

Application Note

LCT Premier: Extended Dynamic Range

Waters Corporation



This is an Application Brief and does not contain a detailed Experimental section.

Abstract

The Waters LCT Premier Mass Spectrometer is the highest performance bench-top orthogonal acceleration time-of-flight (oa-ToF) LC-MS system available today. Prior to LCT Premier, oa-ToF mass spectrometry had limited dynamic range due to instrument detector saturation at high ion intensities. This resulted in limited quantitative capability, and thus was not a suitable instrument for certain applications. In addition, exact mass measurement was compromised at high ion intensities.

Benefits

The LCT Premier: wide dynamic range oa-ToF mass spectrometry for both exact mass measurement and quantitation.

Introduction

The Waters LCT Premier Mass Spectrometer is the highest performance bench-top orthogonal acceleration time-of-flight (oa-ToF) LC-MS system available today. Prior to LCT Premier, oa-ToF mass spectrometry had limited dynamic range due to instrument detector saturation at high ion intensities. This resulted in limited quantitative capability, and thus was not a suitable instrument for certain applications. In addition, exact mass measurement was compromised at high ion intensities.

Technology

With the LCT Premier Mass Spectrometer's innovative design, the detection system of the instrument has been improved and now incorporates new technology: Dynamic Range Enhancement (DRE). With DRE, the detection system of the LCT Premier has been extended by an order of magnitude, now providing four orders of dynamic range for both quantitation and exact mass measurement. This provides the user with an oa-ToF LC-MS system that can acquire sensitive, full spectral data for applications requiring either qualitative or quantitative answers over a wide range of ion intensities.

With the additional benefit of exact mass measurement, the LCT Premier Mass Spectrometer is the ideal choice for applications such as Open Access exact mass measurement, pharmaceutical compound screening, impurity and metabolite identification, biomarker analysis and protein identification. The LCT Premier also has the potential to be used for environmental/toxicology applications requiring quantitative information on very

complex mixture/multiple component samples without any loss in sensitivity.

Results and Discussion

Figure 1 shows the quantitative LC-MS analysis of sulfadimethoxine, a small molecule with a molecular weight of 310 Da, analysed by positive ion electrospray LC-MS with and without DRE. The range of analysis covers 0.5 to 5000 ng/mL and a linear fit has been made to all points. Without DRE, you can see that the points measured produce a curve at the higher sample concentrations due to detector saturation. With DRE on the LCT Premier, the same samples analyzed over the same four orders of magnitude produce a linear graph through the points - ideal for routine quantitation.

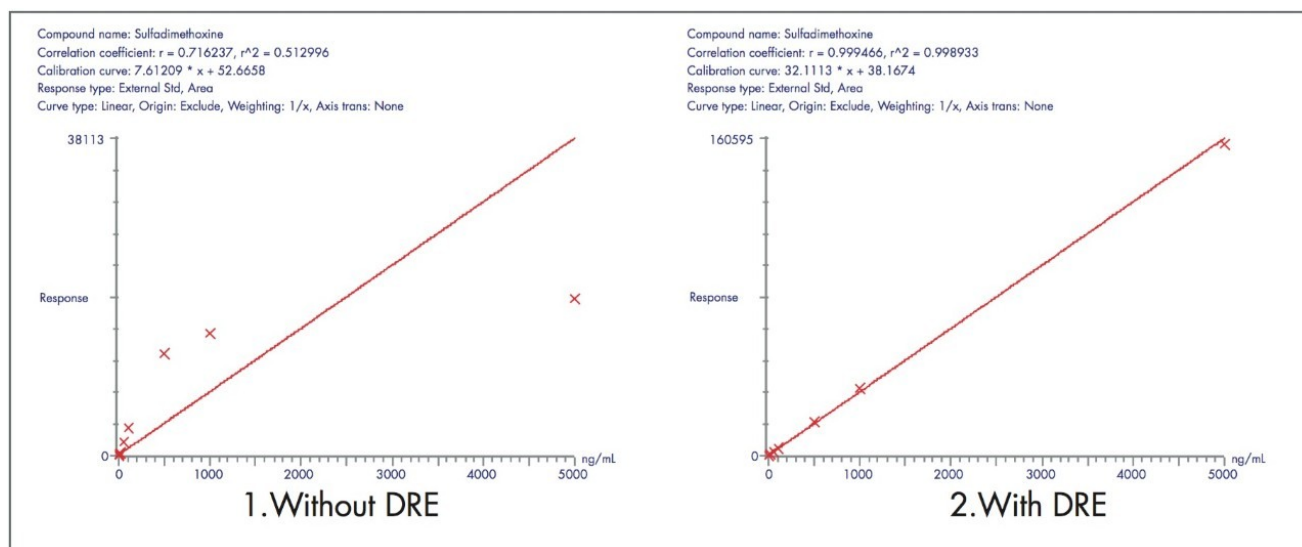


Figure 1. Quantitative analysis of sulfadimethoxine with and without Dynamic Range Enhancement (DRE).

