

DART-based Thermal Profiling of Solids and Powders as a Screening Tool for Quality Assessment

*Brian Musselman, Elizabeth Crawford, and Jordan Krechmer • IonSense, Inc. 999 Broadway, Suite 404, Saugus, MA USA
Corresponding author; musselman@ionsense.com

Direct ionization in real time (DART) desorption ionization mass spectrometry has been successfully used for the rapid screening of solids including powders and tablets, and for organic materials on the surfaces of objects. An automated sample positioning system facilitates rapid screening of these by reducing or eliminating the need for sample preparation. Improvements in sample positioning reproducibility enable acquisition of a series of desorption ionization mass spectra for a given solid at successively higher temperature values. This collection of spectra describes a qualitative and quantitative profile of the chemical content for comparison with standards. The method shows promise as a high-throughput screening tool to identify contaminated raw materials or the presence of hazardous chemicals in the finished product using existing laboratory LC/MS instrumentation.

Introduction

The growth of criminal activity focused on the adulteration of food products and counterfeit pharmaceuticals have increased the workload of analytical chemist. The full impact of these activities on targeted companies and their products is not yet known, however, it is increasingly likely that more testing will be required to address concerns related to product liability and satisfy government regulations. Traditional quality analyses to verify legitimate content may need to be expanded to include searches for unknown substances for which no specified methods exist. For example, the recent contamination of milk with melamine has already provoked discussions regarding new testing regulations for food produced in China. The need exists for rapid and simple methods to detect a wide range of potential contaminants in order to keep pace with the increasingly-sophisticated criminal elements. The potential of DART-MS method as a screening tool for determination of these contaminants has been documented with publications addressing melamine in dog food⁽¹⁾, the prevalence of counterfeit pharmaceuticals in third world countries⁽²⁾ and the determination of trace pesticides and environmental contaminants in food⁽³⁾

The potential of DART⁽⁴⁾ for rapid screening of raw materials and finished products was first demonstrated at the Pittsburgh Conference in 2005. At that meeting a DART source fitted to time of flight mass spectrometer (TOF-MS) was used to ionize and identify chemicals

present in samples provided by the attendees at the meeting. No sample preparation was used, in part due to the prohibition of the use of solvents in the conference hall. The inventor of DART, Dr. Chip Cody of JEOL USA, held samples between the DART source exit and the atmospheric pressure inlet of the TOF-MS and desorption ionization produced intact protonated molecular ions of each of the chemicals present. The accurate mass values derived from these experiments helped to ascertain the composition, purity, and identification of contaminants. However, the most popular experiments conducted were the detection of cocaine, insecticide, sunscreen, and even Ritalin[®] on bank notes.

Since that first Pittcon, implementation of an automated sampling system (AutoDART) for analysis of liquids has been completed using a CTC HTS-PAL laboratory robot⁽⁵⁾. Determination of the composition of a wide variety of foodstuffs, pesticides, and even direct determination of drug molecules in plasma and blood have been demonstrated using this technology^(5,6).

DART and Tablet Analysis

The DART source was interfaced to a commercially-available ion-trap MS for this series of experiments. Inside the DART source an inert carrier gas, helium, is activated during passage through a high-voltage electrical discharge. This produces helium ions and neutral "metastable" helium atoms. After this process, the carrier gas passes into a

heating chamber and then flows past an electrical grid which blocks transfer of the ions to the desorption ionization region so that only the high energy, heated metastable atoms are used in the ionization process. The sample positioned in the desorption ionization region is heated and molecules desorbed into the activated helium carrier gas where ion formation occurs within seconds. The ions are drawn into the MS through the atmospheric pressure inlet by the effect of the mass spectrometer vacuum. One capability of this method is that the carrier gas temperature can be changed over a significant range, typically from ambient to 5000C. The collection of mass spectra at successively higher temperatures enables detection of a wider range of sample constituents than using a single temperature. This use of successively higher gas temperatures has been described as "thermal profiling"⁽⁷⁾.

