

Preparation and Rapid Analysis of Dry Powders with an Ambient Pressure Desorption Ionization Equipped Mass Spectrometer

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ABSTRACT

Mass spectrometry is literally the step-child of separation science. GC/MS and LC/MS dominate analytical chemistry laboratory environments in large part because it is easier to handle chemicals after they are dissolved in liquids. However, some sample matrices are not readily soluble and some chemicals may react or degrade in solution.

The advent of ambient pressure desorption ionization sources such as DART and DESI has made it possible to analyze chemicals directly from solid surfaces. Many chemicals are present in a loose powder form which cannot be compressed into solid tablets or easily dissolved for LC/MS. Use of these desorption techniques for the direct analysis of these powders would be an important analytical advantage. An example is the detection of melamine in food products. The EU-required limit of 2.5ppm in processed food and 1ppm in infant formula is easily detected by LC/MS methods. However, these require lengthy (>1hr) sample preparation to extract melamine from lipid and protein rich powders. Here we discuss methods for the direct, rapid analysis of loose powders such as dried milk.

INTRODUCTION

A magnet anchors powder-coated metal particles to facilitate ambient pressure desorption ionization mass spectrometry without source contamination.

Our initial attempts at desorption ionization of powder involved restricting the movement of the powder by using small mesh screens. This method proved difficult, however, since the powder was displaced by the movement of the gas across the surface. The use of screens was also difficult to automate. In this study we have investigated the use of fine metal powders dispersed in powder samples to enable transport and analysis of appropriate quantities of samples. Several methods were developed and evaluated for effectiveness in automated sampling and presenting spectral data.

Novel and effective methods of preparing and sampling powder samples without contaminating the inlet of the mass spectrometer were designed and implemented. An investigation was carried out to determine the overall and relative effectiveness of these methods.

Illustration of Powder Sampling Problem

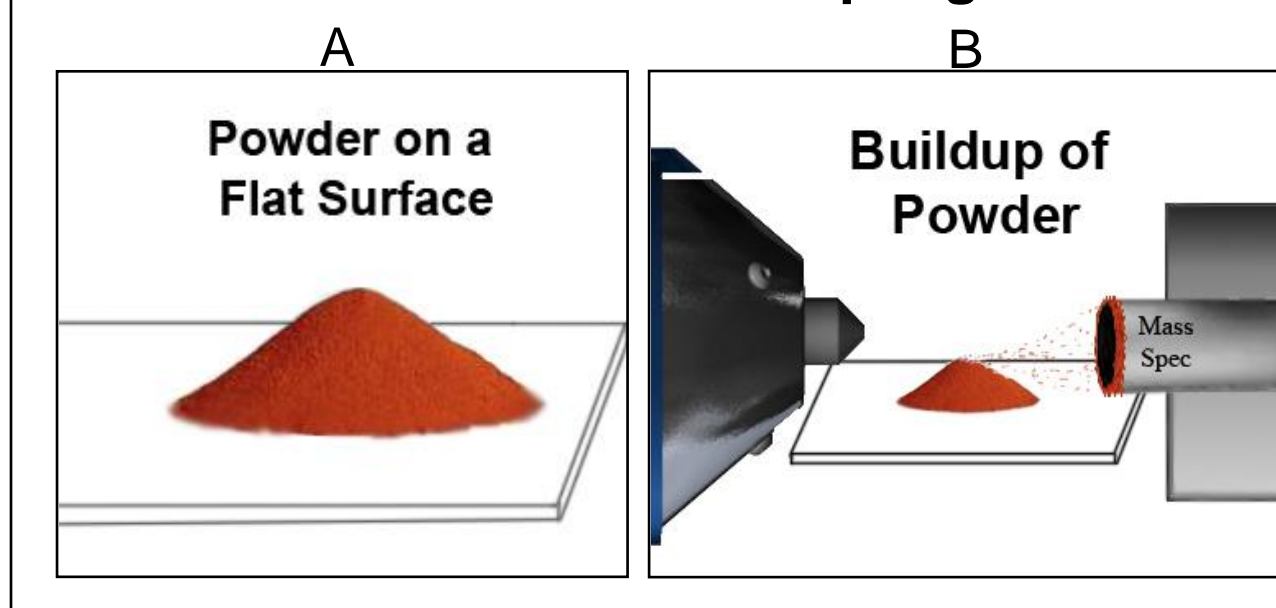
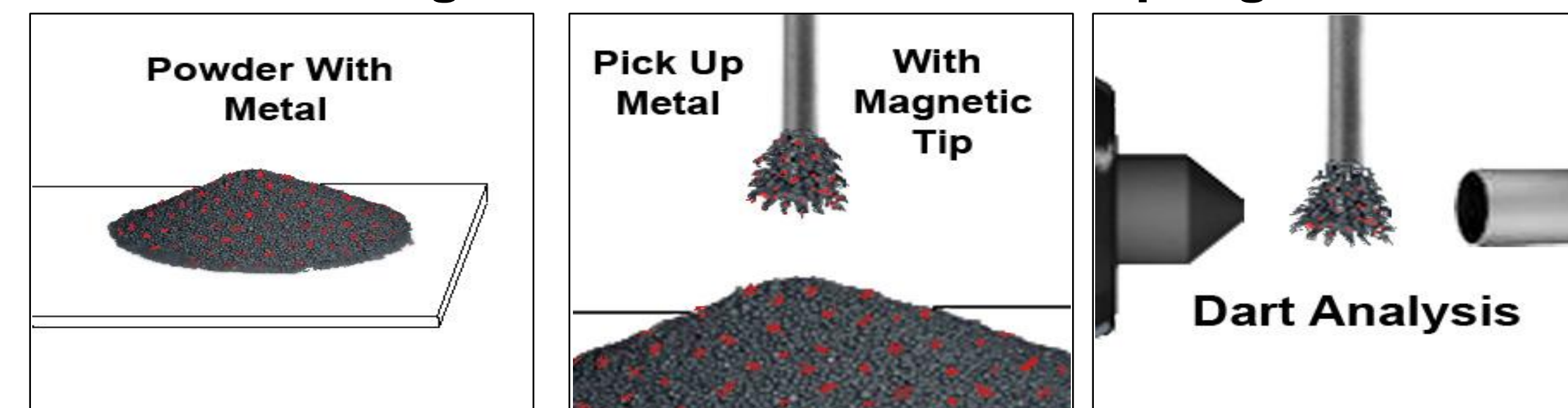


