

Overview

- Rapid thermal profiling and analyte detection
- Increased sample throughput using a motorized X-Z scanner
- Improved sample handling allowing for MS tuning with DART

Introduction

Rapid screening for small molecule compounds whether they be in biological matrices, foods or herbal supplements is facilitated by using ambient pressure desorption ionization methods such as DART, DESI and ASAP. The utility of these methods has been limited in the past due to the difficulty of reproducing the ionization exposure time, sample positioning and sample shape. The determination of small molecules directly from in-vitro assays, including microsomal metabolism studies, as well as for other applications ranging from pesticide detection in foods to quantitation of caffeine in energy drinks has been improved by enabling a new ionization method called transmission mode (TM) ionization.

A series of TM experiment modules, 1-D transmission and higher throughput X-Z transmission modules, have been developed for DART-MS to improve sample handling, reproducibility and overall throughput. This new approach to sample presentation with DART entails mounting the sample holder vertically in front of the source allowing the heated desorption gas to flow directly onto the sample spot and then through the porous sample surface directly to the MS inlet. One major improvement in this experimental set-up over previous configurations for DART is that the samples can be placed significantly closer to the inlet of the mass spectrometer resulting in an increase in analyte sensitivity, as well as the ability to better control the sample deposition on to the sample surface. Analyses using the 1-D transmission module allows for up to 10 samples per analysis run, while the X-Z transmission module offers a higher throughput option analyzing up to 96 per run in just under 20 minutes.

Specifically in the bioanalytical setting, previous DART studies have always been performed off of solid glass surfaces^{1,2,3}, which set the benchmark for DART-MS/MS analysis directly from plasma. Moving forward, analysis of drug candidates directly out of whole blood off of blood spotting papers will be one of the main focuses for this new technology and is still under development. In this presentation we show TM-DART for rapid screening in an in-vitro hepatic clearance study.

In other applications, the transmission module has been demonstrated to monitor for pesticides in foods and for caffeine levels in popular energy drinks. In addition to the above mentioned benefits for TM-DART, this set-up has also enabled us to tune for compound dependent MS parameters directly using DART ionization.

References

1. Yu, S. *et al.* Anal. Chem., 2009, 81(1): 193-202.
2. Zhao, Y. *et al.* Rapid Comm. in Mass Spec., 2008, 22(20): 3217-3224.
3. Gordon, J. *et al.* Quantitative analysis of dried blood spots by DART (direct analysis in real time)/MS/MS without sample preparation. Presented at: 58th ASMS Conference on Mass Spectrometry and Allied Topics. Salt Lake City, UT, USA, 23-27 May 2010.
4. Edison, S. *et al.* Rapid Comm. Mass Spec., 2011, 25(1): 127-139.

Acknowledgements

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Methods

Instrumentation

- A fourth generation DART ionization source (DART-SVP (Standard Voltage & Pressure)) was fitted with either a 1-D transmission module or with a 2-D 96-well plate footprint X-Z transmission module.
- The transmission module is designed to hold a woven wire cloth sampling surface vertically in front of the DART ionization source. The sample surface is then moved systematically within the DART ionization region for direct analyte desorption under ambient conditions.
- MS Platforms:
 - LCQ Deca Ion Trap with Vapur Interface
 - API 4000 with Vapur Interface

