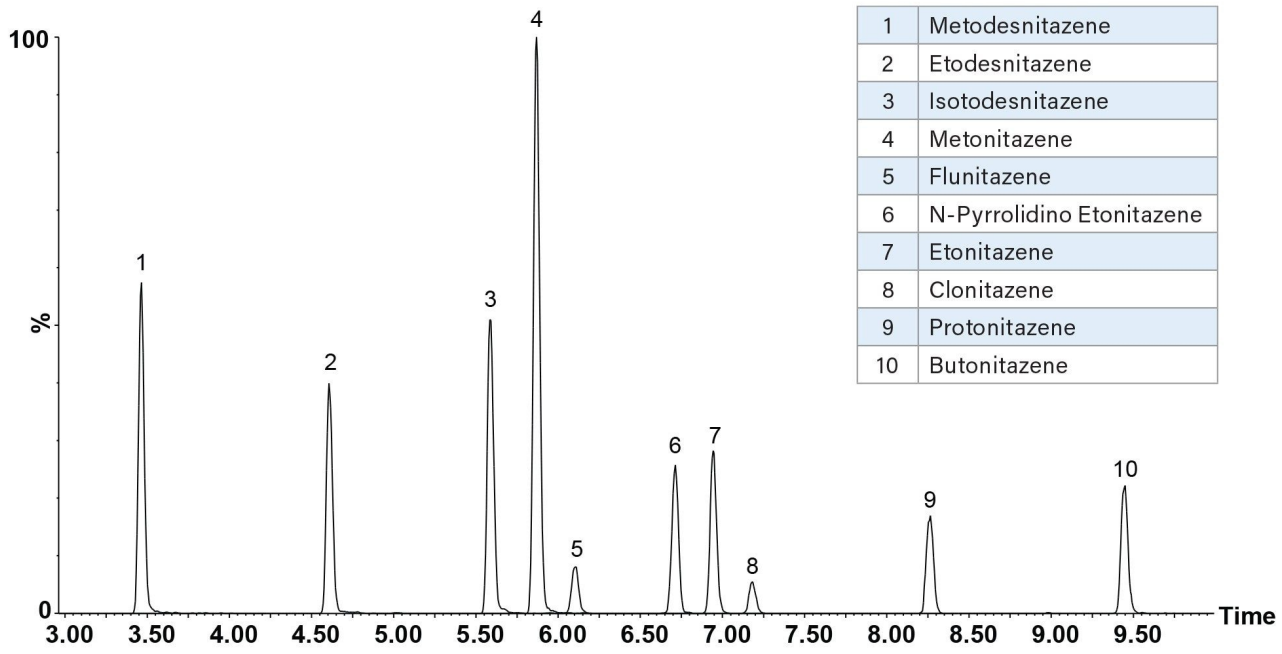

Figure 2. Chromatogram showing benzimidazoles spiked into pooled blank urine detected by the Xevo TQ-S micro using the supplied targeted MRM method. The quantifier ion transition is displayed.

Conclusion

The MRM nominal mass toxicology screening methodology for use with the ACQUITY UPLC I-Class/Xevo TQ-S micro Mass Spectrometer has been updated. These latest developments, together with the existing dedicated method for negatively-ionizing analytes, now provides ready-to-implement methods for >400 toxicologically-relevant analytes.

The new additions improve the ability to screen for numerous “designer” drugs and NPS. The inclusion of performance enhancing drugs have also been incorporated within this update, which are of specific interest to sports doping laboratories. This revised ESI+ MRM screening method is intended for immediate use with the ACQUITY UPLC I-Class/Xevo TQ-S micro Mass Spectrometer and can be simply substituted in favor of the previous MRM method, as all other parameters (MS method, UPLC conditions) remain unchanged.

References

1. Lee R and Wood M. Targeted MRM Screening Using the ACQUITY I- Class/Xevo TQ-S micro. Waters Application Note. 720005606. 2016.
2. Roberts M and Wood M. Forensic Toxicology Screening Using the ACQUITY UPLC I-Class System with the Xevo TQD. Waters Application Note. 720004602. 2013.
3. Lee R and Wood M. Targeted MRM Screening for Forensic Toxicology in Negative Electrospray Ionization Mode Using the Xevo TQD or Xevo TQ-S micro. Waters Application Note. 720006512. 2019.
4. Forensic Toxicology Screening solution media available at https://marketplace.waters.com/login?1698708110 <https://marketplace.waters.com/login?1698708110> .

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