Video Article

A New High Sensitivity Tandem Quadrupole Mass Spectrometer for Quantitative LC/MS/MS Analysis of Low Exposure Pharmaceuticals - ADVERTISEMENT

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Abstract

The quantification of trace levels of any analyte in a complex matrix requires a highly selective and specific detector. The Waters Xevo™ TQ-S is a new high performance tandem quadrupole mass spectrometer, equipped with new StepWave™ Technology, allowing unprecedented levels of sensitivity and spectral quality.

The detection of trace levels (pg/mL) of analytes such as pharmaceuticals, metabolites, pollutants or toxins in complex matrices such as plasma, blood, or foodstuffs plays a critical role in ensuring drug and food safety. When operated in multiple reaction monitoring, or MRM, mode, LC/MS/MS has proven to be the technique of choice with exceptional selectivity, specificity and sensitivity.

As the mass spectrometry system's sensitivity is a balance between the signal from the ion(s) of interest and the signal from the unwanted background noise (the signal-to-noise ratio), the overall sensitivity depends on the instrument's efficiency of the ion sampling in the ion source and the transfer optics. Ion sampling is a delicate balance between having a large enough orifice to maximize the sampling of the ions in the electrospray source, but not too large to compromise the overall vacuum in the system. However, the source sampling process draws not only charged ions, but neutral species into the mass spectrometer vacuum region. These must first be separated from the charged ions. This process is performed in the original ion guide where the ions first enter into the MS, and is normally achieved by a hexapole-type system.

The new Waters Xevo™ TQ-S Mass Spectrometer is equipped with a novel StepWave™ ion guide. This ion guide provides an offset path via which desired ions can travel via an electrostatic charge. The unwanted, uncharged background neutral compounds are not able to make it through the offset ion path, and are exhausted to waste. This new process maximizes the ion sampling efficiency, leading to lower levels of sensitivity.

Here, it will be demonstrated how the Xevo TQ-StepWave Technology can increase the sensitivity for the analysis of low-exposure pharmaceuticals and their metabolites in plasma and blood samples.

Video Link

The video component of this article can be found at http://www.jove.com/video/2266/

Protocol

Xevo TQ-S Sensitivity for the Bioanalysis of Low Exposure Pharmaceuticals in Plasma

1. A series of six pharmaceutical compounds (Fig. 1), that when dosed to humans have a low systemic circulating concentration, were dissolved and diluted into plasma in the 0.1-100 pg/mL range.
2. The target pharmaceuticals were extracted from the plasma using solid phase extraction with Oasis® SPE. The extracted samples were then re-suspended in methanol/water solutions.
3. The extracted samples were chromatographically separated using an ACQUITY UPLC® System with a ACQUITY UPLC Bridged Ethyl Hybrid BEH C18, 2.1 x 50 mm, 1.7 µm Column and a reversed phase gradient over 2 minutes.
4. The MS analysis was performed on a Xevo™ TQ-S Mass Spectrometer operated in positive ion electrospray MRM mode, with simultaneous acquisition of full scan data. The sensitivity of this new UPLC/MS/MS system was compared to that obtained from a similar mass spectrometer with a conventional hexapole ion guide, as well as with other tandem quadrupole MS systems.

Representative Results for the Bioanalysis of Low Exposure Pharmaceuticals in Plasma

The sensitivity of the UPLC/MS/MS system with the StepWave ion guide was compared to the conventional ion guide using model pharmaceutical compounds and showed that the system sensitivity was 10 times that of the conventional system. The overall levels of sensitivity

obtained for six model pharmaceutical compounds are listed (Figure 1 and Table 1). The response level for a 5 pg/mL standard of fluticasone propionate was determined to be 574 with the conventional system and 12053 with the new StepWave-enabled system (Figure 2).