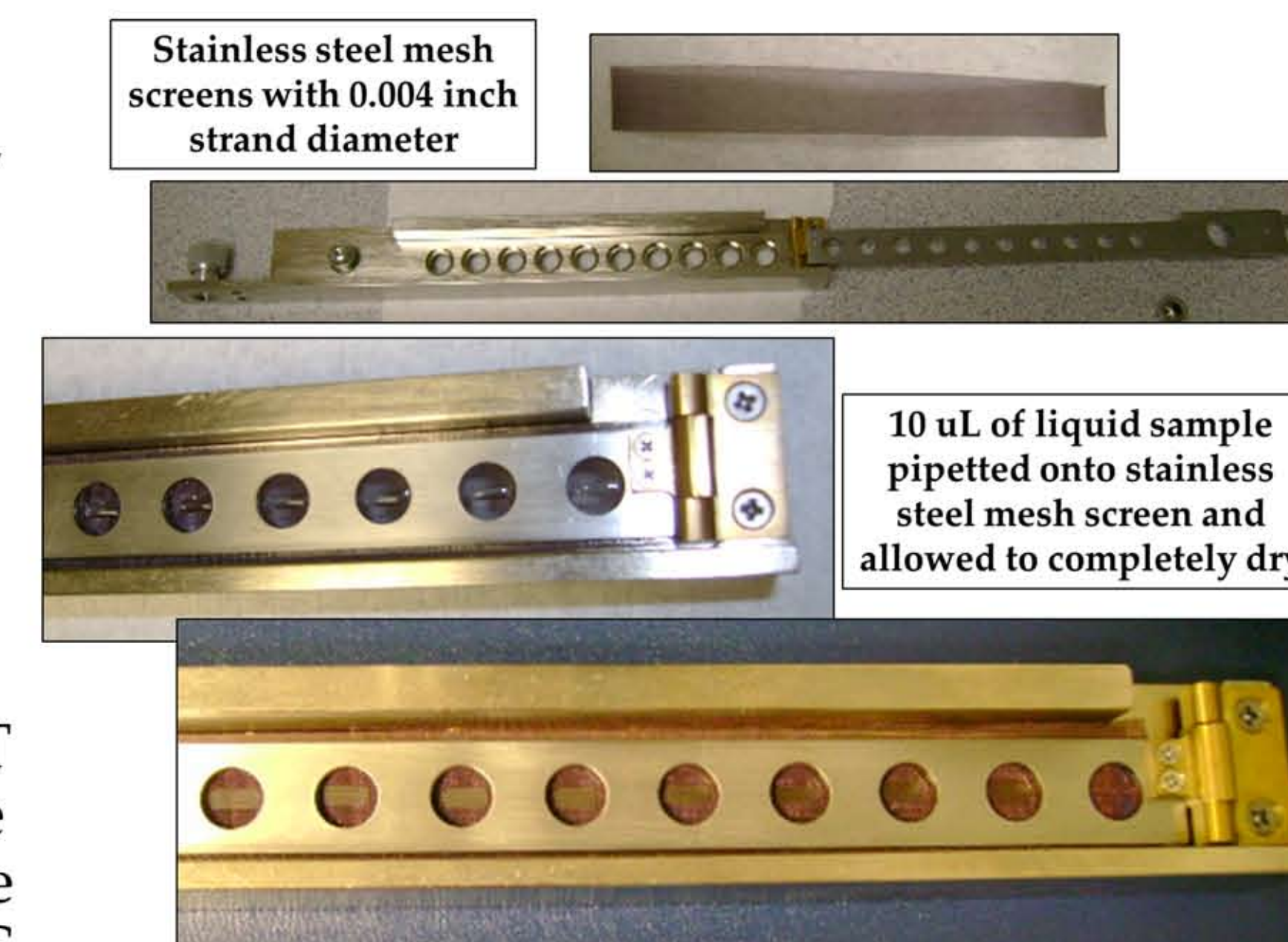