Figure 1: Sampling pure powder on a flat surface (pictured in frame A) results in contamination of the mass spectrometer inlet (frame B).

Magnet-Enabled Powder Sampling



EXPERIMENTAL

Mass Spectrometry

The basic configuration for the experiment comprises the following: a Finnigan LCQ Deca LC/MS mass spectrometer (Thermo Fisher Scientific, Waltham, MA); a DART ET ionization source (IonSense Inc., Saugus, MA); and a linear rail (Parker Automation LP 28 Series Linear Actuator).

Sample Preparation

Chemicals Used: Iron Oxide Blend #98121510004022 (V&P Scientific, San Diego, CA) Quinine, Methyl Paraben, and Melamine were purchased from TCI America. Bayer-brand Aspirin and Tylenol-brand acetaminophen capsules,

Powdered pharmaceutical products (aspirin, acetaminophen), raw crystalline chemicals (quinine, methyl paraben), and baby formula spiked with melamine were co-mixed with magnetite (Fe_3O_4 , 231.5333 g/mol) in various proportions to give 50%, 20%, 5%, and 1% (w/w %) concentrations. The magnetite powder was placed in glass vials containing small amounts of powders and co-mixed using a vortex mixer.

Magnetite proved an ideal mixer for this application. It was not detected in any mass spectral data and has a Curie temperature of 858 K, greater than the highest DART operating temperature. It is non-volatile, readily available, and does not react with any of the investigated chemicals.

The sample/magnetite mixture was extracted from the vial using a custom-designed magnetic micropipette (VP Scientific, San Diego, CA) and analyzed with the DART source. All sample concentrations greater than 1% ($\leq 99\%$ magnetite) contaminated the ceramic transfer tube or capillary of the mass spectrometer, leaving a residual signal of quinine or methyl paraben in the mass spectrum, visible after the sample was removed from the path of the DART source. These results were confirmed through visual inspection of the capillary area and can be observed in quinine and methyl paraben mass spectra after the samples have been removed (Figure 2).