An over-the counter cold-cure pharmaceutical, Tylenol[®] Daytime Caplets, was used to demonstrate this. The formulation is supplied as a sweetener-coated caplet containing three active pharmaceutical ingredients;- 325mg Acetaminophen, 10mg dextromethorphan HBr, and 5mg Phenylephrine HCl. For these experiments, the activated helium desorption gas temperature was set to 150°, 250°, 350°, and 450°C for four successive experiments. The mass spectra generated from a single caplet analyzed at multiple temperatures are shown in figure 1. The protonated acetaminophen at m/z 152 (A) was observed

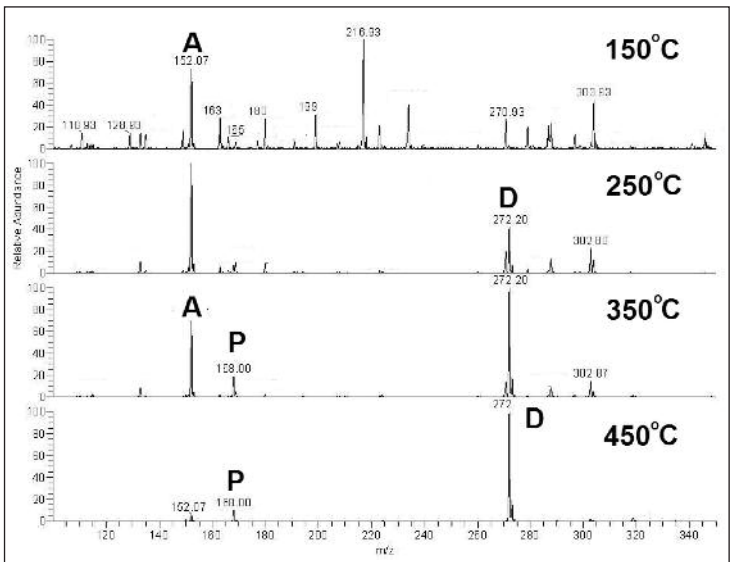
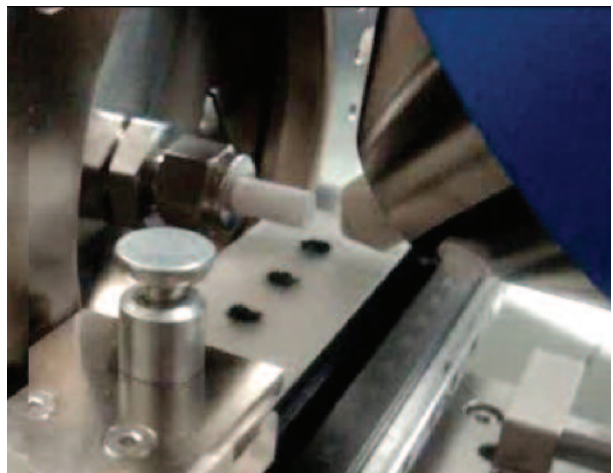


Figure 1: DART MS analysis of a Tylenol Daytime Caplet at four successively higher temperatures. All of the active pharmaceutical ingredients are detected using 350oC helium as the DART gas.



Heated carrier gas exits blue DART source mounted 45 o off-axis with respect to the sample surface. The ceramic tube connects the ionization region to the atmospheric pressure inlet of the LC/MS. Sample dispersed in metal powder is held in the desorption ionization region by using magnets mounted on the bottom of the etched glass slide.