Figure 2 shows the exact mass measurement error of sulfadimethoxine for each of the peaks analysed. Without DRE, as the concentration of the sample increases, the exact mass measurement error deviates in a negative direction from the expected mass, which is due to detector saturation at high ion currents. With DRE, the exact mass measurement is maintained to within 3 ppm of expected over the four orders of magnitude.

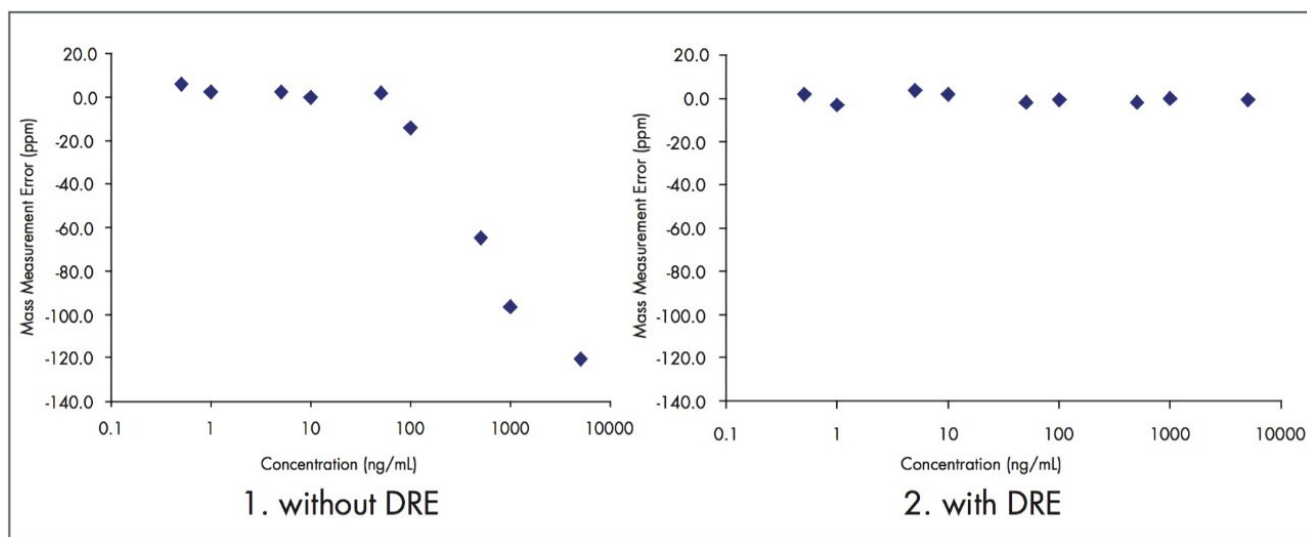


Figure 2. Exact mass measurement of sulfadimethoxine.

Sulphadimethoxine has also been analysed by LC-MS with APci (atmospheric pressure chemical ionisation) over the concentration range 1 to 10,000 pg/ μ L. Figure 3 shows the quantitation report, displaying that excellent linearity is obtained with APci and DRE on the LCT Premier. The correlation coefficient over the analysed concentration range is better than 0.999.