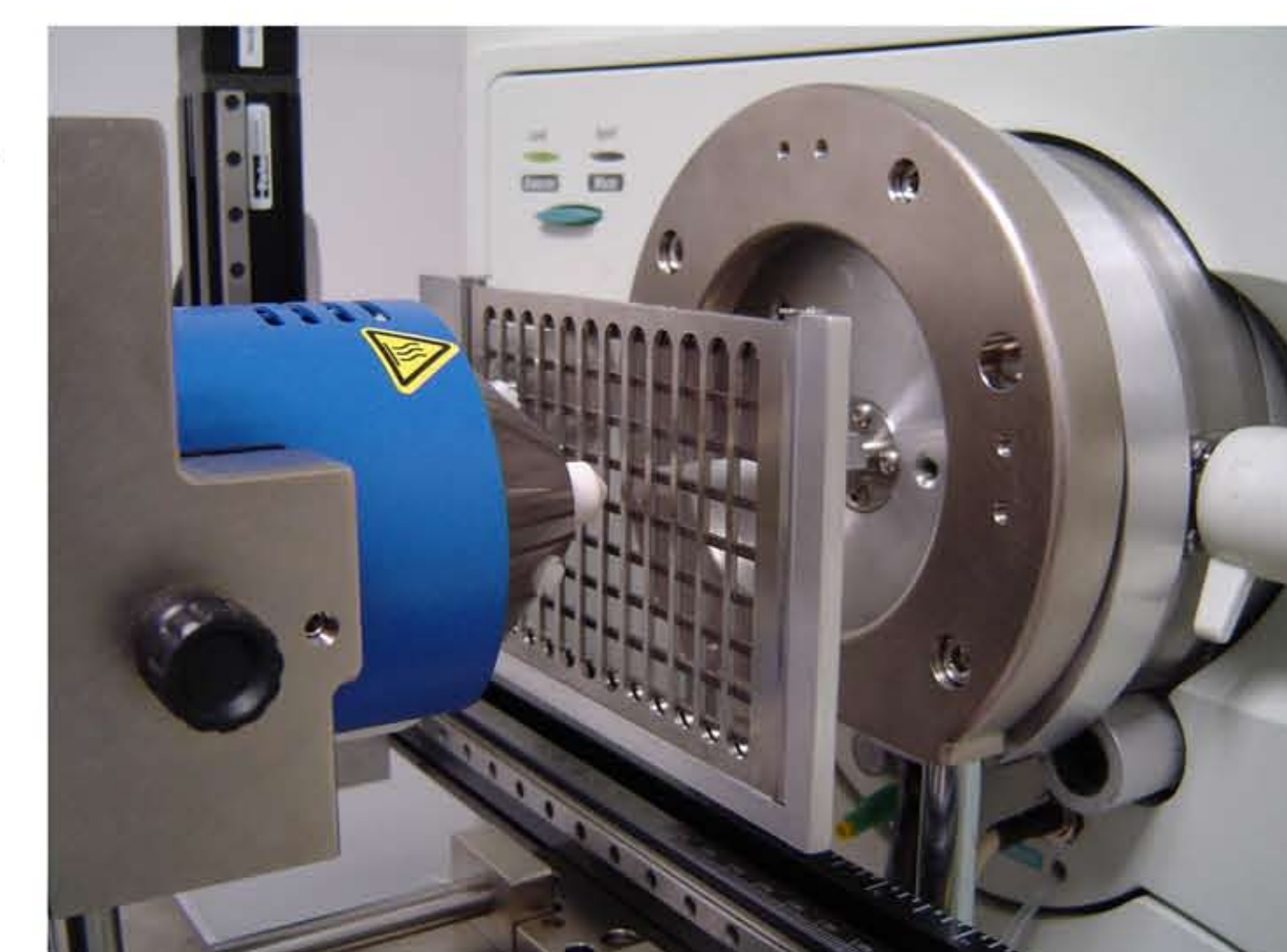