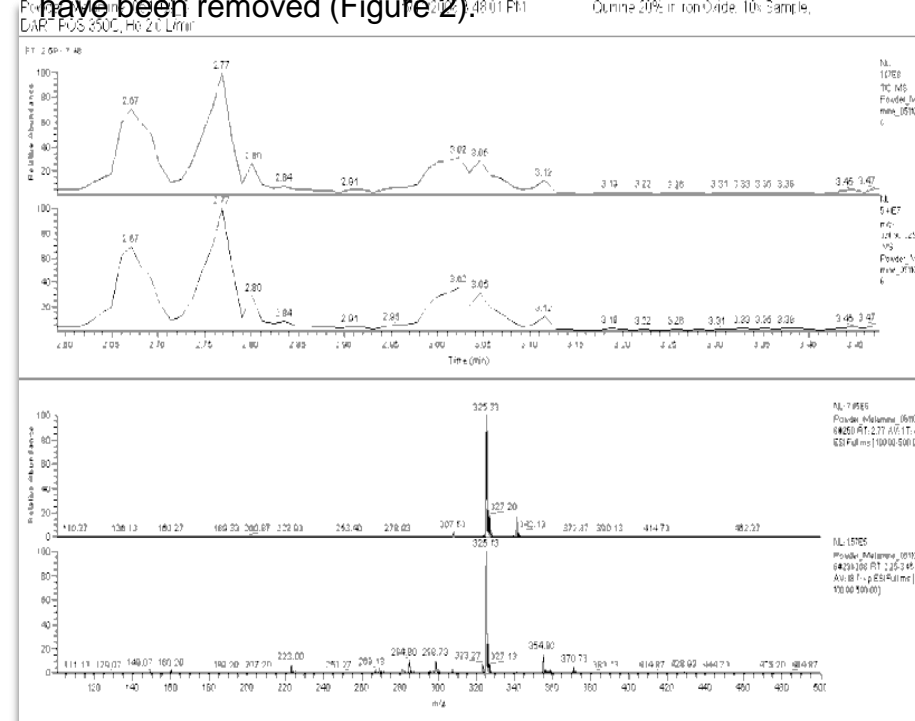


Figure 2: The mass spectra show the quinine signal at m/z 325.4 during sample insertion (top) and residual quinine after the sample was removed (bottom).

RESULTS AND DISCUSSION

Initial automation – Different ratios of Sample: Magnetite Spotted on a Glass Slide

The sample/magnetite mixture was transferred to a glass microscope slide where it was held in place with a neodymium disc magnet (K&J Magnetics, Jamison, PA) taped to the underside of the glass (Figure 3). The slide and sample were moved through the path of flowing helium on a linear rail and a custom-fabricated mounting stage. The mounting stage was designed so that the DART ET, raised and angled downward at 45 degrees, directed the path of carrier gas containing metastable helium at the powder sample on the slide.



Figure 3: Metal powder is transferred to the glass slide with a magnetic micropipette and held in place by the neodymium magnet underneath.

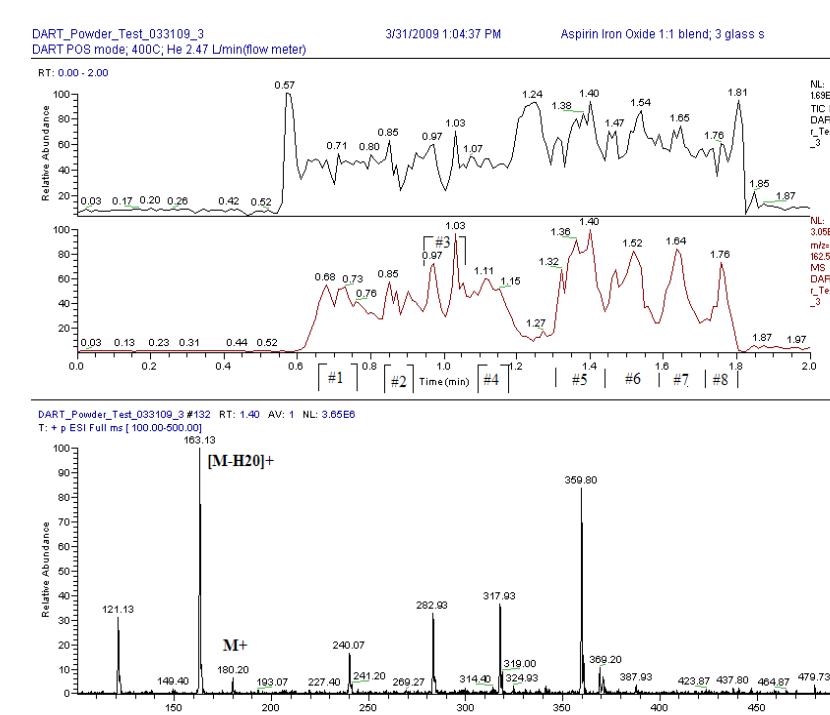


Figure 4: Four spots of 50% aspirin/magnetite were placed on the slide and run back and forth across the ion stream. High ion counts were generated of the base peak in the mass spectrum at m/z 163 (aspirin), and its dimer at 359.8. 8 poorly-defined peaks are visible in the mass chromatogram. Also visible after 1.8 minutes is the high residual ion count for m/z 163, a result of the 50% aspirin concentration.