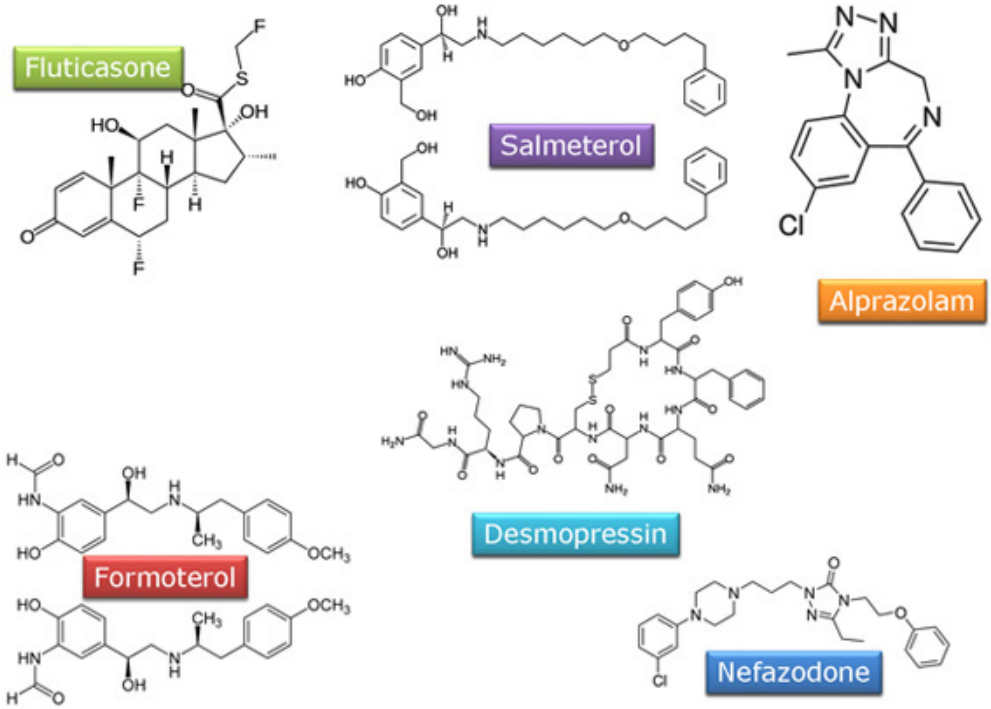

Figure 1: Six model pharmaceutical compounds used in this experiment.

Compound	Compound Class	Increase In Response
Fluticasone Propionate	Steroid	12
Salmeterol Succinate	B2-Agonist	15
Alprazolam	Benzodiazepine	13
Formoterol	B2-Agonist	20
Desmopressin	Peptide	25
Nefazodone	Antidepressant	16

Table 1: The increased response levels obtained for six model pharmaceutical compounds when the StepWave ion guide was compared to the conventional ion guide.

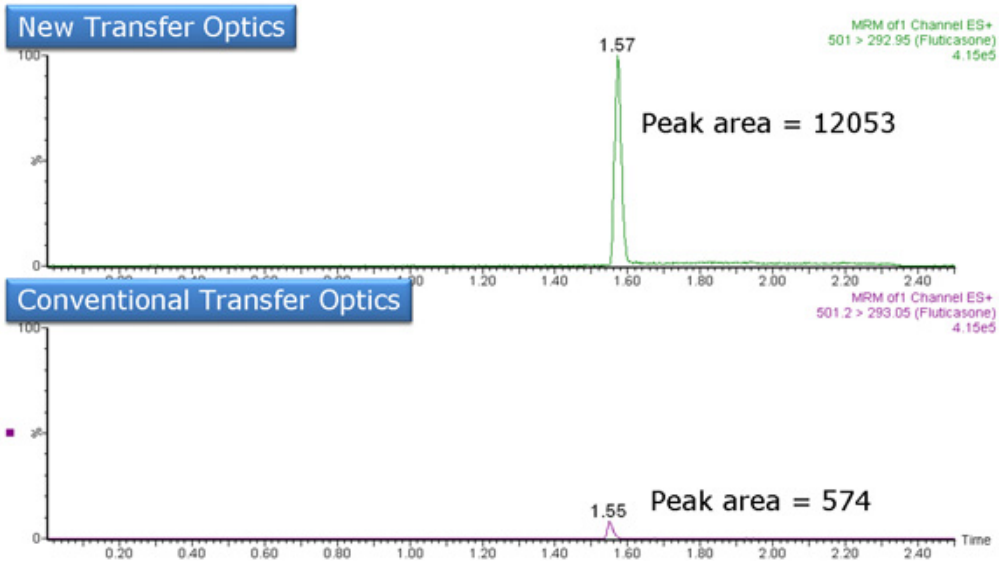

Figure 2: The response level for a 5 pg/mL standard of fluticasone propionate was determined to be 574 with the conventional system and 12053 with the new StepWave-enabled system.

Discussion

The new Xevo TQ-S MS with StepWave technology significantly increases the sensitivity of the UPLC/MS/MS system. The ability to achieve very low levels of sensitivity allows compounds to be detected in complex matrices such as plasma and serum at very low levels. The low levels of detection afforded by the Xevo TQ-S MS with StepWave technology allows the pharmacokinetic elimination phase of candidate drugs to be more accurately determined, improving both data quality and safety evaluation.

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