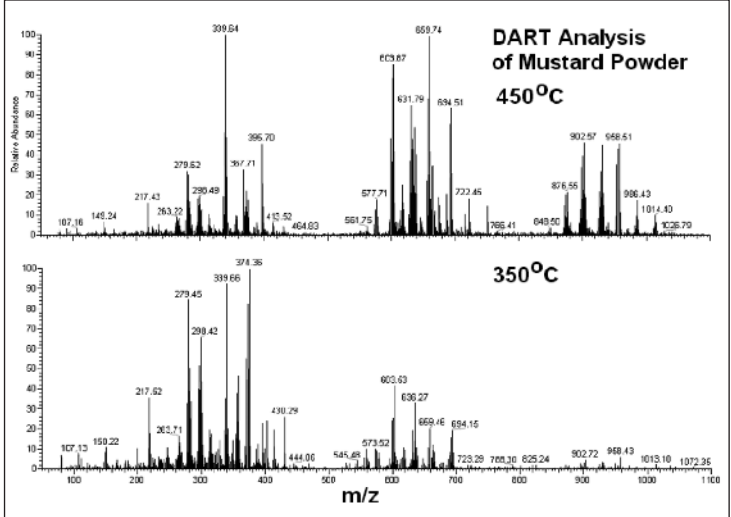


Figure 2: DART-MS of mustard powder at 350 oC and 450 oC showing the ionization of different intact lipids as gas temperature increases. The ratio of mustard powder to Magnetite (metal) powder was 1:100. Each sample was exposed to the heated DART gas for 10 seconds.

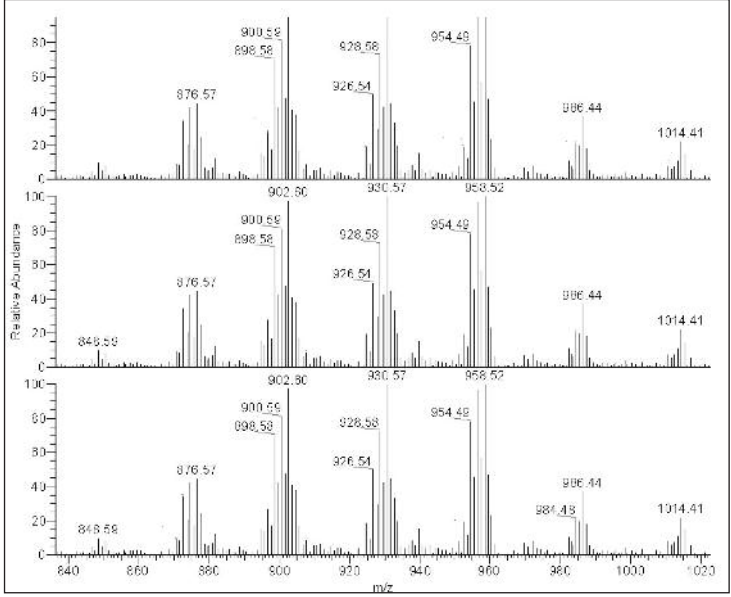
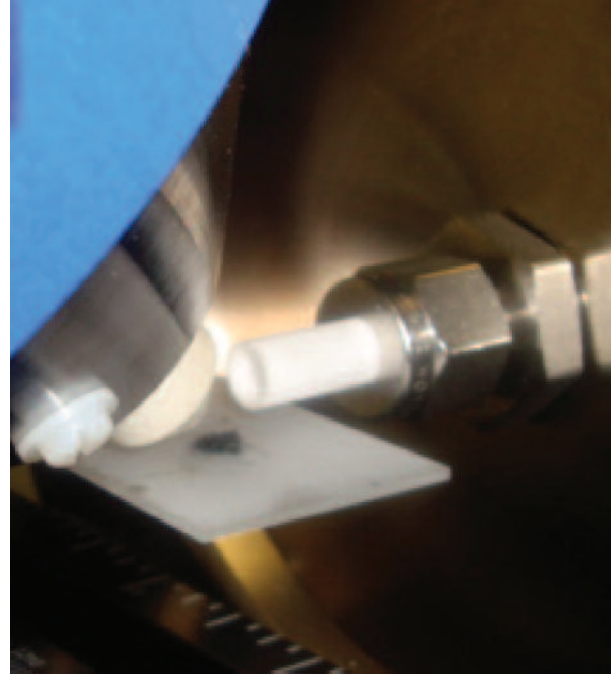