High-Throughput Automated Analysis Using Pins

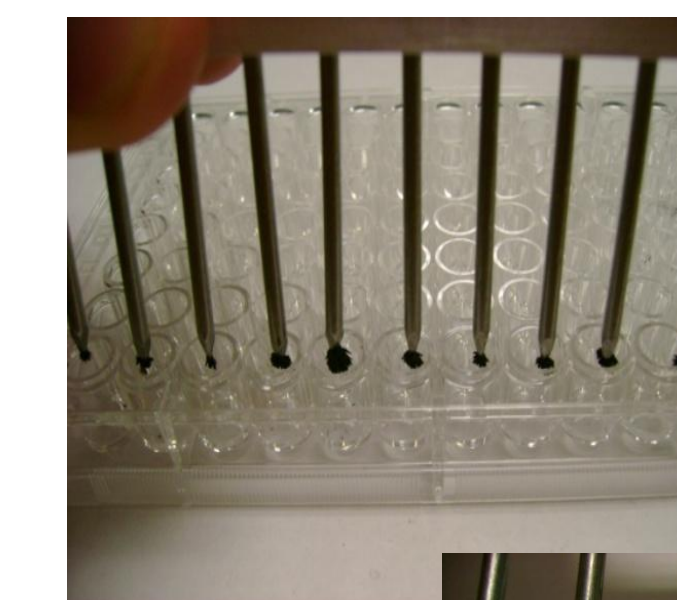


Figure 5: 2mg of mixed sample were placed into the wells of a 96-well microtiter plate. A custom piece with extended ferromagnetic pins spaced to correspond with one row of a 96-well plate was topped with a strong (3080 Gauss) neodymium bar magnet. The block was dipped into the well plate, collecting all the powder.

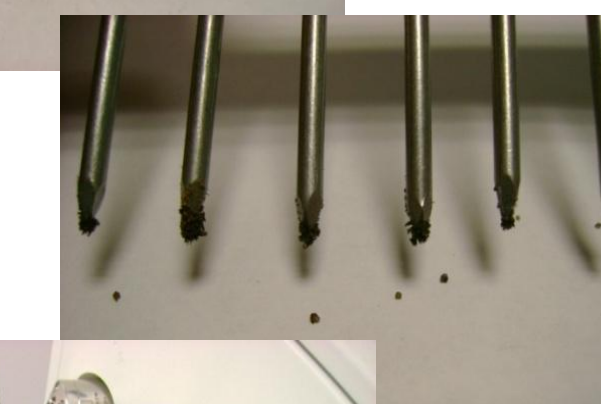


Figure 6: Loose powder was removed by gently shaking the block.

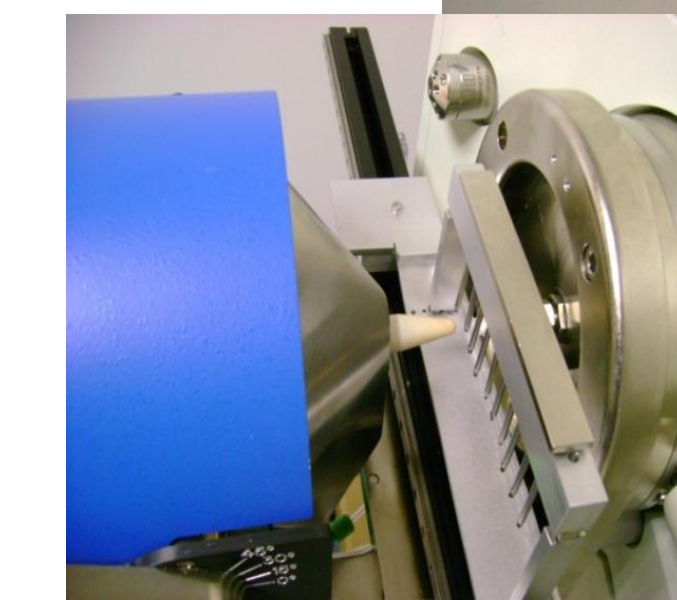


Figure 7: The block was positioned on the linear rail with the pins facing downward and were pushed through the ion stream at a rate of 0.5mm/s. After the data were collected, the bar magnet was removed and the sample was wiped off so the pins could be reused.