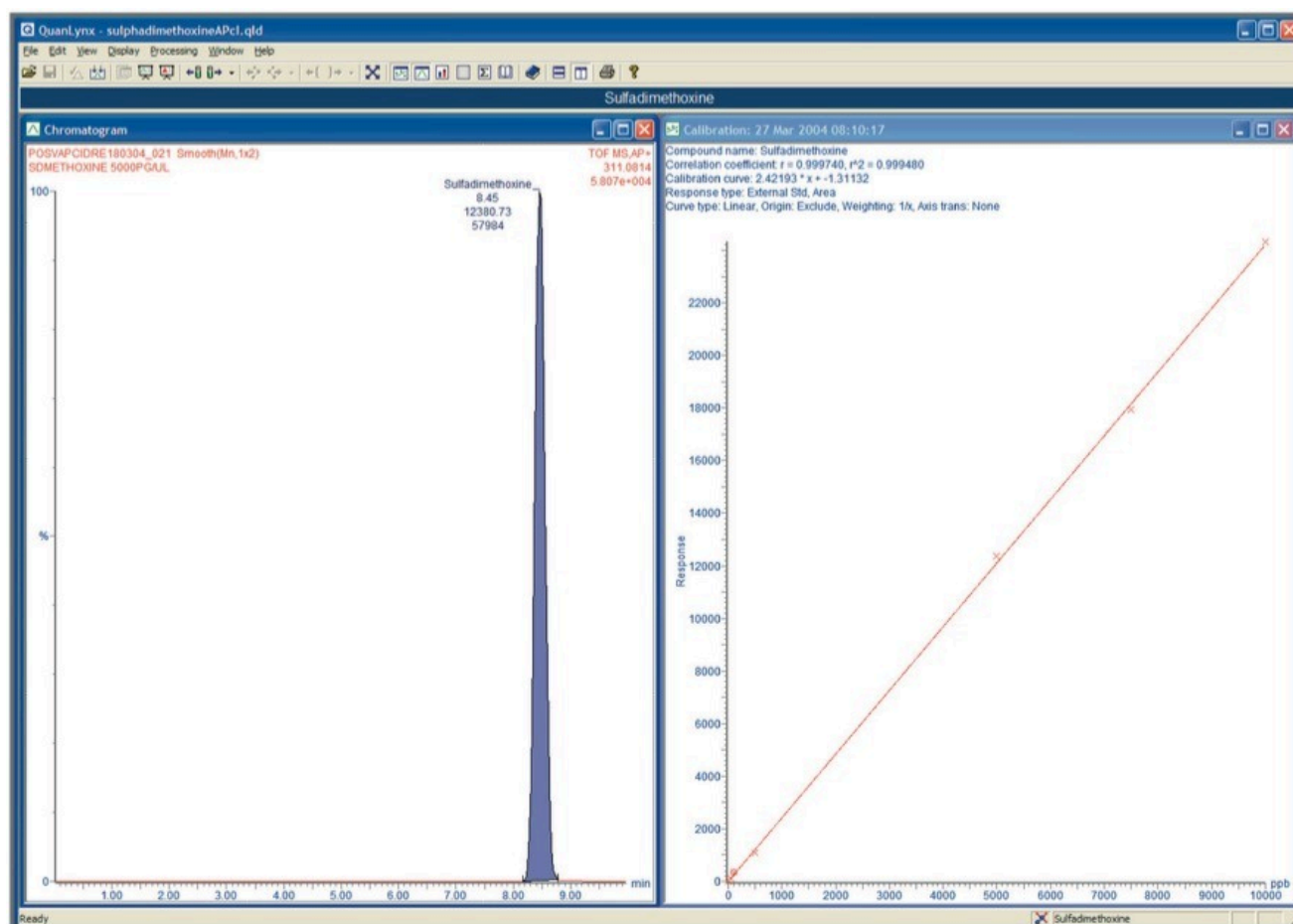


Figure 3. Analysis of sulphadimethoxine with APCL and DRE.

Use of the LCT Premier Mass Spectrometer with DRE also offers an application for the analysis of peptides with nano-scale chromatography. Glu-fibrinopeptide (GFP) has been analysed by nanoLC and detected by the LCT Premier using NanoLockSpray. GFP produces a doubly charged ion at m/z 785.8, with an exact mass in positive nano-electrospray of m/z 785.8426. The amount of GFP injected on column was from 0.5 femtomole to 5000 femtomoles. Figure 4 shows the quantitation curve with a linear fit from the 0.5 to 5000 femtomole sample with DRE. No internal standard was used.

