

응용 자료

High Sensitivity Analysis of Prostaglandin D2 in Plasma using UPLC and Xevo TQ-S

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Abstract

In this application note we describe the use of a new high-sensitivity tandem quadrupole mass spectrometer for the analysis of prostaglandin D2 in plasma.

Benefits

This new tandem quadrupole MS system provides significant increase in sensitivity for the analysis of prostaglandins in negative ion mode.

Introduction

Prostaglandins are lipid compounds, containing 20 carbon atoms, including a five-carbon ring. They are derived enzymatic action from fatty acids and have many important functions in the animal body including causing dilation in vascular smooth muscle cells, aggregation of platelets, regulation of inflammatory mediation, control of hormone regulation, control of cell growth, and acts on the thermoregulatory center of the hypothalamus to produce fever.

These prostaglandins have several clinical uses such as to induce childbirth, prevent closure of patent ductus arteriosus in newborns with cyanotic heart defects, and treat peptic ulcers. During treatment, the systemic concentrations of these prostaglandins is very low, thus the accurate quantification of prostaglandins in biological fluids requires a very high-sensitivity assay. In this application note we describe the use of a new high-sensitivity tandem quadrupole mass spectrometer for the analysis of prostaglandin D2 in plasma.

Experimental

Chromatography

LC system:	ACQUITY UPLC (binary solvent manager, sample manager, HT column oven)
LC column:	ACQUITY UPLC BEH C ₁₈ , 1.7 μm, 2.1 x 50 mm
Gradient:	0.1% NH ₄ OH (Aq), Methanol 5-95% over 1.5 min
Flow rate:	600 μL/min
Injection vol.:	10 μL

Mass Spectrometry

MS system:	Xevo TQ-S and Xevo TQ Negative ion
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	electrospray mode
	MRM data acquisition 351 =>189 prostaglandin D2
Voltages:	Capillary, cone, and collision voltage where optimized for each mass spectrometer as well as cone gas flow
Source temp.:	140 °C
Desolvation temp.:	625 °C
Nebuliser gas flow:	1200 L/Hr

Data Management

MassLynx 4.1

Quantification using TargetLynx Application Manager

Results and Discussion

The Xevo TQ-S is a new ultra-high-sensitivity tandem quadrupole mass spectrometer. It is equipped with new StepWave technology, which is a revolutionary off-axis ion source. The design of this source significantly increases the efficiency of ion transfer from the source to the quadrupole analyzer while the off-axis ion path eliminates neutral contaminants, Figure 1. These two factors combine to dramatically increase the sensitivity of the LC-MS/MS system. The use of stacked ring electrode, T-Wave,* ion optics allows the use of very fast multiple reaction monitoring (MRM) acquisition rates, less than 10 ms dwell time, with no loss in sensitivity. This makes the Xevo TQ-S the ideal tandem quadrupole MS to be used with narrow peaks developed by ACQUITY UPLC.

* The traveling wave device described here is similar to that described by Kirchner in U.S. Patent 5206506; 1993.

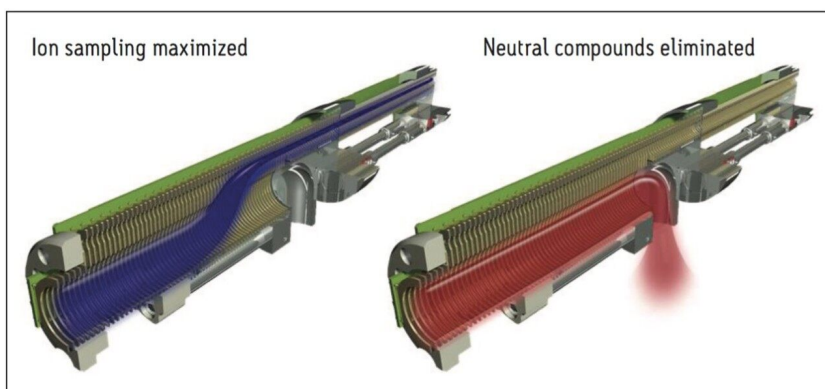


Figure 1. Schematic of the StepWave transfer optics, showing the path of the charged analyte ions of interest (left) and the neutral compounds being exhausted to waste (right).

Prostaglandin D2 is found in the brain and mast cells in mammalian systems. It binds to the receptor PTGDR, as well as CRTH2, and is critical to development of allergic diseases such as asthma. To evaluate the performance benefits of the new tandem quadrupole mass spectrometer, prostaglandin D2 was prepared and an aliquot injected onto both the Xevo TQ and the new Xevo TQ-S utilizing an ACQUITY UPLC System. The compound was eluted using a linear gradient from 5 to 95% aqueous ammonium hydroxide/methanol over 1.5 minutes at a flow rate of 600 $\mu\text{L}/\text{min}$. The peak of interest eluted with a retention time of 1.14 minutes.

The data displayed in Figure 2 shows the sensitivity benefits of the new StepWave ion source versus a conventional ion optics design. Here we can see that the new design gives a 400-fold increase in peak area and 34-fold increase in signal-to-noise (RMS).