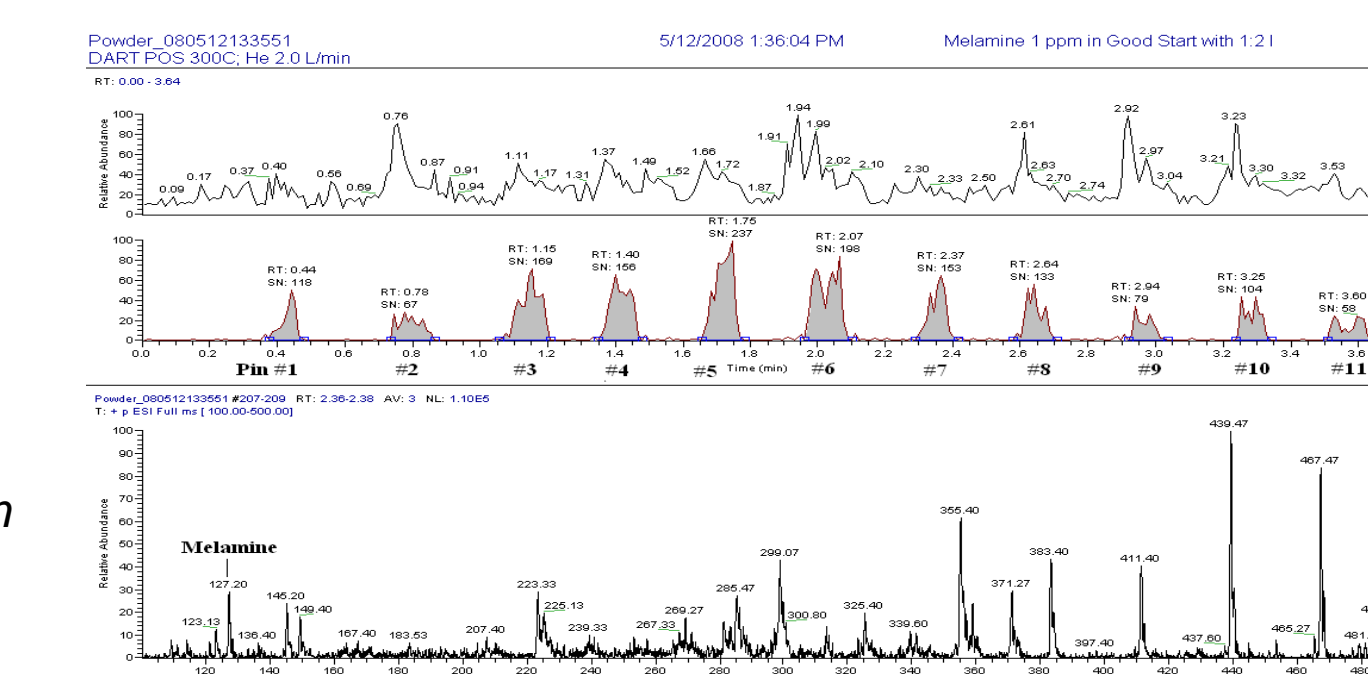


Figure 8: The positive ion mass spectrum and mass chromatogram of m/z 127 for protonated melamine, spiked into baby formula at 0.5ppm. Other ions in the spectrum arise from the composition of the baby formula. Melamine detection has traditionally presented a challenge because nutrient-rich baby formula contains dozens of active ingredients that fragment easily. Melamine was observed with a relative abundance of ~25%, proving the metallic-powder method is comparable in effectiveness to previous experiments using DART to detect melamine in liquid baby formula.

IR Heating Preparation

Some molecules, such as quinine, need a very high DART gas temperature for efficient desorption. Because of the high heat capacity of the magnetite, a method of sample preheating immediately prior to DART desorption and ionization was investigated. The tip block was placed in front of an infrared heating source (ICX Photonics, Billerica, MA) with an operating temperature of 700 degrees C. Each pin was left in front of the infrared light for 5 seconds to melt the mixture onto the pin (Figure 9). The sample was then analyzed by DART using the same high-throughput method.

Results below show the positive ion mass spectrum and chromatogram for quinine, one using an IR heat lamp during sample preparation (A) and one without (B). Use of the lamp does not appear to offer any improvement in results. Indeed, the signal to noise ratios in the spectrum without the IR lamp are approximately 3-4 times higher than those with the IR lamp. This was most likely due to the evaporation of the sample during the burn procedure.