Figure 1. 1-D transmission module showing stainless steel mesh loading and sample spotting.



Figure 3. Direct analysis from food and other complex matrices such as plasma and whole blood. Dimethoate pesticide spiked into apple juice matrix.



Figures 5 & 6. X-Z transmission module allows for up to 96 samples to be analyzed in a single method run. The wire cloth mesh holder easily slides in and out of the X-Z module and maintains the 96-well titer plate format for automated sample loading.



Figure 2. 1-D transmission module mounted for DART analysis. Typical analysis speed is 0.5 - 1.0 mm/s through the DART ionization region.

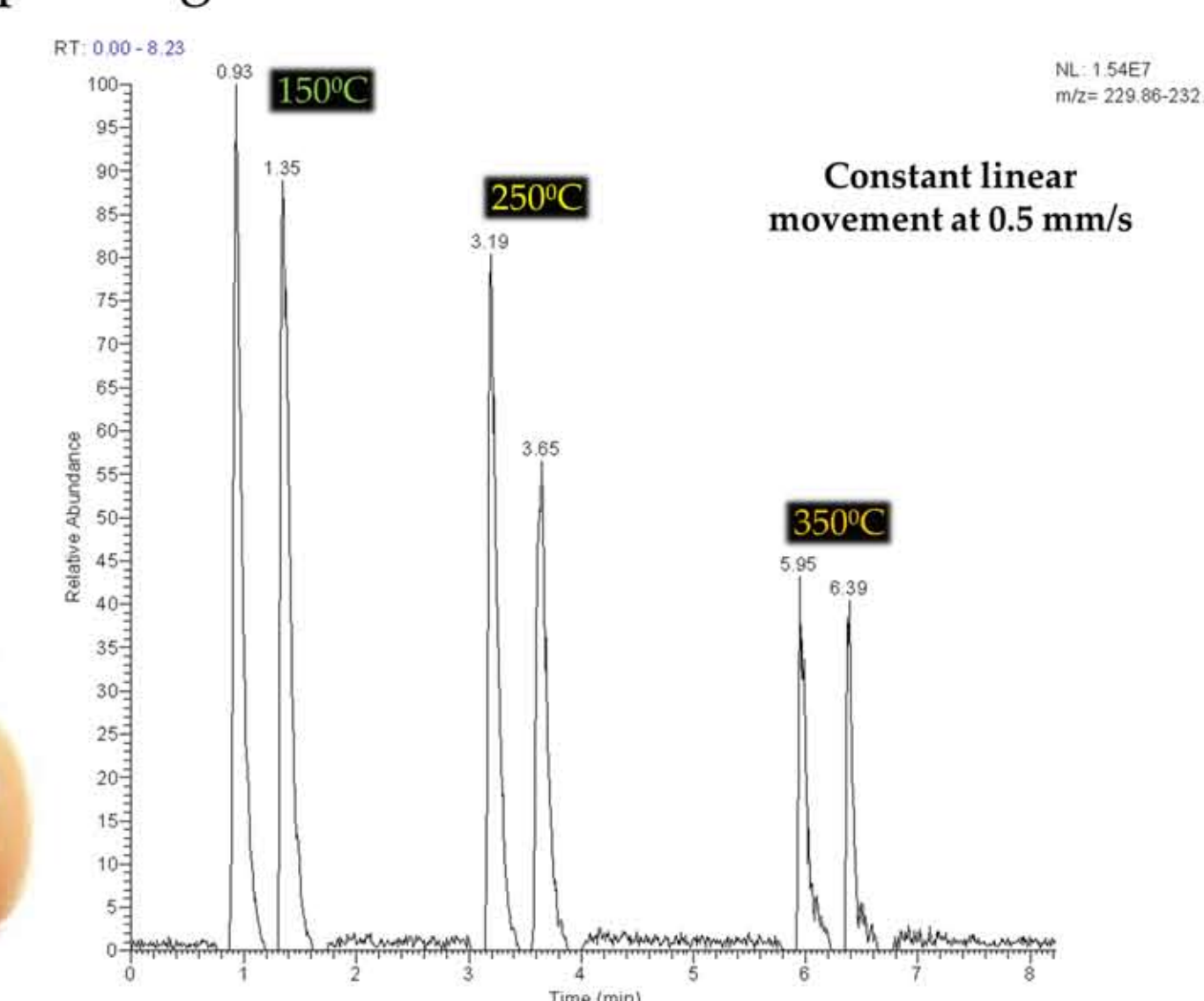


Figure 4. The optimal DART heater temperature must be experimentally determined. A temp ramping method used to optimize DART desorption.

Results

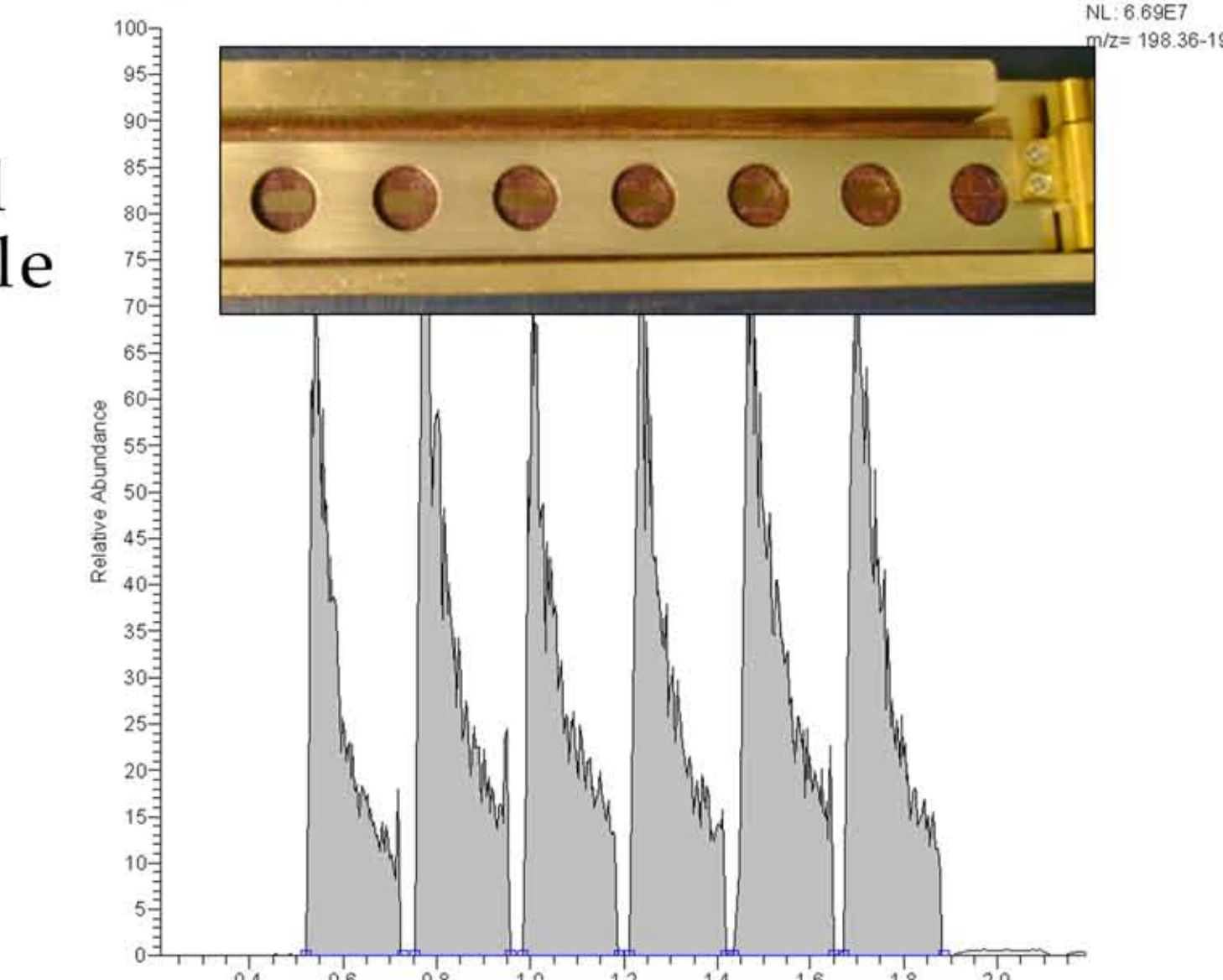


Figure 7. MS/MS condition tuning for dimethoate using the stainless steel mesh, m/z 233 -> 199 at 23% CE.