Figure 2: DART-MS of mustard powder at 350 oC and 450 oC showing the ionization of different intact lipids as gas temperature increases. The ratio of mustard powder to Magnetite (metal) powder was 1:100. Each sample was exposed to the heated DART gas for 10 seconds.

to desorb at the lowest temperature while the protonated phenylephrine at m/z 163 (P) was not detected until desorption temperatures reach the higher range. Finally, protonated dextromethorphan at m/z 272 (D) dominated the mass spectrum at the highest temperatures even though its concentration in the tablet is comparatively less than the other active ingredients. There are many low-intensity peaks in the low temperature desorption profile; these are probably the flavor and sweeteners present in the outer coating of the tablet.

Results from the Direct Analysis of Powders:

One application of this technique is the analysis of mustard. Pound per pound, the value of a spice compared with other foodstuffs is often very high. Routine QC for spices usually involves solvent extraction followed by time-consuming gas chromatography (GC) or GCMS analysis. Unlike solid tablets, analysis of powders with ambient pressure desorption analysis can be a challenge because it is possible to displace very light powders with the ionising gas. For DART analysis it is sometimes necessary to immobilize the powder. For the determination of mustard powder we dispersed

a small amount of the spice into magnetite, a fine iron powder typically used in fireworks formulations. Since magnetite is magnetic, mixing the powder with it enabled manipulation of the materials using magnets. For these experiments a 10mg sample of McCormick's Mustard Powder was dispersed in 990 mg of metal powder to create a 1% w/w mixture in preparation for analysis. A sample transfer device was made by fixing a small 3mm diameter x 2mm neodymium magnet to the distal end of a 1.75 inch T-shaped quilting pin. The magnetic field at the opposite end of the pin was sufficient to attract a 3 - 4 milligrams of the powder-coated metal onto the pin. The sample was then transferred to a glass slide to which several small magnets were fixed on the underside with epoxy adhesive. The sample-laden glass slide was placed on the TLC plate scanning module fixed on the linear rail of the DART. As in the earlier experiments, sampling at successively higher temperatures was used to complete the thermal profiling. The mass spectra generated at 350° and 450°C are shown in figure 2. The lower temperature desorption ionization experiment yielded two distributions of ions at mass values corresponding to organic acids and monoglycerides and diglycerides at 250 – 350 and 500 – 600 dalton respectively. Both the low and high carrier-gas temperature experiments produced these ion species. However, from the high temperature DART result it is evident that the increase in temperature enabled detection of the intact triglycerides. Although not used for these

experiments, previous analyses with a high resolution TOF-MS documented the use of these high mass ions as a means of identification of adulteration of edible oil by comparison of the distribution of intact triglycerides⁽⁸⁾. The partial mass spectra shown in figure 3 demonstrate that the distribution of these ions from one analysis to the next is comparable for replicate analysis of the mustard powder. That the relative abundances of each ion in the high mass region is nearly identical suggests that development of a method for triglyceride distribution would provide a real time alternative to longer GC and GC/MS analysis.