Figure 9: Sample held in front of IR light source

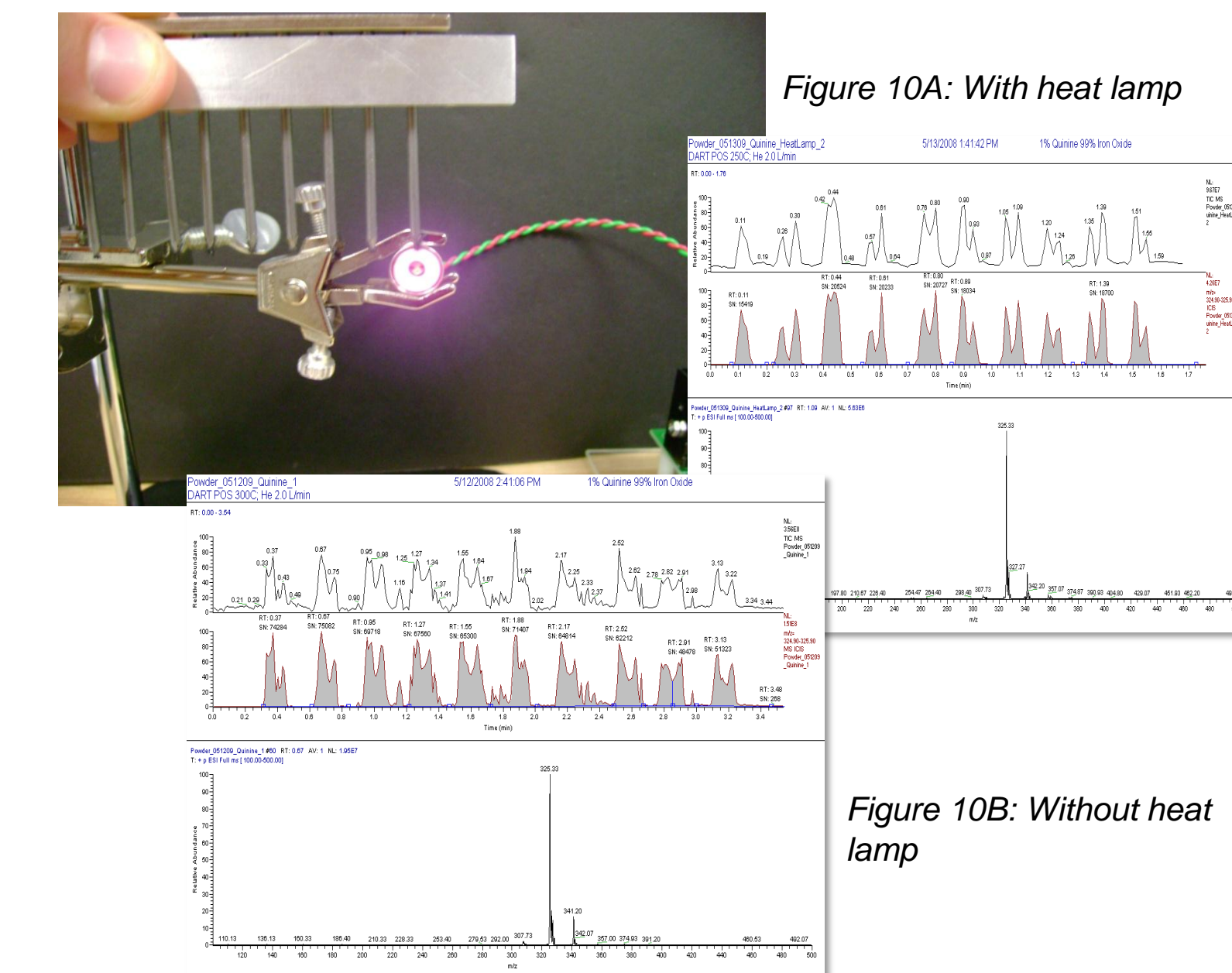


Figure 10A: With heat lamp

Figure 10B: Without heat lamp

CONCLUSION

- Use of magnets to hold co-mixed powder samples in place prevents contamination of the mass spectrometer inlet.
- The magnetic fields have no noticeable effect on the mass spectrometer.
- Ferromagnetic pins proved to be a better sampling device than glass slides.
- Feasibility for high-throughput automatic sampling using a motorized linear rail was demonstrated.
- Use of an IR heat lamp to melt the sample before introduction into the sampling area failed to improve results.