Compound	Eh by LC/MS/MS	Eh by DART/MS/MS
Dextromethorphan	0.507	0.573

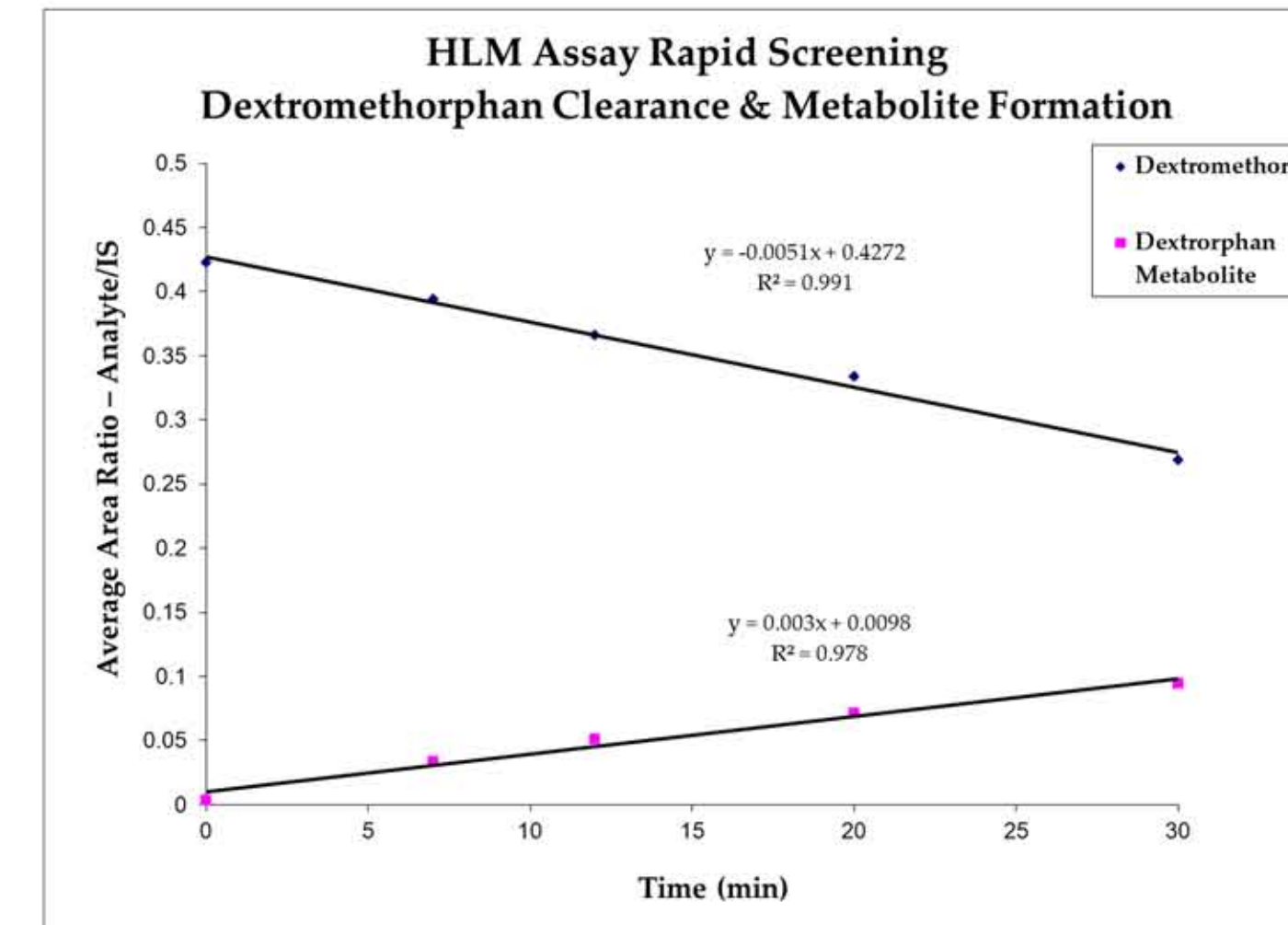


Figure 10. Rapid DART-MS/MS screening of parent and metabolite concentrations in a HLM clearance study.