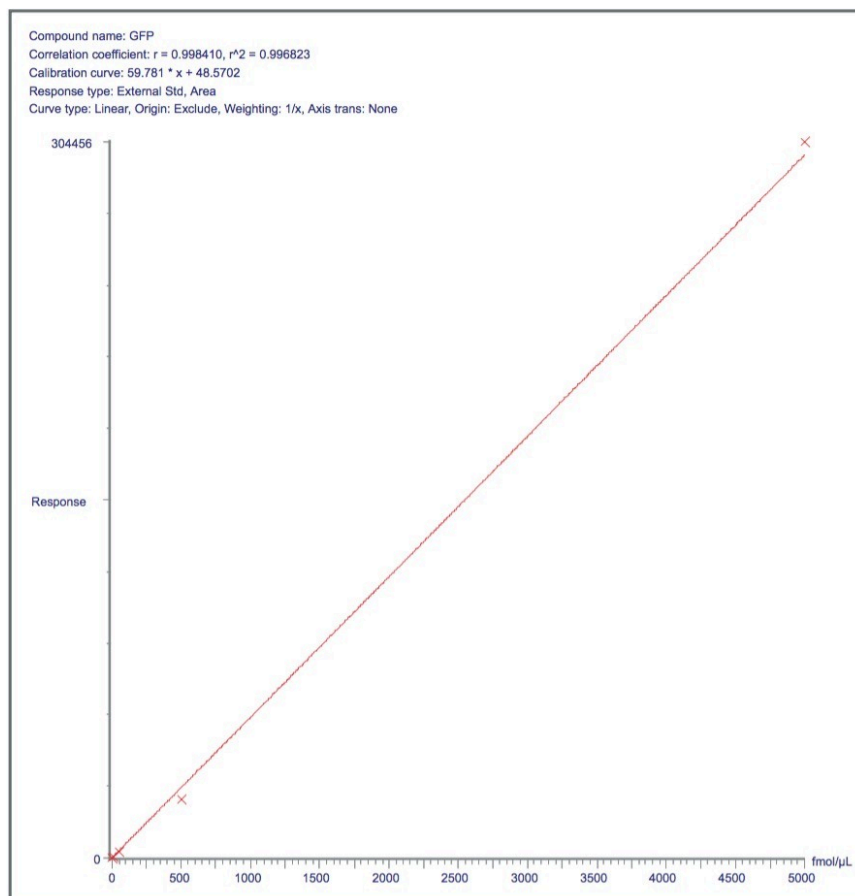


Figure 4. Quantitation graph for Glu-fibrinopeptide.

Figure 5 shows the mass spectrum of the lowest level GFP standard (0.5 femtomole) with an exact mass measurement error of -1.4 ppm from expected. Figure 6 plots the exact mass measurement error for each of the standards over the 0.5 to 5000 femtomole quantitation range. As can be seen with DRE, exact mass measurement is maintained to within 3 ppm of expected even for the high intensity samples.

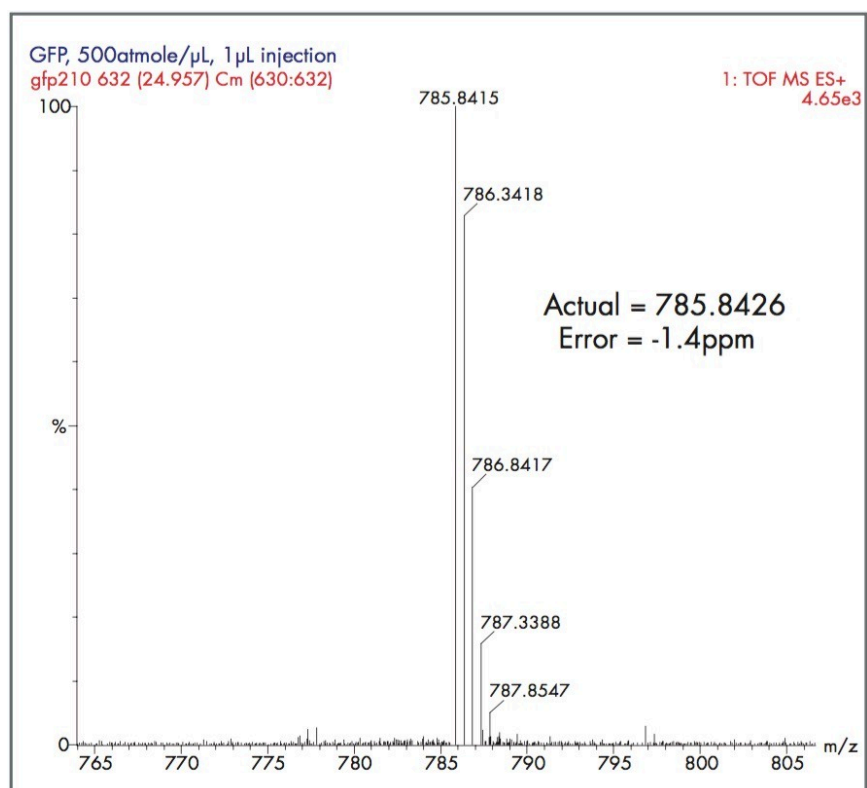


Figure 5. Exact mass measurement of GFP (500 atmole sample).