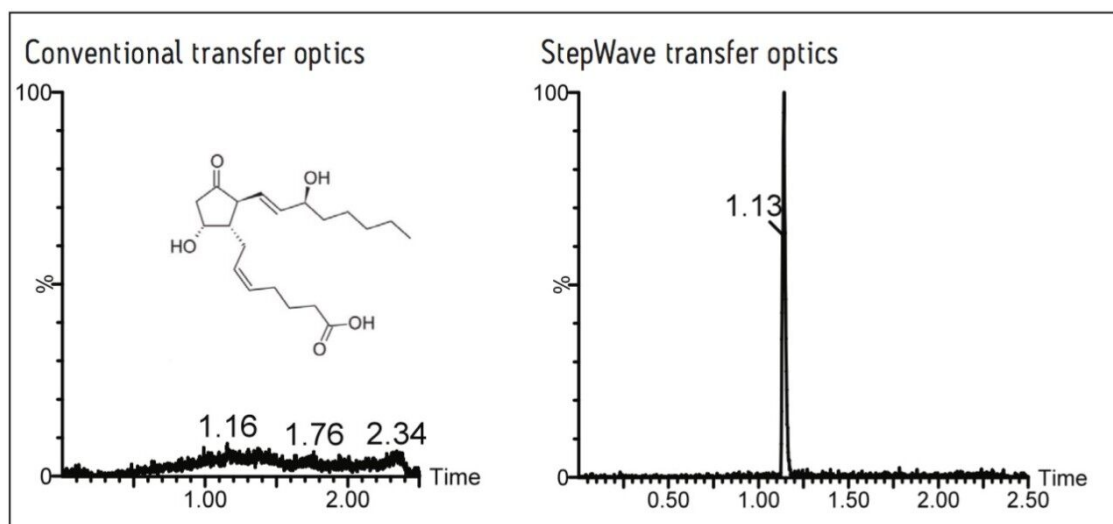


Figure 2. Comparison of the peak response for prostaglandin D2 with convention transfer optics (left) and StepWave transfer optics (right) when analyzed by UPLC-MS/MS in MRM mode.

The data displayed in Figure 3 show a comparison of the signal response of the two systems with the baseline expanded. Here we can see that with the conventional quadrupole based transfer optics, the prostaglandin peak is not detectable, whereas with the new StepWave design the peaks are clearly visible above the base line.

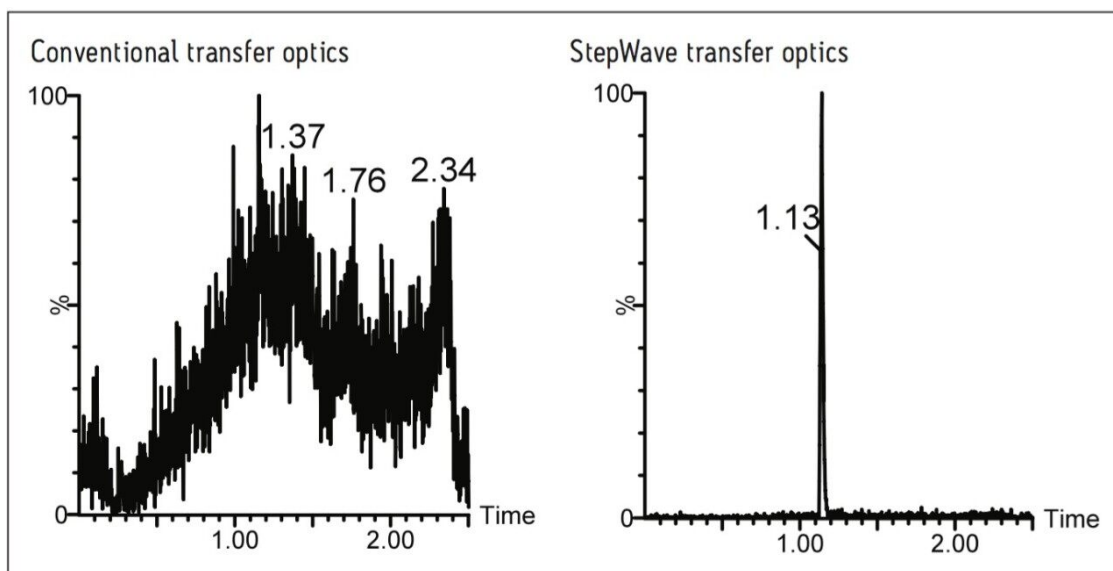


Figure 3. UPLC-MS/MS analysis of prostaglandin D2 with the baseline expanded to show the limit of detection. Conventional transfer optics on left, StepWave optics on right.

Conclusion

The new Xevo TQ-S combined with ACQUITY UPLC offers significant increases in both peak area and signal-to-noise performance for the analysis of prostaglandins in negative ion mode, by 30-fold. The novel off-axis geometry design prevents unwanted, neutral compounds from entering the analyzer stage of the instrument. Meanwhile, the use of T-Wave ion optics and collision cell design allowed more than 12 points to be acquired over a very narrow UPLC peak with no loss in sensitivity. For bioanalysis, these factors translate into:

- Lower levels of detection that can be achieved easier
- Methods that are developed faster
- Peak detection is simplified
- Assays are more robust

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[MassLynx MS Software <https://www.waters.com/513662>](https://www.waters.com/513662)

[TargetLynx <https://www.waters.com/513791>](https://www.waters.com/513791)

[StepWave <https://www.waters.com/134673601>](https://www.waters.com/134673601)

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