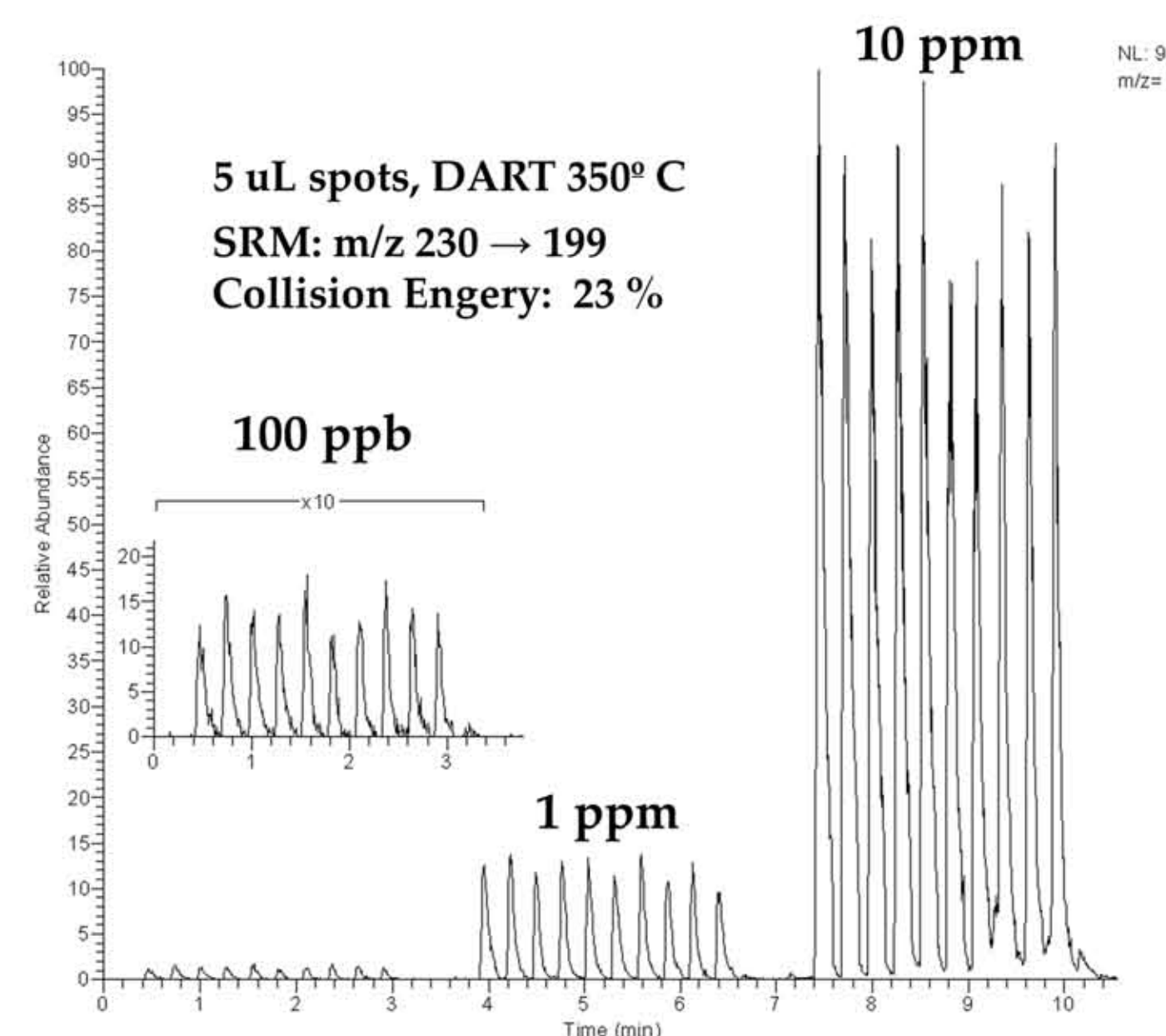
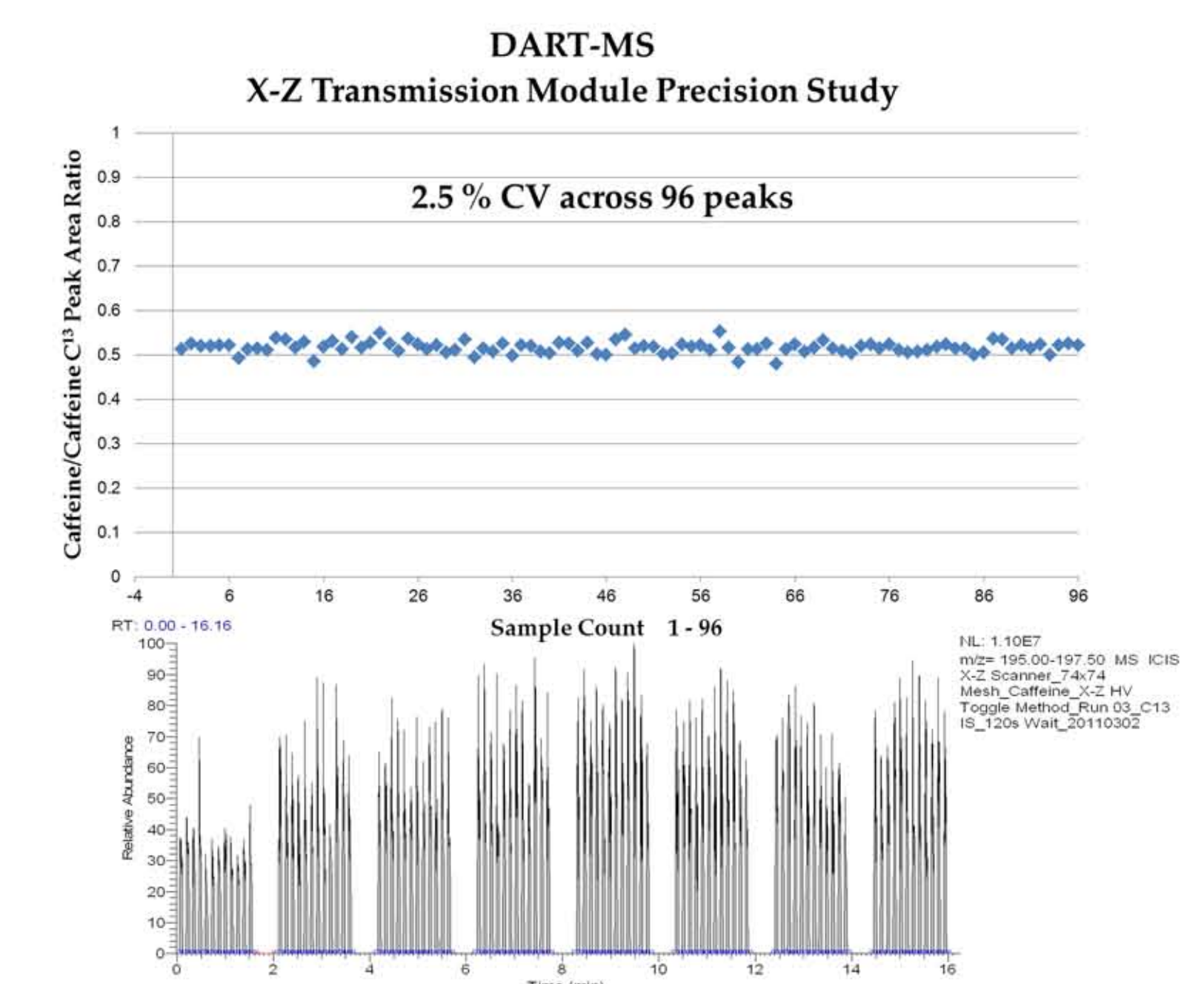