Larger Objects

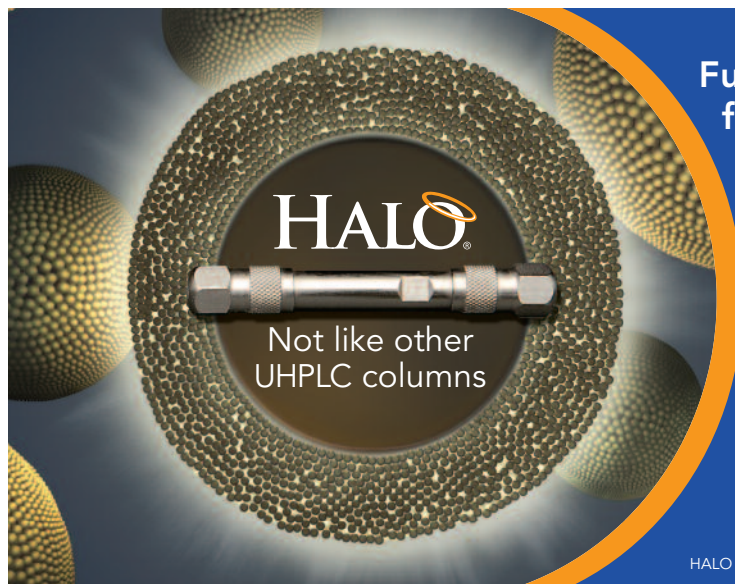
In order to profile chemicals on larger surfaces such as inks on bank notes and paper⁽⁹⁾, coatings, and contaminants, a 2-D scanner module was developed. The unit provides the means to scan an area equivalent to the size of a 96-well microtiter plate. Since the desorption ionization region can be further from the API inlet because of the large size of the sample, a vacuum-assist VAPUR[®] gas ion separator (4) is used to transfer ions to the mass spectrometer. In the example shown in figure 3, determination of the distribution of cocaine on euro note was determined to be related to the density of the dye on the surface. Alternative experiments include the identification of blemishes or off-color spots on fabric or packaging material in order to improve production processes and identify the possible sources of contamination.

Conclusions

The ease-of-use of DART facilitates screening of both raw materials and finished products for a wide range of chemicals. The individual measurements described here are completed in less than 10 seconds and the time required to change the operating temperature of the DART gas by 100° C is typically less than two minutes making collection of a three temperature thermal profile in less than 5 minutes feasible. Once a thermal profile has been determined the potential for use of a single optimum temperature is often possible, reducing the analysis time even further. The data suggests that DART-MS is an extremely useful additional screening tool in support of the LC/MS laboratory particularly now that deliberate contamination or criminal activity may warrant a more extensive surveillance program to augment traditional product quality control analyses.

References

1. Vail, T.M., P.R. Jones, and O.D. Sparkman, *Journal of Analytical Toxicology*, 2007, 31(6): p. 304-312.
2. Fernandez, F.M., M.D. Green, and P.N. Newton, *Ind. Eng. Chem. Res.*, 2008, 47(3): p. 585-590.
3. Vaclavik, L., Schurek, J., Cajka, T., Hajslova, J., *Chemicke Listy*, 2008, 102: p. s324-s327.
4. Cody, R.B., J.A. Laramée, and H.D. Durst, *Anal. Chem.*, 2005, 77(8): p. 2297-2302.
5. Zhao Y., L.M., Wu D., Mak R., *Rapid Communications in Mass Spectrometry*, 2008, 22(20): p. 3217-3224.
6. Yu, S.; Crawford, E.; Tice, J.; Musselman, B.; Wu, J.T., *Analytical Chemistry*, 2009, 81(1): p. 193-202.
7. Malekina, S.D., Vail, T.M., Cody, R.B., Sparkman, D.O., Bell, T.L., and Adams, M.A., *Rapid Commun. Mass Spectrom.* 2009, 23: p. 2241-2246
8. Vaclavik, L.; Cajka, T.; Hrbek, V.; Hajslova, J. *Analytica Chimica Acta*, 2009, 645, p. 56-63.
9. Jones, R.W., R.B. Cody, and J.F. McClelland, *Journal of Forensic Sciences*, 2006, 51(4): p. 915-918.



Fused-Core[®] particle technology for hyper-fast and super-rugged UHPLC columns

HALO UHPLC columns deliver the separation efficiency of sub-2 µm columns but at half the pressure. HALO columns can be used with either UHPLC or conventional HPLC equipment to deliver reliable, rugged ultra-fast separations. Now available—HALO Phenyl Hexyl



Hichrom Limited - Authorised UK Distributor
Tel: 0118 930 3660
Email: technical@hichrom.co.uk
Web: www.hichrom.co.uk