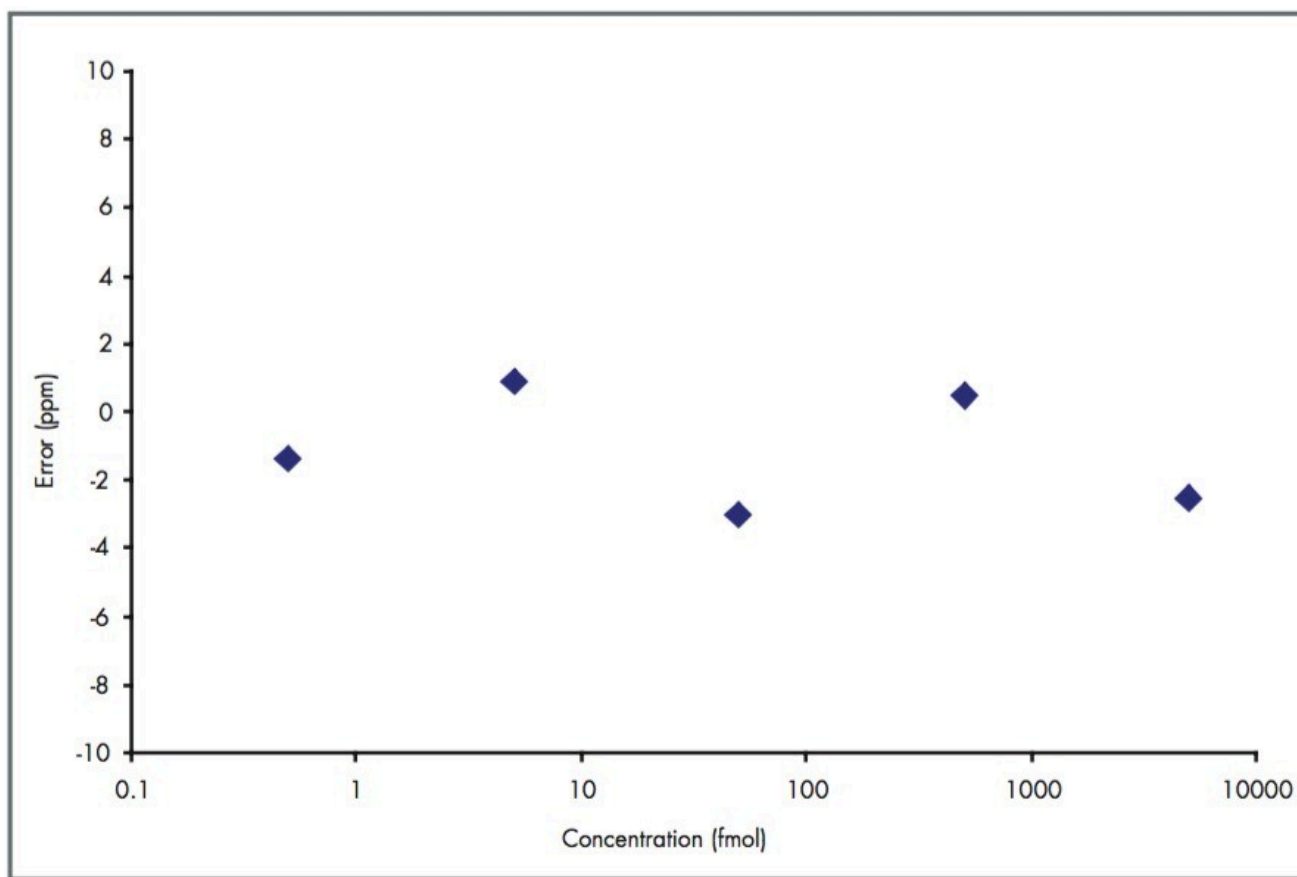


Figure 6. Exact mass measurement of GFP over 0.5 to 5000 fmol concentration range.

Conclusion

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