Figure 12. SRM run monitoring dimethoate directly out of apple juice. Spotted 5 uL volume/sample spot.

Conclusions

- TM- DART offers:
 - Rapid sample screening - 96 samples in just under 20 minutes
 - Controlled sample application with liquid handling devices and application of larger sample volumes with respect to prior sampling techniques with DART for improved sample loading
 - Longer lasting signal as a result of increased sample loading for direct MS tuning
 - X-Z transmission module with a 96-well titer plate footprint permits the use of robotic liquid handling devices for streamlining sample application



Figures 8 & 9. X-Z transmission module precision study. For 96 samples 2.5% CV was achieved with internal standard.

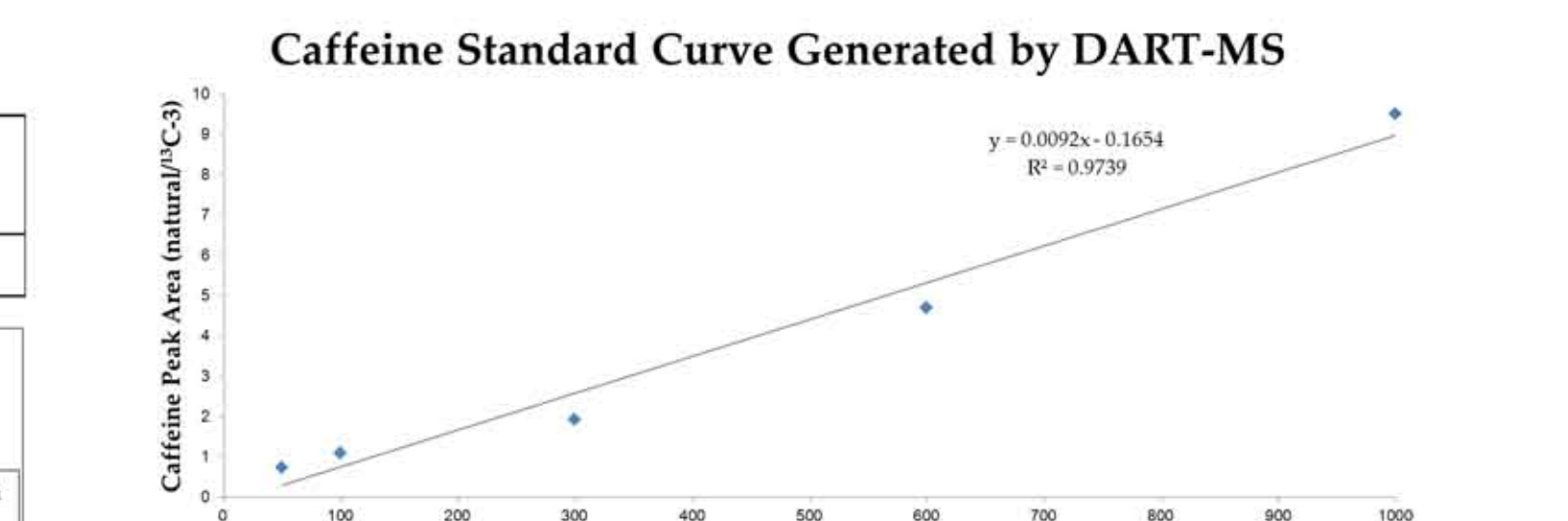


Figure 11. Monitoring caffeine levels in coffee & popular energy drinks, including the US FDA warned Four Loko.

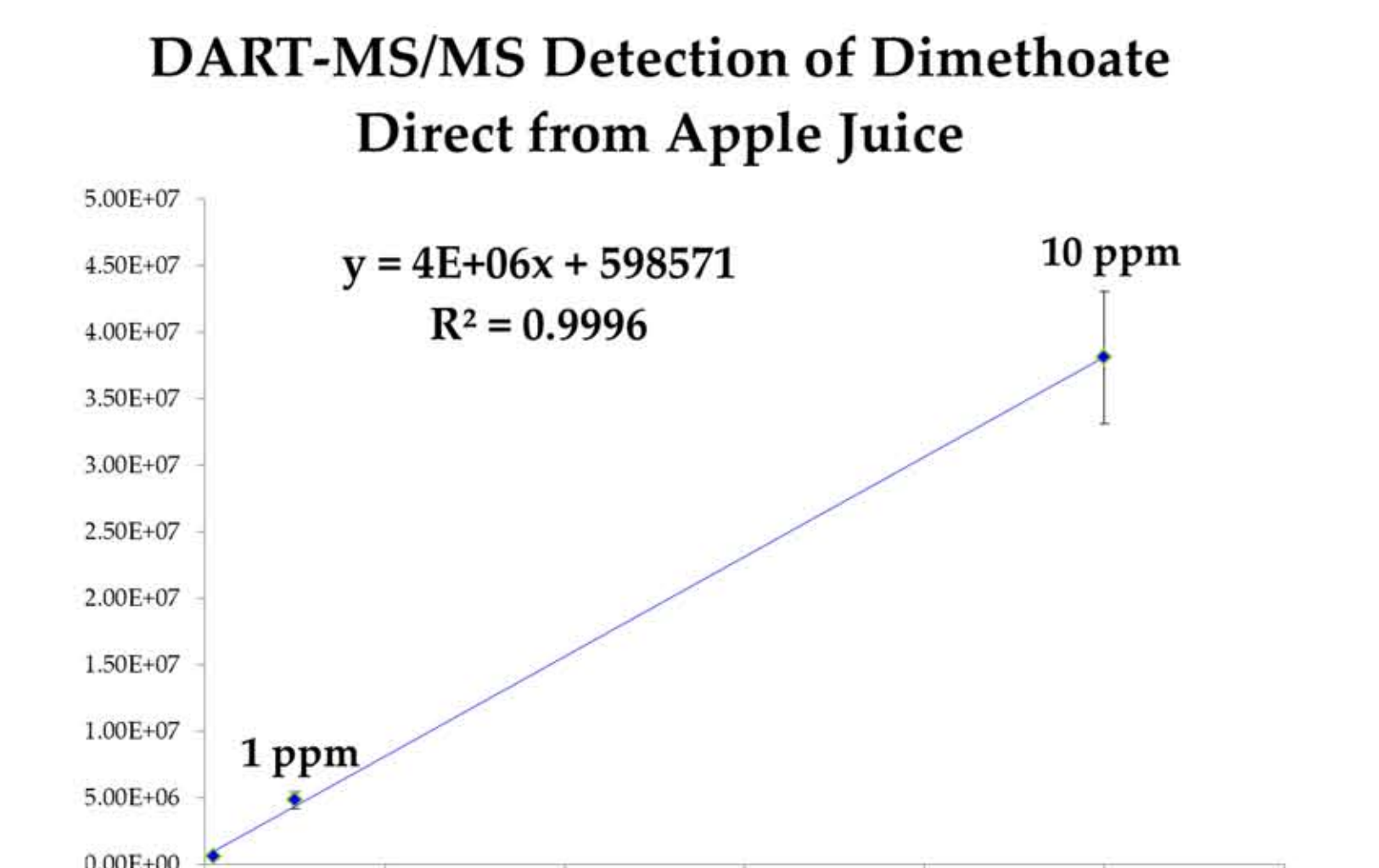


Figure 13. Data from Figure 12 plotted showing acceptable linearity across two orders of magnitude.